

1118

Regd. No. 9 M. 429.

MAY, 1940

Vol. XXXVII. No. 5.

The Antiseptic

A Monthly Medical Journal

Edited by

Dr. U. Rama Rau, M.L.C. & U. Krishna Rau, M.B., B.S.

CONTENTS.

Original Articles.

- RATIONAL INTRANASAL MEDICATION.** By V. R. Kamath, M.B.B.S., D.L.O. (Eng.), Madras. ... 377
- FUNCTIONAL IMPOTENCE.** By M. V. Govindaswamy, M.A., B.Sc. M.B.B.S., D.P.M. (Eng.), Superintendent, Mental Hospital, Bangalore. ... 385
- SPINAL ANÆSTHESIA—ITS COMPLICATIONS.—Part II.** By C. K. Kurup, L.M.P., L.O.P. & S. Kumily, Travancore. ... 394
- EVOLUTION OF CATARACT SURGERY FROM THE PRE-HISTORIC AGE UP TO THE PRESENT TIME.** By Nabin Kishore Bidyadhar, M.B.B.S., (Pat.), Susruta Clinic, Sonapur Raj, Orissa. ... 400
- SULPHANILAMIDE IN THE TREATMENT OF CERTAIN EYE CONDITIONS.** By S. Sanyal, M.B. (Cal.), Visiting Ophthalmologist, Ashtanga Ayurveda Hospital, Calcutta. ... 421

Cases and Comments.

- A CASE OF ACUTE EXFOLIATIVE DERMATITIS FOLLOWED BY MYASTHENIA GRAVIS AND DEATH.** By Capt. P. S. Gupte, M.B.B.S., Nasik. ... 425

Editorial :—

- CARDIAC EMERGENCIES—DIAGNOSIS AND TREATMENT.** ... 427

Gleanings from Medical Press.

- MEDICINE & THERAPEUTICS.** ... 432
- SURGERY.** ... 435
- OPHTHALMOLOGY.** ... 437
- OBSTETRICS AND GYNÆCOLOGY.** ... 438

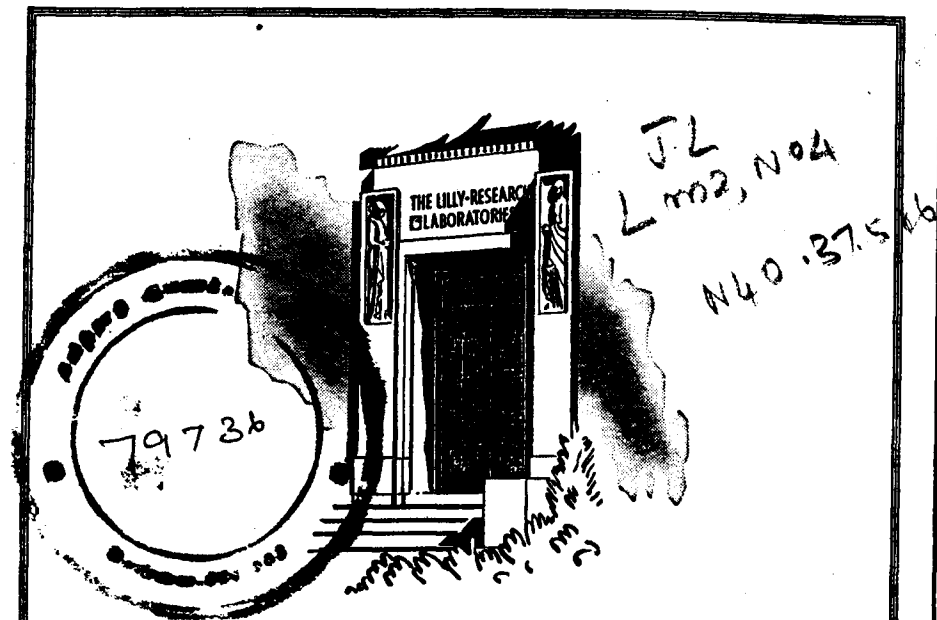
- Notice.** ... 440

Editorial and Publishing Offices: 323, Thambu Chetty Street, G. T., Madras.

London Office: 34-40, Ludgate Hill, E. C. 4.

Subscription Rs. 5. Foreign 10 sh. a year. Post paid. Single Copy As. 12—In advance.

Index to Advertisements, see page 34.



The Red Lilly stands for quality products, progress through research, and ethical dealing with the medical profession. These precepts are not an idle pose but are the basis on which the Lilly Laboratories have operated for over sixty years.

'SULFO-MERTHIOLATE' (Sodium *p*-Ethyl Mercuri Thiophenylsulfonate, Lilly) 1:1,000 Surgical Powder has many general uses. It is protective and soothing as well as antiseptic to body surfaces which are bathed in perspiration. The antifungicidal action of 'Sulfo-Merthiolate' makes the powder especially valuable in the treatment of ringworm or hyperhidrosis of the feet.

'Sulfo-Merthiolate' 1:1,000 Surgical Powder is supplied in sprinkler-top cans containing 1 1/2 ounces.

Distributor: KEMP & CO. LTD.

BOMBAY, CALCUTTA, DELHI, MADRAS, NEW DELHI

ELI LILLY AND COMPANY • INDIANAPOLIS, INDIANA, U.S.A.

1940]

THE ANTISEPTIC

In all cases

of malaria, influenza and
bronchitis

WINCARNIS is a pleasant-tasting, effective tonic composed only of purest health-giving ingredients. It contains no drugs, and may be prescribed with the utmost confidence for all convalescents or patients suffering from debilitating illnesses. It is especially valuable in cases exhibiting a tendency to anæmia, as it rapidly strengthens the bloodstream. Wincarnis is basically a blend of matured and selected red wines, combined with exact quantities of finest strengthening elements and vitamin malt extract (4,850 International Units Vitamin A per ounce, 700 Units Vitamin D). One or two glasses a day is the usual prescription, and Doctors recommend it because it not only stimulates appetite for food, but facilitates digestion of it. It is extremely efficacious in inducing sound, healthy sleep, and its general tonic effect restores vitality and resistance. For all cases where vitality is low—influenza, bronchitis, tonsilitis, anæmia—

Prescribe

WINCARNIS

The Tonic Wine

● OVER 25,000 RECOMMENDATIONS FROM MEDICAL MEN

Coleman & Co. Ltd., Wincarnis Works, Norwich, England

LM/W/67

When writing to advertisers, please mention the "Antiseptic"



When Occupation interferes with -

Chronic constipation frequently occurs amongst sedentary workers and others who are unable to take time from their work to go to stool. For these patients it is important to re-establish Habit Time of Bowel Movement.

Patients may be assisted to

establish regularity with the aid of 'PETROLAGAR' because it renders the faeces soft and moist to facilitate normal, comfortable evacuation.

'PETROLAGAR' is available in four varieties: Plain, with Phenolphthalein, Alkaline and with Cascara.

'Petrolagar'
BRAND PARAFFIN EMULSION
Regd.

Distributors in India:

KEMP & CO. Charni Road, Queens Road, Bombay, India.

Sole Proprietors:

JOHN WYETH & BROTHER LTD., 25, OLDHILL PLACE, LONDON, N. 18.

When writing to advertisers, please mention the "Antiseptic."

LACTOPEPTINE

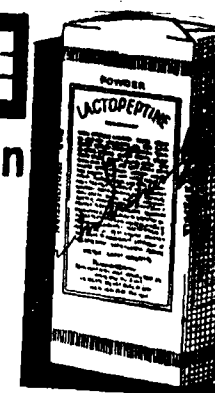
The **POSITIVE** Remedy for Indigestion

To prescribe LACTOPEPTINE in any case of Digestive Weakness, Disorder or Distress, is to provide the patient with the positive means of restoring adequate digestive action. For LACTOPEPTINE represents, in combination, the active principles of digestion as supplied by Nature in the human body.

It is an accurately constituted compound of Pepsin, Pancreatin and Diastase together with Lactic and Hydrochloric Acids. Thus the Digestive Organs are allowed to rest and recuperate, whilst distressing symptoms are quickly conquered.

FREE SAMPLE together with further details may be obtained from:-

Messrs. Muller & Phipps (India), Ltd.,
P.O. Box 773, BOMBAY.



**IN 3 FORMS
TO SUIT ALL CASES**

To suit the needs of all patients, LACTOPEPTINE is obtainable in 3 forms, viz: Tablets, Powder and Elixir.

DIGESTS LIKE NATURE DIGESTS

CASPRETTE

BRAND

Tablets of Aspirin and Caffeine

Trade  Mark

For the relief of all kinds of pain

Safe and Dependable

Does not affect the heart or upset digestion

MADE IN MYSORE

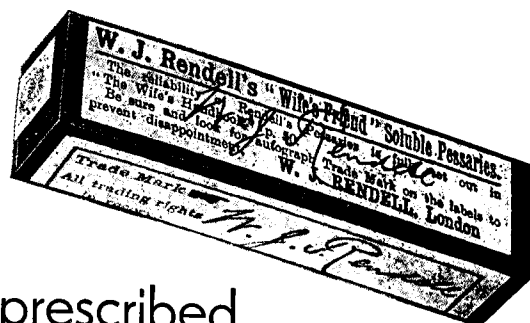
BY

The Government Industrial & Testing Laboratory

MALLESWARAM, BANGALORE.

When writing to advertisers, please mention the "Antiseptic."

When
further pregnancies
are undesirable



can
be prescribed
with confidence

This contraceptive is known throughout the world and has been used successfully for 50 years.

Made under conditions of scrupulous hygiene, it is the one Product which fulfils the exacting demands required of a contraceptive product.

Rendells may be prescribed in all cases with complete confidence. It is also a convenience to patients that supplies can be obtained from all good chemists.

For special literature apply

W. J. RENDELL LTD
161/165 ROSEBERY AVENUE, LONDON, E.C.1

When writing to advertisers, please mention the 'Antiseptic'

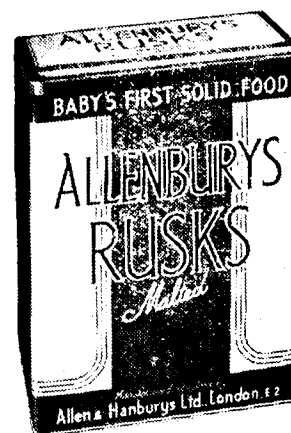
*Baby's
First Solid
Food*

Allenburys Malted Rusks are a valuable food from the age of ten months onwards, and may be used even earlier as a stimulus to salivary secretion and a help to teething. Their use encourages the development of a strong, wide jaw in which there is ample room for the teeth.

Vitamin D (calciferol), in the form of irradiated ergosterol, is added to the Rusks in the process of manufacture, in order to ensure normal calcification of bones and teeth.

The Rusks retain their crispness and flavour under the most varied climatic conditions.

In tins containing $\frac{1}{2}$ lb., 1 lb., 2 $\frac{1}{2}$ lbs.



Allenburys
RUSKS

ALLEN & HANBURYS Ltd., Clive Buildings, CALCUTTA
(Incorporated in England) and at 37, Lombard Street, London, E.C.3

When writing to advertisers, please mention the 'Antiseptic'

MALARIA!!!

USE
JAVA QUININE
TRADE MARK



ALL QUININE SALTS
PLAIN & SUGAR-COATED TABLETS
CINCHONA FEBRIFUGE
AND OTHER
DERIVATIVES OF CINCHONA
ALKALOIDS

High Degree of Purity and Solubility.

Sole Agents for India & Burma:
MARTIN & HARRIS LTD.,
CALCUTTA — BOMBAY — MADRAS
KARACHI — RANGOON.

Some recent pronouncements on the value of QUININE IN MALARIA

Extract from the

*"Resolutions of the Inter-Governmental
Conference of Far Eastern Countries on
Rural Hygiene." Bandoeng, Java,
3rd-13th August 1937.*

*"...that wide distribution of quinine is a
public duty which, whenever and wherever
necessary should be organised and paid for
by the State."*

*"The Conference further is in agreement
that the Cinchona derivatives remain the
drug of choice for mass distribution."*

*"QUININE is not only still the best and
safest remedy against MALARIA.*

*QUININE is also of proved value in the
prevention and cure of INFLUENZA."*



BI-COLATES

(STEARNS)

DEPENDABLE CHOLERESIS and CHOLAGOGUE ACTION

A scientific combination of the bile salts,
Sodium Glycocholate and Sodium Taurocho-
late, with Cascara Sagrada, Phenolphthalein,
and Oleoresin Ginger.

Bi-Colates (Stearns) are particularly indicat-
ed in cases of hepatic insufficiency, either
functional or in association with early cirrho-
sis, catarrhal and other forms of jaundice,
bilious attacks, intestinal auto-intoxication
and the prevention and treatment of gall-
stones.

Bi-Colates (Stearns) are also indicated in all
conditions in which a true cholaretic and
cholagogue is required.

Manufactured by:

FREDERICK STEARNS & CO., DETROIT, U.S.A.

Sole Agents in India & Burma.

MARTIN & HARRIS LTD.,
CALCUTTA—BOMBAY MADRAS—KARACHI—RANGOON.

PRESCRIBE

OSTERMILK

an infant food of such high
quality that it has been used
and prescribed since 1928 by
over 2,000 British Clinics

In Great Britain today, Ostermilk
is accepted as the successful
substitute whenever breast feeding
is inadequate or impossible. Over
2,000 British Infant Clinics have
recommended Ostermilk continu-
ally for the last eight years.

The doctors in charge of these
clinics include the leading British
infant specialists.

Only an infant food of un-
impeachable quality giving the
highest possible degree of success
in practice could maintain the
respect of such eminent physicians
over such a long period of years.

Representatives in India:

H. J. FOSTER & Co. LTD.,

P. O. Box 202, Bombay.
P. O. Box 2257, Calcutta.
P. O. Box 108, Madras.
P. O. Box 244, Lahore.

THE REASONS FOR THE SUCCESS OF OSTERMILK IN GREAT BRITAIN

The formula of Ostermilk,
a dried milk-food, approx-
imates to that of human
breast milk. Both the
fat and protein contents
are lowered to be in ac-
cord with the standards
set by nature, and to
suit the digestive
capacity of the youngest
infant. The special roller-
drying process used in
making Ostermilk
renders the protein more
easily digestible by re-
ducing the size of the
clot, which becomes light
and flocculent. The in-
corporation of vitamin
D and iron in measured
prophylactic amounts
provides factors which
build not only for the
present but for the
future. Constancy of
composition and the
greatest possible purity
are accepted features of
Ostermilk. No better or
safer food is available
anywhere.

When writing to advertisers, Please mention the "Antiseptic"

The CONSTIPATED CHILD

Agarol simplifies the treatment of constipation by making it pleasant; children not only take Agarol with the greatest of ease but actually enjoy it.

This palatable emulsion of mineral oil and agar-agar with phenolphthalein is the ideal treatment for constipation in children. It is gentle in action and furnishes the natural stimulus to a comfortable and normal peristalsis. Its capacity for lubricating the bowel, softening the faecal mass and easing its passage to the rectum and final expulsion, is unsurpassed.

Further advantages of Agarol are that it is not habit-forming and, by mixing freely with the intestinal contents, it makes the occurrence of seepage extremely improbable.



AGAROL

A trial supply to Physicians on request.

MARTIN & HARRIS LTD.,
Mercantile Buildings, Lall Bazar, Calcutta.
Also at Bombay, Madras, Karachi and Rangoon.

Prepared by **WILLIAM R. WARNER & CO. LTD., LONDON, ENGLAND.**

When writing to advertisers, please mention the "Antiseptic"

1940]

THE ANTISEPTIC

GLYKERON

*Coughs, Bronchitis, Asthma
Laryngitis, and other Res-
piratory Affections . . .*

A Bronchial Sedative

Control the cough that weakens your patient.

GLYKERON quickly relieves this distressing symptom because it contains medically approved respiratory sedatives.

Your patients with respiratory affections do better when they sleep better—*without coughing.*

GLYKERON may be administered to diabetics freely as it contains no sugar or syrup and causes no disturbance of digestion.



Stimulating Expectorant

GLYKERON loosens the mucus in the bronchial passages and aids in its expulsion.

It lessens the hazard of complications by getting rid of germ-laden secretions. Prescribe it for the symptom of cough. Very palatable.

GLYKERON supplied in 3 oz. as well as 16 oz. bottles.

DOSAGE: Adults, one to two teaspoonfuls every two or three hours or at longer intervals as the individual case requires. Children, from ten drops to one teaspoonful, according to age.

Literature on request

MARTIN H. SMITH COMPANY · NEW YORK

HEWLETT'S MIXTURE

MIST. PEPSINÆ CO. C. BISMUTHO (HEWLETT'S)
THIS PREPARATION IS ALSO SUPPLIED "SINE OPIO" WHEN DESIRED
**OVER 60 YEARS' REPUTATION AS A REMEDY FOR
INDIGESTION, DYSPEPSIA AND ALL DISEASES OF
THE STOMACH.**

MEDICAL OPINIONS

"It is clear, mixes easily with water, and is undoubtedly a valuable and convenient preparation."—*The Lancet.*

"Obviously likely to be of much advantage in the frequent cases of irritative dyspepsia with atony of gastric or intestinal muscular layers."—*The British Medical Journal.*

Supplied in 4oz., 10oz., 22oz., 40oz., and 90oz., bottles.

INTRODUCED AND PREPARED ONLY BY
C. J. HEWLETT & SON., LTD.,
Wholesale and Export Druggists and Surgical Instrument Makers,
35-43, Charlotte Road and 83-85, Curtain Road, London, E.C. 2.

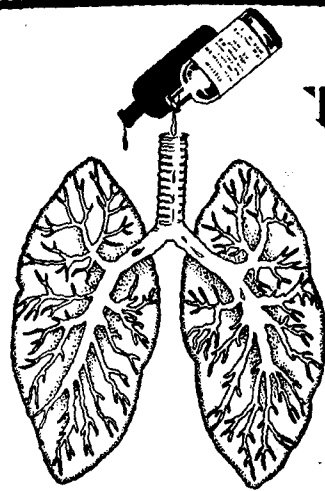
Agents who stock Hewlett's Preparations.

BOMBAY:—	Amersey Khimjee & Co.	Jadavji Goverdhandas & Co.
CALCUTTA:—	Smith Stanistreet & Co.	M. Bhattacharyya & Co.
MADRAS:—	Madras Drug Store.	Dadha & Co.
		B. K. Paul & Co. Ltd.
		Appah & Co.



When writing to advertisers, please mention the "Antiseptic"

**WASH
THE LUNGS CLEAN**



Being a combination of pulmonary antiseptics & expectorants of proved therapeutic value viz. pot. Guaiacol Sulphonate, Ammonium Chloride & Vinum Antimonii & containing, as it does, the tonic properties of Calcium Hypophosphite

PULMOLIN

not only clears the lungs of bronchial mucus but strengthens them against future attacks.

KILLS COUGH & HEALS THE LUNGS.

LISTER ANTISEPTICS & DRESSINGS COMPANY (1928) LD. CALCUTTA

SUCCINOL (Regd.) Is a satisfactory injection for **LEPROSY** (J. N. Missra) in all stages which has always stood the strictest test of the profession equally in official and non-official circles. Doses:— .02 Grm. to .2 Grm. in ten graduated ampoules.

DERMOL (Regd.) Is an unchallenged, stainless, bland, and the (J. N. Missra) most effective remedy for all skin diseases, swellings, ulcers, carbuncles, cuts, bruises, insect bites, ear troubles, burns; joint, gland and chest troubles etc. In short, an unfailing application for any and every disease externally.

IODINOX (J. N. Missra) (Regd.) The best, stainless, bland, and non-irritative preparation of Iodine "superior to other similar preparations" containing 5% of the active principle. Equally efficacious on skin and mucous surfaces. Indicated for use in cases.....requiring Iodine without irritation.

HYDROXY ERYTHRIN Hydroxy Erythrin also called Hydroxy Anthocyan--discovered by Dr. Missra is a synonym **HYDROXY ANTHOCYAN** (Regd.) (J.N. Missra) satisfactory injection for T. B. infection. It shows its effects both as preventive and curative only after a few injections. For detailed description leaflets will be sent on request.

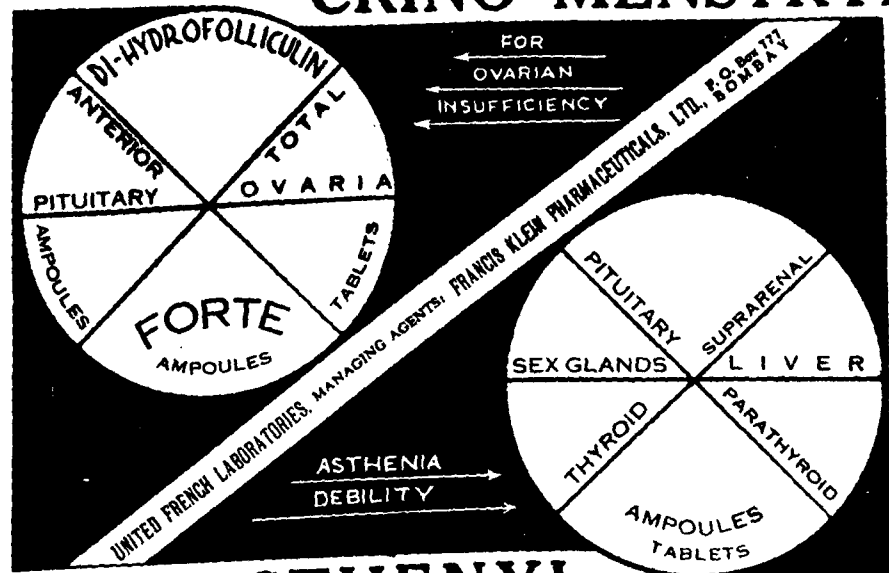
To be had from:—**GALLENO PHARMACEUTICAL WORKS,**

P. O. Waini, Ry. St. Pusa Road, B. N. W. Ry. Dist. Darbhanga. BIHAR, (INDIA).

Main Stockists:—Messrs. **SMITH STANISTREET & CO., LTD.**, 18, Convent Road, Entally, Calcutta.
Messrs. **SRI KRISHNAN BROS.**, 323, Thambu Chetty St., Madras.
Messrs. **E. STELLA & CO.**, Marshall's Building, Ballard Road, Bombay.

When writing to advertisers, please mention the "Antiseptic"

CRINO-MENSTRYL



CRINO-STHENYL

**NEDERLANDSCHE ARSPHENAMINENFABRIEK
N.V. BANDOENGSCHE KININEFABRIEK**

BANDOENG, JAVA &
AMSTERDAM, HOLLAND

THE SAFEST AND MOST
RELIABLE SPECIFIC FOR
TREATMENT OF
TREPONEMA
INFECTION

ALASPHIN
NEO-ARSPHENAMINE

In
ampoules of
graduated dosage
.15, .3, .45, .6, .75,
&
.9 grammes

Tested and controlled both
chemically and biologically

SOLE AGENTS FOR INDIA & BURMA
MARTIN & HARRIS LTD. MERCANTILE BLDGS, LALL BAZAR, CALCUTTA

When writing to advertisers, please mention the "Antiseptic"

MYALGIAS OF THE EXTREMITIES BACK AND NECK

are almost invariably benefited by heat therapy.

Antiphlogistine is a most useful and efficient form of applying prolonged moist heat, plus medication, for the relief of muscular aches and pains and associated stiffness.

It is distinctly beneficial, also, as a supporting measure to electro-therapy.

Sample on request

ANTIPHLOGISTINE

THE DENVER CHEMICAL MFG. CO.
163 Varick Street New York

Agents in India:—MULLER & PHIPPS (India) LTD., P. O. BOX 773, BOMBAY



The GLAXO surety of safety and purity

During the hot season, when it becomes impossible to obtain liquid milk at the required standard of purity for infant feeding, a dried milk food is essential. Glaxo is of particular value since its freedom from harmful pathogenic organisms gives protection against milk-borne diseases. Its lowered fat content is specially suited to the infant's digestion; its extra measured vitamin D and iron are safety measures against rickets and nutritional anaemia.

Glaxo

MILK FOOD

PRODUCT OF THE
GLAXO LABORATORIES



Glaxo Laboratories Ltd., Greenford, Middlesex, England.
Representatives in India: H. J. Foster & Co., Limited.
P.O. Boxes 202 Bombay; 2257 Calcutta; 108 Madras
244 Lahore.



HORLICKS

in

DIGESTIVE DISTURBANCES



Physiological tests show that Horlicks is easily digested, readily absorbed and well utilised. It forms a valuable diet in ulceration of the stomach and duodenum, gastritis, and digestive disorders generally, furnishing adequate nourishment without burdening the weakened digestive powers of the patient. In some cases an emulsion of Horlicks and olive oil is beneficial. The nutritive qualities of Horlicks also make it an ideal diet not only in acute illness and during convalescence, but in the many chronic conditions of ill-health which are favourably influenced by correct dieting.

HORLICKS

AVAILABLE EVERYWHERE

When writing to advertisers, please mention the "Antiseptic"

Crookes'

COLLOSOL CALCIUM

with VITAMIN 'D'

As a therapeutic agent, Calcium is of paramount importance. Although present in the blood serum only in very small concentration, the maintenance of this level is vital, and a small daily intake of Calcium is necessary to ensure it.

During pregnancy and lactation this becomes even more important as the requirement of Calcium during this period is greatly increased.

Equally important with the supply of Calcium is Vitamin D as without it Calcium cannot be absorbed. Failure to absorb Calcium because of lack of Vitamin D is the cause of Rickets in children and Osteomalacia in adults.

Rickets and Osteomalacia are extreme cases of Calcium deficiency but many other indications are benefitted by Calcium administration e.g. Tuberculosis, Nervous debility, Dental Caries, Urticaria, Neurasthenia associated with emotional disturbances, etc.

'COLLOSOL' CALCIUM with VITAMIN D (Injection)

Contains 0.05 per cent Calcium in Colloidal Suspension with 5,000 International Units of Vitamin D per c.c., and is specially prepared for subcutaneous injection.

Packings: Ampoules (box of 6) $\frac{1}{2}$ c.c., 1 c.c., 2 c.c.
Vials (rubber cap) 15 c.c., 30 c.c.

'COLLOSOL' CALCIUM with VITAMIN D (Oral)

Contains 1 per cent of Calcium Salts of fatty acids in Colloidal Suspension and is Standardised to contain 250 International Units of Vitamin D per fluid dram.

Packings: Bottles of 4 oz. and 10 oz.

'COLLOSOL' CALCIUM is available in the same forms and sizes as 'Collosol' CALCIUM with VITAMIN D.

THE CROOKES LABORATORIES (British Colloids Ltd.) PARK ROYAL, LONDON, N.W.10, ENGLAND
BOMBAY: 10 GRAHAM ROAD, BALLARD ESTATE

When writing to advertisers, please mention the "Antiseptic"

gaining the patient's confidence

It is axiomatic that unless the patient fully relies on his medical attendant, no treatment can have its full benefit. Some tendency to this unbalanced and unjustifiable lack of confidence lengthens most convalescences. Hall's Wine is a specially valuable tonic in such cases, for its mild alcoholic stimulus is immediately felt, and a psychological control is established over the anxiety-neurosis.

As a food the medicated properties of Hall's Wine give it a much higher thermal-energy value than that of unmedicated Wines and Spirits. Since no activity of the digestion is required for the assimilation of grape sugar and alcohol, Hall's Wine is without contra-indications for cases of gastric disorder or weakness. Hall's Wine improves the metabolism and hence the nourishment derived from other foods.

The matured wine which forms the basis of this preparation is unusually rich in iron, which makes it a very rapid reconstructor of haemoglobin. The tendency to anaemia so common in tropical countries is efficiently counteracted by a course of Hall's Wine.

To hasten recovery from illness, Hall's Wine may be prescribed with perfect confidence.

HALL'S WINE

Tonic Restorative



Distributors: J. HALLEY & CO., LTD.

P. O. Box 133,
Calcutta

P. O. Box 84,
Lahore

P. O. Box 34,
Karachi

P. O. Box 466,
Bombay

HW 98

When writing to advertisers, please mention the "Antiseptic"

Ergoapiol-(Smith)

REG. U.S. PAT. OFF. AND FOREIGN COUNTRIES

A Menstrual Regulator...

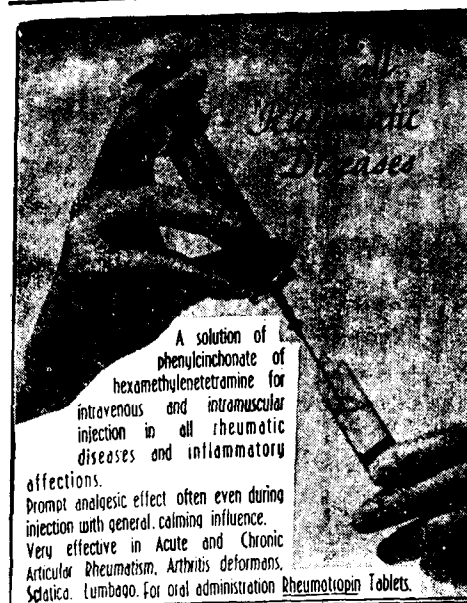
When the periods are irregular, due to constitutional causes, ERGOAPIOL (Smith) is a reliable prescription. Containing superior ergot and apiol (M.H.S. special) together with aloin and oil of savin of the highest quality, this preparation effectively stimulates uterine tone and controls menstrual and post-partum bleeding.

In cases of Amenorrhea, Dysmenorrhea, Menorrhagia and Metrorrhagia, Ergoapiol serves as a good uterine tonic and hemostatic. Valuable in obstetrics after delivery of the child and for the menstrual irregularity of the Menopause.

Prescribe 1 to 2 capsules 3 or 4 times daily. Supplied only in packages of 20 capsules. Literature on request.

As a safeguard against imposition the letters MHS are embossed on the inner surface of each capsule, visible only when the capsule is cut in half at seam as shown.

MARTIN H. SMITH COMPANY
NEW YORK, N.Y., U.S.A.



SILBE BRAND **LEUCOTROPIN**
Ask for booklet and free sample from
VYAS Bros., Princess Street, BOMBAY.
Manufactured by Silben Ltd., 27 Porchester Road, London W 2

The most recent advance in the treatment of

Pyelitis and other Urinary Infections

UROMALINE

Ammonium Mandelate in a Palatable Solution, B.R.I.

Prepared for the first time
in India

One fluid drachm or one
teaspoonful contains an
equivalent of one gramme
of Mandelic Acid.

Pamphlets on Uromaline are sent free
on application to:

The Brahmachari Research Institute,

82-3, Cornwallis Street, Calcutta.

DIABETES

Successfully treated by the oral administration of the active derivatives of the pancreas which control the several phases of diabetic pathology:

Trypsogen

Bottles of 100 tablets.
Enterosol Coated if desired.



G. W. CARNRICK CO.
20 MT. PLEASANT AVE. Consult NEWARK, N. J., U. S. A.
MULLER & PHIPPS (ASIA) LTD.
NICOL RD., BALLARD ESTATE, BOMBAY

INFANTILE LIVER AND SPLEEN COMPLAINTS

It is generally believed that these cases of Infantile Liver & Spleen Complaints are difficult of treatment. Most Medical Men are thoroughly convinced that by the use of Jammi Venkataramanayya's 'LIVERCURE' (Regd.) the unique Specific remedy invented and perfected by Jammi Venkataramanayya Garu, the disease could be successfully treated.

For further particulars, please write to:—

JAMMI VENKATARAMANAYYA & SONS,
'LIVER CURE' OFFICE,
2 & 8, SALAI STREET, MYLAPORE, MADRAS.

When writing to advertisers, please mention the "Antiseptic"



IRON MEDICATION FERRONE, ELIXIR

Each fluid ounce contains:

Iron and Ammonium Citrates... 120 grs.
Yeast Extract equivalent to approximately
125 Sherman Units of Vitamin B
25 Sherman Units of Vitamin G
in an acidulous elixir base.

The distinctive features of this preparation are its simplicity and the fact that it provides a surprisingly pleasant fluid form of iron medication which permits massive dosage. It is appropriate in all types of iron deficiency and nutritional anæmias (the various forms of secondary anæmia) and is particularly adapted to the treatment of nutritional anæmias because of the high content of vitamins B & G.

Dosage: 1 to 2 teaspoonfuls three times daily.

Available in Bottles of 8, 16 & 128 ounces.

Manufactured by:

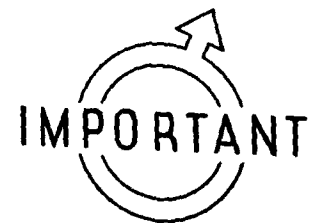
THE UPJOHN COMPANY,
Kalamazoo—Michigan.
U. S. A.

Sole Agents:

T. M. THAKORE & CO.,
43, Churchgate Street, Fort, Bombay.

Branches:

Calcutta: 12, Dalhousie Square.	Karachi: 123, Bunder Road.	Lahore: 124, Anarkali.
Madras: 1/10, & 10A, Stringer St., G.T.	Nova-Goa: Rua 31 de Janeiro.	
Rangoon: 65, Taseekai Mg. Taulay Street.		



PLASTULES' For The Treatment of ANÆMIAS & DEBILITY



As a **Reconstructive Tonic** for anæmias, debility and "run-down" conditions 'Plastules' have proved exceptionally effective.

You and your patients will be astonished at the rapid results. Colour returns to the patient's face in four days, appetite returns with a feeling of "well-being".

The dosage of 'Plastules' is small—3 a day. This small dosage results in lower cost, and is simple to administer. The usual after-effects of constipation and digestive upset associated with massive iron doses are absent when 'Plastules' are prescribed.

3 'Plastules' (daily dose) are equivalent to 18 x 5 grains Blaud Pills, 19 x 5 grains capsules of reduced iron, 16 x 17½ grains capsules of iron and ammonium citrate.

'PLASTULES'
HEMATINIC COMPOUND

FOR ANÆMIA AND DEBILITY

Distributors in India:—KEMP & CO., LTD.,
P. O. Box 937, Bombay.

Sole Proprietors:—
JOHN WYETH & BROTHER LTD.,
25, Oldhill Place, London, N. 16.

When writing to advertisers, please mention the "Antiseptic"

33 YEARS' RECORD OF STANDARD QUALITY

STANDARD DRUGS AND MEDICINAL
SPECIALITIES OF PROVEN MERITS.
RIGHT IN QUALITY: RIGHT IN PRICE.



Alembic CHEMICAL WORKS CO. LTD.

BOMBAY

BARODA

MADRAS CALCUTTA

High germicidal efficiency without danger



'DETTOL' can be used at really effective strengths without danger, discomfort or staining—a marked superiority over carbolic and cresylic antiseptics. It is thus a most useful disinfectant for first aid at home, for personal hygiene, and for gargling and bathing. 'DETTOL' maintains high bactericidal efficiency in the presence of blood, pus and other organic matter, and is the antiseptic now widely used for all obstetrical purposes. 'DETTOL' is a clean, clear fluid, non-poisonous and non-staining, with a distinctly pleasant smell.

'DETTOL'
THE MODERN ANTISEPTIC

Send postcard for free literature to:

ATLANTIS (East) LTD., (Dept. V. 9) 20, 1, Chetia Road, Calcutta
Marketing Agents for Reckitt & Sons, Hull & London, England

When writing to advertisers, please mention the "Antiseptic"

STILBOESTROL B.D.H.

Laboratory and clinical trials have established that stilboestrol possesses all the physiological properties of the natural oestrogenic hormones. In addition it is as active orally as parenterally and its use is therefore both economical and conducive to the comfort of the patient as well as convenient for the physician.

Stilboestrol dipropionate is available as Stilboestrol D-P for use in those rare cases in which the patient may display some degree of intolerance to Stilboestrol B.D.H.

For the treatment of menopausal patients with symptoms of involutional melancholia the use of the natural oestrogenic hormone, Cestroform, is recommended since it has proved to be more effective in controlling the nervous symptoms than stilboestrol.

Stocks of Stilboestrol B.D.H. and of Stilboestrol D-P as well as B.D.H. Sex Hormone Preparations are held by leading chemists and full particulars are obtainable from:

THE BRITISH DRUG HOUSES LTD.
(Incorporated in England)

Imperial Chemical House Ballard Estate
BOMBAY

Stil/In:405

When writing to advertisers, please mention the "Antiseptic"



Children who need
additional vitamins
need—

TRADE **'KEPLER'** MARK

COD Liver Oil **MALT** Extract
with

The value of this nutritious vitamin-containing food has been proved by its effects upon the backwardly-developed child. Physically and mentally the improvement is quickly noticeable.

It gives healthy, well-developed children also increased resistance against infection.

Bottles of two sizes

Literature to Medical Men, on request

 **BURROUGHS WELLCOME & CO., LONDON**
(THE WELLCOME FOUNDATION LTD. INCORPORATED IN ENGLAND)
AND COOK'S BUILDING, HORNBY ROAD, BOMBAY
D 692 Ex. COPYRIGHT

When writing to advertisers, please mention the "Antiseptic"

CHEMOTHERAPY OF PURE AND MIXED
STREPTOCOCCAL INFECTIONS

3 years of research,
the testing of over 200 substances

HAVE PROVED THAT

RUBIAZOL
AN AZOIC DYE
(formerly known as Bacteramide)

is
the **MOST ACTIVE**
the **LEAST TOXIC**
the **BEST TOLERATED**
TREATMENT

DAILY DOSE
6 TO 12 TABLETS
1 TO 3 AMPOULES



LABORATOIRES DU DR. ROUSSEL

89, RUE DU CHERCHE-MIDI - PARIS

SOLE AGENTS FOR INDIA, BURMA AND CEYLON:

G. LOUCATOS & CO.

CALCUTTA
P. O. Box 2239
Tel. 2455.

BOMBAY
P. O. Box 783
Tel. 20849.

MADRAS
P. O. Box 1273
Tel. 3454.

The Antiseptic

Estd. 1904.

A Monthly Journal of Medicine and Surgery.

Editors: Dr. U. RAMA RAU, M.L.C., & U. KRISHNA RAU, M.B., B.S.

Editorial and Publishing Offices: 323, THAMBU CHETTY ST., MADRAS.

Annual Subscription Rs. 5. Foreign, 10 Sh. Post Paid.

37.

MAY, 1940.

No. 5.

ORIGINAL ARTICLES

Rational Intranasal Medication*

BY

V. R. Kamath, M.B.B.S., D.L.O. (ENG.)
Madras.

O-RHINO-LARYNGOLOGY has in recent years undergone such a rapid evolution in the realm of surgery, that ear, nose and throat specialists are generally considered, by their medical colleagues as well as by the laity, to be strictly surgeons, either incapable of treating or unwilling to treat their patients by non-surgical means. It has to be admitted, however, that they are themselves largely to blame for such an attitude on the part of medical practitioners and the public, for they have tended to omit or neglect the study and understanding of the problems of oto-rhino-laryngological medicine.

The pioneer work of A. W. PROETZ of America on the physiology of the nose and paranasal sinuses, followed by the experimental and clinical studies of WALSH and CANNON, PARKINSON, LIERLE and MOORE, HILDING, and others, ushered in a new era of rational medical treatment of nasal and paranasal sinus affections. One cannot, within the limits of a paper on intranasal medication, enter into the details of nasal physiology and bio-pathology, but a brief review of the outstanding advances in our knowledge regarding these will be useful as an introduction to the new intranasal therapy.

The main physiological function of the nasal chambers may be summed up in the term 'air-conditioning'. It has been estimated that, in temperate climates, a litre of water is evaporated from the nasal mucosa in 24 hours, in order to saturate the inspired air with moisture, and 70,000 calories of heat are expended within the same

* Specially contributed to 'The Antiseptic'.

period to raise the temperature of the air to blood-heat. Of more direct clinical interest, however, are the various defensive devices that exist in the nose; chief among these is the *mucous film*. It is a thin layer of viscid fluid covering the entire mucosa of the nasal chambers and associated sinuses like a blanket, and constantly moving in a general backward direction at the rate of about 15 millimetres per minute. It entangles dust, bacteria and other particulate matter, thus acting as a dragnet and a physical barrier against invasion; it serves as a humidifier, a conductor of heat, a diluent for irritants, a lubricant, a buffer whose pH value is ideally set for lysozymic action; it is, above all, an almost incomparable antiseptic, capable of destroying bacteria even in 1 in 100 dilution, and equal in power to 1 in 20 carbolic acid without the tissue-harming properties of the latter.

The mucous film is, as Hilding puts it, the central factor of nasal physiology; the motive power for the mucous film is supplied by the *ciliated epithelium* which lines the greater part of the nasal cavities and the paranasal sinuses. Each columnar cell of this epithelium bears about 30 cilia, (each 5 micro-millimetres in length), perpetually undulating with a whip-like motion at the rate of 250 cycles a minute, wafting the blanket of mucus from the depths of the sinuses into the nasal cavities, and backwards in the nose towards the nasopharynx. The marvellous power of this apparatus has been graphically described by PROETZ, who has calculated that if the cilia were each one foot long, the maxillary antrum would proportionately be a mile high, and its cubic contents could supply New York City with water for 14 years; and yet, if such an antrum were filled with thick secretion (as in purulent sinusitis), the little mat of cilia could clear out the antrum *within a few hours*!

Among other features of the series of defensive mechanisms in the nose are: the adaptability of the nasal epithelium, by virtue of which it alters its form according to changes of humidity, modifications of intranasal air-currents, etc; the property of facile sloughing and rapid regeneration of the mucosa; and the important sub-epithelial defences, consisting essentially of the reticulo-endothelial system and the erectile tissue of the turbinals.

Curiously enough, this remarkable array of tissue defences does not appear to be invulnerable to infection, if one is to judge by the considerable incidence of rhinitis and paranasal sinusitis in all classes and ages of population. The complicated nature of the mechanism seems to be the very reason for its failure; nature overshoots the mark. The congestion induced by bacterial invasion upsets the venous and lymphatic circulation in the nose, with resultant oedematous swelling of the mucosa, narrowing or closure of the various ostia by means of which the sinuses communicate with the nasal cavities, accumulation of inflammatory products in the sinuses, and ultimately paralysis of the cilia and destruction of epithelium.

Rational intranasal therapy aims at preventing or checking this vicious cycle; it recognises the nasal and sinusal mucous membrane to

be "a functioning organ rather than an inert lining" (PARKINSON), it employs drugs and methods which are suited to the physiology and pathology of the nose, and above all, it is based on experimental and clinical evidence of real utility rather than upon the empiricism and traditions of the pre-physiological era.

The chief considerations in connection with the selection of the drug, the vehicle, and the method to be employed in intranasal medication, may be summarised as follows:—

1. *The nasal and sinusal mucosa must not be injured*:—It is well to accept as an axiom that no antiseptic must be used in the nose. "There are valid objections to the intranasal use of all antiseptics and preservatives available today. These objections are particularly important during acute colds and sinusitis." (PARKINSON). Temperature is another factor; the use of boiling water for vapour inhalations (such as Tr. Benzoin Co.) is definitely an instance of adding insult to injury.

2. *The mucous film should be respected*:—It is to be regretted that the practice of advising 'nasal alkaline douches' has become so universal, by specialists and general practitioners alike. In cases of acute rhinitis or sinusitis, their employment may be said to amount to malpractice, and even in chronic infections they can do much harm and no good. Again, oily solutions of drugs are unsuitable, as they block the normal flow of mucus and prevent the drugs dissolved in them from penetrating the mucous blanket, thus frustrating their own purpose. WALSH and CANNON have amply demonstrated that patients who have used oily solutions for nasal instillations during fairly long periods of time, are prone to suffer from lipoid pneumonia, broncho-pneumonia, pulmonary oedema, etc. as a result of continual aspiration of the tiny oil particles into the lungs.

3. *Ciliary activity must not be hampered*:—The prescription of hypertonic or hypotonic solutions for intranasal medication is the surest way of interfering with the ciliary mechanism, and thus retarding recovery from inflammation. Such solutions 'sting' or 'smart' when instilled into the nose, and the simplest test of proper strength of a drug or vehicle used in the nose is that it produces no sensation whatever. Apart from the importance of isotonicity, it must be remembered that several drugs commonly employed for 'nasal drops' hamper or paralyse ciliary activity, irrespective of their relation to the tonicity of the epithelial cell-contents. In this connection, the hydrogen-ion content of the solution is of importance, since any shift from the normal value for nasal mucus (about pH7) interferes with its lysozymic action.

4. *The vasomotor balance of the turbinals must not be disturbed*:—The erectile tissue of the turbinals is very sensitive, and displays an embarrassing predilection to reactions following the desired action of drugs applied locally. Menthol, for instance, which is used so widely for inhalations or as a constituent of 'nose drops', is an arch-offender

in this respect; the gratifying vaso-constriction it produces, being too often replaced by greater congestion than existed before its use; Adrenalin sprays may act in a like manner. Drugs used intranasally should therefore be such as will produce no side-effects or reactions.

5. *The drug must be brought into contact with the whole area which requires to be treated, and should remain in contact with it for a sufficient length of time:*—Consideration of this factor entails a brief review of the various methods employed in intranasal medication, some of which have been alluded to previously; they comprise:

(i) **APPLICATIONS**:—Of caustics, pigments, ointments, etc. The topical application of Trichlor-Acetic Acid crystals to a bleeding point on the septum, or the use of Silver Nitrate (10% solution) or of Mercurial Ointments for dermatitis or eczema of the nasal vestibule, are examples of this method. It is, however, very limited in its scope, and cannot be employed in the great majority of nasal and sinusal infections. The practice of introducing cotton-wound applicators (kutchies) deep into the nose for the purpose of treating rhinitis and allied conditions is greatly to be deprecated; it cannot serve any useful purpose, whatever the drug employed, and more often than not, it results in injury to the inflamed epithelium, thus paving the way to complications.

(ii) **IRRIGATION**:—Syringing or douching. This mode of therapy has been already referred to. Even in the very few circumstances in which irrigation is indicated (as in some cases of atrophic rhinitis, and in myiasis), it should be carried out by the rhinologist himself, and never entrusted to the patient.

(iii) **PACKS**:—Tamponage of the nasal cavities with cotton-wool pledgets or gauze pieces impregnated with Argyrol was once in vogue for the treatment of sinusitis (Dowling's method). The technique, however, requires the skill of a trained rhinologist rather than that of a general practitioner, and the results of this therapeutic measure have not been satisfactory in the experience of many observers. Moreover, recent investigations by various workers have demonstrated that mild protein silver has no bactericidal effect in the nose. Packing the nasal cavities is nevertheless rational and effective for the purpose of obtaining anaesthesia for the performance of intranasal operations, and also as a means of temporary arrest of profuse epistaxis.

(iv) **INHALATIONS** of powders, vapours, or gases. Medicated snuffs have gone out of fashion, and rightly so. The inhalation of the vapour of Friar's balsam is very popular, and is probably of some psychological value to the patient; the *rectified* Tincture Benzoin Co. should be prescribed (not the commoner methylated variety), and the water used should not exceed a temperature of 60°C.; boiling water which has been left to cool for ten minutes usually serves the purpose; a drachm of Chloroform added to an ounce of the tincture enables the latter to vaporise at a lower temperature. The inhalation of the vapours of solids such as Menthol, Camphor, Benzadrine, etc. cannot

be commended, owing to their proneness to produce reactions and other undesirable after-effects.

(v) **INSUFFLATIONS** of powders, for ulcerative conditions, are hardly ever employed.

(vi) **SPRAYS**:—Antiseptic, decongestive, or anaesthetic. The first variety may be dismissed at once, for reasons already shown. Adrenalin solution sprayed into the nose is very effective as an immediate vaso-constrictor, but the result is short-lived, the reaction may be marked, and besides, the drug can hardly be said to fulfil the criteria that have been enumerated. One practical disadvantage of all sprays is that a special apparatus is required, which is expensive and apt to go wrong when it is needed. For preliminary anaesthesia, a Cocaine and Adrenalin spray is useful and not irrational.

(vii) **INSTILLATIONS**:—The number and diversity of preparations prescribed and patented for the purpose of instilling into the nose is evidence of the wide-spread employment of this method of treatment. Very few (if any) of these, however, can lay claim to physiological correctness, and their popularity rests upon the production of a partial and temporary decongestion, their appeal to the sense of smell, or their publicity by efficient advertisement. When oily solutions or silver preparations are used for prolonged periods, there is the real danger of pulmonary complications ensuing. Even if the drug and vehicle are physiologically suitable, the method of putting 'drops' into the nose has little to commend it; the solution merely flows backwards along a limited area of the nasal chambers and immediately makes its presence felt in the pharynx.

What then, is the proper drug, the physiological vehicle, and the correct method for intranasal medication? Can we devise a means of combining physiological righteousness with practical simplicity, and applicability to the majority of nasal and sinusal infections? ARTHUR W. PROETZ and SIDNEY N. PARKINSON have supplied the answer. The Proetz-Parkinson technique (if one may so name it, though they have not been collaborators in their work) bids fair to replace all other non-surgical methods for the treatment of non-specific intranasal and sinusal inflammations, and to render unnecessary many surgical procedures that have been so fashionable in the past. The present writer has employed the technique (which is described below) in a large series of cases, both in hospital and private practice, and considers it to be one of the most striking and important advances in the field of rhinology during the past decade.

The Proetz-Parkinson Technique.—The formula consists of a 0.9 per cent solution of Ephedrine Hydrochloride in normal saline; in other words, four grains of Ephedrine Hydrochloride and four grains of Sodium Chloride to the ounce of water. The solution may be boiled and cooled; it is issued to the patient in a clean bottle, along with a clean glass medicine-dropper (or ink-filler) fitted with a good rubber teat capable of drawing up about half a drachm of liquid. As

PARKINSON emphasizes, the solution should contain "No preservative; no antiseptic; no volatile oil." It is isotonic, it has a stable hydrogen-ion content, it is compatible with the nasal secretions, it does not damage the epithelium or interfere with ciliary action, it produces reasonably prompt and prolonged vaso-constriction without side-effects or reactions, and last but not least, it is inexpensive.

The method is simple enough when intelligently understood, but depends for its efficacy on meticulous attention to several details. The underlying principle is purely a physical one,—the displacement of air in the paranasal sinuses by liquid forced into them from the nasal cavities, by creating a negative pressure. The actual technique may be described in a series of stages, for the sake of clearness, although the whole process is a continuous one and takes less than three minutes to perform.

1. The patient lies on a cot or table, with one or two pillows beneath his shoulder-blades, the shoulders projecting beyond the upper edge of the pillow and the head resting on the cot. He then turns over to one side, (the lower shoulder still projecting beyond the pillow), and bends his head as much as possible so as to bring it close to the lower shoulder (lateral flexion). In this posture (termed the 'lateral head-low position' by Parkinson) the important points therefore are that the side of the chest and the lower shoulder are elevated, and the head tilted so that the anterior edge of the nose is almost vertical; the vertex rests comfortably on the cot. The lateral head-low position can of course be assumed in one movement, without previously making the patient lie on his back, but when the method is demonstrated for the first time, it is less confusing to the patient if he is instructed in the manner described.

2. The patient is now told to open his mouth and breathe audibly through it. Unless one concentrates on mouth-breathing, one is apt to lapse unconsciously into nose-breathing, and such concentration is best accomplished and maintained by panting audibly through the mouth.

3. Two dropperfuls of the solution (that is about a drachm) are poured into each nasal cavity, holding the tip of the dropper at the anterior angle of the nasal orifices, that is to say, at the junction of the septum with the outer wall of the external nose. (One dropperful in each nasal cavity is sufficient for children.) For about two minutes, the patient continues to breathe through the mouth, thus retaining the liquid in the nasal cavities and giving time for the nasal mucous membrane to shrink; the various ostia of the paranasal sinuses are under the level of the liquid in the nose, and they become wider in consequence of the shrinkage of the surrounding mucosa. During this waiting period of two minutes, the patient should be completely relaxed, should refrain from making swallowing movements, and should devote his attention to mouth-breathing.

4. When the two minutes are over, the patient's nostrils are occluded with the balls of the thumbs (this manoeuvre is better than

pinching the nostrils between thumb and index finger) and he is directed to shut his mouth and attempt to inhale strongly *through the nose*; this attempt is repeated two or three times, keeping the mouth closed and the nostrils occluded *all the time*. The strong muscular action results in a negative pressure being created in the nose; the air in the sinuses is thereby sucked into the nose, and the solution rushes into the sinuses through their various ostia.

5. The thumbs are removed from the nostrils, and the patient turns face downwards, to allow any excess of the liquid in the nose to escape. If the technique has been properly carried out, hardly a drop of the solution comes out of the nose, and of course, none of it has found its way into the throat; it has disappeared completely into the paranasal sinuses. During the course of the next few minutes, however, the solution is gradually wafted into the nasal cavities by the cilia in the sinuses, and its taste is then felt in the throat.

Recapitulation of the more significant details of this essentially simple technique would perhaps be helpful, in the absence of a practical demonstration.

(1) The exact posture is important. "In the same sense that the medication may be termed physiological, the posture for its administration may be termed anatomical." (PARKINSON). A child may be put across one's lap, with its head hanging along the side of one's thigh, and the solution instilled into the nose in this position.

(2) Breathing through the mouth is essential, during the two minutes in which the solution is allowed to remain in the nose. It is very easy, provided the patient is not apprehensive and if he relaxes, rather than screwing up his eyes and holding his throat muscles taut. Children can be taught to breathe orally by a little persuasion and gentleness.

(3) Plenty of the solution must be used. Excess does not matter, it will escape from the nose at the end of the manoeuvre; too little of the solution may mean that all the ostia are not under fluid level, and so some of the sinuses may be left untreated or may be incompletely filled. Both nasal cavities are treated in the same posture, the patient need not turn from one side to the other. The left lateral position is convenient, for the patient can then use his right hand to fill his nasal cavities himself; most patients, however, prefer to have the method carried out on them by some one else.

(4) The attempts at inhalation must be forcible; otherwise, enough negative pressure may not be created in the nose. The mouth should *not* be opened between each attempt at inhalation,—both mouth and nose are kept closed all the time, which means for about five seconds.

(5) The treatment is done once daily, preferably at bed time; never more than twice daily, lest too much Ephedrine should get into the system. Ill-effects of such absorption are not met with if the technique is correctly followed. A course of three weeks daily treatment

is usually required for an average case of chronic catarrhal rhinitis or paranasal sinusitis.

The clinical advantages of the Proetz-Parkinson technique, as apart from its physiological rectitude, may be summed up as follows:—

1. It is ideally suited for routine treatment of nasal and sinusal infections. The present writer has what he calls the 'Proetz-Parkinson procession' of patients every morning in hospital, consisting of cases of rhinitis and sinusitis, which are treated rapidly and efficiently by a nurse who has been instructed in the technique. It is particularly evident that children take delight in the treatment; the solution produces no sensation in the nose, and the whole procedure is like a game to them. In this connection, one may be permitted to observe that chronic maxillary sinusitis is exceedingly common in children and is the cause of much ill-health; this is often mistakenly attributed to the tonsils or to gastro-intestinal disorders, which are really the result of the constant swallowing of pus from the sinuses.

2. The method is equally applicable to nasal or sinusal infections. General practitioners, who cannot be expected to diagnose all cases of sinusitis, can nevertheless employ this technique for all patients who complain of "chronic colds", on the reasonable assumption that the majority of such patients must be having a chronic rhinitis or a chronic sinusitis or both. Acute inflammation in the nose or sinuses, also, responds dramatically to this treatment. The technique is not only easy, comfortable and rational, it is also safe, which is more than can be said of many other methods. Even if the sinuses are not infected, as in simple chronic hypertrophic rhinitis, the writer believes that displacement of liquid into the sinuses by negative pressure is of definite value; the gradual return flow of the solution, by ciliary activity, into the nose serves to prolong the vaso-constrictive action already produced, and to 'wash' the nose in a far more physiological and effective manner than an alkaline douche. PARKINSON does not employ negative pressure displacement in his routine technique, but he permits the solution to remain in the nasal cavities for as long as ten minutes before turning the patient face downwards.

3. The routine employment of this therapy obviates the need for surgical intervention in all but the worst cases. The rhinologist who has adopted the Proetz-Parkinson technique cannot fail to be impressed by the pronounced fall thereafter, in the number of his intranasal operations—cauterisations, turbinectomies, septum resections, and antrum punctures, to mention the most common ones. Nasal polypi will have to be cleared out, septal spurs which produce reflex neuralgia will need removal, and radical operations will occasionally be found necessary; but the new intranasal therapy will still constitute a notable advance in the post-operative treatment of nasal or sinus conditions; it gets rid of residual infection, helps the mucous membrane to regain its normal functions, and gives the lie to that opprobrious phrase, "Once a sinus operation, always a sinus operation!"

One cannot do better, by way of conclusion, than to quote from PARKINSON'S admirable article in a recent number of *The Journal of Laryngology and Otology*: "However, the daily use of tampons, trocars, probes and lavage inclines one to be impatient of unspectacular 'hands off' methods. The desire to do something and do it quickly is strong. Especially for a busy man, a doubting period of re-education is necessary. How can he be sure that the ciliary cleansing mechanism can be efficient in an acute case? Can it remove large accumulations of pus from the sinus unaided? His senses have long been attuned to sights, sounds and acts peculiar to the pre-physiological era, and these are not relinquished without effort. But of one thing I am certain: the patient will give up these nostalgic items without lament."

References:

1. Hilding, Anderson. "The Physiology of Drainage of Nasal Mucus" *Arch. Otolaryng.*, January 1932.
2. Lierle, D. M. and Moore, P. M. "Effects of Drugs on Ciliary Activity and Mucosa of Upper Respiratory Tract." *Arch. Otolaryng.*, January 1934.
3. Parkinson, Sidney N. "A Lateral Head-low Position for Nasal and Sinus Treatment." *Arch. Otolaryng.*, June 1933. "Non-traumatic Ventilation Treatment of the Nose and Sinuses." *J. Laryng. and Otol.* October 1939.
4. Proetz, Arthur W. "Displacement Irrigation of Nasal Sinuses." *Arch. Otolaryng.* July 1926.

Functional Impotence*

BY

Dr. M. V. Govindaswamy, M.A., B.Sc., M.B.B.S., D.P.M. (ENG.)
Superintendent, Mental Hospital, Bangalore.

MY interest in the problem of functional impotence was first aroused about three years ago when the husband of patient—discharged after recovery from the Mental Hospital, Bangalore—a very intelligent, healthy, youngman in the middle thirties, came up to the hospital for advice, panic-stricken at his inability to have conjugal relations with his wife, and fearful of impending impotence.

It was easy to conclude that in this case, the disability was primarily due to the unconscious feeling, not to have anything to do sexually with a woman labelled as 'mental', and secondarily to oversolicitude and consideration for the wife. All that was necessary, was a little reassurance and explanation, and everything went on well subsequently. Since then, whenever possible, I have tried to question, the husbands of patients, similarly situated, regarding their sexual relations, and I have been rather impressed with the fact that functional impotence, usually temporary, is very common amongst them. In view however, of the intimate nature of the questions asked, one is not always sure of the accuracy of the answers, and the conclusions are in consequence more in the nature of impressions than

* Specially contributed to "The Antiseptic".

scientific deductions. But because of the intense misery which the sufferers from this disability undergo, and which, in the majority of such patients, is temporary and curable, a detailed study seems to be necessary.

The following is a preliminary report based on detailed interviews with fifty healthy husbands. The disability is commonest in the age group thirties, less in the forties, while it is rather erratic in the twenties. In about ten of the fifty interviewed, the mental breakdown on the part of the wife, was more in the nature of a release, and freedom from domestic worries and anxieties to the husband, and as her return to health and home meant domestic trouble and unhappiness, the unconscious resentment against such a return, exteriorised itself as functional impotence. In most of the others, the explanation was not so simple, while in a few no explanation could be found. The factors considered in every case were:—

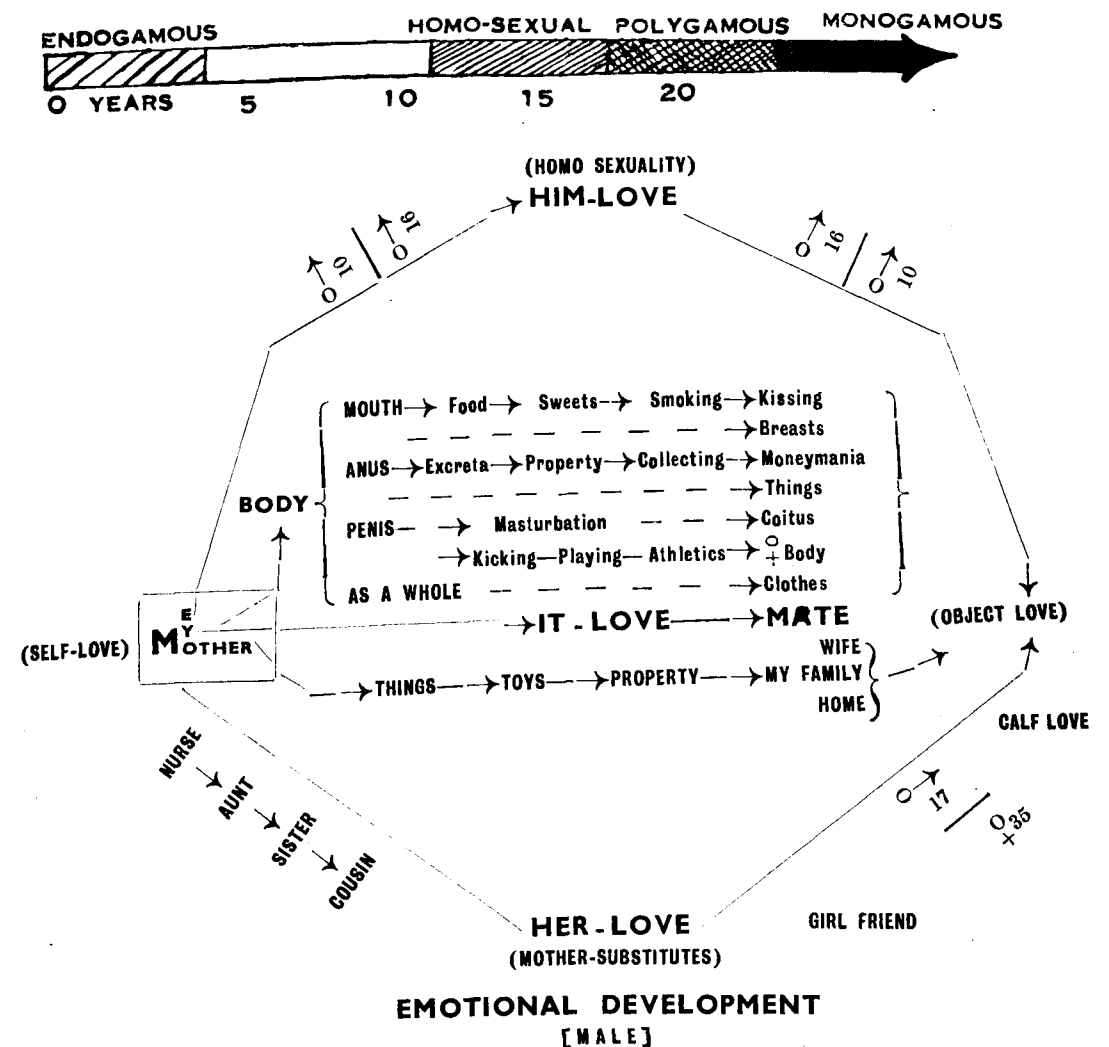
- (1) The personality of the couple.
- (2) Their emotional attitude towards each other.
- (3) Marital and extra marital relationships on the part of either.
- (4) Presence or absence of children.
- (5) Domestic worries and anxieties.
- (6) Economic security.
- (7) Compatibility of temper, and
- (8) Cultural levels.

Companionship between husband and wife, a harmonious household, freedom from penury, presence of children, but not too many, and absence of neuropathic heredity in either, prevent such a development. Functional impotence is rare in such a group, and even if it should arise, it is usually due to over-solicitude on the part of the husband for the welfare of his wife, or to removable superficial causes and is only temporary. It is more common, and less amenable to treatment, in those groups where in addition to absence of children, incompatibility, domestic worry, intense penury, or in the other extreme, great luxury and neuropathic heredity are evident, and the husband is the possessor of a dreamy imaginative personality, full of phantasies, and is sloppily sentimental. The larger the number of such adverse factors, the worse the prognosis.

But mental breakdown on the part of the wife is not the only shock that a man has to face, and functional impotence presents itself in various forms and degrees in different situations. To appreciate the significance of the several etiological factors which by their interaction lead to the symptom-complex 'functional impotence' and to outline the necessary treatment, a brief review of the psychosexual development of the individual, is necessary.

II. Psycho-Sexual Development.—The accompanying diagram from Howe's 'Motives and Mechanisms of the Mind' helps to

understand the continuity of psycho-sexual development in the male, but should not be taken literally as depicting what actually happens.



The emotional development of an individual consists in a series of transitions from the completely selfish, possessive and competitive behaviour of the child to the varying degrees of altruism and selflessness of the adult. Intermediate phases are usual but not dominant in a fully developed personality. Immature development, despite the passage of years, is attended with the persistence of such intermediate phases.

This development from ego-centricity to selflessness implies a great strain. Neuropathic heredity, poor physical health and an

over-imaginative personality, undue restrictions imposed by the environment (including the well-meant but ill considered suggestions from relatives such as an over-solicitous mother-in-law) add considerably to this strain. The result is sometimes a reversal to a purely phantasy existence, with various signs and symptoms, of which, 'functional impotence' is one.

The psycho-sexual development runs parallel with, and is, influenced by the development of set attitudes towards those who represent law and authority. While the dominant part in the development of affective attitudes is played by the mother and mother substitutes, the dominant part in the other case is played by the father and father substitutes, such as the teacher, the priest and the boss.

A normal development implies:—

- (1) The complete submersion of the sexual component in falling in love towards the mother and mother substitutes, while the feeling must be kept dominant with regard to the mate.
- (2) The feeling which the individual should develop towards law and authority should be free from feelings of guilt, fear, and inferiority.

Fixations occur frequently, which serve as escapes. The simplest escape is unconscious idealisation of the woman, the sexual component being entirely eliminated, as being the primary source of both guilt and fear. This idealisation of the mother figure as virginal, pure, perfect, and with the deepest unconscious emotional appeal, is common to all religions. The mother concept of the Diety amongst the Hindus is too well known to need comment.

There are certain aspects of clinical psycho-pathology which suggest that the sub-conscious motives of a whole group which find expression in the above conceptions underlying various forms of religious belief, also function in individuals. They give rise to several symptom complexes of which functional impotence is one. It is interesting to note that many people who are helplessly impotent with their wives are exceedingly potent where prostitutes or maid servants are concerned. This seems to be due to a sort of disassociation which keeps exempt for sexual purposes the idealised mother figure which includes the wife, but excludes, on the other hand, a woman of lower class and of a vulgar type.

Another explanation could be found for the development of such an attitude. By its means, responsibility is evaded, and satisfaction found where most can be obtained and least given. Many patients suffering from functional impotence speak of women in a high platonic fashion with false intellectualization. The explanation for this is obvious.

The age groups are interesting from the point of view of the incidence of functional impotence.

The early twenties are very erratic. It is the period at which there is a normal increase of sexual feeling and therefore a normal increase in guilt feelings. It is the time of vivid imagination, and of great conquests. It is also a time when home ties have to be broken up and responsibilities assumed. Because of these emotional conflicts instability is the rule, with an intense manifestation of either guilt or callousness.

In the thirties, functional impotence is exceedingly common. Many of my friends have assured me that they have experienced it, some time or other, and that the disability had actually scared them. It is accounted for as being due to an overwhelming sense of responsibility which is entirely sub-conscious. Domestic and occupational troubles are responsible in some, official humiliation in others, and in others still, it is due either to over-solicitude for their wives, or an unconscious desire to have no more children. It must be stressed that in the majority of people the motive is unconscious.

Resentment towards a nagging wife, economic insecurity, a large number of children, over-solicitude for the family, unexplained and unexplainable women, are, the obvious explanation in some cases, but there are many, however, in whom the obvious explanation is by no means the correct explanation.

In later periods, associated with involuntary and degenerative processes, and often due to the secondary consequence of such processes, a morbid ungrounded fear of premature impotence seizes many people. As a result they indulge in various excesses, and get into the hands of quacks with dangerous results.

Summarising the psychological factors responsible for functional impotence, in the earlier age periods, they are either due to inexperience or over-idealisation, in the middle periods, to over-responsibility, and in the later periods, due to overwhelming fear, other factors being equal.

III. **The Term 'Functional'.**—The sense in which the word 'functional' has been used needs some explanatory comment. Generally speaking, any abnormality is the resultant of interaction of factors belonging to the following four groups:—

- (1) Factors dependent on the innate constitution of the individual. (Heredity).
- (2) Factors dependent on sex, ages, and epochs of life.
- (3) Factors dependent on exceptional emotional experiences, recent or remote. (Mental Shocks).
- (4) Gross physical influences. (Deformities, injuries, inflammations, degenerations, new growths).

As long as the etiological factors of a disorder fall into any or all of the first three groups, it is termed functional. It is in this sense that the term 'functional' has been used in this article with reference to impotence and has to be so understood. By this definition, in

addition to purely psychological factors, factors dependent on hereditary or innate constitutional characteristics, and those dependent on various epochs of life have to be taken into consideration. It must also be noted that in any disorder lasting for some time, three groups of symptoms acquire prominence, namely, symptoms due to reduction of function, symptoms due to release of function, and reactive symptoms which are compensatory in nature. Impotence, usually a reduction symptom, might also be on occasions a reactive symptom.

To appreciate the significance of the several etiological factors apart from the purely psychological, consideration of the relevant points in applied physiology is necessary :—

- (1) The psycho-somatic unity of the organism. Thus emotional states may produce visceral effects, and a functional nervous disorder may lead to physical changes.
- (2) The sympathetic nervous system is designed to work as a whole, but, under abnormal circumstances its functions might be dissociated, and there may be perseveration of its action until permanent structural changes result.
- (3) The activity and output of endocrines is determined by heredity, vascular adequacy, infection, diet, the vitamins contained in them, and interrelated chemical substances.
- (4) More important than all these, the output of one endocrine gland is influenced by the output of other endocrine glands.

I have emphasised this aspect primarily, because, in recent years, the glamour of the gonads has tended to ascribe impotence mainly to failure of these glands, and has given rise to the spectacular pseudo science of 'rejuvenation' via the route of the gonadal hormones or gonad implantations. This is absurd because the atrophy of no single endocrine or group of endocrines can, by itself, readily account for the aging process.

Hence, in our study of cases of functional impotence, while excluding cases of impotence due to definite illnesses, and lesions of the nervous system (TABES, G.P.I., neuritis) and of the genital organs, notice must be taken of certain physiological changes in the endocrines and hypoplasias of the tissues with age.

IV. Aging and Functional Impotence.—Two conflicting views are held today by students of aging in man. One considers aging as an involuntary process with the passage of time, and which is revealed in different organs as inevitable modifications of cells, tissues and fluids; the other view interprets the changes found in aged organs as due to infections, toxins, traumas nutritional disturbances or inadequacies, which have forced cells to respond with degenerative changes. It appears, however, that at least some of the changes serve to maintain proper functioning and hence are protective. The issue is to differentiate between the natural physiological changes and pathological changes due to adverse environmental conditions.

Aging cannot be ascribed to any single statement of functional change or failure. Despite the passage of years, many organs possess a capacity for renewal that enables them to function adequately, while others have a potential duration of life greater than that of the organism. The hereditary factor in aging is now considered to be less controlling than previously. The inability of functional efficiency of an organ may be considerably enhanced by more adequate nutrition.

Time is of the greatest significance in all studies of growth and aging. DR. CARREL and others have shown, however, that chronological age by itself does not constitute a homogeneous group, and individuals develop, grow and mature at different rates even at the same chronological age. The same chronological age may have a different significance for different individuals. MINOT suggested some years ago that aging is most rapid in early life. Individual differences arise not only from heredity but has large cultural, social, and psychological implications. Human relationships with feelings and emotions influence bodily and structural damage. Worry, anxiety and unhappiness aggravate the inadequacy of later years.

The findings of HAVELOCK ELLIS and others suggest that, during the fourth decade of life, and even in the middle thirties, there is sometimes sufficient recession of gonadal function to render the individual male liable to fear of impotence. This fear is said to be of less importance in women. A growing sense of inadequacy and consequent repression of inner strivings is also a factor which makes for impotency. Fear of their children's opinions and a tendency of the latter to take over the management of their parents' lives and property increase the importance of this factor. It is interesting to note that psychiatrists like HAMILTON have recorded their experiences that after fifty, the individual derives more satisfaction from auto-erotic, habits than normal hetero-sexual acts. The incidence of masturbation without orgasm is said to be maximum in the seventies. While the young men boast of satisfying sexual experiences, older men boast of the regularity of their bowel movements. The increased pre-occupation with anal functions may be regarded as a compensatory regression to the narrowing of the range and intensity of sexual desires. The old adage that after middle age one tends to dig his grave with his teeth reflecting the importance of oral pleasures is interesting as is also the garrulity of old age (regressive oral eroticism).

V. Treatment.—It is possible that I might be accused of irrelevance and wandering away from the subject in the above paragraphs. It is, however, only apparent. My concern has been with basic principles, and not with descriptions and classifications which are to be found in any text book. My intention has mainly been to place before general practitioners the view that the symptom complex 'impotence' is the resultant of interaction of several factors, and their complexity can be appreciated only if one is aware of them.

The treatment is the treatment of the individual, and is beset with many difficulties. It is not always possible to change the patient's environment, nor, can one think of providing him with a better home or with another wife. What is necessary is to help the patient make the best of what he has got. In intelligent individuals, and whenever possible with the co-operation of the patient's wife, the patient can be helped to have a better insight into his condition. The general lines of treatment which, however, have to be modified and altered to suit individual cases are outlined below.

- (1) The patient must be allowed to discuss his disabilities freely. Never make an appointment with him unless you are prepared to spare at least half an hour.
- (2) Examine the patient thoroughly. He will have usually gone the round of several doctors, and it is not possible to win his regard or confidence (the essential for any treatment) unless you make him feel that you know your job and can be expected to give him your best. Also, without a detailed physical examination, several important clues are likely to be missed.
- (3) Concentrate on the individual, and, not on his genitals—but do not forget his genitals.
- (4) Insist on continence for about two months. It will give the patient more confidence, and time for your treatment to have effect.
- (5) We have come to realise that emotional states may produce visceral effects, and a functional disorder leads to physical changes. Hence, in emphasising the importance of psychological factors, the physical should not be neglected. This includes, (1) Diets and drugs, (2) Physiotherapy and (3) Surgical measures.

The SURGICAL MEASURES consist of testicular grafting, vaso-ligature, and tightening up the ischio-cavernosus and bulbo-cavernosus muscles. With the availability of concentrated testicular extracts, several grafting operations have now become unnecessary.

The METHODS OF PHYSIOTHERAPY consist in the application of diathermy to the testicles, various baths preferably cold, and alternate cold and hot douches to the genitals. The cold and hot water applications have a good deal to recommend them. Suspension of the patient for a couple of minutes at a time by means of Sayre's apparatus, and passage of cold sounds into the urethra are also practised. Several instruments designed for alternate compression and distension of the genitals are on the market, and their value, if any, is more psychological than physical.

MEDICAL TREATMENTS.—1. *Dietetic Measures*:—Plenty of good food, milk and small quantities of spices do certainly act as aphrodisiacs. Drumsticks, a vegetable very popular in South India, is said to be gifted with such powers, as well as soups made of sparrow meat,

Intensive administration of vitamins A. B. (Nicotinic acid, Thiamin Chloride) and C, and regular eating of small quantities of sprouting pulses and grains, especially green gram are beneficial.

2. *Yohimbine*:—(2 tablets twice daily), small doses of Strychnine and Nuxvomica (twenty minims prior to intercourse), small doses of Ergot have all been prescribed, and are occasionally useful. Cantharides is a very powerful aphrodisiac but it leads to such exhaustion that it is dangerous in use.

Small doses of Opium, and Alcohol are found to reduce inhibition in nervous individuals, as also small doses of Bromides and Belladonna. External application of Cocaine ointment is a well known remedy.

I have also tried instilling once or twice a week, five to ten minims of a solution of (one in thousand) Silver Nitrate into the posterior urethra after previous anaesthetisation with Percaine, with fairly good results.

Endocrines.—Thyroid, in half grain doses, is very good and testicular extracts in young individuals are certainly to be advocated. Several preparations are on the market, to be used orally, or as injections and inunctions. I prefer injections of Testosterone Propionate. But unfortunately, elderly individuals, on account of a false sense of shame, prefer self administration of harmful glandular extract whose only claim for distinction is blatant advertisement. They forget that not merely their genitals but their whole selves participate in the sexual act, which is attended with such intense exhaustion, that they may die if there is coincident cardiovascular weakness. Administration of anterior pituitary extract has not lived up to its reputation and it seems to be useless.

STEKEL quotes the case of a man who could only get sexually excited by being led round by a dog collar and chain, and another who had first to crow like a cock. As has been aptly remarked the professional reputation of very few doctors could survive advocating such methods.

Prognosis.—In patients who were previously normal, and whose abnormality could be traced to definite removable causes, prognosis is extremely good, the chances of recovery being nearly eighty per cent. In the case of others who have never had successful sexual relations at any time, and in whom no organic lesions can be discovered, prognosis is either very good or very bad, the chances being only about thirty per cent. Intensive treatment for at least six months is necessary before a case could be given up as a failure.

Summary.—The basic factors underlying the development of the symptom complex 'Functional Impotence' are outlined in the above paragraphs, with a brief summary of the lines of treatment to be followed. The main emphasis in treatment is on psychological methods, such as free conversation, encouragement, reassurance, avoidance of purposeless arguments, the administration of concentrated vitamins, and such physical and medicinal treatment as might be necessary.

Spinal Anæsthesia—Its Complications*

BY

C. K. Kurup, L.M.P., L.C.P. & S.
Kumily—Travancore.

PART II.

FIRST part of this article on spinal anæsthesia was published in June 1936 issue of the Antiseptic. The complications of this form of anæsthesia were not properly dealt with in that article. So, it became desirable to deal with them separately. In this paper, the common complications that are likely to occur due to spinal anæsthesia, and their treatment are mainly discussed.

It is concluded in the first part, that when a proper drug is used by a correct technique, in selected patients, the spinal anæsthesia is as safe as any other form of anæsthesia. So, in fact, the complications of spinal anæsthesia are of very seldom occurrence when every care is taken in all the details of the spinal block. But, at the same time, it may be admitted that complications do occur, once in a while in very rare cases, even when all the necessary precautions are taken. Though such complications are unavoidable, the occurrence of many of the common complications can be reduced to the minimum.

Complications.—1. *Sudden fall of blood pressure and its sequelæ.*
—Generally, the complications of spinal anæsthesia, may be liable to occur, from the time of the injection of the anæsthetic drug into the thecal cavity, to many a month later. But the greatest possibility of a complication to occur is during the anæsthetic period. The gravest complication that is possible to develop during this period is the sudden fall of blood pressure causing cerebral anæmia, which leads to respiratory and cardiac failures.

The possibility of such a grave complication can be limited, by taking the necessary precautions early. Great care is to be taken in selecting a person for spinal. In general, well built and well nourished healthy middle aged persons take spinal well. As a rule, patients who are under severe shock, and whose blood-pressure is abnormally low, and whose myocardium is degenerated, are bad subjects for spinal. Patients whose systolic blood pressure is less than 70, should be avoided. In the case of patients under shock, if necessity demands, spinal can be given, if they show the required improvement, after treating the shock. Some of the patients, especially when they are under primary shock, improve in their condition of shock, by giving Morphia followed by hypodermic clysis or infusion of Saline with Glucose or by transfusion of whole blood. Spinal also should be avoided in patients who are having respiratory embarrassments, or who suffer from diseases of the central nervous system. Very weak, very old and very young persons also may be avoided, as they may not

tolerate spinal well. The presence of any septic process locally contraindicates its use, for then there is the danger of carrying the infection to the central nervous system.

The choice of the level for spinal puncture also is important in relation to the development of complications. In adults, the spinal cord terminates into a cone-shaped part called *conus medullaris* from where it extends as a fine filament. When the spinal column is flexed, the lower end of the cord rises slightly in the spinal canal. So, when the spinal puncture is made above the level of the third lumbar vertebra, there may be greater chance for causing some injury to the spinal cord. Thus, the higher the spinal puncture is made above this level, the greater is the possibility for developing complications. Paralysis of the diaphragm, the respiratory centre and of the lower limbs, are the important of such complications.

As far as possible, the spinal puncture should be done with a single stroke, and without causing the least pain to the patient. Repeated thrusts should be avoided. Such failed attempts will cause greater fear in the patient which may sometimes produce even shock. The possible danger of breaking the spinal needles in the intervertebral disc also is to be borne in mind. By anaesthetising the area and the line of puncture in the intervertebral disc, and by using a very fine spinal needle, lumbar puncture can be done without least hurting the patient.

During the whole of the anaesthetic period, the patient should be carefully watched for any sign of an untoward effect. The rate, volume, and tension of the pulse, and the rate and character of the respiration should be carefully noted from the beginning to the end of the operation. Similarly, the blood pressure also should be noted from time to time, by means of a sphygmomanometer. It is better to tie the rubber bag of the instrument to one hand of the patient, and keep it ready, so as to be able to read the pressure whenever it is required. This arrangement eliminates the delay caused in tying the instrument to the patient's hand when an emergency reading of the pressure is required. If any sign of a fall of blood pressure, or of circulatory failure is noted, according to the demand of the gravity of the situation, a judicious treatment is given.

Immediately, the head of the patient is further lowered, if he is already in Trendelenburg's position. This is followed by an intramuscular injection of 1 cc. of a 1 in 1000 solution of Adrenalin Hydrochloride (of Parke Davis & Co.). Meanwhile, 25 to 50 cc. of a 10% Glucose solution is given intravenously. This may be followed by an intravenous infusion of 50 to 100 cc. Ringers solution or 200 to 300 cc. of Normal Saline. If this treatment is not sufficient to improve the condition of the patient, an injection of a cardiac stimulant such as Veritol, Coramine, Ephedrine, Cardiazol or, Caffein, Sodium Salicylus may be given, and repeated if necessary. This is followed by an hypodermic clysis of 1000 to 2000 c.c. of Normal Saline which, when absorbed, will improve the condition of the pulse and the general circulation. In

* Specially contributed to 'The Antiseptic'.

addition, the patient may also be given half to one ounce of brandy diluted with water, by mouth. A stimulant mixture consisting of Spt. Ammonia Aromaticus, 20 to 30 minims, Spt. Etheris 10 to 15 minims, Spt. Chloroform 15 minims in one ounce of water is given every 3 hours; for, 2 or 3 doses help greatly in improving the general condition of the patient. After the operation, it is better to keep this patient in Trendelenburgs position at least for three hours. If a patient shows no improvement in the fall of blood pressure and signs of circulatory failure, even after giving the necessary treatment, the operation should at once be stopped to avoid any further shock.

Occasionally, some patients show a tendency for nausea and vomiting soon after the anaesthesia is given. This can be prevented by further lowering the patient's head and drawing his attention away from his operation and concentrating his mind on some other object.

2. *Paralysis of the phrenic nerve*:—This is a very rare complication of spinal anaesthesia. This is met with in spinal blocks of high level only. Such a complication can be avoided by using spinal blocks confined to the lower lumbar region.

3. *Headache*:—This is the most common complication during the post-anaesthetic period. Usually, it is noted to occur in 3 to 5 per cent. of spinal cases. It may vary in severity, from the very mild to the severe form of headache. It may either remain for few hours and automatically disappear, or persist for days together. Though the exact causes of this condition are not known, it is usually attributed to the following causes.

(i) *LEAKAGE OF THE CEREBROSPINAL FLUID*.—A small hole made by a fine spinal needle in the dura mater, may close automatically. But a large hole made by a thick spinal needle may not close automatically, and allow the cerebrospinal fluid to leak through it. Thus, the larger the size of the puncture hole in the dura mater, the greater the chance for the leakage of the spinal fluid. This leakage of the spinal fluid is said to be one of the causes of post anaesthetic headache.

The leakage of the spinal fluid can be avoided by making only very fine hole in the dura mater, just enough to tap the fluid, by using a very fine needle. The needle should be smooth, flexible, and with a bore not more than No. 17 standard wire gauge. Its point must be sharp, and the cutting edges also should be short. It must possess a good and easily removable stylet, which accurately fits the needle. When making the spinal puncture, the needle should be inserted into the thecal cavity in such a way that the long up and down fibres of the ligamentum flavum and of the dura mater, are more easily pierced and not torn and thus avoid any laceration of the dura. If the dura tears and lacerates, the leakage of the spinal fluid will happen.

(ii) *ALTERATION OF PRESSURE OF THE CEREBROSPINAL FLUID*.—A sudden change of the pressure of the cerebrospinal fluid, may also play a part in causing the post-anaesthetic headache. Generally, the anaesthetic drug is dissolved, either in the spinal fluid itself, or in

Saline or water. For instance, Neocaine in the spinal fluid, Percaine in Saline, and Novocaine in water are dissolved. Except in the case when the drug is dissolved in the spinal fluid, it is introduced into the thecal cavity through the medium of a foreign fluid only. Usually, in order to introduce this, a certain quantity of the spinal fluid has to be drained before giving the injection. In practice, the quantity of the fluid introduced may not be equal to the quantity withdrawn. It may be either less or more in volume. Naturally, this imbalance of the fluid in the spinal canal alters the existing pressure of the cerebrospinal fluid, more or less suddenly. This sudden change of pressure in the cerebrospinal fluid causes the headache.

The use of a fluid other than spinal fluid as the medium for introducing the anaesthetic drug should be avoided as far as possible. Whenever such a foreign fluid has to be used, the purity and sterility of the solution should be of the highest degree possible. In addition, when it is introduced into the thecal cavity, great care should be taken to maintain the existing pressure of the spinal fluid. Anaesthetic drug such as Neocaine crystals when dissolved in the spinal fluid itself, and injected, more or less maintains the existing pressure of the spinal fluid.

(iii) *TOXICITY OF THE DRUG*.—Certain drugs show a tendency to produce headache due to their toxicity. The incidence of headache, when Percaine is used, is said to be more than when other drugs are used. The percentage of cases who complained of headache after Neocaine was less than other drugs.

(iv) *FAULTY SOLUTION*.—Fault in the preparation of the solution or the presence of impurities and foreign bodies in the anaesthetic solution are also prone to cause headache. Concentrated solution when used also is likely to cause headache.

Great care should be taken for the preparation of a proper solution. Similarly, when the solution is injected, to avoid the concentration of the drug at the point of injection, it must be introduced very slowly only and often diluting the solution with the spinal fluid, by frequently aspirating it into the syringe, and returning it into the thecal cavity.

(v) *MENINGITIS*.—Meningitis, developing from whatever cause, may produce headache, mainly due to the increase of pressure of the spinal fluid. Both aseptic as well as septic meningitis are also seen after spinal anaesthesia. In the case of aseptic meningitis, when there is headache, usually it may be relieved by a second puncture. If the headache persists and the intracranial pressure is increased, repeated lumbar punctures should be done so as to relieve the increase of pressure. In addition, symptomatic treatment may also be given with advantage.

In the case of meningitis due to infection, the condition may be improved by repeated spinal punctures, each time withdrawing small quantities of spinal fluid according to the increase of pressure

of the spinal fluid. The pressure of the spinal fluid may be read by a mercury manometer.

Infection of the meninges should be avoided as far as possible by taking all the necessary precautions, to procure asepsis of the lumbar puncture and the injection of the anæsthetic drug. The presence of bacteria and their toxins, and other impurities should be avoided in the water used for the preparation of the anæsthetic solution. Double distilled and recently sterilised water only should be used for making the solution.

Treatment of Headache.—When the headache is only a mild one, it may be relieved by some analgesic remedies such as a powder or a tablet consisting of, Aspirin grs. 5 to 7, Phenacetin grs. 2 to 5, and Caffein Citras grs. 2 to 4, every 4 hours, for 3 to 6 doses. In the place of this, as an analgesic, proprietary preparation such as Veganin, Veramon, Ortal, Novalgin and Sodium Amytal, may be preferably given. In addition to this, the patient may be asked to lie down flat on the bed with his head kept low, by raising the foot of the bed on blocks. He is encouraged to take plenty of fluid. In more severe and protracted cases, besides the above mentioned treatment, the patient, may be given an injection of Pituitrin 1 c.c. twice a day, and Calcium Lactate 5 to 10 grs. thrice a day by mouth. Pituitrin, if necessary, may be continued, 2 to 3 days only. Ephedrine $\frac{1}{2}$ to $\frac{3}{4}$ grain is also useful. An intravenous injection of 70 c.c. of a 15 per cent Sodium Chloride solution is an helpful adjuvant. An enema of 3 to 6 ounces of 50% solution of Mag. Sulphas, is sometimes found serviceable. Whenever the pressure of the spinal fluid is increased, causing headache, repeated lumbar punctures as mentioned before may be done. During each time of the puncture, small quantities of spinal fluid is withdrawn according to the increase of intra-cranial pressure.

Nervous Complications.—Various kinds of nervous complications were observed resulting from spinal anæsthesia. But they are very rare events. So they may be mentioned as a group. There is no definite time for their occurrence. Some may appear soon after the operation while others develop after a long interval of many months. They range in wider limits, from mild troubles of micturition to grave complications such as paraplegia and even death. These may be either due to the injury of the spinal cord, or of the toxicity of the anæsthetic drug or of infection.

The nature and severity of any of these complications depend upon the level of the injury of the spinal cord or of the degree of the toxicity of the drug and of infection. Some of these may be mild and transient, while others are grave and permanent. There may develop varying degrees of pain over the back, especially over the point of puncture. Sometimes the pain may be turned to be severe, so as to disable the person from walking or sitting up. On X-ray examination, at the site of puncture of the dura mater, which may constrict the spinal cord, its roots and cauda equina.

Meningitis is noted to occur after spinal. Two types were served, one is a benign type with lymphocytosis, and high fever, and another is with polynuclear leucocytosis. The latter form may be due to infection. The patient will be having the associated symptoms of the inflammation of meninges.

In some patients, mild symptoms like difficulty in micturition and defæcation, to retention of urine as well as incontinence of fæces are seen. Sixth nerve palsy is the commonest nervous complication noticed by some. Loss of sensation over the third, fourth, and fifth sacral nerves and loss of sexual functions are also, not rare. Not drop with loss of knee and ankle jerks, and impaired sensation over the outside of the leg are also seen.

Softening of the spinal cord above the point of puncture was also served. In this the grey mater was completely necrosed while the white mater affected in part only. Microscopically, thrombosis and necrosis of the pial arteries were found. Lesions of cauda equina and nucleus medullaris, with symptoms of urinary retention and sexual algesia also occurred. Disseminated sclerosis with muscular atrophy also resulted from spinal.

Radiculo-myelitis of the cord at different levels, and myelitis, transverse, diffuse or ascending, also may result after spinal. Ascending myelitis progressing to encephalo-myelitis is also on record. Transverse myelitis with extensive destruction of myeline sheaths marked at the peripheral and root zones was also noted. A case of myelomalacia in which pain appeared over the left knee with difficulty in walking and numbness over the left leg spreading up was found, which finally came fatal. Sacral Radiculitis with severe spasm of pain and sacral perthesia also occurred.

In one case severe paraplegia appeared on the third day of the operation. Another case in which patient developed paralysis and paresis after spinal, recovered completely. Focal cerebral lesions also have been recorded.

Mental changes were also noted by some resulting from spinal. Hallucinations, dizziness, photophobia were the complaints. Tetanic contractions had also developed. Many of the mental changes appeared after varying interval of time.

No effort should be spared to prevent the development of any of the foregoing nervous complications. Great skill and care is essential in avoiding any injury either to the spinal cord or roots or to its membranes. The drugs used are only of the lowest toxicity available. Concentrating the drug at the point of injection should be avoided. Every care is taken to avoid any possibility of carrying infection to the spinal cord or to the meninges. Asepsis to the maximum extent possible should be observed from the beginning to the end of the technique of spinal anæsthesia.

When any of the nervous complications is developed, the treatment of the condition depends upon the nature and extent of the lesion. Usual line of treatment for nervous disorders may be given in such cases also, according to requirements of the conditions.

Evolution of Cataract Surgery from the Pre-Historic Age up to the Present Time*

BY

Nabin Kishore Bidyadhar, M.B., B.S., (PAT.),
Susruta Clinic, Sonapur Raj, Orissa.

(Contd. from p. 346 of Apr. '40 issue of 'The Antiseptic').

VAGBHATT II divides cataract into the following varieties:—

- | | |
|---|--|
| 1. Cataract with irregular opacity. | } These varieties are not fit for operation. |
| 2. " of uneven consistence. | |
| 3. " with white curd-like consistence. | |
| 4. " with their nucleus. | |
| 5. Greyish white cataract. | |
| 6. Bluish-looking cataract. | |
| 7. Reddish-looking cataract. | |
| 8. Diabetic cataract. | |
| 9. Multi-coloured cataract. | |
| 10. Hard cataract. | |
| 11. Cataract of the colour of bell-metal. | |

VAGBHAT wisely enjoins that a cataract which is fully mature, and which is without any complication, is fit for operation. The contra-indications for the couching operation according to VAGBHAT are the following:—

Those who are unfit for venesection; those suffering from inflammatory eye diseases; those who suffer from rhinitis, bronchitis, pharyngitis; those who suffer from nervous dyspepsia and nervous debility; those who are susceptible to vomiting diathesis and people suffering from migraine.

The operation of lens couching is to be done in an equable season, i.e., when it is neither very hot nor very cold.

Preparation of the Patient and the Eye.—Prior to the operation, the patient's body should be duly cleaned by purgatives and diet regulation and he should be freed from any constitutional disease, especially inflammatory condition of the nose, eyelids and disease of the pharynx etc.

The patient's eye should be duly washed before operation and the surgeon's hands should also be duly cleansed.

The operation is to be done before noon, preferably in the morning after sunrise.

The patient is to be seated in a wooden operation table and the

* Specially contributed to 'The Antiseptic'.

surgeon should be seated on an operation stool as high as the operator's knee.

The eye should be warmed by the breath of the mouth and gently massaged with the fingers of the surgeon. Then the patient's head should be kept steady. The patient would be asked to look steadily at his nose and should not move the eye in any way. His eye should be kept sufficiently open and the eyelids retracted by the fingers of an assistant.

Then the surgeon, holding the Jabamukhi Salaka (the curved barley-mouthed needle) steadily with the thumb and fore-finger and middle finger of the right hand in case of the left eye and *vice versa*, should puncture the sclera on the temporal side just outside the limbus in the horizontal diameter of the eye, and then carefully grade the needle through the natural aperture of the eye on to the surface of the cataractous lens. When the puncture is correctly done, there is exudation of water (aqueous humour) and a sound and there will be no pain whatsoever. The patient should be given due consolation by the surgeon. Breast milk should be sprinkled over into the operated eye. Then, with the tip of the salaka, the surface of the cataract will be gently scratched and scribbled so as not to cause any pain. The patient will, in the meantime, be asked to sniff slowly so as to draw up any phlegm from the eye into the naso-pharynx. Light compress will be applied to the supra-orbital region of the eye. By gentle scribbling manoeuvre of the salaka, the lens will be dislocated and it will then be pushed inside towards the nose. The proper dislodgement of the lens will be indicated by clearance of vision. The needle will now be carefully withdrawn. Then a lint, soaked in lukewarmed clarified butter, will be put over the eye, which will be properly bandaged.

After Treatment.—The patient will be laid undisturbed and quiet in a clean and well-ventilated and duly shaded room. If the right eye is operated, he should lean on the left side, and *vice versa*; if both eyes are operated, he should lie flat on the bed.

The patient's head and feet will be shampooed lightly with medicated oils. His diet should consist of light liquid articles of food and he should take enough of milk during the post-operative period. On the operation day, he should be preferably given a fasting.

For one week after operation, he shall not sneeze, cough, vomit, expectorate or regurgitate food, nor should he take solid food. He should not gaze downwards, should not bathe nor should he brush his teeth.

During the post-operative stage, he should be given fastings according to his capacity. Till the inflammation and pain of the eye are over, warmed clarified butter should be poured into the eye. A plaster composed of fried barley powder with clarified butter, Trikatu (Piper longum, Dry ginger, Black Pepper) and Amalaki (Embalica Officinalis) should be applied over the eye. Every third day the bandage is to be opened, the eye is to be washed with decoction of

antiseptic and antiphillogistic drugs and compressed and bandaged with a fresh bandage. After 7 days the bandages are to be removed once for all.

Till the vision and accommodation of the eye is restored to its normal condition, the patient should remain under control. He should not look at glaring lights, nor should he gaze at small and resplendent articles.

VAGBHAT then goes on to describe the complications arising from injudicious puncture and the treatment thereof.

PAULUS AEGIMETA, the famous Greek surgeon of the 7th century, practised lens couching operation in his days.

We have so far followed the evolution of cataract surgery at the hands of the ophthalmic surgeons of Asia and Europe. We shall now see how a further acceleration to the evolution was given by the translation of SUSRUTA's and VAGBHAT's surgical works into Arabic, Latin and German.

"The work of SUSRUTA was translated into Arabic at the end of the 8th century A.D. It has been translated into Latin by HESSLER and German by VULLERS. The Latin translations formed the basis of European medicine which remained indebted to the Eastern science of Medicine down to the 17th century" (THAKORE SAHEB of Gondal).

"The Arabic version of SUSRUTA is called 'Kitab Shawshoon-al-Hindi' and also mentioned as 'Kitabi-Susrud' or Book of SUSRUTA by IBN ABILSAIBIAL. RHAZES often quotes SARAD as an authority on surgery."

That great patron of learning, the "Caliph, Harun-al-Rashid (786-809 A.D.) had two Indians MANKA and SALEH, as physicians at his Court. MANKA translated the classical work on Medicine 'Susruta'—(cf. *Steinschneider, Wissenschaftliche Blatter*, Vol. I p. 79)".

"We know also that VAGBHAT's Astanga-Hridaya-Samhita was translated into Arabic by the order of Caliphs in the 8th century A.D." (Zeit. dent. morg. Ges. 34, p. 465) the Arabic version goes by the name of *Sindhisara*.

The translations of SUSRUTA's works at the instance of the learned Caliphs of Bagdad at the close of the 8th century A.D., greatly influenced and orientated the surgical knowledge of the Arabic surgeons, who extensively introduced SUSRUTA's method of cataract operation in their ophthalmic practice. From Arabia, his teachings extended to Egypt, Alexandria, Greece and Rome, and through the medium of Latin translations, it extended to the whole of Europe in those days.

The Arabian surgeons of those days adopted SUSRUTA's method with minor modifications. They made a limbal incision with a knife and dislocated the lens with a blunt needle, in case of hard cataracts. In case of soft cataracts, they sucked out the soft lens matter through a tube introduced through the corneal incision.

RHAZES, an eminent Arabic surgeon, who was born in 850 A.D. and

flourished up to 932 A.D., largely followed SUSRUTA's method of cataract operations. He quotes very often SUSRUTA as an authority on surgery.

AVICENNA, the writer of canon of Medicine, flourished about 980 to 1037 A.D. He stands out as a monumental figure from the tenth to the fifteenth century. He was a great eye surgeon. He has left his notes on couching operation from which we learn that the Arabian surgeons of the day modified SUSRUTA's method by using two instruments, namely a two-edged lancet for corneal incision and a blunt needle for depressing the cataractous lens.

BENEVENUTUS HIEROSOLIMITANS who lived in Jerusalem, sometime in the 11th or 12th century A.D., was a most experienced and learned ophthalmic surgeon of the day. He practised couching operation extensively. He had his own modification of the method, the main principles of which are noted below:—The patient is to be purged before operations by means of his own Jerusalem pills. The patient is to be seated astraddle on a bench. Post operative treatment consists in keeping the patient on bed in the dark for 8 days. The eye is to be dressed with white of egg 4 times in the night and day. He recommends the use of a gold or a silver needle in the operation. From CASEY WOOD, we learn that the writings of the Jerusalem surgeon formed the most popular ophthalmic manual of the day.

We have thus far followed how, up to the end of the 11th century, SUSRUTA's method of cataract surgery flourished with modifications at the hands of the learned ophthalmic surgeons of Asia and Europe. The period following between the 12th century up to the latter part of the 17th century witnessed a woeful decline of cataract surgery as, unfortunately, during this Dark Age, there were no learned eye surgeons to teach and practise cataract surgery scientifically. Consequently, the evolution of cataract surgery had to be at a standstill. As bad luck would have it, the cataract surgery was captured by the quacks who knew neither anatomy nor physiology nor surgical principles. The science, therefore, hopelessly degenerated in their hands. These quacks roamed over Asia and Europe, practising the lens couching operation. They are known as charlatans in Europe and as *Mals* and *Vaidyas*, and *Rowals* in India. These quack Rowals are still plying their trade of cataract couching in the remote villages of India and nobody knows how many eyes are being spoiled through their jugglery. It is high time that proper legislation should be invoked to put a stop to their mal-activities.

However, towards the close of the 17th century, the world saw the renaissance of cataract surgery. P. M. BRISSEAU of Tournay revived the lens couching method by inventing his own needle.

Ever since the pre-historic age up to the early part of the 18th century, SUSRUTA's depression method of lens couching by the anterior route was being extensively followed, with or without modifications, all over Asia and Europe; when in 1745, DAVIEL gave a new orientation

to the evolution of cataract surgery, by devising the open method of expression of cataractous lens and performing his first extraction of the cataract. The evolution of cataract surgery entered into a newer and more advantageous phase, when lens couching method of cataract operation gave place to extra-capsular method of cataract extraction.

DAVIEL generally expressed the cataract through an opening incised in the lower part of the cornea. He usually performed the simple capsulotomy operation. He performed iridectomy only in those special cases wherein it was found necessary. The earlier eye surgeons used to make the incision in the lower part of the cornea, but as the disadvantages of the lower corneal incisions were found out, they advantageously adopted the upper corneal incision. The present-day surgeons here universally adopted the upper limbal incision as it has been found out to be the best and the safest procedure.

Ever since the inauguration of DAVIEL's method, the simple cataract extraction (*i.e.* without iridectomy) has been advocated and practised from time to time. The method is also followed in the present day.

The almost simultaneous discovery of antiseptics (1860-1875) and anæsthetics (1880) revolutionised the scientific evolution of surgery and their introduction into the field of ophthalmic surgery has facilitated the development of open methods of eye operations.

The providential invention of extra-capsular operation facilitated by the discovery of antiseptics and anæsthetics, certainly heralded the dawning of the evolution of modern cataract surgery.

Cocaine was discovered by ALBERT NEOMANN in 1855. RICHARDSON used it in producing local anæsthesia in 1866, but the credit goes to KOLLER, who in 1883, used Cocaine in ophthalmology. Novocaine was discovered by ALFRED EINHORN of Ohio in 1904.

To combat the disadvantages and post-operative complications in the shape of iris prolapse etc., following simple extracapsular cataract extractions, the eye surgeons have devised and adopted extraction with iridectomy. The combined extra-capsular extraction has undoubtedly become the safest operation and has become the method of choice amongst the majority of operators—ELLIOT, HEPBURN, BIRCH-HIRSCHFIELD, FUCHS, DUKE-ELDER as well as many others. ELLIOT, with his vast experience of cataract surgery, became a great sponsor of this method.

We shall now briefly describe the technique of the combined method of extra-capsular cataract extraction as it has evolved from time to time up to the present day.

Preparation of the Patient.—SUSRUTA was the first surgeon to enjoin upon the patient being bodily cleansed and freed from the deranged bodily humours before being brought to the operation table, that is to say, SUSRUTA strictly held that the patient should be freed from any constitutional disease, as also bronchitis, pharyngitis, rhinitis, etc., before being subjected to operation. VAGBHAT, CELSUS,

BENEVENUTUS, PAUL, ALBUCASIS, RHAZES, GALEN, AVICENNA and others have equally followed the Susrutian method of preparing the patient. There were no antiseptics and anæsthetics in those days. It was in the middle of the 19th century, after the discovery of antiseptics (1860-1875) and after the discovery and introduction of the anæsthetics (1855-1883) into ophthalmic surgery, that the surgeons began to feel that the preparation of the patient and that of the eye aseptically and anæsthetically is of vital importance to the success of the operation and made the best use, therefore, of the services of antiseptics and anæsthetics, the introduction of which revolutionised the scientific development of surgery and saved humanity from the septic jaws of death. Preparation of the patient includes a thorough investigation of the patients' oral cavity, teeth, tonsils, ear, nose and throat, accessory sinuses; any other likely focus of sepsis should be eliminated. SUSRUTA's advice of cleansing the patient's body should be followed, and his advice to cure any disease of the teeth, nose, pharynx etc., should be scrupulously followed to rid the body of toxins. The patient should be examined for the presence of any constitutional disease and a routine W. R. done to determine whether it is positive or negative, the presence of which should receive adequate attention. The attending surgeon would see if such diseases like gall bladder sepsis, blood-pressure, bronchitis, pharyngitis, tonsillitis exist in the patient, for which he should take proper precaution and give adequate treatment. In case of a patient suffering from diabetes, the surgeon should see that the blood-sugar is brought to normal by Insulin and diet therapy, and if practicable maintained normal by strict control of diet. If the patient suffers from chronic pharyngitis attended with dry cough, he or she should be medically treated and should be given a course of auto-vaccine, or in the case of doubt of a septic focus lurking somewhere either in the oral cavity or nasal sinuses, or the naso-lachrymal duct or the ear, a course of prophylactic polyvalent combined autovaccine might profitably be administered to the patient for increasing the power of immunity. The condition of the palpebral conjunctiva, and the lachrymal sac must be determined to see if there is any inflammation, for which proper treatment must be given.

Preparation of the Eye.—The object underlying the preparation of the eye is to make the conjunctival sac with its appendages as aseptic as possible by removing the maximum number of organisms. A preliminary bacteriological examination of the conjunctival sac, with that of the lachrymal duct is absolutely indicated to know whether the conjunctival sac etc. is septic or aseptic. The usual procedure is to get a bacteriological examination done at least 48 hours before the time of the operation, so that there would be enough time for the growth of Pneumococci in the culture media. If the report of such examination reveals the presence of such organisms as Streptococci, Pneumococci, the operation must be postponed, till after further antiseptic treatment, it is found to be normal on a subsequent examination. "There are some surgeons who do not object to the presence

of *Micrococcus catarrhalis* and *Pneumobacillus*, but these are best regarded as dangerous and a profuse growth of *Staphylococcus albus* is not entirely devoid of risk." (DUKE ELDER).

The lachrymal sac and the naso-lachrymal duct must be thoroughly examined to see if there is any sepsis, and if such sepsis be present, it must be cured antiseptically before operation. Any moderate secretion from the eyelids must be treated with 1% Mercurochrome solution or with 2% Silver Nitrate solution.

A brief review of the different methods of washing the conjunctival sac with antiseptic lotions is given below:—The usual procedure is to wash the eye with 1 in 5000 solution of Bichloride of Hg. for from 1 to 2 minutes. HERBERT advocates irrigating the eye with 1 in 3000 Bichloride solution for from 1½ to 2 minutes; SMITH irrigates with 1 in 2000 solution of Bichloride, while CHATTERJE (N) advises washing with Hydrarg. Bin. Iodide solution of 1 in 5000. COLLINS is in favour of using Zinc Sulphate solution as a collyrium for eight days prior to operation. ELSCHNIG irrigates both the conjunctival sac and the lachrymal sac with a solution of Oxycyanide of Hg. Finally, irrigating or flooding the eye with sterile Normal Saline solution is the usual routine method in universal use.

For the purpose of counteracting sepsis and creating immunity in the conjunctival sac, the eye surgeons have devised various interesting and instructive methods from time to time. Thus, we have the use made of the injection of 20c.c. Treuuch's anti-pneumococcal serum before each operation as advocated by MORAX; 1% Optochin ointment has been prescribed by MOREAU to be applied to the lids for the destruction of Pneumococci; autogenous vaccines are administered (Castresana) to inhibit the bacterial growth; while VOGT, depending upon the bactericidal property of blood, washes the conjunctival sac with fresh blood obtained by deep external canthotomy.

In resistant cases, however, where all methods of antiseptic treatment have failed to produce the desired effect, the technique of local radiation of the conjunctiva by ultra-violet light suggested by LAW (1934), provides a way out of the difficulty (*Law, Proc. Roy. Soc. Med.* 1934, XXVIII. 192). According to LAW, ultra-violet irradiation is successful in nearly every case in rendering the eye bacteriologically safe for operation, even when the other methods fail. The routine method is to give six doses of 5 minutes each at two-day intervals, irradiation being carried out at a distance of about 12", number of doses may be increased when necessary.

Of course, it must be emphatically said that too much use of antiseptics in the eye does more harm than good, as thereby, the normal resisting capacity of the organ becomes impaired to a great extent owing to the conjunctival tissue being damaged. The writer agrees with DR. CLAPP when he says that "since the ideal of complete asepsis is practically never attained, the most one can hope for is the removal of the greater number of the organisms". Hence, violent methods of using too much antiseptics should be scrupulously avoided.

The immediate local preparation of the eye is done in the early hours of the operation day. Moderate dilatation of the pupil is done by pouring one or two drops of 1% Atropine solution into the conjunctival sac and if further dilatation is desired, 1 drop of 1% Homatropine is instilled into the eye one hour before operation.

Local Anæsthetisation and Immobilisation of the Eye.—Ever since the introduction of Cocaine into ophthalmic surgery by KOLLER in 1883-1884, it is being extensively used as an anæsthetic agent in cataract surgery. Cocaine Hydrochloride is the salt most frequently used; Cocaine Biborate is also recommended for its greater stability. It is dropped in 4% strength every 5 minutes until four applications are made. If anæsthesia is not complete after this, a single drop of 10% solution will suffice to produce insensitiveness. We owe it to THEOBOLD who, for the first time in 1907, suggested the indications for the employment of Adrenalin Chloride (2 to 5 drops of 1 in 1000 solution) in alternation with Cocaine in eye operation. Adrenalin not only increases the anæsthetic effect of Cocaine, but it has the additional advantage of checking bleeding (KILLICK).

In the Susrutian age, antiseptics and anæsthetics had not been discovered. SUSRUTA probably managed this with the decoction of certain antiseptic drugs which he used in washing the eye. To arrest bleeding, SUSRUTA advised sprinkling of mother's milk into the conjunctival sac. Thus, it is evident that SUSRUTA was the first to know the hæmostatic property of mother's milk and that in the pre-epinephrin days mother's milk took the place of modern Adrenalin.

Besides the conjunctival instillation, some surgeons inject two or three minims of 2% Cocaine solution at the upper limbus. This helps to anæsthetise and elevate the conjunctiva so as to enable flaps to be fashioned easily and also to produce anaesthesia of the iris. Besides Cocaine, many synthetic drugs, viz. Novocaine, Holocaine, Butyn, and Pantocaine are being used in cataract surgery.

Novocaine is used in 0.5 to 2% strength in conjunction with sterile Adrenalin solution (2 drops of 1 in 1000 solution). This is used mostly for blocking the facial branches of the lids to produce immobilisation thereof.

Holocaine—used in 2% solution instilled every 2 minutes until 5 instillations are made. The anaesthesia lasts for from 10 to 20, minutes. KNAPP and TOROK use this as anaesthetic agent.

Butyn—used in 2% solution at ten minutes' intervals for half an hour along with instillation of 2 drops of Adrenalin 1 in 1000 just prior to operation (CLAPP). DE SCHWEINITZ advocates 4 instillations of 2% solution at 3 minutes' intervals.

Pantocaine—introduced into cataract surgery by WILMER and PATON in 1932. 2 drops. of 0.5% solution instilled into conjunctival sac before the patient is brought to the operation table and then the instillation of 4 drops one after another. The action of Pantocaine is

quick and sure, with little toxicity. Hence, the drug is largely recommended for use with perfect safety in modern cataract surgery.

From time to time, there have evolved different methods of inducing paralysis of the orbicularis muscle by anaesthetising the branches of the facial nerve, the involuntary contraction of which, during operation, produces squeezing with its attendant complications of prolapse of iris and vitreous. The principle underlying the induction of paralysis of the orbicularis is to block the branches of the facial nerve by deep infiltration with solution of Novocaine cum Adrenalin.

Von Lint's Method.—VON LINT devised in 1914, his method of paralyzing the orbicularis by deep infiltration with 2 c.c. of 2% solution of Novocaine combined with 2 drops of Adrenalin solution 1 in 1000. The injection blocks the branches of the facial nerve in about 10 to 15 minutes.

Wright's Method (1921–1923) consists in blocking the branches of the facial nerve by injecting the lid with 2% Novocaine, and also blocking the main trunk of the facial nerve by injecting into the molar region towards the stylomastoid foramen.

Elschnig's Method—(1932)—Retrobulbar injection of 1 c.c. of 2% Novocaine solution into the conjunctiva.

Fixation of the Eye is done by grasping the conjunctiva, with some conjunctival tissue with a fixation forceps, near the limbus on the nasal side below. Some surgeons—AXENFELD, KALT, ELSCHNIG effect fixation of the eye by passing a suture through the superior rectus at its insertion, while others (COPPER) advocate grasping the superior rectus tendon with a pair of fixation forceps, from 5 to 6 m.m. behind the limbus. BARRAQUER fixes the eye with a large lid-elevator and the use of the Landolt forceps placed 1 m.m. below the vertical meridian of the cornea.

The Incision.—The incisions that are advocated from time to time are the corneal and the sclero-corneal or the limbal. SUSRUTA, the founder of cataract surgery, in performing the depression method of cataract operation passed the barley-mouthed needle through a point situated just outside the junction of the black and white regions of the globe i.e. the sclero-corneal junction or the limbus and is a line dividing the white portion (Sclera) equally into two segments. SUSRUTA was, therefore, the first to advocate the sclero-corneal puncture as the best and the safest.

Now, a word or two about the comparative merits and demerits of these two incisions:—

Corneal Incision suffers from many disadvantages:—Wound heals slowly due to corneal nutrition being less active; union being weak, any accidental pressure during post operative stage may easily lead to the prolapse of vitreous by the bursting out of the wound, thereby augmenting the chance of intra-ocular infection. The only advantage

is that in corneal incision, the prolapse of iris is less liable to occur. In pre-historic age, CELSUS, AVICENNA made punctures through the cornea in doing the couching operation.

Sclero-corneal Incision:—To SUSRUTA must go the credit of being the first surgeon to devise that the puncture, and for the matter of that, incision through the sclero-corneal region is the best and the safest. The advantages are manifold; wound heals quite rapidly and soundly; calibre of the wound is uniform and even. Union sufficiently strong, hence prolapse of iris and vitreous rare; chance of intra-ocular infection almost nil. This is the most advantageous method and one that is universally followed. The only disadvantage which is minor, is that it bleeds which is effectively checked since the introduction of Adrenalin.

"The section which has now been universally adopted in the extraction of cataract is one which involves the limbus over an extent varying between $\frac{1}{3}$ to $\frac{1}{2}$ and which is invariably placed in the upper half of the globe" (DUKE-ELDER).

The surgeon holds the cataract knife, with its cutting edge looking upward, in his right hand in case of right eye and *vice versa*, steadily and lightly between his thumb and the first two fingers. The point of puncture is at or slightly below the limbus on the temporal side above the equator. The point of the knife is lightly but confidently thrust into the point of puncture and after it has penetrated into the anterior chamber, it is rapidly passed steadily through it, in front of the iris, to a corresponding point on the other side, where the counter puncture is made. After the counter puncture is made, the knife is slowly and gently pushed on under the scleral conjunctiva upward for about 4 to 5 m.m. so as to fashion a conjunctival flap. The advantage of taking a conjunctival flap is:—the wound seals up quickly, thereby minimising the chance of iris prolapse and post-operative intra-ocular infection. The disadvantages are, however, minor in character—there is a little more bleeding which is checked by Adrenalin; it interferes with manipulation and easy introduction of instruments which would be overcome with a little care and caution. The fashioning of the conjunctival flap is done by many operators; some surgeons, however, make the section with a conjunctival bridge, while others again pass a suture through the apex of the flap and the conjunctiva above and then tie the suture after the completion of the operation.

Historically, we owe it to DESMARRES who devised the method of conjunctival bridge as early as 1588 and utilised it in practice. Subsequently, we find that VACHER (1899), PANSIER (1901), and CLUCKIE (1909) were enthusiastic advocates of this method and popularised its practice.

In recent years, ELSCHNIG (1921), BUTLER (1922), VON PFLUGK (1923), and KILLICK (1923) have practised the method of utilising a conjunctival bridge in cataract extractions and each of them has

published his own observation for or against the method. BUTLER says that corneal astigmatism is higher in such cases. ELSCHNIG recommends the operation in high myopia and exophthalmos. According to VON PFLUGK, the method of keeping a conjunctival bridge is indicated in patients with emphysema and heart diseases. KILLICK (1923) reviewing a series of 100 cases of cataracts, removed under a conjunctival bridge, gives a favourable opinion of this method. SALVA (1925) is an enthusiastic exponent of this method in both simple and combined cataract extractions. BUTLER recommends the bridge being made directly upward as otherwise oblique astigmatism will result while some surgeons (EWING and PATON 1928) advise the bridge to be advantageously constructed to one side, as it facilitates the easy delivery of the lens. The utility of keeping a conjunctival flap cannot be questioned, as it has been an important factor in preventing the tendency to prolapse of the iris followed later by intra-ocular infection.

The Iridectomy.—Some surgeons are in favour of making a preliminary iridectomy in certain cases *i.e.* in complicated, and immature and diabetic cataracts and in cataracts of one-eyed people. PARSONS advises preliminary iridectomy to be performed in immature cataracts. COLEMAN has discussed the question of preliminary iridectomy in the extraction of senile cataracts and CRITCHETT and TERSON recommend it in cases of diabetic cataract.

The Classical Iridectomy.—The majority of the operators usually perform the iridectomy immediately after the incision is made. SMITH, KNAPP, TOROK, ELSCHNIG, SINCLAIR, and BARRAQUER and others all perform iridectomy after the incision is made and before the delivery of the lens. "The iris is gently grasped near the pupillary margin and withdrawn through the incision and excised. The amount of iris tissue should not be large" (CLAPP). There are however variations from the classical iridectomy. Thus HESS (1912) advocates a peripheral iridectomy; VERHOEFF (1906) performs a small iridotomy as near the root of the iris as possible; while ELSCHNIG (1911 and 1912) advocates a peripheral iridotomy.

DUKE ELDER (1934), however, holds that "an iridectomy should not be performed until the lens has been expressed. If, during the extraction, the torn anterior capsule is pushed up into the wound, the process of replacing the iris automatically replaces the capsule at the same time, but if an iridectomy has been performed before the lens is expressed, the practically invisible capsule may lie in the wound, and its replacement is difficult and is very likely to be incomplete." (DUKE ELDER).

Capsulotomy.—In extra-capsular extractions, the question of doing a capsulotomy arises in order to dislocate the lens from its capsular bed. There have evolved various methods of doing capsulotomy. Some surgeons incise the capsule at the time of completing the limbal section by the tip of the cataract knife; some do this by using the various types of cystitomes; while others perform capsulotomy

either by use of sharp toothed capsule forceps or by blunt capsule forceps.

To BENNETT (1919) goes the credit of devising the first method of immediate capsulotomy in the extra-capsular extraction of senile cataract. While passing the point of knife through the anterior chamber over the anterior surface of the lens, the handle is elevated slightly in order to pierce the anterior capsule, thereby slitting up a small section. DUKE ELDER says that although it requires a slight additional manipulative dexterity, it is the best method of capsulotomy as it does away with the subsequent introduction of a second instrument. The second method of opening the capsule with cystitome is the one most frequently in use. The surgeon introduces the cystitome through the corneal incision, and by a process of gentle scribbling of the blade on the capsule, the opening in the capsule is made. Amongst the cystitomes that are in frequent use may be mentioned those of VON GRÆFFE, ARLT, KNAPP or LANDOLT.

Preliminary capsulotomy is performed by some surgeons (DRAKE-BROCKMANN, HOMER SMITH). It is indicated in immature cataracts. This is a most efficacious procedure of hastening maturation of an immature cataract.

After capsulotomy is done, the lens is to be expressed out of its capsular bed. At this stage, the speculum which was put between the lids is to be removed. The surgeon holds a spoon or a hook in his right hand, and a loop with the left. The assistant would be asked to retract the lower lid gently and the patient would be asked to look downwards. The surgeon would now exert gentle pressure by manipulating with the instrument in the right hand at the lower limbus towards the centre of the globe, at the same time applying counter pressure with the loop upon the posterior lip of the incision. By means of this manoeuvre, the lens presents itself in the wound and is delivered out.

The irrigation of the anterior chamber comes in after delivery of the lens. The idea underlying the irrigation is to remove the remnants of soft lens matter either from the anterior chamber or from within the capsule. Intra-ocular irrigation after cataract extraction was first practised by GUERIN as early as 1773, but it was left to McKEOWN to standardise and popularise the practice of irrigation since 1898. The most common solutions that are used for irrigation are Normal Saline solution (DUKE-ELDER 1934) and RINGER's solution (CLAPP). Careful replacement of the iris pillars is done after this. The eyes are dressed and bandaged and the patient sent to bed.

We have so far given briefly the technique of the extra-capsular method of cataract extraction. "The majority of the ophthalmic surgeons have always preferred the extra-capsular method of cataract extraction, the technique of which has remained unchanged, since it was introduced by DAVIEL in 1745" (DUKE ELDER 1934).

But the extra-capsular method is not the ideal method of cataract

extraction, as in this operation, the posterior capsule along with part of the anterior capsule still remains, and this may grow into an after-cataract, requiring subsequent surgical intervention.

Hence, the ideal method of cataract extraction would be the removal of the entire cataractous lens in its capsule, without infliction of trauma and too much instrumental interference to the ocular structures, both inside and outside.

Therefore, it was but natural that as cataract surgery advanced in its path of Evolution, a method free from the defects of the extra-capsular extraction method would be devised. Hence, we find that towards the latter part of the 18th century, the ophthalmic surgeons began to feel the necessity of extracting the cataractous lens entire in its capsule. Besides eliminating the defects of the extra-capsular extraction, the intra-capsular method has the further advantage in that cataracts can be extracted in any stage of maturity.

We shall now chronologically enumerate the glorious names of the various ophthalmologists who invented various operative techniques in order to introduce and popularise the intra-capsular extraction of cataract.

DAVIEL (1748) is accredited by some with having tried the intra-capsular extraction, but he gave it up due to some disadvantages.

We have it on the authority of HUBBAL that SAMUEL SHARP was the first surgeon to make the corneal incision in cataract extraction with a single knife and recommended the removal of the lens with capsule by use of external pressure. His method was advocated before the Royal Society in April and November 1753.

GREEN (1914) associates the names of the eye-surgeons BEER, CHRISTIAEN and MORENHEIM for having developed and perfected the technique of intra-capsular extraction.

Credit must be given to the Pagenstecher Brothers—ALEXANDER and HERMANN—who in 1865 and 1888 dealt with the subject more elaborately. Their method consisted in the use of a spoon to extract the lens in capsule.

In 1878 LINDESBURG published his method of intra-capsular extraction with spoon and application of pressure.

In 1884, J. W. WRIGHT advocated his method of intra-capsular extraction. He made an incision about $\frac{1}{2}$ way down the limbus in the upper part of the cornea and expressed the lens in capsule without prolapse of vitreous by applying digital pressure to the upper segment and counterpressure by the finger of the other hand over the sclero-corneal junction.

In 1888, HIGGINS advocated his own method in which he extracted the lens in capsule by inserting a flexible wire loop to the back of the lens.

The first surgeon to make an extensive utilisation of this method

was COL. MULRONEY working at Amritsar in India. MEHER CHAND published MULRONEY's work in 1894 at Calcutta.

While the intracapsular cataract surgery was yet in its infancy in the surgical nurseries of Europe and Asia, it was left to COL. HENRY SMITH, working at Jullundhur in India, to devise a radical improvement in the technique of the intra-capsular extraction, as a result of which, the intra-capsular extraction method attained a truly scientific status and became so widely popularised and so extensively practised. It is an unique piece of coincidence that cataract surgery had its birth in India more than 1000 years before Christ and attained a high stage of evolution in India in the dawn of the 20th century.

Indeed the publication of SMITH's method caused a great awakening in the ophthalmic world, leading to the standardisation of SMITH's method and the elaboration of several other well-known methods of intracapsular extraction.

The different methods of intra-capsular cataract extractions that have evolved from time to time may conveniently be discussed as belonging to the following groups:—

The first method is devised by the Pagenstecher Brothers, and known as the Pagenstecher method in which the cataractous lens is delivered in capsule by introducing an instrument such as a scoop or a loop to the hind part of the lens.

The second method is that invented by SMITH in India; this depends upon the exertion of pressure on the outside of the eye-ball in order to rupture the lenticular ligaments and to express the lens in capsule entire from its fossa.

The third method is that devised by KNAPP. It consists in delivering the lens in capsule by application of traction and external pressure employed either simultaneously or one after another. VERHEFF, SINCLAIR and ELSCHNIG and others have elaborated modifications of this method.

The fourth method is demonstrated in the Hulen and Barraquer vacuum extraction operations or in the Kalt and Stanculeanu technique. In this method the cataractous lens is dislodged out of its fossa, and removed by grasping its anterior capsule either with special forceps, a vacuum cup or by electro-coagulation.

We shall now give a concise description of each of these methods in the order in which they evolved from time to time.

The First Method of Extraction by Scoop or Spoon.—This method was first described and popularised by the Pagenstecher Brothers, ALEXANDER and HERMANN (1865—1888). By this method, the lens in capsule is removed by means of a spoon, a loop or a lens hook introduced from behind the lens. It was left to BORYSIEKIEWICZ (1880) to draw attention to the drawbacks of the Pagenstecher method. BORYSIEKIEWICZ remodelled the Pagenstecher method in which he inserted a hook between the lens and the iris and then, by rotating

the hook backward, he grasped the lens and effected delivery by traction.

In 1922, JOHNSON published a new method of removing the lens in capsule, in which he effected delivery of the cataract by means of a bent spoon and a strabismus hook.

All these methods, however, are not easy going ones, hence, they are not in popular use; but they are to be remembered as important landmarks in the road of evolution of cataract surgery.

Smith's Intracapsular Cataract Extraction.—After preparation of the patient, anaesthetisation of the eye is done by dropping 2 drops of Cocaine solution at 5 minutes' intervals. Eyelids are washed with soap and water; the trimming of the eyelids (outer one-third) is done. Conjunctival sac is thoroughly irrigated with 1 in 2000 solution of Bichloride of Mercury. A catchless spring speculum is inserted and fixation of the eye is done with SMITH's forceps. SMITH makes the corneal incision by puncturing at the sclero-corneal junction and the incision involves nearly one-half of the circumference. SMITH completes the incision with the first thrust of the knife, or with the drawing back of the first thrust. Then having made a broad iridectomy, the speculum is removed, after which the assistant retracts the upperlid with a special strabismus hook, while the lower lid is retracted either by finger or thumb. The surgeon takes a strabismus hook in the right hand and a spatula in the left. With the point of the hook directed towards the centre of the lower third of the cornea, the surgeon exerts gentle pressure directly backwards towards the optic nerve; by lightly and firmly exerting pressure with gentle manoeuvre on the hook, the dislocation and final delivery of the lens in capsule is effected.

After delivery of the lens in capsule, reposition of the iris pillars is done. In case of vitreous prolapse appearing in between the edges of the wound, it should be cut off. The eye is now bandaged with antiseptic dressings, and it is left untouched until the 7th or 8th day, when on opening it will be found usually free from any intra-ocular inflammation.

After SMITH's publication of the intra-capsular cataract extraction method, keen interest in the subject was aroused. Several modifications in the technique of SMITH's method were made; GREEN (1914) made a small iridectomy in place of a large one; and LISTER (1919) made the use of assistants, one in controlling the orbicularis and the other to retract the lids. In 1926, SMITH himself made a modification in his technique in which the lens was subluxated in its transverse axis till the rupture of the zonular ligament and by application of pressure from below, the lens was finally delivered in capsules.

Knapp's Intra-capsular Extraction Method.—After dilatation of the pupil with 1 drop of Atropine and anaesthetisation with Holocaine the speculum is inserted and left in situ till the completion of operation, unless otherwise indicated. KNAPP makes a large incision involving nearly one-half of the corneal circumference and a conjunctival flap is made at the completion of the section. Iridectomy is

now made and the Kalt forceps having been introduced to a point below the pupillary centre, KNAPP grasps the capsule and, with a gentle but firm traction manipulation, subluxates the lens with rupture of Zonular fibres. Then with a Smith's hook, he applies gentle but steady pressure to the lower corneal margin, as a result of which the lens in capsule is tilted up and delivered. The iris pillars are replaced and speculum removed. Atropine ointment being applied to the conjunctival sac, a dry dressing is given. KNAPP keeps both eyes bandaged and for the first four days the affected eye is not dressed. KNAPP published his method in 1915.

KNAPP's technique has undergone a modification at the hands of VERHOEFF (1916) whose method consists in grasping the capsule with the modified KALT forceps below the centre of the lens and by a process of applying traction forward on the lens capsule combined with application of pressure from below, the lens in capsule is delivered.

Stanculeanu Intra-capsular Extraction.—In 1912, STANCULEANU published his method of intra-capsular extraction which consists in removing the lens in capsule with the capsule forceps. He dilates the pupil with Homatropine and makes a rather large corneo-scleral section. Inserting the capsule forceps, he grasps the lens capsule immediately below the centre. Gentle pressure is exerted to and fro till the zonular fibres are ruptured, after which the lens in capsule is delivered off.

Torok's Method—In 1916, TOROK published his intra-capsular method. He operated under Holocaine anaesthesia and his corneal incision involved nearly one half of the circumference, with the retention of a conjunctival flap. A small iridectomy is done and pillars replaced, after which he grasps the anterior capsule just below the centre with the Kalt forceps, and makes gently to and fro movements until the zonular fibres are ruptured. Then taking a Daviel spoon in the right hand, he applies pressure at the lower limbus, as a result of which the lens in capsule is delivered, the lower edge appearing foremost. Iris pillars are now replaced. TOROK makes the first dressing at the end of 48 hours.

Elschnig's Intra-capsular Method (1931).—ELSCHNIG irrigates the conjunctival sac and the lacrimal sac with Mercury Oxycyanide solution and also applies the yellow oxide of Hg. ointment to the lids until bacteriological examination shows the eye to be aseptic. Anaesthetisation of the eye is done by 3% Cocaine solution; the immobilisation of the lids muscles done by injecting 2% Procaine-Hydrochloride-Epinephrine solution into the subcutaneous tissues on the outer half of the zygomatic arch, and a retro-bulbar injection of 1 c. c. of the solution is made. Having put the sutures for fashioning a conjunctival flap, a corneal incision involving the upper two fifths of the limbus is made. Conjunctival flap is lifted with forceps, and by opening the anterior chamber, a small basal iridotomy is made. ELSCHNIG grasps with his own capsule forceps the lens at the lowest possible part of the dilated pupil and tosses the lens to and fro by gentle manoeuvres on the forceps for about 8 to 10 seconds. Then by

continuing forward traction on the lens, re-inforced by gentle exertion of pressure with a hook applied against the cornea at the level of the lower limit of the dilated pupil, the delivery of the lens in capsule is effected. Suture having been tied, the iris is replaced into position by inserting the repositor underneath the flap. Eserine having been dropped into the eye, the wound is touched with 5% tinct of Iodine, and after applying Eserine Oxycyanide ointment, the eye is bandaged.

Sinclair's Method.—SINCLAIR of Edinburgh is another enthusiastic advocate of the intra-capsular extraction. He published his latest technique of the operation in 1932 which consists in delivering the lens in capsule by the simultaneous action of pressure applied from without by means of an instrument "the expressor-guard of SINCLAIR" and traction from within by means of a specially designed extraction forceps which has a "double cross action", being opened by pressure of the fingers and closed by releasing the fingers.

Now, we shall describe the evolution of the vacuum extraction method: The Arabian surgeons were the first to use suction methods in extracting soft cataracts from very early times. Next, the Greek surgeons utilised this method in their ophthalmic practice. It was, however, in the beginning of the 20th century that the eye-surgeons began to build up the method of vacuum extraction on a scientific basis.

In 1906, STOWERS described his method of vacuum extraction which consisted in extracting the lens in capsule by grasping the anterior capsule with a hollow spoon connected with a rubber ball.

The method received greater attention and further elaboration at the hands of HULEN who in 1910 published his modified method of vacuum extraction, which consisted in extracting the lens in capsule by means of a hollow spoon connected by a rubber tube to a receptacle connected with negative pressure.

While STOWERS and HULEN are to be remembered for having paved the way for the evolution of the scientific vacuum extraction method, BARRAQUER is to be remembered as the builder of the method; because, it was due to the laborious and enthusiastic investigations of BARRAQUER that the operation of phaco-erises has been raised to a really scientific status in cataract surgery.

BARRAQUER published his phaco-erisis method in 1917. A brief description of his method is given below:—After dilating the pupil and anaesthetisation of the ocular sac, a rather large corneal incision is made. BARRAQUER introduces the erisiphake through the dilated pupil behind the iris, and places it on the lower-half of the lens. When the vacuum pump is turned on, the lens becomes tightly attached to the cup, and by moving the handle of the erisiphake, the lens is rotated round its horizontal axis. This rotation of the handle of the erisiphake facilitates the rupture of the zonular fibres, and the lens in capsule is delivered adherent to the erisiphake, which is a small spoon or a cup on a hollow handle in connection with an air pump capable of creating a finely controlled vacuum.

BARRAQUER's method has a large group of advocates. FOSTER MOORE (1923), A. and L. GREEN (1921); MARBAIX, URRÁ, McDANNALD (1921); GALLEMAERTS (1921), KOEPPE (1923), CROSSLEY, CASTROVIEJO and FISHER (1932) have all adopted BARRAQUER's method with modifications in individual cases.

The latest evolution in the sphere of intra-capsular cataract surgery comes from the brain of LACARRERE (1932), who advocated the method of extracting lens in capsule by means of diathermy. He uses an instrument known as the 'Electro-diaphake'. After the usual preparation and anaesthetisation of the eye, a limbal incision involving $\frac{2}{3}$ th of the corneal circumference is made. After iridectomy the needle of the electro-diaphake is introduced, its point being applied to the anterior capsule below the centre of the lens. As the current is turned on, it passes through the terminals of the instrument into the lens tissue which becomes coagulated and firmly adherent to the top of the 'electro-diaphake'. By the movement of the needle of the diaphake the dislocation of the lens with rupture of Zonular fibres is done, thereby facilitating the final delivery of the lens in capsule.

Conclusion.—We have briefly enumerated the various stages through which the evolution of cataract surgery passed ever since the hoary pre-historic age up to the present time.

We have found that up to the middle of the 18th century A.D., SUSRUTA's method of lens couching operation was exclusively practised throughout the world. Everybody would frankly admit that at a time when antiseptics and anaesthetics had not been discovered, open methods of operation, especially open operations on such a delicate organ as the eye, could not be undertaken for fear of intra-ocular sepsis. Hence, SUSRUTA, the founder of cataract surgery and the first surgeon of the world was prudent enough not to adopt open methods of cataract operation and invented the depression method of lens couching operation which gave him the best results. Indeed, that was the only method left for the treatment of cataract in the pre-antiseptic and pre-anaesthetic days. Hence, SUSRUTA cannot be blamed and branded as a cataract coucher.

The extra-capsular method of cataract extraction is decidedly better than the depression method of lens couching operation. But the extra-capsular method has its defects, as in this case, the capsule is left behind, leading to the formation of after cataract necessitating subsequent surgical intervention. Hence, the best and the most ideal method of cataract surgery would be the intra-capsular method of cataract extraction. After DAVIEL devised his extra-capsular method of cataract extraction in 1745, it did not take long for the intra-capsular method to appear in the field of cataract surgery. Towards the middle of the 19th century, ophthalmic surgeons were busy devising and standardising the intra-capsular method of cataract extraction, and the dawn of the 20th century saw the highest stage in the evolution of cataract surgery.

SUSRUTA was well aware of the shortcomings and disadvantages of the lens couching method, as would be evident from his writings, but he was greatly handicapped in undertaking open methods of cataract extraction for want of anæsthetics and antiseptics in his days. It was only after the discovery of antiseptics and anæsthetics that open methods of cataract extractions have been standardised and popularised. Hence, SUSRUTA cannot be blamed for his adopting the lens couching method in his days.

Even in the present day, when extra-capsular and intra-capsular methods of cataract extractions are being widely practised, there are eminent eye-surgeons who advocate lens couching operation under certain conditions.

POWERS in 1901 advocated lens couching to be adopted in the case of very old, in deep sunken eyes, in deaf people, in lunatics, in cases of dislocated lens, and in patients suffering from a hæmorrhagic diathesis.

JOHNSON published in 1925, a paper entitled "A plea for reviving the operation of couching, thereby advocating the use of this operation.

CLAPP (1934), says—"Possibly in cases of cataracts occurring in the mentally deranged or deficient, the operation of lens couching might be justified."

FUCHS (1934) says—"In a case in which one eye has already been lost by a hæmorrhage, instead of the extraction, the old reclination (depression) method of cataract, long given up because of the uncertainty of its results, is to be chosen. For an operation with 50% bad results is always better than the entire loss of the only eye."

SUSRUTA's instructions for the post-operative management of the patient stand as effective to-day as he taught so many thousand years before Christ.

His advice regarding the change of eye dressings and conduct of the patient during the post-operative period is quite sound and scientific and is followed even in the present day. His injunctions to the patient not to sneeze, cough, yawn, nor spit are quite in concordance with scientific principles.

His knowledge about the anatomy of the eye was so perfect that he advocated the passing of the Jabamukhi Salaka only through the natural aperture of the eye, as otherwise, it would puncture the iris, ciliary body and other vital structures of the eye. SUSRUTA's advice for puncturing the eye just outside the limbus on the temporal side of the globe is being followed even to-day.

The existence and efficacy of vitamins was known to SUSRUTA in the pre-historic age, who was wise enough to emphasise the necessity of the patient's taking enough of fresh milk during the whole of the post-operative period.

SUSRUTA recognised the properties of mother's milk as a hæmostatic,

soothing and nutritive agent in ocular therapy. Indeed, it was his fertile brain that discovered the hæmostatic property of breast milk, which was the 'Adrenalin' of the pre-Epinephrin days.

Nor was SUSRUTA dogmatic about his teachings. Like a true prophet of science, he frankly admitted that he taught only the fundamental principles of ophthalmic surgery, and that it was left to the future votaries of the science to enlarge its scope by their researches.

Indeed, SUSRUTA's teachings have greatly influenced and moulded the scientific evolution of cataract surgery.

The extra capsular method of cataract extraction is being largely practised by the majority of ophthalmic surgeons in the present day. But it has its defects. The most ideal method of cataract extraction is the intra-capsular method. We have now on the field so many intra-capsular methods, each with a delicate and complicated technique; and as DUKE-ELDER says "that all the methods of intra-capsular extraction are difficult; they require skill in the selection of cases, and they demand a long apprenticeship and a delicacy of technique not readily attained." "The value of an operative procedure cannot be usefully assessed on the results of its most skilful interpreter, but must stand or fall on those reasonably attained by a surgeon of average ability."

We cannot, therefore, at this stage say that the evolution of cataract surgery is complete. We still hope for the evolution of an intra-capsular method whose technique would be simple in nature and which would be universally accomplished by the specialist and the non-specialist alike.

Two names stand out prominent in the domain of cataract surgery—SUSRUTA, the first surgeon ophthalmologist will ever be remembered as the inventor and founder of cataract surgery; and as he and all the eye surgeons who followed his teachings had to live in the pre-antiseptic and pre-anæsthetic age when open methods of eye operations were deemed risky, SUSRUTA's lens couching operation had to be followed till the middle of the 18th century when DAVIEL devised the extra-capsular method of cataract extraction.

Hence, if SUSRUTA is to be honoured universally for ever as the inventor and founder of cataract surgery, DAVIEL is equally to be honoured as the architect of modern cataract surgery, and the names of SHARP, BEER, PAGENSTECHEERS, WRIGHT, SMITH, FUCHS, SINCLAIR, GRÆFE, KATT, BARRAQUER, ELSCHNIG, KNAPP, TOROK, STANCULEANU, VERHEFF, LACARRERE and MORENHEIM will ever be remembered as master-builders of the edifice of cataract surgery in the modern period.

In preparing this article, I have freely consulted the works of many learned authors, to whom I gratefully acknowledge my indebtedness, the bibliography of which is appended herewith.

References :

1. *Susruta-Samhita*,—Edited By Jadeva Sherma, Bombay—2nd Edn.—1931.
2. *Vagbhat's Astanga-Hridaya-Samhita*.
3. Mukkerji, G. N.—'Surgical Instruments of the Hindus' 1913.
4. Clapp, C. A.—'Cataract, its Etiology and Treatment', 1934.
5. Duke-Elder—'Recent Advances in Ophthalmology' 3rd Edn. 1934.
6. Green, Armytage—'The Debt of the Western Medicine to the East', Bristol Medico-Chirurgical Journal, Vol. LIV, P. 239, 1937.
7. Roy, A. T.—'Peep into Hindu Medicine', I. M. Record, Dec. 1929. 'Hindu Medical Science' I. M. G., July 1929.
8. Fuchs—'Diseases of the Eye—X English Edn.—1933.
9. Visagrathna, K. L.—*Susruta-Samhita* (Eng.) Vol. I. 1907.
10. Thakore Saheb of Gondal—*History of Aryan Medical Science*. 2nd Edn. 1927.
11. Hoernle—*Studies in the Medicine of Ancient India*. Part. I, Osteology Introductory.
12. *Medical Annual*, 1936.
13. Parsons—'Diseases of the Eye' 7th Edn. 1934.
14. Roy, P. C.—*History of Hindu Chemistry*.
15. *Atharva-Veda*—'On the Date of Atharva-Veda'. pp. CXL-CLXI, Prof Lanman's Edition of Whitney's Translation.
16. Schultz—*Historiae Medicinae*.
17. Royle—*Antiquity of Hindu Medicine*, 1937.
18. Wilson—*Oriental Magazine*, 1823.
19. Max Muller—*Works on Hindu Medicine*.
20. Heins—*Tracts on India*.
21. Captain Johnston Saint—*Sir George Birdwood Memorial Lecture*, June, 1929.
22. Wise—*Commentary on Hindu Systems of Medicine*, 1845.
23. McDonnell—*History of Sanskrit Literature*, 1900.
24. Somade Koros—*Journal of the Asiatic Society of Bengal Transactions*.
25. Sen, D.N., Kaviraj.—*Dravya-Guna—Hindu Materia Medica*.
26. Smith—*Cataract and its Treatment*.
27. Bidyadhar, N. K.—'Susruta and his Ophthalmic Operations'—*Archives of Ophthalmology*, Oct. 39, Vol. 22, pp. 550-574.

Sulphanilamide in The Treatment of Certain Eye Conditions*

BY

S. Sanyal, M.B., (CAL.).

Visiting Ophthalmologist, Ashtanga Ayurveda Hospital, Calcutta.

EFFECTIVE campaigns against Streptococcal infections became feasible with the famous discovery of Prontosil by DOMAGK. With the ever-increasing field of indication, Sulphanilamide group of drugs have been tried mainly on three types of eye diseases viz., trachoma, gonorrhoeal ophthalmia and panophthalmitis; but the administration has been limited to injections and oral routes. It goes without saying that the results of these methods (oral and parenteral routes) of treatment were not unsatisfactory.

It is a known fact that the diseases of the conjunctiva and cornea are mainly local and a desired result should be forthcoming by direct application of these drugs in an effective concentration and in such a form which could be kept in prolonged contact with the affected part. With this end in view, I was inclined to use Urea-Sulphazide, Sulphanilamide compound manufactured by Messrs. Union Drug Co., Ltd., in my cases in the form of a 5 per cent ointment (Red) and solution, the concentration of which varied from 1 to 5 per cent according to individual requirement. My group of 50 cases comprises conjunctivitis, kerato-conjunctivitis, keratitis, corneal ulcer and trachoma. I confess that in this small series of cases, thirty were of the first two types and the remainder belonged to the other varieties. It would, therefore, seem that my observations on kerato-conjunctivitis and conjunctivitis were more conclusive than the rest of the cases.

Before I deal with the main issues, I should like to dispose of one incidental topic. This is about kerato-conjunctivitis. It is perhaps known that classical trachoma does not exist among the people of Bengal. Kerato-conjunctivitis is somewhat similar to trachoma in the formation of pannus, papillary hypertrophy and granule formation. Pannus may occur in this disease in acute, subacute or chronic stages. Papillary hypertrophy is seen in sub-acute stages but granules are very rare in this disease. But as a rule, the manifestations are acute. More commonly, the corneal affection is manifested in the form of keratitis or ulcerations of various types. It is mainly distinguished from trachoma by the absence of scar tissue formation either of the conjunctiva or of the cornea. In trachoma, loss of vision results mainly from slow but relentless progressive fibrosis of the conjunctiva, cornea and lids; but in this condition, blindness is the outcome of either acute destruction of the cornea or, in favourable cases, by the formation of leucomatous patches with its known defects. Bacteriologically, smear examination with Giemsa's stain shows acidophilic coccoid bodies similar to those in trachoma; but basophilic bodies are

* Specially contributed to "The Antiseptic".

not found. Histologically, it is more of a cellulo-exudative nature than trachoma which is a lymphocytic infectious granuloma with selective follicular localisation and very little reticulum or endothelium (KRUCKMANN, 1932). Another form of conjunctivitis (Sanyal's conjunctivitis) described by the writer also is distinguished clinically by the absence of yellow areas of degeneration, corneal complications and pre-auricular gland enlargement and bacteriologically, by the absence of coccoid bodies.

Coming to the consideration of the results of my observations on cases of kerato-conjunctivitis with Urea-Sulphazide, I should like to mention that the relief of subjective symptoms sometimes begins within an hour of the first insertion of the drug and lasts for about 12 to 18 hours after each application. Characteristic flat yellow areas of degeneration on the palpebral and bulbar conjunctivae are removed within 24 to 72 hours depending on the size and specially the depth of the degenerated areas and the superficial marginal ulcer if any, heal up within a day or two. In this condition, only the Urea-Sulphazide ointment was inserted twice daily—once in the morning and again before retiring at night. Light massage of the lids was done after each insertion.

CASE 1.—Sabita, H. F., aged 20 years, reported herself for pain, lachrymation, photophobia of the left eye for 4 days;

- (1) The lids—Œdematous.
- (2) The Conjunctiva.
 - (a) Lower—Slightly congested.
 - (b) Bulbar—Congested from the periphery towards cornea. Marked on the medial side.
 - (c) Upper—Slightly congested.
- (3) Cornea—Inflamed.
- (4) Keratitis—Present.
- (5) Ulcer—Nil.
- (6) Infiltration—Present.

Urea-Sulphazide ointment was advised b. d. The very next day the patient said that the lachrymation and photophobia were markedly less but slight pain still persisted. On the third day, the pain totally disappeared. Congestion of the conjunctivae was decidedly less. Treatment was conducted for 5 more days to effect a cure.

With regard to conjunctivitis, my series includes acute, subacute and chronic cases and the observations are based on three different methods of application. The first group had only the ointment inserted twice a day, the second, instillation of the solution alone thrice daily and in the third, the insertion of the ointment was supplemented by instillation of the solution, both preparations being administered twice during 24 hours. The best results were achieved as it should be, with the last method and was mainly employed in the more severe forms of acute cases. In these cases, the combined method produced

desired results within 12 to 24 hours. The gritty sensation, lachrymation and photophobia and to some extent, the pain are first to disappear. The redness, œdema of the lids, etc., then gradually pass off. One distinctive feature of Urea-Sulphazide application is that there is an early relief of the subjective symptoms. On an average, in this series, a five days' combined treatment was necessary to effect a cure. To free the conjunctivae from the infective process, it was found necessary to continue the insertion of only the ointment for about a week more. But, in the Out-patients' Department, this desirable condition of the conjunctiva was not always possible as most of the patients disappeared as soon as their subjective symptoms were relieved. In many cases, congestion of the palpebral conjunctiva persisted even after the conjunctiva was bacteriologically free. These required some astringent lotion.

CASE 2.—Hindu, Female, aged 50 years, complained of pain, lachrymation, photophobia and gritty sensation of both eyes for 3 days. Examination revealed the lids to be œdematous. The upper and bulbar conjunctivae moderately congested while the lower was densely congested.

Cornea—marginal haziness. Keratitis—nil.
Ulcer cornea—small superficial marginal present.
Infiltration—Present.

TREATMENT:—Urea-Sulphazide ointment and instillation of a 2½ per cent solution were prescribed. Within 12 hours after the treatment was commenced, the gritty sensation, pain, lachrymation, photophobia were less and the patient felt much relieved. From the third day onwards, the congestion in the conjunctiva and oedema of the lids were decidedly less. The small superficial ulcer was also on the way to recovery and healed up completely at the end of treatment. This combined method of treatment was done for a period of five days and was followed up with the ointment for another week.

As far as the treatment of sub-acute cases of conjunctivitis are concerned, the combined method enumerated above is perhaps the best. With regard to the chronic cases, the ointment alone inserted twice daily has yielded the desired results and most of my chronic cases were free from symptoms within a period of two weeks.

Out of the four trachoma cases I have had, one failed to respond, two others left the treatment after 3 days.

CASE 3.—In the fourth one (an acute case), the pain, photophobia, lachrymation and gritty sensation were relieved within a few hours and within an hour of the application of the ointment, the conjunctiva became congested and velvety with slight œdema of the lids. As far as the granules are concerned, the general hyperæmia and œdema induced by the drug made the yellowish white points less distinct within a few hours. Most of the granules became flattened within 4 days. But the few which still remained resisted the treatment for 2 weeks. Thickening of the lid took about a week to

become normal. But the improvement observed in this case deserves further trials to draw a definite conclusion as to the efficacy of the preparation in trachoma cases.

With reference to corneal ulcer cases, I would mention that superficial ulcers are quickly amenable to the ointment alone. The deep ulcers specially with hypopyon required the usual methods in addition. But control of the condition was noticeable within 24 hours.

CASE 4.—*Secondary ulcer*:—Acute kerato-conjunctivitis of the right eye with small superficial ulcer at the sclero-corneal junction about the size of a pin head. Urea-Sulphazide ointment was applied. Within 24 hours, the ulcer failed to give any reaction to Methelyne Blue.

CASE 5.—*Acute ulcer (R. E.)*:—History of injury while working in the paddy field. Sub-acute spreading ulcer covering about the middle third of the cornea developed with hypopyon in the anterior chamber. There were acute pain, photophobia and lachrymation. Urea-Sulphazide ointment was applied b.d., in addition to hot compress, Atropine and Normal Saline wash. The ulcer healed up within a week.

In the keratitic group, the superficial ones, specially those in the outer-third, are quicker to respond than the central ones. With regard to the deeper ones, the results are not so encouraging. It might be mentioned that these keratitis cases—specially the superficial punctate ones—were very difficult to treat and because of the epithelial covering, the usual drugs failed to reach the infecting agents, but this drug seems to shorten the course of the disease.

In conclusion, it should be emphasised that this being a preliminary report, no definite conclusion can be drawn, but from the results so far observed, it seems that Sulphanilamides (Urea-Sulphazide) used locally, in eye practice, is worthy of further trials.

I must thank Messrs. Union Drug Co., Ltd., for the free supply of the required quantity of (specially prepared red) ointment and solution for my trials.

References :

1. Sanyal S.—*Kerato-Conjunctivitis with Adenitis in Calcutta*—*Am. J. Oph.* 19, 82—88, Nov. '36.
2. Duke-Elder Sir W. S.—“*Sanyal's Conjunctivitis*”, *Text Book of Ophthalmology*, Vol. II, pp. 1659.

ARSENICAL THERAPY BY MAY & BAKER

Intravenous injection in SYPHILIS

*N·A·B·NOVARSENOBILLON

Ampoules of 0.15 gm., 0.30 gm., 0.45 gm., 0.60 gm., 0.75 gm. and 0.90 gm. Also available in "Bipoule" double ampoules.

Painless intramuscular injection in SYPHILIS and YAWS

*ACETYLARSAN

Boxes of 10 x 3 c.c. and 1 x 5 c.c. ampoules of solution for adults, and boxes of 10 x 2 c.c. ampoules of solution for children.

Oral administration in AMOEBIC DYSENTERY

*STOVARSOL

Bottles of 30 x 4 grain tablets

Intravenous injection in NEUROSYPHILIS

TRYPARSAMIDE

Ampoules of 1, 2 & 3 gm.

★ TRADE MARK



**MAY & BAKER (INDIA) LTD.
11 CLIVE STREET, CALCUTTA**

BERIN

VITAMIN B₁ "GLAXO"

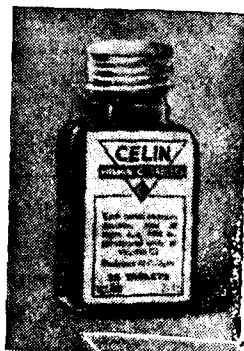
AMPLE STOCKS NOW AVAILABLE

The success of vitamin B₁ in beri-beri is generally recognised; in addition the therapy has a wide use in every-day practice. In gastro-intestinal disorders vitamin B₁ will improve impaired digestion and alleviate intestinal obstruction. It is of value in neurological disorders; for correct carbohydrate metabolism; and in pregnancy when the nutritional requirement of the vitamin is increased.

PRODUCT OF THE
GLAXO LABORATORIES

GLAXO LABORATORIES LTD., Greenford, Middlesex, ENGLAND.
Representatives in India: H. J. FOSTER & CO., LTD.
P.O. Boxes: 202, Bombay. 2257, Calcutta. 108, Madras. 244, Lahore.

To supply the urgent demand for VITAMIN C in FEVERS



PRODUCT OF THE
GLAXO LABORATORIES

Many diseases become complicated by a marked deficiency of vitamin C—particularly in fevers such as typhoid, malaria, pneumonia, whooping cough etc. For in these conditions a much greater intake of the vitamin is needed than normally. Yet, by the very nature of the illness the patient has to live on a restricted diet. Hence a vitamin C supplement becomes imperative. Celin Tablets (Glaxo) offer the simple and convenient method of providing it. Three or four of these small tablets daily are ample to maintain and safeguard the patient's vitamin C reserves.

When the parenteral route is preferred, Celin (Glaxo) is available in ampoules.

Celin

VITAMIN C (GLAXO)

Glaxo Laboratories Ltd., Greenford, Middlesex, England. Repts. in India: H. J. Foster & Co., Ltd.
P. O. Box 202, Bombay. P. O. Box 2257, Calcutta. P. O. Box 108, Madras. P. O. Box 244, Lahore.

When writing to advertisers, please mention the "Antiseptic"

NOW AVAILABLE FROM GLAXO LABORATORIES LTD *

the accepted contrast medium for INTRAVENOUS PYELOGRAPHY

PYELECTAN

brand of IODOXYL injection

(the disodium salt of 3:5-di-iodo-4-pyridoxyl-N-methyl 2:6-dicarboxylic acid)

There is one organic iodine compound which completely fulfils the exacting requirements of intravenous pyelography. This substance is accepted everywhere by urologists and radiologists as the most satisfactory of all contrast media for producing a dense and strongly defined shadow in the renal pelvis and ureter. Glaxo Laboratories Ltd. now prepare this substance and offer it in solution under the registered trade mark, 'Pyelectan.'

Excretion of 'Pyelectan' is rapid: the iodine is firmly bound and the substance excreted unchanged. Thus 'Pyelectan' is safe in use and causes no inconvenience to the patient.

One ampoule of 'Pyelectan' (20 cc.) is the amount to be injected for an adult. The pelvis is usually filled in 10 minutes, pyelograms being obtainable within 10-30 minutes. Each 20 cc. ampoule of 'Pyelectan' contains 15 grams of the salt in stable aqueous solution.

GLAXO LABORATORIES LTD., Greenford, Middlesex, ENGLAND.
*Representatives in India: H. J. FOSTER & CO., LTD.
P.O. Boxes: 202, Bombay. 2257, Calcutta. 108, Madras. 244, Lahore.

PRODUCT OF THE
GLAXO LABORATORIES

When writing to advertisers, please mention the "Antiseptic"

TWO USEFUL PRESCRIPTIONS
IN CASES OF
INDIGESTION

Colic, Diarrhoea, Flatulence, Hyperacidity, Stomach pains and nervous eructations, and where a General stomachic with sedative action is required, are

Alembic
 MIXT. PEP SIN
 BISMUTH CO.

Alembic
 MIXT. PEP SIN
 BISMUTH CO.
 WITH OPIUM

ALEMBIC CHEMICAL WORKS CO., LTD
 BOMBAY BARODA MADRAS CALCUTTA

UREA SULPHAZIDE-T
 $\text{NH}_2 \text{ CO CH}_3\text{—NH—C}_6\text{H}_4\text{—SO}_2 \text{ NHCO NH}_2$

HAS BEEN FOUND VERY EFFECTIVE
 IN CASES OF GONORRHOEA
 AND PNEUMONIA.

Manufactured by:
THE UNION DRUG CO., LTD.,
 CALCUTTA.

Sole Agents for Madras Presidency:—MESSRS. APPAH & Co.

When writing to advertisers, please mention the "Antiseptic."

CASES AND COMMENTS

A Case of Acute Exfoliative Dermatitis followed by Myasthenia Gravis and Death

BY

Capt. P. S. Gupte, M.B.B.S.,

Nasik.

(With notes from Major Dani, I.M.S. Retd.).

A FEMALE patient aged 64, suddenly got an attack of suffocation in the throat in the early hours of 26th December 1939. Her pharynx was a little red and swollen. Tongue looked dry and coated and the mouth was sore. She complained of pain below the larynx and in the chest. Temperature was 99° with pulse rate 120. When I saw her, she was extremely restless. I gave her one Camphor-in-oil injection. Inhalation of Amylnitrite made her more uncomfortable. Breathing was rapid and shallow. Voice became husky and changed. Next four days she kept temperature between 99°—101° with a few rales and rhonchi in both lungs. I treated her for influenza and she felt well after a week's treatment.

Previous history.—She had severe menorrhagia at the menopause for nearly one year. During the last three years, she was complaining of vague pains in various parts of the body and vertigo. I gave her Benerva and Theelin injections without much relief. Her eyesight was failing and the eye specialist declared that the failure of vision was due to arteriosclerosis and prescribed her some Iodine preparation for internal use.

After a week of her recovery from her so-called 'influenza' she started severe urticaria with redness and intense itching all over the body. Itching was intolerable and deprived her of her rest and sleep. The skin of the whole body became thick and infiltrated. Face was swollen to such an extent that it was impossible to recognise her. After severe scratching she felt burning sensation which made the condition extremely unbearable. Sepsis on the scratched parts brought on fever. Ointments, oils, cooling antiseptic lotions and various powders and baths had no effect on the disease. One Sodium Thiosulphate injection was given, but further injections were discontinued owing to difficulty in finding out veins in the thick and swollen skin.

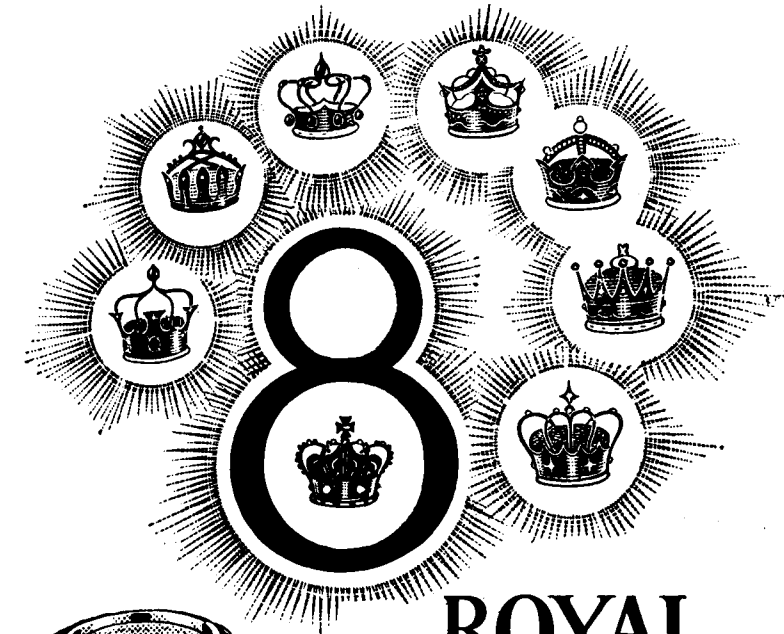
After two months, MAJOR DANI gave her a few exposures of Ultra-violet rays which brought the disease under control; but the colour of the skin remained dark particularly on the face.

The patient was showing signs of improvement when she began to find difficulty in swallowing on 14th March '40. She swallowed solids and liquids with difficulty. Speech was possible but with a

distinct nasal twang. The general appearance of the patient was apathetic. Face looked flabby and swollen to some extent. Eyes were partially closed due to ptosis. On further examination, it was evident that the muscles of deglutition were partially functioning owing to paresis which caused regurgitation of fluids through the nose and gave rise to nasal twang. Patient's general musculature was atonic probably due to recent illness. All the reflexes were slow but present. She had a few front teeth infected with P. A. There was no temperature. A thorough examination of other systems was carried out and no obvious cause for the condition could be found out. A diagnosis of myasthenia gravis was thus arrived at.

Treatment.—Prostigmine injections were tried. They caused colic in the abdomen but did not produce any effect on the face or deglutition muscles. The condition was getting worse day by day. Nasal feeding was resorted to as the patient could hardly sip any liquid. After a few days, nasal feeding became difficult owing to rawness of nasal and pharyngeal mucous membrane. She was conscious upto 24th March, when she got a sudden rise of temperature and developed signs of pneumonic consolidation. Patient died on the forenoon of 25th March 1940.

In this case it is difficult to say whether myasthenia gravis has anything to do with exfoliative dermatitis. What was the cause of exfoliative dermatitis? Was it due to influenza? Were the initial symptoms of suffocation the usherers of the final fatal malady? There was no fatigue, paralysis of deglutition or face muscles as is described in text books. Probably, this was an acute type of the disease. OSLER says, "In severe cases paralysis persists". What was the cause of failure of vision? Was it really a beginning of myasthenia and not diagnosed as such?



ROYAL MOTHERS CAN'T BE WRONG!

There is nothing more difficult to remedy in later life than defective feeding in infancy.

It is an assurance then to every doctor to know that in recent years Cow & Gate has been the food of no less than **eight Royal Babies**—eight little ones whose care and nutrition has been supervised by the most eminent specialists in the world.

The gratitude of the mother, the definite progress of the child will follow your prescription of



By Appointment
to H.M. the King
of Yugoslavia.



By Appointment
to H.M. the King
of Iraq.

©2559

COW & GATE MILK FOOD

"THE FOOD OF ROYAL BABIES"

"Ample stocks are available in India and will be maintained"

AFTER THE MOST EXACTING TESTS

LEXIN

The famous treatment of Snakebite has been recognized by the five Faculties of Medicine in Central America—the habitat of the Rattle snakes.—“LEXIN works wonders” they recorded.

Sold by Chemists. Re. 1 per bottle (4 drs.) Doz. Rs. 10-8.
Box of 6 Ampoules. x 2 c.c. Rs. 2-4.

P. BANERJI, MIHIJAM E. I. Ry.

Agents:—Messrs. SRI KRISHNAN BROS., MADRAS.

CALCUTTA MEDICAL JOURNAL

(Journal of the Calcutta Medical Club)

A Monthly Record of the
Medical Sciences as applied to the Tropics

Annual Subscription

In India	...	Rs. 9/-
(For Junior Practitioners	...	Rs. 5/-)
Foreign	...	18 sh., \$ 4.00

THE BEST MEDIUM FOR ADVERTISEMENTS

For specimen copies, please send two annas in stamp to:

Editorial & Publishing Offices at
91B, Chittaranjan Avenue, Calcutta, India.

Contract Rates on Application to:

THE PUBLICITY SOCIETY OF INDIA LTD. 1, Waterloo St., CALCUTTA.

When writing to advertisers please mention the "Antiseptic"

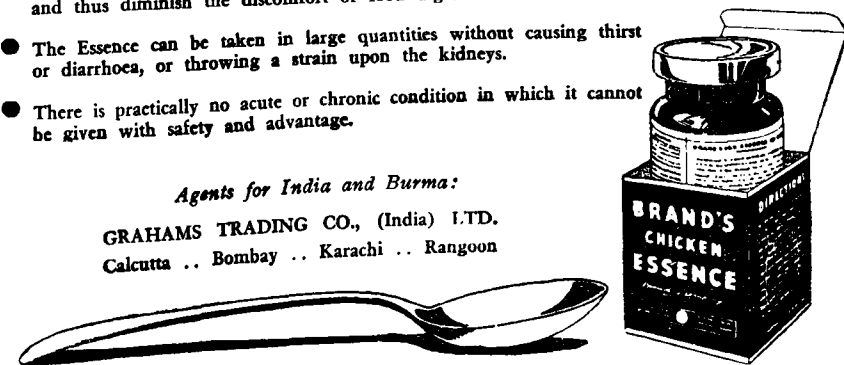


All your
patients
will readily
accept & enjoy

BRAND'S ESSENCE OF ENGLISH CHICKEN because—

- Brand's Essence is easily and quickly digested without the formation of any solid precipitate—as may occur in the case of milk, raw white of egg, or even the best home-made chicken broth. Where there is gastric insufficiency, full digestion of these fluids sometimes takes many hours.
- This absence of precipitate at all stages of the digestion of Brand's Essence indicates that the system absorbs it with a minimum of effort. The stimulating properties of the Essence take speedy effect owing to the high degree of solubility of the natural protein.
- Even when the gastric juices are enfeebled by acute and chronic disease, there is always enough of the digestive ferments present to deal with the protein present in the Essence. For this reason, it may confidently be prescribed in conditions involving minor degrees of hypochlorhydria.
- Brand's Essence liberates and strengthens the gastric juices. It provokes neither irritation of the delicate lining membranes of the stomach nor the spurious stimulation induced by alcohol and similarly-acting drugs. Most of the resultant free acid is absorbed by the soluble protein. This is present in sufficient quantity to protect the stomach membranes and thus diminish the discomfort of food digestion.
- The Essence can be taken in large quantities without causing thirst or diarrhoea, or throwing a strain upon the kidneys.
- There is practically no acute or chronic condition in which it cannot be given with safety and advantage.

Agents for India and Burma:
GRAHAMS TRADING CO., (India) LTD.
Calcutta .. Bombay .. Karachi .. Rangoon



When writing to advertisers, please mention the "Antiseptic."



CREMAFFIN

(Cream of Magnesia with Liquid Paraffin)

A pleasantly flavoured emulsion free from any oily taste. Cremaffin is an ideal antacid and gentle laxative.

CREAM OF MAGNESIA WAFERS

Each wafer contains the equivalent of one teaspoonful of Regesan Cream of Magnesia.

BURNOL

A creamy emulsion containing 0.1% of the powerful non-toxic antiseptic Neutral Acriflavine presented in handy collapsible tubes ready for immediate application.

BURNOL has given excellent results in the treatment of burns and scalds, tropical sores, tinea infections, Dhobie Itch, insect bites, minor injuries, ophthalmia of all types, suppurating wounds, and septic conditions generally.

For Prices and Particulars of Agents and Stockists apply to :

BOOTS PURE DRUG CO. LTD.
10, LALL BAZAR, - - - CALCUTTA.

MANUFACTURED BY
BOOTS PURE DRUG CO. LTD. NOTTINGHAM. ENGLAND

DMK 30

When writing to advertisers, please mention the "Antiseptic"

The Antiseptic

Estd. 1904.

A Monthly Journal of Medicine and Surgery.

Editors: Dr. U. RAMA RAU, M.L.C., & U. KRISHNA RAU, M.B., B.S.

Editorial and Publishing Offices: 323, THAMBU CHETTY ST., MADRAS.

Annual Subscription Rs. 5. Foreign, 10 Sh. Post Paid.

Vol. 37.

MAY, 1940.

No. 5.

EDITORIAL

Cardiac Emergencies—Diagnosis and Treatment

AMONG the most alarming of the medical emergencies are those arising from acute conditions within the heart. Immediate treatment is very imperative. In a very interesting and learned article on this subject in the Journal of the American Medical Association, DR. J. A. LYON discusses the various emergencies that the physician may often be called upon to treat.

Cardiac arrhythmias are first to be considered. Probably, in no cardiac emergency does death seem more instantly impending than in the Adams-Stokes syndrome. If the ventricles cease to pulsate for as long as eight or ten seconds, cerebral anæmia results and the patient suddenly loses consciousness. If the ventricles remain in diastole for more than fifteen seconds, the Adams-Stokes syndrome appears with convulsive seizures accompanying the syncope. The ventricular standstill, if untreated, may continue until sudden death occurs. The diagnosis of this condition is not difficult when the patient is seen in an attack. The very slow heart rate, or the absence of the apex beat, and the rapid venous pulsations in the neck due to the uninterrupted auricular action, distinguish it. As an emergency measure in the treatment of a prolonged attack of ventricular standstill, Adrenalin Hydrochloride (Epinephrine Hydrochloride) should be directly injected into the heart. From 0.5 to 1.5 cc. of a 1:1,000 solution of Epinephrine Hydrochloride may be injected through a long needle inserted into the fourth left interspace about 2.5 cm. from the sternal border. During the less severe attacks of convulsive syncope or when the attacks are recurring from 0.25 to 1 c.c. of a 1:1,000 solution of Adrenalin should be injected subcutaneously every few hours for as long as is necessary to maintain a heart-rate of over 30 beats per

minute. This drug stimulates ventricular irritability and shortens the diastole. It has an immediate but not a prolonged action. Ephedrine, Barium Chloride and Atropine Sulphate have all been used to control Adams-Stokes seizures, but they have not produced as uniform a result as Adrenalin.

A rapid ventricular rate approaching 200 beats per minute will at times produce alarming symptoms in persons without organic heart disease. Palpitation, dyspnoea, vertigo, syncope and severe præcordial pain may result. When such a rapid rate is superimposed on organic heart disease such as mitral stenosis or aortic regurgitation, acute congestive heart failure may supervene and may cause death if the ventricular rate is not decreased.

If the rapid beating of the ventricles is due to paroxysmal auricular tachycardia originating in the sinus node, the attack may be terminated by vagus pressure. If this does not benefit, it is claimed by the writer, that a drug called Mecholyl, (Acetyl-Beta-Methylcholine Hydrochloride) injected subcutaneously, in doses of one-sixth to one-third grain for young or light patients and one-half to 1 grain for elderly or obese patients, gives relief. The author emphasizes the necessity for knowing the reactions and disagreeable symptoms accompanying the action of the drug.

In all cases of paroxysmal ventricular tachycardia as well as in those cases of paroxysmal auricular tachycardia, where Mecholyl is contraindicated, Quinidine Sulphate should be given orally from 3-6 grains every two hours for six doses or more. However, in giving Quinidine, it is safer to test the patient for Quinidine idiosyncrasy. Electro-cardiograms should be taken at intervals in order to note any toxic effect of Quinidine calling for discontinuance of the drug.

In the treatment of paroxysmal auricular fibrillation, the use of Quinidine Sulphate is specifically indicated. Quinidine acts directly on the heart muscle, decreasing its irritability and conductivity and prolonging the period of diastole. Its administration is contra-indicated in cases of long standing or permanent auricular fibrillation, because of the possibility that with the restoration of normal auricular pulsation, portions of mural thrombi might be detached and carried into the circulation. When the ventricular rate is accelerated in a case of chronic auricular fibrillation, Digitalis should be administered.

Acute congestive heart failure is one of the most commonly seen conditions demanding emergency treatment. Cases of organic heart disease such as valvular incompetency and stenosis may remain compensated under a normal regimen; but when the burden of infection, fatigue, excitement, prolonged nervous strain or a rapid ventricular rate is added, congestive heart failure may suddenly appear. If the precipitating factor is not removed, the attack of failure may develop rapidly into an emergency.

In left ventricular failure, dyspnoea, orthopnoea and air hunger

appear and increase in severity with the degree of failure. The associated pulmonary congestion may give rise to a productive cough and to hæmoptysis. Patients with failure of the left side of the heart are subject to alarming and not infrequently fatal attacks of acute paroxysmal dyspnoea. The attacks which are usually nocturnal are marked by extreme dyspnoea and a cough which is productive of profuse frothy blood-tinged sputum. The blood pressure is at first elevated but later falls. As the pulmonary oedema becomes acute, circulatory collapse occurs accompanied by pallor and cyanosis, marked perspiration and a rapid feeble radial pulse. If treatment is delayed, death may ensue. The most important emergency measure is the subcutaneous administration of Morphine Sulphate, one-fourth grain, repeated in fifteen minutes if relief has not been obtained. Oxygen when available should be administered promptly. Phlebotomy of from 300 to 500 cc. of venous blood is frequently followed by striking improvement.

With regard to the use of Digitalis in acute emergency conditions, opinions differ, but the writer objects to its use in acute attack for the following three reasons: (1) The dosage is usually too small to be effective; (2) even though enough be given, its action is too slow to combat an emergency, and (3) the use of Digitalis may divert attention from more effective measures that should be employed.

When right ventricular failure is predominant, there are dyspnoea, marked fatigue, gastric and abdominal flatulence, nausea, venous engorgement, enlargement and tenderness of the liver, ascites, oedema of the extremities and at times, anasarca and hydrothorax. When a rapid elimination of the oedema is necessary, Salyrgan 1 c.c. of a 10 per cent. solution, should be injected intravenously, with or without the oral administration of Ammonium Chloride, 22½ grains (1.5 Gm.) four times daily, in enteric coated capsules of 7½ grains. The initial dose of Salyrgan may be repeated after the lapse of from two to three days, when, if needed, the dose may be doubled. If large accumulations of transudates are present in the thoracic or peritoneal cavities, it may be necessary to give the patient prompt relief by aspirating the fluid, in which case, a thoracentesis or an abdominal para-centesis should be carried out. The Karel diet should be instituted at once. Oxygen should be administered as an emergency measure, and Morphine Sulphate should be given freely to relieve the patient of dyspnoea and nervousness. The slow intravenous administration of from 50 to 100 c.c. of a hypertonic solution of Dextrose, of 50 per cent. concentration, has value in some cases in that it aids the failing heart muscle in replenishing lost glycogen. Absolute bed-rest should be maintained. Patients, even children, find an upright or semi-recumbent position more comfortable than recumbency, as pressure from the engorged liver is less distressing. The use of a cardiac bed, when available, is of value.

In extreme cases of failure, involving either the left or the right side or both sides of the heart when the circulation is gravely embarrassed, the patient must be given immediate relief. Strophanthin

should be administered intravenously, 1/100 grain, provided the patient has not been properly Digitalized as evidenced by an electrocardiogram. If the patient has been taking small doses of Digitalis during the preceding fourteen days, the dose of Strophanthin must be regulated accordingly. Strophanthin exerts an action on the heart similar to that produced by Digitalis: but, unlike Digitalis leaves, it acts almost at once. Its full effect is produced in about one hour and is prolonged for from twelve to twenty-four hours. The initial dose of Strophanthin may be followed by two subsequent doses at intervals of from eight to twelve hours. When possible, an electrocardiogram should be taken to determine the degree of Digitalis effect. After the acute stage has subsided, the patient may be put on the oral administration of powdered Digitalis leaves.

A discussion of congestive heart failure should not be closed, without making clear the distinction between cardiac failure and a failure of the peripheral circulation. Peripheral failure produces the symptoms and signs of collapse and shock, including pallor, perspiration, cold clammy skin, weak heart sounds, rapid thready pulse and low blood pressure. These phenomena are seen occasionally in surgical cases, in severe hæmorrhage, in dehydration, in coronary thrombosis, in arterial embolism and in other conditions which for any reason produce a sudden decrease in the volume of the circulating blood or a sudden collapse of the vascular bed. In certain of these cases, the heart itself may be entirely normal in its capacity to function properly, but the vascular system fails to return a normal volume of blood to heart.

The circulatory type of failure may require either of the two kinds of treatment, depending on the factor which has produced the collapse. If a sudden decrease in the blood volume from hæmorrhage or dehydration has been the precipitating factor, a transfusion of whole blood or the intravenous administration of small doses of 20 per cent Dextrose solution or of Salt solution is beneficial. If, however, depression of the central nervous system has been a contributing factor in the production of the shock through loss of vascular tone, drugs which act on the central nervous system should be administered, such as hot coffee, brandy, Strychnine Sulphate—one-sixtieth to one-fortieth grain (0.001 to 0.0015 gm.) subcutaneously, or Caffeine with Sodium Benzoate—7½ to 15 grains subcutaneously, or intravenously, if a more prompt response is desired. These drugs, as well as Coramine, Theobromine, Camphor and Aminophyllin, have at times been regarded as cardiac stimulants, but it is now generally accepted that their value lies in the effect which they produce on the peripheral vascular system or on the respiratory centre, secondary to a primary effect on the central nervous system. It has been pointed out that although Caffeine has an important stimulating effect on the nervous system and vasomotor centre and Coramine and Aminophyllin often stimulate and regulate a depressed respiratory centre, they are not known to have a direct effect on the action of the Myocardium. None of these drugs, therefore, should be substituted

for Digitalis in the treatment of congestive heart failure. Digitalis, however, is not known to exert a direct effect on the vascular system and, therefore, should not be administered in circulatory failure. It should be clearly understood by surgeons as well as by clinicians, that Digitalis therapy not only has no value in collapse or surgical shock but may even do harm in that it slows the heart rate. Much of the confusion concerning the results of Digitalis therapy in coronary thrombosis has come from an attempt to institute Digitalisation while vascular collapse was a predominant factor in the clinical picture. In the presence of shock, associated with low venous pressure, the use of digitalis is contraindicated.

The syndrome of acute coronary thrombosis is too well known to be discussed in detail. If pain is present, its continued intensity and prolonged duration and the ineffectiveness of the nitrites to control it, will differentiate it from the pain of angina pectoris. Pain may be absent in coronary thrombosis, and intense dyspnoea may be the striking symptom. Peripheral vascular failure with signs and symptoms of collapse and shock may be present without pain or dyspnoea. On even a tentative diagnosis of coronary occlusion, the patient should be put at complete rest in bed. If, within twenty-four or thirty-six hours, signs of infarction appear, such as a rise in temperature, an elevation of the leucocyte count and a pericardial friction rub, the patient should remain at rest for several weeks. The important drug in the emergency treatment of acute coronary thrombosis is Morphine Sulphate, which should be given promptly and in sufficient amounts to quiet the patient and to relieve him of pain. From one fourth to one half grain may be given subcutaneously and the dose repeated if necessary. If there is cyanosis, rapid heart action, dyspnoea, orthopnoea or other signs of myocardial anoxemia, Oxygen in concentrations of from 50 to 80 per cent should be administered by means of a tent. When dyspnoea is persistent or when vomiting is producing dehydration, the intravenous administration of a hypertonic solution of Dextrose, from 50 to 100 c.c. of a 50 per cent solution should be carried out slowly and cautiously and repeated once or twice daily as needed. Caffeine with Sodium Benzoate, 7½ grains, may be given intravenously, if there is circulatory collapse or shock. The intracardiac or subcutaneous injection of Epinephrine should be resorted to in the rare instances in which the Adams-Stokes syndrome complicates coronary occlusion. Quinidine Sulphate should be given orally when there is a rapid ventricular rate, but the drug should be administered guardedly. Digitalis therapy has no place in the treatment of coronary thrombosis, except when auricular flutter or chronic auricular fibrillation is present with a rapid ventricular rate or when congestive heart failure has supervened. It should be borne in mind that massive doses of Digitalis are not well tolerated during the healing stage of myocardial infarction. It should also be borne in mind that in an occasional heart, there are extensive areas of coronary sclerosis, myocardial degeneration and massive infarction which leave no cardiac muscle for drugs to act on.

A cardiac emergency occasionally arises in cases of acute pericarditis when a rapid accumulation of fluid in the pericardial sac causes marked cardiac compression. As the cardiac compression develops, the force of the ventricular contractions is diminished and signs of circulatory embarrassment appear. The venous pressure increases and the veins of the neck appear dilated and engorged. The arterial pressure falls and the pulse volume is diminished. The heart sounds become distant and faint. The area of cardiac dullness is increased usually to the right and to the left. Friction rub may sometimes be heard. Ewart's sign, due to compression of the left lung may appear at the angle of the left scapula as dullness, bronchial breathing and bronchophony.

Treatment should be directed both to the relief of the cardiac compression and to the control of the underlying condition whatever the infection may be which is responsible for the acute pericarditis. If pain is present and severe, Morphine Sulphate from one-eighth to one-fourth grain is administered. If the pain is not severe Codeine, Salicylates or Bromides may be given. For pericardial effusion accompanied by marked circulatory embarrassment, pericardiocentesis, promptly carried out, may be a life-saving measure.

In the treatment of cardiac emergencies, the time element is often of inestimable importance. The proper drug, if administered promptly, will give immediate relief and may, in some cases, be a means of saving the patient's life. We would strongly advise our readers to read the excellent article in the original referred to in the first paragraph of this article.

GLEANINGS FROM MEDICAL PRESS

Medicine and Therapeutics

Injection of Sodium Salts in Sciatica.—SUTTON says that this investigation was instigated by a report which PORTER made in 1925. The treatment consists of the administration of both Sodium Salicylate and Sodium Iodide in a single solution by intravenous injection. Each injection consisted of 20 cc. of an aqueous solution containing 1 Gm. of Sodium Salicylate and 1 Gm. of Sodium Iodide. The solution was prepared as follows: The Sodium Salts were dissolved in previously sterilized and twice distilled water without warming. The solution was filtered through a Jena glass bowl and put up in 20 cc. sterile ampules, which were quickly sealed, care being taken that the solution did not become too hot. Sterility was further insured by heating to 70 C. for an hour on three consecutive days. The solution is readily decomposed by heat over 80 C. and by light. The ampules were of plain (not colored) glass, so that any subsequent decomposition of the solution would be readily detected. Prepared in this way the solution remains clear for three months or longer. The injections were made slowly with an ordinary 20 cc. record syringe. Any inadvertent

injection into the tissues causes great pain, without, however, any subsequent sloughing. The author resorted to this treatment in thirty-two cases of sciatica, of which twenty were primary and twelve secondary. In the twenty cases of primary sciatica, pain ceased usually after about ten minutes. If a second injection was necessary the result was better than that of the first injection. In the twelve cases of secondary sciatica due to some extraneous pathologic condition, pain was diminished but not abolished and a second injection tended to produce less effect than in the first. Any improvement in secondary sciatica is probably due to the analgesic action of the sodium salicylate, but in primary sciatica, in all likelihood "rheumatic," the effect of the Sodium Salicylate appears to be specific rather than symptomatic. The cases treated this way are too few to justify definite conclusions, nevertheless, the intravenous injection of Sodium Salicylate and Sodium Iodide does rapidly cure uncomplicated cases of sciatica; on the other hand, its lack of effect on secondary sciatica suggests its value in diagnosis.—J. A. M. A.

Treatment of Acute Gonorrhœal Urethritis.—To evaluate four different methods of treating acute anterior gonorrhœal urethritis, MORSE and HIRSCH treated twenty-five cases by each method: Sulfadilamide, Sulfanilamide and anterior injections of Silver Protein, anterior irrigations with Silver Protein preceded by Potassium Permanganate irrigations, and daily anterior irrigations with a suspension of colloidal Silver. All the patients were seen within five days from the onset of discharge before having any previous treatment and only initial infections were selected. The dosage of Sulfanilamide of the first group of patients was 80 Gm. For the first two days 5.33 Gm, was given each day in four divided doses, 4 Gm. for the following two days and then 2.66 Gm. until the entire amount had been taken. The average duration of the disease in these cases was 39.1 days with extremes of from nine to ninety-three days. From the standpoint of complications, 56 per cent had none. Arthritis or epididymitis did not develop in any patient. Prostatitis developed in 8 per cent and the infection extended into the posterior urethra in 36 per cent. The average duration of the disease in the second group was fifty-one days. The extremes were sixteen and ninety-three days. There were no complications in 32 per cent of the cases, the infection in 52 per cent extended to the posterior urethra, epididymitis developed in 12 per cent and prostatitis developed in 4 per cent. The average duration of the disease of the third group of patients was fifty-one days with extremes of from thirty-eight to eighty-two days. The incidence of complications in this group was significantly higher. In only 30 per cent of the cases was the infection kept localized to the anterior urethra. In 20 per cent the only complication was a posterior urethritis, but in 50 per cent epididymitis or prostatitis developed. The average duration of the disease of the remaining twenty-five patients treated by daily anterior irrigations of a suspension of colloidal Silver was 46.9 days, with extremes of eighteen and ninety-six days. Of these

cases 64 per cent remained uncomplicated for the duration of the disease, in 24 per cent the disease extended into the posterior urethra and in 4 per cent prostatitis, epididymitis or arthritis developed. The authors' conclusions are that Sulfanilamide without supplementary Silver irrigations gave the most satisfactory results and that a colloidal suspension of metallic Silver is preferable to protein Silver preparations in cases in which the use of Silver is desirable.—J. A. M. A.

The Treatment of Heart Failure During Anæsthesia.—Following extensive experimentation D. DANIELOPOLU and I. MARCOU (*Presse medicale*, January 16, 1940, 48, 44) advocate a method of cardiac resuscitation in cases of heart failure during anæsthesia by means of the injection of a solution of Atropine, Adrenaline, and Strophanthin, followed by cardiac massage to ensure the penetration of the solution into the coronary circulation. Adrenaline has been used by other authors as a cardiac stimulant, but the addition of Atropine prevents the inhibitory parasympathetic action of the Adrenaline, and Strophanthin strengthens the Adrenaline action. The formula of the mixture used is:—

Atropine Sulphate	...	5 cgm.
Adrenaline	...	10 cgm.
g-Strophanthin	...	1 cgm.
Distilled water	...	100 gm.

1 c.cm. of the solution contains $\frac{1}{2}$ mgm. Atropine, 1 mgm. Adrenaline, and $\frac{1}{10}$ mgm. Strophanthin.

The technique is as follows:—Artificial respiration must be begun immediately. Meanwhile the abdomen is opened above the umbilicus to permit diaphragmatic massage of the heart, and an injection of 2 c.cm. of the Atropine-Adrenaline-Strophanthin solution is made into the left ventricle (the action of Adrenaline is more rapid in the left ventricle than in the right), which must be penetrated so that 1 c.cm. of the solution is left in the cavity and the other 1 c.cm. is injected on withdrawing the needle, whereby the solution reaches the right cavities as well as the left, and also the myocardium for stimulation of the muscle. Immediately after the intracardiac injection the surgeon begins to massage the heart—it is emphasized that intracardiac massage should not be begun before the administration of Atropine, or ventricular fibrillation may result. If the procedure is not successful the first time a second intracardiac injection can be given, again followed by cardiac massage until the contractions are reinstated. During the entire procedure an assistant carries on artificial respiration and, from time to time, carotid sinus compression. The compression must be made after the administration of Atropine, however, in order to prevent the inhibitory effect of the carotid sinus reflex on the heart. The authors state that the ventricle can be injected fifteen to twenty times without causing cardiac injury or hæmorrhage.—*Practitioner*.

Surgery

Rupture of Liver.—LAMB reviews sixty cases of rupture of the liver and shows that it is most commonly due to violent injuries but that seemingly trivial injuries may likewise cause laceration. Rupture of the liver is much more frequent in young people than in older ones. This can be accounted for on the basis of violence alone, for the young engage in many more daring activities than do the old. Another reason is that the bony protection in the young is much more supple and that minor blows are therefore more likely to reach the liver. The ratio of male to female patients in this series was 5:1. Every one of the women had sustained injury as a result of an automobile accident. Although the men had been injured in all sorts of accidents, most of their injuries had been produced by automobiles. One child fell while walking the curbing and struck his right lower ribs. Another coasted into a tree. Another was kicked in the side by a horse. A few were injured while playing games, chiefly football. The wheel of some vehicle traversing the abdomen was a common cause of injury. Falling from a height was the etiologic factor in a number of cases. It is absolutely essential to recognize rupture of the liver early in order that proper care may be instituted promptly. THOLÉ states that the mortality increases from 2 to 5 per cent with each hour's delay in treatment. The author's statistics confirm this assertion. An exact diagnosis cannot be made except on exploration, but the need of immediate laparotomy can be shown without great difficulty. Given a patient who has met with a blow to the midtrunk and soon shows signs of shock, together with tenderness in the right upper quadrant, rebound tenderness (blood in the peritoneal cavity) and an elevated white cell count (bleeding in a serous cavity), an exploration is mandatory. The patient should receive whole blood before, during and after the operation in sufficient quantities to keep the blood pressure within the range of safety. He should be treated for his shock on the operating floor and if possible on the operating table, so that movement may be reduced to a minimum. Except for exposure, no type of incision possesses any special advantage. Transverse incision gives a better exposure for barrel-chested patients but is of doubtful advantage for thin patients. Infection after liver injury is common. Drainage of bile occurs in 50 per cent of the cases but ceases in every case by the third week. The commonest postoperative complications are in the order of frequency: peritonitis, postoperative hæmorrhage, subdiaphragmatic abscess, intrahepatic abscess and abscess of the lesser peritoneal cavity. In the present series, twenty-six patients died before operation could be performed. Of the thirty-four operated on, fifteen died and nineteen recovered, a mortality rate of 44 per cent. The mortality rate, however, for the entire series of sixty cases was 68 per cent.—J. A. M. A.

Zinc Peroxide in Treatment of Diabetic Gangrene.—Diluted solution of Sodium Hypochlorite and other Hypochlorites do not act favorably on tissues which have impaired circulation, as in diabetic

gangrene of the extremities. They inhibit the development of granulation tissue and thus delay the reparative process. Zinc Peroxide, MELENEY states, markedly inhibits the growth of the hemolytic streptococci and all anaerobic bacteria, including the organisms causing gas gangrene and the anaerobic streptococci. It neutralizes or inactivates the toxins formed by these organisms and at the same time encourages the reparative process by the stimulation of granulation tissue. Zinc peroxide, which is a white powder, should be suspended in sterile distilled water and applied to every part of the wound surface. The wound should then be covered with fine meshed gauze soaked in the same material. This should be covered with compresses saturated with sterile distilled water and these compresses in turn covered with petrolatum gauze or some other impermeable material to prevent evaporation. The dressing should be changed every twenty-four hours, the old material irrigated off, and a new dressing applied. It is important to use material which has been proved to be effective in the production of Oxygen, and it is essential that adequate contact be obtained between the Zinc Peroxide suspension and every part of the wound surface. The use of Sulfanilamide are present. If hemolytic streptococci and anaerobic organisms are present at the site of amputation, Zinc Peroxide should be used as a prophylactic to prevent the development of infection in the stump, or if infection has developed it should be used as early as possible to control it. If reamputation is necessary, it should be used immediately to prevent infection in the second operative site.—J. A. M. A.

Surgical Treatment of Hypertension.—DAVIS and BARKER find that the majority of hypertensive patients observed by them respond favorably to the administration of Potassium Thiocyanate as evidenced by a drop in the systolic and diastolic blood pressures and a fall in the blood cholesterol, total proteins and hematocrit reading. Headache, insomnia, nervousness, fatigue, dyspnoea and heart consciousness are relieved, and an actual decrease in the size of the heart occurs. However, there is a small group of patients who are resistant to Thiocyanate therapy. The drug must be pushed to the toxic level in treating these individuals before any effect can be obtained, and the lack of a safe margin makes it impossible to control symptoms or blood pressure successfully. In their experience with these patients, bilateral supradiaphragmatic section of the splanchnic nerves alone has failed to decrease their blood pressure or to cause a fall in the chemical constituents of the blood. However, after operation the authors noticed that four patients responded to the administration of Thiocyanate. The blood pressure, systolic and diastolic, has shown a definite drop and there has been a decided improvement in the condition of the patients. There has been a parallel decrease in the blood cholesterol, total protein, urea nitrogen and hematocrit readings which compares favorably with the same responses obtained by patients with hypertension who are sensitive to the Thiocyanates.

The authors believe that section of the splanchnic nerves has in some unknown manner increased the sensitivity of a small number of patients to Thiocyanates.—J. A. M. A.

Ophthalmology

Vitamin D Complex in Progressive Myopia.—KNAPP selected fifty-three patients because it was believed that their myopia would progress. Their age varied from 3 to 20 years. Their myopia ranged from -0.25 to -41 diopters. Vitamin D and calcium were prescribed. The dosage of the latter varied with the milk intake. For each glass of milk less than a quart two tablets of the calcium were added. Of the fifty-three patients, insufficient data were obtained on seven. Of the remaining forty-six, only twelve patients took their medication regularly. Six of these twelve showed a reduction in their myopia, two remained stationary and four progressed. Considering the forty-six patients without regard to the regularity of medication, sixteen had a reduction in their myopia, seven remained stationary, twenty-one progressed and two displayed a decrease of myopia in the left eye and a progression in the right. In other words, 66 $\frac{2}{3}$ per cent. of the patients who had medication either manifested a reduction in their myopia or remained stationary. It appears to the author that a disturbance in the vitamin D calcium-phosphorus metabolism is concerned in the etiology of myopia. In the presence of a calcium imbalance there may be a weakening of the fibrous tunic, which may give rise to myopia. Once a condition of progressive myopia has been established, treatment with the vitamin D complex is indicated. The myopic eyes that respond to this therapy may undergo an actual shrinkage of the globe. For the prevention of the onset of myopia, the vitamin D complex probably has another field of usefulness. Given a patient showing a diminishing degree of hyperopia and one who is approaching the axial myopia side, it would be well to fortify his diet with vitamin D and calcium. Assuming a disorder of the vitamin D complex metabolism to be a basic factor in the etiology of myopia, the author believes that the rarity of myopia in the American Indian, the fact that the rural inhabitant is free from this complaint than the one residing in a city, that fewer myopic eyes are found in high altitudes and the prevalence of myopia in China are readily explained. Greater food consciousness, especially in relation to vitamin supply, explains why fewer cases of progressive myopia are seen today.—J. A. M. A.

Electrical Cataract Following Electrical Trauma.—SKYDSGAARD thinks that, of eye injuries resulting from electrical trauma in persons struck by lightning or in those who work with high tension currents, one of the most important is the delayed cataract which occasionally appears. He reports the history of a man aged 44 who was employed on high tension work and who, about a year and a half ago, received an electric shock (6,000 volts). He lost consciousness and when brought to the hospital he was found to have extensive burns on the

left hand and wrist and on the right arm. There were also burns on the left side of the face and on the nose. During the first half year after the accident the patient noticed nothing wrong with his eyes, but after that there was a gradually increasing loss of vision in the right eye and a cataract was discovered. The anterior surface of the lens had a cataractous opacity of somewhat irregular polygonal form, measuring about 1.5 by 1.5 mm. Slit lamp examination showed that the opacity was localized in the anterior capsule and the outermost sub-capsular parts of the lens. The opacity projected slightly above the level of the remainder of the lens capsule; the shagreen pattern of the other parts of the anterior surface of the lens was normal. In addition to the cataractous part there was seen in the remainder of the most anterior part of the lens capsule a net work of fine, linear, cataractous opacities, resembling cotton fibres, their arrangements having no relation to the lenticular structure. In the interstices there were fine, punctate opacities. Ophthalmoscopy revealed a normal fundus and the tension was normal. The field of vision was normal for hand movements. The left eye was healthy in all respects. The author is convinced that this cataract was caused by the electrical trauma. He says that electrical cataracts often present only features that are common to a large group of cataracts. He stresses that the electrical cataract appears late and that it may be either unilateral or bilateral. Contrary to the opinions of some investigators, he maintains that electrical lesions in the proximity of the eye are not an essential condition for the development of the cataract. The strength of the current does not appear to be of decisive importance in the production of cataract. A tension of 500 volts may result in mature cataract, while tensions even up to 80,000 volts have been known to produce only partial cataract. It is probable that in this respect considerable importance attaches to the duration of the passage of the current. The cataract may be regarded as due (1) to the mechanical effects of the electric current or the lightning on the lens or on its suspensory ligaments, or to calorific or chemical (electrolytic) changes resulting in the destruction of the epithelium of the lens capsule or (2) to impairment of the nourishment of the lens owing to inflammation produced in the ciliary body and in the iris. Finally, (3) the aqueous may be altered by the electrolytic effect of the current. None of these theories alone would appear to suffice for the explanation of all cases, whereas a combination of them provides a plausible explanation.—*J.A.M.A.*

Obstetrics and Gynaecology

Amyl Nitrite in Treatment of Bandl's Ring.—In 1934 CROFT published in the 'Lancet' two cases in which the inhalation of only few drops of Amyl Nitrite effected such complete relaxation of Bandl's ring that labour could be terminated in a couple of minutes. Impressed by this, E. HOLM determined that when next he encountered Bandl's ring he would let the patient inhale Amyl Nitrite, but with no success. Quite recently, however, he has verified CROFT's claims.

In a 2-para, aged 26, pregnancy began at the end of Jan. 1938, and labour on Sept. 22. The membranes having ruptured, and the progress being slow, she was admitted to hospital. Labour pains had ceased, and the infant's heart-sounds could not be heard. The head had descended into the pelvis, and the cervix was fully dilated. In the hope that labour could be completed with forceps, they were applied under ether anaesthesia, but even on forcible traction the head hardly moved. Episiotomy having been performed, the head of a macerated foetus was made to protrude beyond the vulva, but the rest of the body did not follow. On exploration, a deep-seated, very tense Bandl's ring was found to grip the neck so tightly that it was almost impossible to insert one finger between them. Even under deep anaesthesia the ring remained contracted, and an attempt to twist the foetus out proved abortive. The patient inhaled three drops of amyl nitrite while the obstetrician's hand remained within the pelvis, controlling the behaviour of the ring. Within a minute it had suddenly relaxed, so that without difficulty it was possible to extract the foetus. There was no great hæmorrhage, but as the placenta could not be expressed from without, extraction from within was undertaken. Bandl's ring had formed again, and gripped the placenta, half of which was above it. A couple of fingers could, however, be inserted between the two, and the placenta coaxed out of the uterus intact. Uneventful recovery followed.—*Clinical Journal*.

Abortion as Complication of Operation in the Pregnant Woman.—J. E. LOCKNER and A. S. TULSKY (*American Journal of Surgery*, 46:362, Nov. 1939) report that in 108 operations on pregnant women (excluding operative delivery), there were 5 abortions, an incidence of 4.66 per cent. Of the 108 operations 90 were intra-abdominal and 18 extra-abdominal; all the abortions occurred in the intra-abdominal group. Most of the operations were done in the first trimester of pregnancy and all the abortions occurred in this period; 4 of the 5 abortions resulted from operative procedures done eight weeks after the last menstrual period; the fifth twelve weeks after the last period, i.e. "close to the date upon which the patient would have menstruated had she not been pregnant." One abortion occurred after appendectomy on the thirteenth post-operative day (one in 32 appendectomies). One occurred after myomectomy (one in 17 myomectomies); cramps and bleeding developed on the fifth postoperative day; one occurred after cholecystectomy. Two abortions occurred after ovarian operations (2 in 27 oophorectomies and ovarian resections); in 5 of these operations it was noted that the corpus luteum was removed, and both of the abortions occurred in this group; one abortion occurred on the second, the other on the eleventh post-operative day. In 9 of the cases in this series corpus luteum hormone was given post-operatively, none of these patients aborted; the number of cases so treated is "too small to make any deductions." But it has been shown that this hormone inhibits motility of the pregnant uterus, and the authors are convinced that the administration of

Progesterone following operation on pregnant women should be tried with the aim of decreasing the incidence of post-operative abortions. —*Medical Times*.

Palliative Treatment of Dysmenorrhea.—AINLAY used a combination of three drugs for the palliative treatment of thirty-four cases of primary and four cases of organic or secondary dysmenorrhea. The ages of the patients ranged from 14 to 44 years. The combination treatment consisted of 5 grains (0.3 Gm.) of Acetylsalicylic Acid, 3 grains (0.2 Gm.) of Acetophenetidin and three-fourth grain (0.05 Gm.) of Propadrine Hydrochloride. The value of Acetylsalicylic Acid as an analgesic with little depression is well known. It is, however, ineffective for severe pain, and especially cramplike pain. Acetophenetidin, while probably possessing more analgesic properties, is apparently much more depressing in its action and seems to be especially so during menstruation. Like Acetylsalicylic Acid it is not capable of relieving cramplike pains. Propadrine Hydrochloride increases the effectiveness of the other two ingredients but counteract any tendency to depression afterward. It is believed but not proved entirely that Propadrine Hydrochloride is a marked antispasmodic and decongestant without side effects and with no possible chance for anuria or nausea. The patients were given three capsules of the combined drugs daily at the first onset of distress. This medication was continued until the third day of the period. Pain after the third day is not relieved well by the preparation and should lead one to suspect some organic lesion. The capsules were given the first month, skipped the second month and repeated the third month, in an attempt to cover the variation that may be expected in some women. The results showed that the combination of the three drugs is more effective in the primary type of dysmenorrhea and also if taken immediately on the appearance of symptoms. There is a marked effect within a few minutes after taking the capsule. All patients were either partially or completely relieved. The relief from physical and mental depression is often more gratifying to the patient than the relief from pain. The treatment does not depress the kidneys, nor does it influence the regularity or the amount of the menstrual flow.—*J. A. M. A.*

NOTICE

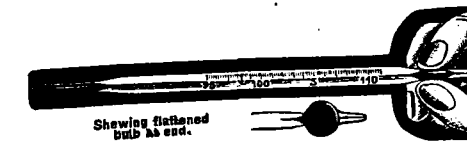
A. P. Parikh, Registrar, Bombay Medical Council, Bombay, notifies as follows:—

DR. V. L. HINGORANI, L.C.P.S. is administered a warning by the Executive Committee of the Bombay Medical Council for contravening the provisions of Clause (a) of Rule 6 of the Warning Notice relating to advertising in the matter of printing his letter heads. He is also warned to so regulate his conduct hereafter as to conform strictly to the provisions of the Code of Medical Ethics, this being the second occasion when he is administered a warning.

ZEAL'S CLINICAL THERMOMETERS THE REPELLO (REGD.)

A 30-second pushed back in an instant.

GUARANTEED
ACCURATE



NO
SHAKING DOWN
REQUIRED

NEW IMPROVED LENS FINDER

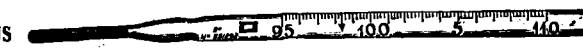
THE ORIGINAL AND RELIABLE MAGNIFYING CLINICAL ON THE MARKET

IN FOCUS



GUARANTEED

OUT OF FOCUS



ACCURATE

REGISTERED
TRADE MARK

THE SQUARE MARK ENGRAVED ON THE
LENS FRONT LOCATES THE MERCURY
COLUMN IMMEDIATELY
BEWARE OF IMITATIONS

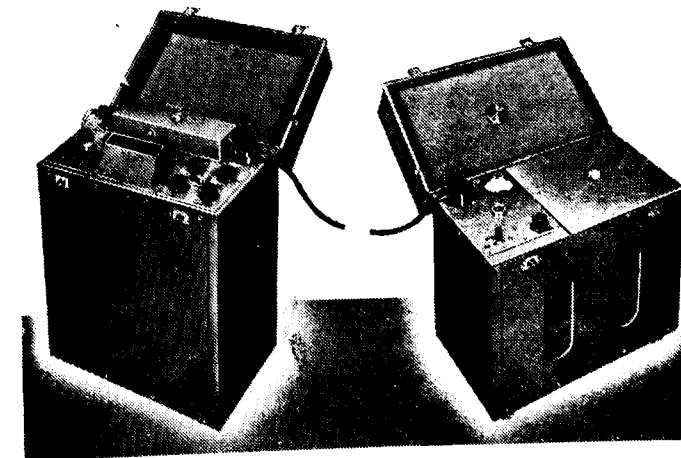
REGISTERED
TRADE MARK

G. H. Zeal Ltd., Morden Road, Merton, London, S.W. 19, Eng.
THERMOMETER MANUFACTURERS.

Established 1888

Cables, Zealdom Smith, London.

COSSOR-ROBERTSON ELECTROCARDIOGRAPH



Developed through the collaboration of physician and engineer, this practical and reliable Electrocardiograph has many unusual advantages. Continuous visual and photographic recording is a unique feature indispensable for accurate and thorough diagnosis. Of all recording devices, the Cathode Ray Tube (as used) alone can produce an instantaneous two-dimensional and true picture of the heart potentials.

Simple • Silent • Portable • Rapid Direct Visual Observation •
Distortionless Automatic Photo-Recording • Universal Operation

Full technical details and prices of equipment for A. C. Mains and Battery use
will be gladly supplied on application.

Sole Distributors in India:

THE SCIENTIFIC INSTRUMENT CO., LTD.

5A, Albert Road,
ALLAHABAD.

240, Hornby Road,
BOMBAY.

11, Esplanade East,
CALCUTTA.

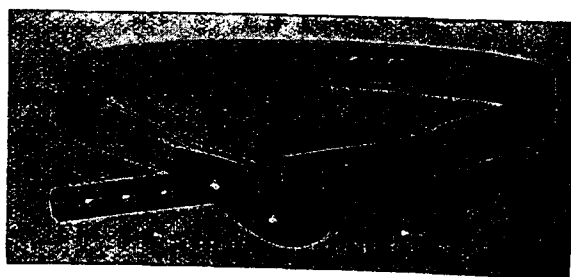
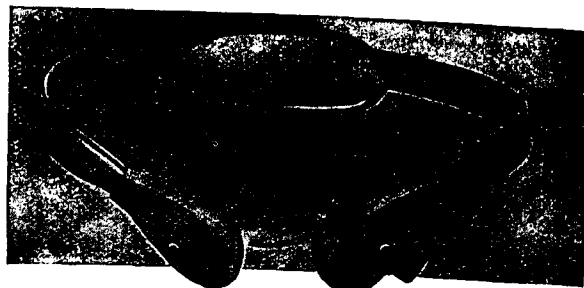
30, Mount Road,
MADRAS.

INDEX TO ADVERTISERS, MAY, 40.

	PAGE.		PAGE
Alembic Chemical Works Co. Ltd.	21, 28	Horlick's Malted Milk Co.	14
Allen and Hanburys Ltd.	5	Indian & Eastern Chemist	38
Antiseptic Press	36	Krishna Pharmacy	37
Astier Laboratories	37	Lister Antiseptics & Dressings Co.	10
Atlantis (East) Ltd.	21	Jammi Venkataramanayya	18
Banerji P.	30	Journal of Indian Medical Association	36
Bench T. C. & Co.	3	John Wyeth & Brother Ltd.	20
Bengal Chemical and Pharmaceutical Works.	Inside of back cover	Loucatos G. & Co.	24
Bonnaire & Co., Ltd.	11	Martin & Harris Ltd.	6
Boots Pure Drug Co., Ltd.	32	Martin H. Smith Co. N. Y.	9, 17
Brahmachari Research Institute	17	May & Baker Ltd.	25
Brand & Co. Ltd.	31	Parke Davis & Co.	2
British Drug Houses Ltd.	22	Petrolagar Laboratories Ltd.	4
Burroughs Wellcome & Co.	23	Rendell W. J. Ltd.	33
Calcutta Medical Journal	30	Scientific Instrument Co.	37
Carnrick G. W. Co.	18	Seller L. H.	17
Coleman & Co., Ltd.	1	Silten Ltd.	34, 36, 39
Cow & Gate	29	Sri Krishnan Bros.	16
Crookes Laboratories Ltd.	15	Stephen Smith & Co., Ltd.	38
Denver Chemical & Mfg. Co.	12	Thacker Spink & Co. Ltd.	19, 37
Eli Lilly & Co.	Inside Front Cover	Thakore T. M. & Co.	28
Galleno Pharmaceutical Works	10	Union Drug Co. Ltd.	11
Glaxo Laboratories Ltd.	7, 13, 26, 27	United French Laboratories	35
Govt. Industrial & Testing Laboratory	3	Victor X-Ray Corporation (India) Ltd.	8
Health	40	William R. Warner & Co.	33
Hewlett C. J. & Son Ltd.	9	Zeal G. H. Ltd.	

Trusses for
Hernia

We have a large assortment of various sizes for infants and adults.

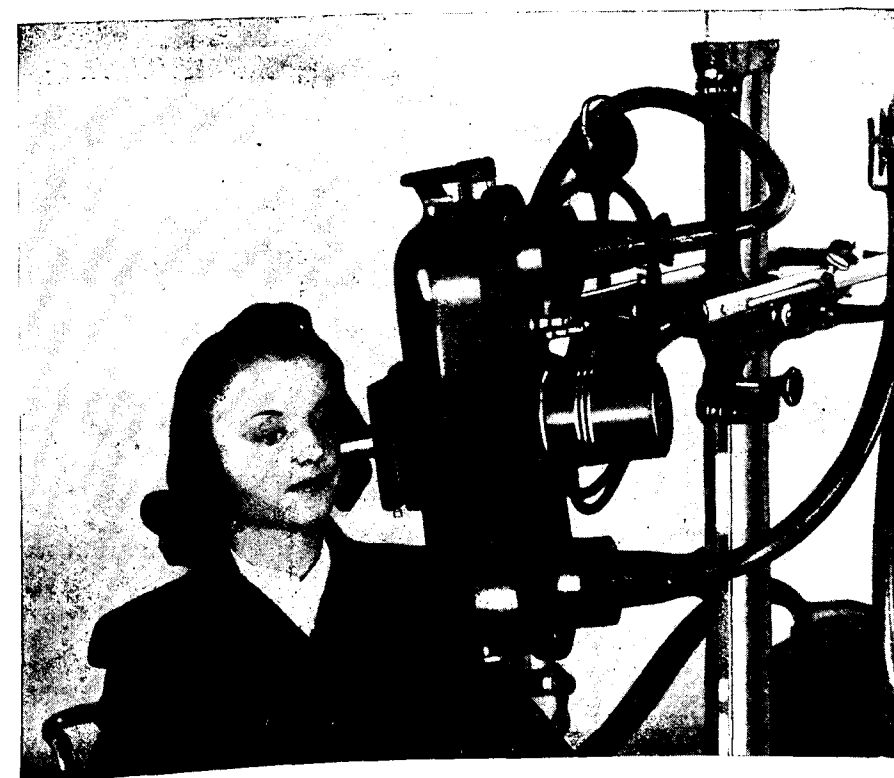


PRICE

Leather, Single	Rs. 6
Do Double	Rs. 12
Vulcanite, Single	Rs. 10
Do Double	Rs. 20

Booklet how to measure for and fit up a truss for hernia will be sent free.

From SRI KRISHNAN BROS., Post Box 166, MADRAS.



DESIGNED TO DO ONE JOB WELL

WHAT do you consider essential in an X-ray tube for superficial and intermediate therapy?

To this question radiologists answered: "The tube which covers the largest single treatment areas at the shortest focal-skin distances offers very definite advantages."

Accordingly, Coolidge tube engineers sought a means of obtaining the maximum possibilities in this respect. And the ultimate design, the Model S.P. 140 Coolidge tube, in which a 30 degree target is used, presents distinct operating advantages in the 60-140 kv.p. therapeutic range. For example, with this tube you can irradiate a field equal in diameter to the focal-skin distance used. Moreover, a focal-skin distance as short as 9.5 cm. is obtainable.

The 30-degree target is only one of a number of reasons why the Model SP-140 is ideally adaptable to the varied requirements in superficial and intermediate X-ray therapy, and provides those operating advantages which radiologists consider of first importance. You will find more interesting facts about the SP-140 in the new free booklet, Pub.—"7A. 430A. 1." Send for your copy today, naturally there is no obligation.

GENERAL ELECTRIC
X-RAY CORPORATION

2012 Jackson Boulevard Chicago, Ill., U.S.A.

FORMERLY VICTOR X-RAY CORPORATION

Exclusive Distributors in India:

VICTOR X-RAY CORPORATION (India) LTD.,

Bombay:	Ballard Estate P. B. 992.
Lahore:	The Mall, P. B. 181.
Calcutta:	13, Hare St., P. B. 2007
Bangalore City:	Narasimharaja Road
Lucknow:	1715, Birkett Road
Colombo:	3, 44th Lane, Wellawatta.

When writing to advertisers, please mention the "Antiseptic".

ARTIFICIAL EYES



The disfigurement caused by loss of an eye may be removed by the substitution of an artificial one. Artificial eyes, when properly matched defy detection. We keep a very large assortment of Artificial Eyes, and shall be pleased to send a selection on receipt of a deposit of Rs. 25 which will be refunded on return of the packet.

When ordering kindly furnish us with the following particulars:

Is the eye required for the right or the left one? Is the sound eye prominent or shrunken? What is the colour of the eye, clean white or of a yellowish tinge?

Full instructions as to how to insert and remove the eyes will be given.

Price Rs. 5 to 10 each.

SRI KRISHNAN BROS., OPTICIANS,
P. O. BOX 166 **MADRAS.**

JOURNAL OF THE Indian Medical Association

EDITED BY
SIR NILRATAN SIRCAR,
KT., M.A., M.D., D.C.L., ETC.

WITH THE HELP OF
A STRONG ALL-INDIA EDITORIAL
BOARD

*The Official Monthly Publication of the
Indian Medical Association.*

Features:

1. Original Articles.
2. Case-Reports.
3. Society Proceedings.
4. Valuable abstracts from leading Medical Journals from all over the world.

Published on the First Day of the Month

Annual Subscription Rs. 6 post free.

Free to members of the Indian Medical Association.

AN EXCELLENT MEDIUM FOR ADVERTISEMENT

For particulars write to Secretary,
Samavaya Mansions, Calcutta

Printing for the Medical Profession. ANTISEPTIC PRESS

Equipped with high-class machines, types and under expert supervision, offers efficient service in matters of display, promptitude and neatness. Good printing of any size and magnitude in English, Tamil, Telugu and Canarese, and Book Binding. Publishing and Colour Printing are undertaken. Prices competitive, consistent with quality.

Apply to:

Manager, 10, Thambu Chetty Street,
G. T., Madras.

THE HIGHEST AWARDS AT INTERNATIONAL EXHIBITIONS
EXCELLENT ARHEOL BALSAMIC
 $C_{15}H_{24}O$
THE PURIFIED ACTIVE PRINCIPLE OF
SANDALWOOD OIL IN A DEPENDABLE
AND NON-IRRITATING FORM.
For GONORRHEA, CYSTITIS,
PYELITIS, PYELO-NEPHRITIS,
PROSTATITIS, URETHRITIS
AND VESICAL CATARRH.

NEO-RIODINE

Iodine Treatment without Iodism
in 2 Forms.

An aqueous solution of organic iodine.

**IMMEDIATE AND INTENSIVE ACTION BY
NEO-RIODINE.**

For Internal use RIODINE CAPSULES.

Ask for literature

Dr. P. ASTIER LABORATORIES

P. O. B. 740, P. O. B. 460, P. O. B. 248,
Bombay. Madras. Karachi.

DIABETES

An entirely New Invention of herbal combination for the complete and permanent cure of **Diabetes** by Dr. D. R. Mehta, M.P.L., L.P.H. Price Rs. 4 only for 16 powders for 8 days.

Manager, **KRISHNA PHARMACY,**
'KRISHNA BUILDING'
Ludhiana (Punjab) India

YOUR EYE

Does it trouble you? If so, try **SELLER'S LOTUS HONEY**, the safest, surest and most highly praised Nature's cure for Eye-diseases. Cures even Cataract etc. Literature free.

SRI KRISHNAN BROS.,

Post Box 166, : : G. T., MADRAS.

A-O

INDICATED IN CASES OF

A SPECIFIC VACCINE Made of TUBERCLE BACILLI OF HUMAN TYPE

There are three practical uses to which

A-O

may be put

- (I) Prophylactic
- (II) Diagnostic and Prognostic
- (III) Therapeutic

Literature on request.

Prepared by:

THE ARIMA INSTITUTE,
Osaka, Japan.

Head Office: 43, Churchgate Street, Fort, Bombay.
Readymoney Mansions.

Agents: **T. M. THAKORE & CO.,**
1/10 & 10'A, Stringer Street,
G. T., MADRAS.

- Latent or frank tuberculosis.
- Pulmonary tuberculosis (Apical catarrh)
- Surgical and urogenital tuberculosis.
- Ophthalmological tuberculosis.
- Dermal tuberculosis.
- Pleurisy and Peritonitis in Convalescence
- Disorderly menstruation due to innate weakness
- Glandular affections
- Laryngeal and intestinal tuberculosis.
- Is also useful as a diagnosticum and as a prophylactic of tuberculosis.
- A-O is an agent which calls forth or increases in an organism the immunizing powers through a biological reaction of its own.

When writing to advertisers, please mention the

CLINICAL OBSTETRICS

By A. L. MUDALIAR, B.A., M.D., F.C.O.G.

Professor of Obstetrics, Madras Medical College, University of Madras; Second Obstetric Physician and Gynaecologist, Government Hospital for Women and Children, Egmore, Madras.

With 213 Text Illustrations of which 9 in colour. Price Rs. 23-10

This is a well-illustrated practical guide to normal midwifery and the diagnosis and management of obstetrical difficulties. The teaching incorporated is modern and up to date, and in addition there is to be found throughout an expression of personal opinion which is the result of a wide and mature experience.

The introduction of a comprehensive section on tropical diseases in relation to obstetrics is a noteworthy feature of the book. Here the reader cannot fail to be impressed with the even greater scope and increased value of adequate antenatal care in countries where these diseases are met with.

It will be of great value to practitioners and to students in India, the East, and tropical countries.

THACKER SPINK & CO. (1933) LTD.
Post Box 54, CALCUTTA.

Advertise to the TRADE



Published exclusively for the Chemical, Drug and Allied trades throughout India, Burma and Ceylon.

Official Organ of the Bengal Pharmaceutical Association and the United Provinces Pharmaceutical Association.

in INDIAN AND EASTERN CHEMIST

Subscription rate Rs. 5 per annum, post free. The news and literary articles have special interest for the Medical Profession.

Specimen copy and advertising rates on application to:—
5, MISSION ROW, CALCUTTA.

When writing to advertisers, please mention the "Antiseptic"

CUTS AND WOUNDS! BURNS AND SCALDS!! SHOCKS AND FRACTURES!!!

The havoc caused by the above is more than that of any other ailment in times of War. This danger, though at the present moment seems to be far removed from us, may at any time be brought right up to our door on account of the lightning speed of the modern Warfare.

It is therefore the duty of every conscientious medical practitioner to prepare the lay public for any emergency by teaching them how to give first aid to the injured. No public measure of protection will succeed without the co-operation of every individual. They must therefore be taught to help themselves. This seemingly difficult problem has been simplified by Dr. U. Rama Rau in his book "FIRST AID IN ACCIDENTS." This fully illustrated book is available in English as well as in the South Indian Vernaculars at 12 as. for any edition and will be very helpful for doctors to teach their fellowmen. Equally useful are the booklets of Health Lecture series.

For further particulars, please write to:—

Sri Krishnan Bros., Post Box No. 166, Madras.

HEALTH

[ESTD. Jan. 1923]

An Illustrated Monthly devoted to Healthful Living
Published in English.

Editors and Proprietors:

Dr. U. RAMA RAU and U. KRISHNA RAU, M.B., B.S.

Dear Doctor,

Perhaps you are already aware of our monthly publication "Health," which is being published from 1923 and is devoted to healthful living.

"Health" aims at bringing into every home, in a simple and informal way, the truths about health and disease as discovered by eminent Medical and Public Health authorities. It advocates vegetarianism, temperance, purity, simplicity and moderation in all phases of life—in short, nature's way to better health and longer life. The social and health worker will find it as the best means to keep him informed of the progress made in kindred subjects throughout the world.

We invite from the Medical Profession and Public Health Authorities in India and abroad, contributions on Vital Health Topics, such as Diet, Nutrition, Prevention of disease, Care and feeding of infants, Child training, Management of the sick, Guidance for the prospective mother, Healthful beauty, Exercise, Occupation, Recreation, Contagious diseases, School hygiene, Sanitation, First-Aid in Accidents, Health News, Views and Inventions, Vital statistics &c., Each article should not exceed about 2000 words in length.

The contributions may be in the usual form or in the form of Dialogues, Dramas, Poetry, Court Proceedings, or Personal stories of health building or even pen pictures (line drawings), condensed extracts of useful contributions appearing in other journals with or without comment, practical hints, recipes, healthy menus, experiences, statistics, communications &c. The choice of the subject is left to the contributors so that they may select the best subject in their own special line. Contributions should be in an entertaining, non-technical style, and must pass the acid test of scientific approval before being published. No questionable or unproved theories can find a place in the Journal. Contributions are accepted on the distinct understanding that they are sent solely to "Health."

Further details may be had from:—

THE EDITORIAL AND PUBLISHING OFFICES,

THE "ANTISEPTIC" Post Box No. 166, Madras.

P.S:—Annual Subscription for Health (inland) is Rs. 2/- post paid. A specimen copy will be sent on request.

1121

Regd. No. 9 M. 429.

JUNE, 1940

Vol. XXXVII. No. 6.

The Antiseptic

A Monthly Medical Journal

Edited by

Dr. U. Rama Rau, M.L.C. & U. Krishna Rau, M.B., B.S.

CONTENTS.

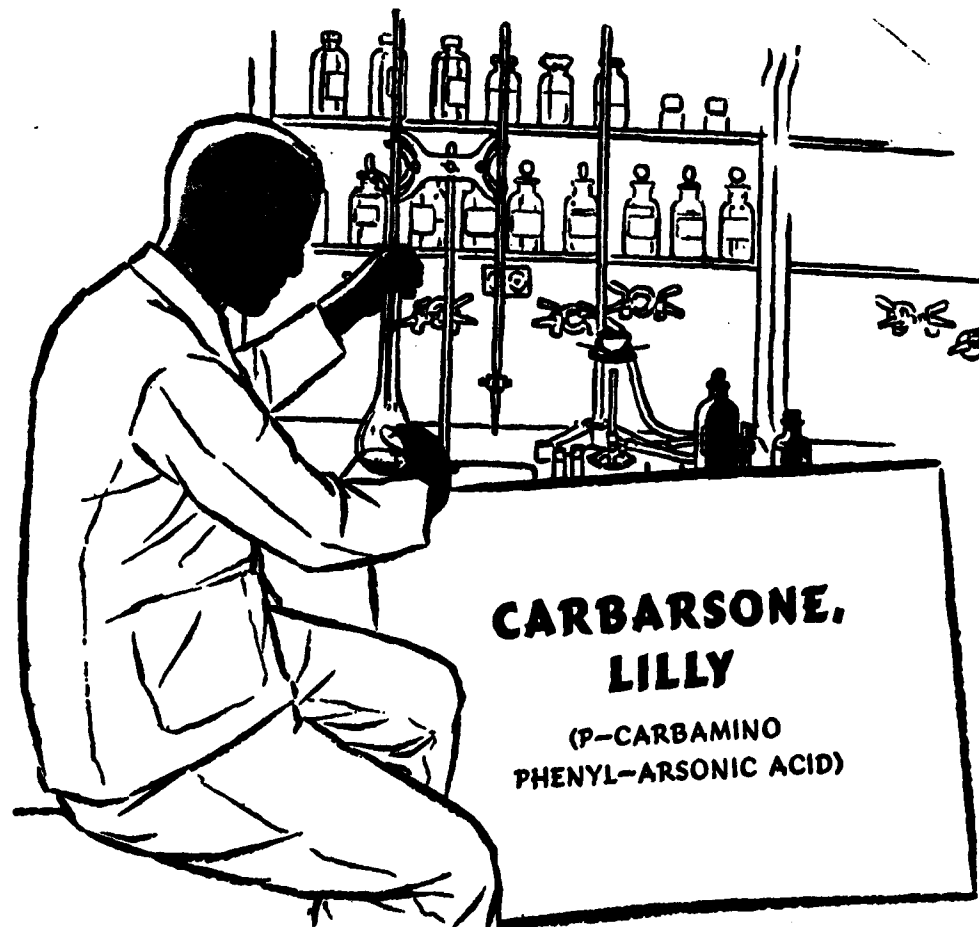
A Short Historical Review of the Development of the Present Knowledge of Diabetes Mellitus. By Chandulal C. Merchant, M.B.B.S., Bombay.	441
A Review on the Genesis of Diabetes. By A. Chakravarti, B.Sc., M.B. (Cal.), F.R.C.P., F.R.S. (Edin.), Calcutta.	455
A New View on Diabetes. By H. N. Mukherjee, B.Sc., M.B., D.I.C. (Lond.), Calcutta.	460
Clinical Observations on Some Aetiological Factors in Diabetes. By K. Narayanamurthi, M.D., Madras.	467
Metabolism in Diabetes. By G. B. Mankad, M.D., M.R.C.P., F.C.P.S., Ahmedabad.	471
Protein Metabolism in Tropical Diabetes Mellitus. By P. Gopalachari, M.B., Madras.	475
Habitus and Diabetes. By R. Krishna Rao, F.R.C.S., L.R.C.P., Vizagapatam.	480
Diagnosis of Diabetes Mellitus. By D. R. Dhar, M.B., D.T.M. (Cal.), M.R.C.P. (Lond.) Calcutta.	483
Laboratory Tests and their Significance in the Diagnosis of Diabetes Mellitus. By S. K. Bose, M.B. (Cal.), Bhopal.	489
Treatment of Diabetes. By Rao Bahadur Raman Tambi, M.D., Trivandrum.	494
Pathology of Diabetes Mellitus and Role of Zinc Protamine Insulin. By Capt. P. Ganguli, B.A., D.T.M., P.G. ZEUG., (University of Vienna), I.M.S., (Late) Calcutta.	499
A Survey of Remedies Used in Diabetes. By Major K. N. Waghay, M.B.B.S. (Allahabad), M.R.C.P. (Lond.), Hyderabad, Deccan.	507
Difficulties in Treating Diabetics. By N. C. Appayya, M.R.C.P.I., Pallatur.	510
Management of Diabetes Mellitus in Rural Practice. By Major P. C. Dutta, M.B., F.R.C.S. (E.), D.G.O., I.M.S., Montgomery.	514
Insulin and its Combinations. By K. N. Sinha, M.B.B.S., F.R.F.P.S., Lucknow.	521
Theories of Action of Insulin. By S. Sankara Raman, M.B.B.S., Cuddalore.	527
Non-Surgical Emergencies of Diabetes. By R. B. Billimoria, B.A., M.D., Bombay.	529
Surgical Diabetes. By B. N. Lahiri, M.B., F.R.F.P.S. (Glas), Calcutta.	538
Diabetes and Sepsis. By T. H. Somervell, M.A., M.B., B.Ch., F.R.C.S., Neyyoor.	547
Prognosis and Treatment of Infections of Hand and Foot in Diabetes. By Capt. D. Kanakasabesan, M.S., F.R.C.S.E., A.I.R.O., Madras.	554
Management of Surgical Diabetics. S. N. Choudhury, M.B., Hooghly.	561
Pyogenic Infections in the Diabetics. By Capt. J. M. Ghosh, M.B. (Cal.), D.T.M. & H. (Cantab.), D.P.H. (Lond.), Katmandu, Nepal.	568
Carbuncle as Seen in the Delta Areas. By K.S. Appu Mudaliar, M.B. Kumbakonam.	570
Operation on Diabetic Patients and its Precautions. By S. C. Das Gupta, Nepal.	573
Eye in Diabetes Mellitus. By G. S. Guha, M.B., D.T.M., M.D., Shillong.	576
A Few Observations on Eye Affections in Diabetes. By Md. Shafi Mehkri, Bangalore.	583
Diseases of the Ear, Nose and Throat and Diabetes. By P. V. Cherian, M.B., F.R.C.S. (E), Madras.	586
Diabetes Complicating Diseases of the Ear, Nose and Throat. By M. Sanjiva Rao, M.B.B.S., Madras.	588
The Interactions of Diabetes Mellitus and Pregnancy. By G. A. W. Wickramasuriya, F.R.C.P., F.R.C.S. (E.), F.R.C.O.G., Colombo.	591
Diabetes in Obstetrics. By B. N. Purandare, M.D., F.R.C.S.E., Bombay.	607
Pregnancy and Diabetes. By B. I. Kapur, M.D., Lahore.	612
Diabetes and Pulmonary Tuberculosis. By K. S. Sanjivi, M.D., Madras.	616
Obesity and its Relation to Diabetes. By K. K. Mehta, P.C.M.S., Multan.	618
Towards the Close of Diabetic Lives in India. By A. Singh, M.B., Benares City.	620

Editorial and Publishing Offices: 323, Thambu Chetty Street, G. T., Madras.

London Office: 34-40, Ludgate Hill, E. C. 4.

Subscription Rs. 5. Foreign 10 sh. a year. Post paid. Single Copy Rs. 2—In advance.

Index to Advertisements, see page 38.



ARSENIC can be safely used in amebiasis by prescribing Carbarsono. The treatment is rapidly effective, no other drugs are required, and the activities of the patient are not restricted in most cases.

Give Carbarsono retention enemas, 2 Gm. in 200 cc. warm sodium bicarbonate solution, during acute amebic dysentery.

Prescribe Carbarsono in pulvules (filled capsules) of 0.25 Gm., two pulvules daily for ten days and repeated as required, in subacute and chronic forms of the disease.

Distributor:

KEMP & CO., LTD.

BOMBAY, CALCUTTA, DELHI, NEW DELHI

Lilly

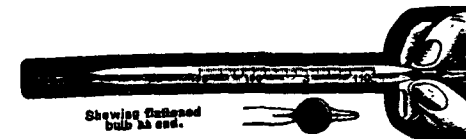
ELI LILLY AND COMPANY
INDIANAPOLIS, INDIANA, U.S.A.

ZEAL'S

CLINICAL THERMOMETERS
THE REPELLO (REGD.)

A 30-second pushed back in an instant.

GUARANTEED
ACCURATE

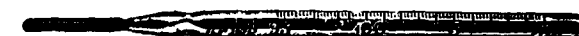


NO
SHAKING DOWN
REQUIRED

NEW IMPROVED LENS FINDER

THE ORIGINAL AND RELIABLE MAGNIFYING CLINICAL ON THE MARKET

IN FOCUS



GUARANTEED

OUT OF FOCUS



ACCURATE

REGISTERED
TRADE MARK

THE SQUARE MARK ENGRAVED ON THE
LENS FRONT LOCATES THE MERCURY
COLUMN IMMEDIATELY
BEWARE OF IMITATIONS

REGISTERED
TRADE MARK

G. H. Zeal Ltd., Morden Road, Merton, London, S.W. 19, Eng.

THERMOMETER MANUFACTURERS.

Established 1888

Cables, Zeal-dom Smith, London.

CASPRETTE

BRAND

Tablets of Aspirin and Caffeine

Trade  Mark

For the relief of all kinds of pain

Safe and Dependable

Does not affect the heart or upset digestion

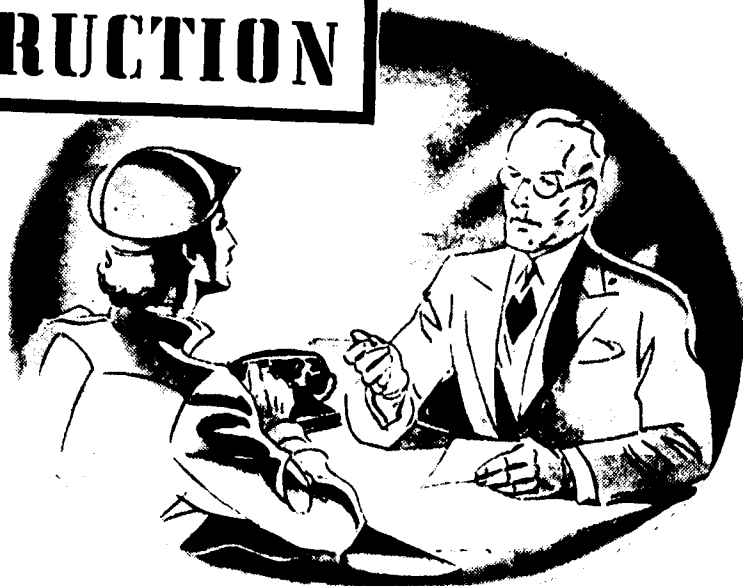
MADE IN MYSORE

BY

The Government Industrial & Testing Laboratory
MALLESWARAM, BANGALORE.

When writing to advertisers, please mention the "Antiseptic"

INSTRUCTION



The key to the problem of constipation is Habit Time of Bowel Movement . . . Food has its bearing, exercise and mechanical aids their places,

BUT

for easy, complete, comfortable bowel movement, natural contraction waves of the colon must be brought about.

'Petrolagar' fits this regimen . . . 'Petrolagar' emulsion will mix with the intestinal contents and help to make up the deficiency of moisture and mass to bring about a normal faecal consistency. Copies of the treatise "Habit Time of Bowel Movement" will be sent to physicians on request.

'Petrolagar'
BRAND PARAFFIN EMULSION Regd.

For the convenience of physicians 'Petrolagar' is prepared in four varieties—Plain, with Phenolphthalein, Alkaline and with Cascara.

Distributors in India:

KEMP & CO. LTD., P. O. Box 937, Charni Rd., Queens Rd., Bombay.

Sole Proprietors:

JOHN WYETH & BROTHER LTD., LONDON, N. 16,
DISTRIBUTORS FOR PETROLAGAR LABORATORIES.

When writing to advertisers, please mention the "Antiseptic"

In all cases

of retarded convalescence and weakness

YOU can recommend Wincarnis with confidence. Persistent weakness and slow recovery of strength are the forerunners of relapse and complications. To avoid such dangerous possibilities, prescribe Wincarnis. Composed of finest strengthening properties and vitamin malt extract carefully combined in exact quantities with matured wine made only from the finest grapes, Wincarnis should be administered once or twice a day in all cases of weakness, slow convalescence, nervous debility and general run-down conditions. Its delicate aroma and taste quicken the most capricious appetite; its strengthening vitamin elements restore resistance and vitality; enrich impoverished blood-streams, and induce healthy sleep. Wincarnis is easily assimilable, and is not only an excellent stimulant, but counteracts any tendency to anæmia.

Prescribe

WINCARNIS

The Tonic Wine

● OVER 25,000 RECOMMENDATIONS FROM MEDICAL MEN

Coleman & Co. Ltd., Wincarnis Works, Norwich, England

EM/W/68

When writing to advertisers, please mention the "Antiseptic."

In Acute Genito-urinary Inflammations

the use of Antiphlogistine constitutes a rational aid to the treatment. Its heat and medication tend to exert a modifying influence on the inflammatory phenomena.

As a local adjuvant to other therapeutic measures, it is often beneficial.

Sample on request

ANTIPHLOGISTINE



Hypertrophic prostate.
1. Accretions ("prostatic pearls").
2. Overgrowth of connective tissue.

THE DENVER CHEMICAL MFG. CO., 163 VARICK ST., NEW YORK

Agents in India:—MULLER & PHIPPS (India) LTD., P. O. BOX 773, BOMBAY.



As Development Proceeds

The needs of the growing infant call for increased amounts of mineral elements; these, with small variations in the proportions of fat, protein and soluble sugars, form the *raison d'être* for the use of Allenburys No. 2 Humanised Milk Food instead of Allenburys Milk Food No. 1 from the beginning of the fourth month.

*Descriptive literature
will be sent on request.*

ALLEN & HANBURY LTD.

(Incorporated in England)

Clive Buildings, CALCUTTA

and at 37, Lombard Street, London, E.C.3

When writing to advertisers, please mention the "Antiseptic"

MALARIA!!!

USE
JAVA QUININE
TRADE MARK



ALL QUININE SALTS
PLAIN & SUGAR-COATED TABLETS
CINCHONA FEBRIFUGE
AND OTHER
DERIVATIVES OF CINCHONA
ALKALOIDS

High Degree of Purity and Solubility.

Sole Agents for India & Burma:
MARTIN & HARRIS LTD.,
CALCUTTA — BOMBAY — MADRAS
KARACHI — RANGOON.

Some recent pronouncements on the value of QUININE IN MALARIA

Extract from the

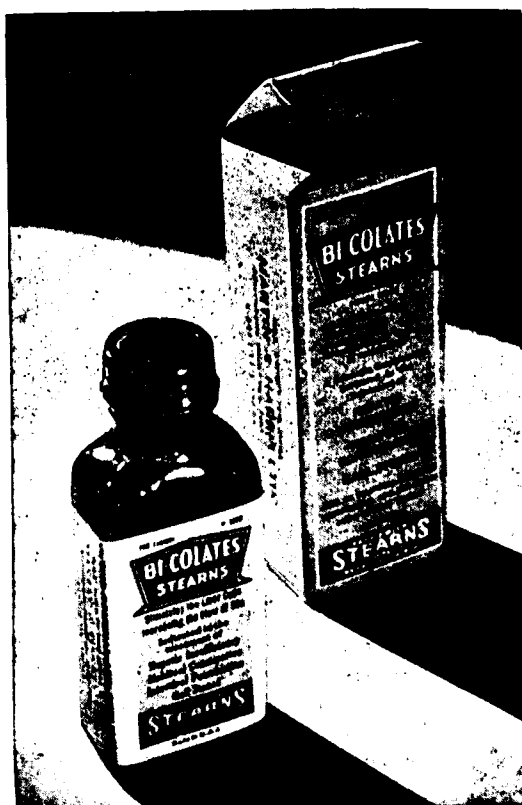
*"Resolutions of the Inter-Governmental
Conference of Far Eastern Countries on
Rural Hygiene." Bandoeng, Java,
3rd-13th August 1937.*

*... "that wide distribution of quinine is a
public duty which, whenever and wherever
necessary should be organised and paid for
by the State."*

*"The Conference further is in agreement
that the Cinchona derivatives remain the
drug of choice for mass distribution."*

*"QUININE is not only still the best and
safest remedy against MALARIA.*

*QUININE is also of proved value in the
prevention and cure of INFLUENZA."*



BI-COLATES

(STEARNS)

DEPENDABLE CHOLERESIS and CHOLAGOGUE ACTION

A scientific combination of the bile salts,
Sodium Glycocholate and Sodium Taurocho-
late, with Cascara Sagrada, Phenolphthalein,
and Oleoresin Ginger.

Bi-Colates (Stearns) are particularly indicat-
ed in cases of hepatic insufficiency, either
functional or in association with early cirrho-
sis, catarrhal and other forms of jaundice,
bilious attacks, intestinal auto-intoxication
and the prevention and treatment of gall-
stones.

Bi-Colates (Stearns) are also indicated in all
conditions in which a true cholagogue and
cholagogue is required.

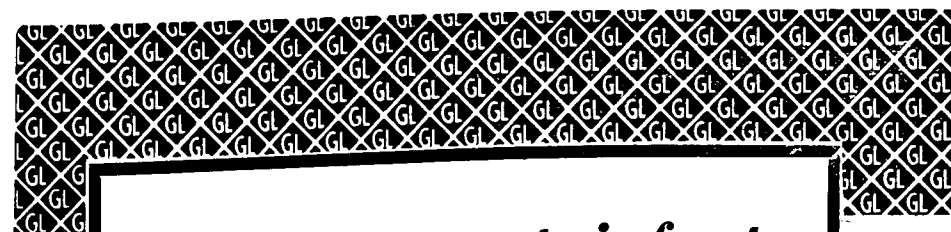
Manufactured by:

FREDERICK STEARNS & CO., DETROIT, U.S.A.

Sole Agents in India & Burma.

MARTIN & HARRIS LTD.,

CALCUTTA — BOMBAY — MADRAS — KARACHI — RANGOON



*The youngest infant
can digest*

Glaxo
MILK FOOD

The fat, carbohydrate and protein
content of Glaxo has been modified
to suit the infant's delicate diges-
tion. The curd formed is soft and
flocculent—ensuring that the food
will be properly assimilated even
by the most "difficult" baby.

Only good fresh milk is used
in Glaxo—and the natural
goodness of this milk is
supplemented
further by added
vitamin D and iron.



Glaxo Laboratories Ltd., Greenford,
Middlesex, England.

Representatives in India:
H. J. Foster & Co. Ltd., P.O. Boxes
202 Bombay; 2257 Calcutta; 108 Madras;
244 Lahore.



When writing to advertisers, please mention the "Antiseptic"



A perfectly balanced blend of DEXTRINS, MALTOSE & DEXTROSE, "KARO" has been well known abroad for many years as an

OUTSTANDING MILK-MODIFIER for bottle-fed infants.

The highly gratifying results already obtained with "KARO" by hundreds of doctors in this country fully confirm the opinion of Prof. Marriott given in his book "Infant Nutrition".

"We have found it (Karo) the most satisfactory form of carbohydrate for the feeding of normal and most sick infants".



DEXTROSOL

The Brand name which stands for PURITY and ALL-ROUND EXCELLENCE in glucose in powder form.

Literature and further particulars gladly supplied free and post-free on application.

CORN PRODUCTS CO. (INDIA) LTD.

P. O. BOX 994, BOMBAY.

When writing to advertisers, please mention the "Antiseptic"

GLYKERON

*Coughs, Bronchitis, Asthma
Laryngitis, and other Res-
piratory Affections . . .*

A Bronchial Sedative

Control the cough that weakens your patient.

GLYKERON quickly relieves this distressing symptom because it contains medically approved respiratory sedatives.

Your patients with respiratory affections do better when they sleep better—without coughing.

GLYKERON may be administered to diabetics freely as it contains no sugar or syrup and causes no disturbance of digestion.



Stimulating Expectorant

GLYKERON loosens the mucus in the bronchial passages and aids in its expulsion.

It lessens the hazard of complications by getting rid of germ-laden secretions. Prescribe it for the symptom of cough. Very palatable.

GLYKERON supplied in 3 oz. as well as 16 oz. bottles.

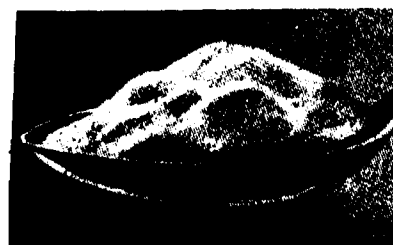
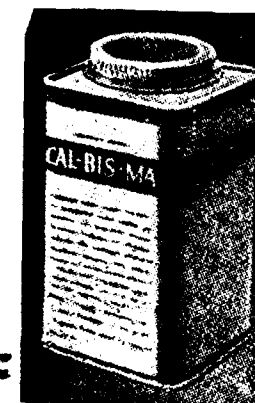
DOSAGE: Adults, one to two teaspoonfuls every two or three hours or at longer intervals as the individual case requires. Children, from ten drops to one teaspoonful, according to age.

Literature on request

MARTIN H. SMITH COMPANY · NEW YORK

A single teaspoonful of CAL-BIS-MA

The first teaspoonful or the last—there is no difference in the composition of CAL-BIS-MA. In every teaspoonful there is just the right proportion of sodium bicarbonate and magnesium carbonate for quick gastric neutralization; every single teaspoonful has the proper amount of calcium carbonate and bismuth salts to prolong the neutralization. Ingredients of matched density, incorporated in a colloid base, assure a uniform product throughout. But Cal-Bis-Ma goes further. With colloidal kaolin it obviates gaseous distension; with bismuth and colloidal kaolin it soothes and protects the irritated gastric mucous membrane and prevents secondary acid rise. Descriptive literature and trial supply of Cal-Bis-Ma gladly sent on request.

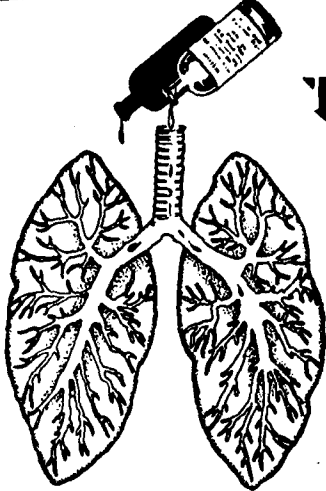


MARTIN & HARRIS LTD.,
Mercantile Buildings, Lall Bazar, Calcutta.

Also at Bombay, Madras, Karachi and Rangoon.

Prepared by WILLIAM R. WARNER & CO., LTD., LONDON, ENGLAND

**WASH
THE LUNGS CLEAN**



Being a combination of pulmonary antiseptics & expectorants of proved therapeutic value viz. pot. Gualacol Sulphonate, Ammonium Chloride & Vinum Antimonii & containing, as it does, the tonic properties of Calcium Hypophosphite

PULMOLIN

not only clears the lungs of bronchial mucus but strengthens them against future attacks.

KILLS COUGH & HEALS THE LUNGS.

**LISTER ANTISEPTICS &
DRESSINGS COMPANY (1928) LD.
CALCUTTA**

SUCCINOL (Regd.) Is a satisfactory injection for LEPROSY strictest test of the profession equally in official and non-official circles. Doses:— .02 Grm. to .2 Grm. in ten graduated ampoules.

DERMOL (Regd.) Is an unchallenged, stainless, bland, and the most effective remedy for all skin diseases, swellings, ulcers, carbuncles, cuts, bruises, insect bites, ear troubles, burns; joint, gland and chest troubles etc. In short, an unfailing application for any and every disease externally.

IODINOX (Regd.) The best, stainless, bland, and non-irritative preparation of Iodine 'superior to other similar preparations' containing 5% of the active principle. Equally efficacious on skin and mucous surfaces. Indicated for use in cases requiring Iodine without irritation.

HYDROXY ERYTHRIN Hydroxy Erythrin also called Hydroxy Anthocyan—discovered by Dr. Misra is a satisfactory injection for T. B. infection. It shows its effects both as preventive and curative only after a few injections. For detailed description leaflets will be sent on request.

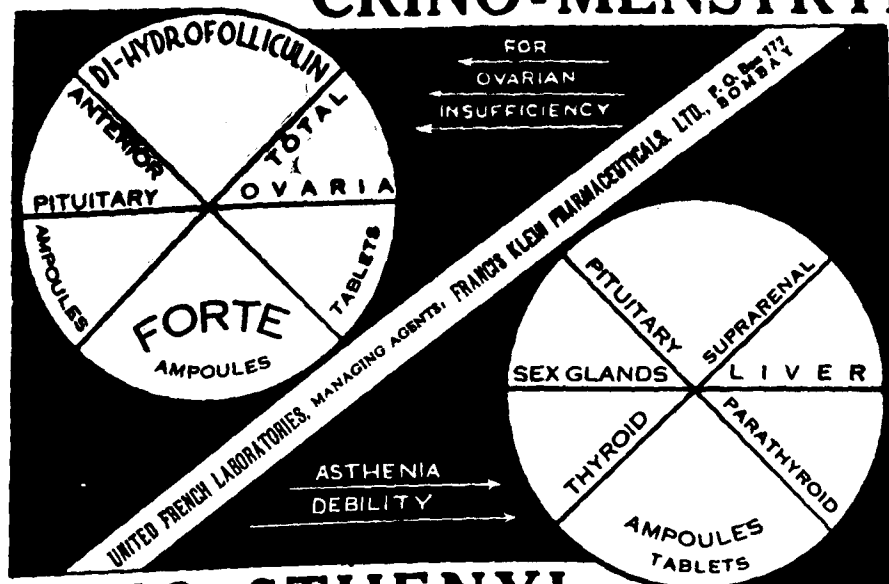
To be had from:—**GALLENO PHARMACEUTICAL WORKS,**

P. O. Waini, Ry. St. Pusa Road, B. N. W. Ry. Dist. Darbhanga, BIHAR, (INDIA).

Main Stockists:—Messrs. SMITH STANISTREET & CO., LTD., 18, Convent Road, Entally, Calcutta.
Messrs. SRI KRISHNAN BROS., 323, Thambu Chetty St., Madras.
Messrs. E. STELLA & CO., Marshall's Building, Ballard Road, Bombay.

When writing to advertisers, please mention the "Antiseptic"

CRINO-MENSTRYL



CRINO-STHENYL

Treatment of Insanity and Mental or Nervous Disorders

by
INSANIL

Also indicated as the most powerful yet harmless sedative and regenerator known to medical science that can be opposed to all sorts of violent mental and nervous disorders, hysteria, epilepsy, insomnia, after effect of excessive worry and severe emotional shocks, neurasthenia, high blood pressure, etc. It also acts as a sedative, hypnotic antispasmodic and if continued for sometime it acts as an alternative.

Used successfully by doctors, hospitals, lunatic asylums all over the world. Contains no depressing drugs like Luminal, Chloral Hydrate, Potassic Bromides, Opium, Morphia, Henbane, etc.

For free clinical sample and literature apply on
your own prescription form to:

HERING & KENT

Post Box 323 (A. S. M.)

Reay House, Opp. Lloyds Bank, Hornby Road, Bombay.

Stockists: APPAH & CO., China Bazar Road, Madras.

When writing to advertisers, please mention the "Antiseptic"

OVER 60 YEARS' REPUTATION.

HEWLETT'S MIXTURE

Mist. Pepsinæ Co. c. Bismutho (Hewlett's)

Useful in all forms of Dyspepsia, Pyrosis, Gastric pain and vomiting, and for alleviating the pain in cases of Ulcer and Cancer of the Stomach.

DOSE—Half to one fluid drachm, diluted.

"Messrs. Hewlett's preparation of Pepsine and Bismuth is of standard excellence. The combination is a particularly good one for the treatment of diseases of the stomach which require a sedative." Medical Review.

LIQ. SANTAL FLAV. c. BUCHU et CUBEBA (Hewlett's)

Since its introduction it has been largely prescribed all over the world as a specific for certain cases.

DOSE—3j to 8ij in water or milk.

"Experience has shown this preparation to possess the same efficacy as Santal Oil itself." Practitioner.

LIQUOR ERGOTÆ PURIF.

(Hewlett's)

PHYSIOLOGICALLY STANDARDISED.

Superior to the ordinary Liquid Extracts, etc.
Reliable and unalterable.

"A very excellent preparation of the drug."

Medical Times & Gazette.

"A reliable preparation of Ergot, and well adapted for obstetric practice."

London Medical Record.

HEPATAGEN

An elegant and palatable general Aperient and Cholagogue, specially recommended in cases of so-called "Biliousness," Hepatitis and Chronic Gastritis.

DOSE—10 to 60 minims, diluted.

Introduced and Prepared only by

C. J. HEWLETT & SON, LTD.

"ESTABLISHED OVER A CENTURY"

Wholesale Druggists and Manufacturing Chemists
35-43, CHARLOTTE ROAD & 83-85, CURTAIN ROAD,
LONDON, E. C. 2.

When writing to advertisers, please mention the "Antiseptic"

IN BRITAIN TO-DAY
the leading infant
specialists prescribe

OSTERMILK

For the last eight years Ostermilk
has been the choice of over 2,000
British Infant Clinics



BEFORE Ostermilk was made generally available in Great Britain, it was subjected to clinical trials extending over two years. The success of Ostermilk in these trials and the national acceptance of this dried-milk infant food during the following years has amply fulfilled the high expectations of the specialists who devised its formula.

The variable vitamin D content and the deficient iron content of cow's milk and its ordinary dried food derivatives is corrected in Ostermilk by the incorporation of these protective elements in dependable and appreciable amounts. The fat and protein content is adjusted to approximately that of breast milk. Extensive precautions are taken to assure constancy of composition and the greatest possible bacterial purity.

These qualities may well explain the sound and satisfactory progress shown by infants fed solely on Ostermilk. But it is undoubtedly this success in practice which has maintained the respect of the doctors in charge of 2,000 British Infant Clinics during the past eight years. Over this long period, these eminent specialists have continually recommended Ostermilk for the infants under their care.

Representatives in India: H. J. FOSTER & CO., LTD.,

P. O. Box 202, Bombay.

P. O. Box 108, Madras.

P. O. Box 2257, Calcutta.

P. O. Box 241, Lahore.

When writing to advertisers, please mention the "Antiseptic"

THELESTRIN

OVARIAN FOLLICULAR HORMONE

A standardized preparation of the ovarian follicular hormone for intensive ovarian therapy by hypodermic injection.

Indicated in the treatment of scanty menstrual flow, amenorrhea and the vasomotor and nervous symptoms of the menopause.

Doses of 6 1-cc. ampoules.
400 international units in aqueous solution.
2000 international units in oil.

G. W. CARNRICK CO.
20 MT. PLEASANT AVE. NEWARK, N. J., U. S. A.

Consult
MULLER & PHIPPS (ASIA) LTD.
NICOL RD., BALLARD ESTATE, BOMBAY

INFANTILE LIVER AND SPLEEN COMPLAINTS

It is generally believed that these cases of Infantile Liver & Spleen Complaints are difficult of treatment. Most Medical Men are thoroughly convinced that by the use of Jammi Venkataramanayya's 'LIVERCURE' (Regd.) the unique Specific remedy invented and perfected by Jammi Venkataramanayya Garu, the disease could be successfully treated.

For further particulars, please write to:—

JAMMI VENKATARAMANAYYA & SONS,
'LIVER CURE' OFFICE,
2 & 8, SALAI STREET, MYLAPORE, MADRAS.

When writing to advertisers, please mention the "Antiseptic"

Crookes'

COLLOSOL CALCIUM

with VITAMIN 'D'

As a therapeutic agent, Calcium is of paramount importance. Although present in the blood serum only in very small concentration, the maintenance of this level is vital and a small daily intake of Calcium is necessary to ensure it.

During pregnancy and lactation this becomes even more important as the requirement of Calcium during this period is greatly increased.

Equally important with the supply of Calcium is Vitamin D as without it Calcium cannot be absorbed. Failure to absorb Calcium because of lack of Vitamin D is the cause of Rickets in children and Osteomalacia in adults.

Rickets and Osteomalacia are extreme cases of Calcium deficiency but many other indications are benefitted by Calcium administration e.g. Tuberculosis, Nervous debility, Dental Caries, Urticaria, Neurasthenia associated with emotional disturbances, etc.

'COLLOSOL' CALCIUM with VITAMIN D (Injection)

Contains 0.05 per cent Calcium in Colloidal Suspension with 5,000 International Units of Vitamin D per c.c., and is specially prepared for subcutaneous injection.

Packings: Ampoules (box of 6) $\frac{1}{2}$ c.c., 1 c.c., 2 c.c.
Vials (rubber cap) 15 c.c., 30 c.c.

'COLLOSOL' CALCIUM with VITAMIN D (Oral)

Contains 1 per cent of Calcium Salts of fatty acids in Colloidal Suspension and is Standardised to contain 250 International Units of Vitamin D per fluid dram.

Packings: Bottles of 4 oz. and 10 oz.

'COLLOSOL' CALCIUM is available in the same forms and sizes as 'Collosol' CALCIUM with VITAMIN D.

THE CROOKES LABORATORIES (British Colloids Ltd.) PARK ROYAL, LONDON, N.W.10, ENGLAND
BOMBAY: 10 GRAHAM ROAD, BALLARD ESTATE

When writing to advertisers, please mention the "Antiseptic"



HORLICKS

is a modified milk food with a fat content protected by the valuable mixed sugars lactose, maltose, and dextrin. It forms a balanced diet which is easily digested and assimilated.

It is a valuable aid to the physician in the dietetic treatment of many diseases associated with childhood. Marked success has attended its use in digestive disturbances, epidemic diarrhoea, and in infective and respiratory conditions with which acidosis is associated.

During recent years acidosis has attracted much attention, and it is now recognised that many children who exhibit vague symptoms of illhealth, are debilitated, or who are liable to bilious attacks, suffer from it in some degree. In many cases the condition is due to an intolerance for fat, and is made worse by efforts directed towards improvement by feeding-up the patient with unmodified cows' milk, extra cream and fatty foods.

To prescribe Horlicks for these children is to know that they will speedily regain full health and vitality.

HORLICKS

AVAILABLE EVERYWHERE

When writing to advertisers, please mention the "Antiseptic"

MOBILISATION

|||
To Combat Bacterial Invasion
Nature Attempts to Mobilise the
Defence Forces of the body.

|||
Help Nature

|||
use

STERODIN

The ideal Nonspecific Immunising Agent

Sole Agents for Madras Presidency,

Messrs. APPAH & CO.,
Madras.

Manufactured by

THE UNION DRUG CO., LTD.
Calcutta.

A-O

Prices reduced from May 1, 1939.

INDICATED IN CASES OF

A SPECIFIC VACCINE

Made of
TUBERCLE BACILLI
OF HUMAN TYPE

There are three practical
uses to which

A-O

may be put

- (I) Prophylactic
- (II) Diagnostic and Prognostic
- (III) Therapeutic

Literature on request.

Prepared by:

THE ARIMA INSTITUTE,
Osaka, Japan.

Head Office: 43, Churchgate Street, Fort, Bombay.
Readymoney Mansions.

- Latent or frank tuberculosis
- Pulmonary tuberculosis (Apical catarrh)
- Surgical and urogenital tuberculosis
- Ophthalmological tuberculosis
- Dermal tuberculosis
- Pleurisy and Peritonitis in convalescence
- Disorderly menstruation due to innate weakness
- Glandular affections
- Laryngeal and intestinal tuberculosis
- Is also useful as a diagnosticum and as a prophylactic of tuberculosis
- A-O is an agent which calls forth or increases in an organism the immunizing powers through a biological reaction of its own.

Agents: T. M. THAKORE & CO.,
1/10 & 10/A, Stringer Street,
G. T., MADRAS.

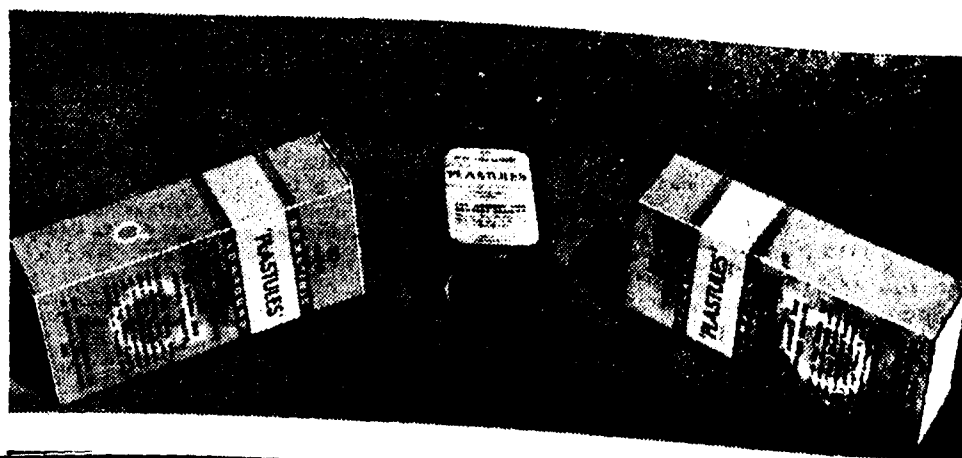
When writing to advertisers, please mention the "Antiseptic"

IRON

THE therapeutic value of iron is directly proportional to the ease with which ferrous ions are liberated. Recent experiments have shown the ferrous salts to be the most effective in the treatment of anaemia because they are more rapidly assimilated, require smaller doses and are more economical than other forms of iron now in use. An effective form of ferrous ion is available in 'Plastules' brand Haematinic Compound. Actual tests reveal that the haemoglobin regenerating power of 'Plastules' is four to five times greater than that of

ferric ammonium citrate, 15 times greater than that of reduced iron, and is more readily adaptable to metabolism in the human body. Three 'Plastules' Plain provide the average patient with an adequate daily dose of iron to show a marked increase in haemoglobin..... 'Plastules' provide ferrous ion and vitamins B₁ and B₂ in an edible oil in the form of a semi-fluid mass, enclosed in soluble gelatin capsules which quickly dissolve in the stomach..... 'Plastules' are available in two types Plain and with Liver Extract.

Distributors in India:—KEMP & CO., LTD., Charni Road, P. O. Box 937, Bombay.
Sole Proprietors:—JOHN WYETH & BROTHER LTD., 25, Oldhill Place, LONDON, N. 16.



When writing to advertisers, please mention the "Antiseptic"

33 YEARS' RECORD OF STANDARD QUALITY

STANDARD DRUGS AND MEDICINAL SPECIALITIES OF PROVEN MERITS. RIGHT IN QUALITY: RIGHT IN PRICE.



Alembic CHEMICAL WORKS CO. LTD.
BOMBAY BARODA MADRAS CALCUTTA



Confidence in Antisepsis

The high germicidal efficiency of 'Dettol' with its safety and convenience, have won for it a leading position in hospitals and private practice, and make it a most useful disinfectant for first aid at home, for personal hygiene, and for gargling and bathing.

'DETTOL' maintains its efficiency in the presence of blood and other organic matter, and can be used in high concentration, thus giving a wider margin of safety. It is absolutely non-poisonous and non-staining and possesses a distinctly pleasant smell.

'DETTOL'
TRADE MARK
THE MODERN ANTISEPTIC

Send postcard for free literature to:

ATLANTIS (East) LIMITED., (Dept. A. 6) 20.1, Chetla Road, Calcutta.
Marketing Agents for Reckitt & Sons, Hull & London, England.

When writing to advertisers, please mention the "Antiseptic"



ANAHÆMIN B.D.H.

In Nutritional Macrocytic Anæmias

Nutritional macrocytic anæmias are stated to be due primarily to a deficiency of Castle's extrinsic factor. It is logical, therefore, to assume that they will respond to the exhibition of Anahæmin - the product of interaction of intrinsic and extrinsic factors.

Convincing evidence of the value of Anahæmin in nutritional anæmias is provided in a report (Response of Nutritional Macrocytic Anæmia to Anahæmin, *Lancet*, August 12th, 1939, p. 360), in which it is shown that Anahæmin is at least as active in its curative effect as less highly-purified preparations of liver.

In other words, Anahæmin is of high and unvarying activity not only in pernicious anæmia which is due to lack of intrinsic factor, but to nutritional anæmias which are due to lack of extrinsic factor. This latter fact accounts for the restorative effect produced upon patients after operation or who for one reason or another are maintained on a restricted dietary.

Stocks of Anahæmin B.D.H. are held by leading chemists and full particulars are obtainable from:

THE BRITISH DRUG HOUSES LTD.

(Incorporated in England)

Imperial Chemical House

BOMBAY

Ballard Estate

An/tn/406

When writing to advertisers, please mention the "Antiseptic"

STILBÆSTROL

(4:4'-dihydroxy- α : α' -diethylstilbene)

A Compound Possessing Powerful
Æstrogenic Activity

Stilbæstrol is a synthetic compound which faithfully reproduces the effects of the naturally-occurring æstrogens, and may be used in all conditions where the natural æstrogenic hormones are indicated. It is of particular value in conditions of menopausal irregularity and amenorrhœa.

Preparations

'TABLOID' BRAND
STILBÆSTROL

(For Oral Administration)

0.5 mgm., 1 mgm. and 5 mgm. Each in bottles of 25 and 100

'HYPOLOID' BRAND
STILBÆSTROL

(For Intramuscular Injection)

1 mgm. in 1 c.c. and 5 mgm. in 1 c.c. Each in boxes of 6 ampoules

Recent clinical investigations have shown that oral administration is as effective as intramuscular injection.



Literature to Medical
Men on request



BURROUGHS WELLCOME & CO., LONDON
(THE WELLCOME FOUNDATION LTD. INCORPORATED IN ENGLAND)

AND COOK'S BUILDING, HORNBY ROAD, BOMBAY

© 700 Ex.

COPYRIGHT

When writing to advertisers, please mention the "Antiseptic"

Special Number on 'Diabetes'.

The Antiseptic

Estd. 1904.

A Monthly Journal of Medicine and Surgery.

Editors: Dr. U. RAMA RAU, M.L.C., & U. KRISHNA RAU, M.B., B.S.

Editorial and Publishing Offices: 323, THAMBU CHETTY ST., MADRAS.

Annual Subscription Rs. 5. Foreign, 10 Sh. Post Paid.

Vol. 37.

JUNE, 1940.

No. 6.

A Short Historical Review of the Development of the Present Knowledge of Diabetes Mellitus

BY

Chandulal C. Merchant, M.B.B.S.,

Pharmacology Dept., G. S. Medical College, Bombay;

Author of "Prevention of Diabetes Mellitus", Dossabhoy Hormusji Cama Prize Essay (University of Bombay), 1938.

"Quod non est in actis non est in mundo"
(Whatever is not in the record, is not in the world.)

THE disease, diabetes mellitus has a long and fascinating history which is assumed to date as far back as "before the Christian Era" (B. C.). It seems certain that diabetes afflicted mankind since the remotest times, the earliest indication of anything suggesting diabetes being found in the old Egyptian compilation "Papyrus Ebers" (1500 B. C.) which is considered to be one of the oldest of all medical documents.

From the earliest times, diabetes has attracted the attention of medical men of almost all ages and all climes, and it may be well to note that the modern knowledge of the disease is the cumulative outcome of hundreds of years of most carefully planned and patiently carried out experiments being correlated with accurate clinical observations, and not a chance discovery of one or two individuals.

During the last two decades, many and important advances have been made in the knowledge pertaining to diabetes; still, it is felt that its story is far from being complete and that there are many wide gaps which still require to be bridged over. Much of the matter is

CHEMOTHERAPY OF PURE AND MIXED
STREPTOCOCCAL INFECTIONS

3 years of research,
the testing of over 200 substances

HAVE PROVED THAT

RUBIAZOL

AN AZOIC DYE
(formerly known as Bacteramide)

is
the MOST ACTIVE
the LEAST TOXIC
the BEST TOLERATED
TREATMENT

DAILY DOSE
6 TO 12 TABLETS
1 TO 3 AMPOULES



LABORATOIRES DU DR. ROUSSEL
89, RUE DU CHERCHE-MIDI - PARIS

Sole Agents for India, Burma and Ceylon:

G. LOUCATOS & CO.

CALCUTTA
P. O. Box 2739
Tel. 2455

BOMBAY
P. O. Box 783
Tel. 2039

MADRAS
P. O. Box 1273
Tel. 355

still vague and controversial, especially with regard to its causation, and requires further study and research. Luckily, however, adequate methods for routine diagnosis and successful control of the disease in a majority of cases, have been found and developed as to be practically within reach of all, rich or poor alike.

Voluminous literature has, until now, appeared on the subject, especially during the past twenty years—the period of most active growth in the evolution of our modern knowledge of diabetes. It is not an easy task to trace the history of the disease, extending as it does over some 2000 years, in a short limited space, except in its major aspects, mentioning only those events which appear to serve as distinctive landmarks in its study.

Advances in the knowledge of diabetes mellitus have come at different times and through a large number of investigators and in many cases, they have been only rendered possible through improved methods of technique and advanced knowledge in various medical subjects such as anatomy, physiology, pathology etc. as well as in other sciences, particularly organic and bio-chemistry. In fact, were it not for the organic chemists, it would not have been possible to unfold the many mysteries surrounding the nature and causation of the disease, least or not to speak at all of the diagnosis and the present-day treatment with Insulin—which, not only has allowed the diabetic of to-day to live much longer, but also has made possible for him to enjoy a comfortable and active life just like his non-diabetic associates.

In tracing the history, in order that the continuity of the link may not be broken, it is planned to describe the various advances under their several respective heads more or less in the order of their sequence rather than to record the events in their strict chronological order.

I. Observations on Symptomatology of Diabetes Mellitus.—

In the writings of medical authorities of very early days are to be found a large number of references which indicate the prevalence of diabetes in the most ancient times, perhaps some two thousand years from now. CELSUS (25 B.C.—50 A.D.), often called the 'Roman Hippocrates', a reputed compiler of medical knowledge during the reign of Tiberius Cæsar, wrote of a disease in which wasting and passage of excessive amounts of urine were the characteristic symptoms.

It was, however, the Greek physician ARETÆUS of Cappadoica (Asia Minor) (150 A.D.) who gave the name 'Diabetes' (Dia.=through and benein=to flow) by which the disease has ever since been known. He is considered to have given the first accurate and graphic account of diabetes that has passed down to us from ancient times. He described the disease as "..... melting down of the flesh and limbs in incessant as if from the opening of aqueducts; thirst unquenchable as if scorched with fire". It may be noted that luckily such unpleasant symptoms are seldom or never experienced by the

diabetics of to-day, thanks to Insulin which has of late greatly revolutionized the treatment of the disease.

GALEN (131 to 201 A.D.), the most prolific of ancient medical writers, describes the symptoms which he observed in two diabetic cases which he is said to have treated.

In India too, diabetes seems to have prevailed and been well-known to physicians in ancient times. It is stated to have been first described by CHARAK (Charak Samhita 200—A.D.), who is said to have obtained his materials from the earlier works of AGNI VESA, who again seems to depend for his writings upon the teachings of his master ATHEYA (6th B.C.). It was, however, SUSHRUT (50 A.D.) who noticed and described for the first time, the sweetness of diabetic urine and gave the name मधुमेह (Madhu Meha=honey urine) to the disease.* The disease has also received the name इक्षुमेह (Ikshu Meha) on account of the close resemblance of the urine to sugar-cane juice.**

In China, diabetes was noted and described by the well known Chinese physician TCHANG TCHONGKING (about 200 A.D.) as a "disease of thirst."

AVICENNA (Ibn Sina) known as "Prince of Physicians" was a court physician (980–1037 A.D.) to several Caliphs and he noted the sweetish taste of the urine and the intense thirst as characteristic symptoms of the disease. PARACELSUS, a reputed author of over 100 books, wrote about diabetes as "a disease of chronic thirst."

There is little further of historical interest to report until the middle of the 17th century. As a matter of fact, with the fall of the Roman Empire (3rd century A.D.), Medicine ceased to be progressive and passed into a stage of degeneration along with the rest of civilization and culture. Few medicinal advances are known to have occurred until the Italian renaissance, which began about the middle of the 15th century. During the two hundred years that followed, great advances were made in different branches of Medicine such as anatomy, physiology, pathology etc., as well as in other sciences. They greatly influenced the study of diabetes and made possible many and important discoveries which ultimately led to the discovery and isolation of Insulin, only some twenty years ago.

The first outstanding contribution to diabetes came from THOMAS WILLIS (1621–1675 A.D.) who in 1675 noted the sweetish taste of the diabetic urine which was for the first time, at least in England, regarded as a criterion for diagnosis. He believed in under-nutrition as a part of the treatment, an idea which was, centuries later, developed and successfully applied by ALLEN (1913).

In France, the sweet taste of diabetic urine seems to have been

* मधुरयच्च महेषु मायोमध्विव महेति ।

सर्वेऽपि मधुमेहारव्या माधुर्याच्च तनोरतः ॥

** इक्षोरसामिवा त्यर्थ मधुरंचुक्षु महेतः ॥

known before 1674, as a reference to the sweet tasting of urine occurs in one of the early plays "Le Medecin Volant" written by MOLLIERE in 1650.

In 1775, MATHEW DOBSON of Liverpool, proved for the first time that the sweetness of the diabetic urine was actually due to sugar. He evaporated the urine and showed that the mass thus obtained underwent alcoholic as well as acetic fermentation. He also noted the sweetish taste in the blood of diabetic patients and may thus be credited to be the first to discover hyperglycæmia.

In 1815, CHEVREUL showed that the urinary sugar was glucose (dextrose). In 1835, AMBROSIANI noted that the diabetic blood had a higher content of glucose than normal blood.

The adjective "Mellitus" (= sweetish) came to be applied to diabetes in about the middle of the 18th century and was first used by CULLEN in 1776 to differentiate cases of polyuria with sugar (diabetes mellitus) and without sugar (diabetes insipidus) in the urine; but it remained for JOHANN P. FRANK, a German, to clearly differentiate (1792) the two varieties of diabetes which he described as diabetes mellitus or verus and diabetes insipidus or spurius respectively. The latter condition was stated by J. CAMUS (1872-1924) and ROUSSAY (1913) to be due to disorder of the hypothalamus without involvement of the posterior lobe of the pituitary.

During the latter part of the 19th century, many important advances were made towards the modern knowledge of diabetes. Diabetic coma which was first recognized by WILLIAM PROUT (1785-1850) was explained by KUSSMAUL in 1874 as being due to an excess of acetone in the blood. He applied the term acetonæmia to this condition which was later called acidosis by NAUNYN (1839-1925). KUSSMAUL also drew attention to the clinical syndrome of air hunger which usually precedes the onset of coma in diabetes.

In 1871, FROISIER described bronzed diabetes which results from hæmochromatosis, and which was investigated later in 1889 by VON RECKLINGHAUSEN.

Tests for Sugar in Urine and Blood.—The testing of sugar in urine and blood which is of paramount importance in the diagnosis and control of diabetes, was in early days carried out in a crude and disagreeable manner by tasting the urine. Later, it was done by fermenting the sugar which was also a clumsy and inaccurate method. In 1833, BIOT discovered the polariscopic method which was based on the ability of a sugar solution to bend a beam of light. In 1841, TROMMER, a German chemist, invented the Trommer's test (copper reduction) for testing the urinary sugar, which was announced after his death by JOHN MOORE in 1844. A few years later, in 1848, HERMANN VON FEHLING published the methods for qualitative as well as quantitative tests for the urinary sugar. These tests were later modified by PAVY in 1879 and BENEDICT, an American chemist, in 1911.

BENEDICT's tests are simple to perform and the results are accurate. They are until now, not surpassed by any other better method.

The estimation of blood sugar has been made possible by methods devised by BANG (1906), FOLIN and WU (1919), MAC LEAN (1919) and CALVERT (1929). The more recent methods to be employed are those of HARTMAN, SCHAFER and SOMOGYI, BENEDICT and HAGEDOEN—JENSEN.

II. Observations on Pancreas and its Anti-Diabetic Functions.—

1. *Islands of Langerhans*—MONDINO (1270-1326) of Bologna, described the pancreas (sweet bread) and mentioned its duct which in 1642 received its name after G. WIRSUNG, professor of Anatomy at Padua, who gave an account of it. The duct was also described by HOFFMANN in 1648 and SWALRE in 1667. REGNIER DE GRAAF in 1663 found that in man, there was sometimes an additional duct, which was also noted later by SANTORINI (1724) and J. MECKEL (1781-1833).

In 1869, PAUL LANGERHANS discovered the presence in the pancreas of bunches or groups of cells (Islands) which differed in several respects from those forming the alveoli and ducts which carry the external secretion to the duodenum. These islands were named after him in 1893 by E. G. LAGUESSE (1861-1927). KUHNE and LEA in 1882 described the islands as collections of lymphoid tissue, but this was corrected by LAGUESSE in 1893 and by HARRIS and GOW in 1894. The same workers also showed that these collections of cells had a definite and abundant supply of blood. CLARKE in 1913 estimated the number of islands to be between $\frac{2}{3}$ to $1\frac{1}{2}$ millions (750,000 to 1,750,000) in the pancreases of non-diabetic adult persons. HEIBERG in 1906 and BENSLEY in 1911 showed that the islands were twice as numerous in the tail (splenic end) as in the head or body of the pancreas; HEIBERG estimated that the islands formed nearly 3% of the pancreatic tissue.

ROBERTSON in 1933 observed, as a result of a large number of post mortem examinations, that the islands were more numerous and larger than a quarter of a century ago and ascribed the changes to the increased consumption of sugar.

LAGUESSE in 1896 demonstrated specific granules in the cells of the islands; DIAMARE in 1899 and SCHULZE in 1900 described two kinds of cells called "alpha" and "beta" cells in the islands. M. A. LANE in 1907 detected and devised methods for distinguishing the two types of granules from each other and also from the zymogen granules; he showed that the granules differed amongst themselves in their size, solubility and staining properties.

It was in 1915 that HOMANS suggested that the cells containing beta granules secreted Insulin—the sugar-reducing hormone of the pancreas.

A third variety, gamma cells, has been described by BENSLEY in 1911 and BLOOM in 1931.

BENSLEY (1912), HOMANS (1913) and GRAUER (1926) expressed the

view that the islands were derived from the epithelium of the pancreatic duct, which had three developmental possibilities viz: (i) to form ordinary acini (ii) alpha cells and (iii) beta cells.

DIAMARRE in 1889 and RENNIE in 1903 observed that in the abdominal cavities of certain Teleostei fish were to be found structures which very closely resembled those of the islands of Langerhans in the pancreas of the higher vertebrate animals, and that these structures were very often capsulated and distinct from the zymogenous acinar tissues.

2. *Insulin—the anti-diabetic hormone of the pancreas—and its isolation.*—In early times, pancreas was regarded as a mechanical packing in the abdomen to support the various branches of the aorta and to serve as a cushion for the stomach (JOHN BANISTER 1578). According to THOMAS WHARTON, the pancreas removed the supposed excrement from the plexus of the vagus. GIBSON in 1862, wrote, expressing the view current in the 17th century that “it (the pancreas) brought the chyle to perfection and was the gall bladder of the spleen”.

The first step in the discovery of Insulin—the anti-diabetic hormone—may be considered theoretically to date from the time of VON BRUNNER's experiments in 1682, when he first noted glycosuria and intense thirst in dogs in which varying portions of the pancreas were removed. At that time, no importance was attached to his experiments.

During the nearly 150 years that followed, no progress of any importance was made until 1846, in which year, the French physician, BOUCHARDT carried out experiments of a very similar nature. He tied the pancreatic duct of some dogs and attempted total removal of the pancreas in others. He found that the dogs with closed ducts did not develop diabetic symptoms, indicating that the pancreatic juice was not concerned with diabetes. During nearly fifty years since then, CLAUDE BERNARD and many other investigators, with a view to determine the role of pancreas in carbohydrate metabolism, tried the experiments of extirpating the pancreas as a whole or in part, with little or no success, until at last in 1887, MINKOWSKI and VON MERING, pupils of BERNARD NAUNYN (1839—1925), a leading figure in diabetes in his time, working at the latter's famous laboratory at Strassburg, succeeded in producing marked diabetes in dogs by complete removal of the pancreas and proved the pancreatic origin of diabetes mellitus.

Whilst passing, it may be worth mentioning that the true foundations of our modern knowledge of diabetes were laid by CLAUDE BERNARD (1813—78), who is looked upon as “the father of modern experimental physiology”. His contributions are many and important. He studied the exact role of pancreatic juice in digestion and was the first to determine with reasonable accuracy the percentage of sugar in the blood. He discovered glycogen and the glycogenic function of the liver. He suggested the possibility of sugar formation from protein. He produced glycosuria by the puncture of the floor of the 4th

ventricle and showed that the nervous system had a more or less influence on carbohydrate metabolism by regulating the activity of the pancreas through the vagus.

CLAUDE BERNARD in 1856 and SCHUFF in 1872 had observed that blocking of the pancreatic duct did not affect the health of the animals. LANGERHANS who had described the islands in 1869 was not able to suggest any definite function for them.

DIAMARRE (1889) and LAGUESSE (1893) were probably the first to suggest that the island tissues were concerned in the production of an internal secretion which controlled carbohydrate metabolism. They showed that the island cells were distinct from the secreting cells and recommended a close search for lesions affecting the islands of Langerhans in diabetes. Their view was supported by the later work of SCHULZE and SSOROLEW, who in 1900 found that the blocking of the pancreatic duct by means of Paraffin wax led to the destruction of the acinar tissue but left the islands and their blood vessels intact and did not produce diabetic symptoms.

Other investigators, LANCEREAUX (1892), SAUERBECK (1904), HEIBERG (1906), MAC CALLUM (1909), KIRKBRIDE (1912), BENSLEY (1912) and KAMINARE (1917) also noticed the atrophy of acinar gland cells after the duct was ligatured, without any disturbance in the normal function of the island tissue.

KUHNE and LEA (1882) noticed that the capillaries supplying the islands were prominent and that there were no lymphatics in the islet tissues. They opined that the secretion of the island cells entered the blood stream directly. GLEN showed in 1901 that diabetes resulted when the pancreatic circulation was stopped by tying the veins.

The first positive evidence for the existence of an anti-diabetic hormone secreted by the pancreas was provided by the experiments of MINKOWSKI (1892) and HEDON (1893) who showed that pancreatic grafts in the abdomen of animals in which pancreas was subsequently removed, prevented the onset of diabetic symptoms as well as any serious disturbance in carbohydrate metabolism.

In 1912, KNOWLTON and STARLING observed that when a fluid containing glucose was perfused through the isolated heart of a diabetic dog, the rate at which the sugar was removed from the fluid was much less than through that of a normal animal. They noticed that when a weak acidic extract of the pancreas was added to the fluid perfused through the diabetic heart, sugar disappeared practically as quickly as when the solution was passed through a normal heart. These results have not, however, been supported by other workers.

The possibility that the pancreas produced a secretion which directly entered the blood stream was strongly suggested by HEDON's cross circulation experiments made in 1915, in which, normal dog's blood coming from the pancreatic vein was circulated through the body of a depancreatized dog. Both the blood and urinary sugars in the diabetic animal were found to be greatly reduced. Similar results

were obtained by CARLSON and GINSBURGH in 1915. LA BARRE in 1927, by means of cross circulation experiments, was able to show the presence of Insulin in the blood.

CLARKE A. H., working in the laboratory of MAC CALLUM, made an attempt to demonstrate the presence of the anti-diabetic hormone by perfusing Locke's fluid through a mammalian heart and succeeded in showing that the heart removed glucose more rapidly when the solution was first passed through the blood vessels of the pancreas than otherwise.

3. *Isolation of Insulin.*—Towards the close of the 19th century—the end of the “dark ages” in the history of Diabetes—pancreas came to be distinctly regarded as the organ concerned in the production of an internal secretion which was responsible for the maintenance of normal carbohydrate metabolism. In view of this belief, from 1890 onwards, numerous attempts were made to prepare active and serviceable extracts of the pancreas, but they almost all failed until 1922, a most eventful year in the history of diabetes, when BANTING and BEST, two young Canadian workers, succeeded in preparing their first active crude extract which, when injected, was found to control symptoms, in both experimental and clinical diabetes.

As early as 1892, MINKOWSKI tried and injected pancreatic extracts but was not able to notice any visible effect. HEDON (1892) and CAPPARELLI (1893) prepared and injected pancreatic extracts in experimentally made diabetic dogs, but they were unable to observe any noticeable change in the sugar content in blood. MACKENZIE (1893) and several other workers tried the effect of freshly prepared pancreatic juice given orally, but could not detect any change in the output of urinary sugar, nor in the level of blood sugar.

In 1898, BLUMENTHAL tested the freshly pressed juice from the pancreas after removing the protein material, but his results were inconstant and often marred by severe toxic reactions following upon injections of the extract. DIAMARRE and RENNIE, and FRASER prepared active extracts from the island tissues of certain fish, which appear to contain considerable amount of Insulin. These extracts, when given orally, were found to be almost inert, but, when injected, produced severe toxic reactions. ZUELGER in 1908 prepared an alcoholic extract by a method which very nearly resembles the modern method of isolating Insulin. Promising results were obtained but, on account of the extract, the use of such extracts was soon discontinued. During the summer of 1911, E. SCOTT, working at the University of Chicago, prepared an active alcoholic extract which he termed *Insuline*, and showed that his extract was capable of relieving some of the diabetic symptoms. After the publication of his discovery in 1912, he did not proceed further with his work on account of the frequent appearance of severe toxic reactions coming on after injection of his extract. Meanwhile, SHARPLY-SCHAFER, not knowing the active extracts prepared by SCOTT, and assuming that there was produced an

internal secretion by the island cells, gave the name *Insulin* to the hypothetical active principle.

Later in 1913, MURLIN assisted by KRAMER, prepared alkaline extracts of the pancreas and also duodenum and showed that he reduced glycosuria in depancreatized dogs. He, however, did not proceed further with his investigations, as it was soon known that alkalis also were capable of reducing glycosuria to a certain extent. KLEINER and MELTZER in 1915 prepared weak saline extracts which, when slowly administered to diabetic animals, produced a temporary but well marked reduction in the percentages of both blood and urinary sugars. They regarded their findings as direct evidence in support of the pancreatic theory of diabetes mellitus.

In 1921, PAULESCO in France prepared an extract of the pancreas with ice cold water, which lowered the percentage of sugar as well as urea in the blood, and also greatly reduced the amount of sugar excreted in urine of the diabetic animals. He (1922) suggested the name “Pancreine” for the active principle of his extract. MACKENZIE WALLIS prepared and tried alcoholic extracts of the pancreas made *in vacuo* and observed reduction in blood sugar in certain diabetic cases.

Finally, we come to the epoch-making discovery of Insulin. In the month of May 1921, two young Canadian investigators, FREDERICK G. BANTING, once an orthopaedic surgeon, and CHARLES H. BEST, a second-year medical student, set to work under the guidance of PROF. J. J. R. MACLEOD, in his laboratory at the University of Toronto and, towards the end of the same year, succeeded in preparing a somewhat crude but physiologically active extract which, they showed, was capable of alleviating hyperglycemia and glycosuria, the two leading symptoms of diabetes, in both diabetic animals as well as patients. They further showed that under the influence of their extracts, not only did the diabetic animal improve in health and activity but also lived much longer than the untreated control which usually died within a few days of the removal of the pancreas. Their first active extract was prepared according to the method suggested by BANTING, who assumed that the active principle was destroyed by the proteolytic enzyme trypsin, secreted by the acinar cells, and ligatured the pancreatic duct and allowed several weeks to elapse before removing and extracting the pancreas in order to allow the acinar tissue to atrophy and degenerate.

Soon after, it became evident that the original method of BANTING was inadequate for preparing extracts sufficiently pure and in quantities large enough to meet the clinical demands. Improved methods were, therefore, sought for and soon developed and in 1923, Insulin was made available in the form of crystal clear solution, in amounts big enough to supply the then existing demand. For this brilliant achievement, a greater share of the glory goes to B. COLLIP, another worker at the Toronto University. Mention must also be made of the firm of MESSRS. ELI LILLY & Co., one of America's greatest pharmaceutical houses, as being pioneer in undertaking and perfecting the methods for the manufacture of Insulin on a large commercial scale in

order to supply the needs of the millions of diabetics all over the world. Insulin is now also marketed by a number of other firms.

BANTING and MACLEOD were awarded Nobel Prize for medicine for the year 1923, which they most magnanimously equally shared with BEST. In 1930, the magnificent Banting Institute of the University of Toronto was built and dedicated to the man who discovered Insulin at the young age of thirty. The names of BANTING and BEST will ever gratefully be remembered in the history of medicine for giving one of the few, most valuable, life-saving remedies in the form of Insulin.

In 1926, ABEL first prepared Insulin in a pure crystalline form, which, in the light of recent investigations, is regarded as a protein-like substance of a high molecular weight, containing Sulphur exclusively in di-Sulphide (—S—S—) linkage. Insulin was included in the British Pharmacopœia 1932 and its manufacture in England is controlled by the Therapeutic Substances Act of 1925.

4. "*Slowly-acting*" forms of Insulin.—Soon after Insulin was discovered and introduced into therapeutics, it was found that it was very soluble in the body fluids and its action was short lasting and in certain severe cases, even multiple injections failed to control hyperglycemia and glycosuria. Attempts were, therefore, made to prolong the blood sugar lowering action of Insulin, and as early as 1923, BURGESS, NORMAN, CAMPBELL, OSMAN, PAYNE and POULTON experimented with Insulin in a 70% gum arabic solution. DE JONGH, and E. LAQUEUR also studied similar preparations (1925). LEYTON (1929) experimented with mixtures of Insulin with Lecithin, Arachis oil, and Castor oil, whilst CLAUSEN (1934) tried small amounts of Adrenalin, Pituitary extract and Ephedrin, mixed up with Insulin, with a view to limit its absorption.

So far, none of the methods was found suitable for practical application in therapeutics. Later, endeavours were made to chemically modify Insulin in such a way that the new compound was absorbed much less rapidly. In 1936, HAGEDORN of Copenhagen and his collaborators succeeded in preparing a compound which was introduced in the market under the name Insulin retard or Protamine Insulin, by mixing Insulin with a properly buffered solution of Protamine—a component of fish sperm. The new compound was formed in the form of a fine precipitate and, when injected as a suspension, it was found that Insulin was very gradually liberated by the body fluids and the hypoglycemic effect lasted from 2 to 4 times as long as that of unmodified Insulin. Though the new compound was a distinct advance on the original Insulin, it proved irregular in its action and not to last long enough when given in one single dose, however large, to control symptoms in severe diabetes.

Practically at this time, SCOT (1934), working at the University of Toronto, found that crystals of Insulin could only occur in the presence of zinc, nickel, cobalt or cadmium. He and FISCHER also discovered that Insulin solution containing 0.01% of zinc exerted in rabbit, a mild but prolonged action lasting over a period of over 10 hours, and that

the amount of sugar metabolised was equal or greater than that metabolized by a similar quantity of Insulin.

A newer compound, having a more stable and more prolonged action lasting for nearly 24 hours, was prepared by the Toronto workers (1937) and marketed by MESSRS. ELI LILLY & Co. under the name of Zinc Protamine Insulin. This compound soon replaced the Danish one, as it made possible to control hyperglycemia and glycosuria by one injection a day, instead of two or three of the original Insulin.

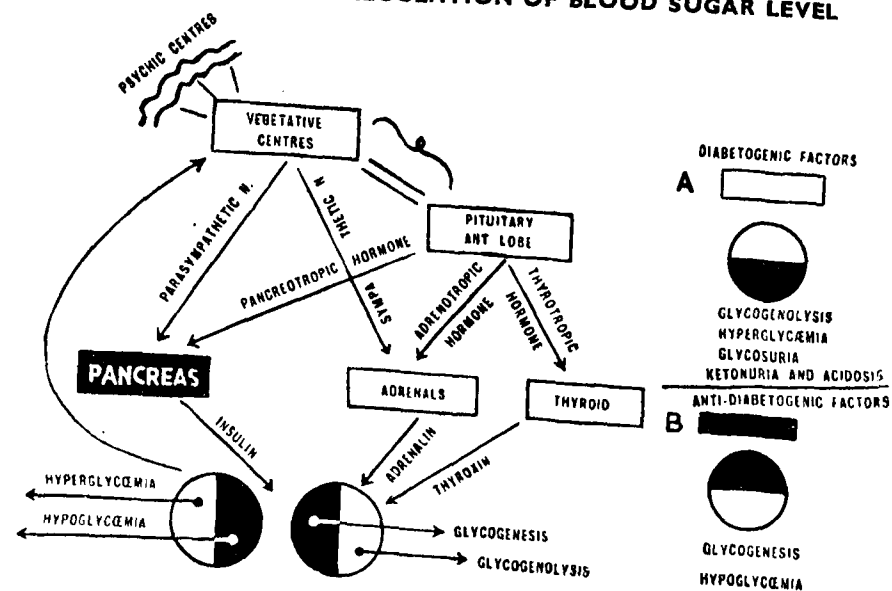
The newer compound, with increasing experience, has been found to possess certain drawbacks, but it is very likely that it will be improved upon in the near future.

III. *Observations (clinical and experimental) on the relationship between the Pancreas and Diabetes Mellitus.*—The association of diabetes mellitus with pancreas was suspected since the time of BRUNNER's experiments on depancreatized dogs, but their full significance was not recognized until many years later. Isolated observations on the morbid anatomy of the disease were made by a number of independent observers, but no attempts were made to correlate them. Thus in 1778, THOMAS CAWLEY, chief surgeon to the forces of Jamaica, recorded a case of diabetes mellitus associated with a pancreas full of stones. CHOPART (1792), VON RECKLING HAUSEN (1864) and LANCEREAUX (1877) described pancreas containing calculi. JOHN ELLIOTSON (1833), BOUCHARDT (1851) and FRERICHS (1884) noticed at autopsies, gross morphological changes in the pancreas of their patients. It was, however, in 1889 that MINKOWSKI and VON MERING, by their classical experiments definitely proved that in dogs, a diabetic condition was produced by removal of the pancreas. MINKOWSKI (1892) and later HEDON (1893) demonstrated that the experimental diabetes could be prevented by pancreatic grafts, and conclusively proved that the pancreas produced an internal secretion, the lack or deficiency of which was responsible for the diabetic condition. Later, LAQUESSE (1893) OPIE (1901), SSOEOLEU (1902), MAC CALLUM, HEIBERG and WEICHELBAUM (1911), CECIL (1911), ALLEN (1913) and several other workers noticed morbid morphological changes in the island cells of the pancreas in diabetes and favoured the Insular theory of diabetes, first championed by SAUERBECK (1904), and which seemed almost completely established when BANTING and BEST in 1922 isolated Insulin in an almost pure form, which, when injected, controlled the symptoms both in experimental and human diabetes, at least during the period it lasted in the body.

Mention may also be made of the rival theories that were current at one time or other before Insulin was discovered. Essentially, there were two *viz.*, (1) the acino-insular hypothesis, which held responsible the "malfunction of pancreas as a whole" for diabetes and was supported by LOMBROSO (1910) REITMANN (1905), HERX HEIMER (1905), KARAKASCHOFF (1906) and SAGUCHI (1920) and (2) the acinar hypothesis—It is more or less of historical interest only and was founded on the belief of HANSEMAN (1894), that the acinar cells are the seat of regulation of carbohydrate metabolism.

The success of BANTING and BEST in isolating Insulin held out high hopes for an early and complete elucidation of the problems connected with diabetes and led to many researches being undertaken with a view to study the chemical, physical and physiological properties of Insulin, a necessary step preliminary to attempts to unfold the mystery which still surrounds the disease—particularly as regards its nature and origin. As a result, extensive literature has appeared during the 20 years that have elapsed since Insulin was discovered; to review it is beyond the scope of this article and would require a separate volume by itself. Suffice it to say that nothing has happened to merit historical importance and the "Insular theory"—a legacy from the workers of the 19th century, has remained the favourite till the present day, though as a result of growth of knowledge in the subject of carbohydrate metabolism and in the realm of endocrinology, doubts have begun to be expressed, in very recent years, as regards the correctness of the "Insular theory" of diabetes. The functional evidence, though convincing by itself, has not been supported by observations made in search of demonstrable morphological lesions in the islands of pancreas. At autopsies, the lesions have been found to vary widely qualitatively as well as quantitatively and not to run parallel with the severity of the clinical symptoms. Moreover, lesions similar to those commonly found in diabetic pancreas, have been found in non-diabetic cases dying of other diseases.

SCHEME TO SHOW REGULATION OF BLOOD SUGAR LEVEL



(From "Münchener Medizinische Wochenschrift".
(No. 5 1938).

Consequently, many workers have directed their attention elsewhere outside the pancreas, in search of influences which act antagonistically to or neutralize the effect of Insulin—the anti-diabetic

hormone of the pancreas. Recent researches, carried out independently by HOUSSAY and his co-workers in America (1937), and YOUNG and RICHARDSON (1938) in England, strongly tend to favour the view that endocrine glands and particularly the anterior pituitary are involved in the development of diabetes.

It may be well to note that the present knowledge of diabetes is still very fragmentary and is based on knowledge derived from observations made during recent years on the mechanism of normal blood sugar regulation particularly by HOUSSAY and his collaborators. The latter may be summarized as follows:—The regulation of blood sugar is automatic and very finely adjusted and in this regulation, both liver and pancreas play a fundamental role and they are greatly influenced and controlled by the co-ordinated activities of the various endocrine glands, possibly through the anterior pituitary and the central nervous system. (*Vide Diagram.*)

IV. **Heredity.**—RICHARD MORTON in 1689 is said to have first drawn attention to heredity being probably associated with the causation of diabetes. It is believed that Hindu physicians of old too knew diabetes to be hereditary and familial. FRERICHS in 1884 estimated that a family history was present in 10% of the cases; other observers MOSLER, NAUNYN, KULZ and WILLIAMSON also noticed the influence of heredity on diabetes. JOSLIN (1928), CAMMIDGE (1934) and LAURENCE (1934) found that family history was obtainable in nearly 30-40 per cent of cases. WHITE PINCUS (1937) concluded that "the potentiality for developing diabetes is inherited and that the disease in most cases is transmitted as a simple Mendelian recessive type." Studies of BAUER, FISCHER and LANG and others also support this view. A few cases of dominant and irregular Mendelian transmission have also been found.

V. **Observations on Diet.**—As early as 1797, JOHN ROLLO had recommended meat diet in the treatment of diabetes. In pre-Insulin days, from 1895 to 1914, the type of diet advocated contained very little carbohydrate but more of protein and fat in order to make up the caloric deficit necessitated by restricted amount of carbohydrate. An occasional starvation-day was generally the rule. In 1913, ALLEN emphasized the evils of high fat diet and pointed out the value of undernutrition which is even to-day recognized as a part of treatment. From that time onwards till very recently, short fasts were almost always prescribed and were shown to be safe and effective in animals and in man by FOLIN and DENIS, particularly in mild cases. GUELPE (1910) and GRAHAM (1917) also referred to the value of under-nutrition in the treatment of diabetes. In 1912, SCHAFFER and WOODYATT pointed out that the amount of fat which could safely be given without producing ketosis was limited by the amount of available sugar in the diet (Ketogenic-antiketogenic ratio.)

From the time of discovery of Insulin, a gradual change has come in the trend of opinion and diet containing relatively large amounts of carbohydrate has been advocated and prescribed in a large number of diabetic clinics. Amongst those who have studied and advocated

the use of new liberal carbohydrate diet—rendered possible by Insulin—may be mentioned the names of GEYLIN (1926-35), SANSUN (1926-33) ADLERSBERG (1929-1932) POULTON (1931), RABINOWITCH (1930-1935) DYKE (1932), GRAHAM (1932), NIXON (1932) HIMSWORTH (1931-1934), BARACH (1930—1937) and PECK and RICHARDSON (1936). It is believed that the inclusion of a large amount of carbohydrate diet leads to an increase in sugar tolerance, and some of the diets (RABINOWITCH and RICHARDSON) contain on an average 200 to 300 grammes of carbohydrate, but a greatly reduced amount of fat, not more than 40 to 50 grammes per day.

Besides, in the past, from time to time, many systems of diet have been recommended and tried with claims of success by their respective authors; thus there were VON NOORDEN's oat-meal cure, DONKIN's milk cure, MOSSE's potato-cure, DURIY's rice-cure, PINNEL's liver-diet, but none of them survived for a long time.

VI. Observations on the Medicinal Treatment of Diabetes.—

Various organic preparations and drugs have been recommended in the treatment of diabetes but none of them has been found to give a cure though some have been found to reduce the severity of glycosuria. Thus, Incretin, extract of duodenum (LA BARRE), extracts of raw pancreas, Succenic Acid (GYRI 1937), Opium Synthalin, Myrtillin Decholin, Copper Sulphate and Gold preparations have been empirically prescribed and found to be useless if not harmful.

Since the time ZUELGER proposed the theory that adrenals have an important part in the development of diabetes, various surgical procedures such as cutting off the splanchnic nerves, resection of the sympathetic ganglia have been tried. Exposure of the adrenal region to roentgen rays have been recommended with a view to suppress the adrenalin secretion.

The present day treatment does not recognize, however, the use of any drug, except to treat the complications as they arise, and may be summed up in three words namely, diet, Insulin and exercise, the last being recognized, as a valuable adjunct in the treatment, by JOHN BROWN as early as the middle of the 18th century.

In concluding, it may be remarked that though diabetes mellitus has existed for over 2000 years and in spite of many valuable advances that have been made particularly during the past fifty years, we are still much ignorant as to why and how it is caused and that the present methods of diagnosis and particularly treatment at their best cannot be considered to be perfect and without fault or reproach.

In almost all civilized countries, during recent years, the incidence of diabetes has been known to rise gradually but steadily to a fearful degree, and yet no method has been known at least to keep its incidence under control, if not to completely eradicate it. To achieve it, further researches are absolute necessities. But it is not unlikely that one day, perhaps not very far, a new startling discovery is made which would completely metamorphosize all previous ideas about diabetes and make it possible to completely eradicate it or at least make it a rare disease, and write a new but concluding chapter in the history of diabetes.

A Review on the Genesis of Diabetes

BY

A. Chakravarti, B.Sc., M.B. (CAL.), F.R.C.P., F.R.S. (EDIN.)

Hony. Visiting Physician, North Suburban Hospitals, Calcutta.

DIABETES is understood to mean a condition of persistent hyperglycæmia with or without glycosuria. Sugar is not an excretable product and ordinarily would not appear in the urine (excepting a very little trace 0.001%), unless the blood sugar level is beyond 150 to 160 mgms. per 100 c.c.—the average normal kidney threshold for sugar. In fasting, the blood sugar level is usually 80 to 90 mgms. per cent. and after a meal, there is a steady rise till it reaches 130 to 140 mgms. per cent. within one hour and, with the simultaneous storage in the liver and muscles as glycogen and utilisation in the tissues by oxidative processes, the level gradually goes down to the normal level within two hours. In a diabetic, the fasting level is high, being 120 to 130 mgms., showing failure of efficient storage and utilisation and after a meal, the level goes up much beyond the threshold *i.e.*, 200 to 250 mgms. or more and the level would remain longer and would, owing to the same defects, go down very slowly to the high fasting level. In a diabetic, the threshold tends to go up and cases are not uncommon where there is hyperglycæmia without glycosuria. The reversed condition is also found—where there is glycosuria without hyper-glycæmia—the renal glycosuria, often encountered during pregnancy, in experimental phlorhizin diabetes, where the renal threshold is definitely lowered.

Thus in a diabetic, the absorption of sugar is assumed to be normal, the oxidation of glucose is deficient, so also glycogen synthesis and as a result, there is persistent high blood sugar and excretion of sugar. A further pathological process is in evidence in the abnormal conversion of some of the amino-acids to glucose, adding fuel to the fire.

Diabetes is not by itself a clinical entity and cannot be accounted for by any particular pathology or a particular causative factor. Researches into the etiology of a condition like this have been quite extensive and quite a varied type of etiological factors and pathological findings have been brought to light.

1. Predisposition or heredity is an important etiological factor and according to JOSLIN and GRAFE, quite a good number of cases are definitely accountable.

2. High carbohydrate diet and pancreatic exhaustion have been found to be important factors in a fair number of cases.

3. Congenital deficiency or abnormality—either of the pancreas or of other endocrine glands—may be responsible for at least some of the diabetic subjects. Hyper-thyroidism and hyper-pituitarism are frequently associated with hyper-glycæmia, while obesity has been frequently found in many of the diabetic patients. According to

KARUSE¹ and TRAUBE, most of these obese patients have had over-action of the anterior pituitary with increased basophil cells. Over-growth of pancreas by tumors has been associated with hyper-insulinism and occurrence of hypoglycæmia and in a large majority of diabetic autopsies, gross pathological lesions have been observed in the *beta* cells of the islets of Langerhans. A specific hormone² has been isolated in the pituitary extracts, called *diabetogen*, which definitely counteracts Insulin action, either inactivating Insulin by forming a pituitary-insulin combination or else by depressing the cellular activities of the islets by altering capillary circulations and thus inhibiting Insulin production. The contra-insulin hormone of the anterior pituitary controls secretion of the Insulin.

Insular cells are sensitive to the concentration of the blood-sugar and hyper-glycæmia would result from the inability of the body to maintain blood sugar within limits. The rate of absorption of sugar normally is 0.8 to 0.9 gram per kilo per hour. Insulin induces glycogen synthesis in the liver and in the muscles, the muscle glycogen differing from the liver glycogen, the latter being more stable. Insulin is *activated*³ inside the liver and Insulin so activated has been found to be only effective in initiating oxidation of sugar in the tissues. The action of Insulin is probably catalytic—a linkage of the active disulphide with the active aldehyde group of the dextrose molecule may be a possibility.⁴ In diabetes, there is unquestionably less oxidation of glucose in the tissues, not entirely accountable to deficiency of Insulin or any definite lesion in the islets and other factors play their parts. About 30 to 40% of the autopsies reveal pancreatic or endocrine lesions. Insulin hypoglycæmia may be combated by simultaneous injection of human plasma.⁵ Anaerobic oxidation of glucose does occur in the tissues with the formation of lactic acid, some of which is transported to the liver where it may be converted into glycogen.⁶ In pancreatectomy glucose oxidation is impaired and hepatic glycolysis is increased—there is hyperglycæmia. In more severe condition of diabetes, the venous blood sugar may be even higher than of the arterial—the tissues adding more sugar.⁷

4. Diabetic ketosis is analogous to the ketosis of starvation owing to the incomplete oxidation of fats as a result of inefficient carbohydrate oxidation. Diabetic lipaemia is due to the mobilisation of fat stores for the energy requirements as carbohydrate metabolism contributes less. The body starts katabolising tissue proteins in an attempt to supply more anti-ketogenic materials, converting about 58% of the amino-acids into glucose and the other amino-acids producing keto-acids make the condition worse. The acid-base equilibrium⁸ is upset—the plasma bicarbonates may go down and acidosis manifests. There is decrease of plasma chlorides and simultaneous reduction of the plasma bases. The fluid balance is finally lost by dehydration, there is impaired circulation and renal inefficiency—oliguria and uræmia follow and finally anuria.

5. The nervous system is concerned in the integrity and ordered activities of the live tissue cells. Any derangement, either in the

centre or in the branches, is reflected in the functional disturbance of the general or local tissue-cell activity. Infections, trauma, shock, long-standing worry, anxiety or strain, all tell heavily on the nervous system and the effect is, more or less, temporary or permanent in accordance with the nature of the causative factors.⁹ Any cerebral accident by disease or injury would, in a phase, exhibit glycosuria. The lesion in the brain itself may be responsible in causing depression in an all-round nerve control and consequent metabolic paresis leading to accumulation of absorbed and unutilised food products and the occurrence of proteinuria, glycosuria etc. The pituitary itself may be affected primarily by any trauma or disease or else secondarily affected by any lesion in the brain and the absence or deficiency of the pituitary hormone may remarkably inhibit metabolism, by affecting paresis in the sympathetic nervous system.

The work of HOUSSAY¹⁰ and YOUNG, and later on, by HINGSTON, have established that crude extracts of anterior pituitary facilitates glycolysis in the liver, inhibits oxidation of sugar and storage of glycogen in the periphery by paralysing Insulin work and also induces conversion of larger quantities of amino-acids and glycerol to sugar. Possibly, there is no specific diabetogenic hormone in the anterior pituitary extract but the combined effect in the various tissues results in the condition of hyper-glycæmia and glycosuria. The effect may be temporary and may go back to a normal state after discontinuance, but if very large doses are given for some days, the condition may be permanent, showing that certain definite pathological changes are brought about and evidences of such changes have been found in the liver, pancreas, adrenals and in the hypothalamus.¹¹

6. The process of tissue metabolism of the available food factors is evidently under neuro-hormonal control—the autonomous nervous system is principally concerned in the local secretory activities of the various glands with or without ducts and the actual engine work is under the control of the hormonal operatives—starting ignition and carrying on the combustion work. Insulin is undoubtedly concerned in the oxidation of glucose in the tissues—how it acts is not fully established: but from the extensive work in this field, it may be deduced that in this work of Insulin, there is an activator just as much as there is an inactivator or a controlling switch. The part played by the adrenals is really an emergent one, operated though the sympathetics, including glycolysis and sugar transport from the mobile storage in the liver but the action of hypophyseal hormone in diabetes is more profound and longstanding. The transient glycosuria in hyperthyroidism or in conditions of acute nerve strain or shock is evidently of the adrenal-sympathetic type. Some cases of hyperthyroidism may be highly glycosuric and these cases do not recover normal sugar level even after thyroidectomy. The condition may possibly be due to an associated hyper-function of the hypophysis. Cases are on record, where supra-renal cortical adenoma was associated with marked glycosuria and hyperglycæmia and there was complete recovery after successful removal of the tumour. Simultaneous removal of the pancreas and

adrenals exhibited mild glycosuria, no ketonuria and if further cortical hormone was administered, there was definite increase of glycosuria^{1,2}. These observations strongly suggest that the adrenals play an intimate and probably an intermediate role in the action of hypophyseal diabetogenic hormone. WEINSTEIN's case of pituitary glioma¹³ with emaciation (pituitary cachexia), anaemia, eosinophilia and hyperglycaemia exhibited, on autopsy, marked atrophy of more than 50% of hypophyseal tissue, complete atrophy of testes, prostate and thyroids. The gonads are intimately related to hypophysis, the hypo or hyper-activity of the pituitary leading to hypo and hyper-activity of gonads. Oestrin¹⁴ is supposed to repress the activity of anterior pituitary. If injected it may alleviate the symptoms of diabetes to some extent. OGILVIE found that obesity after artificial menopause is frequently marked by hyperglycaemic condition, but not so in natural menopause. Temporary glycosuria during pregnancy so often found is due to the disturbances of ovarian and pituitary functions occurring during pregnancy and cases are on record where the threshold of the kidney only is lowered, hyperglycaemia is not marked, but ketosis very much in evidence. After delivery, these cases invariably returned to complete normality. Occasionally, however, true diabetes with profound hyperglycaemia manifests itself for the first time during pregnancy, but such cases are very few, and the detection might be accidental. DUNLOP¹⁵ reports a peculiar case of young diabetic in his ward with physical and sexual infantilism. Radiologically, the pituitary fossa was very small. DOTT¹⁶ had a similar case. The anomalous condition is explained to be due to an encephalitic hypothalamic injury causing Insulin secretory deficiency and at the same time, there was damage or a congenital deficiency of the anterior pituitary interfering with growth-promoting and sex-maturing hormone.

7. The occurrence of carbuncles, cellulitis etc., have long been recognised as a very common complication in a diabetic subject. Again, diabetic condition has been manifest for the first time during such an infection. Staphylococcal infection is the commonest type and the effect, till the introduction of Insulin, was, quite disastrous. Another interesting feature in such an infective condition is the marked Insulin resistance demanding incredibly large doses of Insulin to make the urine sugar-free. I have known several such cases, who would ordinarily be aglycosuric simply by dietetic control, requiring 80 to 100 units of Insulin daily, while suffering from carbuncle or cellulitis by staphylococcal infection¹⁷. Evidently, the bacterial bodies or their toxins somehow prove antagonistic to Insulin, either by interfering with Insulin activation inside the liver, or else making Insulin innocuous by some physico-chemical process.

From what have been said, it is apparent that the diabetic condition may be occasioned by a wide variety of different conditions. Usually, there are three types of diabetics—the young diabetic, the fat diabetic and the senile diabetic. It may be seen in hyper-pituitarism, in hypo-thalamic lesions, in hyper-thyroidism, in hyper-adrenalism, in pregnancy and in infections. Excepting in the case of the young, acute

diabetics and the senile diabetics, the sugar is capable of being controlled or the condition returning to normal. It is only in the young diabetic that permanent pancreatic changes have been found. In the senile type, the changes are a part of the slow degenerative arteriosclerotic process. In the young, the condition looks very much like the experimental diabetes created by a few massive injections of anterior pituitary extracts.

References :

1. Grafe, E., *Metabolic Diseases and Treatment*, pp. 155, 1934.
2. Burn, *Jour. Physiol*, 57, 318, 1923.
3. Himsworth, H., *The Activation of Insulin—Lancet*, 2 : 935, 1932.
Do. *The Physiological Activation of Insulin—C1 in. Sc. 1 : 1, 33—34.*
4. Cori, C. F., *Comparative Study of the Blood Sugar Concentration in the Liver, Vein etc., during Insulin injections—J. Phatak Exp. Ther.* 22 : 355, 1923—24.
5. Karlitz, S., *Insulin Inactivation by Human Blood—Arch. Int. Med.* 45, 546, 1930.
6. Cori, C. F., *Glycogen Formation in the Liver from Lactic Acid—J. Biol. Chem.*, 81 : 339, 1929.
7. Rabinowitch, I., *Simultaneous Detection of Arterial and Venous Blood Sugar in Diabetes—Brit. Jl. Expt. Med.* 8 : 76, 1927.
8. Peters, J., *Total Acid—Base Equilibrium of Plasma in Health and Disease—J. Chm. Invest* : 21 167, 1925—26.
" *Studies in Diabetic and Acidosis, Do. : 2 : 377, 1933.*
9. Joslin, E. P., *The Nervous Factors in the Etiology of Diabetes—The Treatment of Diabetes Mellitus—1937.*
10. Houssay.
11. Do.
12. Long and Lukins—*Proc. Soc. Expt. Biol. and Med.* 1934—35.
13. Weinstein : *Am. J. Med. Sci.* 189, 245, 1935.
14. Grafe, E., *Ovarian Prep. in Diabetes—Metabolic Disease and their Treatment*, —pp. 187, 1934.
15. Dunlop, D. M., *The Significance of Glycosuria, Ed. Med. Jr. N. S. IV.* p. 369, 1939.
16. Do.
17. Do.

A New View on Diabetes

BY

H. N. Mukherjee, B.Sc., M.B., D.I.C. (LOND.)

Sir Nilratan Sircar Research Institute, Charnichael Medical College, Calcutta.

THE hyperglycæmia of diabetes has been so long considered as a pathological process. DR. B. C. ROY, however, has held for more than a decade that the hyperglycæmia is a physiological response to certain metabolic defect which is at the root of diabetes. This view has been already reported elsewhere (ROY & MUKHERJEE, 1935, 1939). In view of the fact that during recent years somewhat similar views have been put forward by other workers (HIMSWORTH, 1939), it is considered worthwhile to develop our conception in more detail in the present paper. In order to form a comprehensive idea of the physiology of carbohydrate metabolism, it is necessary to trace the development of our ideas beginning from the classical experiments of the great physiologist CLAUDE BERNARD. From the observation that the blood flowing from the liver of an animal contains more sugar than the blood entering that organ, BERNARD came to the conclusion (1853), that "sugar is manufactured in the liver which must, therefore, be considered as an organ producing and secreting sugar". His further investigations showed that in liver, there is a substance which does not give the ordinary tests for glucose but could, in suitable circumstances, give rise to sugar. BERNARD isolated and called this substance *glycogen*, which is the immediate precursor of sugar liberated by the liver. The next important observation is that by SANSON (1857), who found that the muscles also contained glycogen and the work of HERMANN (1867) and of others showed that muscular contractions were associated with decrease in muscle glycogen and appearance of lactic acid. By 1877, CLAUDE BERNARD came to the conclusion that sugar is never formed in the muscle but muscle glycogen is always broken down to lactic acid and that, in the living animal, sugar is destroyed in the muscles and not formed therein. This meant that the level of sugar in the blood was the resultant of the action of two forces: (1) the production of sugar in the liver and (2) the absorption and utilisation of sugar by the muscular tissues. The constancy of the blood sugar level was the result of a dynamic and not a static equilibrium. The fact that the blood sugar remains so remarkably constant and naturally tends to re-establish itself at the original level after a disturbance in one direction or the other, showed that a very sensitive mechanism for mutual adjustment must exist between the processes in the liver and muscle tissues. Such a theory, brilliantly conceived by BERNARD, appears to be fundamentally correct according to modern research (e.g., the work of MANN which demonstrated that hepatectomy causes hypoglycæmia in normal and pancreatectised animals). BERNARD believed that glycogen is formed from non-carbohydrate sources and it is a secretion by the liver and not a passive storage form of sugar and according to his conception the liver of an animal which is not receiving carbohydrate food manufactures sugar

from non-carbohydrate sources—"the formation of sugar being preceded by the production or secretion of glycogen".

In discussing the origin of this glycogen, we will first consider the three obviously possible sources:—

- (1) Carbohydrate—ingested as food.
- (2) Protein matter—exogenous or endogenous.
- (3) Fats.

It has been, however, amply demonstrated (CORI & CORI), that liver glycogen level rises considerably after ingestion of many carbohydrate substances. In this respect fructose appears to be a better glycogen—far more than glucose.

We can account for the rise of liver glycogen level during carbohydrate absorption by two simple ways.

- (1) The sugar absorbed is directly converted to glycogen.
- (2) The glycogen which the liver is normally manufacturing and hydrolysing is conserved by the liver during carbohydrate absorption causing an increase in the glycogen content.

There is apparently a normal rate and level of glycogenesis and also of glycogenolysis *i.e.*, two processes (1) first glycogen is formed and secreted at a normal rate to reach a normal level; and (2) sugar is formed from it at a normal rate to reach a normal level.

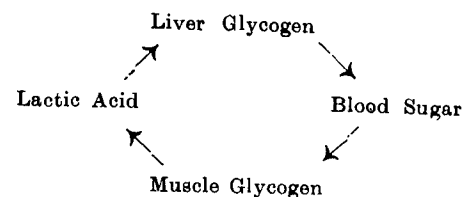
The experimental work of MANN (1927) and his co-workers, have demonstrated that the liver of a fasting 10Kg dog is secreting about 60g of sugar daily. Calculated at this rate the liver of a fasting man is producing about 300 to 400g of sugar in a day.

It is thus evident, as CLAUDE BERNARD originally stated, that the constancy of the blood sugar level depends on a very accurate mutual adjustment between sugar production by the liver and sugar absorption by the tissues. The mechanism controlling this mutual adjustment is an extremely complex one and, according to modern physiological research, is associated with at least three important hormones *viz.*, (1) Insulin (2) adrenalin and (3) the anterior pituitary factor. Besides these hormones, certain nervous centres in the floor of the 4th. ventricle and hypothalamus and the adrenal cortex may be implicated.

Now, we shall consider how sugar is produced in the liver and what part the three hormones play in it.

Normally, sugar is formed from the ingested carbohydrate and proteins of the food but for some reasons the formation of sugar from fats is a matter of difficulty, the process being accompanied by the formation of ketone bodies. The liver stimulates the formation of sugar from fatty acids only when it is forced to do so by lack of sufficient alternative sources; that is, fatty acids are only converted into

sugar when there is great demand for sugar and protein and carbohydrate sources alone are not sufficient to meet it. The whole process of normal carbohydrate metabolism can be conceived as occurring in a cycle.



The fate of absorbed sugar is in part the replenishment of the glycogen stores of the muscles which are reduced during muscular activity while part may be oxidised directly. Conversion to fat or lactic acid as already indicated is also possible.

We shall now briefly consider the action of Insulin, Adrenalin and the Anterior Pituitary factor in the regulation of normal carbohydrate metabolism.

Insulin.—Injection of Insulin lowers the blood sugar level and brings about the disappearance of diabetic ketosis rapidly in the presence of adequate supplies of sugar. Insulin raises the R. Q. It increases the amount of muscle glycogen and diminishes markedly the rate at which sugar is secreted by liver and perhaps antagonises the glycogenolytic action of adrenalin on the liver. It apparently does not increase the liver glycogen and has no effect on the metabolic rate though it reduces the increased protein katabolism in diabetes. It would thus appear that the hypoglycæmic action of Insulin is mainly due to inhibition of glycogenolysis in liver and conversion of circulating sugar into muscle—glycogen.

Adrenalin:—It causes glycogenolysis in the liver; so, the blood sugar is increased and the liver glycogen is decreased. Muscle glycogen under the action of Adrenalin is broken down to lactic acid and the metabolic rate may be increased. Adrenalin secretion is automatically increased during hypoglycæmia as a protective measure (CANNON ET AL 1924). The main effect is to check possible hypoglycæmia and to raise blood sugar level at the cost of liver glycogen during times of strife and strain, when more work has to be done.

Anterior Pituitary Factor:—The association of glycosuria and disturbance in growth with the pituitary gland has been observed for a long time (MARIE, FROHLICH). It is, however, the work of HOUSSAY (1929) and his co-workers, which first clearly demonstrated the important role played by this factor in diabetes. Hypo-physectomy makes the animal very sensitive to the action of Insulin—a very small dose may cause convulsion and death. In depancreatized dogs, hypophysectomy alleviates the symptoms of diabetes. Fasting, even for a short period, may cause fatal hypoglycæmia in such animals.

From recent research (SOSKIN ET AL, 1935), it appears that the

anterior pituitary factor stimulates the conversion of fats to sugar and in its absence, Adrenalin cannot initiate glycogenolysis. Hypo-physectomy hinders the ability of the liver to liberate sugar. In the depancreatized and hypo-physectomized animal (the Houssay dog), the capacity to oxidise and utilise carbohydrate is almost normal.

If it is believed that Insulin is necessary for the utilisation of sugar in the normal animal, so that the depancreatized dog is unable to oxidise sugar at all, then it must be conceded that, in the absence of pancreas, the pituitary gland is normally inhibiting sugar utilisation in the tissues although these tissues left to themselves (Houssay dog) can utilise sugar when the pituitary as well as the pancreas are removed.

The available evidence suggests that the pituitary gland stimulates the formation of sugar from protein (HOUSSAY) and from fat (SOSKIN) and that the alleviation of diabetes following hypophysectomy is, perhaps, due in part to the diminution of sugar production from these sources. There is also evidence that the pituitary can retard the peripheral utilisation of glucose. So, its effects are generally antagonistic to that of Insulin. So far, we have considered briefly the complicated process of carbohydrate metabolism. We shall now try to consider the nature of the metabolic defect in diabetes. As first enunciated by CLAUDE BERNARD, there are two possible causes of the diabetic condition (1) excessive secretion of sugar by the liver, (2) Inability of the extrahepatic tissues to absorb and utilise sugar.

BERNARD himself favoured the over-production theory. PFLUGER and VAN NOORDEN also subscribed to this view.

MINKOWSKI (1893) and in recent times LUSK, on the other hand, favoured the second or the under-utilisation theory.

More recently, MACLEOD and his school (1928), have suggested that the cause of diabetes is uncontrolled hepatic gluco-neogenesis i.e., sugar production from non-carbohydrate sources with which some decrease in utilisation of glucose in muscles might be associated.

But it is natural to enquire how does this over-production of sugar,—this gluco-neogenesis take place? Is it a cause or an effect of diabetes? Any how, it is obvious that in diabetes, there is disturbance in the rate of glycogenesis and glycogenolysis in the liver with increased secretion of sugar.

From certain experimental evidence we, (ROY and MUKHERJEE, 1935, 1939) suggested a possible explanation of the nature of the diabetic condition,—that the primary factor in the pathogenesis of clinical diabetes is a condition of acidosis and the hyperglycæmia is an active body mechanism to combat acidosis. We shall now try to develop this thesis from experimental and other evidence.

Acidosis and Hyperglycæmia.—Experimental work in animals have demonstrated that hyperglycæmia is produced by acid intoxication. CAMMIDGE and HOWARD (1923) have reviewed the earlier literature on the subject. Thus NAUNYN, as far back as 1868, observed

glycosuria in a dog poisoned with Hydrochloric Acid. ELIAS (1912) produced hyperglycaemia in rabbits and dogs with Hydrochloric Acid. UNDERHILL (1916), on the other hand, showed that intravenous injection of Sodium Carbonate into normal animals may induce a fall in the blood sugar level. From these and other experiments, it can be concluded that hyperglycaemia may be expected to arise in acidosis and the opposite condition of hypoglycaemia will occur in alkalosis.

If we again consider the condition of hyperglycaemia after Ether or Chloroform anaesthesia, the same factor of acidosis becomes apparent as in these conditions the hyperglycaemia is associated with a lowered alkali reserve and can be controlled by administration of alkali and glucose. Moreover, it has been observed that prolonged fasting can lower the sugar tolerance in experimental animals. This condition was originally described by CLAUDE BERNARD who noticed that dogs, after a long fast, passed sugar in their urine when they were given a large carbohydrate meal (hunger diabetes).

ELIAS AND KOLB (1913) have shown that the glycosuria of "hunger diabetes" in dogs is associated with hyperglycaemia and that the excess of sugar in the blood and urine can be reduced by administration of alkali which brings about an increase in sugar tolerance. So, in this condition also, the hyperglycaemia is the result of acidosis developed during breakdown of proteins and fats in the liver during starvation (starvation acidosis). A similar condition is found in man also, in tramps and poorly-nourished fasting individuals, and known as "vagabond glycosuria", the condition reacting quickly to alkali and glucose. The proper understanding of the condition of "hunger diabetes" or "vagabond glycosuria" is of great importance in forming a correct idea about the pathogenesis of clinical diabetes in man. Apparently, acidosis antagonises Insulin and prolonged acidosis damages the Insulin secreting mechanism.

From available recent experimental evidence (DONNELLY, 1938), it may be safely concluded that glycogenolysis varies directly and glycolysis varies inversely with the total acidity of the system. The breakdown of glycogen with resulting hyperglycaemia, which follows acidosis, demonstrates according to DONNELLY, 1938, the necessity of treating the acid intoxication in hyperglycaemic conditions or, in other words, the primary acidosis factor in diabetes is here again emphasised.

From these findings it is evident that hyperglycaemia is a natural physiological corollary of acidosis. But is it only a passive phenomenon? If, however, it is considered, as suggested in our previous paper (ROY and MUKHERJEE, 1935), that the hyperglycaemia is an active body mechanism to combat acidosis, the significance of the hyperglycaemia becomes more important.

ROY and MUKHERJEE (1923) found that, in most cases of diabetes, the alkali reserve is low even in mild types of the disease. Again, the administration of glucose has long been known to be effective in combating acidosis. So, it is natural to conclude that the same phenomenon may occur in the body i.e., hyperglycaemia is produced to combat acidosis. In other words the hyperglycaemia in diabetes is a

natural protective reaction of the system against acidosis. We shall now try to picture the nature of the metabolic disturbance in *Diabetes* as follows:—The liver normally produces glycogen from proteins and carbohydrates and secretes sugar in the circulation at a rate according to body needs. In acidosis, rate of glycogenolysis is increased and hyperglycaemia results. Proteins and fats are also under abnormal conditions broken down in the liver to form glycogen and from this source also sugar is formed and secreted into circulation according to body needs. But, in the process of abnormal sugar formation from proteins and fats, ketone bodies are formed, resulting in acidosis and ketosis. For complete oxidation of ketone bodies sugar must be available in sufficient amounts as the combustion of adequate amount of glucose must occur for the oxidation of ketone bodies to proceed to completion. In the normal individuals, this takes place near about a blood sugar concentration of 0.1%. But if by any means the rate and quantity of protein and fat breakdown in the liver are increased, acidosis and ketosis result. The first effect of this results in lowered carbohydrate tolerance (as in hunger diabetes or vagabond glycosuria) or, in other words, the blood sugar level is raised. The system can then work in this higher concentration which is a proper and natural body reaction to deal with acidosis. But, if this condition is allowed to persist for a long duration, a permanent hyperglycaemia with damage to the insulin secreting mechanism may follow. In a large number of diabetic individuals, a history of over-nutrition is present. Commencing with a normal metabolism and a normal blood sugar level, these patients by over-eating force the liver to produce more glycogen at a greater rate resulting in a tendency to hyperglycaemia. To cope with this state of affairs, the system has to react with greater production of Insulin to keep down the blood sugar level within normal limits. Ultimately, this state of affairs results in damage to insulin secreting mechanism due to over-strain and the higher blood sugar level becomes normal with this group of individuals; but, the resulting increased production of ketone bodies damages the insulin mechanism further and diabetes results. In our previous paper (1935), we have suggested that the same factor which causes acidosis also depresses Insulin action. This view becomes clear in the light of recent research with the anterior pituitary factor.

Normally, the function of the anterior pituitary factor is obviously to initiate the breakdown of proteins and fats in the liver. The factor has thus two effects: (1) diabetogenic or anti-insulin and (2) ketogenic or acidotic. Prolonged treatment with this factor in dogs results in hyalinisation of the *beta* cells of the islet tissues of the pancreas (RICHARDSON and YOUNG 1938). It is thus clear that the same factor which causes acidosis also depresses Insulin action.

That Insulin itself does not directly play a very important part in the oxidation of glucose is apparent from experimental work. ROY and MUKHERJEE (1935) found that glucose, when given intravenously in diabetes, was utilised by the tissues. The effect of intravenous glucose in these cases was to increase the blood sugar level still higher

and, at this higher blood sugar level, oxidation and utilisation of glucose were possible. The introduction of glucose in adequate amounts intravenously quickly brings available glucose to tissues and liver and thus stops hepatic gluconeogenesis and reduces acidosis and ketosis and ameliorates the diabetic condition.

Recent physiological work has corroborated these findings of ours. MIRSKY ET AL (1937) found from investigations on completely depancreatized dogs that in the absence of Insulin, glucose itself administered intravenously in big amounts reduces ketosis and acidosis. From further work on depancreatized and nephrectomized dogs, they found that glucose thus administered stops the breakdown of proteins and is thus a sparer of body nitrogen.

MIRSKY ET AL (1937) came to the following conclusions which, interpreted rightly, fully confirm the views of ROY and MUKHERJEE (1935) that the metabolic disturbance in diabetes was due to an alteration in the balance between hepatic glycogenesis and glycolysis. The associated production of ketone bodies was due to a compensatory acceleration of breakdown of fats and proteins in the liver in consequence of a decrease in the amount of carbohydrate available for oxidation.

We may thus conclude that the first stage in diabetes is a condition of acidosis. This may result from ingested acid bodies or from faulty method of living which causes retention of CO_2 or greater production of acid ketone bodies in the system. Hyperalimentation specially with rich protein and fat foods introduces a large amount of organic acid bodies into the system and if continued for a long time, may bring about acidosis. This automatically brings about a tendency to a condition of hyperglycemia. So long as the insulin mechanism is intact, the blood sugar level is kept within normal limits and diabetes does not supervene but when Insulin fails due to the damaging effect of the acid bodies, diabetes results.

References :

1. Cammidge and Howard (1923)—*New Views on Diabetes Mellitus*, 72.
2. Cannon et al (1924)—*Amer. Journ. Physiol.*, LXIX, 46.
3. Donnelly (1938)—*Amer. Journ. Physiol.* 123 (2), 448.
4. Elias (1912)—*Biochem. Zeit.*, XLVIII, 120.
5. Elias and Kolb (1913)—*Biochem. Zeit.*, LII, 331.
6. Mann (1927)—*Medicine*, VI, 419.
7. Himsworth (1939)—*Lancet*, July 1, 1.
8. Houssay and Biasotti (1929)—*Endocrinology*, 1931, XV, 511.
9. Mirsky et al (1937)—*Amer. Journ. Physiol.* 118 (2), 290; 120 (4), 681.
10. Naunyn (1868)—*Arch. f. Physiol.*, 413.
11. Richardson and Young (1938)—*Lancet*, CCXXXIV(I), 1098.
12. Roy & Mukherjee (1923)—*Calcutta Med. Jour.* March.
13. Roy & Mukherjee (1935)—*Calcutta Med. Jour.* December, 367.
14. Roy & Mukherjee (1939)—*Jour. Indian Med. Assoc.* March, Vol. VIII, No. 6.
15. Soskin et al (1935)—*Amer. Journ. Physiol.*, CXIV, 110.
16. Underhill (1916)—*Jour. Biol. Chem.*, XX, 463.
17. Young (1936)—*Lancet*, CCXXXI(II), 237; 297.

Clinical Observations on Some Ætiological Factors in Diabetes

BY

K. Narayana Murthi M.D.,

Hony. Physician, General Hospital, Madras.

Diabetes is a constitutional disorder due to defective secretion of Islets of Langerhans in the pancreas resulting in disturbance of utilisation in storage of carbo-hydrates as evidenced clinically by hyperglycemia with or without glycosuria. Animals like the dog and horse are also susceptible to this disease. Normally, urine may contain some amount of glucose which might not be sufficient to give positive result with Fehling's or Benedict's. FOLIN, BENEDICT, MACKENZIE and others estimated the quantity of sugar in normal urine as varying between .06 to .09 %.

The varied manifestations of cases do not depend upon the damage to the pancreatic acine but to the diseased condition of the Islets of Langerhans, though it is not understood what conditions brought about such change in the Islets. There are several explanations offered by various people like VON MERING, MINKOWSKI and ALLEN, but none of them offered convincing explanations. However, the following few observations will be of some help to understand the ætiology of the disease.

1. *Nature of Food* seems to do a great lot in the cause of diabetes in India though it does not by itself act as a contributory cause, because as we know the Japanese are a rice-eating population but diabetes is not common among them. The other instance is the poor working classes in India who live exclusively on carbohydrates with practically no variation in the diet they take from day to day. It is possible to think that over-eating and indolent habits bring about strain on the liver and pancreas resulting in diabetes. So long, however, as the liver retains the power of converting glucose into glycogen of the combustion of sugar in tissues remains normal, the person or individual does not suffer from diabetes. But, sooner or later, liver and pancreas give way with the invariable result of occurrence of sugar in the urine. If a case is discovered initially at this stage, the occurrence of sugar in the urine can be corrected but, if it is allowed to pass on from "alimentary glycosuria", a true diabetes mellitus results.

2. *Lack of physical exercise*, coupled with great mental activity or strain, is supposed to be one of the contributing factors in the causation of the disease. Exercise increases the self production of Insulin but in severe cases this is not possible. LAWRENCE (1926) has shown that exercise increases the hypoglycemic action of Insulin and the author is also of opinion that the dosage of Insulin should be small if the patient is allowed some exercise. ALLEN, HILL and BOSE

proved conclusively that the combustion of carbohydrates improves under the stress of physical exercise. But it should, however, be remembered that in severe cases of diabetes, exercise should not be allowed as it might result in acidosis and coma. Mild and moderate cases must be advised to take some exercise. Mental worry and anxiety are some of the common causes for diabetes.

3. *Obesity*:—Diabetes seems to start with obesity but later on these people become so unrecognisably thin. Therefore, obesity may be considered a prediabetic condition—among the Indians at any rate—and these people may be asked to take exercise from the beginning. LAWRENCE in his book on Diabetic Life considers that slight underweight “is an insurance against diabetes”. JOSLIN considers diabetes to be “a penalty to obesity; the greater the obesity, the more likely is Nature to enforce it”.

4. *Climate*:—There is a general opinion in the medical world that the tropical and sub-tropical climates lower the carbohydrate tolerance and further diabetes mellitus is more severe in hot regions than in cooler and hilly cold places. It is in our experience that the course of the disease is more severe in summer than in winter. LANGEN and SHUT have found a rise of blood sugar in the white inhabitants of Java living near the sea-shore while their blood-sugar was below normal when they had gone to a more elevated and cool place.

5. *Heredity*:—It is a curious coincidence that obesity and diabetes are considered hereditary. There are many families in which diabetes can be traced to three or more generations. GRAHAM and BEGG are of opinion that heredity is an important causative factor in diabetes, but JOSLIN who collected a large statistics on this head hesitates to attach too much importance to heredity. Therefore, it is always wise to view diabetes as a familial disease rather than of heredity as we have no positive proof that diabetes can be transferred from parent to child. But, most observers find a hereditary element of 25% in their cases, which need not cause much terror of the disease.

6. *Age*:—Majority of the cases occur between the age periods of 35 and 45. BOSE reported a case of acute diabetes in an Indian boy of 16 months old. Though no age is exempt from the disease yet, generally, middle-aged persons suffer from it. If young people get diabetes it is very severe and the mortality rate is also high. But, in old people, the disease runs a comparatively mild course.

7. *Sex*:—Females seem to suffer more from diabetes than males according to JOSLIN. But, as Indian figures show, the sex incident is 77% in males and 23% in females. But, really this may not represent actual state of affairs as the existing social and religious customs, coupled with their reluctance to complain to their husbands till they are actually ill, is probably the explanation for the difference in incidence.

8. *Race*:—Certain races are more prone to this disease than others. Jews seem especially liable but it is probably their sedentary

habits and rich diet rather than their racial tendency which make them develop this disease. It is less common among the Chinese, the Japanese and the Negroes. In France and U.S.A., the disease is mostly prevalent. In India, the Bengalese are more prone to this disease than any of the other races. Ill-balanced diet, over-eating, disinclination for exercise and intellectual work, which are inseparable from the present struggle for existence, all probably act as some of the ætiological factors.

9. *Social position and profession*.—The higher the social position in life, the greater is the incidence of the disease. A long continued strenuous life may be considered one of the important ætiological factors. According to BOSE, 9.1% of the sufferers are his physicians. This is explained by the fact that physical and mental work which entails their profession cause the disease. The following is the table classified according to profession and occupation in life (BOSE):—

	Per Cent.
Landholders	22.3
Lawyers (including judicial officers)	19.3
Merchants	16.8
Physicians	9.1
Railway Officers	8.7
Teachers (including clergymen)	6.5
Clerks (including accountants)	6.3
Engineers	3.7
Police Officers	1.9
Students	1.1
Unclassified	4.2

10. *Nervous Factor*.—Mental strain, emotion and constant worry have been found to bring about existence of sugar in urine. Sudden shock as death in the family or sudden failure in business are causes for diabetes of an acute type. Students going for an oral examination have been found to have sugar in their urine as a result of the ordeal of the examination. The temporary presence of sugar may be due to excitement and anxiety causing a sympathetic disturbance and the consequent outflow of Adrenalin. Some direct and indirect ætiological factors such as injuries to the head, spine, brain tumours, lesions in the medulla are always to be remembered.

11. *Insanity*.—10% of insane persons pass sugar in their urine. The author had a case of severe diabetes referred to by the Superintendent, Mental Hospital, Madras, which gave interesting facts relating to dosage of Insulin, the occurrence of acetonuria and loss of weight and absence of secondary sexual character in the case. Whenever an effort was made to reduce the blood-sugar, there was a preponderance of acetone bodies making the person slightly dull. The dullness, the author was sure, was not due to hypoglycæmia as several blood-sugar examinations were done. At one stage, the author thought whether the

case was an Insulin resisting one. But, before he could arrive at that conclusion, several factors had to be taken into consideration such as syphilis, infections of various kinds, injuries, mental condition and internal secretions. It has been found that gonadal extracts were of some help in lessening the dosage of Insulin. Of late, DR. VENKATACHALAM PILLAI and RATNAGIRISWARAN showed that vagus inhibition produced sugar in the urine in their experiments on animals. Psychotics are found more in acute types of insanity than in chronic ones and certainly the prognosis in an insane diabetic is more grave.

12. *Infection*—bacterial, toxic or otherwise,—lowers the carbohydrate tolerance and increases the severity of the disease. Influenza, middle ear disease and recurrent boils which occur in an aggravated form in an elderly person, necessitate the examination of urine. Unless these infections are cured, the diabetic condition will not very much improve. Syphilis produces to some extent a defective function of the pancreas. Septic condition such as pyelitis, cystitis, urithritis caused by gonorrhœal infection may aggravate the condition of the disease.

13. *Hormone*:—Thyroid, supra-renal and pituitary glands give rise to hyperglycæmia and defective secretions of them are followed by increased tolerance for carbohydrates. Glycosuria is a very common manifestation of Graves' disease. In Acromegaly, sugar is often noticed. In Adiposis dolorosa and in Addison's disease, myœdema shows increased tolerance for sugar. Of late, the author is trying to find out if there are any gonadal defects which have to do with diabetes.

References :

1. J. S. Bose. *A handbook on Diabetes Mellitus.*
2. R. D. Lawrence. *The Diabetic Life.*
3. E. P. Joslin. *Treatment of Diabetes Mellitus.*

Metabolism in Diabetes

BY

G. B. Mankad, M.D. (BOM.), M.R.C.P. (LOND.), F.C.P.S. (BOM.)
Ahmedabad.

DIABETES is a condition in which there is disturbance of metabolism in general, with particular perversion of carbohydrate metabolism. The departure from the normal metabolism is, as far as is known to us at present, presumed to be due to the deficiency of the internal secretion of the pancreas, which is one of the factors to regulate the carbohydrate metabolism. The metabolism of carbohydrates, as of anything else, consists of processes called ingestion, digestion, absorption, and assimilation or storage, utilisation, accumulation of waste products and their excretion. Of all these various stages, storage and utilisation of carbohydrates are chiefly perverted in diabetes. The perverted utilisation leads to deficient utilisable carbohydrate, which acts as a draught to complete the combustion of fat to its final katabolites CO_2 and H_2O . In the absence of sufficient draught, the combustion of fats stops short at the stage of ketones, which, circulating in the blood on the way to be excreted, give rise to the condition called acidosis which is the chemical basis of diabetic coma, and in which there is thus disturbance of fat metabolism initiated by a faulty carbohydrate metabolism. Normally, carbohydrate is a source of readily available energy. When this is not utilised as in diabetes, the energy has to be obtained from other and less convenient sources *e.g.*, proteins. More proteins are, therefore, ingested but from these proteins, when assimilation is effected, as there is no storage mechanism for the proteins, the absorption units *i.e.*, the amino-acids, except those for immediate use, are separated into amino and acid radicles. The former tax the excretory organs, the latter are changed into carbohydrates and fats. Thus, with more proteins ingested, more of carbohydrates and fats are formed in the body and, with both of them, the metabolic difficulty is existing in diabetes, as mentioned above.

Thus, cutting off carbohydrate from the food of the diabetic does not solve the problem entirely and permanently as, without it, the proteins will continue to pour in the carbohydrate, and the fats will not be katabolised to the final stages of CO_2 and H_2O in the absence of sufficient carbohydrate.

We know thus that the remedy lies in correcting the disturbed carbohydrate metabolism rather than in removing, from the food stuffs of the diabetic, this important proximate principle of diet. This raises the question where is the disturbance in the carbohydrate metabolism. It is not in the ingestion or digestion or absorption: because, if the material is not digested well, it will not be absorbed and unabsorbed material will be cast out. This will be starvation but not diabetes. The disturbance is really after absorption. It is in the storage mechanism in the liver, where the sugar is warehoused to be despatched on demand by tissues using it. This storage by and its release

from the liver are regulated by mechanisms—chemical and nervous. The chemical mechanism consists of hormones and ferments while the nervous mechanism consists of a centre in the medulla with its afferents from the tissues and efferents down the splanchnics to the liver. The hormone Insulin, the internal secretion of pancreas, controls the storage of sugar, and its release is effected, when needed, by nervous mechanism reacting to the needs of the tissue and helped by hormones like adrenalin, pituitrin etc. After the release of the sugar from the store in the liver, it is carried in the blood stream to the tissues, mainly the muscles, which require it the most. Here again, it is said that Insulin acts as an intermediary, making the muscles more capable for using or making the sugar more utilisable. Anyway, under its influence, the sugar of the blood is utilised better by the muscles.

The storage of carbohydrate by the liver is by synthesising the monosaccharoses absorbed from the alimentary canal into a polysaccharose glycogen. On account of the blood glucose being consumed in the muscles or stored in the liver to be supplied when needed, the amount of glucose in the blood is maintained at a standard level, variable only within narrow limits. This level is from 80 to 180 mgm. per cent. If, on account of storage being faulty or consumption being lessened, the amount of sugar in the blood tends to rise above that level, excretory capacity of the kidney comes to play and the surplus is passed out in the urine. The excretion of surplus sugar in the urine is thus an abnormal means adopted to maintain the normal blood sugar level.

"The total amount of blood sugar is about 5 mgm. i.e. one average lump of sugar." The total amount of sugar stored as glycogen in the liver is about 5 ounces i.e., an average sugar-pot-full on a tea table. The muscles also store glycogen in as much amount as the liver.

Though the exact role played by Insulin is not quite understood, we presume that it promotes storage of glucose as glycogen in the liver and also promotes utilisation of blood glucose by the muscles when they exhibit energy. The following is the train of events and their regulation.

(1) All carbohydrates which can be digested to monosaccharoses, (mostly glucose) are carried as glucose to the liver via the portal vein. Some passes to the general blood stream and the rest, (2) under the influence of Insulin, is stored as glycogen. (3) When need for glucose arises, the glycogen is decomposed into glucose under the influence of Adrenalin and of the nerve impulses to and from the medullary centre acting on the liver cells to free the stored glycogen. (4) This glucose is carried to the muscles via the blood stream. (5) Some of this is again stored in the muscles as glycogen to be broken into glucose and used later and some used immediately, (6) when used glucose is katabolised to CO_2 and H_2O and energy evolved.

The Adrenalin, whatever role it plays in the carbohydrate metabolism, is helped in it, by posterior pituitrin and thyroid. The

parathyroid is similarly assisting the Insulin. Thus adrenalin, pituitrin and thyroid work together to break glycogen into glucose and thus to flood the blood stream with glucose. They induce hyperglycaemia, and lessen the sugar tolerance. The Insulin and parathyroids are arrayed on the opposite side and they promote storage of glycogen, lessen the blood sugar content, and increase the sugar tolerance of the individual. In diabetes, where there is hyperglycaemia due to defective storage and lessened consumption, Insulin is assumed to correct both these defects and over-dosage may induce hypoglycaemia, which can, in turn, be corrected by adrenalin.

The depancreatized dogs cannot be kept alive even by carefully regulated Insulin doses, but their diabetes could be made to disappear if, in such depancreatized dogs, anterior pituitary be completely removed. Removal of adrenal cortex has also a similar but less pronounced effect on the diabetes of the experimentally depancreatized dogs. In such dogs, it is certain that there could be no Insulin and such experiment would certainly theorise that Insulin is not *sine qua non* for the carbohydrate utilisation by the tissues.

Conversely, it has been recorded that patients, who have died of diabetic coma, have their pancreas showing normal amount of Insulin meaning that in their case normal amount of Insulin could not promote storage or utilisation of the carbohydrate.

The Insulin produces hypoglycaemia in normal animal with depletion of glycogen stores while in the diabetic, it increases and restores glycogen of the liver to normal. If an over-dose of Insulin be given and hypoglycaemia is induced, the glycogen even in the diabetic is again depleted by Insulin as in normal animal.

These considerations show that Insulin does not seem to work only in one direction but it acts in response to the varying metabolic and biochemical alterations and association with other endocrinological factors e.g. anterior pituitary and adrenal cortex etc. The exact role of Insulin in the carbohydrate metabolism though undoubted is not, therefore, perfectly understood. It seems very queer that two decades have nearly passed during which Insulin is used as the most useful therapeutic weapon against diabetes and hypo-insulinism has been recognised even longer to be the main aetiology of diabetes mellitus of pancreatic origin, no theory of insulin action completely elucidates its nature, its variable effects on the diabetes of human beings, or in experimental animals. In pre-Insulin days we had no treatment. Now with Insulin the responsibility of treatment has increased and every case has to be considered in the light of his response to the drug and this response varies from case to case, and sometimes in the same case from time to time. When the action of Insulin will be more precisely understood, we would be able to predict the effect of Insulin more accurately. We all know that the method of giving Insulin has so often been changed. First, it was used with any diet, then opinion prevailed that with insulin the need for diet adjustment was greater and this diet allowed only a basal requirement of

carbohydrate. This has now been proved to be not only unnecessary but definitely harmful and we are at present in an era when fair ration of carbohydrate is considered a necessary adjunct to Insulin in the treatment of diabetes. The hitherto ill-understood action of Insulin is the cause of all these oscillations.

In pre-Insulin days, the diagnosis of diabetes was easy in as much as any glycosuria was accepted as diabetes. In those days, it was folly to be wise when ignorance was bliss. Then came a period when hyperglycæmia and glycosuria combined, formed the diagnostic criterion of diabetes. We live in an age when this does not hold good. The diagnosis of diabetes today is more difficult than it ever was. No case can be said to have a true diabetes unless a definite hyperglycæmia is present and a diabetic blood-sugar curve is obtained on sugar tolerance test. Even such a curve is compatible with normal pancreas if the patient has been on much restricted carbohydrate diet and a normal curve is seen in a definite case of diabetes if the test is carried out under conditions of such carbohydrate restrictions. Unrestricted carbohydrate ration must be given prior to the day of the sugar tolerance test and that is as necessary a preliminary to that test as the administration of the required grams of glucose.

Some normal individuals do pass sugar in their urine after ingestion of 100 grams glucose and some do not even after as many as 500 grams. This variation is due to the variable rate of storage in the liver. If starch be given in any quantity the digestion of starch to glucose has to be effected and thus the absorption is delayed and, therefore, even with slow storage-rate, the blood stream is not flooded with glucose, and glycosuria ex amylo is never a normal event. It is always abnormal.

The parathyroid is helping the Insulin in an indirect way. Its function is that of detoxication. Infection and toxæmia throw extra strain on the parathyroids and when the latter are exhausted, Insulin has to regulate the glucose metabolism without its helper. Thus in the presence of infection, hyperglycæmia develops even in a normal person. In the diabetic, the same happens with greater force and this explains the increased Insulin requirement and the increased liability of the diabetic to drift into acidosis and coma in the presence of even a mild infection.

Protein Metabolism in Tropical Diabetes-Mellitus

BY

P. Gopalachari, M.B.B.S.,

Diabetes Research Worker, Madras.

1. **Abstract.**—Much work has been done on the role and fate of individual amino acids in metabolic process. The ketogenic nature or otherwise of these amino-acids, has been worked out. While they are of academic interest, they would seem to possess no bearing on the clinical side as amino-acids as such are not consumed. Nevertheless, a study of the chief proteid foods as are used on diabetes would bring out the relative value in respect of their utility or harmfulness in a diabetic organism. It is not merely the protein in its quantitative aspect but also the quality thereof that counts much in the successful dieting of a patient, with diabetes.

2. Such a work pre-supposes an idea of the nature of the normal blood or tissue proteins in the human organism. However, knowledge on this count is inadequate except that DEFT has brought out, from his experimental study on animals, that the more closely the food protein resembles the body protein, its biological value is increased.

3. Blood analysis has, therefore, been done on diabetes of South India and the results are tabulated as hereunder, and conclusions drawn.

The importance of adequate and suitable food protein to a diabetic organism cannot be over-estimated, as myo-cardial degeneration has been demonstrated by electro-cardiogram in every case of diabetes, in all its varying grades of severity. A successful dietetic therapy, advocated before medical treatment, involves a knowledge of food chemistry and a classification of food into the allowed and the forbidden.

Clinical and Bio-Chemical Studies

Analysis of Diabetic Blood at Resting Conditions

No.	R. S.	N.P. N.	Urea Mg. N%	Amino Mg. N%	Total Mg. N%	Cholesterol. Mg.	Age.	B. P.	Urinary Deposit.	Clinical Complaint.
1	.1379	36.1	10.826	14.05	3.751	200	36	$\frac{100}{80}$	Epithelial cells and casts.	Weakness.
2	.2350	44.4	25.59	28.9	2.773	100	24	—	Do.	Pruritis.
3	.1600	58	7.8	9.13	3.113	262.6	38	$\frac{90}{70}$	Do.	Weakness.
4	.1000	39.92	17.7	10.2	2.826	181.8	26	$\frac{145}{95}$	Do.	Weakness.

Clinical and Bio-Chemical Studies—(Contd.)
Analysis of Diabetic Blood at Resting Conditions—(Contd.)

No.	R. S.	N.P. N.	Urea Mg. N%	Amino Mg. N%	Total Mg. N%	Cholesterol. Mg.	Age.	B. P.	Urinary Deposit.	Clinical Complaint.
5	.3478	44.2	13.9	10.5	2.677	133.3	18	$\frac{108}{58}$	Epithelial cells and casts.	Tuberculosis Lung.
6	.140	27.92	7	18.3	1.519	150	60	—	Do.	Diarrhoea.
7	.2500	70.72	13.55	17.1	3.24	160.0	60	$\frac{138}{76}$	Do. + Albumin	Asthma and giddiness at other times.
8	.1834	46.92	16.73	14.03	3.170	150	66	—	Do.	Cataract.
9	.1754	59.16	8.4	8.4	3.761	125	54	$\frac{145}{98}$	Do. + Albumin	Pallor of optic disc.
10	.238	44.66	16.3	8.9	2.911	142	36	$\frac{110}{35}$	Do.	Gangrene finger.
11	.210	46.05	14.9	12.03	3.385	235	54	$\frac{130}{78}$	Do.	Pain in the legs and thighs.
12	.125	42.82	6.8	11.3	3.206	222.2	20	—	Do.	Oligomenorrhoea and Sterility.
13	.2312	69.36	29.4	8.2	3.017	185.5	78	$\frac{124}{74}$	Do. + Albumin	Gangrene toes.
14	.1146	38.42	7.46	8.2	2.167	100	14	$\frac{74}{44}$	Do. + Acetone	Wasting.
15	.120	48.68	14.06	10.6	3.015	100	40	—	Do.	Synovitis.
16	.1274	55.25	13.53	6.9	3.251	142.9	52	$\frac{105}{75}$	Do.	Myocardial failure and oedema feet.

Discussion.—1. The investigations were all on samples of blood drawn at resting condition, 12 to 16 hours after the last dinner. The N.P.N. and total Nitrogen were determined in duplicates with Pregli's Micro Kjeldahl technique. That the results are reliable have been verified by the author's ability to distil off the Nitrogen of a known substance like Leucine, and comparing the practical yield of Nitrogen with the theoretical yield. The former was 10.602% of Nitrogen in Leucine as against a theoretical yield of 10.68% N, resulting in an experimental error of 0.7% that is permissible.

The consistently higher values of N.P.N. in all the diabetics, investigated irrespective of their resting sugar value or age, is to be noted, as against a text-book description of the increase only in grave and neglected cases of diabetes over the normal range of 25 to 35 mg. %. It is due to the renal damage as is demonstrated in the present series by epithelial casts in centrifuged urinary deposits. This organic renal damage is the direct result of a chronic protein under nutrition. MACAY (1908).

2. The total Nitrogen is within normal limits except in gross or relative inanition as in cases with tubercular or acetonuric complications or a sequel to diarrhoea. The absolute value of albumin fraction, however, would throw additional light as to the real state of nutrition obtaining in the diabetes of South India, as advocated by BRECKMANN, ET AL (1930).

3. The urea Nitrogen is determined by Conway's micro method of analysis using water melon urease for the enzyme. No extraneous urea has, therefore, been introduced through the enzyme—DAMODARAM (1937).

The experiments were done in duplicates. It is to be noted that in all diabetics, uncomplicated by albuminuria, the urea Nitrogen content of blood is within the normal range of 10-15 mg. N%. If Neuberg's findings from tissue culture are to be applied, it apparently leads to an inference that all is well so far as general nutrition is concerned. This interpretation, however, would seem to be untenable from a knowledge of the amino acid Nitrogen of blood in diabetes. Its full import, nevertheless, can be studied in correlation with Nitrogen balance experiments of different proteids at various levels of intake, as it is now known that the biological value of the same protein for maintenance and growth differs in the same organism.

4. The amino acid Nitrogen of blood:—OKADA-ET-AL (1922) have observed that amino Nitrogen is unaltered in endocrine disorders. C. H. GREEN-ET-AL (1923) observed it to be remarkably constant in normals and almost all pathologic states except leukæmia and tissue autolysis. Their findings are not corroborated in the present series of investigations on diabetes of South India. The amino Nitrogen was determined in duplicates by Folin's Colorimetric method. The increased amino Nitrogen content of diabetic blood, over and above the normal range of 5 to 8 mg. %, now reported is possibly suggestive of an autolysis of body tissues to make up for the starvation of a suitable protein that is necessary for diabetic metabolism. The more closely the food protein resembles that of body protein, the higher is its biological value—LLOYD and SHORE 1938. It impresses the need for an increase in the intake of appropriate protein diet to tone up the individual. The asthenia, indicated by a low blood pressure and the myo-cardial impairment borne out in successive electro-cardiograms again call for such a reform in the diet of South Indian diabetics.

OSBORNE's compilation of the amino acid content of ovalbumin, ox muscle and casein go to show the superiority of casein to the rest in respect of glutamic acid whose role in the combustion of carbohydrate through a formation of succinic acid cycle has been recently worked out by KREBS and others. This casein is nearly equalled to, in the modulation of glucose tolerance curve, by the protein of P. Mung dhal when either is given to a diabetic in the same proportion of Nitrogen to starch in the food mixture. The beneficial effect of this dhal's amino acids in levelling down the blood sugar concentration curve—like that of Insulin—is possibly due to glutamic and aspartic

acid present as 16.16% of its total N.P.N. and to its non-amino non-basic nitrogen fraction like Proline present as 16.52% of the total N.P.N.—(BHAGWAT 1936). The ketogenic effect of Proline is possibly availed of in the synthesis of ketoglutaric acid by exchange of radicals on the lines of BROWNSTEEN and KRETZMENN's experiments. This intermediary product of protein metabolism is, as already referred to, necessary to the evolution of succinic acid and its derivatives that are found to play an important role in the metabolism of carbohydrates.

That proteins from all sources are not equally utilised by the body is well-known. There are two factors involved herein: (1) digestibility (2) the nature of the linkages of peptides of amino acids, that are required for the different purposes of growth or maintenance. NYOGI and NARAYANA have isolated pure globulin, in the same proportion in the two common pulses, *Cicer arietinum* and *P. Mung*; when either dhal is administered to a diabetic, the changes in the blood sugar concentrations subsequent thereto are different.

After *Cicer Arietinum*, Blood-Sugar Concentrations in a Diabetic

No.	1 Hr.	2 Hr.	2½ Hrs	3 Hrs.	3½ Hrs.	4 Hrs.	Remarks.
1	·2208	·2758	·2666	·2500	·2150	·2564	The rise after an initial fall following <i>Cicer</i> administration is to be noted.
2	·1379	·1444	·1905	·1219	·1123	·1232	
3	·1914	·2340	·2062	·1835	·2106	·2539	
4	·2041	·1905	·2259	·2222	·1818	·1905	

After *P. Mung*, Administration to Diabetics

5	·2477	·2454	·2260	·2162	·2094	·2030	The gradual decline in blood sugar level is to be noted. It bears testimony to the usefulness of this dahl to a diabetic metabolic process.
6	·3203	·2919	·2914	·2900	·2814	·2811	
7	·2516	·2000	·1941	·1932	·1835	·1830	

CHOUDURI and KAHLI (1936) have demonstrated that the average absorption co-efficient, at the optimal concentration of glucose from the bowel, is lowered by subcutaneous injection of Insulin. Proteins that have a similar effect when given per oral, in retarding a very rapid sugar absorption from the bowel, or lowering the existing blood-sugar levels and preparing the patient for the next carbohydrate meal, are desirable to a diabetic. In both ways, the nitrogenous fractions of *P. Mung* have been found to answer the purpose well. It is superior to *Cicer*. This only suggests the supplemental value of non-protein Nitrogen present in the *P. Mung* dhal in influencing the digestibility and biological value of the pulse protein.

A diet that is enough to enable human beings to lead an energetic life at a reasonably high level of working capacity, is the ideal to be aimed at in modern dietetics. A diabetic is no exception to this rule. A well-chosen diet should help him to build up a constitution, healthy

and strong so as to withstand successfully any infection and live his full span of life.

Conclusions.—1. There is positive need for an increased protein intake in diabetes of South India, as supported by bio-chemical evidence to arrest the morbid processes consequential to a chronic protein under-nutrition that is generally obtaining in dietaries, as brought out by AYKROYD.

2. *P. Mung* dahl, among vegetable proteins is found to answer the requirements of a diabetic metabolic process, better than *Cicer arietinum*. It nearly equals casein in utility to a diabetic.

3. A list of forbidden foods can be drawn up, based on such studies. A mere withholding of these, would tend to improve the carbohydrate intolerance of the diabetic—as adumbrated by EMBLETON

Acknowledgement.—My thanks are particularly due, among the many, to Col. Cruickshank, who had obtained the necessary grant of facilities, from the Government of Madras, and to Dr. M. Damodaram, D. Sc., for all help rendered in the conduct of the investigations.

References.

1. Bhagavat, K. and Sreenivasaya, M. R.—1935, *Bio-Chem. Journal*, Vol. 19, p. 909.
2. Chouduri, C. H. and Kahali, B. S.—1936, *I. J. M. R.*, Vol. 23, p. 963.
3. Damodaram, M. and Siva Ramakrishnan, P. M.—1937, *Bio. Chem. Journal*, Vol. 31, p. 1041.
4. Embleton, D.—1938, *Proc. Roy. Medl.*, Vol. 31, p. 1183.
5. Green, C. H. et al.—1923, *Jour. Bio. Chem.*, Vol. 58, p. 845.
6. Lloyd and Shore—1938, *Chemistry of Proteins*, J. A. Churchill, London.
7. Macay, D.—1908, *Scientific Memoirs* No. 34, Govt. of India.
8. Nyogi et al.—1932, *I. J. M. R.*, Vol. 19, p. 1041.
9. Okada et al.—1922, *Jour. Biol. Chem.*, Vol. 51, p. 121.

Habitus and Diabetes

BY

R. Krishna Rao, F.R.C.S., L.R.C.P.,

Professor of Anatomy, Medical College, Vizag.

Introduction.—When I was asked by the learned editor of *'The Antiseptic'* to contribute an article for incorporation in the special number on Diabetes I felt rather hesitant and diffident at first and thought of pleading an excuse for non-compliance on the score of my isolation and segregation from the clinical section of the college as non-clinical Professor of Anatomy. On carefully considering the question whether an anatomist is justified in assuming a defeatist attitude, I came to the conclusion that the study of Anatomy is absolutely futile if it can throw no light on problems of disease. I am again fully conscious of the fact that most of the articles by experienced physicians, surgeons and specialists, will deal in detail with the history and antiquity of diabetes, its incidence and etiology, pathology and symptomatology, complications and sequelae, diet, drug and operative treatment and so forth. I propose however to confine myself to body mechanics in its relation to diabetes.

Diabetes Mellitus has been known to occur mostly in adults of both sexes after middle life and to a lesser extent in adolescents, children and even in infants. While it is easy to explain the factors responsible for the causation of the malady in adults and adolescents, it becomes rather difficult to account for its incidence in infants and children. The physician is necessarily confronted with heredity and its baffling and complicated problems.

SIR A. KEITH has vividly described how man, who is indisputably the crown and culmination in the vast scale of creation, has paid a pretty heavy price for the noble, dignified, exquisitely graceful upright posture and plantigrade mode of progression by this proneness and susceptibility to hernia, visceroptosis and static disabilities of various kinds. PROFESSOR DWIGHT of the Harvard University was perhaps the pioneer to draw attention to the wide divergencies in the build of the body and departures and deviations from the normal ailments. A detailed anatomical and roentgenological study was made of thousands of individuals by WALTER MILLS, GOLDTHWAIT, BEAN, BRYANT, LUCAS, MONTESSORI and others. The results of the investigation have revealed that mankind (including women) admits of being classified, from the point of view of physical conformation, under two principal types, the heavy and the slender, besides an intermediate type and that most of the chronic diseases owe their origin to the disturbance in the bodily poise and balance with the concomitant displacement of viscera brought on by the assumption of faulty attitudes, and faulty living. The human body, which has been justly described as a marvel of creation, can function properly and efficiently, only when the various parts comprising it are placed in

their respective and relative positions. Habitus has been defined as the resultant general build of the body arrived at by combining the two components of weight and stature. By adopting this as the basis of classification of individuals, three types have been evolved and described, the thin, heavy and medium ones. The thin type has various synonyms such as the splanchnoptotic (GLENARD), hyperontomorphic (BEAN), macroscelous (MONTESSORI), linear (LUCAS), carnivorous (GOLDTHWAIT) the narrow-back (industrial) and the grey hound type (CLENEDENING). At the other end is the heavy type which too has variously been designated by the expressive epithets of herbivorous (GOLDTHWAIT), hyperontomorphic (BEAN), brachyscelous (MONTESSORI), lateral (LUCAS), broad-backed (industrial) and the broad stocky clydesdale (CLENEDENING). There are numerous points of difference in the anatomical configuration between the sthenic and the asthenic types. About 60% of people of advanced age belong to the latter type, or in other words, this is the type that conduces to longevity. In this type the viscera maintain their proper high positions and tonus and function efficiently. The former on the other hand, is the ptotic type with a tendency to stasis. There are again temperamental and psychical differences between the two types; whereas, the heavy-typed individual is a gourmand and gastronome, connoisseur of the cuisine, an extrovert and epicure given to guzzling and swilling, a happy-go-lucky, devil-may-care sort of a fellow, enjoying life to the lees, clubable and convivial, gay and buoyant, laughing and making merry, the lean one is a dyspeptic, cynic, misanthrope and possibly a misogynist, ever planning and plotting, reforming, scheming and intriguing. It is the heavy type that is susceptible to diabetes. His lungs are comparatively smaller; he does not breathe regularly in and out to burn all the food he eats, a moiety of which becomes deposited in the form of fat; he develops a tendency to corpulence and obesity which increases with careless, intemperate, easy and luxurious living. It is these that

“When to the age of forty they come
Men run to belly and women to bum.”

Bum is said to be the Warwickshire slang for the gluteal regions. The sag or the droop is consequent on the accumulation of fat. This manifests itself in the protuberant lower abdomen, the paunch, usually considered to be a sign of prosperity and good living. The result is pressure, congestion and interference with the vascular supply of the digestive organs concerned with carbohydrate metabolism, viz., the liver and pancreas, duodenum and small intestines.

Anatomy of the Pancreas:—This is a gland having an external and internal secretion and becoming deranged in diabetes. It is fixed against the posterior wall of the abdomen across the two biggest blood vessels of the body, the aorta and inferior vena cava, opposite the bodies of the first and second lumbar vertebrae. It lies between the two cardinal arteries of the alimentary canal, the coeliac (digestive artery of Hilton) above and the superior mesenteric artery below. It

occupies the C-shaped concavity of the fixed part of the gut, the duodenum. It has the pylorus in front and the kidneys and solar plexuses (the abdominal brain) which regulates the blood supply to the alimentary canal. It is peculiar again in that it is related to the largest of blood vessels. In obese subjects the pancreas is subjected to pressure by the coeliac axis artery and stomach and to traction by the transverse mesocolon. It is, therefore, not at all a matter for surprise that the islets of Langerhans, numbering about a million, contained in the pancreas, begin to dysfunction. It is the lack of Insulin secreted by the islets that is so characteristic a feature of the diabetic and that leads to the abnormal accumulation of glucose in his blood which passes off as sugar in the urine. With the relaxed abdomen, there is a progressive tendency toward a drooped chest, narrowed costal angle, forward shoulder, prominent shoulder blades, exaggerated curves of the spine, hollowness at the sides of the epigastrium, etc. Life insurance companies have noted that applicants weighing 20% above the average of their height and age, show a much higher death rate than those conforming to the standards. The excess in weight is due to high living, sedentary life and want of exercise. It is a hard, stubborn and undeniable fact that diabetes is a disease prevailing in prosperous persons, holding high positions in life, though this is not to say that it is confined to the well-to-do. These constituting the upper and the upper middle classes have neither the time nor the inclination for taking active exercise. Mental strain, worry and anxiety are additional factors that have to be reckoned with. Many of them, unlike the Westerners, are incapable of taking and enjoying a real good holiday by completely forgetting for a time all about their normal routine activities and relaxing perfectly.

It is not the purpose of this paper to deal with the treatment of the disease. It seeks but to stress and emphasise the importance of the body mechanism as a potent aetiological factor of the disease which is apt to be overlooked by the ordinary physician, who more often than not, concentrates on diet and drugs in the treatment of the patient.

Diagnosis of Diabetes Mellitus

BY

D. R. Dhar, M.B., D.T.M. (CAL.) M.R.C.P. (LOND.)

*Hony. Deputy Physician, Medical College of Bengal,
Associate Professor of Medicine, National Medical Institute,
Visiting Physician, Chittaranjan Hospital etc., Calcutta.*

Causes in short.—That diabetes mellitus is caused by the lack of the insular element derived from the *Beta* cells of the islands of Langerhans of the pancreas, is proved conclusively by experimental results and by the discovery of Insulin by BANTING and his co-workers. Though manifesting mainly a derangement of carbohydrate metabolism with hyperglycemia and glycosuria, yet there are, in diabetes mellitus, numerous other side issues of deranged metabolism, including those of fats, proteins, etc.

Mostly a disease of *overweight individuals of sedentary habits*, at the fourth to sixth decade of life, though juvenile diabetes in thin underweight individuals of young age is not uncommon. JOSLIN in a large series showed 4.7 per cent of diabetes in persons during the first ten years of life¹. Indians, of certain habits and dispositions, commonly suffer. Bengalis, Hindus, Jews, Maltese, Ceylonese and persons of Hebrew race seem to suffer more commonly, but persons of no race or climate appear to be exempt. People of both the sexes appear to suffer almost equally. There is a hereditary tendency² to perpetuate this disorder, though JOSLIN thinks that the hereditary cases are always of a milder nature. *Excesses in dietary*, leading to accumulation of fat, notably through carbohydrates and fats, by over-increase of body weight may contribute. How far an unbalanced diet, with an overwhelming proportion of carbohydrate in it, taken for a long time, may predispose to this disordered metabolic state, one cannot say definitely. May avitaminosis for a prolonged period contribute to it? We do not know.

Any nervous strain or shock, probably acting through the sympathetic and adrenals, by producing hyperglycemia or by lowering further the sub-normal power of utilisation of carbohydrates, may make a latent condition manifest. The over-production theory seems now again in vogue³. The inter-relation between the glands of internal secretion in the production of this disorder is interesting. A deficiency of Insulin and excess or over-activity of pituitary,⁴ adrenals and thyroid secretions cause hyperglycemia.

Septic foci, acute infectious diseases may be the immediate and apparent precipitating factor of this disorder. Arterio-sclerosis, though more commonly an effect rather than a cause, syphilis, gout, repeated affections of the biliary passages⁵, disorders of pancreas, and other glands of internal secretion, injury to the brain, loss of reserved alkali⁶, ketosis etc., have been ascribed to be the cause of this, sometimes elusive metabolic disorder.

These are mentioned not only to show what a multitude of variable factors may play a part more or less in initiating this disorder having very far-reaching metabolic ramifications, but also to demonstrate how much better results are expected, if due attention is paid to the probable etiological factor, may be, an emotional shock, a nervous over-strain, a gastro-intestinal upset, hyperthyroidism, and prolonged and undue intake of an unbalanced carbohydrate diet without proper vitamins by a corpulent individual, loss of alkali reserve in a stout man, and so on.

Clinical Types.—Though the cases have been classified in various clinical groups such as mild, moderate or severe, yet they are all empirical and have no scientific basis, as the mild cases may, if left untreated or uncared-for, drift into the severe group. "According to NAUNYN, if the glucose disappears with the patient on a non-carbohydrate diet, the case belongs to the former type (mild). If, on the other hand, he continues to excrete glucose, the case is a severe one, for it means that sugar is being produced from body proteins. The presence of a high ammonia secretion, low respiratory quotient, low CO_2 combining power of blood, and *Beta*-oxybutyric acid and its derivatives, acetone and diacetic acid, is also indication of a severe type".

Pathogenesis of Symptoms.—Owing to the increased percentage of glucose in the blood, the latter becomes hypertonic and fluids of the tissues are absorbed into the circulation in greater amounts than in normal persons, hence the tissue dehydration causes *thirst*. This to be satisfied makes the patient drink more of fluids (polydipsia) leading to increased volume of blood, whose excretion causes *polyuria* with consequent *dehydration*. The amount of urine may range even up to ten to fifteen liters instead of normal 1,500 ccs. The amount excreted is usually in direct proportion to the degree of hyperglycemia. As the person cannot utilise carbohydrates, the normal easily combustible fuel of the system, he takes more food to excrete more sugar giving rise to the insatiable appetite (*polyphagia*). Such sugar-rich blood forms a good culture medium for all bacteria, hence the latter can grow easily and trivial infections which do not affect the normal individuals, may cause serious sepsis in diabetics, not uncommonly with grave consequences. The face may be red and the skin dry and harsh.

Patient's Complaints.—When a person comes complaining of some of the classical symptoms of diabetes such as polyuria, polydipsia, polyphagia, undue weakness, loss of weight, dehydration, easy fatigability, or of some of the well known complications such as pruritus, carbuncle, neuralgia, neuritis, premature cataract, gangrene etc., careful examination of the urine may settle the diagnosis.

Urinary Findings.—A sample urine collected from twenty-four hours specimen, or a sample from the mixed urine passed at bed time after meals and early in the morning may show raised specific gravity near about 1040 and the total quantity if very large is highly suspicious. Early morning specimen may not show sugar. "Renedict's

solution is better than that of Fehling's as the former reagent detects sugar even when present in traces. Fermentation test of the sugar and other tests in order to exclude the probable fallacies giving a positive or pseudo-sugar test, should be done^{8, 9}. Tests should be done for the presence of the ketone bodies too. *Renal glycosuria* in which there is lowering of renal threshold for sugar from normal of about 0.18 per cent has got to be distinguished in doubtful cases by estimation of fasting blood sugar and by sugar tolerance test.

Blood Sugar.—Blood sugar level normally varies usually between 0.08 to 0.12 per cent, and mild and moderate cases of diabetes mellitus may show fasting blood sugar level of near about 0.15 to 0.20 per cent or higher.

Mild or Liminal Cases.—There are numerous cases of mild diabetes only detected by the routine examination of urine at the time of life insurance, and such other purposes. Transient glycosuria after a big meal, notably of carbohydrate excess, should serve as a warning and prompt the patient to seek immediate treatment.

Complications.—*Coma*:—The person may seek medical aid for one of the numerous complications of which *coma* is the most important. Clinically, three types have been described. (1) The typical air-hunger type of KUSSMAUL or dyspnoic coma; the premonitory headache, lassitude, epigastric pain, vomiting and diarrhoea, mental unrest etc., are helpful and suggestive complication. The speech becomes the beginning of this impending complication. The speech becomes thick and incoherent and the mind gets duller to pass eventually into deep coma. The pulse becomes soft, small and quick. At the onset, the deep noisy but deep inspiratory efforts are quite characteristic and, once fully developed, the respirations are full and voluminous in contrast with the short hissing respiratory excursions of uræmic coma. It was probably this wide excursion and the increased volume of the chest at each inspiration that led KUSSMAUL to designate the phenomenon as "*air hunger*". The temperature is usually sub-normal. Due to exhalation of acetone, the breath may give out a fruity odour. The other two less common forms are:—(2) The alcoholic form—in this the patient appears as if intoxicated by alcohol—a rather serious form and without much of dyspnoea. (3) The collapsing type. In this the patient shows signs and symptoms of collapse and the typical respiratory excursions are not marked. In both these last mentioned forms, one can only diagnose by a careful history, in the absence of which, a thorough examination of a catheter specimen of urine and the presence of ketone bodies besides sugar will help to clarify the mystery. Coma of diabetes has got to be differentiated from other common causes of coma which, without a good history, is rather difficult to clear up.

Disturbances of Metabolism.—In the urine, one finds ketone bodies like acetone, aceto-acetic acid and beta-oxybutyric acid, because the hot flame of carbohydrates being depleted out, fat cannot be completely oxidised; hence the above intermediary toxic products of

incomplete combustion of fat circulating in the system conduce to this unconsciousness. In severe cases, the excretion of urinary nitrogen may be double that of normal. This indicates not only much increased ammonia co-efficient, but that there is profound disturbance metabolic ratio of dextrose and nitrogen called in short D. N. ratio. Such changes usually show that carbohydrates derived from protein elements even cannot be utilised by the system. From normal five per cent. the ammonia co-efficient may rise even upto eighteen per cent. or more.¹⁰ The fall of the CO₂ tension in the alveolar air from normal 4 to 6.2 per cent. to one to two per cent.¹¹ in ketosis are helpful where well equipped laboratory aids are available. Loss of alkali reserve of blood is also helpful diagnostically besides other tests.

DODDS and ROBERTSON¹² (1930) tried and failed to find out any co-relation between the symptomatology and biochemical deviations from normal in the loss of alkali-reserve, lowering of alveolar CO₂ tension, ketosis etc. Only the alkali reserve though low at coma, rose as the patient improved. This led ROY and MUKHERJEE of Carmichael Medical College, Calcutta, to investigate the problem from a somewhat different angle.

Common Causes of Coma.—*Coma is common in.*—(1) acute and undiagnosed cases of diabetes, (2) over-eating with a severe disorder (3) severe untreated cases (4) persons of diabetes with sepsis.

PRECIPITATING CAUSES USUALLY ARE:—(1) Incidence of acute infections, may be febrile and apparent like influenza, carbuncle, cellulitis, appendicitis or hidden deep-seated abscesses and infections. (2) Omission of the usual dose of Insulin. (3) Taking of large amount of carbohydrate. (4) Hyperthyroidism. (5) Nervous shock or strain etc. (6) Operations or surgical interferences, and others.

Infections:—Due to hyperglycæmia, such blood is a better culture medium than normal blood, hence trivial erosions or breach of skin or pimples not affecting the normal may initiate serious infections common amongst them being, boils, carbuncles, pruritus, gangrene of the extremities, partly from sepsis and arteriosclerosis, probably the latter by poor blood supply to the parts contribute; persisting eczema; perforating ulcers notably when neuritis is present. In long standing cases, the scene may be closed by tuberculous infection of the lung or the kidneys. Cutting of corus in these subjects, is not uncommonly attended with serious even fatal sepsis.

Heart and blood vessels:—Hypertension in elderly diabetics may be the cause or effect of this disease. Sclerosis of the vessels of the brain, heart, kidneys, may curtail their respective functional capacity. Pain in the præcordium due to coronary sclerosis or thrombosis is not uncommon. One has seen three cases of coronary thrombosis in diabetics of long standing within two years. But this has got to be differentiated from temporary glycosuria in coronary thrombosis in non-diabetics. Arteriosclerosis and gangrene have already been mentioned.

Renal:—Albuminuria is frequent. True arteriosclerotic nephritis may follow.

Edema:—Local or general œdema is not uncommon and in the absence of renal, cardiac or other conditions producing œdema, may be traced to too much intake and retention of the Sodium ions in the system. Treatment of this œdema by withdrawal of Sodium ions may precipitate coma causing dehydration, whereas too much of Sodium ions may increase œdema, hence the dilemma in the treatment.

Digestive:—Pyorrhœa alveolaris is common and is more commonly a contributory factor of diabetes than otherwise. Its proper care often ameliorates the glycosuria and its train of events. Nausea, vomiting, diarrhœa, and abdominal pain¹³ may herald the onset of coma, and should be seriously taken in a diabetic. Obstinate constipation may be a troublesome symptom; its relief usually helps the patient.

Nervous:—Peripheral neuritis, preceded by neuralgia is common, more frequent when coupled with arteriosclerosis¹⁴ than in uncomplicated diabetics. Trophic disturbances and perforating ulcers and such like changes are not infrequent. Loss of knee jerk, hyperæsthesia, numbness are met with. Cramps of a painful nature due to dehydration may also be encountered.

Special senses:—Cataract, retinitis and optic atrophy may follow in long standing cases. Strabismus due to palsy of ocular muscles may be seen. The fundus oculi should always be examined in all diabetics.

Lipæmia:—There is excess of fatty acid or cholesterol in blood in all severe cases of diabetes. This can be best seen in the retinal vessels. By itself, except denoting some profound disturbance of metabolism of lipoids, it does not mean much, as such cases respond quite well to treatment.

Sexual:—Though not much affected at the beginning yet in advanced cases, the males become impotent and pregnancy in females usually makes the condition worse. Not uncommonly, the pregnant diabetic gives birth to a dead child.¹⁵ Uterine inertia and even coma following child-birth are not uncommon.

Differential Diagnosis.—Presence of reducing substance in the urine is easy to detect; but its nature and that it is caused by glycosuria have got to be established. Fehling's solution is reduced by glycuronic acid, uric acid and creatinin besides by glucose. Unless the urine is very concentrated, the other substances are seldom in sufficient concentration to reduce Fehling's solution. Benedict's solution is reduced by almost all the sugars, and these have got to be differentiated from glucose. Bronzed diabetes in hæmachromatosis is a rare condition and is diagnosed by pigmentation, enlarged liver and so on. Acute pancreatitis causing glycosuria is easy to diagnose. In all cases of diabetic glycosuria, renal diabetes need be excluded. Sugar tolerance test, and estimation of fasting blood sugar are

very important diagnostic features in establishing the diagnosis of true diabetes.

Test for ketone bodies should always be made in all specimens of urine in diabetics. All other causes of increased quantity of urine as in contracted kidney, diabetes insipidus etc., have got to be distinguished from diabetes mellitus. In the chronic kidney condition, there is large quantity of limpid urine of low specific gravity of about 1010 with traces of albumin, granular casts, may be with hypertrophy of the heart having booming first sound at the downwardly displaced apex, accentuated aortic second sound, may be retinal changes and raised non-protein nitrogen content of the blood. In diabetes insipidus, the quantity of urine is very profuse, the specific gravity near about 1003, but no albumin casts etc. are there and it responds well to injections or intranasal insufflation of Pituitrin, and oral administration of Valerian etc., and restriction of salt and water.

References :

1. Mosenthal—(1927), *Diabetes Mellitus; Practice of Medicine*, Edited by Tice, Vol. IX.
2. Joslin and others—(1937), *Amer. Jour. of Med. Sci.*, 193, p. 8.
3. Soskin Levine—(1937), *Amer. Jour. of Physiol.*, 120, Dec. p. 761.
4. Campbell and Best—(1938), *Lancet*, I, p. 1444.
5. Lande and Pollack—(1936), *Ibid.*, May 23rd, p. 1161.
6. Roy and Mukherjee—(1935), *Cal. Med. Jour.*, Dec.
7. Fletcher—(1926), *Osler's Modern Medicine*, Vol. III, p. 139. *Diabetes Mellitus* Lea Febigers Publication.
8. Benedict—(1918), *Jour. of Biol. Chemistry*, 34, p. 203.
9. Benedict and Wu—(1919), *Ibid.*, p. 91.
10. Beaumont and Dodds—(1936), *Recent Advances in Med.*, 8th Edition, p. 109-110.
11. Dodds—(1921), *Jour. Physiol.*, 54, p. 342.
12. *Lancet*—(1930), I, p. 852.
13. Bread Wood—(1935), *Jour. Amer. Med. Assoc.*, 105, p. 1168.
14. Jordan—(1936), *Arrh. of Int. Med.*, 57, p. 307.
15. Krans—(1936), *Med. Klin.*, 32, p. 375.

STOVARSOL

TRADE

MARK

*The
Arsenical
with the
double
action*



Bottles of 30 x 4
grain tablets.

AMOEBICIDAL

STOVARSOL has a well-established usefulness in the treatment of amoebic dysentery, effectively eradicating amoebæ and cysts.

TONIC

STOVARSOL exerts a remarkably beneficial tonic action on the system and is of particular value in anaemic and debilitated states.



MAY & BAKER (INDIA) LTD
11 CLIVE STREET, CALCUTTA

BERIN

VITAMIN B₁ "GLAXO"

AMPLE STOCKS NOW AVAILABLE

The success of vitamin B₁ in beri-beri is generally recognised; in addition the therapy has a wide use in every-day practice. In gastro-intestinal disorders vitamin B will improve impaired digestion and alleviate intestinal obstruction. It is of value in neurological disorders; for correct carbohydrate metabolism; and in pregnancy when the nutritional requirement of the vitamin is increased.

PRODUCT OF THE
GLAXO LABORATORIES

GLAXO LABORATORIES LTD., Greenford, Middlesex, ENGLAND.
Representatives in India: H. J. FOSTER & CO., LTD.
P.O. Boxes: 202, Bombay. 2257, Calcutta. 108, Madras. 244, Lahore.

To supply the urgent demand for
VITAMIN C in FEVERS



PRODUCT OF THE
GLAXO LABORATORIES

Many diseases become complicated by a marked deficiency of vitamin C—particularly in fevers such as typhoid, malaria, pneumonia, whooping cough etc. For in these conditions a much greater intake of the vitamin is needed than normally. Yet, by the very nature of the illness the patient has to live on a restricted diet. Hence a vitamin C supplement becomes imperative. Celin Tablets (Glaxo) offer the simple and convenient method of providing it. Three or four of these small tablets daily are ample to maintain and safeguard the patient's vitamin C reserves.

When the parenteral route is preferred, Celin (Glaxo) is available in ampoules.

Celin
VITAMIN C (GLAXO)

Glaxo Laboratories Ltd., Greenford, Middlesex, England. Repts. in India: H. J. Foster & Co., Ltd.
P. O. Box 202, Bombay. P. O. Box 2257, Calcutta. P. O. Box 108, Madras. P. O. Box 244, Lahore.

When writing to advertisers, please mention the "Antiseptic"

urgent in
lactation

The "key" minerals—iron and calcium—are those most commonly deficient in the average diet. In pregnancy and lactation the demand for them is even more urgent. Unless an adequate supply is maintained, a deficiency of iron and calcium may result in severe debility in the mother and thus prejudice the health of the infant. Caldeferrum supplies in balanced and rational combination iron, calcium and vitamin D. Four of these tablets daily during pregnancy and lactation form an efficient dietary supplement and will in most cases be sufficient to raise the maternal reserves of calcium and iron to the optimum level.

GLAXO LABORATORIES LIMITED, Greenford, Middlesex, England.
Representatives in India: H. J. FOSTER & CO., LIMITED.
P. O. Box 202, Bombay. P. O. Box 2257, Calcutta.
P. O. Box 108, Madras. P. O. Box 244, Lahore.

CALDEFERRUM



KAPSEALS DILANTIN SODIUM

DILANTIN SODIUM (sodium 5,5-diphenylhydantoinate), an anticonvulsant with little or no hypnotic effect, is supplied for the treatment of epileptics not responsive to other medication. Extensive clinical use indicates that Dilantin Sodium will prevent, or greatly decrease the frequency and severity of, convulsive seizures in a majority of epileptics. However, since the significance of observed reactions to Dilantin Sodium is not fully established, patients receiving the drug should be closely observed.

Dilantin Sodium is accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Non-official Remedies.

The name "Dilantin Sodium" designates the sodium salt of diphenylhydantoin. Dilantin Sodium is available as 0.1 gram (1 grain) capsules in bottles of 100.

PARKER, DAVIS & COMPANY

OVALTINE

In Wasting Diseases

TO replace the tissue wastage and decrease in energy associated with wasting diseases, is a problem often rendered more difficult by the fact that there is frequently an associated anorexia and enfeeblement of the digestive and assimilative processes.

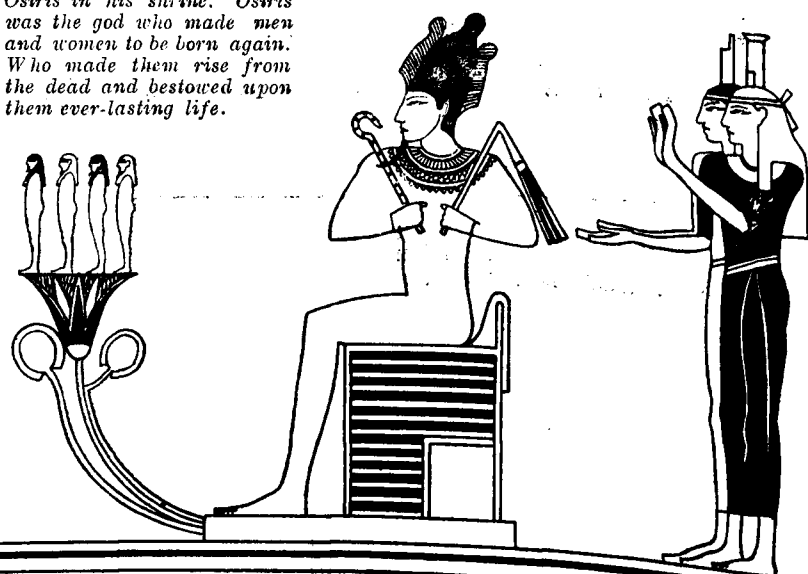
'OVALTINE' has proved to be the ideal stand by in many such cases, because it is an energizing and reconstructive nutrient, complete in all the essential food elements. It is almost invariably well tolerated even by disordered stomachs and is practically completely absorbed into the blood-stream.

The unique dietetic value of 'OVALTINE' is derived from its content of fresh food substances—ripe barley malt, pure creamy cow's milk together with valuable natural phosphatides and vitamins. Noteworthy features are its high percentage of maltose and its entire freedom from cane sugar, starch or other undesirable constituents.

A liberal supply for clinical trial sent free on request.

Indian Distributors: Messrs. GRAHAMS TRADING CO. (India) LTD.
Cathness Hall, Third Floor, 310-311, Linghi Chetty Street, Madras.
Also at Calcutta, Bombay and Karachi.

Osiris in his shrine. Osiris was the god who made men and women to be born again. Who made them rise from the dead and bestowed upon them ever-lasting life.



M 284

Laboratory Tests and their Significance in the Diagnosis of Diabetes Mellitus

BY

S. K. Bose, M.B. (CAL.),

Pathologist, Prince of Wales Hospital, Bhopal.

Prelude.—Though the presence of some reducing substances in urine affords a considerable help in the diagnosis of a case suffering from the cardinal manifestations of diabetes mellitus, viz., polyuria, great thirst, and loss of weight, sometimes an accidental discovery of a reducing substance in the urine of a patient suffering from incipient diabetes or in those of life insurance and routine hospital examinations, calls for certain complicated laboratory tests for its identification. In other words, the patient whose urine reduces either Fehling's solution or Benedict's qualitative solution, may not necessarily suffer from glycosuria, not to speak of diabetes mellitus. In order to confirm the diagnosis of glycosuria the reducing substance must be identified as glucose, and the presence of glucose in urine should arouse suspicion that the patient might be a case of diabetes mellitus. And the next laboratory procedure for its confirmation is to determine the blood sugar of the patient under certain conditions. Though an isolated blood sugar over 0.2% fairly indicates that the person has a low sugar tolerance, a glucose tolerance test giving a characteristic curve of diabetes mellitus is, more or less, a conclusive evidence in the diagnosis of the disease.

Tests employed to detect a reducing Substance in Urine.—The two reagents employed for the detection of a reducing substance in urine are Fehling's solution and Benedict's qualitative solution, the latter being recent, less cumbrous, more standardised, and is not reduced by certain other urinary constituents. In view of these advantages, it should replace Fehling's solution at least where the qualitative examination of sugar in urine is concerned. Moreover, by the standardised way of performing Benedict's test, an experienced laboratory worker may get a fairly accurate idea of the amount of sugar present in the urine by the varying grades of colour of the reduced copper. I personally prefer Benedict's solution for the identification and preliminary rough estimation of the sugar in urine and Fehling's reagents for its quantitative determination, in spite of the prevalent objection regarding the difficulty of the end-point determination. With a little experience, if the experiment is conducted in the open light, there should not be any difficulty in finding out the end-point.

Fehling's Test.—Equal quantities of albumin-free urine and freshly-mixed solution of Fehling's solutions no. 1 and 2 are taken in two separate clean test-tubes and boiled separately. Both are then mixed and allowed to stand for 2 to 3 minutes. If a reducing substance is present in the sample, the cuprous hydrate will be reduced

to yellow cuprous hydrate or even to red cuprous oxide. There are certain important points to consider with regard to this test.

Fehling's solution, if kept for a long time, gives a precipitate of cuprous oxide on boiling. As preliminary to carrying out the test, the efficacy of the reagents is to be ascertained. To test it, equal quantities of water and the reagents are taken in test-tubes and boiled for two minutes. If the solution remains clear, the reagent is safe.

Fehling's solutions No. 1 and 2 are to be freshly mixed when the actual test is done. On no account, the mixed solution should be kept for use on subsequent days.

The urine to be tested must be free from albumin. If required, the albumin should be separated by boiling the acidulated urine and filtering. The filtrate is then neutralised with Calcium Carbonate solution.

Strongly ammoniacal urine prevents precipitation of cuprous oxide.

Besides glucose, Fehling's solution is also reduced by Uric Acid, Creatinin, excess of Oxalates, Hippuric Acid, Lactose, Glycuronic Acid, Homogentisic Acid, Chloral, Chloroform, Glycerine, Benzoic Acid, Salicylates, and Carbohic Acid. It is also reduced by the urine in which Formalin has been added.

Benedict's Test:—Either 5 c.c. of the reagent and 8 drops of urine or 3 c.c. of the reagent and 6 drops of urine are taken in a clean test-tube and the contents boiled for two minutes. The test-tube is then set aside and allowed to cool. If the reducing substance is present, there will be a precipitate of green, yellow, or red colour depending on the concentration of the substance in the urine.

The reagents keep for a sufficiently long time and are only reduced by glucose, lævulose, lactose, pentose, and homogentisic acid. It should be emphasised at the very outset that if a sample of urine reduces Benedict's solution, the chances are that the reducing substance is glucose unless it is proved to be otherwise.

Identification of the reducing Substances.—The presence of homogentisic acid in urine indicates an inborn error of metabolism (Alkaptonuria) and is readily ascertained by the fact that if the sample of urine is kept for sometime in the open light, the colour changes to black. Lactose may sometimes be present in the urine of a lactating mother and considerable difficulty may arise in examining the urine of such a person suspected of diabetes mellitus. Pentosuria is a harmless error of metabolism. For the convenience of description, the points of differentiation in the identification of the urinary substances reducing Benedict's solution are given below in a tabular form.

	Glucose.	Levulose.	Lactose.	Pentose.	Homogentisic acid.
Optical activity	D	L	D	D or I	I
Fermentation with yeast	+	+	—	—	—
Formation of Osazone crystals	+	+	+	—	—
Special test	—	Seliwanow's Test.	—	Bial's Test.	Addition of weak sol. of Ferri Chlor. gives a momentary deep blue colour.

D = Dextrorotatory. L = Laevorotatory. I = Optically inactive.

Of these methods of differentiation, preparation of Osazone crystals requires careful technique, and the cost of a suitable polarimeter limits the determination of optical activity in many cases. The easiest and the best way is to carry out fermentation test. The only things required are three fermentation tubes and a little yeast. One of the fermentation tubes is filled up with a paste made by mixing a little of the yeast with the urine to be tested. The other two tubes are used as positive and negative controls. The tubes are then incubated overnight. If glucose or lævulose is present, gas will collect in the fermentation tube. In this connection, it is very important to note that controls are parts of the actual tests and they should never be omitted, as there are some forms of yeast which do not produce any gas from glucose and there are other forms which will produce gas when no glucose is present.

Blood Sugar Estimation in Cases of Glycosuria.—Sugar is a threshold substance, and as such, no sugar is excreted in urine of a normal individual after a carbohydrate meal, although the blood sugar increases to a certain extent. The presence of glucose in urine, therefore, should invariably be followed by blood sugar estimation. If it is more than 0.2%, it is certain that the person has a low sugar tolerance; if it is lower than 0.2%, the patient should be subjected to Glucose Tolerance Test. It is to be remembered in this connection, that although the blood sugar of a normal individual is not increased more than 0.18% even after a carbohydrate meal, it may be increased to about 0.2% in moments of emotion and nervous strain. Blood sugar may be appreciably increased with the resultant glycosuria in patients suffering from thyrotoxicosis, multiple boils or carbuncle.

Collection of blood:—The time of collection of blood for the estimation of sugar from a case of suspected diabetes mellitus is very important. It is customary to collect the fasting blood for examination; but this routine procedure has also its drawbacks. The blood sugar of a case of mild diabetes mellitus may only be raised for a short time and thus the estimation of the fasting blood may lead to a wrong diagnosis. Consequently, the best time for the collection of blood in these cases is one or two hours after a meal containing about 1½ to 2 ounces of carbohydrates. In a moderately severe case of

diabetes, the blood sugar is raised throughout the day, and hence it may be collected at any time. It is only in certain number of cases where Insulin is being given for treatment and in those cases where Glucose Tolerance Test is to be performed, the examination of fasting blood is essential.

If the patient is in the laboratory, about 2 c.c. of blood is drawn out of a vein and poured in a clean test-tube containing a small crystal of Potassium Oxalate which acts as an anti-coagulant. As too much of Potassium Oxalate tells upon the accuracy of the result, it is essential that the amount of Potassium Oxalate should be just sufficient to prevent the coagulation of blood. For the sake of simplicity and exactness, what I do is this: I take a piece of cloth $1\frac{1}{2}$ inch square, soak it in the saturated solution of Potassium Oxalate and allow it to dry. This piece of cloth may be safely kept for use for a considerable period of time and a single piece of thread removed from it, is just sufficient to prevent the coagulation of about 2 c.c. of blood. If the patient is not in the laboratory, in order to prevent the coagulation of blood and disappearance of sugar, GRAHAM advocates a solution of Potassium Oxalate 4 parts and Potassium Fluoride 1 part. For 5 c.c. of blood, 0.2 g. of the above solution is quite enough.

Method of FOLIN and WU for blood sugar estimation:—This is the easiest and rapid method of blood sugar estimation provided a colorimeter is available. The procedure is divided into four stages.

(1) *Precipitation of protein:*—7 c.c. of distilled water, 1 c.c. of theoxlated blood, 1 c.c. of 10% Sodium Tungstate solution and 1 c.c. of $\frac{2}{3}$ N. Sulphuric Acid are taken in a clean test-tube and the mixture is shaken thoroughly. It is then filtered. (Folin's filtrate).

(2) *Reduction of copper solution:*—In a Folin's tube, 2 c.c. of this Folin's filtrate and 2 c.c. of a specially prepared alkaline Copper Sulphate solution are taken. Similarly, in another Folin's tube 2 c.c. of a standard glucose solution (containing 2 mgms. of glucose in 10 c.c.) and 2 c.c. of the alkaline Copper Sulphate solution are taken and the two tubes are then boiled in a water bath for 8 minutes. After boiling they are allowed to cool.

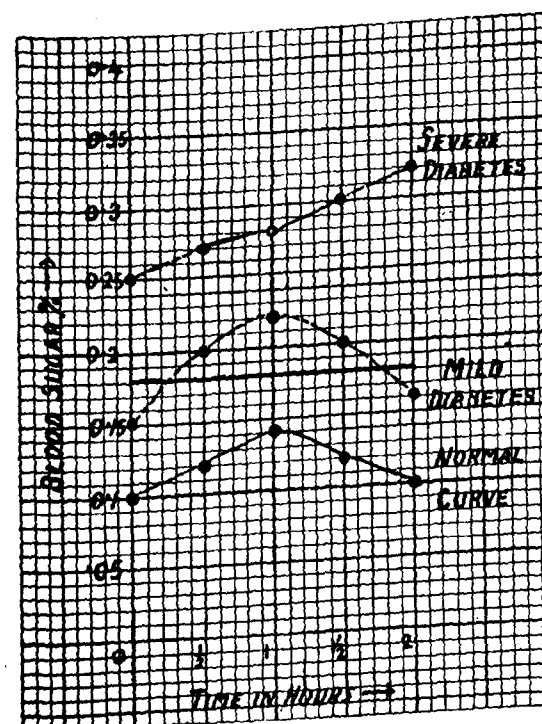
(3) *Reduction of the phosphomolybdic acid reagent:*—Now, in each of the two Folin's tubes, 2 c.c. of the phosphomolybdic acid is added which is reduced by the cuprous oxide giving blue coloration. The tubes are well shaken and the volume of each are made upto 25 c.c. with distilled water.

(4) *Comparison with a colorimeter:*—The colours of the solutions in the two Folin's tubes are then matched and from the known percentage of sugar in the standard solution, the amount of sugar in 100 c.c. of blood is found out.

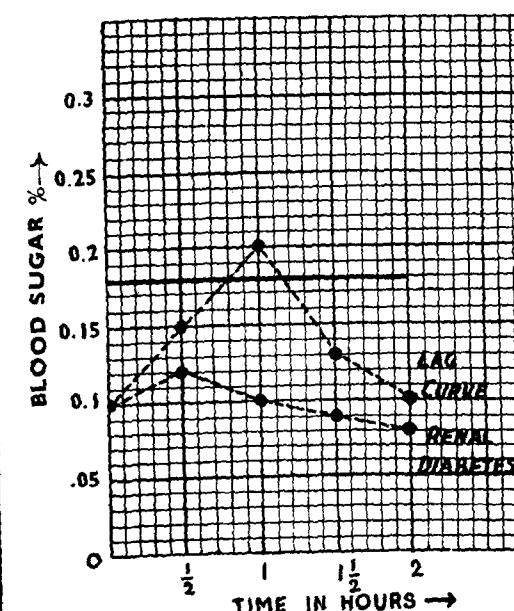
Glucose Tolerance Test:—The patient's fasting blood is collected in the morning. Fifty grammes of glucose dissolved in some water are given to the patient to drink and further specimens of blood are collected at half-hourly interval after the meal for two hours. Glucose content of each of these five specimens of blood is determined. For

the sake of simplicity, the results of the different types of glucose tolerance values are given below in graphs.

No. 1.



No. 2.



Tests for Acetone Bodies.—An account of the laboratory tests for the diagnosis of diabetes mellitus is incomplete without some remarks on the tests for acetone bodies, because their presence in large amount in the urine of a case of diabetes means that he is in imminent danger of coma. Of the two well known tests—ROTHERA and GERHARDT's tests—the former is more satisfactory and there are practically no fallacies of this test.

Rothera's Test:—Half a test-tube full of unboiled and fresh urine is saturated with Ammonium Sulphate and to this, a few drops of freshly prepared aqueous solution of Sodium Nitroprusside is added. A few drops of strong Ammonia is then poured by the side of the test-tube. If acetone bodies are present, a permanganate ring develops at the junction.

References :

1. Dodds and Dickens—*Lancet*, 1924, I.
2. Bennet and Dodds—*Lancet*, 1925, I, 429.
3. Dodds and Robertson—*Lancet*, 1930, I., 852.
4. Folin—*Laboratory Manual of Biological Chemistry*.
5. Price—*Text Book of Medicine*.
6. J. P. Bose—*Hand Book of Diabetes*.
7. Beaumont and Dodds—*Recent Advances in Medicine*.
8. *The Clinical Interpretation of Aids to Diagnosis*, Published by the Lancet Ltd., 7, Adam St.; Adelphi, London.

Treatment of Diabetes

BY

Rao Bahadur Dr. Raman Tambi, M.D.
Presidency Surgeon, Trivandrum.

DIABETES is a disease which has claimed numerous victims from the intellectual classes in India. Fifty years ago, the disease was very common among the officials in Travancore. In my youth, I had seen many promising men cut off in the prime of life by this dire disease. While I was studying Medicine in Great Britain, I availed myself of every opportunity I had, for studying the comparatively few cases of diabetes I saw there. The first thing that struck me was that, while in India, I had seen the disease commonly among the well-to-do and the disease in Great Britain. I once had occasion to discuss this subject with the late SIR DYCE DUCKWORTH, who had spent several years in India. He said the cause of the disease could be summed up in three words: *Wine, Women, Worry*. In England, drink was a potent factor whereas, in India, licentiousness and worry were the chief factors in causing the disease. Eating a large quantity of starch and sugar was also a contributory factor. Heredity also had some influence. Children of diabetics have a tendency to acquire the disease late in life. I shall next proceed to the treatment of the disease. This subject can be considered under two well-defined heads:—

- I. Treatment before the discovery of Insulin.
- II. Treatment after the discovery of Insulin.

I. Treatment before the discovery of Insulin.—More than thirty years ago, I tried the effect of Von Noorden's diet on several patients. I determined the amount of sugar by keeping them on ordinary diet for two days. Then they were given a purgative. They had almost a complete fast for 24 hours except for two cups of tea or two bottles of soda. In moderate cases, these measures were sufficient to make the urine sugar-free. Then I put them on Von Noorden's diet.

Breakfast:—7-30 A.M.—6 ozs. of tea or coffee. $\frac{1}{4}$ lb. of mutton, one or two eggs.

Lunch:— $\frac{1}{2}$ lb. of mutton: 2 ozs. of boiled vegetables or cucumbers or tomatoes in vinegar and salt. 5 tea-spoonfuls of whisky in 12 ounces of water. 2 ozs. of coffee without milk or sugar.

Dinner:—6 P.M.—8 ozs. of clear soup. $\frac{1}{2}$ lb. of mutton, three table-spoonfuls of well-cooked green vegetables. 3 sardines—5 teaspoonfuls of whisky in 13 ounces of water. (Whisky is not absolutely essential to the treatment).

Supper:—9 P.M.—2 Eggs. 13 ounces of water. This diet, with slight modifications, enabled several patients to keep themselves sugar-free for several years.

For pure vegetarians, treatment by diet alone is not satisfactory.

Drug Treatment.—Opium and its derivative Codeine have been used for a long time.

Dose:—Crude Opium in doses of $\frac{1}{2}$ grain, thrice daily, has been given and gradually increased to 12 grs. or 15 grs. in a day. This greatly reduces the amount of sugar but the patient runs the danger of contracting the Opium habit.

The drug is pushed on till the maximum amount of sugar reduction has been obtained and then the dose is maintained at that level. Codeine Phosphate has been given in doses of $\frac{1}{2}$ grain, thrice daily, combined with $\frac{1}{2}$ gr. each of Ext. Nuxvomica and Extract Cascara. The dose of Codeine phosphate can be gradually increased to two grs. thrice daily.

Sodium Salicylate.—This can be given in doses of 10 or 15 grains, three or four times a day. In recent and moderate cases of glycosuria, this drug has been found useful.

Hexamine in 5 grain doses, thrice daily, is said to be beneficial in some cases. I have no personal experience of this drug in diabetes.

Among proprietary medicines, I have found Pancreaptine and Panmellitus useful in moderate cases of glycosuria—Synthalin B. has also been found in a few cases to be very efficacious in reducing the quantity of sugar in the urine. For improving the general weakness of diabetics, I have found Elixir of Glycero-Phosphates without sugar (P.D. & Co.) in doses of a teaspoonful in half an ounce of water, extremely useful. So far, no drug has been found which, if given by the mouth, can be said to cure diabetes.

Insulin.—This was discovered by BANTING and BEST who were working in the laboratory of Professor MCLEOD of Toronto. They found that an extract of special cells of the pancreas which, when refined, was called Insulin and on injection into a diabetic, controlled the disease.

Indications for the use of Insulin:—FITZ and MURPHY state that “as a general rule, Insulin should be given in cases occurring in children (juvenile diabetics) and in people under forty, in all cases of coma or severe acidosis, in all cases complicated by an infectious process causing either a temporary or permanent lowering of tolerance, in all cases of proved severity in which a surgical operation is necessary and in all cases in which the tolerance without Insulin as determined by adequate dietetic control is so low as to make efficient living impossible. Insulin is not necessary in many cases of mild diabetes in elderly people, when the disease is uncomplicated and the patient can get along quite well on a reasonably restricted diet.”

Treatment with Insulin:—Insulin is not a specific for diabetes. Diet restriction is very necessary when Insulin is used. As Insulin can control the disease, methods of treatment with diet and Insulin are not uniform. In my experience, a preliminary starvation treatment is

useful. While treating diabetes, it is advisable to look for foci of infection in the teeth, throat, alimentary tract etc., and have them attended to.

There are four methods of beginning diabetic treatment :—

(1) Fat in the food is first reduced and along with it, the total number of calories in the food is also reduced. The amount of carbohydrate is also reduced. This is useful for mild cases in fat people.

(2) The patient is given a basal diet *i.e.*, enough food for the body at rest, according to height and weight. Food is then gradually increased and when sugar appears in the urine, enough Insulin is given to counteract it. Basal requirement of diet varies with the weight and age of the patient. Roughly 12 to 15 calories are required for every pound of body weight. Women require 10% calories less and children require proportionately more.

(3) Patient is given a full diet sufficient for his maintenance and then sufficient Insulin is given to prevent the appearance of sugar in urine.

(4) Patient is asked to fast till sugar disappears. Food is increased gradually till the patient has enough to eat or till sugar returns. When sugar returns, sufficient Insulin is given to check the sugar.

It has been found that a diabetic cannot tolerate more than 30 to 60 grammes of carbohydrate. He will require $\frac{1}{2}$ to $\frac{3}{4}$ gramme of protein per pound of body weight.

The remaining calories can be obtained from fat. The diabetic should know something of the composition of food stuffs to enable him to make a selection.

1 Gramme of carbohydrate	equals	4	calories.
1 " protein	"	4	"
1 " fat	"	9	"

The chief sources of carbohydrate are vegetables, fruits and nuts. These can be grouped as follows:—

Vegetables A.	... 0—5 %
Vegetables B.	... 5—10 %
Vegetables C.	... 10—15 %
Vegetables D.	... 15—20 %
Vegetables E.	... 20—30 %

Common Articles under Vegetable A:—Cabbage 1%; Cauliflower 1.3%; Spinach 1.3%; Gooseberries (unripe, stewed) 1.5%; Cucumber (raw) 1.75%; Coconut milk 2.4%; Tomatoes (raw) 2.4%; Pumpkin (raw) 2.4%; Turnips 3.5%; Straw Berries (ripe, raw) 4.4%; Spring Onions (raw) 4.7%; Coconut (edible fruit) 4.8%; Apricots (ripe raw) 4.6%; Apples (stewed) 4.7%; Walnuts 5%.

Vegetable B:—Gooseberries (raw) 5.3%; Onions (after boiling) 5.4%; Carrots 5.9%; Pomegranate (ripe, raw) 6.1%; Oranges

(without skin) 6.2%; Almonds (weighed without shells) 6.5%; Figs (green, imported raw) 6.9%; Apricots (dried, stewed) 9.4%; Pineapple (fresh) 9.9%; Grapes 10%.

Vegetable C:—Peas (fresh) 12.8%; Prunes (stewed with stones) 18.6%; Figs (raw) 14.4%.

Vegetable D:—Potatoes 15.6%; Bananas 18.7%.

Vegetable E:—Chestnuts (shelled) 29.2.

1 oz. of oatmeal contains 18 grms of carbohydrate.

A shredded wheat biscuit contains 23 grms of carbohydrate.

Ragi can also be used by the diabetic occasionally in place of oatmeal.

Soyabean can also be taken by the diabetic as most of its carbohydrate is not assimilable.

Amount of protein in the diabetic diet is to 1.5 grms per kilogram of body weight in adults. In children, up to 3 grms per kilogram of body weight may be allowed.

For non-vegetarians, best sources of protein are meat and fish.

Fat:—Too much fat may lead to acidosis. The proportion of fat to carbohydrate in the diet should be as 1 : 2.

Fat can be taken either as cream or milk. Butter is also useful, as 30 grammes of butter yield 25 grammes of fat.

For children, Cod Liver-oil may be given as a source of fat. The amount of carbohydrate allowed should be divided into three portions. The smallest portion $\frac{1}{5}$ th should be taken in the morning as at that time there will be more sugar in blood and urine than at other times. First, find out the maintenance diet of the patient. If he cannot do work and lead a healthy cheerful life on that diet, increase it gradually, especially by adding more carbohydrate. When the patient feels that the diet is sufficient in everyway, examine his urine, see if there is sugar. Then give him sufficient Insulin to make him sugar-free as far as possible. At first, when Insulin was discovered, every one thought that a sure cure for diabetes had at last been found. The experience of a few years made the physicians realise its limitations. Restricted diet with Insulin has enabled many people to lead cheerful and active lives. Diabetic children have been enabled to grow into adult life. With the advent of Insulin, the life of the diabetic has been considerably prolonged, diabetic coma which was formerly dreaded by the doctors has become very rare. Formerly, diabetics did not have restricted diet. They used to over-eat because of their abnormal appetite. There was no restriction of fat. Fatty acids formed in the system and this led to acid intoxication and coma.

Methods of using Insulin.—As a preliminary, the patient's blood sugar and quantitative estimation of sugar in the urine should be done. It will be advisable to have blood sugar estimations periodically, as guide to progress in treatment. Before injecting Insulin, it is always advisable to test the urine because the dose of Insulin has to

be regulated by the amount of sugar present in the urine. In mild cases, one injection of 15 or 20 units of Insulin before breakfast will be enough. If large quantities of Insulin have to be given, it is best to give the Insulin in two doses, the larger dose being given before breakfast and the smaller dose before the evening meal. The action of Insulin is greatest about an hour after it is injected. Generally, it is given half an hour before a meal, to counteract the wave of sugar in the blood which occurs half an hour after a meal. Within twenty or thirty minutes after Insulin, the patient must have some carbohydrate food to avoid the danger of hypoglycæmia. As the effects of Insulin wear away in about eight hours, attempts have been made to produce some varieties of Insulin whose effects will last longer. In 1936, HAGEDORN used Insulin in suspension. He called it Protamine Insulin. As it was in suspension, it was absorbed slowly by the tissues. Its action lasted twice as much as the ordinary Insulin. Later, Zinc Protamine Insulin was produced. The action of the Zinc Protamine Insulin starts only three hours after injection. The action may continue for 24 to 48 hours. For mild cases, one injection of Zinc Protamine Insulin a day will be enough. Start with five units and increase gradually by three units up to 15 units once a day. This should be enough for a moderate case. Zinc Protamine Insulin can be cumulative in its action and so increase in dosage should be made very carefully. Severe cases may be controlled by combining Zinc Protamine Insulin and ordinary Insulin. In surgical complications, the quantity of Insulin will have to be greatly increased. In diabetic coma, 50 units of Insulin may be given at once, followed by large doses till the patient shows definite signs of improvement. After the introduction of Insulin, death rate from diabetic coma has been considerably reduced. A patient who takes physical exercise regularly will need less Insulin as exercise can burn up some sugar. For effective treatment with Insulin, the hearty co-operation of doctor and patient is absolutely necessary. Whenever possible, the patient should stay in hospital for some weeks to enable the doctor to investigate the case thoroughly and to stabilise the patient's diet and also regulate the dosage of Insulin. The manipulation of the diet and Insulin calls for the best energies of the doctor. When we consider the great havoc caused by diabetes, and when we recognise that the diabetics are very susceptible to tuberculosis, we can realise how important it is for the patient to be under the watchful eye of the doctor. The diabetic patient, even when he has been sugar-free for a long time, should not grow negligent. He must always remember that any neglect on his part will lead to relapse. I had under my care, a patient who remained sugar-free for eleven years. After that he became reckless in dieting and died in a few months owing to an attack of severe diabetes. Diabetes is a disease in which idiosyncrasies with regard to certain articles of diet have been found. One patient may tolerate one variety of carbohydrate while another patient passes sugar in the urine with this same carbohydrate. For the successful treatment of the disease, every patient has to be watched for several years.

Pathology of Diabetes Mellitus and Role of Zinc Protamine Insulin

BY

Capt. P. Ganguli, B.A., D.T.M.,

P.G., ZEUG, (UNIVERSITY OF VIENNA), I.M.S. (LATE)

Calcutta.

DIABETES is a metabolic disease caused by disorder of the metabolism of the proximate principles of food and especially of the carbohydrates in which a link is missing for converting sugar into energy and heat of the body.

Exogenous Sources of Blood Sugar.—The end products of digestion of carbohydrate in the gastro-intestinal tract are monosaccharides of which glucose forms the chief variety. These monosaccharides are absorbed and carried through the portal vein into the liver. Here all the monosaccharides other than glucose are transformed into glucose. Most of the glucose is transformed into glycogen and stored in the liver cells. But, if the quantity of absorbed glucose is large, then part of it overflows into the systemic circulation. The end products of digestion of proteins are amino-acids. When these are absorbed and carried to the circulation through liver, a certain portion, which is necessary for repairing the tissue waste, is taken up by tissues and built up as tissue proteins, the balance is deaminised into ammonia and non-protein residues. The liver cells transform ammonia into urea, and the residues are transformed into glucose, acetone bodies, bile salts and other substances. In diabetes, about 60% is converted into glucose by liver cells and some of the amino-acids give rise to acetone bodies. The glucose derived from protein by transformation in the liver cells is not readily stored in the liver, unless the liver cells are in need of it, as during very much reduced carbohydrate intake. But usually, when the store houses of the liver cells are filled up by readily available glucose from carbohydrate diet, the glucose subsequently formed from amino acids passes out into the blood and serves to maintain the level of the blood sugar and to raise it after meals in case of large intake. The rise of blood sugar after meals is due principally to the glucose of amino-acids (and fats) and then to the glucose derived from monosaccharides other than glucose and lastly, to the excess of glucose which cannot be stored in the liver. The glycaemic cycle in the blood of a normal patient rises after meals from 0.09 or 0.1% of the fasting blood sugar level to 0.15 or 0.16% within half to one hour or so. The threshold level of blood sugar is normally 0.18%, beyond which sugar leaks out into urine. If a massive quantity of sugar or glucose (more than 300 grms.) is taken, this threshold level of blood sugar is exceeded even in normal persons and sugar appears in the urine. But, if other carbohydrates are ingested, even in very large quantities, the rise of blood sugar does not reach the leak-point, as the gradual overflow of sugar into t

blood is quickly dealt with by Insulin, which the pancreas is stimulated to secrete by the excess of sugar in the blood. When fat is ingested, about 10% is converted into sugar, but when there is a great demand for sugar in the body, almost the total quantity can be thus utilised.

Endogenous Sources of Blood Sugar.—Besides the exogenous source of blood sugar derived from meals, there are endogenous sources from which a continuous supply of sugar is maintained to keep the level of the blood sugar constant in between the meals, after the initial rise of blood sugar after meals is restored to normal level. This continuous stream of endogenous flow of sugar into the blood continues till exogenous supply is again derived from the next meal. The meals bring alkalis in the blood, which check acidosis and consequent hyperglycæmia and are excreted with the alkaline tide of urine. If no meals are given, the endogenous supply continues, but as acidosis is increased, glycogenolysis of the tissue glycogen is also increased, which may, in extreme cases, actually raise the blood sugar above the threshold level. We thus get examples of "hunger diabetes" or "vagabond diabetes" in which the blood sugar is thus raised from endogenous sources. Although this sugar is mainly derived from glycolysis of liver and muscle cells, almost all the other cells of the body, especially of the heart, brain, kidneys and such others, take part in carbohydrate metabolism. The role of vitamin B₁ is very important in carbohydrate metabolism as an adjuvant of Insulin, and is of utmost importance in the treatment of diabetes.

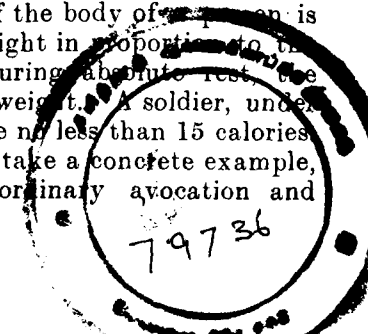
Basal Secretion of Insulin.—The sugar derived from endogenous sources is always proportional to the need of supplying nourishment to the cells and as this sugar can only be utilised by the tissue cells through the intermediary of Insulin, a continuous flow of the latter is maintained, which is known as the *basal secretion of Insulin*. This basal secretion helps to keep the blood sugar, more or less at a constant level during fasting and checks its rise. Ordinarily, it is a continuous secretion and rarely varies in amount. But, when a person takes a meal, the temporarily increased amount of Insulin, which the pancreas is excited to secrete, makes the storage derived of sugar from carbohydrate possible, especially in the liver and muscle cells and prevents the formation of sugar from protein in liver, so that the rise of blood sugar is kept within proper limits.

Von Gierke's Disease. Hyperglycæmia. Hyperinsulinism.—The transformation of glycogen thus stored in the cells is effected by impulse from the brain through the sympathetic and a constant secretion from suprarenal gland, thyroid and posterior lobe of the pituitary glands produces a continuous glycogenolysis ensuring a continuous supply of glucose in the blood necessary for metabolism in all parts of the body. If, for any reason, this supply fails, the glycogen becomes increasingly stored in the liver, heart and other organs producing increase in size of these organs due to accumulation of glycogen. This is known as Von Gierke's disease. Similarly, if for any reason, the B-cells of the islands of Langerhans are affected by over-

feeding, acidosis, hereditary predisposition for dysfunction and such others, there is a failure of basal supply of Insulin, the balance goes in favour of glycogenolysis, and the failure of muscle and other cells of the body to utilise all the glucose circulating in the blood leads to an accumulation of unusually high amount of sugar in the blood or *hyperglycæmia*. Again, in adenoma or adenocarcinoma of the islands of Langerhans, excess of Insulin is secreted and much more blood sugar becomes taken up by the cells of the body leading to diminution of the blood sugar or *hypoglycæmia*. This condition is known as *hyperinsulinism* and can be prevented by taking excess of sugar in the diet; otherwise, various symptoms of hypoglycæmia set in.

Pathology of Diabetes Mellitus.—We can thus understand that there exist two different processes of entry of sugar into the blood, one being a continuous production of endogenous sugar during fasting conditions, which is controlled by basal secretion of Insulin, and the other an increased access of sugar in the blood circulation after meals, which has to be controlled by increased activity of the islands of Langerhans and resulting increase in the secretion of Insulin. In diabetes mellitus, both these supplies are defective and the severity of the disease depends upon the degree of insufficiency. In mild type of diabetes, the basal supply of Insulin is not affected to any marked extent. It is only the increased secretion of Insulin to deal with increased blood sugar after alimentation that is affected. The diseased or dysfunctional B-cells of islands of Langerhans cannot cope with the normally increased work. There is an analogy with diseased heart in that although the normal function can be maintained by such heart during rest, it becomes quite incapable to cope with the increased work or exercise leading to circulatory failure. Just as in this case, the treatment should be directed to avoidance of exercise and ensuring rest, so also in the treatment of diabetes, the first and the most important indication is the reduction in the quantity of the meals to such an extent that the percentage of blood sugar is not raised above the threshold level, which is normally 0.18%, so that the function of the B-cells is not overtaxed.

Treatment of Diabetes Mellitus.—I. Mild type of first degree.—The study of diabetic animals shows that liver elaborates glucose principally from proteins or amino-acids and that this glucose cannot be readily stored in the liver but quickly passes into circulation. The intake of protein should, therefore, be limited to the minimum quantity required for tissue repairs and it has been found that for this purpose no more than 1rd to 3rd gm of protein per pound of body weight is all that is necessary. The total caloric value of the diet necessary to maintain the basic metabolic requirement of the body of a person is from 10 to 15 calories per pound of body weight in proportion to the amount of exercise he has to undergo. During absolute rest, the caloric requirement is 10 per pound of body weight. A soldier, under conditions of heavy active service, will require no less than 15 calories. Each gm of protein yields 4.1 calories. To take a concrete example, a person, weighing 120 pounds pursuing ordinary avocation and



moderate exercise, will require 1500 calories, calculating at the rate of 12.5 calories per pound of body weight. His protein requirement should not exceed 80 grms or 328 calories. Deducting this value from 1500 calories, the balance of 1172 calories should be met from fats and starch. The caloric value of each gm of starch and fat is 4.1 and 9.3 respectively. In hot countries, the intake of fat should be reduced as much as possible, so that the bulk of food or caloric requirement should be obtained from starch. Proper quantities of salts and vitamins should be taken. Vitamin B₁ is particularly needed for diabetics.

It has been shown by PORGES, ADLESBERG and others of Vienna, that the old method of dieting the diabetic patients with abnormally low amounts of carbohydrates (60 to 80 grms) was conducive to acidosis and hyperglycæmia and they suggested increase of the carbohydrates to 100 or 150 grms, and proportional reduction of fat. It was found, however, that even this method of dieting, without reduction of protein, was insufficient to prevent reappearance or even increase of glycosuria. This is certainly due to large amount of protein in the diet and hence, it is imperative to reduce the amount of protein to $\frac{1}{3}$ rd or even $\frac{1}{4}$ rd gm per pound of body weight, and to get the balance of calories from as much carbohydrates as possible.

Now, if the balance of calories has to be obtained chiefly from carbohydrates, the nature of the starchy food exerts a remarkable influence on the curve of the blood sugar, the height of which becomes directly proportional to the rapidity of absorption of monosaccharides from the alimentary canal. If sugar or very rapidly assimilable starchy food like rice, potatoe or white flour is taken as principal diet, a massive quantity of monosaccharides is so quickly absorbed, that very little time is given to liver with limited supply of Insulin to convert it into glycogen, and prevent its overflow into the circulation. This sudden access of sugar into the blood raises the blood sugar above the threshold level.

It has already been mentioned that the fasting blood sugar level of normal persons is 0.09 or 0.10%. In the case of diabetics, this level is usually higher than normal except in most mild cases. It is, therefore, indispensably necessary that slow absorption of alimentary sugar takes place from intestines so that the rise is gradual and does not overstep the limit. The starch of green vegetables is enclosed in cellulose framework and the digestion takes place mostly in the large intestines, where *B. coli* disintegrate the cellulose, liberating the precious starchy granules. The rise of blood sugar is, therefore, slowly effected, as ample time and opportunity are given to the liver cells for converting them into glycogen with the limited supply of Insulin.

It is, therefore, necessary to avoid sugar and sweet fruits and also to limit the amount of rice, potatoes and bread to as small a quantity as possible. The principal meals should consist of a large quantity of boiled green vegetables, which are mainly composed of cellulose with very small percentage of starch granules confined in their meshes.

There are plenty of green vegetables which contain 1 or 2 per cent. of starch. Bran bread is better suited than ordinary bread.

The stomach of the Indians, especially of the rice-eating people, is more dilated than that of the average Europeans and hence in order to quench their appetite, larger bulk of food is necessary. The diet of a diabetic Indian should mainly be composed of boiled green vegetables, as a large bulk can thus be provided. The following vegetables are recommended. Cauliflowers, cabbages, beans, carrots, radishes, cucumbers, brinjals, egg fruits, kohl rabi or ol kabi, tomatoes, lettuce, asparagus, okras or vindees, onions, unripe pumpkins, turnips, parowal, squash, karela, kolha, mugree, gourds or kadu, gawaree, ghosali, spinach and sags of all sorts, especially poee sag, green telakucha and such others.

Small quantities of fruits should be taken in between principal meals and they should not be too sweet. Among the fruits, oranges, papaya, pomegranates, lucarts, mangosteins, copras, fresh cocoanut pulps, melons, kharmujas may be taken. Many Indians take raw cucumber (*khira*), muli, and such others in place of fruits. Mangoes, bananas, custard apple, (*ata*) grapes, jack fruits, lichis and other sweet fruits should be avoided.

In order to get the allowance of proteins, meat should be avoided. Small quantities of fish may be taken. Eggs should be avoided, especially the yellow part which contains fat. Protein is contained in rice, bread and dhal or other leguminous vegetables. Bread contains 11.5 per cent protein and 1 % fat. Rice contains 8 % protein and 0.3 % fat. Fresh white fish contains 10 % protein and 1 % fat. Milk contains 3.3 % protein and 3.7 % fat, potatoes contain 1.8 % protein and 0.1 % fat. Dhal contains 24 % protein and 1.3 % fat. Proteins which are deficient in any of the essential amino acids are of inferior biological value. Animal proteins are, therefore, regarded as far superior to vegetable proteins.

Interval between meals :—The interval between meals should be so arranged that the temporary rise of blood sugar should go back at least to its own fasting level, which, in very mild cases, is like that of normal persons, viz., 0.09 to 0.1 %. But, as the severity of diabetes increases, the fasting blood sugar level rises as well as the threshold level. Besides these, the time for coming back to the previous level is always increased, so that the intervals between meals is to be prolonged accordingly. The total diet should be divided into five meals, of which two should be primary and the rest secondary. The two primary meals (lunch and dinner) should consist of a little rice or bread, plenty of boiled green vegetables, salads, pickles, and fish or skimmed milk. The other three meals (tiffin, breakfast and supper) should consist of tea, or coffee, one or two slices of brown bread, without butter, and fruits. The intervals between lunch and tiffin and between dinner and supper should be not less than 4 hours, so as to allow the blood sugar fall to his fasting blood sugar level. The rise of blood sugar after the smaller meals will necessarily be small and should not take more than

3 hours to fall to his original fasting level. If the time exceeds the above limits, the patient will require the help of Insulin and the disease is already advanced.

The patient should be weighed every week at least, in order to see whether he is losing weight with the strict basic metabolic diet. If it is found that he is losing weight, it must be assumed that he is not assimilating the diet to the full extent and the allowance should be increased. If, on the other hand, he gains in weight, curtailing the diet should only be done if he passes sugar in his urine. If his weight remains stationary, and his urine becomes free from sugar, the same diet should be continued, and cautiously increased afterwards.

II. Mild type of second degree (Moderately advanced).—If the blood sugar rises above the threshold level even after taking basic metabolic diet, the case is moderately advanced and the help of Insulin is needed for its treatment. In these cases, the basal secretion of Insulin is not diminished, but the increased secretion of Insulin, for coping with hyperglycæmia after meals, is interfered with. The basal secretion of Insulin is sufficient to keep the level of the blood sugar normal or nearly so during fasting periods. The best way of determining whether the basal secretion is normal or not, is by testing two samples of urine, the first being that voided for the first time after the night meal and the second being the next one, which is usually passed in the morning. The first sample shows presence of glucose, but if the second sample is free from sugar, it means that the percentage of blood sugar falls at least below the threshold level, *before* the first urine is passed. The assumption is that the basal secretion of Insulin has kept down the blood sugar, during fasting period, derived from endogenous sources. If the patient takes two principal meals, the level of blood sugar rises twice above the threshold level after each meal for want of proper quantity of Insulin. In order to prevent this glycosuria, pure unmodified Insulin should be given half an hour before each of the two principal meals, and the quantity of Insulin will depend on the amount of deficiency of Insulin depending on the degree of dysfunction of the B-cells of the island of Langerhans. The effect of Insulin reaches maximum within two or three hours and vanishes within five or six hours. It goes parallel with the curve of glycæmia after meals and keeps the blood sugar within proper limits.

Zinc Protamine Insulin:—In order to avoid two daily punctures of Insulin, which are not liked by patients, only one administration of Zinc Protamine Insulin may be sufficient to make the urine sugar-free gradually within a week. The fine suspension of minute particles containing Insulin is deposited under the skin and is slowly dissolved and liberated within 24 hours. In these moderately advanced cases, 15 units of Zinc Protamine Insulin may be given daily once before morning meals. Some prefer evening administration, others yet recommend administration just before retiring. Whatever be the time of administration, the full effect of Zinc Protamine Insulin treatment will not be manifested before a few days are over. The sugar in the urine is gradually diminished and disappears within a week.

III. Moderately severe type of diabetes. (Third degree).—In these types of cases, the basal secretion of Insulin is diminished in addition to increased secretion after ingestion of food. Slight acidosis is almost invariably present, but ketone bodies are not found in the urine. LAWRENCE¹ usually gives in these cases 30 units of Zinc Protamine Insulin daily before the morning meal to begin with and the urine is examined for sugar at 11 A.M., 1 P.M., 4 P.M., 7 P.M. and 10 P.M. In comparatively mild cases of this type, sugar usually disappears from urine within a week. Such a dose of Zinc Protamine Insulin comes into action in three hours and acts mainly by day in helping to deal with the day's meals. The level of the fasting sugar is kept within normal limits partly by Insulin liberated from the part where the Zinc Protamine Insulin has been injected and partly by patient's own endogenous sources.

If, however, it is seen that 30 units of Zinc Protamine Insulin control the endogenous secretion of sugar but not the sugar after ingestion of meals, the dose of Zinc Protamine Insulin is increased. Care must be taken to avoid hypoglycæmia and the patients should be warned against it and trained how to deal with it. In severe cases, 30 units of Zinc Protamine Insulin are insufficient even to check the hyperglycæmia due to endogenous secretion. In these cases, the dose of Zinc Protamine Insulin can be increased more safely and frequently both the endogenous and increased formation of sugar are controlled in a week or two.

IV. Severe type of diabetes. (Fourth degree).—If, however, Zinc Protamine Insulin is unable to control the rise of sugar above the threshold level after meals, but is able to control the endogenous sugar only, in big doses, and if ketosis is present, pure unmodified Insulin should be administered *with* Zinc Protamine Insulin. In fact, the latter is not efficacious in combating acidosis or diabetic coma. In these cases, Zinc Protamine Insulin is given for ensuring continuity of the effects of Insulin. In severe types of diabetes, although the patient feels better and increases in weight, yet he is never free from sugar in urine and ketosis is not controlled. In these cases, pure Insulin should be given in addition to Zinc Protamine Insulin in sufficient quantities to control the rise of blood sugar after breakfast so that, it cannot go beyond the threshold level and to come back to normal level before lunch, or midday meal. This combined dose of Insulin should be given before breakfast. In these cases, blood sugar may be estimated once at noon to find whether the doses are too heavy to have a combined effect of producing hypoglycæmia at that time. If such is the case, the dose of modified Insulin is to be reduced as the dose of Zinc Protamine Insulin as a substitute for basal secretion, has been already adjudged, or the quantity of food in breakfast may be raised a little. In that case, the quantity of night meal be reduced a little. Usually, by this procedure, the morning urine passed first after the night meal may be made sugar-free as well as the urine passed in other times.

V. Very severe cases of diabetes. (Fifth degree).—In very severe cases, this morning urine cannot be made sugar-free by only one injection of un-modified Insulin combined with Zinc Protamine Insulin and a second dose of unmodified Insulin is necessary for that purpose. This second dose of Insulin is to be given 20 minutes before night meal and the dose regulated so as to prevent hyperglycaemia going above the threshold level.

Method of Administration of Combined Insulin and Zinc Protamine Insulin.—In the pamphlets supplied with each bottle of Zinc Protamine Insulin by SHARP and DHOME and ELI LILLY and Company, strong exhortations have been made against mixing together of two preparations either in a syringe or otherwise. R. D. LAWRENCE (in an article on the subject published in *B. M. J.*, May 27, 1939), advocates the use of Insulin and Zinc Protamine Insulin drawn in the same syringe, with the only precaution that the un-modified Insulin should be drawn first. He also advocates that these combined Insulins should be injected *immediately* before morning meal.

After Treatment.—It must be borne in mind that a continuous attempt should be made to carefully note the effect of these different methods of administration with a view to diminish the dose of Insulin as the sugar tolerance increases. In a vast majority of cases, ketosis can be quickly controlled and sugar tolerance gradually increased permitting gradual reduction of the doses of Insulin.

Reference :

1. R. D. Lawrence—*B. M. J.*, May, 1937, 92,

A Survey of Remedies Used in Diabetes

BY

Major K. N. Waghray, M.B.B.S. (ALLAHABAD), M.R.C.P. (LONDON.),
Hyderabad, Deccan.

NEED for a survey of remedies used in diabetes arises particularly because there is still, both in the lay mind as well as in a great number of practitioners, a belief or a tendency to believe that medicines given orally will check the progress of disease. This feeling, evidently, has for its cause the disinclination of the patient to adhere to rigid observances of diet indefinitely and the inconvenience of taking injections or getting facilities for the same.

Diabetes has been known from early A.D.'s, and all schools of Medicine have recognized it generally as a disease entity characterized by thirst, weakness and polyuria with the result that it has been ascribed to diseased condition of the kidney and/or generative organs. All, however, recognize sedentary habits and excess in diet as contributory factors. Thus, remedies to decrease the polyuria, directions to control the intake of fluid, aids to improve general health and thereby sexual health, to help liver function etc., have been recommended from time to time. Again, several remedies have been recommended empirically by virtue of their counteracting the sweetness of sugar and sugary substances.

It was not until MINKOWSKI, in the latter part of the 19th century, described the specific lesion responsible for diabetes to lie in the islets of Langerhans of the Pancreas, that attempts at rationalizing treatment by using pancreatic extract came to the field. Many forms of extracts of the pancreas and of its enzymes began to be favoured in the treatment of diabetes till in 1921 BANTING and BEST showed that these whole extracts were inert and toxic and that a pure potent extract which is known by the name of Insulin could be isolated which would give the desired effects. Clinical results of Insulin therapy have made it to stay as the one single scientific and rational remedy against diabetes.

While Insulin does control hyperglycaemia, acidosis and glycosuria, the role of dietetic regime cannot be overstated. All schools of Medicine agree on the important role of dietetic regime in the treatment of diabetes.

All of us have had occasions to try one or more of these Herbal, MINERAL and ORGANIC remedies, of which the following comprise the main in general use:—I. Jambul. II. Opium. III. Karela. IV. Kandori. V. Sulphur, Gold, Mica. VI. Pan Mellitus and Trypsogen (Pancreatic Extracts): Pancreaptine. VII. Glukorment. Anti-Comen and Synthelin.

I. **Jambul.** - Has been most commonly in use. It has been reputed to reduce sugar in the urine and I have certainly found, along with a certain amount of reduction in the excretion of sugar in diabetic urine, a fair amount of a general feeling of well-being also by the patient under Jambul, although I did not notice any marked changes in the level of blood sugar. I did not know whether this reduction has been

so much due to the use of Jambul, or to the dietetic regime. Lasting effects have not been noticed.

II. **Opium.**—Has been highly talked of as being responsible for controlling sugar. Perhaps the beneficial effect of Opium lies in its property of generally depressing or slowing metabolism. I have known of several cases of mild glycosuria who have kept more or less free from it under the use of Opium and yet I also know of a good few recognized cases of diabetes who have not had the slightest beneficial effect from its use. In one case which I had to treat for myocarditis, the patient gave the history that he was suffering for 20 years previously from a high grade glycosuria and that the use of Opium had completely checked it, but in my routine examination, I found him to be having not only sugar in the urine, but also ketones.

There is no doubt that one does meet with opium addicts who have led a life, more sedentary than which could not be imagined, and who have indulged in excesses worse than which could not be thought of, and yet they have escaped diabetes. This raises an interesting point worth investigation as to what role Opium does or can take.

III. **Karela.**—Karela powder, specially the white Karela has been ascribed to have the property of curing diabetes. The whole Karela is taken, dried in shade and powdered. Some use it in doses of one teaspoonful on empty stomach with fresh milk, others use it in smaller doses, repeated two or three times a day. I was tempted to treat some of my cases with this stuff, because one of my patients whose urine and blood tests had previously proved him to be a true diabetic of mild type, and who denied having put himself under any other treatment, is now free from glycosuria without any restriction in diet (his present blood sugar could not be estimated however). I have found no uniform results. In some, undoubtedly a little reduction in glycosuria has occurred and that too temporarily. Even in the more advanced and established cases, I have noted a very temporary diminution of glycosuria, but this, I am inclined to think, may be due to dietetic restrictions.

IV. **Kandori.**—The leaves of this plant are said to counter the sweet taste of sugar. Perhaps it is this that has brought its use in this disease. I have known of several diabetics who have used it as a regular treatment and for prolonged periods to no appreciable advantage. There have no doubt been, during its use, periods of diminished excretion of sugar in the urine. But here again other factors especially diet may have been responsible for the same.

V. I have no experience of Sulphur, Gold, Mica, but I should certainly think it worthwhile trying Sulphur as it has been claimed that the beneficial effects of Insulin are proportionate to the amount of Sulphur it contains.

VI. Of the pancreatic extracts, Pancreaptine and Panmellitus have been highly talked of. In some cases, a certain amount of reduction in glycosuria is noted, while generally there is no diminution in glycosuria nor any change in the patient's feelings.

VII. Glukorment and Anti-Comen have been similarly praised. Both help considerably more in reducing glycosuria, but not being constant in their results are undependable. Synthelin with Decholin control glycosuria and glycæmia much more effectively, but cannot be recommended for prolonged use being toxic. Oralin is a chemical compound of Insulin said to be absorbed when administered orally. Results are so erratic that no reliance in a disease like diabetes can be placed on it.

The only remedy which is constantly effective and certain in its action is Insulin administered sub-cutaneously in controlled and adequate dosage. Insulin is indicated in all diabetics with complications, especially in the ones who have marked ketosis and those who are getting denutritioned. The drawback with Insulin is the short duration of its effects and, therefore, the necessity for repeated injections. Also the fluctuations in glycæmia that result from its interrupted injections. An improvement over it so as to spread out its absorption at a more uniform rate for a prolonged period has been made available now in Zinc Protamine Insulin also injected subcutaneously. This product is indicated in all cases of diabetes where quick action is not demanded (*e. g.* Coma.) particularly in the young and fresh cases where it offers best chances of a more lasting relief from the disease, and also in cases where myocardial disease, arterial disease, or pulmonary tuberculosis complicate diabetes. Further, it is more conveniently administered in one single dose at any hour of the day irrespective of hours of meals.

In cases with acidosis and high level of glycosuria, a combination of the original plain Insulin to counteract the glycæmia of the meal following the injection with Zinc Protamine Insulin to meet the Insulin requirements of the day has met with great success and satisfaction in practice. But, whatever the remedy used, it is of the greatest importance to adopt a strict dietetic regime in every case of diabetes from the very beginning and keep it up all through and almost indefinitely provided it does not fall short of the needs of the patient in maintaining his general health and weight. Most of the Indian cases are, in my experience, amenable to simple dietetic regimen.

There is no need at the present time with Insulin at our disposal to starve a patient, as practised under ALLAN's method of treatment, nor of restricting the carbohydrates from the patients' diet very rigidly. The modern principle of dietetic treatment is to give a fairly liberal share of carbohydrates in a diet framed to meet adequately the requirements of a patient.

Summary.—1. The ineffectiveness, unreliability and inconsistency of results from herbal, mineral and other patent medicines recommended for oral use is pointed out.

2. The universal need for dietetic regimen with not too rigid restrictions of carbohydrates is stressed.

3. The safety and advantages of Insulin treatment particularly the new combination, *viz.*, Zinc Protamine Insulin, have been brought out.

Difficulties in Treating Diabetics

BY

N. C. Appayya, M.R.C.P.I.

A. M. M. Hospital, Pallatur, Ramnad Dt.

ALARGE majority of diabetics do not know that they are suffering from diabetes until their urine is examined, as a routine for Insurance Companies or when being admitted to the hospital as an in-patient for some other disease. Others consult medical men because of frequency of micturition during the nights and of excessive thirst, chronic ulcer, or ants collecting in the chamberpot used by the patient.

Once diabetes is diagnosed definitely after the examination of urine and blood, one would think that there would be no more difficulty in treating these patients. But, it is not so because, it unfortunately happens to be a disease for which no definite cure has been discovered, though the discovery of Insulin has reduced the mortality to a considerable extent. People suffering from any sort of disease generally go to the doctor because of the suffering caused by the disease and would not ordinarily like to be treated for months and years together.

Diabetes is generally known as a disease of the middle and upper classes of people, the poor among us being very fortunately immune from it.

The upper and middle classes, being in a position to afford for medicine and medical attendance, one would think there will be no difficulty in treating them. But, here again, it is not the case. While the poor would be willing to take his medicine from the hospitals for months and even years, the well-to-do expect to be cured in a few days, because he pays for it. If one medical man cannot cure him, he goes to another and if one system of medicine cannot help him, he of his disease, he will go to another system—thanks to the several systems of medicine that exist in India,—and eventually, he will realise that he, as a rolling stone, has gathered no moss.

The treatment of diabetes may be classified under three headings. I. Prevention, II. Treatment of the disease and III. Treatment of complications.

I. Prevention—Consists in regulating one's mode of life in general and in particular one should be asked to live an orderly life, regular habits in eating, exercise and sleep. When one reaches the age of 40 or so, he should reduce the consumption of fats and carbohydrates if he is overweight and fond of good things in life. He should be warned that, unless he takes good physical exercises in the open air, he runs the danger of getting diabetes, especially so, if there is a definite history of diabetes in the family. Very rarely athletes and people, who, due to their profession, spend their working hours in manual labour in open air, get diabetes. The commonest type of person easily subjected to diabetes is the one who consumes large

quantities of carbohydrates and fats and leads a sedentary life. This induces the accumulation of fat; and fat people loathe to take hard exercises that would bring the sweat out of their body and reduce the excess of fat in them. Is it not possible that the islets of Langerhans are destroyed by the fatty deposits that are found in every organ of the body including the pancreas? Here the difficulty is that the rich and indolent will not listen to the advice of his medical attendant however well meaning he may be.

II. The difficulties of treating the disease itself is not less because ordinarily the disease gives no trouble to the patient in the early stages. As I said earlier the patient is made known of the disease more by accident than anything else. So long as the disease does not trouble him with excessive thirst, frequency of micturitions causing sleeplessness and worry, he will not abstain from rich and fatty foods. He will also refuse Insulin injection and if after some time he takes the injection it will be at long intervals resulting in one or two complications of the disease.

Now let us discuss for a while whether there is any difficulty at all in treating a patient who has one complication or other as a result of diabetes.

III. One would naturally think that because the diabetic patient has complications he would give the doctor no trouble in being treated. But, in practice most of you know that it is not so.

Let me take a few complications of diabetes and discuss its treatment and difficulties.

I. Boils and Carbuncles.—In the early stages, when a few boils appear, the patient would want you to treat the boil by dressings etc. and cure it while he would continue with his lazy life, rich food and indiscriminate eating of forbidden foods. If his boils and ulcers get worse, he will blame you and threaten to change you, while he will cling to his favourite but dangerous habits and refuse to change. Next, when you wish to use your knife either to scrape the ulcer, drain the wound or to cut out sloughs which prevent proper healing, the patient or his relation will strictly order you not to bring the knife or scissors while dressing the wound. Besides, he will complain that the injections are painful and so refuse to take two or three injections a day or even one.

II. Cellulitis and Gangrene.—This is the most dangerous of the complications which gives a lot of trouble to you for want of co-operation from your patient and his relations. Here again, when you advise that the wound has to be freely opened and drained, he will not allow, but would request you to continue to dress the wound as usual. When the limb becomes gangrenous, your advice to have this limb amputated early and high will be refused. Even if the patient is willing, his relations will stand in the way and will only consent when such an operation may be of no use.

I have known at least two cases when the patient in each case refused amputation. The result was that a 'quack doctor' was called in, who promised a cure in a few days. The 'quack' undertook the case and the patient felt so happy because here came a man who could cure him without injection and without sacrificing his limb. But alas! the happiness of the patient was short-lived because he went downhill rapidly and died of coma.

In the second case admitted to the hospital, the ulcer started on the 2nd toe and rapidly the whole of the toe became gangrenous and spread to the sole of the foot, to the great toe. I advised amputation of the leg. He refused and I discharged him. He was taken up by a 'quack' who promised to cure him without amputation, injection or dieting. I have been hearing all sorts of stories about this man being miraculously cured and sent home. Of late, I have heard that his ulcer has not healed but is spreading and the patient has gone back to the 'quack doctor'. It is three months since he left the hospital and it remains to be seen what is going to happen to the patient now that the ulcer has begun spreading.

What I have described above is some of the few difficulties that one meets with in practice.

I know that in Western countries, where the well-to-do man is more educated than ours, the difficulty of treating diabetes is less. They usually follow their doctors' advice from the beginning, take injections of Insulin twice or even three times a day, and rarely get diabetic coma and die.

I have known of one man, however, in this place who, since the last 20 years or more, had been taking Insulin injections once, twice or even 3 times a day. The injections were given by the cook or attendant and he died a few months ago, though he suffered from urinary fistulas for the last 15 years. Several doctors had operated on his scrotum, perineum and penis and when he died, his scrotum, penis and perineum were riddled with holes and yet he had lived for several years.

Before going further, I would like to impress upon my readers, that a great deal of good may be done to the patient if tact is used in treating diabetic patients. It is worth your while to spend more time with your patient than is necessary to dress his wound and give an injection. Besides this, I think at the outset, the patient and his near relations—preferably his wife and children—should be told that giving injections is an easy matter and they should be taught how to give injections. If the minimum dose is prescribed and directions given according to the condition of the patients, there is no fear of an overdose. An injection given just before the principal meal does not lead to severe complications even if a small over-dose is given.

The latest preparation of Insulin *i.e.*, Protamine-Zinc-Insulin is a much safer drug to be handled by the patient or his relations themselves, as its action is slower and lasts longer than simple Insulin.

In all cases where there is no urgency such as threatened coma and in cases where the patient refuses to take repeated injections, Protamine-Zinc-Insulin should be used. Besides, this Insulin is superior to ordinary Insulin, in cases where there is a necessity of giving an injection at midnight or in the early hours of the morning. Protamine-Zinc-Insulin, given at bed time, will keep the blood-sugar of the patient low until the morning.

Next in importance to the injections of Insulin, is the dieting of the patient. Unfortunately, there is much controversy regarding the quantity and quality of food to be consumed. One school of thought holds the view that there should be a strict dieting of the patient, the carbohydrates and fats to be restricted to the minimum and proteins and salts to be given more liberally, while the other school thinks that it is bad to restrict carbohydrates and fats and the patient should be allowed to eat what he likes and in any quantity and should be given injections of Insulin in large repeated doses.

A majority of the medical men are of the view, however, that it is better to follow a middle course and give injections of Insulin now and again, or in severe cases, once a day, the Protamine-Zinc-Insulin being the drug in preference to Insulin alone.

Management of Diabetes Mellitus in Rural Practice

BY

Major P. C. Dutta, M.B., F.R.C.S. (E), D.G.O., I.M.S.
Civil Surgeon, Montgomery, The Punjab.

WITH the introduction of Insulin and its various forms, the treatment of diabetes has become increasingly difficult and the more so for the rural practitioner. The newer Insulins promise to be more useful for the rural practitioner.

Each case of diabetes has to be treated on its own merits. The patient's general condition, economic condition, his environment, occupation, means of livelihood and the severity of the disease, all have to be taken into consideration and no rule of thumb can be laid down; in other words, it is the patient who has to be treated according to his means and requirements and not the disease.

The urine in all cases should be tested with Benedict's solution. This also gives a rough idea of the amount of sugar present in the urine. Estimation of blood sugar, although it has been made mechanical and easy, is neither required nor possible in most cases.

Benedict's Solution.—*Preparation*:—170 gm. of crystallised Sodium Citrate and 100 gm. of Sodium Bicarbonate are dissolved in 700 c.c. of water. 17.3 gm. of fine crystallised Copper Sulphate is dissolved in 100 c.c. of water. The Copper Sulphate solution is poured into the former solution and the volume made up to 1000 c.c. with addition of water.

Testing for Sugar:—Take 5 c.c. of the reagent in a test-tube and add to it, 8 drops of urine. It is boiled over a flame for 2 minutes and then allowed to cool. The following will indicate a very rough estimation of the quantity of sugar present:—

- (1) Greenish opalescence, no red colour, no precipitate—0.1%.
- (2) Same as above but slight yellowish precipitate, fluid blue on standing—0.2%.
- (3) Green colour with slight orange precipitate, fluid blue on standing—0.3%.
- (4) Definite orange precipitate, fluid still blue on standing—0.5%.
- (5) Heavy orange brown precipitate, still some blue colour in the fluid on standing—1.0%.
- (6) Bright heavy red precipitate, blue colour of the fluid has almost disappeared—2.0%.

Although it is a very rough estimate, it will give the practitioner an idea whether the sugar is increasing or decreasing in the urine.

Data for Treatment.—An individual at rest needs 12 calories per pound of body weight to maintain the body in health. One with sedentary habits needs 15–20 calories per pound of body weight, and one doing hard work 25–30 calories per pound.

Each gram of protein and carbohydrate roughly yields 4 calories and each gram of fat 9 calories.

Calculation of the Proportions of Various Food Constituents.—The total number of calories required is divided between protein, carbohydrate and fat in the following proportions:

Protein:— $\frac{1}{2}$ – $\frac{2}{3}$ Gm. of protein per pound of body weight.

Carbohydrate:—Find out the carbohydrate tolerance of the patient and that will be the amount that can be given, if it is not possible to use Insulin.

Fat:—The proportion of fat should bear a definite relation to the carbohydrate, otherwise ketosis will result from unburnt fat. The proportion should be, 1 of carbohydrate to 1.3 of fat, or in other words, the total amount of fat should not be more than $1\frac{1}{3}$ of the carbohydrate.

It is now generally agreed, that the amount of carbohydrate should be considerably higher than considered desirable in the above statement, and the fat correspondingly lower. In uncomplicated cases of diabetes, 130–200 Gm. of carbohydrate may be allowed according to the age, appetite and occupation of the patient. The protein may well be increased by 10–20 Gm. Fat should not exceed 100 Gm. Under this diet, the patient will often require no more Insulin and sometimes less. The amount of carbohydrate should not be less than 100 Gm.

Outline of Treatment.—Remove all sources of infection. Improve the general health of the patient.

A slight under-nutrition may teach the body economy and the basal metabolism may fall one fifth below normal. Therefore, a diabetic can usually live 2–3 calories per pound less than normal.

Mild cases.—Qualitative restriction of food. It is quite unnecessary to condemn the patient to weighing all his food. The patient should avoid what LAWRENCE calls 'dangerous' foods i.e., those which contain a very high amount of carbohydrate. Moderate amounts of proteins and fats are allowed. Those vegetables which contain the least amount of carbohydrate are best. A small but definite amount of 'dangerous foods' should be added, e.g., half a chapati, a piece of toast, a small potato or a small orange or a table spoonful of rice, at each meal. If the urine becomes sugar-free on this regime, it is desirable to estimate the blood sugar to make sure that this is also normal.

Moderate cases.—1. *Patients who cannot afford Insulin*:—If the patient cannot afford Insulin, he must live within his sugar tolerance, i.e., the maximum amount of carbohydrate, which he can metabolise without producing glycosuria or hyperglycaemia. In a moderately severe case, this may be attained by cutting down the caloric requirements of the individual i.e., by limiting his bodily activities, just as a patient with heart disease must live within the limits of his crippled heart. Find out the carbohydrate tolerance of the patient.

Give the patient a standard diet containing 50 Gm. of carbohydrate and known proportionate amounts of proteins and fats. If sugar appears in the urine, gradually cut down the carbohydrate until

no sugar appears in the urine. Conversely, if no sugar appears in the urine with 50 Gm. of carbohydrate, gradually add more carbohydrate in the diet until sugar just appears in the urine. The carbohydrate tolerance will be the maximum amount of carbohydrate that the patient can consume without passing any sugar in the urine.

Cut down the work of the patient compatible with the limited amount of food that may be allowed.

Now prepare several lists of complete daily diets, keeping the amount of carbohydrate within the limits of the tolerance, fat not more than $1\frac{1}{3}$ of the amount of carbohydrate and protein $\frac{1}{2}$ — $\frac{3}{4}$ Gm. per pound of body weight, or slightly more.

2. *Patients who can afford Insulin*.—Put the patient straight on a diet containing 100 Gm. of carbohydrates, 100—120 Gm. of fat and protein as equivalent to the body weight. Give injections of Insulin according to the directions given below.

Severe cases.—If the patient is much under-weight, lacking in energy and muscular strength, or if peripheral neuritis or some other complication due to deficient nutrition is present, the diet should be raised from a basal to maintenance diet (15 calories per pound of body-weight) or even higher (20 calories per pound), until the desired increase in weight and strength takes place. If the patient cannot tolerate this necessary increase of diet without glycosuria or hyperglycæmia, he then passes into the class in which Insulin is necessary.

Another plan is to put the patient at once to a permanent maintenance diet (of about 15 calories per pound of body weight) and not on a basal diet (12 calories per pound). This is usually quite satisfactory and has the advantage that no further change is necessary.

Preparation of diet.—There are several mechanical methods for the preparation of diabetic diets of which Lawrence's (line ration) is most popular. It costs 6d. and can be had from H. K. LEWIS & Co., 136, Gower Street, London. These are hardly satisfactory for Indians and it would be better for the practitioner to prepare a few lists of diets according to various seasons in India. Composition and caloric values of most Indian Foods are given in several books published in India, e.g., OMERA's Medical Guide, CHOPRA's Tropical Therapeutics, DUTTA's Modern Advances for Rural Practice, BOSE's Diabetes, and Food Values of Indian Diets, published by Nutrition Research Laboratory, Coonoor, compiled by AYKROYD.

Insulin Treatment.—*Indications*.—1. When it is not possible for the patient to take the required amount of food to maintain himself in good health without hyperglycæmia or glycosuria.

2. When the patient is very ill, severe thirst is present or obviously a severe case.

3. Presence of severe ketosis, Ferric Chloride Test being positive.

4. Presence of intercurrent disease, sepsis, pneumonia.

5. Diabetes of sudden onset, specially in the young.

Method of administration of ordinary Insulin.—The most important factor in the successful administration of Insulin without blood sugar

estimations is maintenance of a constant diet with slow increase of Insulin until the correct dosage is established.

One unit of Insulin usually burns 1—3 gm. of sugar, but unfortunately, this is far from constant. If the loss of sugar estimated by Benedict's quantitative method is 30 gm. a day the Insulin requirement per day will be about 15 units at the commencement of treatment. This usually requires modification and with experience, a good guess can be made. It needs 24 hours' sample of urine and, therefore, is not so suitable for private practice.

Commence with 5 units, half an hour before the two main meals of the day, arranging most of the food at these times. If, after 3 days' treatment (5 units twice a day), urinary sugar is not appreciably diminished, increase the Insulin to 10 units in the morning and 10 units in the evening. If, after another 3 days, the sugar is appreciably diminished but the amount of Insulin is obviously insufficient, 15 units in the morning and 10 units in the evening should be given. At the same time, the urine should be tested at 2 hourly intervals to obtain a more accurate idea of the Insulin effect. Usually, by the 13th day, 15 and 10 units a day prove too much. This is shown by low level of blood sugar in the afternoon and clinically by slight symptoms of hypoglycæmia which may be put right by a meal in the afternoon or may require administration of sugar before it. If the treatment is being regulated by urine sugar tests alone, it is not always possible to avoid slight attacks of hypoglycæmia. This experience is unpleasant but harmless. It has the further advantage of teaching the patient the early symptoms of overdose of Insulin, knowledge of which may be useful later. Such symptoms call for the reduction of Insulin, which, in the above case, may be reduced to 12 and 8 units on the 14th day.

More severe cases may require 2 to 3 times this dose to obtain control of the sugar. Occasionally, two doses may be insufficient and three doses may be necessary.

During this period and for the next two or three weeks, the patient's pancreas may recover further tolerance for carbohydrates and we may be able to reduce the Insulin. Insulin relieves the overstrain on the islands of pancreas and enable them to recover to a certain extent. This improvement may go on for months and is specially frequent in elderly people. A progressive reduction of Insulin must be made in this condition. Unless this necessary reduction is made, the patient may feel wretched and weak and may be tempted to give up Insulin as unsuitable for his case. For this reason, blood sugar estimation at this time is useful. If this is not feasible, the amount of carbohydrate may be slowly and gradually increased and the effect noted. Instead of reducing Insulin, this may be the suitable time for increasing the diet from 12 to 15 or more calories per pound of body weight or increasing the carbohydrate alone by giving higher carbohydrate and low fat diet, specially when the patient is too thin and gaining insufficiently in weight.

Less Insulin should be given at night to avoid any risk of

hypoglycæmia during sleep—5/8 of the total dose in the morning and 3/8 in the evening are recommended. The maximum effect of Insulin takes place 3—6 hours after injection.

Initial treatment of emaciated cases who have been on severely restricted diets before commencing Insulin.

Although the blood sugar of these patients may be high, they have little or no store of carbohydrate in the body, practically only what is present as glucose in tissues and circulating blood. Very small amount of Insulin suffices to de-sugarise them and then hypoglycæmia is easily induced after the first day or two. They will require more Insulin after the first few days, because Insulin has enabled them to build up a store of glycogen which, in its turn, requires more Insulin to balance it. Subsequent increase in weight and strength, as the treatment proceeds, commonly requires an increased dose of Insulin. Paradoxical as it may seem, the more they improve the more Insulin they require up to the point where the weight becomes constant.

Best time for Urine Test.—While the dose of Insulin is being worked out, it is very helpful to examine the urine every 2 hours. When the leak-point (threshold) is known to be normal, and Benedict's test is carefully carried out, we can often dispense with blood sugar tests. Later on, a sample before the morning dose of Insulin and another later in the morning, when the Insulin action is at its maximum. Bladder should be emptied 3 hours after the Insulin and again after 5 hours. The last sample should always be sugar-free, if the renal threshold is normal. Presence of sugar in the earlier sample is not so serious, as it is very difficult, if not impossible, to keep severe cases always sugar-free. Moderate and mild cases should always be sugar-free.

If Insulin is not being given, sample passed 2 hours after the evening meal or after the largest carbohydrate meal of the day, should be examined.

Ketone bodies in the urine—Ferric Chloride Test is more important. Its presence calls for radical adjustment of treatment.

Complications of Insulin Injection.—1. *Pain*:—Often due to blunt needle or the injection being given too superficially or too deep into the muscles.

2. Allergic reaction. If they persist, (a) Change to Insulin made from another animal or different brand, or (b) Dilute the Insulin and desensitize the patient, the dosage is then gradually increased, injections being given hourly or two hourly until the full dose can be given without reaction, or (c) Use crystalline Insulin (very expensive.)

3. Areas of local fat atrophy, specially if injected at the same site always.

4. Repeated injections at the same spot sometimes produces localised swellings.

5. *Hypoglycæmia*:—Impending symptoms of hypoglycæmia should be explained to the patient. Patients under Insulin treatment should always have some sugar at hand and as soon as one is aware of

the early symptoms of hypoglycæmia, it should be taken with some orange juice.

Treatment of hypoglycæmia—Give 10 gm. of carbohydrate as glucose or sugar. If the symptoms persist, repeat after 10 minutes. If the patient is unable to swallow, give glucose by nasal catheter, stomach tube or per rectum, but it is wise to inject 1 cc. of posterior pituitary extract first. If these fail, repeat pituitary extract and administer 10% pure glucose intravenously until consciousness returns.

New Insulins.—Zinc-Protamine-Insulin.—By combining Insulin with Protamine and Zinc, it is very slowly absorbed and, therefore, the effect lasts for a long period. It is now believed that the new Calcium combination will prove more satisfactory.

Advantages over ordinary Insulin:—(1) It diminishes wide fluctuations of blood sugar and, therefore, reduces the risks of glycosuria and hyperglycæmia. (2) Gives more physiological rest to the pancreas. (3) Injections are painless. (4) The number of injections are reduced, and that is of great advantage to the rural practitioner.

Zinc Protamine Insulin should be given as early as is convenient before breakfast. The dose of Zinc Protamine Insulin required will roughly be the total dose of soluble Insulin previously required in 24 hours.

Most severe cases of diabetes can be well controlled and patient maintained in excellent health by one injection a day of Zinc Protamine Insulin alone or with the addition of some soluble Insulin. The initial stages should be carried out under close observation.

Ordinary Insulin and Zinc Protamine Insulin can be injected at the same time. The substances mix very little in the syringe, but it is very possible that when 20 units of old Insulin and 12 units of Zinc Protamine Insulin are given together, the actual dose may be 18 of old Insulin and 14 of Zinc Protamine Insulin. It is important to prevent mixing the two Insulins in the bottle, so two separate needles should be used to draw the Insulins from the bottles and by injecting the required amount of air into the bottle before withdrawing the solutions.

Method of treatment with Zinc Protamine Insulin:—When fasting, blood sugar estimations are not available, two specimens of urine should be taken before breakfast; one immediately on waking (and to avoid any sugar that might have entered the bladder soon after bed time), and a second just before breakfast to indicate the approximate level of blood sugar at that time. Even when the first specimen contains sugar the second is often sugar-free, indicating that the dose of Zinc Protamine Insulin is sufficient to last for 24 hours. If the second specimen contains sugar, the dose of Zinc Protamine Insulin must be increased. If there are symptoms of hypoglycæmia (sweating, palpitation, trembling), between midnight and breakfast, the basal dose is too high and must be reduced. In most cases, the basal dose will be between 20—30 units and in more severe cases, 30—50 units. Carbohydrate must be spread throughout the day in small and frequent feeds.

It has become the general practice to allow liberal amounts of carbohydrate in the diet of diabetics, if the patient can afford the required amounts of Insulin. Diets containing 120—200 gm. of carbohydrate can be tolerated satisfactorily on Zinc Protamine Insulin, but the carbohydrate distribution must be carefully regulated. The action of Zinc Protamine Insulin is slow in the beginning, gathers strength and acts for 24 hours and may produce hypoglycæmia any-time when no carbohydrate has been taken for 3 to 5 hours. Therefore, the carbohydrate must be spread throughout the day in smaller and more frequent feeds. A meal in the afternoon (Tea time) and bed time (about 10 O'clock) are essential to prevent hypoglycæmia. A suitable arrangement for 150 gm. carbohydrate diet, Zinc Protamine Insulin, before breakfast, and then a meal at 8-30 A.M.—30 gm.; 12 noon—30 gm.; 4 P.M.—30 gm.; 7 P.M.—40 gm.; 10 P.M.—20 gm.

Insulin Resistance.—This is generally associated with damaged condition of the liver. The antagonising substance is present in the blood. Liver of Insulin-insensitive patient fails to activate the injected Insulin. It appears that ascorbic acid in some way or other may activate the Insulin in Insulin-insensitive patients.

Diabetic Coma.—In the treatment of diabetic coma, Insulins with retarded effect obviously have no place as immediate action is essential. Ordinary Insulin must be used.

Treatment.—1. Insulin 20 units intravenously and 20 units subcutaneously. Thereafter, give 20 units subcutaneously every half hour until there is clinical and chemical improvement. Blood sugar estimations are the best guide, if this is not possible, 20 units should be given for a red or orange precipitate with Benedict's solution, 15 units for yellow and 10 units for yellowish green.

2. Glucose—Give as many grammes of glucose as units of Insulin by stomach tube, or nasal tube. If there are signs of circulatory failure, 300-500 cc. of a 10% solution should be given intravenously.

3. Sodium Bicarbonate—one dram may be given every hour.

4. Combat dehydration—3-6 pints of saline must be given intravenously for over 1-2 hours until the tension of the eye ball is normal.

5. Gastric lavage, if there is vomiting.

6. Rectal enema, to clear the bowels.

7. Resumption of diet—Soft bland nutrients *e.g.*, gruel, junket, custard.

Preparations of Insulin for Oral Administration.—1. Synthelin—The reduction of hyperglycaemia is not due to an increased deposition of glycogen in the muscles or liver, but to a diminished formation of dextrose due to toxic action of the drug on the liver cells. Therefore, it should never be used in the treatment of diabetes.

2. Phosphotungstate of Insulin may be given orally and in big doses brings the blood sugar down. But it is very expensive when compared to the effect produced.

Insulin and its Combinations

BY

K. N. Sinha, M.B., B.S., F.R.F.P.S.,

Lecturer in Pharmacology, King George's Medical College, Lucknow.

History of Insulin.—The relationship of Insulin with the pancreas was first demonstrated by MERING and MINKOWSKI in the year 1889. They observed that the complete removal of the pancreas caused glycosuria and death in an animal.

If seven-eighths of the pancreas were removed in a dog, it caused mild symptoms of diabetes (ALLEN). If anymore of the gland was removed, it caused severe diabetes.

Since the year 1889, efforts have been made to obtain an extract of the pancreas which may be useful when given therapeutically in cases of diabetes mellitus. After twenty three years, efforts were crowned with success when, in the year 1922, BANTING and BEST obtained a preparation from the Islands of Langerhans which they consequently named 'Insulin'.

Chemistry of Insulin.—The chemistry of Insulin has not yet been properly worked out. The molecule, however, must be very complex as it contains twenty-three to twenty-four Tyrosine groups as well as some Sulphur atoms.

Properties of Insulin.—Insulin is rapidly destroyed by alkalis but is stable in acid solution. As Insulin is destroyed by Pepsin and Trypsin, it cannot be administered per os. It has, therefore, to be given by sub-cutaneous injection. When administered by this method, it produces a remarkable fall in blood-sugar which may drop from the normal, which is 0.12 per cent to 0.05 per cent, or 0.03 per cent or even less. Though Insulin has been prepared from various sources and by diverse methods, yet the potency of the drug is rather constant at twenty-four units per milligram.

The essential properties of the Insulin are :—

(1) That it restores to the tissues, the power of utilising sugar, which power is lost by the tissues in diabetes mellitus.

(2) That it promotes deposition of glycogen in the muscles and under certain circumstances in the liver.

Normal Mechanism for the Control of Blood-Sugar.—In health, the amount of sugar in blood is kept at about 0.10 per cent by a small continuous supply of Insulin. After meals and especially after carbohydrate meals, the amount of sugar in blood tends to rise but is kept down to normal, as at those periods a greater amount of Insulin is poured out in the blood. Thus, a mechanism exists which never allows the amount of sugar in blood to rise above 0.17 per cent. If somehow the sugar in blood rises above this level, which is a leak point, the excess is excreted in the urine. It is thus evident that the

amount of Insulin needed is variable—more Insulin is required after meals, less in the night, but some is needed all the time. If the amount of Insulin so needed is supplied by the person's own pancreas, it is well and good, otherwise, it will have to be supplied from outside.

Mode of Administration of Insulin.—Insulin is given by subcutaneous injection. Soluble Insulin is given about half an hour before breakfast and is repeated if necessary before luncheon and dinner, and in certain cases, a small dose may have to be given even at bed time.

Injections of Insulin have sometimes led to the occurrence of localised tumefaction and rarely to a more serious condition called 'Insulin Atrophies' which may appear at the site of injection or quite frequently at some distance from the spot where the injection was given. These "Insulin Atrophies" are characterised by depression of skin, with disappearance of sub-cutaneous fat and even the underlying muscles. The cause of these Insulin Atrophies is not known. To avoid such a catastrophe, the site of injection must be varied from time to time, so that a single area is not injected more than once a month. Moreover, repeated injections at one place hinder absorption as they lead to the tumefaction of the skin. If injections are scattered, less Insulin will be required.

Insulin and its Combinations.—Soluble Insulin is rapidly absorbed from the site of injection. A dose of twenty units is at its maximum in two or three hours and is active for six hours (HIMSWORTH, 1937, LAWRENCE, 1938). Due to its rapid absorption and rapid excretion, it causes great fluctuation in the amount of sugar in blood. The chief utility of this Insulin is to deal with the post absorptive rise in blood-sugar. It is not able to deal with the natural requirements between the meals. To avoid this oscillation in the blood-sugar, efforts have been made to introduce Insulin into the body in such a form in which it will be slowly absorbed, and hence supply Insulin in a more gradual manner. With this end in view, HAGEDORN of Denmark introduced a product, known as Protamine Insulinate. This is a combination of Insulin Hydrochloride and Protamine derived from a species of trout, *Salmo-iridius*. It has a minimum solubility at pH 7.2. It is injected as a turbid suspension. It is slowly broken down and the active Insulin released over a longer period of time. The maximum effect is produced in six to ten hours and the action is spent up at the end of twelve to eighteen hours. This keeps the blood-sugar at a lower level and avoids the high peak of the amount of sugar in blood between the injections of soluble Insulin. HAGEDORN and his colleagues gave Protamine Insulin at night and soluble Insulin in the morning.

Protamine Insulinate was further improved by DR. SCOTT of Toronto by adding a small amount of Zinc. This combination has further slowed and prolonged the action of Insulin. The maximum effect of the action continues upto the end of twenty-four to thirty hours (HIMSWORTH 1937). Large doses of this Insulin may act for twenty-four to forty-eight hours or even more (AITKEN, 1938).

Thus, there are three kinds of Insulin that are available in the market :—

- (1) Insulin Hydrochloride in solution in weak acid, pH 3.4. Synonyms for this kind of Insulin are :—Old Insulin, Ordinary Insulin, Regular Insulin, Quick Acting Insulin and Soluble Insulin.
- (2) Protamine Insulin which is a suspension at neutral reaction, pH 7.2. Synonyms of this kind of Insulin are :—Leo "Insulin Retard", Protamine Insulinate, and Danish Protamine Insulin.
- (3) Zinc Protamine Insulin which is also a suspension at neutral reaction. Synonyms for this type of Insulin are :—Protamine Zinc Insulin, Canadian Protamine Insulin.

Nomenclature of Insulins.—Till the year 1935, there was available only one kind of Insulin. The word "Insulin" meant only one thing. Since Protamine Insulin has come from Denmark and Zinc Protamine Insulin from Toronto, there has been a lot of confusion because of the multiplicity of names. To distinguish the old Insulin from the other recently introduced Insulins, one may call the old Insulin as Soluble Insulin and the others as Suspended Insulins.

Soluble Insulin—Its Advantages and Disadvantages.—(1) *Advantages* :—It acts quickly and is, therefore, able to deal with the post-absorptive hyperglycæmia. The hypoglycæmic attacks if they occur, are followed by spontaneous recovery.

Suspended Insulin—Its Advantages and Disadvantages.—1. *Advantages* :—It is a slowly acting Insulin. The prolonged action allows reduction in the number of injections. The injection of this Insulin given late in the afternoon, controls the disease throughout the night. In less severe cases, one injection of Insulin before breakfast may control the disease throughout the twenty-four hours. The slow acting Insulins are less affected by exercise and hence hypoglycæmia is infrequent.

2. *Disadvantages* :—Hypoglycæmic attacks, when they occur, are severe and prolonged. The warning symptoms of a hypoglycæmic attack are not evoked as the slow action causes the blood-sugar to slide down gradually till a level is reached, when a severe attack becomes inevitable. The hypoglycæmic attacks are not followed by spontaneous cure. On the other hand, it progresses to severity if untreated. In the treatment of hypoglycæmic attack, the administration of sugar has to be done repeatedly so as to counteract the series of relapses caused by the persistent action of suspended Insulin.

The suspended Insulins are less efficient to control the post-absorptive hyperglycæmia. Moreover, as in the case of soluble Insulins, so with the suspended Insulin, the susceptibility of the body varies at different times of the day. The susceptibility to Insulin is least marked at breakfast, more marked in the evening and most marked in

the middle of the day. Therefore, the suspended Insulins are still less efficient to control the hyperglycæmia after the breakfast. If an attempt is made to control this by increasing the dose, greater liability to hypoglycæmic attacks occurs during the night or the evening.

The Object of Treatment is to produce normal sense of physical health and mental well-being in the diabetic patient. The aim of the treatment is to see that the patient possesses sufficient energy for his requirements, maintains his weight proportionate to his height and age and does not get hypoglycæmic symptoms. With that end in view, patients may be treated with diet alone or with diet and Insulin. As Insulin has to be given by subcutaneous injection, the aim of the physician is to give as few injections during the course of the day as possible. The aim is to control the disease with one dose of Insulin in twenty-four hours. If need be, the various Insulins may be given in one injection from the same syringe. The suspended Insulins, especially Zinc Protamine Insulin, enable the practitioner to do so and is, therefore, the practitioner's Insulin for choice.

Insulin in Diabetes.—The introduction of Insulin has revolutionised the treatment of diabetes mellitus. During the period of last eighteen years, i.e. since the introduction of Insulin in 1922, the treatment of diabetes has passed through various stages.

The first stage of this period was to adapt the use of Insulin to the dietetic treatment. The second stage was to give a relatively high carbohydrate diet to the patient and to control hyperglycæmia with Insulin. The third stage was the artificial modification of the Insulin itself to meet effectively the requirements of the diabetic patient.

Both the soluble Insulin and the suspended Insulin have their own limitations in the treatment of diabetes. Soluble Insulin is better able to control hyperglycæmia after the carbohydrate meal. Its drawback is that it acts in strong waves which may even produce hypoglycæmia without preventing relapse of hyperglycæmia and ketosis when its action is exhausted. The suspended Insulins on the other hand, provide a small continuous supply of Insulin but are not able to control hyperglycæmia after carbohydrate meal. The suspended Insulins are comparable to basal anæsthetics, whose effect is both mild and prolonged, while soluble Insulin is like volatile anæsthetic which is given on the top of basal anæsthetic when more powerful anæsthetic is required. The suspended Insulin is more irregular in action because of more irregular absorption. Normally, (LAWRENCE and ARCHER, 1936), a small continuous supply of Insulin, called the basal secretion, is poured by the pancreas which controls the endogenous production of sugar, and an increased secretion of Insulin which deals with the post absorptive sugar. The suspended Insulin works as the basal Insulin in the body while soluble Insulin controls the post absorptive sugar.

When a case of diabetes comes in, it has to be decided whether Insulin is required and if so, whether soluble or suspended Insulin. The

suspended Insulin is chiefly indicated (1) when nocturnal glycosuria reveals that soluble Insulin is not able to control the disease during the night, (2) when exercise produces hypoglycæmia in patients treated with soluble Insulin and (3) when it is desirable, as it should always be, to reduce the number of injections per day.

Mild cases in which there is still some production of Insulin, may be treated with diet alone, or with added Insulin to deal with post absorptive hyperglycæmia. More severe cases, in which the internal secretion of the pancreas is not enough even for the basal requirement, Insulin is required to control both the endogenous, and the post absorptive sugar.

In treating a case of diabetes, the presence of ketonuria in more than traces is an indication for the immediate use of Insulin. If, however, there is glycosuria but no ketonuria, the diabetic treatment should be tried for three weeks. If it does not control the sugar, Insulin has to be used. The first step is to determine what is termed as the basal dose of Insulin which will continue its action for twenty-four hours and will keep the blood sugar normal before breakfast, and not produce hypoglycæmia in the night. For this purpose, Zinc Protamine Insulin is used. The first dose of this type of Insulin does not show its effect for two or three days, as the absorption is irregular, the action is slow and cumulative. Hence, one should wait for three or four days before one decides whether the dose given should be increased or decreased. By trials, one is able to determine the basal dose of Zinc-Protamine Insulin. Mild cases are controlled by the dietetic arrangements and one injection of Zinc-Protamine Insulin given before breakfast.

In severe cases, it so happens that one injection of Zinc-Protamine Insulin does not control the disease. If the dose of Zinc-Protamine Insulin is increased, it leads to hypoglycæmia during the night. Glucosuria and hyperglycæmia can be minimised in such cases by reducing to a minimum, the carbohydrate in the food. This, however, is not liked by the patient. Such a state of affairs can fortunately, be rectified by adding soluble Insulin to the basal Zinc-Protamine Insulin. Luckily, the soluble Insulin can be drawn in the same syringe along with Zinc-Protamine Insulin, and the two Insulins injected together sub-cutaneously. When so given, both the types of Insulins retain their individual action—the soluble Insulin showing a quick action and the suspended Insulin a prolonged action. While making use of both the types of Insulin in the same syringe, it is advisable to draw into the syringe, first the soluble Insulin which is acidic in reaction, and Zinc-Protamine Insulin afterwards. This precaution is necessary because a drop or two of acid Insulin entering the phial of Zinc-Protamine Insulin will not matter whereas a little of Zinc-Protamine Insulin which is alkaline, may make the soluble Insulin alkaline and therefore inert.

Barring very severe individual cases, most of the diabetics can be controlled by diet and one injection of either Zinc-Protamine Insulin alone or Zinc-Protamine Insulin with added soluble Insulin in the same

syringe. This has been a great advance in therapeutics which has been rendered possible by the introduction of suspended Insulin. Protamine Insulin introduced by HAGEDORN and improved upon by Dr. A. SCOTT by combining Zinc with Protamine Insulin. Zinc-Protamine Insulin is the suspended Insulin of choice.

Summary.—1. The chemical nature of Insulin and its combinations, Protamine Insulin and Zinc-Protamine Insulin are described. The various types of Insulins are classified into: (a) Soluble Insulin. (b) Suspended Insulin.

2. Properties, advantages and disadvantages of soluble and suspended Insulins are described.

3. The suspended Insulin enables the physician to control all except the most serious cases of diabetes mellitus by one injection of either Zinc-Protamine Insulin alone or with added soluble Insulin, taken in the same syringe and injected together before breakfast.

4. Zinc-Protamine Insulin is the practitioner's Insulin for choice. It has made the treatment so simple for the practitioner and so comfortable for the patient.

References:

1. Bose, J. P.—(1939), *I.M.G.*, 2,749.
2. Cushney's *Pharmacology and Therapeutics*, 1936.
3. Himsworth, H. P.—(1937), *B.M.J.*, 1,541.
4. Lawrence, R. D. and Archer, N.—(1937), *B.M.J.*, 1,487.
5. Lawrence, R. D.—(1939), *B.M.J.*, 1,1077.
6. Spriggs, E.—(1939), *Practitioner*, 1,549.

Theories of Action of Insulin

BY

S. Sankara Raman, M.B.B.S.

Cuddalore.

EVER since BANTING and BEST of Toronto isolated Insulin in a pure form for injection, the action of the drug has been and is the subject of much speculation. When we cannot make dogmatic statements with regard to the carbohydrate metabolism, we can still less make dogmatic statements about the mechanism of action of Insulin.

It has been established that the action of Insulin is antagonistic to that of Adrenalin. Since Adrenalin acts by increasing glycogenolysis in the liver and also by inhibiting sugar utilisation of the peripheral tissues, it is presumed that Insulin must act either by inhibiting glycogenolysis in the liver or by utilising the sugar in the tissues; or by both.

We know that blood-sugar level is the main controlling factor in the secretion of Insulin. But we are at a loss to understand the mechanism regulating the secretion of Insulin. The blood-sugar level by itself is not sufficient to stimulate the secretion of Insulin. The factors at work are (1) either a direct stimulation of the nerve cells of the islets of Langerhans by the blood-sugar or its metabolic product; or (2) indirect stimulation of the central nervous system by the blood-sugar or its metabolic product. It has also been established by experiments that Insulin sometimes favours glycogenolysis in the liver and also sometimes favours laying down of glycogen. This anomalous action of Insulin is attributed by CORI, BARBOUR and MACLEOD and ORR, to the amount of dosage administered *i.e.* while 1 to 2 units per kilo of body-weight of Insulin produce a fall of liver glycogen during the first 1½ hours followed by a slight rise after 2 hours, injections of 3 units per kilo of body-weight produce a fall in the glycogen content of the liver. DONO found that in depancreatized dogs, the liver was free from glycogen after 48 hours' starving and that glucose and Insulin restored the glycogen to normal levels, thus demonstrating that the state of the animals is also a factor. So, any attempt at explanation of the action of Insulin must satisfy the above findings.

Theory of Cori and Cori.—According to this theory, the main action of Insulin is to bring about increased oxidation of glycogen in the peripheral tissues. Experiments on normal fasting rats showed that most of the absorbed sugar was utilised in the peripheral tissues and little sugar was left for glycogen, storage in the liver. According to CORI and CORI, the following cycle exists in the organism: Blood glucose, and CORI, the following cycle exists in the organism: Blood glucose, muscle glycogen, blood lactic acid, liver glycogen, blood glucose. Adrenalin accelerates the conversion of muscle glycogen into liver glycogen while Insulin accelerates the conversion of blood sugar to muscle glycogen leading to depletion of liver glycogen and hypoglycæmia.

Theory of Laufberger.—SOSKIN found that the administration of fat to totally de-pancreatized dogs was followed by an increase in the excretion of glucose, which led LAUFBERGER to conclude that Insulin acted by inhibiting the formation of carbohydrate from fat and protein. This theory fell to the ground when later workers found that Insulin does not exhaust the liver glycogen.

Theory of Oxidation of Glucose.—This suggests a new formation of glycogen under Insulin treatment. Glucose is split up into two molecules of a trios, the simplest being glyceric-aldehyde. This may tautomerise to either Methyl-Glyoxol or di-Hydroxy-Acetone. Usually di-Hydroxy-Acetone forms and it has been shown by MASON to be more completely oxidised than glucose in the normal person and less completely in the diabetic. It has been found that di-Hydroxy-Acetone is excreted by a diabetic person as glucose and that when Insulin is given, it is readily utilised by the system.

di-Hydroxy-Acetone	Without Insulin	Glucose
	With Insulin	

Neo-Glucose Theory.—Neo-glucose is obtained by incubating ordinary alpha beta glucose with muscle tissue and Insulin at 37°. But later researches do not confirm this observation.

Enzyme Theory.—The reduction of the blood sugar by Insulin is effected by enzyme action. THALLINER and PERRY suggest that Insulin acts as an oxidase and indirectly stimulates oxidising ferments in the tissue cells to act on the sugar present. But BRUGSCH and HOSTERS put forward the theory that Insulin is an activator or co-enzyme for phosphates. Later research workers, however, do not confirm their views.

Catalytic Action of Insulin.—GLASER and HALPERN found that Insulin acted best in the presence of Ferric and Nickel Chlorides. But observations on the diabetic do not confirm this observation.

Theory of Goldblatt.—GOLDBLATT found that there was always a rise in the glycogen content of the liver of starved young rabbits after injection of Insulin. He found that Insulin prevents the discharge of glycogen from the liver. The absorption of glycogen-producing substances from the gut and the blood continues freely while glycogenolysis is prevented, and peripheral utilisation continues until the blood-sugar level is reduced. When liver glycogen reaches a certain level, absorption stops. Insulin locks the glycogen found in the liver and utilises the sugar both peripherally and in the gut until a limiting value is reached in the liver glycogen which prevents absorption of sugar from the gut. There is a free passage of sugar through the liver without conversion into glucose.

In the above theories, Insulin acts by increased carbohydrate utilisation. If that is so, Insulin must deplete both liver and muscle glycogen to replace the peripheral losses and when these two sources are exhausted, the animal must naturally die of carbohydrate starvation. But GOLDBLATT has shown that starved animals can lay new formation of glycogen under the effect of Insulin. This work has been confirmed by FRANK and HARTMANN. Hence, this could not have come from the muscle glycogen. So, we are forced to conclude that Insulin glycogenolyses the liver rich in glycogen followed by a steady fall in the blood-sugar. The theory of GOLDBLATT is a fair attempt at justification of the action of Insulin in the light of current literature.

References:

1. American Journal of Physiology.
2. Insulin by D. W. Hill and F. O. Howitt.
3. Bombay Medical Bulletin.



The FOOD of ROYAL BABIES

Two more Royal Babies are being fed on Cow & Gate.

Thus eight Royal Babies have been fed in recent years on this famous English Food.

Cow & Gate is to-day the best authenticated Infants Food in the world.

Used in all the 3,000 Municipal Clinics and Welfare Centres of the U.K.

Used in the last ten years for over a million babies.

Recommended by Royal doctors and world-famous paediatricians

AND NOW PRESCRIBED BY YOU

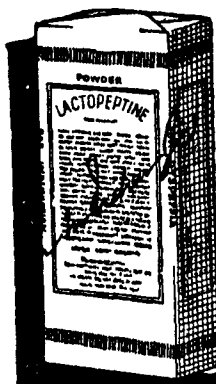
Agents for India: CARR & CO. LTD., Witter Road, Ballard Estate, Bombay; and at Calcutta, Karachi, Madras and Marmagao.

© 2156

COW & GATE MILK FOOD

"THE BEST MILK FOR BABIES WHEN NATURAL FEEDING FAILS"

"Ample stocks are available in India and will be maintained"



When INDIGESTION is the Cause

When Indigestion is the cause, then something more than mere relief from symptoms is required. The digestive organs themselves must be assisted. With this fact in mind, one remedy instantly commends itself. LACTOPEPTINE is the remedy which contains all the substances necessary for Perfect Digestion.

LACTOPEPTINE is the remedy prescribed with remarkably consistent results, even in the most obstinate cases of Indigestion. Not only does it relieve painful symptoms, but actually assists in the digestion of all foods—thus enabling the harassed digestive organs to rest and recuperate.

IN 3 FORMS TO SUIT ALL CASES

To suit the needs of all patients, LACTOPEPTINE is obtainable in 3 forms, viz: Tablets, Powder and Elixir.

LACTOPEPTINE is the Positive Remedy

FREE SAMPLE together with further details may be obtained from:—
Messrs. Muller & Phipps (India), Ltd., P.O. Box 773, BOMBAY.

AFTER THE MOST EXACTING TESTS

LEXIN

The famous treatment of Snakebite has been recognized by the five Faculties of Medicine in Central America—the habitat of the Rattle snakes.—“LEXIN works wonders” they recorded.

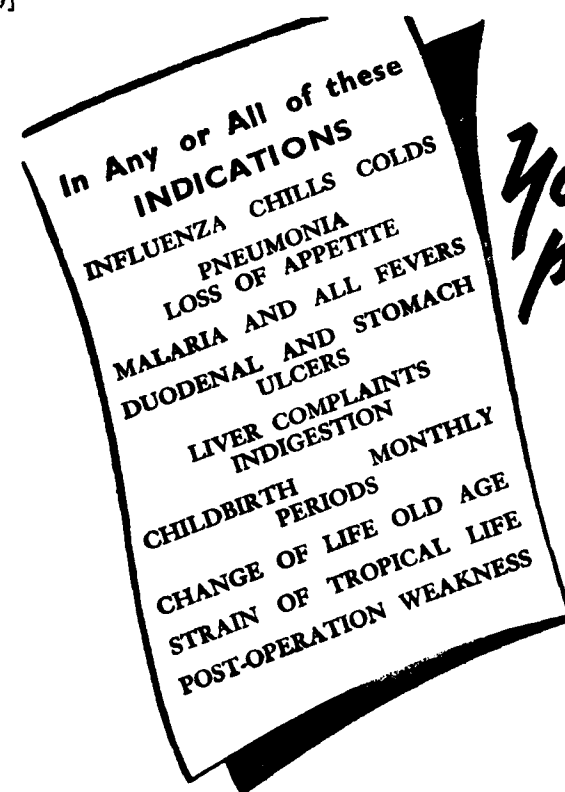
Sold by Chemists. Re. 1 per bottle (4 drs.) Doz. Rs. 10-8.

Box of 6 Ampoules. x 2 c.c. Rs. 2-4.

P. BANERJI, MIHIJAM E. I. Ry.

Agents:—Messrs. SRI KRISHNAN BROS., MADRAS.

When writing to advertisers please mention the “Antiseptic”



*You should
prescribe*

A tonic which not only strengthens, fortifies and stimulates, but which is readily acceptable by the most enfeebled digestion—able to absorb entirely the gastric juice released to digest it and leaving no free acid. In short, you should prescribe Brand's Essence of Chicken—the infallible stand-by of the medical profession for over 100 years.

Brand's Essence is a practical and efficient stimulant at all times when the minimum energy can be spared for digestive effort. The ease and speed with which Brand's is assimilated are due to a complete

absence of solids and irritants. Protein-sparing action takes place to a marked degree. The essence does not cause thirst and can be given at a moment's notice with a teaspoon.



BRAND'S ESSENCE OF ENGLISH CHICKEN

Agents for India and Burma:
GRAHAMS TRADING COMPANY, (India) LIMITED.
Calcutta, Bombay, Karachi, Rangoon.

When writing to advertisers, please mention the “Antiseptic.”



CREMAFFIN

(Cream of Magnesia with Liquid Paraffin)

A pleasantly flavoured emulsion free from any oily taste. Cremaffin is an ideal antacid and gentle laxative.

CREAM OF MAGNESIA WAFERS

Each wafer contains the equivalent of one teaspoonful of Regesan Cream of Magnesia.

BURNOL

A creamy emulsion containing 0.1% of the powerful non-toxic antiseptic Neutral Acriflavine presented in handy collapsible tubes ready for immediate application.

BURNOL has given excellent results in the treatment of burns and scalds, tropical sores, tinea infections, Dhobie itch, insect bites, minor injuries, ophthalmia of all types, suppurating wounds, and septic conditions generally.

For Prices and Particulars of Agents and Stockists apply to:

BOOTS PURE DRUG CO. LTD.
10, LALL BAZAR, - - - CALCUTTA.

MANUFACTURED BY
BOOTS PURE DRUG CO. LTD. NOTTINGHAM. ENGLAND

BMK 30

Non-Surgical Emergencies of Diabetes

BY

R. B. Billimoria, B.A., M.D.

Bacteriological Laboratory, Grant Road, Bombay.

“DIABETES mellitus is a disease of metabolism, characterised by imperfect utilization of carbohydrates, leading secondarily to other nutritional disorders”. The ultimate cause of this disease is not yet known; and quite possibly, there are several causes. Anything which interferes with the functioning of the islet cells of the Pancreas—a damage to its structural integrity, of its nervous control, or interference with its chemical stimulus,—results in diminished out-put of Insulin, thus producing the disease. The utilizable carbohydrate of the food normally is converted into the monosaccharid glucose, and stored as glycogen in the liver. The disaccharids (cane sugar, milk sugar, maltose) are split into glucose and lævulose, galactose and two molecules of glucose. If not thus split up, cane sugar and milk sugar would be excreted unchanged. The stored up glycogen is supplied to the body by the liver by reconvertng it into glucose for being stored or burnt up (oxidised) in the muscles and other tissues by Insulin. Proteins and fats too supply glucose to the body to the extent of 58% and 10%.

Protein metabolism through the specific dynamic action of the protein molecule stimulates metabolism, and thus adversely influences the course of the disease. Another part of the protein molecule is converted at times into fatty acids, which contribute to the production of acidosis.

The fat metabolism is, however, of far greater importance to a diabetic. When the oxidation of glucose is imperfect, fat metabolism is imperfect too, with the result that fatty acids escape oxidation and accumulate in the body—the cause of diabetic coma. The wise maxim—“fat is burnt in the fire of the carbohydrate” must always be remembered.

Lipæmia occurs in severe diabetes, and often in intoxications from liver damage. The average lipoid content of the blood is 0.5 to 0.7 grm. per 100 c.c. The blood plasma is milky when it becomes 0.8 grm. and more as occurs after a fatty meal. In diabetic coma it may reach 1.5 grm. per 100 c.c.; but for reasons still unexplained, it *does not* make the serum milky, thus taking away from us what would have been an easy diagnostic test. The prognostic value of blood fat determination is discussed at length by JOSLIN. The one definite and important conclusion that is reached is that the chief clinical significance of lipæmia is an indication of poor glucose utilization, a factor which is readily amenable to treatment. If we improve the patient's ability to utilize glucose, the lipæmia disappears.

It has been the custom in the past to divide diabetes into the severe, moderately severe and the mild types; and the quantitative

test was held to indicate the severity. The fallacy of this has been well established by now. WOODYATT's method of plotting the sugar percentage curve with isocaloric diet with increasing carbohydrate contents is possible in a hospital or nursing home with a trained staff. But if one finds that gradual increase in the carbohydrate food in the diet is followed by proportionately much increased glycosuria which persists for several days in spite of subsequent dietary restriction, the case may be taken as one of a severe type.

The dextrose-nitrogen ratio (the "D. N." ratio) i.e., the ratio of dextrose to nitrogen in urine is another weapon in our hands for studying the severity of a case. It has been established experimentally that when the excretion of dextrose in the urine is 3.65 grams to 1 gram of nitrogen, the person is incapable of burning the glucose. LUSK takes this ratio of 3.6 to 1 as of the gravest prognostic significance. Estimation of total titratable acidity of 24 hours urine, and the determination of ammonia are further helps, particularly in a case of threatening coma. A sudden appearance of a good number of renal casts in the urine similarly foretells this emergency.

Blood-sugar-curve estimations have come much into vogue, but a warning note has been sounded by POWELSON and WILDER, who take the following four types as belonging to the groups of "innocent glycosurias":

1. *Normoglycæmic glycosuria*:—Outcome of lowered renal threshold. The blood sugar is normal; and the glucose tolerance curve is normal, but urine keeps on excreting sugar continuously. It is not diabetes mellitus.

2. *Alimentary hyperglycæmia*:—The blood-sugar curve shoots immediately to an abnormally high point, but returns to normal within the requisite time. There is sugar in the urine. It is taken to represent "a tardy metabolism of the mechanisms for utilising sugar" or a disturbance in the storage of glycogen. One may take these cases as potentially diabetic.

3. *True diabetes innocens*:—Here there is normal or low blood-sugar, together with a characteristically high peak in the glucose-tolerance curve which is reached tardily but slowly returns to normal. The low renal threshold gives a continuous glycosuria. This condition can be confused with true diabetes with a low renal threshold. But consideration of the duration and course of the disease, the patient's age and general condition, the presence or not of ketonuria can help, though often one is left in the lurch.

4. *The glycosuria of pregnancy*:—Almost all pregnant women have a low renal threshold, and the condition is harmless. But one has to be on the look out, as quite often cases are reported in which true diabetes mellitus began in pregnancy.

5. *Sapremic glycosuria*:—Appears in various infectious diseases, and disappears when the infection subsides.

It is as well worth while noting that *arterio-sclerosis* (not senile)

lowers glucose tolerance, and may lead to the appearance of sugar in the urine. An acute diabetes mellitus in an arterio-sclerotic patient constitutes a grave prognosis from the standpoint of complications.

I may mention here two very interesting cases. The history was almost identical in both: a hard lump in the region of the pancreas, glycosuria, high blood-sugar curve, and rapid wasting. The first sight diagnosis would be cancer of the head of the pancreas, but the characteristic difference was the absence of jaundice and constant presence of glycosuria. Both the patients recovered under the antisyphilitic line of treatment.

I have tried to explain above the carbohydrate metabolism and the pitfalls, as without the full understanding of these, one cannot do full justice to a case of diabetic emergency. Leaving all surgical emergencies aside, one must be prepared to be on the look out for medical emergencies, which I may put down as:—(1) Diabetic coma. (2) Hypoglycæmic shock. (3) Cardiac and vascular emergencies. (4) Uræmia. (5) Senile diabetes.

It is far safer to try and catch a patient in the pre-comatose stage; and particularly, utmost efforts should be made in a septic case, where ketosis almost always threatens. There, the physician has to be most energetic and on the constant look out. In passing, it must be said that as long as the septic condition is acute, Insulin gives poor results when given by the usual standard method; that there are grave chances of severe ketosis developing, and that with the opening of an abscess or giving free drainage to cellulitis, Insulin suddenly begins to work more actively, and thus a continuation of the previous large doses carries with it the risk of hypoglycæmic shock. In a person, with a constitution already severely taxed, this may be too much. In these Insulin-resistant septic cases, it is worth while taking the suggestion of HERBST, and try and break the resistance by intravenous injections of 2—3% Sodium Bicarbonate solution. Further, in cases of asthma, one has always to enquire about any injections of Adrenalin being taken, as much of the Insulin in such cases gets neutralised,—becomes inactive. In some Insulin-resistant cases, the use of depot Insulin may be tried.

Diabetic Coma.—The prevention of coma has always occupied a central place in the treatment of diabetes, anything which upsets the diabetic patient, whatever its nature, may superinduce acidosis and lead to coma. Even the best established carbohydrate-fat ratio diet cannot prevent this dreaded complication. One must not forget that the carbohydrate metabolism is not the sole factor which influences the production and extent of acidosis. JOSLIN has expressed the view that "diabetic coma is a preventable accident or an evidence perhaps of mismanagement." To recognise its approach forms thus a vital subject. In general, it may be said that any change in the patient's demeanour or sense of well-being, peevishness, feeling of exhaustion, restlessness, insomnia, loss of appetite, dislike for fats, feeling of drowsiness, drop in the quantity of urine voided, nausea, (and particu-

larly when such symptoms come on suddenly or after any cause) must put one at once on his guard, and a complete investigation made at once. The simple tests for ketone bodies can be carried out at once, and the pH value of the urine determined as described in this Journal (February 1940, or by the simple use of nitrazine (Phenaphthazine) p. 151) indicator paper. One must not be too scientific and wait for blood-sugar reports, but act at once and energetically too. KUSSMAUL's "air-hunger" type of breathing means that coma is imminent, when one finds that the tension of the eyeballs is giving way, a symptom not observed in any other comatose or semi-comatose condition. The onset of diabetic coma is never sudden, and it means a lot to catch the patient in the pre-comatose phase. Presence of albumin and casts is not a rare occurrence in these cases, and must not make one think of uræmia. At times, one meets with a diabetic patient taking Opium as a remedy; and in such a case, small pupils, with albumin and casts in urine constitute a very deceptive picture. The sudden appearance of casts (a shower of casts) is often taken as a symptom of threatening coma.

Recently, some hot discussion has been going on (B.M.J. 14-x-'39, 4-xi-'39, 6-1-'40) about diabetes complicated with nephritis. I had an opportunity of studying a good many cases of the combined diseases, and have been always struck with the marked fall (and even disappearance) of sugar, in the urine with a corresponding fall as well in the blood sugar; we need not discuss this question here, but it must be said that along with sugar estimation, it is always desirable to apply the albumin test, at least fairly frequently; at times in the pre-comatose stage, there is a fairly severe abdominal pain with leucocytosis in the blood, and many cases are recorded of a mistaken diagnosis of appendicitis, surgical interference and death.

In the threatening condition described above, 40 to 50 units of Insulin are given at once *intravenously*. One may utter a word of warning here, regarding the Insulin. One must always make it a rule to buy Insulin from a chemist who stores it in the cold storage. After the Insulin injection, empty out the bladder with a catheter, so that the next sample of urine is not vitiated by the sugar etc. loaded urine which was present in the bladder before the injection of Insulin. Two hours after the Insulin injection, collect a sample of urine. Examine this urine at the bed-side: if the Benedict's test gives yellow coloration to the solution (*i.e.* 1—2% glucose) 40 units of Insulin are given *intramuscularly*; if the Benedict's solution is greenish, 30 units, and if it is blue (no sugar) then 20 units may be given and at the same time one has to give 150—200 c.c. of 25% sol. of glucose *intravenously*. If the tension in the eyeballs, and the condition of the skin indicate dehydration, one may substitute the above glucose by 100 c.c.—150 c.c. of 25% *intravenously*, and two to four or five pints of normal saline (or more preferably 0.6% Sod. Lactate) with 5% glucose *subcutaneously*. At the same time, it is desirable to give a high bowel wash with 3% of warm Sod. Bicarbonate solution, and leave behind a pint of the same if it can be retained.

This above routine of intravenous glucose and Insulin *subcutaneously* (after urine examination) must be kept up every 4 hours whether the patient has regained full consciousness or not till urine shows no more ketone bodies. It has been suggested to wash out the stomach and combine Coramine or similar drug with Insulin, but personally, I would do neither. The unconscious patient is not a good subject for stomach washing, and the rectal administration of Sodium Bicarbonate solution is quite rapidly absorbed. One has, also, to consider the share of the liver in carbohydrate metabolism, and I would like thus to avoid Camphor and allied synthetic drugs.

As soon as the patient is able to swallow, he must be given fluids freely, with glucose and Sodium Chloride. All efforts must be made to keep the patient warm.

It may be interesting to note here that the recent work of McQUARRIE, THOMPSON and others appears to demonstrate rather definitely that a high intake of Sodium Chloride exerts a beneficial influence upon carbohydrate metabolism in diabetic cases, diminishing glycaemia and glycosuria, and even delaying ketonuria, and improving nitrogen balance. The question has been discussed whether it is the Sodium radicle or the halogenchlorine. Potassium salts neutralise the effect of Sodium Salts; and an increase in glycosuria follows the administration of Potassium Chloride, with a diet low in Sodium.

In a case of coma, if facilities are available, it is desirable to estimate Chlorides in the blood. If the Chlorides are low, the loss of electrolytes has reached a very dangerous stage.

Estimation of the hæmoglobin per centage in the blood is a simple and safe guide for the administration of fluids. A percentage of 120 would mean an urgent call for saline transfusion, and as it drops to normal level, one may withhold it, and not run the risk of hydræmia.

Hypoglycæmic Coma.—With the Introduction of depot-Insulin, some peculiar complications are added to the treatment of diabetes. Whenever one wants to switch on to depot-Insulin from the ordinary type, it is always safe to use a dose 30% less. If the patient's carbohydrate metabolism is unstable *i.e.* the sugar excretion on one and the same standard diet keeps varying, it is advisable to keep on with ordinary Insulin. And thirdly, patients needing 50 units and more of ordinary Insulin require a night attendant who knows fully well his business, if one wants to substitute depot-Insulin. Surgical cases require an absolutely different standard of treatment, and we need not take up that question here.

The object of discussing the effects of depot as contrasted with the ordinary Insulin lies in the important fact that there is marked difference between hypoglycaemia following the use of depot Insulin, and that after ordinary Insulin. The dramatic onset of coma from ordinary Insulin must not be expected from the over-dosage of the depot type, due to the absence of the Insulin thrust effect. With ordinary Insulin sweating, clamminess and limpness precede the neurologic and psychiatric disturbances; whilst with the depot type, the vegetative symp-

toms are absent, and we are suddenly confronted with neurologic and psychiatric manifestations. It may be a mild drowsiness or a complete coma, with all chances of its being missed, coming on, as it has more chances to do so, in the midnight. Or, it may be a muttering mild maniacal condition or an acute mania and even homicidal tendencies. Milder phases of these psychiatric symptoms are often manifested by patients complaining of nightmares, frightful dreams, seminal emissions, sense of choking and suffocation during sleep, a peculiar groaning as if the chest was being squeezed during sleep, or a feeling of complete exhaustion on awakening. Attempts to wake up such a moaning, groaning patient are not as easy as in others with ordinary dreams. If he does wake up, his behaviour is peculiar, he looks stunned, dazed, sleepy,—something suggesting as if he had taken an overdose of alcohol. Thus, the symptoms of hypoglycæmia from over dosage of depot Insulin are very treacherous, and missed. But the still greater danger is that it does not yield to administration of glucose as in the case of ordinary Insulin. One has to remain watching an acute case for at least 24 hours, as the depot Insulin keeps on exerting its influence, and is not so quickly used up as the ordinary one. Some authorities have described some cardiac symptoms, needing careful attention to that as well. But, it must be said as well to the credit of depot Insulin, that in cases of angina pectoris, it is preferred because of its slow action.

One can sound a warning in diagnosing a case of hypoglycæmic shock from urine examination. The urine may be containing sugar, and even some acetone. This was in the bladder before the ordinary Insulin was given (without a complete previous evacuation of the bladder). In a doubtful case, however, it is always safe to give an intravenous injection of 20 c.c. of 25 % glucose solution. If it is a case of diabetic coma, no harm can be done, because the diabetic coma is caused by ketonæmia and not hyperglycæmia. If the response is not there, one may take it as diabetic and treat with a large dose of Insulin intravenously as described above.

The characteristic symptoms of hypoglycæmic shock, from ordinary Insulin is that it is *sudden* in onset, breathing is quick and not eold and clammy, but not the typical dehydrated look, nor with the tension of the eyeballs abnormally low. It is impossible to smell acetone about an unconscious patient, though one reads about it in every medical book. The relatives and friends are rubbing brandy, formenting with "agivan" or onions with free use of *eau-de-cologne*. In the presence of all this, and perhaps a dozen sweating friends and one had suggested that in hypoglycæmic shock the plantar reflex (Babinski's sign) is of the extensor type. Twice I have seen it to be so.

Intravenous injection of glucose brings out an immediate response. But the medical man must not rest there. The patient may be having a combined Insulin with depot-Insulin treatment. He comes out from the effect of the first, and may lapse into that of the second after a period of consciousness. The relatives may think he is sleeping

through sheer exhaustion and because he came out from his first shock so easily and dramatically, their fright is gone, and they take things quite easy. It is thus the duty of the medical man, to enquire beforehand and the best procedure would be to call in his family physician who knows the exact facts.

Differential Diagnosis of Acidosis and Hypoglycæmic Shock.

DIABETIC ACIDOSIS.		HYPOGLYCÆMIA.	
		Regular Insulin.	Depot Insulin.
Onset.	Gradual (12—40 hrs.)	Rapid.	Gradual.
Premonitory symptoms.	Nausea, anorexia, headache.	Hunger irritability.	Loss of memory emotional headache.
Convulsions.	Rare.	May come on late.	May be the first symptom.
Muscles twitchings.	Absent.	Frequent.	Frequent.
Respirations.	Kussmaul type.	Normal (rapid).	Normal.
Breath.	Acetone.	Normal.	Normal.
Skin.	Dry.	Moist.	Normal or moist.
Eyes.	"Soft eyeballs".	Normal.	Normal.
Pupils.	Dilated.	Normal or contracted.	Normal or contracted.
Vomiting.	Frequent.	Absent.	Infrequent.
Abdominal pain.	Common.	Absent.	Rare.
Blood pressure..	Subnormal.	Normal or high.	High.
Temperature.	Subnormal but rises rapidly.	Subnormal.	Subnormal.
Urine.	Sugar and ketone-bodies.	Usually free from sugar.	No sugar, no ketones
Blood.	High sugar, low CO ₂ .	Lower sugar. Normal CO ₂ .	Low sugar, normal CO ₂ .
W. B. C.	Increased.	Normal.	Normal.
Response to glucose injection.	None.	Prompt return to normal.	Promptly normal, but may relapse.

—(International Clinics).

Uræmia.—One of the most ominous developments that can occur, particularly in the course of diabetic coma, is anuria. It is found that this is more likely when the urine fails to excrete ketone bodies; and there is a simultaneous high concentration of non-protein-nitrogens in the blood. Blood pressure is not high, unless it was already so before the grave condition sets in. Rather, without a

previous kidney lesion, the blood pressure keeps falling with all symptoms of "shock". The treatment is administration of glucose in hypertonic saline (or Sodium Lactate); Neptal (Salyrgan) may be ventured though personally, I would feel very shaky about the use of mercurial diuretics.

The presence of albumin in the urine of a chronic diabetic patient is quite a common occurrence. There may be granular casts as well, with this appearance of albumin. I have very often noticed a drop in sugar percentage without any increase in the blood-sugar factor. It need not frighten one about the renal condition, though after a long time, the quantity of albumin excreted goes on increasing with gradual rise in blood pressure. Keeping down the acidity of the urine, and with a strict control on "acid" diet, particularly fats, the percentage of albumin excreted drops, and the rising blood-pressure becomes more steady. But, there are chances of a diabetic developing true nephritis, and developing true uræmia. Blood analysis alone can decide the real condition, and one has to be on the look out to differentiate uræmic from diabetic coma.

Cardio-vascular emergencies.—Before the days of Insulin, the diabetic diet prescribed contained a lot of fat, in the form of butter, cream, eggs (yolks), with the idea of supplying the necessary calories. The metabolism of fat depends very much on the healthy active state of the *alpha* cells of the islets of Langerhan. When these islets are damaged as stated previously, one naturally expects the *alpha* cells too to be damaged. The imperfect combustion of the fat has thus been perhaps the cause of atheromatous degeneration of the inner lining of the aorta and other vessels. In addition to the atheromatous degeneration, a diabetic runs the risk of arteriosclerosis. Whether the constant irritation of the kidneys by the highly acid diabetic urine gives rise to the high blood pressure, with the consequent changes in the arterial wall, or whether the excess of glucose and other products circulating in the blood act directly on the vessel walls, we need not discuss. The fact remains, that a high blood pressure is a fairly frequent complication of diabetes.

The atheromatous degeneration carries far greater risks by involving either the orifices of the coronary arteries, or the coronary arteries themselves. An X-ray examination shows the greater opacity of the aorta, particularly in the oblique position, and one must take it as a grave warning when, coupled with symptoms of fatigue and breathlessness on exertion, there exist oedema of the ankles, flatulence, enlarged tender liver and other signs and symptoms of an imperfect circulation. Coronary thrombosis often terminates the condition. The usual precautions taken for coronary disease are strictly to be enforced; and my personal opinion is to cut off absolutely all fats (ghee, butter, cream, fat, oils, yolk of egg) and put a good restriction on milk as well. To supply the needed calories (in a fairly resting patient) carbohydrates have to be allowed, but no efforts need be made to keep the patient sugar-free as regards his urine. In fact, such patients seem to tolerate

carbohydrates much better than in the past. Though at first sight it appears nauseating, none of my patients have in the least objected to cooking their food in liquid paraffin in place of ghee and oil. Actually, many of them seem to like it and prefer it. Our sole hope in preventing this complication is to get an extract of the *alpha* cells of the Langerhan islets in the same way as we have Insulin to work on the carbohydrates of the food.

In the case of arteriosclerosis, one naturally has to drop the common salt, and avoid all Sodium salts (Sodium Sulphate, Lactate), though for an ordinary diabetic, salt (and Sodium Lactate) is a useful adjuvant to Insulin. With increasing arterio-sclerosis, I have been seeing at times a fall in the sugar contents of the urine. One has to be careful in the use of Insulin in these cases, particularly in patients with præcordial sensations or actual angina. A peculiarity I saw recently in two cases was fleeting paralysis lasting from four to six days or so, exactly the picture of claudication of cerebral blood vessels. This was noticed to be always precipitated by Insulin injection. Insulin was stopped, and to my surprise, there were no more attacks, and a still more strange fact was that the patients began to tolerate carbohydrates better than when taking Insulin, and with a much clearer mental factor too.

In cases of senile diabetes (*i.e.*, over the age of 55), one must not run the risks in complete de-sugarising the patient and elderly diabetic needs sugar very badly, and does poorly on strict diet. WOODYATT showed that glucose in the diet of elderly persons with arterio-sclerosis could be increased significantly without any increase in the glucose excretion in the urine. He suggests that in these patients there were modifying factors in the tissues or cells which had some peculiar destructive (?) effect on Insulin, and warns against large doses of Insulin. The adjustment of glucose intake in a senile patient requires a careful consideration of his sugar tolerance capacity, at the same time paying full consideration to the important factor: is he receiving enough glucose? Upon this his life depends. If otherwise, he either develops acidosis, or other complications (mentioned above) arise. Maximal allowance of glucose prevents in them the progress of arterial degeneration with its consequent complications.

Another peculiarity of senile diabetes is the much higher blood-sugar level as compared to sugar excretion. These high blood-sugar levels are better left untreated, unless a surgical or other complication threatens, and on the whole, I have repeatedly seen that very small (10—15 units) doses of Zinc-Protamine-Insulin produce far more definite results, and that too without exposing the patient to other risks, than ordinary Insulin in larger and even more frequent doses. In senile diabetics, a hypoglycæmic shock is at times manifested by profuse polyuria; and a sudden polyuria in such patients needs careful watch.

Surgical Diabetes

BY

B. N. Lahiri, M.B., F.R.F.P.S. (GLASGOW).
Surgeon, Mayo Hospital, Calcutta.

A CONFIRMED diabetic is liable to most serious surgical complications. Its unknown etiology, obscure pathology and disappointing treatment are of the past. We surgeons no longer hesitate to interfere and thus allow the most precious time to pass in watching the patient when he is in need of urgent surgery perhaps passing through an ordeal of surgical problem and reaching a stage beyond our surgical interference. The year 1921 witnessed BANTING'S most remarkable discovery of Insulin which is a very powerful weapon in our hand to combat the disease and to give a longer protection against the surgical complications. A diabetic with surgical complications can now demand a satisfactory treatment in the same way as a non-diabetic and it may be that his surgical risk, if he is properly prepared, is no greater than a non-diabetic.

Diabetes and Infection.—Diabetics are liable to infection due to their lowered resistance. A diabetic in a crowded room may easily catch "colds" or influenza.

A slight abrasion on his toes may progress to a dreadful gangrene or a crack in callosities, a minor trauma in cutting nails may lead to severe cellulitis.

Infection and sepsis on the other hand lead to rise of temperature, consequently increased metabolism and more glycosuria. The lowered resistance again favours the development of septicæmia.

Diabetes and Ductless Glands.—In disease of thyroid and pituitary glands, we frequently observe glycosuria more where sepsis is a predominating feature. The thyroid, pituitary and adrenals exert an inhibitory action on the islets of Langerhans. If there is an excess in secretion of the former in certain pathological conditions, the function of the latter is arrested and consequently lowered carbohydrate metabolism occurs with associated glycosuria and some degree of hyperglycæmia. This is why glycosuria occurs in GRAVES' disease, acromegaly and basophilic adenoma of pituitary.

The injection of Adrenalin mobilises liver glycogen and causes hyperglycæmia and glycosuria. But in clinical practice, we rarely find glycosuria associated with diseases of suprarenals. Any morbid condition of ductless glands that are antagonistic to pancreas may lead to diabetes and the diabetes of hyperthyroidism is an example. Therefore, in every case of glycosuria, careful observation must be made to exclude morbid conditions of ductless glands because the glycosuria in that case may be one of the symptoms and not a true diabetes.

Surgery may be necessary in a person who is suffering from

diabetes or it may be necessary in treatment of complications of surgical nature occurring as a result of his diabetic state. In treating patients suffering from diabetes, the surgical risks should be ascertained before doing any interference, and in estimating the risk, we consider the following points:—

(1) General condition of the patient.

(2) *Hyperglycæmia*:—It is sometimes present without any sugar in the urine as in the arterio-sclerotic and diabetic of long standing. A high percentage of blood sugar occurs in untreated cases and cases attended with surgical complications. A high blood sugar should always raise the suspicion of obscure septic focus. The higher the blood sugar level the more serious is the progress. We have found that blood sugar level above .35% is a bad risk of surgical interference. With blood sugar at that level, we suspect the presence of acidosis or severe infection.

(3) *Glycosuria*:—In case of severe infection, there may be high blood sugar with sugar-free urine. The result of examination of single specimen may be deceptive.

(4) *Hypoglycæmia*:—The weak emaciated patients with under weight should be considered as surgical risks as they often show sudden hypoglycæmic symptoms as a result of Insulin treatment, especially accompanied by diarrhœa.

(5) *Acidosis*:—Surgical interferences, as incision of cellulitis, opening of abscess have special influence on development of acidosis. The degree depends on the intensity and duration of the disease and the effect of infection on the system. Big carbuncles are commonly associated with acidosis and acidosis again is partly responsible for startling septicæmia from local infections.

(6) *Metabolism*:—The metabolic rate in a diabetic is upset by trauma and anæsthesia. Severe lacerations or cutting of soft tissues in a normal person has the effect of slightly increasing the sugar in blood but in the diabetic, it is of utmost importance for the fact that the post operative disturbance is considerable and the metabolic rate has to be controlled during the after treatment. Similarly, vomiting and diarrhœa in post operative stage have to be adequately combated.

Careful choice of anæsthetic is necessary. It should cause minimum disturbance of metabolism at least for a day after operation and less danger of septic complications such as bronchitis or pneumonia. If general anæsthetic is necessary, Gas and Oxygen are desirable. If surgical condition allows, spinal or local anæsthesia is preferable.

(7) The old standing diabetics are also subjects of arterio-sclerosis and thorough examination of urine with a view to exclude kidney condition should be done. The suppression of urine and uræmia are not uncommon occurrences in these patients. A patient aged 60 was admitted in the hospital for treatment of extensive cellulitis of hand with high fever. His blood sugar was .45% and urine sugar .25%. Urine showed presence of pus cells, casts and micro-organisms. Sulphonamide

1 tablet thrice daily—was given along with other treatment and after 6 tablets, the patient had complete suppression of urine.

Surgery in Diabetic Patients.—As the diabetic condition causes lowered resistance, the impairment of cardio-renal condition, rigidity of blood vessels, and lowered nutrition of tissues, the onset, course and symptoms of certain pathological conditions are modified accordingly. The presence of the acidosis makes the conditions more complex. USADEL reports of a young man with sugar and albumin in the urine who had an attack of violent pain in the stomach. The abdomen became distended and rigid in the course of 12 hours and pulse rapid and small. Diagnosis of perforation and peritonitis was made but the diagnosis was not confirmed on laparotomy. Thus, it is not uncommon to confuse an acute abdominal lesion with acidosis as the symptoms such as nausea, constipation, pain, tenderness and cramps in the abdomen, abdominal spasm, rapid pulse, dry-tongue, and leucocytosis may be met with in both the conditions. In general, the clinical picture of an acute abdomen is more indefinite in a diabetic than a non-diabetic patient. The picture differs in two ways: firstly there is abdominal cramps which may be mistaken as a sign of acute abdominal condition and secondly, the presence of indefinite pain sensation in conditions like acute appendix causes considerable difficulties in arriving at a proper diagnosis. Apart from ordinary surgical risk in a diabetic, a careful history and logical relation between temperature, pulse, blood and urine report and physical findings, should be weighed before deciding for or against an operation.

Acute Appendix:—The most common intra-abdominal lesion that we are asked to tackle is appendicitis of acute type. The signs and symptoms of acute appendix is rather vague in diabetics than in non-diabetics. This is not difficult to understand that in a diabetic, a small superficial ulceration on the toe progresses rapidly and painlessly without any signs of inflammation and ultimately leads to gangrene and complete destruction of the part. Similarly, a small ulceration on the mucosa of appendix may run a painless course without any signs of inflammation, terminates in gangrene and perforation before the patient is well aware of his condition.

A male diabetic patient, aged 50 years, was being treated for infected bursitis at the elbow. He had a few badly infected teeth removed and for several days had temperature of 99° to 100°. He was all right and eating his meals without complaint. One morning, he was awakened with sudden severe abdominal pain and signs of rapidly spreading peritonitis. His abdomen was opened under Novocaine and a big appendicular abscess bursting in the peritoneal cavity was drained. The patient died after a few days.

Nausea and vomiting are more marked in diabetics than non-diabetics, especially if acidosis is present.

Tenderness and muscle spasm are very deceptive signs though tenderness is commonly present. We have noticed that, apart from other factors such as the degree of inflammation, amount of irritating

fluid etc., it depends on the age and degree of acidosis from which the patient is suffering. The older the patient and more marked the acidosis, the less definite the local and general symptoms. Here again, we give importance to exclude the kidney conditions as peri-nephric abscess and ureamia may appear any time in the course of the disease.

TREATMENT.—Appendectomy is the treatment of choice. There is no justification for delaying operation if the patient's condition allows it. The danger of death from delay in operation is greater than expectant treatment. If the diagnosis is obscure, it is safer to establish it by exploration under Novocaine. We do not advocate OCHSNER's treatment. The power of peritoneum in diabetes to localise infection is small and its resistance is smaller and if there is irritating fluid or pus, it should be let out at once.

Gall Stone.—*Relationship of gall stones and diabetes:*—ASCHOFF observes that super-saturation of bile with cholesterine in cholesteræmia is primarily responsible for formation of cholesterine stones and infection may be a secondary factor. In a diabetic patient, there is increase of cholesterine in blood. JOSLIN and his co-workers have shown that lipæmia is more or less constant in diabetes and Insulin and restriction of diet may bring down its level in milder cases. MENTZER also corroborates the view by his observation on 200 diabetic cases where the disturbance of fat metabolism was present. We also find, that in diabetes, there is lipæmia and cholesteræmia and deposition of cholesterine on blood vessels.

Pancreas may be infected by reflux of infected bile into the pancreas and literature shows that pancreatitis with fat necrosis is thus possible. The diabetes, gall stone and arterio-sclerosis—especially of coronary vessels and vessels of leg—seem dependent on some common factor.

Glycosuria is common in gall stone diabetes. The symptoms here again are less marked than in non-diabetics and a case has been reported when the patient made a journey with perforation of gall bladder and abscess formation. One must carefully weigh the severity of condition as in diabetes, the extent of infection and local necrosis is usually greater than the symptoms and signs suggest.

Investigation by cholecystography is no contra-indication in a diabetic patient.

TREATMENT.—Cholecystitis with stones should be treated by removal of stone. The removal is desirable to prevent repeated suffering and serious complications and JOSLIN observes that the removal of stone is a possible prevention of diabetes even in the absence of glycosuria.

Cholecystitis without stone does not demand surgical interference and the risk of operation in this case should not be undertaken in diabetics.

Surgery for Diabetic Complications.—The large number of patients that we treat suffer from infective conditions associated with

diabetes. The frequency of occurrence of sepsis and gangrene in diabetes has been explained due to lessened local and general resistance. It is also believed that increased concentration of sugar in the tissue acts as culture medium for staphylococcus. FOLIN showed that if glucose is injected in animal, a part of it is stored in the skin. We do not as yet know the definite relationship of increase in sugar content and skin infections, but other factors such as arterio-sclerotic conditions of vessels particularly of legs, acidosis and long standing hyperglycemia are collectively responsible for frequency of sepsis and gangrene in diabetes.

Carbuncles—These are most common surgical complications of diabetics in our country. At its onset, the swelling is hard and tender with diffuse oedematous and indurated margin. Later, the centre of the swelling becomes purplish red and softened with multiple necrotic discharging sinuses.

Distribution of 34 carbuncles: Neck—12; back—9; scalp—7; buttocks—6.

Those located at the back have a tendency of earlier localisation than others.

The infective agents are staphylococcus and infections start on the sub-chorium and spread in that layer. In non-diabetics, it is a self-limiting localised condition. But in diabetics, it rapidly spreads due to lowered vitality of the tissue and necrosing action of staphylococcus. Toxæmia due to absorption of toxin from the big infected area, acidosis and septicæmia are common in severe cases. The occurrence of acidosis in carbuncle is explained by the fact that the intense acute infection depresses the power to oxidize the carbohydrates.

Prognosis of fat, aged and frankly septic cases are unfavourable as metastatic abscess, Septicæmia, and broncho-pneumonia are common. Metastatic cortical abscess and carbuncle of the kidney may occur simultaneously with the main lesion. In every case of severity, blood culture should be done.

TREATMENT.—Treatment consists of diabetic condition and of carbuncle. Treatment of carbuncle in the early stages is fomentation by Mag-Sulph solution. Injection of Autogenous Vaccine, Stanoxyl (or per mouth) or Manganese Butyrate. If there is much pain and sleeplessness, Morphine may be given safely.

When there is definite fluctuation accompanied by high temperature, the carbuncle should be opened.

Operation:—Give crucial incision on the carbuncle. The incision should extend beyond the margins of carbuncle. Make the incisions deeper till they reach the bed of the wound. Stitch the corner of the four flaps with skin so that their wound surface is out. Remove slough as much as possible and dress the wound with sterile raw cod liver oil. This is done by pouring it inside the wound. Last of all, Ung. Hydrange Ammoniated should be rubbed all round to the wound.

prevent further spread of infection. In 6 to 7 days time, there will be formation of granulation tissue and then snip the stitches of the skin flap to make them fall back. The whole wound will take a fortnight's course for complete healing. If there is septicæmia, inject Staphylococcus Antitoxin (U. D. Co.) A few exposures of infra-red (for 20 minutes) will facilitate early recovery.

Furunculosis.—The management of furunculosis in a diabetic is a very important problem, especially if they appear on the face. Frequently, they appear on the axilla, on the neck due to rubbing of collars, or on the back with mild fever. Boils or staphylococcal infections start on the papilla of the skin at the side of hair follicles. They should never be incised, especially on the face, as the two venous sinuses situated at the base of each hair follicle, carry the emboli and metastatic abscesses develop elsewhere and in the face, thrombosis of cavernous sinuses is possible.

Apart from general treatment, the local treatment particularly to prevent recurrence should be done. PRICE's advice consists largely of "don'ts,—don't squeeze, don't prick, don't cut and to the diabetic patient, don't show sugar". Wash the infected area with alcohol and apply strap of elastoplast. Boric or Zinc ointment should never be used as they cannot prevent spread of infection. Hydrange Ammoniated ointment should be spread as collar round the boils. Stanoxyl, ultra-violet rays and vaccines should be tried.

Gangrene of the Lower Extremities.—Diabetics are liable to infective conditions of feet which, in non-diabetics, are of little significance. We usually find superficial ulcers such as varicose ulcer, septic abrasions, paronychia and infective corn or callosities. The deeper ulcers are of penetrative type, the examples of which are found in perforating ulcers, and osteomyelitis of metacarpo-phalangeal joints. The diabetic patients differ from non-diabetics in both general and local reactions to infections. Locally, there is sluggish reaction in superficial ulcers but the course of disease is much rapid and the destruction of the tissues is great. We are familiar with the metacarpo-phalangeal joint affections of diabetes, where there is no reaction outside but a tiny sinus is found extending to the bone. The sequestra are not felt though they are present. They are formed of cartilages from the base and head of the bone associated with the joint. The characteristic lesion is not detected by X-ray and is due to poor vascular condition of cartilage in diabetic arterio-sclerotics. These patients again show much less pain and tenderness than a normal patient with such lesion. The treatment of the above conditions is similar to that of non-diabetics but certain points should be attended to.

The diabetic state should be ascertained and controlled by appropriate treatment. The infective condition, if requires draining, should be drained without loss of time, if there is any sequestrum, it should also be removed, the wound cleansed and packed with sterile gauze. The after-care of wound is of great importance and no irritating or strong

antiseptics should be used. They damage the tissues which have very poor blood supply. After a few days, when the wound is in a healing condition, we use Insulin dressing, *i.e.*, a few c.c. of Insulin is sprinkled into the wound and sterile gauze is covered on it. We have got very encouraging results by Insulin dressing.

The simple infective condition described above does not always progress as such, frequently there is œdema at the original lesion spread upwards reaching high up in the leg, thus involving the foot and leg. Red lines of inflamed lymphatics and veins are visible also small areas of gangrenous patch may develop with offensive discharge. The swelling increases the tension of the affected tissues and occlude the deeper vessels. On account of deficient circulation, the infection is not localised so that the condition, instead of remaining as paronychia or septic abrasion, passes on to cellulitis and cellulitis into gangrene.

In all such cases, the general examination of the patient, specially arterial state, should be made.

The condition of the peripheral arteries ascertained by the local colour and temperature change of the affected part, the presence or absence of pulsation in dorsalis pedis artery, posterior tibial artery and popliteal artery.

The examination of heart, brachial and radial arteries should be made as considerable informations are obtained as to the degree of vascular disease in general. The diabetics often are liable to heart attacks due to arterio-sclerotic condition of coronary vessels and failure of peripheral circulation is the result.

The diabetic gangrene is essentially an arterio-sclerotic gangrene, the element of sepsis combined with arterio-sclerosis is responsible for its production. It never occurs in young diabetics and differs from arterio-sclerotic gangrene from being less commonly dry process. The swelling of the foot precedes the gangrene. Infection is common and wet gangrene is the rule.

TREATMENT.—Blood culture should always be done where there is high fever and toxæmia, and staphylococcal septicaemia very often occurs. If the condition is accompanied by severe degree of cellulitis amputation at higher level is called for.

When the condition does not demand immediate surgical interference, the patient should be treated in bed with dry dressings and the condition of the wound carefully watched. If there is improvement especially there is reduction of swelling, a further period of rest may be given.

The level of amputation depends on the general condition of the patient, degree of gangrene present and the amount of arterio-sclerosis as determined by the presence or absence of pulsations of vessels in the leg. The local amputation is done where there is good arterial condition and the degree of gangrene is small. In the old people where the

arterial condition is poor and gangrene is spreading, amputation is above the knee. But if sugar in blood can be controlled, the amputation below the knee may be tried. When there is very rapid spread of gangrene and the patient is toxic to minimise the loss of time, disarticulation of knee is advisable.

In case of emergency the operation is preceded by an injection of 20 to 30 units of Insulin simultaneously with 40 to 60 grammes of glucose intravenously. Spend several days to find a diet which with Insulin clears the urine of sugar and ketone bodies. In the morning of operation, breakfast as usual. Before operation, 30 units of Insulin in 6 % of glucose. Spinal anaesthesia should be tried if possible.

After operation :—Ten units of Insulin with 20 gms. of glucose repeated every six hourly on the first day. Oral feeding should be started as soon as possible.

Fruit juice and glucose after 24 hours. As early a return as possible to the diet established before the operation should be commenced. After the operation, the interval between the Insulin injection must be shorter because anaesthesia shortens the time of Insulin action. Slight glycosuria in post operative period is less serious than hypoglycæmia. The amputation wound dressed with gauze soaked in Insulin.

Cellulitis of the Hand.—The gangrene of fingers due to deficient circulation is rather rare but resulting from severe infection is not an uncommon condition. Generally, we find cellulitis instead of gangrene as a result of minor infection beginning either on the pulp of finger or on the palm. The infection extends upward into the palmar bursa and beneath the anterior annular ligament to the wrist and fore-arm. These patients have as a rule rather a neglectful history of their diabetic condition and the infection they suffer is of a serious nature.

The hand is more accessible to infection than other parts of the body and it is difficult to drain it adequately without destroying important structures. The various tendon sheaths and fascial planes should be known in order to combat the course of extension of the infection and incomplete drainage of a septic focus always results in the extension of the process.

TREATMENT.—Liberal incisions must be made early to prevent extension of suppuration. In the presence of diabetes, prolonged sepsis leads to early sloughing of their tendons and fascia. Such cases should be treated with E. C. Bath and Insulin dressings.

Immediate amputation of hand should not be undertaken unless the patient's condition demands it. With Insulin and proper treatment many patients will respond well. In urgent cases, guillotine type of amputation is called for and Dakin's tube should be placed at the end of the stump for irrigations.

A male patient aged 60, thin and emaciated, admitted with a large collection of pus in the thenar eminence of right hand. The skin on

the back of hand and forearm up to its middle third was sloughed exposing the tendons completely. The patient had a minor infection on the palm and was operated six days back. The patient was running high temperature and toxic. Blood sugar was 48% and urine sugar .27. The diet was controlled and Insulin 60 cc. daily injected with glucose. The hand was put in E. C. bath twice with Insulin dressings. The infection was controlled in ten days' time. Blood sugar came down to 2 % and urine sugar nil. Insulin injection was accordingly modified and a proper diet was established for him so that his urine was sugar-free. His wound responded well to the treatment but he had two attacks of hypoglycæmia.

Some of the cases reported above are published with the kind permission of Dr. H. B. Norrie, M.D., Mch. F.R.C.S., Surgeon Superintendent, Mayo Hospital.

References.

1. Aschoff—*Lectures on Pathology*, New York, Pane B. Hæber, Inc., (1924) p. 213.
2. Folin, Trimble and Newman—*Jour. Biol. Chem.* (1927) p. 75, 263.
3. Hinton—*Ann. Surg.* (1927) p. 85, 104.
4. Joslin, Root and White—*Med. Clin. North America.* (1927) p. 10, 1281.
5. Joslin—*Boston Med. and Surg. Jour.* (1927) p. 196, 127.
6. Joslin, Bloor and Gray—*Jour. Am. Med. Assn.* (1917) p. 69, 375.
7. *Practitioner*—(1939) p. 63, 851.

Diabetes and Sepsis*

BY

T. H. Somervell, M.A., M.B., B.Ch., F.R.C.S.

Neyyoor.

EXCEPT under certain circumstances, diabetes in middle-aged and elderly people may not be incompatible with a very fair state of health. For many such, neither dieting nor Insulin therapy is necessary under ordinary conditions. But when a hand or foot has any septic complication, or in the presence of a carbuncle, diabetes may suddenly assume grave significance. It is of the utmost importance to treat both conditions—the septic focus and the diabetes—with the utmost care and correctness, if the patient is to be spared life and limb.

The treatment of the diabetes itself must aim at keeping the blood-sugar low; in the case of a patient in a country district, or a small hospital without a pathologist, in which estimation of the blood-sugar cannot be done, a rough and ready rule is to keep the percentage of sugar in the urine about 1%, a safe moderate amount, taking frequent specimens of urine for testing both for sugar and acetone. Directly acetone is found, sugar and Insulin must at once be given, and if coma threatens, 40 or 50 units of Insulin should be given, together with 3 ozs. of sugar in water or lime-juice. Low blood pressure must be treated at once by Adrenalin, together with 20 c.c. of a 10% solution of glucose intravenously. It must always be remembered that septic cases are liable to coma and to acetonuria, both of which are grave conditions and demand normal sugar metabolism i.e., Insulin plus sugar, not Insulin alone. In this connection it is right to observe the value and cheapness of sugar in comparison with glucose. Sugar is just as good as glucose for all purposes except intravenous injection, and is far cheaper, besides being easily obtained almost anywhere. The rule to observe, then, with the septic diabetic, is to preserve as far as possible an approximation to normal carbohydrate metabolism, guarding by continual watchfulness against coma, acetonuria, and hypoglycæmia. More will not be said now about the medical treatment, which is dealt with in many other articles in this volume. But as a surgeon, my primary concern is to give advice regarding the surgical side of the treatment of the case.

Carbuncles.—There are three ways in which these can be treated, as far as the use of the knife is concerned.

- (1) Expectant treatment, with Magnesium Sulphate and Glycerine paste applied externally; this should be spread thickly over the whole of the inflamed area, a good Anhydrous paste of equal parts of Glycerine and powdered Anhydrous Mag. Sulph. being used. This is usually the best treatment for carbuncles of face, front of neck, and for the smaller ones on the back of the neck also. Where

*A lecture delivered to the Dist. Medical Association, Trichinopoly—Mar. 1940.

possible, as in the back of the neck, it should be combined with short wave therapy.

- (2) Incisions, crucial in form and each extending to the extreme edge of the carbuncle. The carbuncle is then dressed with strong saline, or with Mag. Sulph. and Glycerine paste, the dressing changed once a day only. This line of treatment, combined when possible with short wave therapy, is best for carbuncles of moderate size, or for large ones on the back of the neck.
- (3) Incision of the skin, with excision of all necrotic tissue, and of all doubtful-looking fibrous tissue, and opening up of all spaces where pus or sloughing exists right to the end of such spaces.

To the wound thus obtained, after hæmostasis of all arterial bleeding, saline (10%) or Mag. Sulph. and Glycerine paste is applied as a dressing. Short wave therapy is very beneficial. This class of treatment is the best for a large carbuncle of the back, abdominal wall, buttock, or other soft tissue, and for any carbuncle which is causing persistent acetonuria or is spreading in the tissues.

Septic Hands.—The treatment of sepsis in the hands, not only of the diabetic but of anyone else, is of supreme importance. Efficient treatment, which is just as easy as inefficient treatment, may save the means of livelihood of a patient, while neglect or carelessness will condemn him to the amputation of his most valuable member, and condemn him to the life of a beggar or an idler. Many doctors do not take nearly seriously enough their responsibility in the treatment of septic hands, and the principles it should follow will therefore be given fairly fully. Except in the case of onychia, sepsis is usually on the palmar surface of the hand, and this locality will be considered first.

I. Palmar Surface.—1. *Finger tip.*—Half an inch below (*i. e.* distal to) the crease marking the distal interphalangeal joint is a septum which extends from the skin on the palmar surface to the epiphysis of the distal phalanx. Incisions for sepsis of the finger can be free, extending if necessary right across the tip of the finger and down each side, parallel with the outline of the finger nail and about a quarter-inch from it all round, but stopping short of the septum. (See Fig. 1).

2. *Fingers, palmar (flexor) tendon sheaths, and radial and ulnar bursae.* (See Fig. 2). The flexor tendon sheaths of the three middle fingers are all confined to the region between the distal interphalangeal crease and the metacarpophalangeal crease on the palmar surface of the hand. If these sheaths are infected, the whole length of this sheath but not more should be incised and laid open in diabetic cases where the sheaths are suppurating. The incision must not be a palmar one, or the case may get contracture afterwards. Incision

must be made along the side of the finger, or if necessary along both sides, laying the tendon sheath freely open, and not going beyond the end of the sheath. If pus exists in the "web", the space between fingers, the incision may continue into the web, opening it well up. But on no account must the incisions extend more than three quarters of an inch beyond the metacarpophalangeal crease, or sepsis may be spread into the great palmar synovial space, or ulnar bursa, and grave damage may be done, as this compartment leads under the annular ligament into the forearm.

3. The little finger has a flexor tendon sheath which extends into the palm and includes, in the proximal half of the palm, all the flexor tendons of the four fingers. Thus sepsis in the flexor tendon sheath of the little finger is likely in diabetics to involve the whole of this palmar synovial space (ulnar bursa), and incision should be made on the medial side of the little finger extending if necessary (it usually is) along this sheath to the wrist, until the sheath stops, its upper end being about half an inch proximal to the end of the ulnar bone. Do not damage the ulnar nerve when making this incision. When the ulnar bursa is involved in suppuration maximum tenderness is usually over the middle point of the hypothenar eminence.

4. The flexor sheath of the thumb similarly extends into the radial bursa, which runs alongside the ulnar bursa and usually communicates with it. This sheath should be opened along the lateral side of the thenar eminence, and a counter-opening made on the proximal side of the anterior annular ligament, extending to three quarters of an inch proximal to the end of the radius. Care should be taken not to damage the radial artery in making this incision. The radial artery is deep to the sheath and need not be touched. The reason for not incising the annular ligament is that the branch of the median nerve to the thenar muscles passes superficial to the radial bursa at this level.

5. The web-space between thumb and first finger can be incised both front and back, the web itself being divided. Care must be taken not to enter the flexor tendon sheath of the thumb, if this is not already involved. If it is, the incision into it can be medial.

6. *Forearm.*—The carpal tendon sheaths, prolongations of those from the thumb and little finger, have already been mentioned as entering the forearm beneath the annular ligament, and terminating half an inch (at least) proximal to the wrist joint. Sepsis, occasionally in neglected cases or diabetics, continues to track upwards from the end of these sheaths. When it does this, it invariably does so in one plane—deep to all the flexor tendons and muscles, and only superficial (anterior) to the bones and the pronator quadratus. (See Fig. 3). The incisions to drain this space should be made along the antero-lateral border of the radius and the antero-medial border of the ulna. These two incisions if necessary can be carried a long way up the forearm, keeping close to the respective bones. In this way, complete drainage of the septic compartment of the forearm can be done without cutting

through a single muscle, or damaging any of the main nerves or arteries. Slashes on the flexor surface of the forearm are inexcusable, and do damage without drainage. Lateral incisions effect drainage without damage.

7. Deep to the tendons of the deep flexors of the fingers, the palm of the hand is divided into two spaces by a fascia which extends from the middle metacarpal to the palmar fascia. On the radial side of this fascial division, is the thenar space, which can be drained (without involving tendon sheaths or other structures), by an incision just radial to the division is the middle palmar space. This must be drained by splitting the web between the middle and ring fingers, and must, on no account, be drained by an incision in the palm of the hand.

II. Dorsal Surface. — 1. *Onychia*. Consists of sepsis near the root of the nail. This usually starts lateral to the edge of the root, and spreads superficial to the root. Two incisions are made, each slightly lateral to the line continuing the sides of the nail across the knuckle, and about half an inch long. (See Fig. 4). The skin of the knuckle is raised so that the two incisions are made to communicate, exposing and draining the whole nail-root. The nail need not be extracted, unless sepsis is also deep to it, and good healing may be hoped for without deformity of the nail. If pus is beneath the nail, the proximal half of the nail must be removed with its root, leaving the distal half in situ to protect the finger from pain and damage.

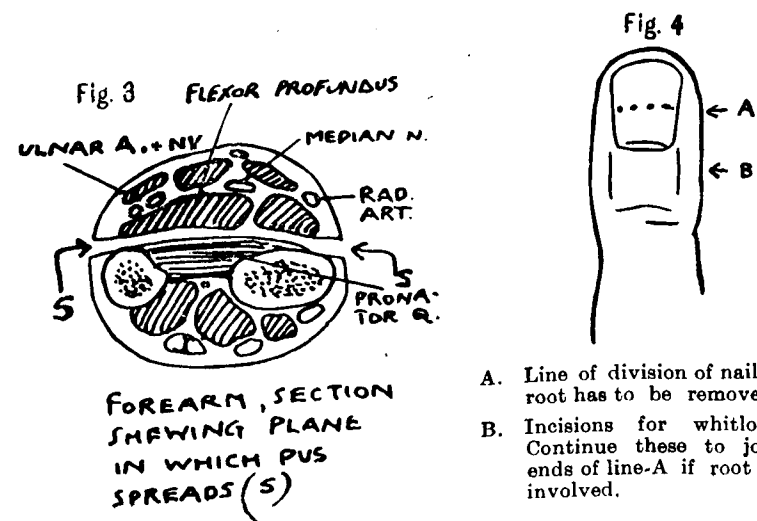
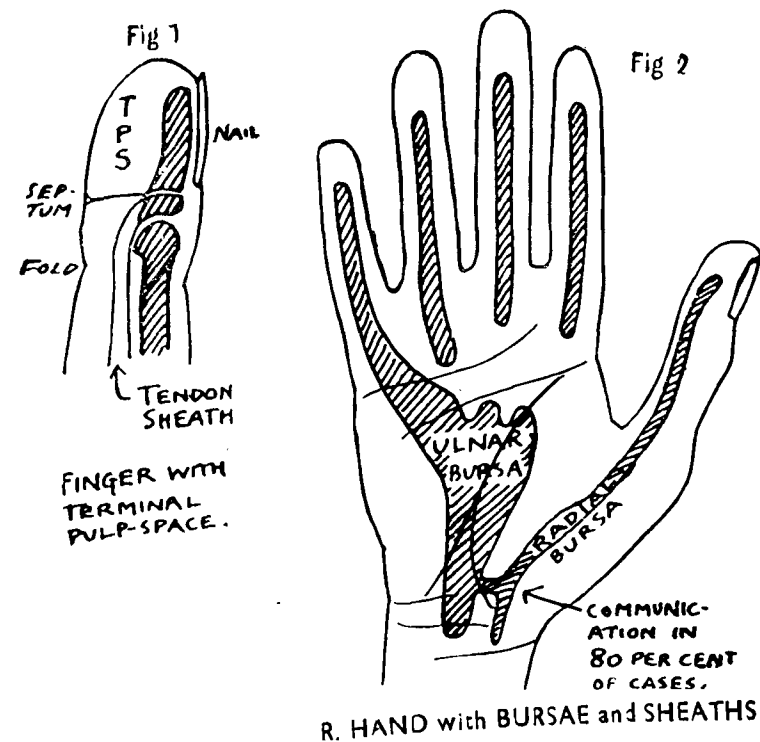
2. *Sepsis in extensor tendon sheaths must be dealt with by lateral incisions* as in the case of flexor sheaths. But, this will rarely have to be done, as sepsis is rare on the extensor side of the hand.

3. A puffy swelling over the dorsum of the hand (metacarpal area) always denotes palmar suppuration. Do not incise this swelling. Look for sepsis on the palmar surface, usually in the large sheath communicating with the flexor sheath of the little finger, or in the middle palmar space. How many of us have incised these swellings on the backs of hands, simply to find nothing except a lot of bleeding?

4. There is, however, a "dorsal space" corresponding to the palmar space on the other side of the hand, and deep to the tendons. Infection of this space may give rise to oedema of the back of the hand, but this feels firm and indurated, not soft and pitting on pressure like the dorsal oedema which accompanies palmar sepsis.

Tendons.—If a tendon sheath suppurates in a diabetic case, and fails to clear up with drainage within a day or two, the tendon will certainly slough, and its continued presence is a danger. It must, therefore, be excised—the whole length of it that is in the sheath being removed. The upper end should be stitched to the tissues around it, to prevent its movement from spreading sepsis further.

III. Some points to be observed:—1. Don't slash, or you may cut important tendons or nerves. Dissect carefully, remembering the



2. Incise adequately. Diabetic septic tracks should always be incised to their very end. I often go an extra quarter-inch for luck.

3. Remove all devitalized tendons. They will not recover, but will slough; remove them adequately, and with a sharp pair of scissors. Don't pull nor tear them, nor cut them with a knife.

4. Use a sharp knife for all work other than the cutting of tendons. Sharp knives do not damage the cut-edges of the tissues.

5. Make all possible use of short wave therapy.

6. Don't use chemical dressings. Saline is the best, as it is non-irritant to the most delicate tissue. Any chemical that will kill organisms will also kill growing, delicate tissues; the days of Carbolic Acid, Eusol, and Mercurochrome are, I hope, over, as far as dressings are concerned. Flavine has its uses, being non-irritant. Hydrogen Peroxide is a great danger to deep tissues, as it opens up new channels for sepsis. The use in deep tissues of Hydrogen Peroxide should be considered a criminal offence.

IV. Splinting and Plaster.—Sepsis in tendon sheaths as well as elsewhere is spread more by the movement of the tendons than by any other factor. To avoid the spread of sepsis and its tracking be obtained by Plaster of Paris. A good "slab" of 4 inch-plaster bandages, 18 inches or so long, is made, and moulded to the dorsum of the hand and forearm, the thumb and fingers being in a comfortable, semi-flexed position. The tips of the fingers, unless they themselves are septic and require incision, are best held by an overlap of the end of the plaster slab, and the hand, as far as possible, (allowing for the incisions to be made), is kept completely immobilised in the plaster splint. In non-diabetic cases, this treatment is even more essential than in diabetics, but in any case of sepsis of fingers, hand, or forearm, immobilisation is the first essential of treatment, and a plaster "slab" is the most effective way of obtaining real immobilisation.

The principles of operating upon the feet in cases of diabetic sepsis and gangrene are, of course, the same as in the hands, but with this great difference, that whereas the preservation of finger movement is the principal consideration in the case of the hand, it matters little in the foot. Stability, strength, and freedom from pain or deformity while walking, are on the contrary, to be considered; but, except for the great toe, absence or stiffness of the toes matters but little. This is just as well, for the foot tends more than the hand to become gangrenous as well as septic, and often toes (with or without their metacarpals) have to be excised bodily for this reason. Amputation of the whole foot is not a very serious affair, as it is in the case of the hand.

The principal points to be observed are as follows:—

The chief tendon sheaths of the foot are separate, each containing but one or at most two tendons. The principal ones—peronei, tibialis anticus and posticus, long flexors and extensors—are channels of

communication from foot to leg and as such, are of great importance to the surgeon. In suppuration of any of these sheaths, the whole sheath must be incised throughout its length at an early stage, and the tendon itself, usually non-viable, removed completely. Only thus will it be possible to avoid the great tragedy of a diabetic foot—spread of the sepsis to the leg, where pus tracks rapidly upwards if once the leg be involved. Incisions must be planned as in the case of the hand so as to limit the sepsis—i.e., incisions of tendon sheaths must never penetrate the plantar or similar fascial spaces, and *vice versa*.

As in the case of the hand, a soft, œdematous swelling of the dorsum of the foot always suggests sepsis in the deep plantar space.

Amputation of the leg at the point of election should be done if the foot is irreparably riddled with pus, or is gangrenous, and foot amputations such as Syme's should never be done. For, in diabetic cases, they are never successful. A foot badly crippled by incisions and amputations of toes etc. can be amputated later if it is a bad orthopædic proposition after all sepsis has subsided. Never delay amputation when it is once indicated. In doing an amputation at the point of election, if sepsis is found to have tracked up to the site of operation, the surgeon must at once change his tactics as well as his gloves, and amputate the limb above the knee. In many cases, I have sewn the flaps up and the wound has healed by first intention; but only if the whole operation is definitely above the level of all septic spaces. Finally, if short wave therapy is available, it should be given to all cases of diabetic sepsis of foot or leg.

Prognosis and Treatment of Infections of Hand and Foot in Diabetes

BY

Capt. D. Kanakasabesan, M.S., F.R.C.S.E., A.I.R.O.
Professor of Surgery, Stanley Medical College, Madras.

INFECTIONS of the hand and foot are frequent and come under the care of the general practitioner at first; while the majority of such infections resolve under prompt treatment, their potentialities for spread and serious damage, resulting in dysfunction, total loss of limb or even death, are great. In the case of diabetics, such untoward complications, sequelæ and terminations are well recognised to be even more frequent and disastrous. It is the province of this paper to indicate the prognosis in such cases, and present a practical guide for the treatment.

Prognosis.—The different degrees and grades of infection are to a certain extent dependent on the site of infection and the virulence of the invading organism; there is, therefore, a great diversity in prognostic significance. Diabetes, however, profoundly alters the already complicated clinical course, and makes the prognosis much worse. To put it tersely, we may say that diabetes predisposes to trauma and infection; and these in their turn aggravate the diabetic state; a vicious circle is, therefore, brought into play, so that an otherwise trivial infection may culminate in disaster.

The special considerations which influence the prognosis may be grouped as follows: (1) general considerations; (2) anatomical and physiological factors; (3) the course of diabetes; (4) the general health of the patient.

General considerations:—Age: It is a matter of special significance that the young diabetics appear to fare worse than the old; while one would naturally expect a more vigorous response and resistance to infection in the younger patients. The explanation for this lies in the fact that frequently, in the latter type of patients, the diabetic state is probably not anticipated or recognised till the infection is well established and probably neglected or mismanaged. It is also probable that the older patients lead more protected and less arduous lives, and are, therefore, careful enough to avoid the numerous minor traumata, resulting in breaches of skin offering portals for infection. A third point of note is the fact that the course of diabetes in the young is more malignant than in the old.

Site:—Infections of the hand are more favourable than those of the foot as (1) there is relatively better blood supply; (2) the hand being nearer the heart, venous drainage is more satisfactory; (3) sensation being better, the part is less liable to trauma, and where infection has set in, sooner likely to attract attention; (4) the hand is better protected than the foot which, particularly in our country, is more

susceptible to trauma, minor injuries and contact with dirt. Apart from the above considerations, there is a great variation in the local inflammatory reaction and tissue response between any two areas dependent on the following factors:—(1) thickness of the skin; (2) the arrangement and nature of the subcutaneous tissue; (3) local susceptibility to pressure, e.g., corns, callosities, etc.; (4) distribution of tendons and the extent of their fibrous or mucous sheaths—particularly offering convenient lines for extensions of infection; (5) the fibrous septa between tendons or muscle bellies influencing the course of spread, and lastly (6) the vascular twigs piercing the connective tissue or muscular planes to effect collateral channels between the dorsum and the plantar aspects of the extremities providing channels for spread.

Co-existing lesion:—Alcoholism, tuberculosis, syphilis, chronic gonorrhœa and leprosy, when they co-exist, aggravate the diabetic state and make the prognosis worse.

The condition of the *cardio-vascular* system determines largely the scope of the inflammatory response that may be forthcoming; a very valuable guide to the probable spread or progress of the disease will be found in the character of the local pulse as compared with the opposite side. Pulseless, painful feet, blanching quickly on elevation and becoming deep red to purple when dependent, indicate primary arterial insufficiency, and these should be carefully distinguished from those primarily due to infection, where the circulation may be adequate but not normal. Low blood pressure and myocardial degeneration are distinctly unfavourable and infections in such patients are prone to be spreading in spite of early and prompt treatment. Streptococcal infections in particular go on quickly from lymphangitis to phlebitis and thrombosis.

Skin:—The condition of the skin is often suggestive of the nature of the prognosis; if it is dry and harsh or moist and greasy, both are equally unfavourable. The presence of numerous pimples, acne, boils or other skin eruptions like ringworm and eczema, are also signs of lowered vitality and indicate poor response to infection. It is not uncommon in such cases to find other foci of suppuration starting up at the sites of hypodermic or intra-muscular injections.

Nerves:—The existence of peripheral neuritis materially affects the course of infection. Impaired sensation in the distal portions of body, the tips of the fingers and toes, might predispose to minor injuries with skin abrasions which may go undetected, till the infection is well established. A point of great importance is the fact that such limbs or extremities may be still more damaged by the injudicious applications of fomentation or local dry heat, e.g., the hot water bottle. It is not uncommon to see numerous ants when the dressings are removed, patient being not even aware of them. The presence of marked peripheral neuritis is, therefore, distinctly unfavourable.

Infecting organisms:—The nature of these is also of great significance. Streptococci with their predilection for causing lymphangitis

and diffuse cellulitis, are particularly unfavourable, while the presence of anærobic organisms like the *Bacillus Welchii*, primarily or acting in symbiosis with other organisms, makes the out-look still more gloomy.

Infections associated with injuries to the bones such as severe crushes or compound fractures involving the bones of the hand and foot, are very serious and call for prompt amputation in the majority of instances, particularly more so, in the case of the lower limbs.

Multiple foci of infection or the presence of metastatic pyæmic manifestations indicate a very grave prognosis.

The diabetic state and the response to Insulin therapy and dietetic regulation determine to a large extent the course of infection. If a patient, put to bed on admission, with limbs slightly elevated and administered, does not show visible signs of improvement both locally as well as of the urinary state, it may be presumed that the infection has probably spread beyond the limits of the local site of entry and has produced systemic poisoning. Such cases should be presumed to be septicæmic and amputation will have to be seriously considered. The condition of the urine—marked and persistent ketosis in spite of large dose of Insulin—is indicative of impending coma. Another disquieting factor is the co-existence of albuminuria indicating renal impairment.

Treatment of Infections.—The general principles of treatment may be summarized as follows:—(1) Relief of tension and promoting drainage (2) Increasing the patient's resistance (3) Control of diabetes.

The general principles of wound treatment are those that are applicable here also; but as we have the patient's resistance considerably lowered in diabetes, greater attention has to be paid in trying to secure increased resistance by mobilizing all the existing protective measures of the body—rest, improved circulation, induction of hyperæmia, supportive measures, prompt removal of waste products, and improving carbohydrate metabolism.

Next in importance is the correct diagnosis of the nature and location of the infection. It is important to differentiate between a diffuse spreading infection in the cellular tissue from a localised infection of one of the closed spaces, tendon sheaths or superficial subcuticular infections. While it is imperative to make an incision early in localized infections to prevent their spread, it may be disastrous to incise in a rapidly spreading streptococcal infection. To err on the safe side, in such cases, the surgeon must stay his hand till he is certain that the infection is tending to localise.

I have found the following outline of procedure to be of great help in guiding one in such cases:—

- (1) Record the temperature, pulse and respiration.

- (2) Weigh the patient if possible.
- (3) Note the state of the skin, tongue and the teeth.
- (4) Note the exact local condition—colour, temperature, swelling, œdema, ulceration, blebs, sloughing—and the voluntary movements of the fingers, toes and the neighbouring joints; note also the presence of any enlarged glands in the neighbourhood and evidence of lymphangitis.
- (5) Examine the heart, the great vessels, and the radial pulse. Take the blood pressure; ascertain the local pulse in the affected region, and compare with the opposite side; note any change in appearance of the limb on elevation or dependency.
- (6) In serious and bedridden patients, and in fat, flabby patients, look out for basal congestion of the lungs.
- (7) Examine the abdomen for evidence of distention, tympanites, rigidity, and tenderness.
- (8) Examine the urine in detail and chart it, and maintain it during the course of the illness.
- (9) Arrange for a blood sugar estimation, and if possible have it repeated twice weekly, to be a check on the urinary record.
- (10) Make a bacterial examination of the exudate.

Preliminary Treatment.—1. Hospitalise the patient if a working man, or institute nursing facilities.

2. Give him a sponge bath,—then only can one find out the true state of the skin.

3. Put him on his usual diet for 24 hours only, and regulate his diet after the 24 hours, ensuring an adequate calorific value—with a liberal supply of easily assimilable carbohydrates, and minimum amount of fat.

4. Elimination of toxins—mild saline purge, unless there is diarrhoea, or the patient is extremely dehydrated and toxic.

5. Put him on an alkaline mixture:—In the presence of marked ketosis, give very large doses of alkalis.

6. Give him, to start with, 20 units of *Insulin* t.i.d., followed by 1/2 oz. of glucose, and study the behaviour of the urine to this dosage, and thereafter regulate the amount of *Insulin*, taking into consideration—(1) the amount of sugar lost per day, (2) the quantity of urine passed in the 24 hours, (3) the weight of the patient, and the total calorific value of the food he ought to take (4) and the presence of other abnormal ingredients in the urine—e.g.—acetone, diacetic acid, albumin, pus, etc.

The progress of a diabetic case can be completely recorded as follows, as it will help the determination of the diet to be allowed, the amount of sugar wastage and the required dose of Insulin.

[illegible]

7. In cases of gas gangrene, give promptly a dose of commercial anti-toxin for *B. Welchii* and other anaerobic organisms.

8. If streptococcal, give the patient 1 to 2 tablets of M. and B. 693 or other Sulphanilamide preparation, t.i.d., and watch its effect.

This 24 hours general plan of treatment gives one the opportunity to decide (1) whether the infection can be localised (2) the extent of involvement, whether confined to fascial spaces, tendon sheaths or sub-cutaneous cellular tissue, (3) the nature of the infecting organism and (4) response to the preliminary Insulin treatment, which will give us an idea for regulating the dosage of Insulin and the course of

The most important step in promoting localisation of the infection even in the presence of an advanced degree of ketosis is (1) to relieve tension by making a suitably large and free incision into the affected area without endangering any of the overlying vessels, tendons or nerves and without infecting any other spaces or compartments not already involved and (2) thereafter, to secure perfect immobilisation of the limb. The course of palmar infection depends chiefly on the original site and nature of infection and usually, it is confined to one of these three main divisions (1) Subcutaneous cellular tissue—taking on the type of lymphangitis and diffuse cellulitis or

(2) tenosynovitis or (3) infection of one of the fascial spaces. The infection is usually confined to one of these anatomical areas until the tension has been increased so much that it has to burst into neighbouring spaces or the surgeon, by careless and indiscriminate incisions, has infected the neighbouring regions. The extent of incision will therefore, depend upon the correct anatomical location of the extent of the original infection. The following facts will guide one to determine where the infection is :

- (1) The site of maximum swelling is not necessarily the site of the pus as the degree of swelling depends upon the amount of loose cellular tissue. To illustrate this, with plantar and palmar infections the swelling is more marked on the dorsum than at the site. Ill advised incisions, therefore, on the dorsum are likely (a) not to relieve tension (b) to increase the area of infection and (c) to add trauma to the already existing toxæmia.
- (2) Careful palpation will reveal the maximum point of tenderness as also a careful observation of the patient's voluntary movements of the fingers and toes and their restriction.
- (3) Local colour changes and œdema should not be relied upon as accurate guides in determining the site of infection. The points of maximum pain and tenderness are of more value than the above changes.

In planning incisions into the infected areas, the infected spaces should be opened up in such a way that maximal drainage is secured while promoting collapse of the walls of the emptied cavity. There should be no necessity for leaving gauze packs or big drainage tubes if sufficiently large incisions are made; at the best, a glove-piece or a thin strip of corrugated rubber drain well soaked in sterilised Paraffin may be kept in for a day or two. Every effort should be made to dispense with these drainage materials as early as possible; free drainage can always be secured by continuing moist warm applications or local applications of Ichthyol and Glycerine. When possible, to prevent maceration of the epithelium instead of moist applications, it will be an advantage to have the use of the Ultra-Therm if available, which will secure a greater degree of penetrating heat without scorching the skin. During the operations, particular care should be taken to see that septic material is not rubbed into the tissue spaces and vascular channels by rough-handling, tearing, or bruising; the thin walled delicate veins are particularly susceptible to injury and will react when rough-handled by promptly undergoing intravascular clotting and probably allow infected clots to be milked up along them and distributed into the circulation.

Immobilisation.—Immediately after the incisions, the limbs should be immobilised by a properly applied supporting plaster cast; this should be so arranged that the dressings can be changed without disturbing the immobilisation. For the hand, a dorsal plaster cast with finger splints should be applied to the forearm while the whole

arm is laid on an abduction splint. In the case of the foot, a similar plaster cast should be applied; this should be suitably interrupted by incorporating in it wire splints opposite the wound areas and the whole limb should be suspended on a cradle. This immobilisation prevents muscular contraction and spasm, and the milking of the veins with every movement. Slight elevation of the limb, not more than 6" above the horizontal promotes venous drainage, while it will not seriously affect the arterial flow. Nothing should be allowed to disturb this immobilisation as long as there is inflammation—in fact it might be several weeks. Frequent dressings should be as far as possible avoided as they are likely to cause pain, to disturb healing and to promote spread of infection. Careful watch should be kept on the temperature, the local skin for œdema, and neighbouring lymph glands for signs of extension or subsidence. If drainage has been adequate and tension has been released, the temperature should drop down, the limb should show signs of shrivelling and the neighbouring glands become painless. Even within a space of 24 hours, it is possible to determine whether the infection has settled down or not; there may be a perceptible reduction in the amount of sugar in the urine while the ketosis should certainly disappear.

In a certain percentage of cases, however, inspite of prompt incisions to relieve tension, adequate immobilisation and suitable drainage, there is an absolute lack of local tissue response. These are the cases of malignant diabetes and probably require more serious surgical measures, further incisions and counter-incisions or even amputation of the limb.

Antiseptic baths: These are mentioned only to be considered as absolutely unnecessary and harmful in the majority of cases. There may be a few cases where it may be advantageous to immerse a foul limb for a few hours, but the disadvantages of having a sodden limb and re-infection from the bath are more than sufficient to argue against them.

Drug Treatment.—The use of Sulphanilamides in the case of streptococcal infection, has revolutionised the treatment of sepsis. A course of 12 to 18 tablets at the rate of 1 to 2 tablets, 3 times a day, may be given; but every patient should be studied carefully for signs of intolerance.

The details of incisions etc. are not specially mentioned in this article as they are available in all text books of Surgery.

LEUKOPLAST ELASTIC

Superior in

ELASTICITY AND ADHESIVENESS

Leukoplast elastic is prepared with the same unequalled plaster base as Leukoplast and possesses the same excellent adhesive and keeping properties.

Increased elasticity is attained because the woven edge which retards stretching is cut away. Greater compression and support is possible.



MADE IN ENGLAND

by

HERTS PHARMACEUTICALS
LIMITED

Welwyn Garden City,
Hertfordshire.

*Sole Agents for
India & Burma:*

GILLANDERS ARBUTHNOT &
COMPANY

8, Clive Street,
CALCUTTA.

Branches at:—

BOMBAY, MADRAS, DELHI,
LAHORE, and RANGOON.

★

FRESH LIVER & SPLEEN
for bloodbuilding

COD LIVER OIL
for its food value

MALT EXTRACT
for its nutritive influence

HYPOPHOSPHITES
for remineralization

A Tonic and Reconstructive of Exceptional Efficiency

Waterbury's Compound is the preparation of choice as a tonic and reconstructive at every age period and at every season of the year. Its unusual palatability, appeals to all—there is no oily taste or odour.

WATERBURY'S COMPOUND

Supplied PLAIN, or with Creosote and Guaiacol.
A bottle of each form is at your service.
May we send them?

MARTIN & HARRIS LTD.,
Mercantile Buildings, Lall Bazar, CALCUTTA.
Also at Bombay, Madras, Karachi and Rangoon.

Made by Waterbury Chemical Co., Inc., New York and St. Louis, U.S.A.

When writing to advertisers, please mention the "Antiseptic"



A Call for Help

Veganin Tablets present acetyl-salicylic acid, phenacetin and codeine in synergistic combination, whereby the individual action of each constituent is greatly enhanced.

Veganin Tablets are not advertised to the public.

Supplied in tubes of 10 and 20

A trial supply to Physicians on request.

MARTIN & HARRIS, Ltd.
Mercantile Buildings,
Lall Bazar, CALCUTTA.

Also at Bombay, Madras, Karachi and Rangoon.

THE CALL OF PAIN

The call of pain is seldom stilled, and relief is of primary importance to the suffering patient. The paroxysmal pain of dysmenorrhœa, the persistent and intense throbbing of migraine, the shooting pains of neuralgia, the pain in affections of the bones and joints, the pain resulting from accidents—all these, and many other conditions, yield with impressive readiness to the sedative and analgesic efficacy of Veganin. With Veganin there is no systemic disturbance, no habituation. It may therefore be safely entrusted to the patient as a dependable means of relieving and preventing pain.

VEGANIN TABLETS

Prepared by
WILLIAM R. WARNER & CO. LTD., LONDON, ENGLAND

When writing to advertisers, please mention the "Antiseptic"

THE RESEARCH LABORATORY.

Telegrams: "IMMUNITY"

MADRAS.

Telephone: 3213.

BLOOD, SPUTUM, URINE, FAECES and other pathological materials examined microscopically, bacteriologically and chemically. **VACCINES, STOCK AND AUTOGENOUS**, prepared.

WIDAL, WASSERMANN AND KAHN'S TESTS
Compliment fixation test for tuberculosis etc. done.

STERILE SOLUTIONS FOR INJECTION: (e.g.) Calcium chloride, Camphor in oil, Emetine, Hexamine (intravenous), Ferri-Cacodyl, Quinine Bihydrochlor, etc., etc., in stock.

Special solutions made up on request.

Glass slides, capillary tubes for Widal, Sterile capsules for Wassermann test, Culture Media for preparation of Autogenous Vaccines supplied on application with direction for their use.

Laboratory stains in common use supplied in solution according to standard formulæ.

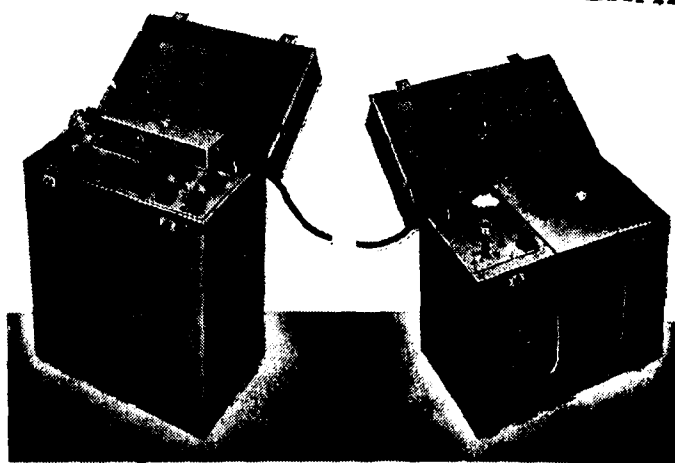
For scale of charges and other particulars apply to:

The Manager,

RESEARCH LABORATORY.

Harris Road, Mount Road, P. O., Madras.

COSSOR - ROBERTSON ELECTROCARDIOGRAPH



Developed through the collaboration of physician and engineer, this practical and reliable Electrocardiograph has many unusual advantages. Continuous visual and photographic recording is a unique feature indispensable for accurate and thorough diagnosis. Of all recording devices, the Cathode Ray Tube (as used) alone can produce an instantaneous two-dimensional and true picture of the heart potentials.

Simple • Silent • Portable • Rapid Direct Visual Observation •
Distortionless Automatic Photo-Recording • Universal Operation

Full technical details and prices of equipment for A. C. Mains and Battery use will be gladly supplied on application.

Sole Distributors in India:

THE SCIENTIFIC INSTRUMENT CO., LTD.

5A, Albert Road,
ALLAHABAD.

240, Hornby Road,
BOMBAY.

11, Esplanade East,
CALCUTTA.

30, Mount Road,
MADRAS.

When writing to advertisers, please mention the "Antiseptic"

Management of Surgical Diabetics

BY

S. N. Choudhury, M.B.,

Assistant Surgeon, Chinsurah, Hooghly.

THE treatment of surgical diabetic has undergone considerable changes during the past 20 years. This has been the result of more intimate co-operation between the physician and the surgeon—one controlling the blood-sugar as required, and the other trying to prevent the onset of the disease. The control of blood-sugar is done by dietetic restriction and Insulin. Insulin has its greatest usefulness in severe diabetics who cannot be brought under control by diet restrictions, and in the treatment of diabetic coma as well as in cases where no time can be lost for controlling diabetes, in other words, in surgical emergencies.

In pre-insulin days, the death rate of diabetics from surgical diseases was about 10% and from coma about 50% or over. But, after the introduction of Insulin, death from coma has come down to about 20% and death from surgical diseases has gone up to about 30%. So, the death rate in diabetes has become more a surgical problem than a medical one. Preventive surgery has a vast field here and much can be done to ameliorate human sufferings.

The pathological processes involved are: diabetes, arterio-sclerosis and infection. These act in a vicious circle and the rationale of treatment is based on a differentiation of the relative importance of these three pathological processes and elaboration of the ætiological factors involved.

Diabetes produces a profound disturbance in the metabolic processes of the body; and the tissues, with faulty carbohydrate metabolism, fail to respond to injury as they should in normal individuals. Thus, the altered metabolism must be corrected. Time permitting, diet restriction and Insulin regimen may be brought into play to control diabetes; but if no time is available, emergency measures are to be had recourse to, preceding or during operation, to ward off diabetic coma or acidosis.

Acidosis:—HENDERSON has said, "Any modification of normal equilibrium between acids and bases within the organism whereby the power to neutralise acid is diminished, is to be regarded as a condition of acidosis."

Acidosis may be a sequel to many diseases—both medical and surgical, but in diabetes, it reaches its maximum intensity. In diabetes, the acid or ketone bodies—diacetic acid, beta-oxy-butyric acid and acetone—have their origin in the perverted metabolism of fats and proteins. This is brought about by the oxidation of insufficient quantity of glucose. Thus, the factors which may produce acidosis are:—

- (1) An insufficient amount of carbohydrate in diet resulting in an increased fat and protein metabolism.
- (2) Lack of oxidation of available carbohydrate which may be corrected by Insulin.
- (3) An increased protein and fat metabolism due to fever hyper-thyroidism, etc.

The main factors in the prevention of acidosis are :—

- (1) Glycogen stored in liver and muscles.
- (2) The carbohydrate of the diet which is available for combustion.
- (3) The extra carbohydrate which can be administered and oxidised by Insulin.

Thus, it is seen that factors (1) and (2) have limited uses and we have to depend mainly on Insulin or Insulin and glucose as the chief means of protection against acidosis.

Insulin.—Insulin is able to combat acidosis where it is imminent. Though it is not a cure for diabetes, yet with its judicious use, the amount of diet can be increased to the desired caloric value—thus giving sufficient food for utilization and storage by the patient. This naturally leads to proper balancing of proteins, fats and carbohydrates with improvement in the general nutrition of the patient. This leads to increase in tissue resistance or, in other words, the resistance of the body against infection. Glycogen is stored in liver as a result of extra oxidation of glucose by Insulin and this ensures against acidosis in the operative period. As blood sugar is brought under control, polyuria is cut short and dehydration is checked. This checking of dehydration is another factor which works favourably in infective condition in patients who are already below par.

Thus, Insulin acts indirectly in surgical affections of the diabetics and it has no direct effect on infection.

Infection and Diabetes.—Infection is one of the bug-bears of diabetic life. The lowered tissue resistance of the patient allows a very mild infection to hang on and a negligible neglected tissue damage may spread hour by hour and day by day, till it endangers life. Further-more, as infection spreads, blood sugar increases and so a definite vicious circle is established—diabetes lessening the local and general resistance of the body, and the infection lowering the sugar tolerance of the diabetic.

How diabetes lowers the resistance of the body is not known yet. This sudden decrease in the sugar tolerance of the diabetic rapidly improves as the infection is removed.

Diabetes and Arterio-Sclerosis.—The changes in the different layers of the vessel wall in the diabetic and the non-diabetic types of arterio-sclerosis are almost similar, and the differentiation is only one of degree of involvement of the different layers. In the diabetic type

intimal changes predominate. The lumen of the peripheral vessels are almost occluded by the lipoid-filled endothelial cells.

Diabetics are generally obese and diabetes generally occurs at an age which may be called arterio-sclerotic age period. At such an age, the non-diabetic is also liable to develop arterio-sclerosis. Diabetes may or may not start the game, but there is no doubt that the final changes in the vessel wall are influenced by the deranged metabolism of the diabetic.

Diagnosis.—The difficulty in diagnosis lies in (1) recognition of the diabetic in the presence of what appears to be a primary surgical condition and (2) recognition of the surgical condition in the presence of diabetes. In frank cases, one is not faced with any difficulty whatsoever, but in border line cases and in cases where previous history of the patient is unknown or inadequate, one has to pause and think, correlate the laboratory findings with that of clinical findings and past history of the patient, if any, and then decide which is the primary condition and to what extent each is responsible for the present state of the patient.

If glycosuria is present—it does not mean that the patient is a diabetic. It might be merely a temporary glycosuria. However, the golden rule is to level such a case as diabetic and treat it as such until the case proves to be a non-diabetic one.

Normal urine contains reducing substances and if the concentration reaches a certain limit, a positive test may be demonstrable with Fehling's or Benedict's solution. This increased concentration of the reducing substances in urine may be the result of dehydration by excessive elimination of water or by reduction of fluid intake. One thing is certain that these normal reducing substances very rarely go above 0.5%.

There is possibility of a transitory glycosuria of nervous origin or renal glycosuria may be present. A long history of sugar in urine—very little fluctuation in concentration, absence of diabetic symptoms, no relation between carbohydrate intake and blood sugar or urinary sugar—all suggest renal glycosuria.

A fasting blood sugar above 0.14% or a blood sugar limit above 0.17% after a meal, indicates that the patient is probably a diabetic. In such a case, if time permits, a sugar tolerance test should be done or blood sugar estimated; but if blood-sugar estimation is not possible, sufficient information can be gathered from finding out the quantity of sugar in the different samples of urine. One must remember that owing to a low carbohydrate diet or owing to fasting, a severe diabetic may have a little or no sugar in urine and so mere examination of one sample of urine without a full history of the case, may be very misleading. If urine is sugar-free, it does not mean that the patient is a non-diabetic. Thus, one should make a definite enquiry about previous diet and treatment before the result of the urine examination can be accepted as a true guide.

It is easy to diagnose a comatose condition in a diabetic but it may be very difficult to find out if the condition is not due to septicaemia, toxæmia or any other disease associated with diabetes or a disease that causes coma and glycosuria at the same time.

The body as a whole reacts abnormally in a diabetic. The pulse, temperature and white blood count respond very slowly in a diabetic, naturally as the defence mechanism is below par, one must remember that in the presence of infection, there is (1) little tendency to localisation, (2) necrosis is more extensive than what meets the eye, and (3) the patient is liable to septicaemia which may creep in insidiously. This shows how important it is to do a blood culture in infected diabetics who are on the verge of acidosis.

Prognosis.—Diabetes is a complication which affects adversely the prognosis in every surgical case, and particularly, where operation is performed; such a patient is always a bad risk. Best results are obtained where the physician and the surgeon co-operate and laboratory facilities are available. The ideal place for treating such cases is, of course, the hospital.

The post operative complications, most feared in the diabetic, are acidosis and coma. Faulty carbohydrate metabolism leads to diminished tissue resistance as already stated and so the chance of wound infection is great. In many of these cases there exists a varying degree of arterio-sclerosis and so healing of wounds by first intention may not take place. Lastly, the patient's mind is full of pessimism, and, unless the surgeon can alter the mental attitude of the patient, the outlook is not at all bright. The common causes of death in these cases are arterio-sclerosis, sepsis, lung embolism and broncho-pneumonia. After the discovery of Insulin, death from coma has become rare.

Treatment.—The cases fall under two groups:—(1) Those which require immediate operation and (2) those which may require operation at a subsequent date. Emergency cases are always bad risks.

CRILE says, "The cardinal principles in the treatment of a bad-risk-patient may be briefly recapitulated as follows:—

- (1) Apply restorative and conserving measures in advance of emergency.
- (2) Supply water and electrolytes by means of saline infusion or by hypodermoclysis.
- (3) Excepting in the presence of jaundice during the acute stages, give Morphine to induce mental and physical rest. After the acute stage is passed, use other narcotics as required.
- (4) Give a transfusion of blood before, during and after operative procedures according to indications.
- (5) Avoid inhalation anaesthesia as far as possible; if required, use Nitrous Oxide-Oxygen to stage of analgesia, relying principally upon local or regional anaesthesia.

- (6) Apply, promptly and efficiently, measures indicated by the special condition which requires relief, but in acute stages, do as little as is required and wait until sufficient restoration has taken place for major procedures to be performed.
- (7) Finally and of prime importance, avoid cooling of the organism as a whole and of the liver in particular by the application of diathermy before and after operation and throughout the course of the disease as indications may demand."

In former days, surgeons shunned all operations on diabetics but now-a-days, it is possible to undertake all kinds of operation as safely or almost as safely as in normal persons. However, one must remember that a diabetic patient is still a diabetic in spite of Insulin therapy, and that a surgical operation even in best hands may have a disastrous result.

Insulin provides an effective means for controlling hyperglycæmia and for preventing and treating acidosis and coma. Uninfected wounds in diabetics, where diabetes has been controlled by Insulin, unite always by first intention and I think vitamin C has a distinct use in these cases in preventing break-down of newly formed granulation tissue. Where healing is not taking place or the granulation looks unhealthy, I have found Padutin injections very useful. In cases where mild infection is present, Insulin and conservative surgical measures often lead to complete subsidence of the inflammation. Where infection is severe, a vicious circle is established and Insulin and conservatism do not show the same tendency to recovery.

It is difficult to outline an exact method for the pre-operative preparation of a diabetic patient or for the post operative care. In non-urgent cases, after determination of blood and urine sugar and plasma-carbon dioxide, a balanced basal metabolic diet, Insulin dosage and method of its administration should be worked out. Unless the Insulin dosage is very carefully regulated in accordance with blood and urine analysis, disaster may result. Hyperglycæmia should be brought under control. If possible, it should be brought to normal limits and maintained there. There should be no ketone bodies in urine. As the infection comes under control, the same amount of Insulin may not be necessary and so regulation of Insulin dosage becomes more and more important and the dose should be modified in the light of blood sugar values.

In cases where immediate operation is indicated and the patient is already comatose, sufficient Insulin should be given immediately, if necessary 100 units or even more and in severe cases even 300 units may be necessary, in the first twenty-four hours, depending upon the blood-sugar estimation.

If operation is immediately necessary in a moderately severe diabetic who is not in coma, Insulin should be given immediately before or just after the operation. I have used glucose combined

with Insulin before operation with good results. If some delay is possible, blood and urine analysis should be done and Insulin or glucose and Insulin should be administered accordingly. Later, it may be possible to make urine sugar-free by controlling the diet but ketosis should always be avoided. Too much diet restriction is decidedly bad for the patient. He should rather have a well-balanced maintenance diet with at least 1 gramme of protein per kilogramme of body weight. Protein at least one gramme per kilogramme of body weight is found to be necessary for proper healing of wounds and adult patients should have at least 3 litres of water per day.

Anæsthesia.—A good general anæsthesia has much to do with regard to success in any operative procedure. The choice of anæsthetic is more important in persons with deranged metabolism. Any general anæsthesia causes a certain amount of acidosis and metabolic derangement, particularly the metabolism of the carbohydrate. It also alters renal function. Thus, respiration is indirectly affected. This upsets the acid base balance of the body and patient suffers from acidosis—the degree of it depending upon the adjustment the body mechanism is capable of.

Even with a healthy kidney, after a general anæsthesia, the excretion rate may fall 20 to 25 per cent and where a kidney lesion is already present, this drop may be even more. In cases where the excretion of ammonia is hampered, the alkali reserve of the body is diminished. It has been found out that after a general anæsthesia, the blood-sugar level goes up and products of incomplete oxidation are found in the blood. Ether may as well diminish the quantity of Insulin in blood in man as it does in animals. So, Chloroform and Ether should never be used. Local, block or spinal anæsthesia should be used wherever possible. Spinal anæsthesia can only be used below the level of umbilicus in these cases and it has another disadvantage that it reduces blood-pressure. This reduction in blood pressure may be combated by the use of Ephedrine-Hydrochloride injections. If inhalation anæsthesia is to be used, Gas and Oxygen or Ethylene anæsthesia may be used. I have found a 0.5 % Novocaine infiltration anæsthesia or block anæsthesia *without Adrenalin* very useful.

The operation should be carried out rapidly with the minimum of trauma to the patient and the wound should be as simple as possible.

Diet.—The diet should be of known caloric value. Blood-sugar should be estimated daily. Twenty-four hours sample of urine should be tested for quantity of sugar and presence of ketone bodies. In emergent cases, diet restriction cannot be carried out; so it is better to order the maintenance diet with Insulin. Where time permits, a diet standard should be reached by controlling diet but starvation or too much diet restriction should never be done as diabetics are prone to develop acidosis and coma. It is far better to work down than to work up the balanced diet scales. These diet scales should be handy showing the total caloric values of the food stuff. The regulation of

diet or of diet and Insulin, as the case may require, is very important and the physician is of great aid to the surgeon here.

Medical diathermy apparatus is a very good source of heat energy in the treatment of hypo-thermia, but in India, its application is only possible in city hospitals where electricity is available. The same object can be reached by hot water bags or bottles. Bottles should be well covered with flannel jackets and applied over the extremities and liver area. The guide is that the patient's body heat should never be allowed to go above 100°F. This heat treatment of hypothermia should be continued once a day till the patient is cured.

Preventive Hygiene.—The prevention of surgical diseases in diabetes is now-a-days receiving more consideration than in the past. Diabetics are coming more and more for advice and treatment and the physicians are in a position to help them by explaining the hygienic principles that should be observed by them.

They should be advised to keep themselves as clean as possible and should seek medical advice for any injury or disease, however trifling it may seem to the patient.

As to diet and Insulin, they have already been dealt with.

The diathermy treatment for hypothermia should also be carried out for diabetics with subnormal temperature even when they are otherwise keeping fit. This improves the temperature and the patient feels better. The effect lasts for about 6 months to one year.

Attention to bowels is also necessary. Even where a diabetic is brought under control by diet restriction or by diet and Insulin, his bowels should be kept open lest toxic absorption may take place from agnant, decomposed or partly digested food materials there.

Dental hygiene is also important and all dental sepsis or decaying eth must be removed. The patient should receive full instructions to how to keep his mouth and teeth clean, and if necessary, should be referred to a dentist.

Pyogenic Infections in the Diabetics

BY

Capt. J. M. Ghosh, M.B., (CAL.), D.T.M. & H., (CANTAB),
D.P.H., (LOND.),
Katmandu, Nepal.

ORDINARILY speaking, a diabetic diagnoses his own condition, when he comes with the history of polyuria, thirst, and having swarms of ants in or about his urinal. Urine is examined and sugar found.

One word about the urine examination. Sugar may not be found in every sample of urine that is passed, and so it should be looked for in a 24 hours' collection, if not found in a particular sample. It should be borne in mind that calcium oxalates, mucous, urates etc. may cause Fehling's to change colour, and hence in doubtful reactions, Benedict's, or charcoal test should be depended on, instead.

Many a time, a carbuncle or a crop of boils or an intractable eczema or an attack of erysipelas etc., draws suspicion to the diabetic state of an individual and an examination of the urine confirms the diagnosis. If, however, no glycosuria is found, blood sugar must be estimated before being satisfied that the condition does not exist.

Sugar in the blood acts as an irritant and when the normal percentage of about 10 is exceeded, it lowers the resisting power of the individual and renders him liable to pyogenic infection—an insignificant scratch developing into cellulitis or erysipelas.

Staphylococcus aureus has almost invariably been the causative organism in our series of cases, rarely the albus.

How to treat these cases?—Say, a small carbuncle has appeared in a diabetic. If we incriminate a high blood sugar for the condition, it is rational to think that by keeping it down to within normal limits, we will be able to re-establish the condition when the natural resisting power will be able to successfully fight out the disease. This is attempted by cutting down the carbohydrates in the food and giving Insulin injections. On several occasions, only such a measure with Sod. Citras or Mag. Sulp. compress has been enough.

Suppose, it is a big carbuncle and there are profound constitutional disturbances, in other words, in a case where the tissue resistance is practically absent. What should be done in such a case? Whether the knife should be taken up? We prefer to differ from the surgeons, and give their heroic measures a very wide berth indeed. If we believe that a tiny scratch can bring on these unfortunate complications, how is it likely to help matters by putting crucial incisions, or by excising the affected part, and thereby leaving extensive wounds to be infected freshly, and by opening at neighbouring lymph channels to favour a further spread, is something which

we do not follow. If it is said that these measures aim to stop the factory pouring forth its output, then obviously, they are trying for the impossible. We do not regret that we have not used a knife in any of our cases up till now.

Having decided against the knife, we advise, locally, Saline compress or Mag. Sulp. poultice, after having taken a sample of pus for culture. As the vaccine will take some 3 days for its preparation, we start immediately either with a good Stock Vaccine or with non-specific protein therapy, and then follow up with the Auto-Vaccine. Sometimes, we combine the Vaccine and the Protein Therapy together and then we give bigger doses of vaccine and at more frequent intervals. We do not use any strong antiseptics nor do we attempt to forcibly remove any slough.

More liberal diet is allowed so far as carbohydrates are concerned. Fat is cut down to a minimum. Fruits (vitamin C), and alkaline drinks encouraged.

Insulin is given once or twice a day according to requirements.

Manganese and Tin preparations have not proved worth while with us.

We have seen some of the operated cases develop sinuses, killing the patients by exhaustion or by bringing in tuberculosis of the lungs.

A few diabetics developed pyuria with low temperature. *Staphylococcus aureus* was cultured from the urine. These cases, unfortunately, all ended fatally—Vaccines etc. did not affect them at all.

The treatment chalked out for a carbuncle holds good, in broad outlines, for the rest of the other conditions.

Carbuncle as Seen in the Delta Areas

BY

K. S. Appu Mudaliar, M.B.B.S.,
Civil Asst. Surgeon, Kumbakonam.

CARBUNCLE is one variety of acute inflammatory gangrene occurring in living tissues. Carbuncle results from infection of the subcutaneous fat by a pyogenic organism—*staphylococcus aureus* in a majority of cases. This may occur following slight injury or as a result of auto-infection, especially in patients debilitated from such diseases as chronic nephritis and diabetes.

The blood supply of subcutaneous fat is poor and should thrombosis occur during inflammation, extensive gangrene and sloughing of fat may set in. In very debilitated subjects, this may involve the muscle and in all cases, the skin over the diseased area will slough following the cutting off of the blood supply from the subjacent tissues. Involvement of large veins close to, may lead to spread of infection with pyæmia or, in the neighbourhood of neck and head, to the infection of intracranial blood sinuses with rapid onset of coma and death. Carbuncle heals by separation of slough from the surrounding tissues, the dead skin having given way, the slough being excluded through the sinuses thus formed leaving a deep ulcer which later heals by granulation.

As with the acute inflammations, we have in carbuncle also local and constitutional signs.

Local Signs.—Hard painful swelling in the subcutaneous tissues often in the back, skin over which becomes dusky and cedematous. Swelling increases in size, centre becomes soft. Meantime, the skin over the area becomes purplish and usually ulcerates in several parts near the centre exposing to view the ashy slough and allowing the exit of thin sero-pus. Occasionally, more than one carbuncle occurs in the same individual simultaneously. In such cases prognosis is grave. Carbuncles are seen mostly on the back, nape of the neck, face, in palm and foot, occasionally in scrotum.

Constitutional Signs are often severe, there being high fever when prognosis is good; but a normal or subnormal temperature is not frequently present and must be viewed with anxiety since it shows patient's poor resistance to the disease. Nocturnal delirium is not uncommon and so is toxic glycosuria.

I have observed in my fifteen years' wandering in the Delta and Ceded District areas that carbuncles are rare in Ceded Districts, probably one sees very few cases in the hot weather which can be counted in finger tips, whereas in the delta areas of Godavari, Tanjore and South Arcot, one meets every alternate day, a case or two. Further, it was noticed that the few cases met with in the Ceded Districts, are

small in size, most of them sugar-free. Most of them responded to the conservative treatment very quickly and so there was rarely any necessity for surgical procedures. Probably, it was due to the diet of these people and non-sedentary habits due to the poverty of these districts where majority have to sweat and earn. The common diet in these areas consists of ragi and maize, little dhall, vegetables, and buttermilk. Probably, it was the intake of ragi and maize which are full of B, vitamins and the low carbohydrate percentage of these cereals which were responsible for this particular variety of carbuncles. I have noticed that these cases respond to autohæmic injections 5 c.c. at the junction of healthy and indurated tissues at 4 places viz., 12, 3, 6, 9, O'clock positions of a clock—with saturated Mag. Sulph. poultice every six hours, rest, opening of bowels, Salicylates internally, and the whole slough separates of its own accord.

Carbuncle seen in delta areas were found mostly in richer classes, most of them vegetarians accustomed to sedentary life and most of them were very flabby and corpulent, being glycosuric from a comparatively young age. Some had combination of sugar and albumin in urine. Most of them were having very bad pyorrhœa and nervous complications such as burning of toes, shooting pain in the legs etc. An enquiry into the diet shows their staple article of diet is polished milled rice with little vegetable and buttermilk and coffee several times a day. Most of them showed pyæmic complications, anorexia and tendency to coma. Percentage of sugar varied from 2 to 6 or even more in the urine. Treatment adopted: (1) Rest. (2) Bowels opened. (3) Thirty units of Insulin with ten units of Zinc Insulin twice a day, as injection with a little fruit juice or glucose, after each injection. (4) If acute pyæmia is present, Pyæmic serum one tube for three successive days, helps. (5) Early stages, Byers Hyperæmia. But rarely patients come in this stage. Still later stages—Mag. Sulph. paste, every six hours till centre feels soft. Mag. Sulph tried to get rid of water of crystallization. (7) After centre feels soft, crucial incision and raising of flaps and using Glycerine carbolic dressing for three or four days followed by Eusol dressing over it. Slough separates out in a week to ten days and later, Mercurochrome or Acriflavine dressing and the carbuncle heals. (8) If a patient has nervous signs, Vitamin B as Benerva or Vibex injections with a tabloid of Ganton daily helps. In cases of late boils during treatment of carbuncle. I have found antipyrogenetic vaccine (Italian) or Stannoxyd tabloids or injection, useful.

If patient has tendency to Coma, intravenous Glucose and Insulin, Soda Bicarb enema dr. 1 to a pint. Soda Bicarb powders by mouth generally help. In extensive carbuncles of the back, which is the only variety wherein my former chief Major General E.W.C. BRADFIELD I.M.S., used to advocate excision, to give short wave therapy and after limitation of the carbuncle, to do the excision. In other cases, he was more for crucial incision and raising of flaps. In cases of facial carbuncle, it was noticed that conservative treatment and, when definite fluctuation is noticed, incision is of use. In cases of

cellulitis of palm and fingers, incision on either side of the phalanges without approaching the joints, without injuring the tendons and sheaths is the rule. In cellulitis of thumb and little finger, after dealing with the phalanges and incision either over the thenar or hypothenar eminences, then cutting the annular ligament of wrist and if there is extension in the forearm, incisions on either side of the forearm reaching the plane between pronator quadratus and superficial layer of muscles of forearm, taking care of radial or ulnar artery as the case may be. The idea is not to injure the median or ulnar nerves and consequent paralysis or contractures. As regards the palm incision extends from the web of the fingers towards the centre to the level of the deep palmar arch. Swelling noticed in the dorsum of the palm does not mean that there is pus there. It may be after all passive oedema. As regards the diet for these patients, my opinion is that no limitation need be placed but only Insulin must be administered to keep the percentage of sugar under one percent.

In this article, I have tried to give out what I have observed during my official career about this particular disease.

Operation on Diabetic Patients And its Precautions

BY

S. C. Das Gupta.

Surgeon-Superintendent, Bir and Town Hospitals, Nepal.

ANY surgical operation on diabetic patients is regarded a little more dangerous and all surgeons should carefully weigh the circumstances before finally deciding to perform an operation which is not quite urgent. In an emergency case, there is of course, no question of option, but still if the operation can be postponed, it should be done in order to properly ascertain the condition and progress of the disease. Often, it happens even in educated and rich classes, that until a carbuncle or cellulitis appeared, the patient or his relatives never thought or had an idea that he ever suffered from diabetes. In one case which I knew, the first examination of urine after the carbuncle appeared showed it to contain 5 p.c. of sugar. Therefore, in all cases of suspected septic infection, urine should be examined above all at once as a routine method. If the patient cannot pass urine by himself, the urine should be drawn by a sterilized catheter for examination. On rare occasions only, sugar may not be found in the urine of even diabetic patients, but still it should be sent for estimation of blood sugar, blood urea and alkali reserve to the Pathological Department.

It is a known fact that glycosuria may develop from some surgical conditions such as head injury, sepsis etc. which may often be relieved by operation.

In fact, the percentage of sugar in urine is not the real criterion for operating or not in a case of diabetic, but it is the blood sugar which is the main point for consideration. There may be no blood sugar with even high percentage of sugar in urine and again there may be high percentage of sugar in blood without any appreciable presence of sugar in urine. This is very deceptive after all. Then again the presence of albumin, acetone and ammonia in addition in the urine renders the prognosis still more grave.

I cannot do better than quote the words of PHILLIP'S (*Lancet*, May 10 and 17, 1902) as to when to operate and when to refuse an operation: "An operation for malignant disease in a diabetic can be performed if the operation would be proper on a non-diabetic individual. Large abdominal tumours can be removed and cosmetic operations are justifiable if the general health is good and there is no marked arterial disease or nerve degeneration. Operations are justifiable in all emergencies without regard to the condition of urine". In a diabetic with a surgical malady, it is often possible to lessen the danger by preliminary medical treatment; but an operation of the greatest urgency should be performed at once. Again, if only 1 gram of ammonia is excreted during 24 hours, the operation is contra-indicated. Therefore, the total amount of urine passed in 24 hours

should be carefully noted and preserved for examination. If acetoacetic acid or a large quantity of albumin be present, every case except the most urgent one should be postponed and subjected to medical treatment. The plan of preparation employed in Mayo's Clinic (*vide* papers 1915) has given excellent results, and should be followed. The urine is freed from sugar by ALLEN's method. "The patient starved for forty-eight hours to seventy-two hours, being given all the water he desires and some black coffee and whiskey three or four times a day. Then he is put upon strict diet of meat, eggs, nuts and small quantity of cream. This diet is continued until urine is free of sugar and remains so for 2 days. Ordinary green vegetables are then added gradually; sugars, starches and all food rich in carbohydrates being still avoided. Should sugar reappear, the strict diet is again enforced". Of course, by simply removing sugar from the urine the risk of operation is not prevented (BERKMAN). Our object should be to increase the tolerance, so that the patient may utilize more carbohydrates and lay up a reserve store of glycogen. A strict carbohydrate-free diet upto operation rather increases the risk of coma by permitting acidosis; slight acidosis does not contra-indicate an operation, but marked acidosis does. Severe nephritis is a positive contra-indication. Transitory (physiological) glycosuria is an uncommon condition. According to RIESMAN, 10 p.c. of pregnant women get glycosuria. In Mayo's clinic, they give one dram of Sodium Bicarbonate by mouth, six to eight times a day, in order to antagonise acidosis, and if it cannot be given by mouth it should be given per rectum or intravenously in 5 p.c. aqueous solution. DA COSTA states that the danger to the kidneys which is already irritated by the secretion of sugar and may induce acidosis or acetonurea. The urine may contain acetone bodies (particularly B-Oxybutyric Acid) Diacetic Acid or both these substances. The blood contains an excess of free fat and shows diminution of alkalinity. There may be an odour of acetone in the breath. In such cases, as little of anaesthesia as possible should be administered and urine should be examined daily after operation and the treatment should be therefore to saturate the patient with alkalis. Carbonates help in stopping acid formation. Dextrose and glucose are also valuable for this purpose and may be given by mouth, rectum or by subcutaneous or intravenous injections. Of all the anaesthetics such as local, spinal, Gas and Oxygen, Ether and Chloroform, the last one should never be used. If the operation is unavoidable, still the patient must not be starved before giving anaesthesia. Just before anaesthesia, 30 units of Insulin should be given with $1\frac{1}{2}$ to 2 ounces of glucose in water by mouth. After the operation, the patient should be put on a milk diet and 20 units of Insulin injected every 6 hours—testing the urine also at the same interval before the injection. If the urine be sugar free, stop Insulin until sugar appears again and then start with 10 units six-hourly.

Diabetic coma is the result of acid intoxication due to accumulation in the blood of acids especially B-Oxybutyric which do not belong there but is formed in the blood because of lack of proper

and diacetic acid is formed from the above acid in the urine and forms acetone and carbon dioxide. Hence acetonuria means acidosis. Ketone bodies are at fault and they are also formed from un-oxidised fat.

In the case of an ensuing operation, the patient should be put at once on what is known as the "basal requirement diet" and Insulin is given in gradually increasing doses, until blood sugar falls within normal limits. In this method, large doses of Insulin upto 60 units daily may be given. Insulin should also be given in cases of coma, gangrene and neuritis; and it should be given with glucose. When estimation of blood sugar cannot be done, 40 to 60 units of Insulin should be given subcutaneously at once without waiting for the report together with 2 oz. of glucose dissolved in 2 pints of water by mouth or through a stomach tube if the patient cannot swallow (BEAUMONT and DONNS). In case of acidosis, it is advisable to administer Soda Bicarb 4 drams by mouth or stomach tube. In a simple diabetic coma the temperature is usually sub-normal, but if there be other complications associated with coma such as septic infection meningitis, pulmonary tuberculosis—the temperature may be high or normal accordingly.

As regards the technique of operation, I have very little to say except that the incision and opening should be just what is absolutely necessary, but drainage of the wound should be thorough and all packets opened out. Most surgeons now advocate high amputation without waiting for a line of demarcation if the gangrene is moist and due to bacteria attacking the tissues (DA COSTA), but if it is dry and due to arterial changes, it is better to wait for the demarcation before amputating; and as soon as demarcation forms, the dead parts are removed and healing is apt to occur. If no improvement occurs with medical treatment and diet restriction, and if acetone and diacetic acid persists in the urine besides sugar, it is dangerous to wait. In a moist gangrene dry hot compress or superheated air should be applied regularly and part kept warm by hot water bags, but if dry hot moist gauze compress must be applied regularly. In operation for carbuncle there are two methods: one the old crucial incision which may be made in a small limited area, but if large and diffused, it is better to make 4 or 5 parallel incisions from above downwards at a distance of $\frac{1}{2}$ inch or so, and at the same time, opening out the packets. If there be deep sloughs and skin over the affected area badly damaged or ulcerated, it is better to divide the flaps by a transverse incision and scrape out the cavity as far as possible. In case of septic wounds, the affected parts should be washed with Hydrogen Peroxide and dressed with Dakin's solution twice or thrice daily according to the severity of the condition. Besides, if possible autovaccine should be prepared and given at regular intervals from the beginning. In strangulated hernia and other urgent aseptic operation the surgeon should strive his best to see that all wounds might heal by first intention. The main point in the treatment of convalescent period should be the improvement of general condition of the patient and making his sugar free by all means at disposal and lastly, maintaining the action of bowels and kidneys.

Eye in Diabetes Mellitus

BY

G. S. Guha, M.B., D.T.M., M.D.

Honorary Ophthalmologist, Government Hospital, Shillong.

THE ocular affections in diabetes mellitus are numerous; in fact practically all the different parts of the eye may be affected in this disease. In no other metabolic disorder, so much pathological changes in the eye are produced. About 20% to 30% of cases of diabetic patients have ocular symptoms. This is the statistics of the European and American countries. In our country, where a large number of diabetic cases are left undiagnosed and untreated, and therefore allowed to advance, the percentage of cases with ocular symptoms is perhaps somewhat more. Indeed, some of the ocular changes in diabetes are so prominent and so significant, that the systematic examination of eyes for defective vision complained of by the patient may be sufficient to diagnose the presence of this disease.

The fundamental defect in diabetes mellitus is the failure to metabolise sugar normally. Both dietary and body carbohydrate are unavailable and therefore there is an effort of the system to obtain carbohydrate from protein and fat. This altered carbohydrate metabolism leads to the increase of blood-sugar concentration or a state of hyperglycæmia is produced. This hyperglycæmia probably acts as a toxin damaging the various parts of the ocular tissue. Again, the normal metabolism of the eye is affected owing to the alteration in the composition of the blood stream circulating in the orbit. In addition to the direct affection of the eye due to the above stated reasons, the eye may be affected secondarily owing to the vascular changes in the brain as a result of this malady.

As stated above the clinical picture of the eye may be sufficient in many cases to establish the diagnosis of this disease and this may be supplemented by the routine examination of urine especially in cataract and in some other conditions where treatment is by surgical procedure. Failure to detect sugar in the urine should lead one to the blood-sugar estimation in suspected cases; because, there is a tendency for the kidneys to become less permeable to sugar resulting that in some cases the output of sugar in the urine may be negligible or even absent. But blood-sugar estimation will reveal here the presence of hyperglycæmia.

The pathological changes in the eye may be dealt with by taking into consideration the affection of each different part of the eye:—

- I. Conjunctiva: Hyperæmic changes.
- II. Cornea: (1) Epithelial dystrophy of; (2) Pigmentation of; (3) Sclerosing keratitis.
- III. Sclera: Relapsing scleritis and episcleritis.
- IV. Iris: Iritis.

- V. Ciliary Body: (1) Weakness or Paralysis of accommodation.
- VI. Ant. Chamber: Pigmentary deposits in.
- VII. Lens: (1) Refraction anomaly; (2) Cataract.
- VIII. Intra-ocular fluids: (1) Refractive changes; (2) Hæmorrhages in; (3) Changes in tension; (a) hypo-tension in diabetic coma and (b) hyper-tension in secondary glaucoma.
- IX. Retina: (1) Retinitis; (2) Lipæmia Retinalis; (3) Retinal hæmorrhage.
- X. Optic Nerve: Retrobulbar neuritis.
- XI. External and Intrinsic muscles of the eye: Ophthalmoplegia externa and interna.
- XII. Vascular changes: (1) Thrombosis of retinal veins leading to hæmorrhages and proliferating retinitis; (2) Optic tract, hemianopsia.

I. Hyperæmic Changes in the Conjunctiva.—Several kinds of hyperæmic changes in the conjunctiva have been described. In some cases, considerable enlargement of the venous branch of the capillaries may be present. These changes, although they may help in the diagnosis, still are not in themselves sufficient to establish a diagnosis of diabetes.

II. Cornea.—1. *Epithelial dystrophy of the cornea*: The epithelial cells of the cornea may swell up in rare cases and form vesicles; anæsthesia of the cornea may be present. The condition is easily diagnosed by means of a magnifying glass and a loupe. The cornea stains with Fluoresceine. The condition generally clears up with proper treatment of diabetes.

2. *Pigmentation of the cornea*:—In old people, it is of frequent occurrence to find the presence of pigment cells on the inner surface of the cornea. This may either be due to senile changes in the stroma of the iris cells or due to diabetes. In diabetic patients, the characteristic of these pigments is that these form a vertical spindle (Krukenberg's spindle) as a result of the disturbance of the aqueous humour.

The author has seen a diabetic patient who complained of seeing streaks when looking through a powerful light. On examining his eyes with a magnifying glass and a loupe, the presence of such pigments on the inner surface of the cornea was found.

3. *Sclerosing keratitis*:—It is a complication of scleritis of diabetic or of other origin when the affection extends from the sclera to the cornea. This is rather a rare complication of eye in diabetes, but in our country, where a large percentage of diabetic cases are either left untreated or not properly treated at all, the condition may not be absolutely rare.

The corneal opacities are grey and greyish yellow, becoming denser until they exactly resemble the sclerotic and hence the name. The prognosis regarding the vision is very bad.

III. Relapsing Scleritis and Episcleritis are rather rare affections of the eye in diabetes. But some cases of scleritis and episcleritis of diabetic origin may be misdiagnosed as of rheumatic, gouty, syphilitic or of tubercular origin and it may become very difficult to cure these conditions. In cases of relapsing scleritis or episcleritis in elderly people, diabetic origin which, although is rather very rare, still should not altogether be lost sight of.

IV. Iritis.—The characteristic of diabetic iritis is the presence of plastic exudates and occasionally a hypopyon in the anterior chamber. In most of the cases, where there is hypopyon, there is probably an associated staphylococcal infection. On careful examination, the presence of new or enlarged vessels in the iris may be seen. The iritis is usually of chronic type.

V. Ciliary Body.—1. *Cyclitis*:—The inflammatory changes from iris may extend to the ciliary body.

2. *Paresis or paralysis of accommodation*:—The tone of the ciliary muscle may be partially or completely lost producing either paresis or weakness or the total paralysis of accommodation. The patient, usually already presbyopic, complains that his glasses no longer suit his eyes for close work. On examination, very high glasses, usually much higher than necessary for his presbyopic correction, may be required. After treatment with Insulin, this symptom gradually disappears.

VI. Anterior Chamber.—Pigments may be seen deposited in the anterior chamber. Such pigments are deposited from the stroma of the iris cells. After extraction of diabetic cataract, such pigments are often seen in the anterior chamber.

VII. Lens.—1. *Changes in refraction of the lens*:—The refractive error is usually in the direction of myopia. This is mostly due to the swelling of the lens in the first stage of diabetic cataract. Such swelling of the lens may also occur in senile or some other form of cataract.

2. *Cataract*:—Formation of cataract is the most common complication of diabetic patients. The characteristic of diabetic cataract is that it begins with the formation of milky spots behind the capsule of the lens especially in the posterior pole. One of the peculiarities of diabetic cataract is often the association of the swelling up of the cells of the iris from which in many cases, the pigments have been lost. This can be easily seen with a magnifying glass and a loupe. Diabetic cataract affects both eyes simultaneously. It may grow very quickly especially in the very young individuals; such a short period as only 24 hours may be sufficient for the complete maturing of the cataract. In children, diabetic cataract is a grave signal of the

severity of the disease. One of the characteristic symptoms in the beginning of diabetic cataract is the refraction anomaly especially myopia. In individuals below 40 years of age, having cataract in both eyes in rather a short time, should be very suspicious of diabetic origin.

The pathology of diabetic cataract is not fully known. Probably the toxic metabolic product of the disturbed intra-ocular fluid damages at first the epithelium of the lens which, in the histological preparations, shows great damage and is very similar to the damages found in the toxic cataract produced by Naphthaline poisoning.

Senile cataracts may also be present in diabetic patients. Here of course, the patients are elderly and the characteristic signs of true diabetic cataract are not present.

Like all other surgical procedures in diabetic patients, the patient must first be made sugar-free by dietetic and Insulin treatment before extraction of the lens.

VIII. Changes in the intra-ocular fluid.—1. *Refractive changes*:—Increase of blood sugar concentration or hyperglycæmia causes increase of sugar in the intra-ocular fluid which varies intimately and directly with that in the blood. The refraction of the eye is changed in the direction of myopia. According to DUKE-ELDER, a rise of blood sugar produces myopia and a fall, hypermetropia through alteration in the crystalline concentration in the ocular fluids. Since Insulin readily alters the blood sugar, such a disturbance has been thought to be due to the introduction of Insulin.

2. *Hæmorrhages in the vitreous*:—Such hæmorrhages are not very common. They are usually of a recurrent nature and frequently associated with retinitis.

3. *Tension of the eyeball*:—Secondary glaucoma may be produced either as a sequelæ of advanced iritis or as a result of severe retinal hæmorrhages leading to proliferating retinitis.

4. *Reduction of tension (Krause's sign) in diabetic coma*. This is a very important sign in diabetic coma. The tension of the eyeball is so low that even slight palpation with the finger should enable the physician to diagnose the condition. In comatose patient, therefore, where the cause of coma is not known before, one should not forget to palpate the eyeball to see if it is not of diabetic origin. It is very important for the physician to diagnose this coma, for the patient can be saved by injection of Insulin (a minimum of 200 units), unless the case is a moribund one. It is also of practical importance to bear in mind that coma may be brought about by hypoglycæmia in diabetic patients due to overdosage of Insulin. In diabetic coma, however, Krause's sign and the smell of acetone in breath will be present while there will be absence of plantar response. In hypoglycæmic coma, on the other hand, Krause's sign and the smell of acetone in breath will be absent, while there will be presence of plantar response. It should be remembered, however, that while Krause's sign is usually present in diabetic coma, it may be absent or difficult to detect it in diabetic

comas of short durations and, according to some observers, it may be present even in hypoglycæmic coma and in some other conditions also. In doubtful cases of comas of non-diabetic origin, diabetic origin may be excluded easily by the examination of the fundus with the ophthalmoscope and the examination of the urine after taking it with a catheter.

The diabetic coma is supposed to be produced when the buffer system of the blood fails to neutralize the bye-products of the fat metabolism so that the whole buffer reserve is exhausted allowing the hydrogen ion concentration of the blood to increase and then resulting in acidosis and dyspnoea.

IX. Retina.—1. *Retinitis*:—The characteristic of diabetic retinitis is the presence of irregular, small and bright white spots around the macula. It occurs in both the eyes. There may also be hæmorrhages and white degenerative spots in the posterior pole and the presence of oedematous condition of the whole retina. In some cases, the picture of a fundus hypertonicus as due to the high blood pressure is also seen. The diabetic retinitis should be distinguished from the albuminuric retinitis where the spots around the macula are brilliant white and have a characteristic stellate arrangement forming a star-shaped figure around the macula. The earlier deposits are cloudy and look like "cotton wool" patches. Besides these, there may be changes in the optic disc which are not to be found in true diabetic retinitis. The hæmorrhages which are often present are with sharp margins and not flat as in diabetic retinitis. But one must not forget that albuminuria is frequently associated with diabetes as one of its complications in its later stage and so sometimes in diabetes also all the characteristics of albuminuric retinitis may be present.

Retinitis is a very serious sign of diabetes. The practitioner should bear in mind that a patient with diabetic retinitis has his span of life for a few years only. About 60 per cent are said to live not more than 2 years.

2. *Lipæmia Retinalis*:—The ophthalmoscopic picture of the fundus is very characteristic. The retinal vessels containing lipæmic fluid look milky white. The arteries are of pale red colour and the veins have bright violet tint.

The presence of this condition of the fundus denotes a very grave significance. It is often found in cases where diabetic coma has set in. The examination of the fundus, therefore, may be helpful in diagnosis in comas of doubtful origin. The condition is frequently found in young diabetic patients. According to some observers, it is really the only lesion of the fundus which may be described as pathognomonic of diabetes.

3. *Retinal Hæmorrhage*:—Retinal hæmorrhages are not very common in diabetes. The hæmorrhages are usually of a recurrent nature and frequently associated with retinitis. A sudden obscuration of vision may be caused owing to such hæmorrhages.

X. Retrobulbar Neuritis.—The condition is diagnosed by taking the field of vision when a central scotoma or less commonly a paracentral or a ring scotoma may be found. The patient may also himself complain of seeing such scotoma. The reaction of pupils to light is very important. When light is thrown on the affected eye, the pupil contracts at first but slowly dilates afterwards when it is still kept on the eye.

The prognosis in regard to vision is good if the condition is diagnosed early and proper treatment carried out immediately.

XI. Ophthalmoplegia.—1. Partial or complete paralysis of nerves supplying the external ocular muscles are sometimes seen in diabetes. The characteristic symptoms are:—Limitation of movement, deviation, squint and diplopia, all of which increase in the direction of the affected muscle. In addition to these, false projection, unsteady gait, vertigo, nausea and head tilting may be present. The 6th nerve is affected most and next to it, is the 3rd nerve. Isolated paralysis of the 4th nerve may also be seen.

2. *Ophthalmoplegia Interna*:—In it, the intrinsic muscles of the eye *viz.*, the sphincter pupillæ and ciliary muscles are paralysed. This is rather rare in diabetes. The symptoms are paralysis of accommodation and the loss of pupillary reflex.

3. *Ophthalmoplegia Totalis*:—In very rare cases of diabetes, paralysis of both external and internal muscles of the eye may take place.

XII. Vascular Changes in the Brain.—1. *In the retinal vessels*:—Arterio-sclerotic changes of the retinal vessels and thrombosis of the retinal veins with or without hæmorrhages may be found in some cases.

2. *In the optic tract*:—Vascular changes, mostly arterio-sclerotic in nature, may cause lesions of the blood vessels situated in any part of the visual tracts from the occipital lobe to the chiasma.

The characteristic symptom of the lesion of the optic tract is hemianopia or loss of vision in one half of the field of vision. The commonest form is homonymous hemianopia, where the right or the left half of the binocular field of vision is lost. The symptom of hemianopia may remain undiagnosed by the patient himself until a proper perimetric examination is made. This is due to the fact that the central vision which remains unaffected, does not cause much inconvenience to the patient unless, when the right field is properly affected, reading is impossible or when the left is similarly affected, it is difficult to see food on the left side of the plate. Similar inconvenience may occur when the lower quadrants of the field of vision are lost.

In addition to the finding of the field of vision by perimetric test, a characteristic pupillary reaction called the Wernick's hemianopic pupil reaction which is often difficult to elicit, should help in the

diagnosis of the lesion of the optic tract. In it, when light is thrown on the two sides of the pupil separately, one side contracts properly while the other side contracts either sluggishly or not at all, showing that the afferent pupil constrictor fibres, which undergo partial decussation at the optic chiasma, have been affected on one side due to lesion of the tract, the type of hemianopia depending on the site of the lesion.

Of the ocular affections in diabetic mellitus, cataract is the most common; next to it is the retinitis. Then comes retrobulbar neuritis and paralysis of the ocular muscles. The more infrequent affections are: disturbances of accommodation and refractive anomalies and iritis. Other affections are still rarer.

Bibliography.

1. Azenfeld—*Lehrbuch und Atlas der Augenheilkunde*—8th Edition, (1935) p. 367, 707.
2. Beaumont and Dodds—*Recent Advances in Medicine* (1939) p. 130.
3. Campbell—*Diabetes Med. Annual* (1930) p. 158.
" " (1931) p. 142.
4. Duke elder—*Text Book of Ophthalmology*, Vol. 1, p. 443.
5. Evans—*Ocular Manifestations of Metabolic Diseases*—"Practitioners Library of Medicine and Surgery", Vol. XI, p. 375.
6. French—*An Index of Differential Diagnosis of Main Symptoms*—4th Edition, (1928) p. 923, 337.
7. Guha—*Ocular Manifestations of Diabetes Mellitus*—"Antiseptic", June (1939).
8. Koby—*Slit lamp Microscopy of the Living Eye*, 2nd Edition (1930) p. 87.
9. Langdon Brown—*Diabetes, Med. Annual* (1934) p. 145.
" " " " (1936) p. 153.
10. Mukerjee—*Ocular Affections in Diabetes*, *Proceed. All India Ophth. Society*, (1935) p. 86.
11. Parsons—*Diseases of the Eye*, 6th Edition, (1931), p. 89, 257, 311, 355, 376, 385, 576.
12. Practitioner.

A Few Observations on Eye Affections in Diabetes

BY

Md. Shafi Mehkri,
Bangalore.

A FEW strides have been taken in recent years in the study of ocular manifestations of diabetes, and many text-books on ophthalmology reserve a separate chapter on the subject. This subject was discussed in a symposium on diabetes at the All-India Ophthalmological Conference held in Lahore in 1936, where eminent ophthalmologists of India expressed their views.

The usual ocular manifestations of diabetes are variously classed under the following headings:—

- (1) Changes in the refraction of the eye. Changes in accommodation.
- (2) Affections of the cornea, vitreous and lens—pitting or epithelial dystrophies of the cornea, opacities in the vitreous, and cataractous changes in the lens.
- (3) Affections of the iris and the uveal tract—iritis and iridocyclitis.
- (4) Changes in the retina—retinitis, hæmorrhages, lipæmia retinalis.
- (5) Palsies of extra-ocular muscles and ptosis.

In this short paper, a few personal observations are mentioned, with reference to South Indian ophthalmic practice.

The most common eye affection in diabetes, in my experience, is a change in the refractive error with alteration in the power of accommodation. At the time of writing, I have five cases of diabetes on hand, the patients being between 40 and 50 years of age, in whom refraction has altered considerably within the past twelve to eighteen months. All these cases had been examined for vision about two years ago, and all were found to have normal sight and normal eye grounds. In the course of the past six to twelve months—according to the history of these patients—their eyesight for distance has diminished, and they were found to be accepting presbyopic glasses of much higher strength than warranted for by their age. Examination of the urine in all these five cases showed presence of sugar in concentrations varying between 1 to 3.5% and acetone was found in the urine of one of them. I had a young doctor aged 34 years of age, whose refraction was constantly changing, according as to whether his glycosuria and hyperglycæmia were under control. In nine months, from being hypermetrope, he became a myope of 2.5 dioptries and required change of glasses almost every three months. Recovery from

these changes of refraction with improvement of the general condition has been reported by WESTCOTT and ELLIS¹ and others. The same applies to power of accommodation, as mentioned by FOSTER MOORE.²

The other eye affection common in diabetes is formation of lens opacities. The typical subcapsular dot-like and saucer-shaped posterior cortical lens opacities clearing up under treatment. This clearing up of the lens opacities occurs more often in young diabetics than in those over 50 years of age, and in whom sclerosis of the nucleus of the lens is fairly established.

Palsies of the extra-ocular muscles come next in consideration. Paralysis of the external rectus is perhaps a little more common than oculomotor paralysis. I have seen three cases of simple ptosis of the upper lid and one of superior oblique palsy due to diabetes. The facial nerve has also to be considered here in as much as it supplies the orbicularis oculi and its paralysis gives rise to lagophthalmos i.e., inability to close the eye. Facial nerve paralysis in diabetes seems to be almost as common as oculomotor affection.

Loss of visual field may be considered as coming next. In 25% of cases, I have met with moderate general contraction of the whole field with superior temporal quadrantic loss and also homonymous hemianopias. The blind-spot is invariably enlarged in these cases and there are smaller scotomata, but all the same, the fundus may not show any changes. Some diabetics complain of sudden depression of vision, perhaps in the course of a few hours or a day. There is no history of pain nor the usual signs of retrobulbar neuritis, nor are there any fundal changes. I have at present a case of a diabetic, 51 years of age, who went to bed after reading the newspapers the previous night, and next morning woke up to find himself unable to read even big types. His urine contained 4.5% sugar and acetone was present. FOSTER MOORE has mentioned a parallel case and opines that it is due to a retrobulbar neuritis. He also draws attention to the fact that "diabetics are more vulnerable to toxic effects of smoking than are healthy patients". Alcohol also is more toxic in diabetics than in others.

Fundus changes and opacities of the vitreous are next in order. There is no need to describe the appearance of patches of diabetic retinitis. The curious thing about the retinal changes is that there does not seem to be any definite relation between the fundus changes and duration of diabetes. I have seen persons suffering from diabetes for 20 years and more, and who have not been under any regular treatment, but whose fundi have been free from any diabetic changes, and I have also seen younger diabetics with a short history of six to twelve months of severe glycosuria showing numerous patches of retinitis. It is not intended to discuss here the possibilities as to what factors determine the retinal changes. One may just say that possibly retinal changes occur more often in longstanding cases of diabetes and in younger diabetics whose disease is fairly severe, with ketonurea and

presence of septic foci in the system. FOSTER MOORE says that when retinitis is present, the knee jerks are often absent.

Though it is the opinion of many workers that diabetics are especially liable to intra-ocular hæmorrhages, retinal and vitreous hæmorrhages do not seem to be very common in South India. I have seen only one case of lipæmia retinalis in the past twelve years. According to PARSONS,³ this condition occurs in young subjects. Prognosis is grave in these cases.

Iritis and iridocyclitis come next under consideration. The affection may be simple serous iritis, but more often, it is a gelatinous exudative iridocyclitis with heavy deposit of keratic precipitates, a hypopyon and firm posterior synechiæ. The lens and vitreous very often undergo degenerative changes as the result of violent inflammation of the iris and ciliary body, and secondary glaucomata are not rare. According to PARSONS,⁴ diabetic iritis is rare. He thinks it is probably a gouty iritis occurring in a diabetic.

In South Indian ophthalmic practice, diabetic affections of the cornea like epithelial dystrophies and annular atrophic keratitis are comparatively rare. I have not yet come across a case of retrobulbar neuritis of purely diabetic origin.

References :

1. Westcott and Ellis—*Jour. American Medical Assoc.*, 1911.
2. Foster Moore—*Medical Ophthalmology*.
3. Parsons, Sir John Herbert—*Diseases of the Eye*.
4. *Proceedings—All India Ophth. Society*, 1936.

Diseases of the Ear, Nose and Throat and Diabetes

BY

P. V. Cherian, M.B., F.R.C.S., (E.),

Surgeon, I/c, E. N. T. Department, Govt. General Hospital, Madras.

INFLAMMATORY diseases of the Ear, Nose and Throat are greatly influenced by accompanying diabetes. As in any other complaint, diabetes, by lessening the resistance of the individual, has an adverse influence on the satisfactory progress of diseases of the ear, nose and throat.

Furuncles in the nose, unless properly looked after, may lead to fatal complications. Several cases are on record where this condition has terminated fatally in diabetics. The venous drainage from the nose is very extensive and infection easily spreads to venous channels in the brain, especially the cavernous sinus. In very many cases, it is easily made out whether the inflammation is likely to spread. The best way to stop this spread is to block the angular vein at the root of the nose. This is easily accomplished by using a pin-point cauterity. The cauterising can be done under local anaesthesia and should be deep. This is a precautionary method well worth making use of, as I am confident, I have saved several lives by this procedure.

Inflammation of the paranasal sinuses too is badly affected by diabetes. The commonest sinus affected is the maxillary. The appearance of the patients in this is characteristic. They are usually between 40 and 50 years of age and the skin of the face has an unhealthy earthy appearance. The discharge is very profuse. The patient often tells you, he has diabetes and on examination, the urine is found to be loaded with sugar. Proper operative treatment in these cases leads to complete recovery.

No operative treatment should be undertaken on the nose and the paranasal sinuses without preliminary accompanying treatment of diabetes, depending on the seriousness of the case.

Except ordinary inflammatory conditions in the throat, there is only one complaint that is characteristic. Some people suffer from a very persistent and irritating dry cough. On examination, you will find no pathological condition. Examination of the urine will, in the majority of cases, reveal the presence of sugar. Successful treatment of diabetes will completely cure the condition.

In the ear, there are two conditions which are badly affected by diabetes. First is furuncles in the external ear. A large number of patients who get them are diabetic and run down in health. The furuncle by itself is not serious but the pain is unbearable and has to be relieved. Very rarely they develop into an abscess

and consequently operative interference is seldom called for. The best treatment for this condition is to put in drops of Ichthyol in Glycerine 10%. It is essential that the external canal is almost filled with the solution and kept moist with it. A dry fomentation also should be applied on the top of this. The best fomentation is from bran or salt. Moist heat is not very beneficial in these cases. Diabetes also should be treated at the same time. If the patient gets repeated attacks, it is advisable to have recourse to an Auto-Vaccine. Drops of Glycerine Carbolic 5 to 10% are also used but it is better to use Ichthyol. In certain cases especially in women, Glycerine Carbolic produces a bad inflammatory reaction with a crop of tiny blisters.

Second is inflammatory affections of the mastoid antrum. Acute suppurative otitis media in diabetics has a great tendency to develop into mastoiditis. It also tends to greater destruction of the bone. In these cases, diabetes should not be considered an impediment to operation. It should really be looked upon as a definite indication for operation. If not operated on, these cases tend to give rise to intracranial complications. Insulin should be administered and the diabetes brought under control. The patient should also have proper dieting. It is not advisable to use a general anaesthetic and if used, Chloroform should be avoided and only Gas and Oxygen should be employed. The technique of local anaesthesia is as follows:—The anaesthetic I usually use is Novocaine 2% with some Adrenalin. The skin should first be anaesthetised along the line of incision to one inch below the tip of the mastoid process. At this point, the great auricular nerve should be blocked by a deep injection. The small occipital also should be blocked by injecting at a point one and a half inches behind the meatus on a level with the floor of the canal. After this, the post auricular groove should be injected deep under the periosteum. Sub-periosteal injections should also be given along the line of incision. It is desirable to wait for a few minutes after the injection before starting the operation. The area of operation will be completely anaesthetised by this method. During operation, every diseased cell should be cleared out and the operation should be as extensive as possible. The results of these operations are very satisfactory and it is only necessary to do the cortical or conservative operation.

It should be clearly understood that diabetes is no contra-indication to any ear, nose and throat operation when it is necessary. The important thing to remember is that diabetes should be treated at the same time with dieting and Insulin.

Diabetes Complicating Diseases of the Ear, Nose and Throat

BY

M. Sanjiva Rao, M.B.B.S.

Ear, Nose and Throat Specialist, Madras.

THE presence of diabetes as a possible complicating constitutional factor has to be constantly borne in mind, during the course of diseases of the Ear, Nose and Throat, to avoid serious pitfalls in treatment. The difficulty of the problem lies in the fact that there are no pathognomonic signs pointing to the presence of this malady and the only way of detecting it, is by routine examination of the urine in every case. This ideal, however, is rarely practicable, as most of us may not examine the urine in the first instance in every case—especially those cases we consider trivial—say a sore-throat or discharging ear. Even in cases, where the patient knows he is a diabetic, he may not tell us the fact, under the impression that it may not have anything to do with his complaint. In other instances, he may complain of symptoms like polyuria or excessive thirst, etc., which should draw our attention to examination of his urine. But, in the majority of acute and painful conditions, like acute otitis, mastoiditis, quinsy, etc., the patient's mind is so pre-occupied by the pain and urgency of its relief, that he may forget to tell us about his diabetes, and we ourselves may be hustled into operative measures to give him prompt relief, which may have to be regretted later.

As mentioned at the outset, a routine examination of the urine is the ideal. But failing this, re-inquiry must be instituted during the course of treatment, if there are—

- (1) Signs of delayed resolution of the inflammation.
- (2) Want of localising power in the tissues.
- (3) Signs of marked toxæmia.
- (4) Unusual severity of the inflammation out of all proportion to the original infection.

I will amplify these points, when dealing with individual diseases, but I wish to stress that not one of these signs is pathognomonic of diabetes, as there are numerous other conditions, which may give rise to these signs—we may more often be disappointed and find no sugar in the urine. All the same, diabetes must be ruled out first.

External Otitis.—In all cases of repeated attacks of external otitis, the urine must be examined, if no other obvious cause is present, e.g., fungus infections, habit of pouring oil into the ear, or wetting the ears or chronic otorrhœa with slight discharge drying up in the canal, etc.

External otitis in diabetics is very often of the diffuse variety

with considerable pain and œdema in and around the external canal. In untreated cases, the canal is completely obliterated to a slit, with confusing retro-auricular œdema, which may render a diagnosis between pure external otitis, and external otitis plus acute mastoiditis, extremely difficult. In all such cases, as also in cases requiring operation, the urine must be examined for sugar and every effort must be made to arrive at a correct estimate of the underlying pathology, including even an examination under an anæsthetic if necessary. Opening a mastoid through a retro-auricular abscess, and finding it healthy is bad enough, but to do so without the knowledge that the patient is a diabetic, is worse.

Diabetes delays resolution in cases of acute otitis media. Factors contributing to delayed resolution are many, and there is no pathognomonic sign to clinch diabetes as the underlying cause. Response to proper treatment is nearly always steady and progressive in most cases of acute otitis media. Therefore, especially in patients of middle age and above, if the response is sluggish or very poor, diabetes must be ruled out first.

Diabetes can also be the cause of *recurrent attacks* of otitis media. There is one patient of mine, whose ears begin to discharge the moment his sugar level rises, and ceases discharging as soon as the urine becomes sugar-free and with no important auxiliary treatment. He is a well-built muscular individual, with strenuous out-door work, who cannot afford diet very much, and he controls his sugar level by ingestion of raw pancreas.

Diabetes and Mastoiditis.—It is not possible to maintain that diabetes favours extension to the mastoid, as that is probably more dependent on the virulence of the infection than anything else and mastoiditis occurs in diabetics as well as in non-diabetics. But having involved the antrum, the further course is different in the diabetic, in whom it tends to spread rapidly to involve all the cellular and diploetic contents of the mastoid usually with extensive sub-periosteal œdema over the mastoid, and zygomatic regions. In such cases, showing rapid breaking down of the cells, it is imperative to examine the urine. In these cases the toxæmia is usually more severe, and it is never safe to unduly delay operative drainage of the mastoid, by expectant treatment, unless such treatment gives rapid and tangible results.

Diabetes is mentioned as one of the causes of nerve deafness, but is extremely rare.

Diabetes is mentioned as a predisposing cause to frequent colds, but I doubt if it is so. In children, excessive consumption of carbohydrates and sugar, does lead to colds and sore-throats, but this may be due to excessive fermentation and gastro-intestinal catarrh.

Diabetics do not suffer from allergic diseases.

Diabetes and Sinusitis.—It is difficult to assess the influence of diabetes on the resolution of sinusitis. Acidosis due to any cause

including diabetes is supposed to delay resolution of acute sinusitis. As far as my experience goes, in diabetics under treatment, the prognosis of cure of sinusitis, is as favourable as in non-diabetics.

Diabetes and Quinsy.—In untreated diabetics, quinsy is apt to be accompanied by severe œdema, extending to the parapharyngeal tissues and aditus laryngis. In fact, in elderly subjects, if the pain of quinsy is not relieved within 24 hours of adequate incision and drainage, the urine must be examined for sugar. In younger subjects, sarcoma of the tonsil should be borne in mind.

Diabetes and Ear, Nose, Throat Operations.—In diabetics under treatment and control, I do not think the ordinary Ear, Nose and Throat operations entail any extra risk. I have done operations like tonsillectomy, submucous resection of the septum, myringotomy, removal of aural polypi, and puncture and lavage of the antrum, without any noticeable prolongation of the healing period. But, as to what would be the result of doing operations without the knowledge that the patient is a diabetic, I cannot say.

In conclusion, it may be said that a little delay in discovering the patient's diabetic constitution is pardonable, but to undertake operative measures or to waste time on un-responsive treatment, not suspecting the underlying cause, is dangerous.

The Interactions of Diabetes Mellitus and Pregnancy

BY

G. A. W. Wickramasuriya, F.R.C.P., F.R.C.S. (E), F.R.C.O.G.

Visiting Obstetrician, De Soysa Lying-in Home, Colombo.

THE supervention of pregnancy in a woman suffering from diabetes constitutes an interesting, though exacting, problem in medicine, demanding for its successful management, the skilled attention of the physician, the obstetrician, and the biochemist, throughout the entire period of pregnancy, labour and puerperium.

In no sphere of medicine is co-operation between the physician, the obstetrician, and the biochemist more essential, and nowhere are the results of such co-operation more gratifying than in this particular field. If this ideal is attainable and if the patient appreciates the full implications of her disability and is willing to co-operate wholeheartedly with her medical advisers, the results can be most gratifying to both mother and child. If, on the other hand, the patient's full co-operation is not forthcoming, either on account of ignorance or poor economic circumstances, the risks to her and her unborn child would be very considerable and she should be counselled against a pregnancy. The maternal mortality is by no means small and the total foetal and infantile mortality very considerable in the absence of correct scientific treatment. Even if the mother survives the pregnancy under such circumstances, there can be little doubt that her life expectancy is considerably reduced in consequence.

In the pre-insulin era, pregnancy was an event most dreaded by the diabetic woman and rightly so; for, her chances of a successful pregnancy were then very remote and, not infrequently, life was lost through the intervention of diabetic acidosis during pregnancy or more commonly during labour. With the introduction of Insulin, by BANTING in 1924, and a better appreciation of the dietetic principles of treatment, the prospects for the diabetic mother and her child have considerably improved. It cannot be said, however, that Insulin has solved the problem in its entirety. In spite of its continued use and the most meticulous care in treatment, many pregnancies still end spontaneously in abortion, miscarriage or still-birth, or neonatal death may occur shortly after birth. The risk to the mother from diabetic acidosis and coma have, however, been considerably diminished as a result of Insulin therapy. These accidents of diabetic pregnancies were attributed until quite recently to the disease *per se* or its complication—ketosis. Whenever interruption of pregnancy or foetal death occurred, ketosis and faulty treatment were at once incriminated. But no such co-relation is discernible in at least some of these accidents of diabetic pregnancies. In the light of these considerations and the fact that a diabetic woman may at times go through pregnancy successfully in the absence of any treatment, and sometimes in

spite of definite ketosis, it would appear that other factors too may be concerned in their etiology than the disease *per se*.

MURPHY in 1933 first directed attention to a possible hormonal imbalance in diabetic pregnancies. He reported that the prolan excretion of two diabetic women exceeded the normal. Later SMITH and SMITH (1935, 1936, 1937) established that an excess of serum prolan "precedes, predicts and perhaps causes pre-eclamptic toxæmia". These latter observers asserted that still-birth, the dreaded accident of diabetic pregnancies, was not at all related to diabetes *per se* or its complication—diabetic acidosis, but was definitely related to pre-eclamptic toxæmia. The onset of the latter can, according to them, be generally predicted by four to six weeks by the rise of the serum prolan. The usual clinical course in such pregnancies is normal behaviour until the sixth month or so, and at any time thereafter, the development of albuminuria, œdema and rising blood pressure. Fœtal death occurs within a few days after the onset of the hypertension and is followed quickly by the subsidence of the pre-eclamptic toxæmia. The whole clinical picture of pre-eclamptic toxæmia can occur and disappear within as short a period of time as one week. PRISCILLA WHITE, after a close study of 34 complete diabetic pregnancies between 1936 and 1939 with examination of serum prolan, makes some very illuminating observations. Thirteen of her patients showed normal values for serum prolan in late pregnancies namely below 200 rat units per 100 cc. of blood. The clinical course of these 13 patients, whose values for serum prolan in late pregnancies were normal, was uneventful; none developed pre-eclamptic toxæmia and none miscarried. There were 12 patients whose values for serum prolan were normal and who received no therapy; all these developed super-tic complications, nine developing pre-eclamptic toxæmia, while the remaining three miscarried. There were 9 patients whose values for serum prolan had been elevated on several occasions but who received replacement Oestrin and Progesterin therapy. These did not develop progressive toxæmia and not one of them miscarried. As a result of her studies, she concluded that the accidents of diabetic pregnancies were not related to the control of diabetes or its complications. Still-birth, neonatal death and spontaneous miscarriage, with only one exception, occurred among those patients whose values for serum prolan were supernormal. The rise of serum prolan predicts the abnormal hormonal balance. Replacement Oestrin and Progesterin therapy have been followed in a few cases by the restoration of the normal value of serum prolan and the successful outcome of the pregnancy. Further studies on these lines are highly desirable.

The problem presented by the diabetic mother is somewhat analogous to that of the sufferer from essential hypertension. Very few women, who begin pregnancy with blood pressure above 150 systolic or 100 diastolic, can go through a successful pregnancy, that is, with a living child and with maternal health unimpaired. There is always the risk that in such cases the pregnancy may precipitate hypertensive encephalopathy or cardiac and renal failure. Similarly, it can be said

that acidosis, pre-eclamptic toxæmia, and fœtal death are the great dangers that lie ahead of the pregnant diabetic with her persistent hyperglycæmia and tendency to hormonal imbalance.

To achieve a rational and successful treatment of diabetes during pregnancy, it is necessary to study closely the manner in which the disease and pregnancy react on each other.

Diabetes interferes with the natural course of pregnancy in the following ways:—

Influence of Diabetes on Pregnancy.—1. *Spontaneous interruption of pregnancy*:—Abortion, miscarriage, and premature labour are exceedingly common among diabetics. Almost every other pregnancy terminates in this manner. Miscarriage may occur in successive pregnancies. One of my diabetic patients has had 5 successive miscarriages.

2. *Intra-uterine death of fœtus*:—This is a characteristic termination of most diabetic pregnancies and occurs in about 50% of the cases. In the majority of spontaneous interruptions of pregnancy, the fœtus had already been killed. The dead fœtus is often retained in utero for days or even weeks. Fœtal death may occur at any time in the course of the pregnancy, but it does so more commonly in the second half and still more often during labour. The sole cause of the intra-uterine death was believed till recently to be ketosis, but the work of MURPHY, SMITH and SMITH, and PRISCILLA WHITE referred to above suggests that pre-eclamptic toxæmia resulting from a hormonal imbalance is a more important factor if not the only factor. Further work is needed before a final decision can be arrived at.

2. *Toxæmia of pregnancy*:—That there is a high incidence of pre-eclamptic toxæmia among diabetic mothers is clinically recognised. Its incidence is stated to be about 30%, an incidence very much greater than that for the general population. As the duration of the toxæmia may be very short, sometimes not more than a week, it is liable to escape detection. I have myself been impressed by the high incidence of pre-eclamptic toxæmia among my cases. As mentioned earlier, according to PRISCILLA WHITE, the concomitant toxæmia would appear to play a very important, if not the most important, part in the causation of the most frequent complication of diabetic pregnancies—namely, still-birth.

Influence of Diabetes on Labour.—By reason of the large size of the child which is a recognised phenomenon of diabetic pregnancies, the normal course of labour is apt to be interfered with. Parturition is often protracted and mutilating operations may be needed to effect delivery. In some cases, Cæsarean Section may be the only alternative to secure a live child. Hydramnios, too frequently, complicates diabetic pregnancies and thus increases the liability to mal-presentations. My last three diabetic pregnancies were associated with hydramnios, in two of them the presentation was abnormal, one being transverse,

and the other breech. This association of hydramnios with diabetic pregnancies may not be purely coincidental.

Influence of Diabetes on the Puerperium.—It is well known that diabetics show a diminished resistance to infection and a lowered vitality. They have, therefore, to be protected against infective complications occurring in the puerperium. Infective conditions in turn aggravate the diabetic state and may necessitate increased doses of Insulin. Another noteworthy feature is that in the early puerperium, there is a special liability to hypoglycæmia on account of the transformation of blood sugar into lactose in the breasts. This must be kept in mind in administering Insulin in the puerperium.

Influence of Pregnancy and Labour on Diabetes.—1. *Influence of pregnancy on diabetes*:—It should be remembered that even in health, pregnancy causes a great diminution in the carbohydrate tolerance, presumably due to the increased activity of the supra-renals, thyroid and pituitary. Thus, ingestion of even 50 grammes or less of glucose would often cause hyperglycæmia and glycosuria. This defective assimilation of sugar is so constant a feature in the first three or four months, that it was at one time even suggested as a test of early pregnancy. This alimentary type of glycosuria is purely physiological and, from a therapeutic view-point, is of no significance. After the pregnancy is terminated, the carbohydrate tolerance usually returns to its normal efficiency but, not uncommonly, it may be permanently impaired. Pregnancy may, therefore, be considered as an immediate cause of diabetes in such instances.

Another noteworthy feature is that pregnancy also causes a lowering of the renal threshold and thus provokes the condition of renal glycosuria in a high proportion of cases. According to some authorities, renal glycosuria is said to be present in about 45% of pregnant women. It is a condition which is said to occur in about 1% of otherwise healthy women, and occurs apart from pregnancy. It is also of no significance therapeutically, but its importance lies in the fact that it is liable to cause confusion in diagnosis.

Apart from these above-mentioned harmless conditions, there is no doubt that pregnancy *per se* causes an aggravation of the disease in the absence of treatment. The symptoms of polyuria, thirst, pruritus, etc., become more marked or become manifest for the first time during the pregnancy. But the most important feature is a pronounced tendency to ketosis. This may be of the fulminating type and can cause death of both mother and child in a very short time. I can recall two instances of this fulminant type of acidosis among my recent cases. In one, the mother died undelivered after an acute illness of only a few days. In the other, the mother was saved only after very intensive treatment in an institution with Insulin and glucose, but the foetus died in utero during the period of ketosis. In both these cases, diabetes was not suspected prior to the pregnancy. It is noteworthy that any infective complication, occurring during the pregnancy such as pyelitis, can be the means of precipitating a diabetic

acidosis and coma. A question that is often asked is whether the mother is benefited by foetal Insulin. The fact that the carbohydrate tolerance often improves in the later months of pregnancy and then deteriorates rapidly after foetal death, is adduced as evidence in support of this hypothesis. SKIPPER, however, believes that there is no good evidence that this gain in carbohydrate tolerance, noted in the later months of pregnancy, is due to the transmission of Insulin from the foetus to the mother.

2. *Influence of labour on diabetes*:—Labour, particularly protracted labour, shows a well marked tendency to provoke acidosis and coma. This tendency is greatly enhanced by Chloroform or Ether anaesthesia. Many diabetics die of diabetic coma during labour.

The Child in Diabetes.—The features characteristic of children of diabetic mothers are (1) high mortality due to still-birth and asphyxia neonatorum (2) gigantism (3) congenital defects (4) foetal hyperglycæmia.

The foetal deaths are generally attributed to diabetic ketosis, but the recent studies of PRISCILLA WHITE and others indicate that foetal deaths occurred largely among those patients whose values of serum prolactin were supernormal, and who received no substitution Oestrin and Progestin therapy. Asphyxia neonatorum or death in utero often follows the development of pre-eclamptic toxæmia. It should also be mentioned that many of the neonatal deaths are due to injuries such as intracranial hæmorrhage inflicted at the time of delivery by reason of the large size of the child.

Gigantism:—This has been thought to be due to over-nutrition of the foetus by maternal and foetal hyperglycæmia, but here again PRISCILLA WHITE and others are definitely of opinion that it is part of the abnormal hormonal picture, because large oedematous children occurred in their series among mothers whose values for serum prolactin were supernormal, and who did not receive any hormone therapy. In support of this hypothesis, may be mentioned experiments of SNYDER (1934) and HOOPES (1934), who have shown that the injections of prolactin into pregnant rats and rabbits produced a picture similar to the diabetic pregnancy, namely spontaneous miscarriage, still-birth or over-development, death and maceration of the giant foetus.

Foetal hyperglycæmia:—A new born child may occasionally show glycosuria due to the hyperglycæmia present at birth. It is not congenital diabetes. The condition passes off quickly. The foetal hyperglycæmia is usually less than that of the mother, owing to the action of foetal Insulin. In cases where the maternal hyperglycæmia has been controlled by Insulin therapy, the new born infant does not show a hyperglycæmia or glycosuria.

Diagnosis.—Lactosuria need not cause confusion in diagnosis. The Ozazone test shows that the reducing substance in the urine is lactose, and not glucose.

Alimentary glycosuria does not cause symptoms, and estimation

of the fasting blood sugar and the sugar tolerance test establishes the diagnosis. The sugar is usually discovered during the routine prenatal examination. Alimentary glycosuria should not be diagnosed merely because there is an absence of symptoms such as thirst, polyuria, or pruritus. Many diabetics do not show these symptoms at an early stage of the disease. According to BROWNE, a fasting blood sugar of 0.13% is diagnostic of diabetes, except in the presence of any infective condition or hyperthyroidism, the normal being 0.09 to 0.11%—the same as in the non-pregnant.

Renal glycosuria can be diagnosed only by the estimation of the fasting blood sugar and the sugar tolerance curve, when it will be seen that the glycosuria is due to the lowering of the renal threshold for sugar. It must be emphasized that not all patients suffering from diabetes show symptoms such as polyuria, thirst, wasting, pruritus. I have encountered not a few young diabetic subjects in whom there were no symptoms at all and the condition was recognised only as a result of the medical examination for insurance. Furthermore, a true diabetes may manifest itself for the first time only during the pregnancy. For these reasons, and in view of the great importance of early diagnosis, it is my practice to do a complete sugar tolerance test in all cases where glucose is discovered in the urine during pregnancy. It is only by the adoption of this as a routine procedure that errors in diagnosis can be avoided.

Hyperthyroidism is also a rare cause of hyperglycæmia and glycosuria. The diagnosis is early established by the presence of the recognised signs and symptoms such as tachycardia, exophthalmos, enlarged thyroid and the increased basal metabolic rate.

Prognosis.—If the disease be at all severe, the outlook is gloomy for both mother and child in the absence of correct scientific treatment. In pre-insulin days, the maternal mortality—immediate and remote, was in the neighbourhood of 50%. The foetal mortality too was very high being about 45 to 50%. The great danger to the mother was diabetic acidosis and coma, which is liable to supervene more particularly during labour.

This danger was always enhanced whenever any infective complication such as pyelitis occurred in the course of the pregnancy. With the introduction of Insulin, the prospects for the mother have become very much brighter. The maternal mortality has now dropped from 50 to 10%. The acidosis and coma are also now more amenable to treatment. With early diagnosis and careful treatment, the maternal mortality can be still further reduced. The outlook for the child, on the other hand, is still very unsatisfactory in spite of modern treatment. The total foetal and infantile mortality still remains at above 50%. The neonatal death rate is also particularly high, largely due to injuries sustained at birth by reason of the abnormally large size of the child. PRISCILLA WHITE attributes the high foetal and infant mortality to an abnormal hormonal balance which is predicted very early by a rise in the serum prolactin. The abnormal hormonal balance causes in

her opinion pre-eclamptic toxæmia, gigantism, and asphyxia neonatorum, conditions which are highly inimical to the life of the child.

By frequent estimations of serum prolactin in pregnancy, particularly during the second half, and its control by replacement Oestrin and Progestin therapy, she has reduced the foetal mortality from 50% to 8% in a small series of cases. Her studies are most convincing and she has made out a strong case for further research on these lines. MURPHY, SMITH and SMITH and PRISCILLA WHITE have clarified the present position, and have added considerably to our knowledge of diabetes in pregnancy.

Management. It should be apparent from what has already been discussed that the diabetic woman who embarks on pregnancy is in need of the most skilled supervision throughout the whole period of pregnancy, labour and the puerperium. Considering the special dangers that lie ahead of her, the need for continued supervision is far more urgent than in the non-pregnant. A glucose tolerance test should be made as early in the pregnancy as possible. The diet and Insulin must be suitably adjusted to render the urine sugar and acetone free. Monthly blood sugar estimations are advisable to check up the diet and Insulin and also to note whether the metabolic condition is deteriorating or not.

The diet should be generous enough to maintain adequate nutrition and to prevent onset of anæmia. Undue restriction of food is definitely harmful and tends to cause anæmia and debility. A generous allowance of carbohydrates should be given, about 200 grammes or more being permitted daily. Fats must be restricted and covering doses of Insulin administered to control glycosuria and ketosis. Strictest watch must be kept on the urine, right through pregnancy and labour to prevent development of acetonuria. Should acetonuria develop, carbohydrate ration should be increased and fats further restricted and more Insulin given. The prevention of ketosis is of paramount importance for the safety of both mother and child.

Estimations of serum prolactin should be a routine laboratory procedure in every diabetic pregnancy. A rise of serum prolactin should be regarded as a warning of impending toxæmia, and points to immediate treatment with replacement Oestrin and Progestin therapy. By the control of serum prolactin during the pregnancy, particularly in the later months, it is claimed that most of the dangers to the foetus can be eliminated. Doses varying from 150,000 to 300,000 international units of Oestrin and ten to twenty milligrammes of Progestin have been administered in those cases, where serum prolactin was supernormal. By the administration of hormones, Oestrin and Progestin, along these lines it had been possible to eliminate to a very great extent the onset of pre-eclamptic toxæmia and its disastrous consequences. Hormone therapy along these lines would thus appear to be an important advance in the rational treatment of diabetes in pregnancy.

Management of labour:—Careful consideration must be given to

the method of delivery. While most diabetics deliver themselves spontaneously, an appreciable proportion find themselves in difficulties owing to the abnormally large size of the child. In some, Cæsarean Section may be the only alternative if a live child is to be secured. Careful examination should be made for signs of disproportion before arriving at a decision as to the mode of delivery. In many cases, I have successfully induced premature labour to prevent the difficulties associated with a large child. If the child is alive and if it is already too large, Cæsarean Section is absolutely indicated. In neglected cases where foetal death has already occurred, craniotomy and other mutilating operations to reduce the bulk of the child may be necessary. Strictest watch must be kept for ketosis, which is particularly likely to develop at this stage. Urine must be tested frequently for acetone and diacetic acid. Insulin 20 units with a covering dose of 40 grammes of glucose should be administered every three or four hours during the labour. Blood sugar estimations at this stage give valuable information regarding the metabolic state of the patient and greatly help in deciding as to the dosage of Insulin. These strict measures are necessary during the labour in all cases and particularly where the labour is protracted. In the absence of skilled medical attention at this stage, the foetus is most likely to perish, whilst the mother herself would be exposed to the tremendous danger of diabetic acidosis and coma.

The question of anæsthesia during labour is also of great importance. Chloroform and Ether should be avoided as they seriously diminish the carbohydrate tolerance, and tend to provoke acidosis. Gas and Oxygen, spinal and local anæsthesia are the methods of choice. Finally, a careful medical examination is necessary to decide whether the mother's health has deteriorated or not, as a result of the pregnancy. The question of permanent sterilization must also be considered. Every diabetic who is not in a position to have scientific treatment should be counselled against becoming pregnant. Such persons should be sterilized or should be given contraceptive advice.

Management of the Puerperium:—Every precaution must be taken to guard against infection occurring in the puerperium. The liability to hypoglycæmia in the puerperium due to the conversion of glucose into lactose in the breasts must be remembered in administering Insulin.

The infant too should receive careful attention in view of the high neonatal death rate. Convulsions resulting from intracranial stress and hæmorrhage may necessitate lumbar puncture.

Illustrative Cases.—The following cases illustrate the more important features of diabetic pregnancies:—

CASE 1.—*Diabetes Mellitus: Pre-eclamptic Toxæmia: Gigantism: Weight of Child 10 Lbs: Intra-uterine Foetal Death: Pyelitis Complicating Puerperium: Recovery.*

An elderly primigravida of 35 years of age sought treatment in

hospital in the 37th week of pregnancy as she had not felt the foetal movements for some time.

Condition on admission:—Foetal heart sounds absent; Urine:—Reaction—Acid; Specific gravity—1022; Albumin+; Sugar+ 1.6%; Granular-Casts+; Hyaline-Casts+; Kidney-Cells+; Acetone—Nil. Blood Pressure: Systolic 120, Diastolic 80.

Sugar Tolerance Test.

	Blood Sugar	Urine Sugar.
Fasting	181 mgs	Trace
$\frac{1}{2}$ hour	193 mgs	1%
1 hour	275 mgs	1%
$1\frac{1}{2}$ hours	293 mgs	1.8%
2 hours	293 mgs	2.2%

Patient put on Insulin—plain as well as Z. P. I. Labour induced by Oil, Quinine and Pitocin injections. Delivery of a macerated foetus weighing 10 lbs.

Sugar Tolerance Test on the 10th Day of Puerperium.

	Blood Sugar	Urine Sugar
Fasting	187 mgs	trace.
$\frac{1}{2}$ hour	256 mgs	trace.
1 hour	237 mgs	trace.
$1\frac{1}{2}$ hours	200 mgs	1%.
2 hours	187 mgs	1.4%.

Pyrexia in the puerperium due to pyelitis. Patient was discharged from hospital on the 21st day of puerperium apparently quite well, though a specimen of 24 hour sample of urine contained sugar.

Comments:—I consider this case to be an instance of true diabetes brought on by the influence of pregnancy. Prior to the pregnancy, the patient had been in excellent health and at no time was sugar detected in her urine. The pregnancy has damaged the carbohydrate tolerance so as to cause permanent hyperglycæmia and glycosuria. In view of her previous good health, she cannot be considered a case of latent diabetes, being accentuated by pregnancy. My own experience has quite convinced me that pregnancy can and often does precipitate a true diabetes, particularly in the elderly and in those predisposed to the disease. It is known that carbohydrate tolerance diminishes progressively with advancing age. It is also recognised that the incidence of diabetes is significantly higher in families of diabetic patients than in families of non-diabetic patients, and the potentiality for developing diabetes is said to be inherited as a simple Mendelian recessive. It can, therefore, be readily understood how a pregnancy may initiate a true diabetes in those predisposed to the disease either by heredity or advancing years.

The case also demonstrates the liability of the diabetic to pre-eclamptic toxæmia, gigantism, and intra-uterine foetal death and its

retention in utero. The foetal death must be regarded as part of the protective mechanism to safeguard the mother from the effects of progressive toxæmia and gradually worsening diabetes. If the disease had been detected early and if serum prolan estimations had also been done, I feel confident that with appropriate therapy with Insulin, replacement Oestrin and Progestin, the pre-eclamptic toxæmia and foetal death could have been averted.

CASE 2.—4 Para—35 years—Diabetes Mellitus—Pre-Eclamptic Toxæmia: Intra-uterine Death of Fœtus with Retention in Utero: Albuminuria and Hypertension persisting in the puerperium.

Obstetric History:—First Pregnancy:—Full time—live baby—No symptoms of diabetes noted.

Second Pregnancy:—Full time—still-birth with maceration of fœtus. Symptoms of diabetes such as polyuria and thirst were present during the pregnancy, and persisted even after the termination of the pregnancy.

Third Pregnancy:—Miscarriage in the 3rd month. Polyuria and thirst well marked. The present pregnancy is her fourth.

When seen in the 5th month of her present pregnancy, her state was as follows:—

Urine:—Reaction—acid; Specific gravity—1022; Albumin—trace; Sugar +; Acetone—nil; Pus Cells—10—12; Red Cells—2—3.

Blood Pressure: Systolic 110; Diastolic 70.

Sugar Tolerance Test.

	Blood Sugar.	Urine Sugar.
Fasting	218 mgs.	1.8%
$\frac{1}{2}$ hour	225 mgs.	2.1%
1 hour	237 mgs.	2.5%
$1\frac{1}{2}$ hours	250 mgs.	2.9%
2 hours	275 mgs.	3.2%

Polyuria marked: 142 ozs. during the 24 hours. Patient had been advised regarding diet and Insulin, but contrary to advice, she had taken no treatment and was readmitted to hospital two months and thirteen days later.

Her condition then was as follows: Foetal heart sounds absent. Blood Pressure: Systolic 160, Diastolic 95. Hæmoglobin 50%.

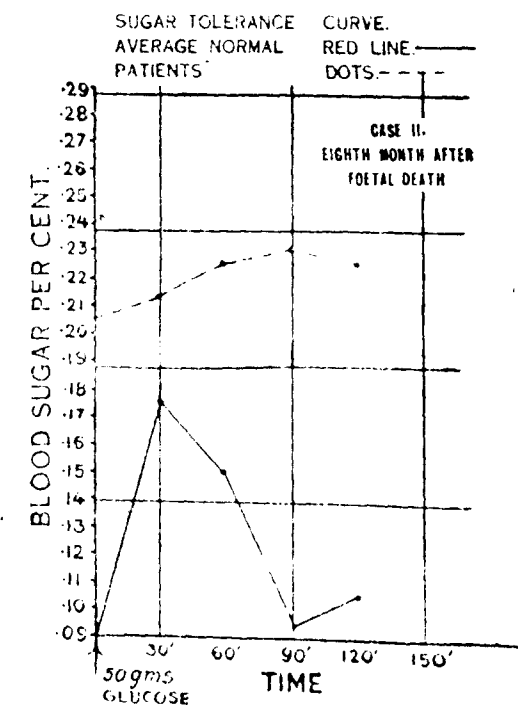
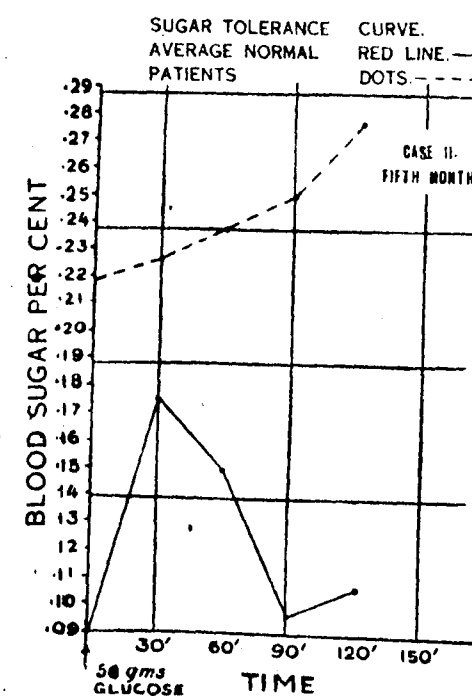
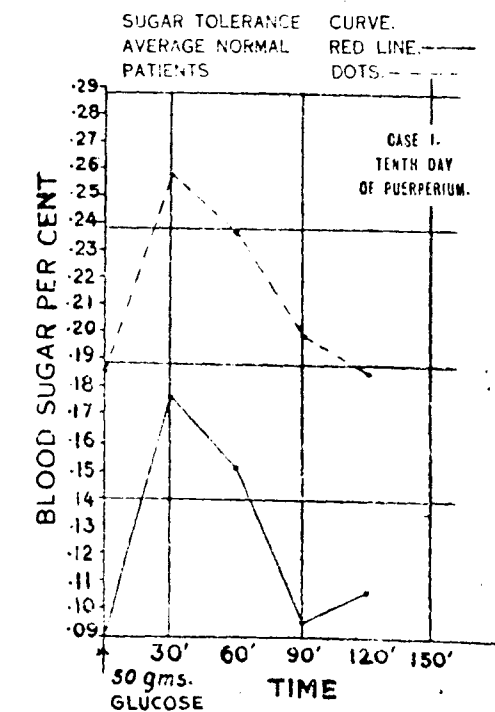
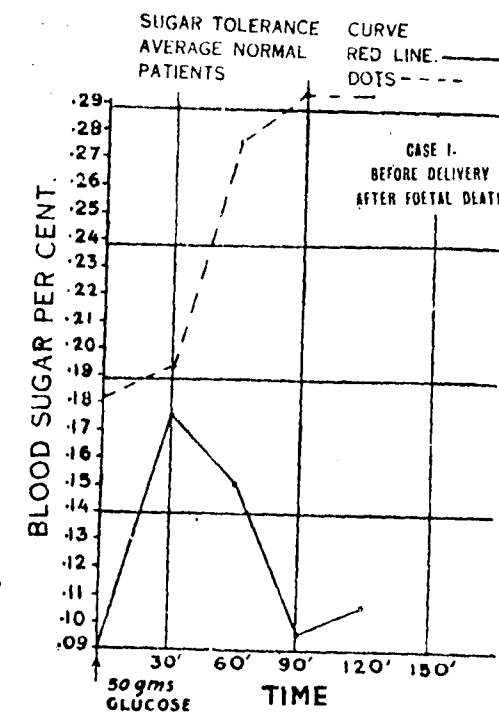
Urine:—Reaction—Acid; Specific gravity—1026; Albumin—trace; Sugar +2.1%; Acetone—nil.

Sugar Tolerance Test at this Stage (after Foetal Death).

	Blood Sugar.	Urine Sugar.
Fasting	206 mgs.	2.1%
$\frac{1}{2}$ hour	212 mgs.	2.8%
1 hour	225 mgs.	3.2%
$1\frac{1}{2}$ hour	231 mgs.	3.8%
2 hour	225 mgs.	3.8%

The Interactions of Diabetes Mellitus and Pregnancy

By G. A. W. Wickramasuriya.



The present pregnancy is her fourth:—The patient had been under medical supervision prior to her admission to hospital in the 37th week of her pregnancy.

Condition on admission:—Hydramnios + +; Presentation: Transverse—converted into vertex by external version. Foetal heart sounds +; Blood Pressure: Systolic 140, Diastolic 100; Urine: Albumin +; Casts +; Sugar +;

Labour induced by artificial puncture of membranes three weeks before the expected date of delivery to prevent foetal death and excessive size of the child. A live baby weighing 9½ lbs. was delivered spontaneously. Baby showed evidence of mild intracranial haemorrhage such as spasms, and spasticity of limbs but recovered with treatment.

Examination of the Amniotic fluid showed:—Specific gravity 1002; Urea 0.1%; Chlorides 640 mgs.; Cholesterol nil; Fats nil; Sugar nil; Deposits—epithelial cells and granular debris; 6th day of puerperium: Blood Pressure: Systolic 145, Diastolic 105. Urine: Albumin +; Sugar +; 16th day of puerperium: Blood Pressure: Systolic 135, Diastolic 96.

Sugar Tolerance Test on 16th Day.

	Blood Sugar.	Urine Sugar.
Fasting	150 mgs	trace.
½ hour	181 mgs	trace.
1 hour	237 mgs	1.8%
1½ hours	187 mgs	2.4%
2 hours	168 mgs	1%

17th day of puerperium: Blood Pressure: Systolic 150, Diastolic 110.; Urine: Albumin +; Sugar +; Patient's general condition is definitely worse than before the pregnancy.

Comments:—In view of the history of three previous unsuccessful pregnancies—foetal death having occurred in the last few weeks of the first two pregnancies, and neonatal death in the third, as a direct consequence of diabetes—it is almost certain that the foetus would have perished on this occasion also, had the pregnancy been permitted to continue to term. There cannot be any doubt that the timely induction of labour not only averted foetal death, but also prevented a major surgical procedure like Cæsarean Section, which would undoubtedly have become inevitable had the induction been further delayed by reason of the excessively large size of the child. Even as it was, the child was already too large and the delivery, though spontaneous, was effected with the utmost difficulty; the mother was nearly exhausted in the attempt and the strictest watch had to be maintained throughout the labour. Delivery took place under Scopolamine-Morphine analgesia. A noteworthy feature is that the pregnancy reached maturity—37th week—without incident in spite of the absence of scientific treatment and continued presence of glycosuria. The symptoms of pre-eclamptic toxæmia had already made their

appearance and foetal death seemed to be imminent when she sought treatment in hospital. Though the child was saved just in time, the mother's general health has greatly deteriorated in consequence of the pregnancy. Hypertensive disease, probably permanent, has been superadded to the diabetic condition, which could have been prevented had the patient submitted herself to correct scientific treatment early.

CASE 4.—3 para—33 years: Diabetes Mellitus: Hydramnios: Breech Presentation: Induction of Premature Labour: Delivery of a Live Baby weighing 8 lbs. following careful Treatment through the Pregnancy and Labour.

Obstetric History.—First pregnancy: Full time—still-birth—weight of baby 8½ lbs. Foetal death said to have occurred during labour. Diabetes was not suspected during the pregnancy.

Second pregnancy: Full time—still-birth—weight of baby 10½ lbs. Delivery effected by embryotomy. Foetal death and gigantism was undoubtedly due to unrecognised diabetes. Polyuria, thirst, emaciation and anæmia became well marked after the termination of this her second pregnancy.

The present pregnancy, which is her third, commenced whilst she was on treatment for diabetes. She was admitted to hospital in the third month. Her condition then was as follows:

Sugar Tolerance Test.

	Blood Sugar.	Urine Sugar.
Fasting	185 mgs	Trace
½ hour	250 mgs	1.5%
1 hour	263 mgs	2.0%
1½ hours	281 mgs	2.5%
2 hours	312 mgs	4.0%

Blood.—Hæmoglobin—65%; Red blood cells—4,400,000; White blood cells—6800; Colour Index—0.7; Reticulocytes—0.5%.

Patient on a regular diet and Insulin injections twice a day.

Sugar Tolerance Test in the 4th Month.

	Blood Sugar.	Urine Sugar.
Fasting	181 mgs	Nil.
½ hour	225 mgs	Trace.
1 hour	243 mgs	1.2%
1½ hours	256 mgs	3.3%
2 hours	262 mgs	4.1%

Patient still on a strict diet with injections of plain Insulin; Combined with Zinc Protamine Insulin; Fasting blood sugar a week later 100 mgs%; Patient feels well. Pregnancy progressing normally; Urine and Blood pressure normal; Tendency to acetonuria off and on.

Patient in the 6th month.

Sugar Tolerance Test.

	Blood Sugar.	Urine Sugar.
Fasting.	148 mgs	Nil.
$\frac{1}{2}$ hour	181 mgs	Nil.
1 hour	181 mgs	1.6%
$1\frac{1}{2}$ hours	150 mgs	1.9%
2 hours	156 mgs	1.5%

Blood Pressure:—Systolic 95, Diastolic 60.

Blood:—Hæmoglobin—60%; Red blood cells—3,880,000; White blood cells—6,400; Polymorphs—60%; Lymphocytes—38%; Eosinophiles—2%; Colour index—0.8%; Anisocytosis +; Poikilocytosis +; Polycromatophila +; Patient put on Iron in addition. The diet and Insulin increased.

Examination in the 37th week:—Blood Pressure—Systolic 100, Diastolic 65; Hydramnios + +; Presentation Breech—Converted easily into vertex by external version; Foetal heart sounds +; Urine: Albumin trace; Sugar + 1.5%. Labour induced prematurely in the 37th week by separation of the membranes followed by artificial puncture.

During labour urine showed: Sugar + 1.5%; Albumin—Trace; Acetone—Nil; Diacetic Acid—Nil.

Blood sugar estimation during labour; 237 mgs %. Insulin 10 units with 20 grammes of glucose given every 4th hour. Blood pressure during labour—Systolic 110, Diastolic 50. Labour delayed due to uterine inertia, and had to be terminated with the forceps as the foetus was showing evidence of distress. Mother's blood sugar immediately after delivery, 140 mgs %. Baby's cord blood sugar, 62 mgs %;

Mother's urine during labour; Albumin—Trace; Sugar—Nil; Acetone—Nil.

Baby's urine immediately after birth: Sugar—Nil; Albumin—Nil; Acetone—Nil.

On the 2nd day of puerperium: Urine—Albumin +; Sugar + 1.4%; Acetone—Nil.

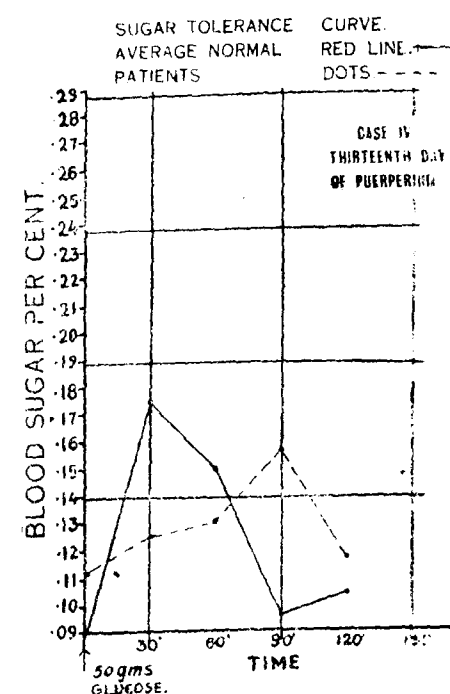
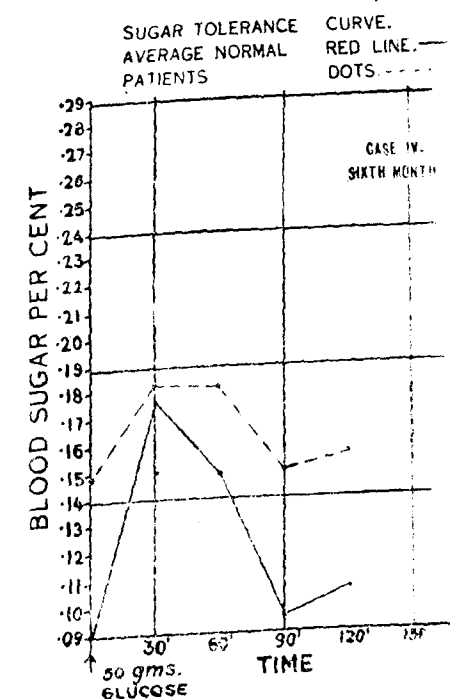
The fourth day of puerperium: Urine: Sugar + 1%; Acetone—Nil; Blood Pressure—Systolic 135, Diastolic 80.

On the 7th day of puerperium: Blood Pressure—Systolic 120, Diastolic 80.

On the 11th day of puerperium—Urine: Sugar—Nil; Albumin—Faint Trace; Blood Pressure—Systolic 120, Diastolic 80.

The Interactions of Diabetes Mellitus and Pregnancy

By G. A. W. Wickramasuriya.



Sugar Tolerance Test on the 13th day of Puerperium.

	Blood Sugar	Urine Sugar.
Fasting	112 mgs	Trace.
$\frac{1}{2}$ hour	125 mgs	Trace.
1 hour	131 mgs	Trace.
$1\frac{1}{2}$ hours	156 mgs	+less than 1%.
2 hours	118 mgs	Trace.

Patient's general health is very satisfactory. She has no symptoms of diabetes—such as polyuria or thirst. The blood pressure is normal. The baby too is in excellent health.

Comments :—This patient was either an unrecognized latent diabetic when she commenced her first pregnancy, the disease being aggravated by the latter, or what is more probable, the diabetes was initiated during the pregnancy and as a direct consequence of it. In view of her bad obstetric history, she had abandoned all hope of having a live child and desired the present pregnancy terminated. However, after full investigation in hospital, she was persuaded to consent to the continuance of the pregnancy. She was put on regular Insulin therapy plain combined with Z. P. I., and her diet carefully adjusted. The course of the pregnancy was uneventful. There was definite improvement in the carbohydrate tolerance in the later months and the Insulin dosage had to be somewhat reduced. This improvement continued on to the late puerperium and at the time of discharge, the patient felt quite well. The old polyuria and thirst had disappeared and the patient considered herself normal. In fact, the impression created was that the patient had been benefited by this last pregnancy. The blood sugar test done on the 13th day of puerperium shows a remarkable gain in carbohydrate tolerance. Whether this gain is real or apparent has to be decided later after the period of lactation is over. The patient has a plentiful supply of milk and I believe, the normal tendency to hypoglycæmia, due to the conversion of glucose into lactose in the breasts, accounts for the improved figures in the tolerance test. In reality, therefore, the carbohydrate tolerance may not be as good as the figures suggest. But one thing is certain: the general health of the patient has in no way deteriorated as a result of the pregnancy. The mother's blood sugar immediately after the delivery was 137 mgs% while the baby was hypoglycæmic at birth, the cord blood sugar being 62 mgs%, evidence of the influence of foetal Insulin. Had the maternal hyperglycæmia not been controlled by Insulin during labour, the baby too, probably would have shown hyperglycæmia and even glycosuria, though to a less extent than the mother, owing to the action of foetal Insulin. This case demonstrates in a most convincing manner the value of scientific treatment.

Summary of Conclusions.—1. In view of the special dangers the pregnant diabetic has to face, the need for skilled attention is far more important and far more urgent in the pregnant than in the non-pregnant.

2. Pregnancy *per se* may at times cause diabetes in the elderly and in those predisposed to the disease by heredity. The position is somewhat analogous to that of the victim of essential hypertension. Just as a hypertensive toxæmia of pregnancy is often the starting point of essential hypertension, developing months or years later, so does the so-called physiological hyperglycæmia of pregnancy lead at times to a true diabetes in those predisposed to it.

3. The control of hyperglycæmia and ketosis during pregnancy, and particularly during labour, is of paramount importance for the successful outcome of the pregnancy.

4. The estimation of serum prolan should be a routine laboratory procedure in every diabetic pregnancy. An increase in the serum prolan, the normal figure being below 200 rat units per 100 c.c. is to be regarded as a warning of impending pre-eclamptic toxæmia. By the control of serum prolan with replacement Oestrin and Progestin therapy, it is claimed that the foetal mortality can be considerably reduced.

5. Special consideration must be given to the method of delivery. The large size of the child may demand Caesarean Section. Induction of premature labour may forestall foetal death in certain cases.

6. Sterilization should be performed or contraceptive advice given in those instances where the patient is unable to carry out scientific treatment.

References :

1. Browne F. J.—*Antenatal and Postnatal Care* (1937).
2. Hoopes E. C.—*Proc. Soc. Exper. Biol. Med.* 31, 1115 (1934).
3. Murphy D. P.—*Surg. Gynec. Obstet.* 56, 914.
4. Skipper E.—*Diabetes Mellitus and Pregnancy. Quart. Jour. Med.* 1933, 26, 353.
5. Smith G. Van S and Smith, O. Watkins—(1935) *Surg. Gynec. Obstet.* 61, 27.
6. Snyder—(1934) *Bull. Johns. Hopkins Hosp.* 54, 1.
7. White Priscilla.—*The Practitioner* (May 1939).

Diabetes in Obstetrics

BY

B. N. Purandare, M.D., F.R.C.S.E.

Bombay.

DIABETES in pregnancy is now-a-days gaining more and more importance so as to form a new problem in obstetric practice, especially during the antenatal care of the patient and the efficient treatment, both of the mother and the child during and after labour. Before the days of Insulin treatment of diabetics, women suffering from this disease seldom became pregnant. If the disease developed in a girl during the first two decades of life, it usually had so serious a course that she had little chance of surviving till the age at which marriage or motherhood was possible. If it developed after twenty or thirty years of age, sterility invariably followed, as the fertility among these women being hardly above 5%. GRAAFE, in 1898, discovered atrophy of the uterus in diabetics and PARISOT in 1911 detected amenorrhœa occurring in 50% of all the cases of diabetes in women and further that it was associated with the disappearance of Graafian follicles from the ovary. This naturally affected the fertility of such a woman. There are similar effects produced in man regarding the sexual function, which fact further produced low incidence of procreation among diabetics. If, perchance, any woman happened to become pregnant, due to want of efficient treatment, she had to face some complications during the pregnancy and puerperium. About one third of these patients ended the pregnancy by the occurrence of an abortion or a miscarriage, and those that reached the full term often succumbed to severe diabetic coma at the time of labour or to severe sepsis thereafter. This led the older obstetricians to be in severe dread of pregnancy in a diabetic, and MATHEW DUNCAN in 1882 laid down the dictum from the survey of case reports, that the association of diabetes with pregnancy was extra-ordinarily serious and that the pregnancy had a deleterious influence upon the course of the disease. But now, the introduction of Insulin treatment has improved the prognosis of a pregnant diabetic patient and also made pregnancy possible in a diabetic by improving her chances of fertility, so that more and more women with this disease do attend now the antenatal clinics. This, however, makes the routine examination of urine for the presence of sugar as essential as that for albumin, during the antenatal visits. But, it does not mean that the cases giving the positive test need necessarily suffer from diabetes mellitus and other conditions of glycosuria, often associated with the changes in the metabolism of carbohydrates during pregnancy, must also be ruled out.

The presence of sugar in the urine of lactating women was first detected by BLUT in 1856. WILLIAMS observes that only 5% of pregnant women give positive reaction for Fehling's test due to lactosuria in the last month of pregnancy. According to HECTOR, the occurrence is as high as 70% in the puerperium, yet it is transitory and disappears

within ten to twelve days after child-birth. Lactose being a non-fermentable sugar with yeast, its presence can be ascertained by a very simple test of keeping an inverted test-tube in the urine, to which a little yeast is added. This should be kept at room temperature for 24 hours when no gas will be collected at the top of the tube if the sugar be lactose. The concentration of lactose in the urine rarely exceeds 0.3% and is more marked if the sucking has to be interrupted. It has no pathological significance and needs no treatment as such.

Another condition, when sugar may be found in the urine during pregnancy, is renal glycosuria. There is lowering of the renal threshold for glucose and hence glycosuria may occur in the absence of hyperglycæmia, due to increased permeability of the kidney cells. LAMBIE gives its incidence as high as 45%. It appears about the end of the second trimester of pregnancy and disappears in the puerperium. When of simple variety, it is not associated with any symptom of diabetes and requires no treatment. The intravenous injection of Calcium Salts seems to abolish it temporarily. D'APRIL, however, considers that renal glycosuria in one pregnancy may be followed by true diabetes in another. In a toxæmic or pseudo-toxæmic type, it is associated with œdema and high blood pressure without any albumin in the urine.

Glycosuria in pregnancy may also be due to early or late alimentary glycosuria. Here, glycosuria is due to hyperglycæmia and not due to lowering of the threshold for sugar. As a result of upset in metabolism, there is lowering of the assimilation limit for carbohydrates. The fasting blood sugar is usually normal or slightly raised, and the sugar tolerance test, after the administration of 50 gms. of glucose, gives a curve which is abnormally prolonged and heightened. In this way, a true diabetes mellitus can be differentiated from alimentary glycosuria. The latter, however, may occur with increasing severity in each succeeding pregnancy and in more severe cases, the complications, like acidosis and coma in the mother, and hydramnios and large size of the foetus, may develop. The various theories of the causation of alimentary glycosuria during pregnancy have been postulated but without definite proof: the factors responsible for the altered sugar tolerance being the enzymes or products of protein hydrolysis in the placenta, hormone of the placenta namely Oestrin which inhibits the action of Insulin, unstable and excitable state of nervous system producing splanchnic stimulation and glycogenolysis or due to the overaction or over-production of pregnancy cells in the hypophysis.

Thus, the renal glycosuria and late alimentary glycosuria, which appear by the end of the 6th month of pregnancy, may complicate the matter regarding the diagnosis of true diabetes.

As stated in the beginning, by the treatment of Insulin more and more diabetic women are seen to get pregnant. There is an intensification of the disease by the intercurrent pregnancy but no lasting ill-effects are produced by it, as at the termination of pregnancy, there

is rapid establishment of marked sugar tolerance. Hence, care should be exercised in continuing the Insulin treatment so as not to overdose the patient and produce hypoglycæmia.

During the first trimester of pregnancy, due to vomiting, there is a danger of acidosis and rapid onset of severe ketosis followed by abortion and then coma. The natural abortion is seen to occur in 12% of the cases. However, the therapeutic abortion is seldom indicated now-a-days, the only cases which require it being (a) where regular treatment with Insulin throughout the pregnancy is not available, (b) severe cases of hyperemesis in whom control of diabetes is impossible, (c) the cases which become worse in spite of Insulin treatment as the pregnancy advances. In the last mentioned condition, there should be no hesitation in terminating pregnancy, since the chances of a living child are practically few.

In the second trimester, there is little change in the carbohydrate metabolism in the mother, and if the Insulin treatment is well regulated, no complications may be expected. During the last trimester, there may even be slight improvement in the condition as regards diabetes due to the utilisation of the excess of carbohydrate in the mother's blood by the ever-increasing demands of the foetus. The old theory of CARLSON that the pancreas of the foetus temporarily compensates for the lack of Insulin on the part of the mother, is not accepted by all, though a definite hypertrophy and hyperplasia of the foetal pancreas are seen on post-mortem examination. Should, however, alimentary glycosuria and renal glycosuria complicate the matter, the diabetes is made worse. At the time of labour, there is a risk of the development of acidosis and diabetic coma if the labour becomes protracted and the patient suffers from vomiting and starvation during that time. WILLIAMS in 1909 gave the statistics of the pre-insulin period as 27% maternal mortality during labour of within two weeks, and an additional 23% during the following two years in severe cases. The prognosis is not, however, so grave as this, with the well-regulated Insulin treatment now so commonly followed. Yet the possibility of the complications at this period of pregnancy still exists and every effort should be made to avoid them. The prognosis is however, better for a diabetic over thirty years of age as compared with that for a young primipara. Following labour, a diabetic woman as a result of lowered vitality, is prone to puerperal sepsis, especially if any sort of instrumental help is required during delivery. In spite of all these complications, one finds that Insulin has really produced marked good effects. For, according to the present statistics of SKIPPER as compared with those of WILLIAMS given above, the maternal mortality at the time of labour and within two weeks is only 9.3% and upto the next two years is only 3.4%.

The prognosis for the foetus is, however, not at all improved to the same extent as in the mother because, the presence of diabetes has definite deleterious effects on the products of conception. There is unusually high incidence of abortion and premature labour and among those cases that reach the full term, about half of them give birth to

still-born children as the foetus is seen to die near the end of pregnancy during the last few weeks. The complications like foetal abnormalities and hydramnios are quite frequent and according to GRAAF, the latter is associated with excess of sugar in the amniotic fluid. This is the result of transudation from the maternal blood and is not derived from the foetus, as no trace of sugar is found in the foetal urine. The foetus too, is overgrown in size due to the deposition of subcutaneous fat brought about by the increased amount of sugar carried to the placenta, or by the high percentage of serum prolactin in the maternal blood. As a result of this, the labour becomes protracted and in some cases, even obstructed, so that asphyxia neonatorum is quite frequent in these cases. Because of the tendency for intra-partum death of the foetus at term, some authorities advise premature Cæsarean Section at the selected time. But if one takes into consideration the high foetal mortality of 25% for the premature babies and the associated risks of a major abdominal operation in a diabetic patient, the vaginal delivery at term seems to be the preferable method from the point of view of the expectant mother, especially if she had easy previous labours with live births. Hence, the routine performance of Cæsarean Section in uncomplicated maternal diabetes is unwise. Those who advocate it put forward the argument that it is inadvisable to risk a repetition of pregnancy and hence the excessive importance of ensuring that each pregnancy in a severe diabetic yields a living, viable child and at the same time affords an opportunity of sterilisation of the mother in very severe cases.

Death of the foetus in utero and the birth of a macerated foetus are not uncommon in spite of Insulin treatment and it is but an indication of poor control of the maternal disease by Insulin treatment. Should the mother develop coma any time during pregnancy or at the time of labour, the chances of getting a live baby are remote. Soon after delivery, the child may develop hypoglycaemia with cyanosis, twitching, convulsive movements and coma, as a result of continued over-action of the islets of Langerhans in the foetal pancreas as in the intra-uterine life. In order to avoid this, the infant's blood sugar must be raised to normal level by early feeding or by giving 10 c.c. of 10% Dextrose either by mouth or intramuscularly.

Thus, despite all the care and new methods of treatment, the foetal mortality in diabetics is still high and SKIFFER gives it as high as 45% so that the out-look for the child is very little improved.

Treatment.—*Antenatal care:*—The diabetic must receive a closer observation during this period. As stated above, seldom is the pre-mature labour indicated. Attention should be directed to thorough eradication of any septic focus in the body. The urine should be examined every week for sugar and the sugar tolerance test and repeated blood sugar test should be carried out. This often requires the patient to be admitted to the hospital. The diet and Insulin treatment should be so adjusted as to keep the blood sugar level well below 0.19% as far as possible.

Management of labour:—Labour is the most critical time during the course of this disease, and it should be managed with all the care as is taken in a diabetic patient when undergoing a major surgical operation. The operative work should be reduced to as much minimum as possible and natural vaginal delivery at term should be encouraged unless the pregnancy is complicated by pelvic disproportion or the patient is an elderly primi-para. Premature onset of labour or the termination of the pregnancy by Cæsarean Section, under these circumstances, may be thought of for getting a live baby provided it is undertaken in the thirty sixth week. During the last fortnight of pregnancy, the dose of Insulin should be readjusted correctly. At the onset of labour, it is wise to give the patient an extra allowance of sugar, because vomiting and anorexia at that time may interfere with her carbohydrate intake and if the usual dose of Insulin be administered, there is danger of the occurrence of hypoglycaemia. Hence, every sample of urine passed should be examined for sugar and acetone and if required, combined glucose and Insulin can be given by injections. Morphine should be used as an analgesic rather than Barbiturates. If Cæsarean Section has to be performed, it should be done under Gas and Oxygen anæsthetic. But, if it is not available, spinal anæsthesia may be used, but at the same time appreciating fully well the possible risk of this type of anæsthesia in pregnancy at term in causing instantaneous death, soon after injection. On no account should Chloroform be used and local anæsthesia should be avoided for fear of wide sloughing.

During the puerperium:—Here again, it is necessary to readjust the diet and Insulin treatment. There is difference of opinion as regards the question of lactation. There is very often poor milk supply and not infrequently, the milk is coloured rich yellow due to excess of fat. There is, however, no risk of transference of the condition to the child, yet suckling is not to be advised because, there is considerable difficulty in the establishment of lactation and also because it necessitates an increase in the diet of the mother.

Conclusions.—Now, with the modern methods of investigation and treatment, one need not regard diabetes as being as deadly a complication as the older writers, who had no such methods at hand, led us to believe. With careful dietary and Insulin administration, diabetics can be taken up to full term without trouble; and under rigid control, pregnancy may take a satisfactory course and yield a normal child.

References :

1. Arnold Walker—271, XXXV, Brit. Jour. Obst. and Gynae.
2. Lawrence—Jan. 1929, Quarterly Jour. of Medicine.
3. Nevinny and Schretter—XXXVII, Brit. Jour. Obst. and Gynae.
4. Lambie.—No. 4, XXXIII, Brit. Jour. Obst. and Gynae.
5. S. Liebmann—XL, 1290, Brit. Jour. Obst. and Gynae.
6. Hernik and Tillmann—No I. Vol. LXVI, 1938, Sur. Gynae. Obst.
7. Randall & Lawrence—(107) 919, 1937, J.A.M.A.
8. Smith Francis Scott—Page 772, Vol. 13, Jour. of Ped. 1938.

Pregnancy and Diabetes

BY

B. L. Kapur, M.D.,

Hony. Med. Superintendent, Lahore Maternity Hospital, Lahore.

It is an admitted fact that the anti-conceptional measures are getting very popular in our country. Practically, all men and women want to be acquainted with the most modern methods. But, in spite of this, the greatest worry of a married couple remains the further progeny especially when they have been sterile for 2—3 years after marriage.

Before the advent of Insulin, pregnancy in diabetes was very rare (ALBERS and CAFFIER). Only 5% conceived (ANTOINE)

The reason is that diabetes has an inhibitory action on the follicle apparatus and produces severe regressive changes which lead to amenorrhœa and thus to sterility.

Uterus becomes smaller and atrophic. Further, diabetes can bring on severe dysmenorrhœa. Probably, the cause for this is diminished function of hypophysis. Infectious vulvar eczema and endometritis are not uncommon.

The discovery of Insulin has been a boon and a blessing to the diabetics. But as far as pregnancy is concerned, only 15% conceive (WHITE).

The mere appearance of sugar in urine is no criterion that a woman is suffering from diabetes mellitus. She can have a harmless glycosuria. In the latter case, the following conditions should be fulfilled:—

- (1) The blood sugar curve is normal.
- (2) The sugar in urine is never beyond 0.5%
- (3) Glycosuria is not dependent on the carbohydrate intake.
- (4) Even by giving dextrose, the blood sugar curve remains normal.
- (5) The patients have no symptoms of diabetes mellitus.
- (6) There is a very low kidney threshold for sugar.
- (7) The condition is refractory to Insulin. According to ANTOINE, there should be no lactosuria in the cases of positive sugar curves of diabetes mellitus.

On studying the histories of the cases of diabetes mellitus, one divides them as follows:

- (1) In most of the cases, diabetes ante-dates pregnancy.
- (2) Diabetes mellitus begins during pregnancy and remains constant after labour.
- (3) Diabetes begins during pregnancy and disappears after child-birth.

In the second type of cases, one is more inclined to believe that pregnancy is the exciting factor of the disease. During pregnancy, a woman undergoes lot of changes in metabolic processes. The thyroid gland increases in size. The same happens with suprarenal glands. The anterior pituitary gland undergoes hyperplasia also. All these organs are antagonistic to pancreas. If enough Insulin is not produced, the monosaccharides cannot be converted into glycogen in the liver and therefore, the patient would get diabetes.

The course of disease during pregnancy can be kept under control. But where the pancreas has reached severer grade of dysfunction, coma may set in. It usually happens in the second half of pregnancy. In OFFERGELD's cases, 17 out of 27 developed coma. According to some writers, the condition can improve in the second half of pregnancy on account of the enlargement of foetal pancreas.

The greatest happiness of woman lies in the knowledge of her conception. She enters a new era of life. She spends all the time of pregnancy in great hopes for her future baby. But, in the diabetics, the hopes are usually not likely to be fulfilled. In CAROLI's cases, 10 out of 85 had spontaneous abortion. Fifty percent die intra-uterine (OFFERGELD and SEITZ). Many babies are born living. But according to KRAUS, 43% die on account of hypoglycæmic coma manifesting symptoms like cyanosis and vomiting (SMYTH and OLNEY). Others die, within the first few weeks after birth, of some disease or other and very few survive. One of the most striking features of the foetus of diabetic mothers is that many are born overweight—that is, about or beyond 5000 grammes (FISCHER).

The multiplicity of the fate of the foetuses is explained by the fact that in the first half of pregnancy, no Insulin is present in the placenta (PAROLI); but afterwards the production of Insulin is taken up by the pancreas of the foetus and, therefore, the foetal liver converts the monosaccharides into glycogen (EUFINGER). This fact is well established by the experiments of CALSON, GINZBERG and PITIMO who removed the pancreas of female dogs in the last days of pregnancy and no glycosuria was observed because, the function was taken up by the foetal pancreas.

Placenta plays an important role in the carbohydrate metabolism (HYENEMAN). Whether it is a filter or an active organ is not very well known. But the molecules of Insulin are large enough as not to pass through the placenta (SCHLOSSMANN). On the other hand, sugar of mother's blood reaches the foetal circulation by diffusion as has been proved by the blood sugar estimation of the mother's blood, the navel vein and navel arteria (REVESE, TUROLT and HELLMUTH.)

So, the second half of pregnancy is relatively a safe period. The increased blood sugar is controlled by the foetal pancreas. On account of its hyperfunction, there is enlargement in size. As already said, the liver of the foetus remains very active in the conversion of monosaccharide into glycogen. A part of glycogen is deposited in the liver and the surplus is converted into fats. Thus, the foetus comes in a condition of a regular mass.

According to CAFFIER, mass is constitutional. But most of these babies die of hypoglycæmia after birth (HOLZBACH, STEPP, NEVINNY, LAMBIER.)

Complication of Pregnancy.—Hydramnion may come off. (BRADSTRUP and OKKELS). The fluid contains large quantities of sugar. *Prophylaxis*:—It is very desirable that the gravida should attend the prenatal clinic from the 3rd month of pregnancy. Their urine must be examined every week. In cases of fatty persons, instructions about proper food should be given and their fats reduced. For the known diabetics, it would be advisable that they do not marry at all, because the object of marriage lies in the procreation of children and that can be accomplished only with very good luck. If, in spite of that, marriage is preferred, then the women should undergo sterilisation, especially if both are diabetics. Because in this case, the diabetes is likely to be inherited by the further progeny.

Things cannot go according to the will of the doctors. People do get married and conception does take place. But, considering the prognosis of the foetus, artificial abortion should be done during the first three months in the moderately severe and too severe cases.

The principle of treatment lies in the following:—

- I. Elimination of excess of blood sugar.
- II. Strictest asepsis.
- III. Improvement of the prognosis of the child.
- IV. Precautions for the mother.

I. The food should be regulated and carbohydrates and Insulin be given as much as the condition of the case requires. Usually, the coma should be treated with high doses of Insulin and glucose controlled by the estimation of blood sugar. The simple cases are best brought under control by administration of yeast one tea-spoonful thrice daily. In the moderately severe classes, Insulin should be added to yeast. The action lies perhaps in the presence of vitamin B and glutathions.

II. Strictest asepsis should be observed whilst conducting the labour of a diabetic. The labour room must be properly disinfected. The persons attending the labour must have masks on and should speak as little as possible. The gloves should be sterilised in a large number and should be changed after each and every vaginal examination which should be avoided as far as possible. The obstetricians should have patience and should be very conservative. The throats of the attending persons should be examined for haemolytic streptococcus.

III. Even Caesarian cannot change the prognosis of the foetus. After the child is born, it should be fed on glucose and if necessary into hypoglycæmic coma.

IV. In severe cases, the mother should not feed the baby.

Conclusion.—1. Only 15% of the diabetics conceive.

2. The prognosis of the mother in second half of pregnancy is usually bad. There is a danger of her getting coma.

3. A very small number of the foetuses reach full term. Most of them are over-weight and do not survive. Quite a number of them die intra-uterine.

4. The diabetics are not advised to marry. Even if they do, they should not conceive.

5. Treatment with yeast and Insulin yeast is recommended.

References:

1. Albers—See Fischer.
2. Antoine Tossilo—Wein. Klin Wsch., 1938, II, 1045-10.
3. Bradstrup, H. Okkels—Hyocumi Acta Obstet. Scand, 18, 136-163, 1938.
4. Caffier—Zentralblatt für Gynaecologie, 1937, II, 2472.
5. Calson and Genzburg—Amer. J. Phys. 36, 1915.
6. Colorni—Ann. Obstr. Milano, 1913.
7. Console Antonino—Monit. Obstet. Gine. 10, 741-751, 1938.
8. Eufinger—Msch. Geburt 92, 1932.
9. Ehrlich—Klin. Wochen 1934, No. 16.
10. Fischer—Zentralblatt für Gynaecologie, 1935, I, 249.
11. Genzburg and Pitimo.
12. Holzback—Zbl. Gynak 1926 No. 41. Arch. Gynae. 137
13. Hyeneman, Z. Geburt—Zeitschrift, 11, 149-163, 1935.
14. Hellmuth—Arch. Gynak 128 (1926).
15. Jaschke—See Fischer.
16. Kraus J.—Diabetes Mellitus and Pregnancy. Med. Klinik, 32, 375, 1936.
17. Liedtke—Diabetes in der Schwangerchaft Jnang.
18. Diss—Berlin, 1937.
19. Nevinny and Schretter—Arch. Gynak. 140.
20. Offergeld—Arch. Gynae. 86, 1908.
21. Lambie, R.—Ref. Zbl. Gynak. 1928, 401.
22. Pittimal—Ref. Ber. Gynak. 1, 342.
23. Revese Turolt—Zentralblatt für gynac. 1226: 15.
24. Schlossmann—Erg. der phys. 34, 1932.
25. Smyth F. Sott. Mary B. Olney—J. Pediatr. 13, 772-786 1938.
26. Stepp—Verh. Ges. Verdgskrkl. 11, 1932.
27. Seitz—Verh. Dtsch Ges. Gynak. 15, No. 1.
28. White P.—Surgect. 61, 324-332, 1935.

Diabetes and Pulmonary Tuberculosis

BY

K. S. Sanjivi, M.D.,

(Madras Medical Service), Madurai.

THE discussion of this subject consists mainly in answering the following three questions:—1. Is the association of the two diseases in the same individual of such frequency as to demand attention?

2. How does the presence of the one affect the course and outlook of the other?

3. What modifications are necessary in the usual individual treatment of the two diseases in view of their co-existence?

1. Tuberculosis of the lungs is undoubtedly common among diabetics. JOSLIN¹ and FISHBERG² have cited authorities supporting and disputing this statement. In a series of 100 diabetics, who have come under my notice, 24 had pulmonary tuberculosis; while, the cases of active tuberculosis in a survey of the general population amounted only to 2.23%.³ The other 76 included many cases admitted into the surgical wards for surgical complications of diabetes; as they have not been under continuous observation, it is not possible to say if any more of these developed lung signs later. Thus, tuberculosis being more than ten times as common among diabetics as among those with a normal carbohydrate metabolism, the answer to our first question must be emphatically in the affirmative.

The incidence of glycosuria among the tuberculous is, however, not high. In a series of 1000 open cases studied by me,⁴ only 1.2% had sugar in the urine. I have no figures regarding the incidence of glycosuria among the non-tuberculous general population.

2. FISHBERG remarks that in the diabetic, the onset of tuberculosis is insidious, the type very frequently exudative and the physical signs few. These observations are indeed so true that I firmly believe that every diabetic must be carefully watched for early evidences of a complicating tuberculosis by periodic skiagrams of the chest.

Since FISHBERG states that gangrene, carbuncle and hypertension are all rare in a diabetic with phthisis, it is worth mentioning that I have recently seen three patients with one of these complications in each.

While JOSLIN claims that he can confirm older writers in the rarity of hæmoptysis, FISHBERG has shown its greater frequency when the two diseases co-exist. In my experience, only 26.4% of a thousand open cases gave a history of blood-spitting while 16 out of the 24 diabetic consumptives or as many as 66.6% had spat blood.

It is generally said that "the outlook is grave when tuberculosis is conjoined with diabetes."⁵ It was thought that the old practice of

starvation to reduce the glycosuria helped the spread of the tuberculous process in the lung. Although McKEAN and MYERS⁶ claim that "the results compare favourably with the results obtained in non-diabetic tuberculosis of like severity and that as long as diabetes is carefully controlled, it does not have an adverse effect on the course of pulmonary tuberculosis," I feel that the presence of diabetes definitely darkens the outlook.

3. The bulk of modern opinion seems to regard that practically no deviation is necessary from the usual treatment of either disease.

The diabetes itself must be treated with a generous diet and the glycosuria controlled with the proper dosage of Insulin. Although FISHBERG sees much danger in using Insulin in the presence of active foci in the lungs, his fears appear to be exaggerated. No untoward effect could be attributed in any of my cases to the regular use of Insulin. Some practitioners even use Insulin in non-diabetic cases to help in the patient putting on weight.

The medical treatment of the pulmonary disease is to be pursued regardless of diabetes. Rest, fresh air and good food—assimilated with the proper dose of Insulin—are the bed-rocks on which the surgical treatment is built. Diabetes does not preclude the use of Sanocrysin or similar gold salts for the case in which they are indicated; and, they are certainly not to be used blindly in every case of tuberculosis.

Surgical Treatment:—Among the contra-indications for artificial pneumothorax, BURRELL and MACNALLY,⁷ in 1922, included "pulmonary tuberculosis intercurrent with some general diseases such as diabetes." But, in 1929, BURRELL⁸ wrote: "It is obviously unwise to induce pneumothorax when the tuberculosis of the lungs is a terminal phase of some intercurrent disease. At the same time, intercurrent disease need not of itself be a contra-indication. For example, many patients with diabetes and tuberculosis do extra-ordinarily well with Insulin and pneumothorax." ALEXANDER⁹ argues that "any complication making tuberculosis more difficult to manage makes the threat of the local lesion more serious and calls for pneumothorax sooner than if the complication did not exist. Complications in this class include pregnancy, diabetes, and syphilis." Seven of my 24 cases were suitable for pneumothorax when first seen; 29% as against only 17.3% in the series of 1000 open cases already referred to. Apart from the fallacy of small numbers, the diagnosis, in the present group of a larger number of cases suitable for pneumothorax treatment, is due to the fact that practically every one of the diabetic consumptives was on a distinctly higher economical level than the average cases of tuberculosis.

One of the seven cases developed an empyema following artificial pneumothorax and died of it. The others had no complications rendering the induction of artificial pneumothorax in diabetics specially dangerous in any way.

I have performed phrenic evulsion in such patients with an uneventful post-operative course. ALEXANDER reports that "Many surgeons have successfully performed thoracoplasty upon patients with varying degrees of diabetes, usually with the aid of Insulin."

I have ventured to briefly review this important subject, although my own experience has been totally inadequate, in the hope that the specialists in diabetes, who see them in large numbers, will watch for pulmonary complications and give us their views on this problem.

My thanks are due to Capt. F. A. B. Sheppard, I.M.S., District Medical Officer, Madura, for permission to publish this paper.

References :

1. Joslin, E. P.—(1923). *Treatment of Diabetes Mellitus*.
2. Fishberg, M.—(1932). *Pulmonary Tuberculosis*.
3. Report of the State of Public Health of the City of Madura. (1939).
4. Sanjivi, K. S.—(1939). *Indian Medical Gazette*, Vol. LXXIV, No. 9.
5. Price, F. W.—(1937). *A Text-Book of the Practice of Medicine*.
6. McKean and Myers—(1936), January 25th.
7. Burrell, L. S. T. and Macnalty, A. S.—(1922), *Report on Artificial Pneumothorax*, Medical Research Council.
8. Burrell, L. S. T.—(1929). *Recent Advances in Pulmonary Tuberculosis*.
9. Alexander, J.—(1937). *The Collapse Therapy of Pulmonary Tuberculosis*.

Obesity and its Relation to Diabetes

BY

K. K. Mehta, P.C.M.S.,

Retired Civil Surgeon, Multan.

THE scientific definition of diabetes is very comprehensive. I define diabetes in a simple and popular language as the morbid condition of the body in which sugar appears in the urine. Sugar is not at all the normal constituent of the urine. It is an abnormal thing. Now let us go back to find out wherefrom the sugar comes in the body and how and why it appears in the urine. Whatever we eat, and more particularly carbohydrates, after undergoing digestive changes in the mouth, stomach, etc., are transformed into glycogen in the liver factory and are stored there as such. According to the needs of the body, this glycogen is constantly converted into sugar and poured into the blood stream like petrol in the cylinder of the car from the carburetter. In order to supply heat energy to the body cells, this blood sugar is burnt in the muscle furnace by an igniting substance (a hormone) called Insulin produced in the island of Langerhans in the pancreas. The quantity of this sugar poured in the blood stream depends on the condition of the body. If the body is at stand still, I mean at do-nothing state, very little sugar is required for the supply of energy to the internal organs which are constantly at work for the well-being of the organism. If, on

physically at work, the amount of sugar needed will be much more than in the former condition. Now then, suppose liver throws more sugar in the blood stream than what is needed by the body cells, the excess must be got rid of; otherwise, the blood will be like syrup and will no longer be able to circulate. So, this excess sugar is expelled by the kidney in the urine. Now, what are the conditions which lead to the excess of sugar in the blood?

1. Over-eating of carbohydrate food with no exercise. To this class belong bankers, capitalist persons with sedentary occupation, sweatmeat vendors in India, literary persons and heavy drunkards. The liver goes on storing glycogen to its utmost capacity. If still the person continues to eat more and more of carbohydrates, the glycogen godowns in the liver factory having been filled up, the excess is converted into fat and is stored in the different fat godowns of the body which nature has provided for it. They are:—

- (1) The first godown is omentum—here fat can be deposited in an enormous quantity, thereby leading to that clumsy figure of the big-bellied person.
- (2) The second fat godowns are serous membranes.
- (3) The third godown is a space between the skin and muscles particularly at the hips and pectoral region.
- (4) The fourth godowns are muscles of the body.
- (5) The fifth godowns are the organs, especially the liver and the heart.

When in their turn all these fat godowns are filled up and the person still continues to march on the path of his destruction, the liver having been left with no godown to store the further input of sugar, begins to pour in large quantities of sugar in the blood stream. Here, now, once again nature tries to protect the organism by moving its defensive forces. What happens now is that the pancreas is called upon to work hard to secrete Insulin in large quantities, in order to burn the sugar in the blood, so that the normal blood sugar proportion is maintained. Even if the person still goes on over-eating, the pancreas working at a strain revolts against this heavy task. Insulin secretion becomes deficient, large quantities of sugar remain unburnt in the blood stream. Now the turn comes for kidneys. They try to throw off the excess sugar and constantly do throw off large quantities in urine. From this above description, it is quite clear how obesity is related to diabetes. This sort of diabetes is absolutely curable by restriction of diet, fastings and regular exercise. In fact, no medicine is required for it. This is one type of diabetes related to obesity. Next time, I will deal with other types of obesity due to disorders of internal secretions.

Towards the Close of Diabetic Lives in India

BY

A. Singh, M.B.,

Chest Specialist, Benares City.

DIABETICS are found all over the world and in all sorts of climates, but the incidence and types of the disease may differ widely from societies to societies and from localities to localities. While racial tendencies depending on the inheritable influences of the "past" do play their parts in producing "the picture," it is mainly in the "dietetics" plus personal habits of the individuals alone that the explanation of the disease is usually arrived at. Thus in cold, temperate and hardy climates, where nature is less bountiful and life is neither so easy nor so neurotic as a rule, it would be difficult to get a "replica" of the Indian picture of diabetes. Yet, in places like New York, Paris or London, where "eating" may be sometimes too much and "artificialities of Life" equally or more "denervating"—with fads of this "ism" or that "ism" in so many things—it may be quite easy to get the "Indian picture" little or not much modified or modified often for the worse.

Before going into the details of the Indian picture, I must say something about the classification of the types of the disease—I mean the types of the *pukka* or hyperglycaemic—diabetes mellitus. It is a patent truth that lesions in the "Islets of Langerhans" in the pancreas are often associated with diabetes of glycosuric forms sooner or later; yet hyperglycaemias with or without temporary glycosurias can be seen without any pathological lesions in the said islets. For the explanation of such hyperglycaemias in the said suria excesses, and anomalies in the glucose-storage-system of the body, are two alternative groups of causes. Of these, the last (anomalies in interplay of endocrines. Thus at the beginning of every real diabetic history, symptoms may begin as a result primarily (1) of lesions in the pancreatic islets, (2) of disturbances in the liver-muscle plus neuro-endocrinal mechanism, or (3) anomalies in the structure and functions of the alimentary canal in respect to the "intake" of sugar or sugar-giving substances. For the sake of facilities in description or references, we may classify all cases of *pukka* diabetes according to their suspected sources of pathogenesis at the beginning as:—

- (1) Primary pancreatic types.
- (2) Liver-et neuro-endocrinal types.
- (3) Alimentary or dietetic types.

The above classification, however, does not mean that there are always something like water-tight compartments between one type and another. Oftener than not, mixed types are to be seen specially towards the "end" in types (2) and (3)—because, hyperglycaemia of

any origin acting for a long time does produce something like secondary pancreatic lesions—thereby adding symptoms of the failure (more or less) of the pancreatic hormone to the previous pictures. Type (1) is more serious and of a more dreaded nature than others because, under it, there are two kinds of defects at the same time *i.e.*, failure in the proper utilization of sugar and failure in keeping patient's glycæmia at the proper level. Failure in "sugar utilization or combustion" produces important side-troubles like defects of fat and protein metabolism—leading to a general devitalization, the details of which are not yet fully known, but which is known to favour the growth of everything harmful for the patient in his own body. Types (2) and (3) in themselves are of equally mild natures in the great majority of cases—being apparently cured at times. Without quoting any authoritative statistics of the country, (because very little is available for the same), it can be safely stated that the incidence of the primary pancreatic type in India is the same as or nearest to "the average" for human populations of the world, while the incidence of types (2) and (3) is much greater in India, possibly far in excess, above "the average" for the human populations of the world.

Peculiarities of Indian Diabetics.—Child diabetics seem to be rarer in India than what can be quoted as "average" for the world and so are the so called acute fulminating cases of pre-Insulin days not very common in Indian practice. The female proportion in incidence also is decidedly much less than the male one.

The great majority of Indian diabetics commence the vague parts of their histories between the ages of 20 and 35 but usually after 25. Oral sepsis, "over-eating" and "Munsif-like" dispositions (sedentary habits etc.) with some "isms" in dietetic history, form some of the usual findings of the early period of the disease. While the histories of the majority of cases in India start earlier than what JOSLIN gives for his majority of cases from American and European experiences, the upper limit of getting the disease here is practically the same as given by him.

The main recruiting ground of Indian cases is formed by the upper-middle class, the rich class and the lower middle class in the order of importance, while the poorer and the working classes give only occasional cases for enlistment.

The advent of Insulin in Therapeutics has markedly improved the expectation of life in diabetics all over the world—not excluding India. Foolish statements like "once Insulin, always Insulin" may apply to certain cases of type (1) even in this country—though, as already pointed out, such cases are much less in the Indian picture, but they are not applicable to the great majority of our cases that fall under types (2) and (3)—in which, it is best used for crossing over periods of "weaknesses" or emergencies due to infections and accidents.

Diabetics of India as a class are more or less fairly intelligent—very often well-to-do people, though not always so. Their disease

discovered usually in some side-activities like examination for life insurance, candidature for posts etc. or for explaining their emaciation, polyuria etc. In their usually long courses of the disease, most of them become impatient or tired out seeking "short cuts to cures" in the numerous *pathies* or alternative systems of treatment—trying and leaving one after another—meeting mishaps or their own ends in experiments or coming back to their first man (or his substitutes) with more faith in what was told to them at the very beginning.

Factors in the Expectation of Life in Diabetics.—1. *Medical control or proper diagnosis and treatment of the patient*:—The diabetic body can be compared in certain respects to a bed containing gun powder or dynamite which can explode at any moment and under certain circumstances unless the nature of the contents are previously known and proper attempts are made to prevent the combination of circumstances favouring the explosion. Unless the possessor of the bed is intelligent, keen and determined, and his advisers are up-to-date or possessed of proper knowledge, the task of prevention is likely to remain defective with chances for death or accidents to the man.

Thus, not only the name of the "disease" has to be disclosed in diagnosis, but a very detailed study has to be made as well of the blood sugar, carbohydrate tolerance of the patient along with those of his or her regular urinary findings, effects of diets given under observations or indications and non-indications of supplementing patient's body-insulin with the Insulin of exogenous sources. The patient and the doctor must evolve such suitable menu for the living, at the same time keeping his urine sugar-free—without or with the introduction of exogenous Insulin. Every hap-hazardism or attempt in finding "short cut cures" may tell upon the expectation of life of the patient. An intelligent diabetic should not have frequent changes in his doctors or meaningless love for alternatives throughout his life.

2. *Exposure to risks*:—The diabetic even of a mild type must know that every pathogenic germ has more chance of growing in his body than in that of any one else. He should specially avoid sources of "droplet infections" or germs of throat and respiratory passages.

He should avoid extremes in temperature and extremes in everything—the commonest source of devitalization for every one. Every chance for a severe infection has a shortening effect on the longevity of the patient.

3. *Operations and choice of anæsthetics*:—(1) No operation upon a diabetic should be lightly undertaken and before every operation, his urine should be de-sugarised without or with the help of Insulin. Among the anæsthetics, Chloroform should always be avoided and preference should be given as far as possible to a local anæsthetic like Novocaine.

4. *Pregnancy in diabetic women* is quite possible now-a-days

under the regime of Insulin, but in cases where births are not of extraordinary importance, it can be better avoided with or without the help of contraceptives. In other cases if the kidneys, hearts and livers are not much damaged, a pregnancy can be encouraged, controlled and led to success through "Insulin cum dietetic regulations".

5. *Marriage*:—Juvenile and adolescent diabetics are not very common in this country so that the question of marriage in diabetics has not got the same importance over here as in European countries. The present consensus of the world opinion on this can be put like this—"while marriages cannot be justly forbidden, pregnancy after the marriage is highly inadvisable in all but the exceptional cases".

6. *Management of complications and treatment of associated or inter-current diseases*:—Insulin has proved to be a great boon for diabetics, if it is used intelligently and in intelligent persons specially for crossing over "emergencies" for short periods. For chronic infections, it is of much utility to the patient in the beginning of his diabetic state, of little help in later periods and of doubtful utility near the end. Cardio-vascular and renal complications, which usually develop after a long period of hyperglycæmic history, are very difficult to treat by drugging orally or parenterally and their existence cannot but go towards shortening the future span of the life of the patient. Previous "Insulinization" ensures success and prevents troubles in over 90% of diabetics in all local operations (cataract etc.) and specific treatments in most of inter-current infections.

The Maximum Span of Life in a Diabetic.—Things are much changed now and it is possible for a confirmed diabetic to live beyond his average expectation of life, if he is careful and fortunate enough. 30—40 years of "diabetic lives" with apparently normal occupations can be easily seen and pointed out. But a "diabetic fool" cannot live long. 10—15 years after diagnosis may be the average span of life for "the mediocre" in intelligence of the usual variety in India.

The Diabetic End.—So, the dreaded end comes to a diabetic as it does everywhere else. While the ignorant, untreated or eccentric cases die usually of coma, with or without acute infections and sepsis (carbuncles etc.), or accidents of varied nature and descriptions, intelligent and medically controlled cases seldom end with any of these at present. They get their "terminal infections" more from their endogenous sources and less from exogenous ones. Their own erstwhile friendly or neutral commensals of the body—the organisms inhabiting the throat, mouth, bowels, etc., with apparent harmlessness up till now, become active and pathogenic when the patients are devitalised beyond a certain limit with or without defects in important organs of the body (kidney, liver, blood vessels, heart etc.) and all contributing towards the complexity of the final picture. "Senilism", with arterial degenerations and gangrenous tendencies plays an important part in such ends and even the best treatment fails because of the multiplicity of the factors to combat at the end. The "coma"

of such ends is seldom a pure diabetic coma. It is usually a mixture of uræmic or cholæmic elements with diabetic elements proper. Sometimes cardiac failure or "syncope" may supervene without anything like coma to be seen at the end. Among the infective manifestations on such occasions "pulmonary tuberculosis of the reactivation type" and "broncho-pneumonia or pneumonias of the endogenous origin" are the commonest.

Summary.—1. The Indian picture of diabetes mellitus differs markedly from the same of other parts of the world like U.S.A., England etc.

2. In India, there is relative insignificance in the incidence of the primary pancreatic type and marked preponderance of the liver-et neuro-endocrinal type and alimentary or dietetic type—the last two varieties being naturally milder than the first.

3. The advent of Insulin in Therapeutics has improved the expectation of life in diabetics everywhere including India.

4. It is possible for an intelligent diabetic to live beyond the average expectation of life now-a-days and it is quite common to see intelligent diabetics having lived 30—35 years of useful lives.

5. A "diabetic fool" cannot afford to live long. He usually dies of coma with or without acute infections or sepsis like carbuncles etc.

6. Intelligent diabetics get more troubles from their endogenous foci of past infections or from their "erstwhile commensals" of the body.

7. Pulmonary tuberculosis of the reactivation type and pneumonias and broncho-pneumonias of "commensal" origin are common troubles towards the end of intelligent diabetics.

8. The comatose condition which is seen at the death-scenes of long standing diabetic histories is very often not due to pure diabetic ketonæmia. Usually, it has mixtures of uræmic or cholæmic elements with or without ketonæmic ones.

Bibliography:

1. Lawrence, R. D.—*The Diabetic Life*, 1927.
2. Langdown Brown, Sir, W.—*Medical Annual*, 1937.
3. Joslin—*The Treatment of Diabetic Mellitus with Observations Based on 3000 Cases*, 1928.
4. Warren, S.—*The Pathology of Diabetic Mellitus*, 1930.
5. Chatterji, H. N.—*A Manual of Diet and Diabetes*, 1929.

Heprona

An active combination of accessory food factors

For
**DEBILITY - FATIGUE
DEPRESSION**
♦ ♦ ♦

HEPRONA is an important contribution to the therapy of debilitated conditions in both sexes, the generous proportions of the active constituents ensuring prompt restorative effects.

HEPRONA is well adapted to the needs of women as it encourages a full and healthy bodily function. During pregnancy and lactation, when heavy demands are being made upon the organs of nutrition, it adds greatly to the comfort of the mother and the well-being of the child.

*Prepared and tested
in modern biological laboratories.*

In bottles 6 and 12 fld. oz.

Composition:
The Vitamins B₁, B₂ and C. Glycerophosphoric Acid.
The anti-anæmic principles of fresh liver.
Colloidal iron with traces of copper, cobalt & manganese

*Alert and
Self-confident*



Depot stocks are held by:

M. J. Batiwala (Box 313), Laxmi Buildings, Phirozsha Mehta Rd., Bombay
Victor & Co. (Box 1353), 10 Broadway, Madras

EVANS SONS LESCHER & WEBB LTD.
LIVERPOOL and LONDON

S. Kushalchand & Co. (Box 2364), 55 Canning St., Calcutta
D. R. Messman, Bunder Road, Karachi

INDEX TO ADVERTISERS, JUNE '40.

	PAGE.		PAGE
Alembic Chemical Works Co. Ltd.	21, 44	Horlick's Malted Milk Co.	18
Allen and Hanburys Ltd.	5	Indian & Eastern Chemist	40
Astier Laboratories	38	Krishna Pharmacy	42
Atlantis (East) Ltd.	21	Kushmol Pharmacy	44
Banerji P.	30	Lister Antiseptics & Dressings Co.	10
Bench T. C. & Co.	30	Jammi Venkataramanayya	14
Bengal Chemical and Pharmaceutical Works.	Inside of back cover	Journal of Indian Medical Association	42
Boots Pure Drug Co., Ltd.	32	John Wyeth & Brother Ltd.	20
Brahmachari Research Institute	17	Loucatos G. & Co.	24
Brand & Co. Ltd.	31	Martin & Harris Ltd.	6
British Drug Houses Ltd.	22	Martin H. Smith Co. N. Y.	9, 17
Burroughs Wellcome & Co.	23	May & Baker Ltd.	25
Carrick G. W. Co.	14	Parke Davis & Co.	2
Coleman & Co., Ltd.	3	Petrolagar Laboratories Ltd.	36
Corn Products Co. Ltd.	8	Research Laboratory	42
Cow & Gate	29	Rosbay & Co.	36
Crookes Laboratories Ltd.	15	Scientific Instrument Co.	42
Denver Chemical & Mfg. Co.	4	Seller L. H.	42
Dhansukhlal & Co.	42	Silten Ltd.	43
Eli Lilly & Co.	Inside Front Cover	Stephen Smith & Co., Ltd.	16
Evans Sons Lescher & Webb Ltd.	37	Thacker Spink & Co. Ltd.	40
Frank Ross & Co. Ltd.	17	Thakore T. M. & Co.	19, 41
Galleno Pharmaceutical Works	10	Union Drug Co. Ltd.	19
Gillanders Arbuthnot & Co.	33	United French Laboratories	11
Glaxo Laboratories Ltd.	7, 13, 28, 27	Victor X-Ray Corporation (India) Ltd.	39
Govt. Industrial & Testing Laboratory	1	Wander A. Ltd.	28
Hering & Kent	11	Waterbury Chemical Co.	34
Hewlett C. J. & Son Ltd.	12	William R. Warner & Co.	9, 35
		Zeal G. H. Ltd.	1

THE HIGHEST AWARDS AT INTERNATIONAL EXHIBITIONS

EXCELLENT **ARHEOL** BALSAMIC

$C_{15}H_{24}O$
THE PURIFIED ACTIVE PRINCIPLE OF
SANDALWOOD OIL IN A DEPENDABLE
AND NON-IRRITATING FORM.
for GONORRHEA, CYSTITIS,
PYELITIS, PYELO-NEPHRITIS,
PROSTATITIS, URETHRITIS
AND VESICAL CATARRH.

NEO-RIODINEIodine Treatment without Iodism
in 2 Forms.

An aqueous solution of organic iodine.

IMMEDIATE AND INTENSIVE ACTION BY
NEO-RIODINE.

For Internal use RIODINE CAPSULES.

Ask for literatures

Dr. P. ASTIER LABORATORIESP. O. B. 740, P. O. B. 460, P. O. B. 248,
Bombay. Madras. Karachi.**DIABETICS
USE COPALTRA**

A marvellous herbal remedy that radically
cures diabetes in all its forms. Approved
to be a rational remedy in Europe and
registered at the National Laboratory Paris
(France) for the control of medicine under
No. 1662-1.

A box sufficient for one month's treatment
costs Rs. 10/- only V. P. P. extra.

A descriptive
booklet sent freeSold by all the
leading chemists of
Bombay, Karachi,
Calcutta, Madras.Sole Agents for India,
Burma & Ceylon**COPALTRA & CO. LTD.,**

127, New Bhatwadi St., Bombay. 4.

Reliable X-Ray Equipment is a Tangible Asset and vitally important to the efficiency of an x-ray therapy service



ONE of the busiest phases of hospital service these days is unquestionably that devoted to tumor therapy. ¶ Experience has shown that once facilities for high-voltage x-ray therapy are made available, it's only a relatively short time before increasing demands on this service give rise to the problem of conveniently arranging daily treatment schedules. ¶ It is at this stage when users of G-E Maximar x-ray therapy units fully appreciate the value and importance of reliable equipment—when correctness of design and precisional workmanship are proved by consistently reliable performance, day in and day out. The abil-

ity to carry on without serious interruption to full treatment schedules, is indeed gratifying to all concerned. ¶ If long experience in design and manufacture, and the satisfactory experience of hundreds of users of G-E high-voltage x-ray units the world over, are criterions, your investment in a G-E Maximar therapy installation will prove unusually sound. Investigate—get all the facts, now.

Exclusive Distributors in India:
VICTOR X-RAY CORPORATION (India) LTD.,

Bombay: Pallard Estate P. B. 992.
Lahore: The Mall, P. B. 181.
Calcutta: 18, Hare St., P. B. 2007.
Bangalore City: Narasimharaja Road.
Lucknow: 1715, Bickett Road.
Colombo: 3, 44th Lane, Wollawatto

*Before buying from
elsewhere*

DRUGS, PHARMACEUTICAL
PRODUCTS, SURGICAL
INSTRUMENTS, SUNDRIES
AND PATENT MEDICINES,

It will be to your profit to try

DHANSHUKHLAL & CO.,

(Union Medical Stores)

Chemists and Druggists,

No. 147, Princess Street, Bombay. 2.

Telegram: "HYPODERMIC"

**JOURNAL OF
THE
Indian Medical Association**

EDITED BY

SIR NILRATAN SIRCAR,
KT., M.A., M.D., D.C.L., ETC.

WITH THE HELP OF

A STRONG ALL-INDIA EDITORIAL
BOARD

*The Official Monthly Publication of the
Indian Medical Association.*

Features:

1. Original Articles. 2. Case-Reports.
3. Society Proceedings. 4. Valuable
abstracts from leading Medical
Journals from all over the world.

Published on the First Day of the Month

Annual Subscription Rs. 6 post free.

Free to members of the Indian Medical
Association.

AN EXCELLENT MEDIUM FOR ADVERTISEMENT

For particulars write to Secretary,
Samavaya Mansions, Calcutta

When writing to advertisers, please mention the "Antiseptic".

FILARIA SPECIFIC

Dr. PAUL'S ROSBAY (Oral or
Injection), the best tried remedy
hitherto proved effective in ELE-
PHANTIASIS, LYMPH SCROTUM,
CHYLURIA, CHYLOCELE, ORCHI-
TES, VARICOSE GROIN GLANDS,
E N D E M I C LYMPHANGITES,
FILARIAL FEVER etc., after failure
of other drugs. Contains Tr. Rosbay
and a radio-active element but not
arsenic, antimony or vaccine. Ra-
tional and safe. No by-effects or
after-effects. Radical and lasting
result assured.

Literatures etc. on request to:

ROSBAY & Co.,

185, Chittaranjan Avenue,

P. O. Box 11418, :: CALCUTTA.

DIABETES

An entirely New Invention
of herbal combination for the com-
plete and permanent cure of
Diabetes by Dr. D. R. Mehta,
M.P.L., L.P.H. Price Rs. 4 only for
16 powders for 8 days.

Manager, **KRISHNA PHARMACY,**
'KRISHNA BUILDING'
Ludhiana (Punjab) India.

YOUR EYE

Does it trouble you? If so, try
SELLER'S LOTUS HONEY, the
safest, surest and most highly praised
Nature's cure for Eye-diseases. Cures
even Cataract etc. Literature free.

SRI KRISHNAN BROS.,

Post Box 166, :: G. T., MADRAS.

**RHEUMATIC
DISEASES**

POLYARTHRITIS - ARTHRITIS -
SCIATICA - LUMBAGO - GOUT

LEUCOTROPIN

eliminates the causes of
inflammation and abridges
the healing process.

LEUCOTROPIN

stops pain immediately,
without fail.

LEUCOTROPIN

acts quicker than mor-
phine without its draw-
backs. Injections are
absolutely painless and
without any after-effects.

Boxes of 5 ampoules for intravenous
or intramuscular injection.

RHEUMOTROPIN TABLETS FOR ORAL USE

given between injections or after treatment will lengthen
the intervals between injections and stabilize their effect.

Samples and literature
gladly on request
from the Sole Agents

SILTEN LTD. Manufacturing Chemists London, E.W.S.

VYAS BROS. PRINCESS STREET BOMBAY

When writing to advertisers, please mention the "Antiseptic".

DOCTORS PREFER

Alembic
INJECTIONS

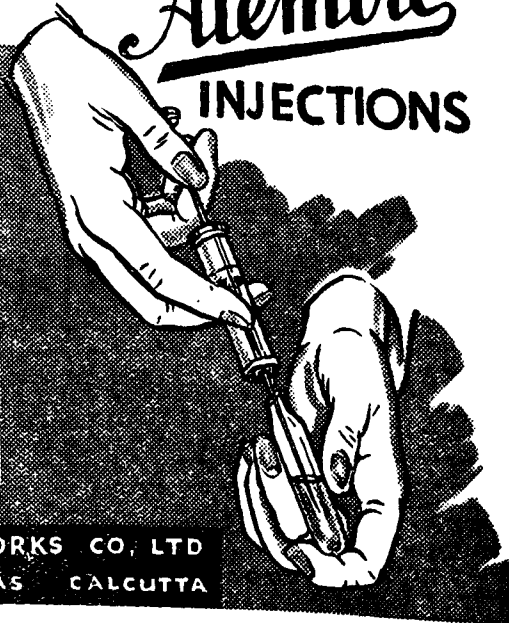
THEY ARE PREPARED CAREFULLY
UNDER RIGID SCIENTIFIC CONTROL.

THEY ARE OF BEST PURITY.
ACCURATE STRENGTH. PROPER
REACTION AND UNIFORM QUALITY.

THEY ARE PROPERLY STERILISED.

THEY ARE WELL PRESERVED IN
NEUTRAL GLASS AMPOULES TO
AVOID DETERIORATION OF THE
CONTENTS.

THEIR MODERATE PRICES ENSURE
ECONOMY WITH QUALITY.



THE ALEMBIC CHEMICAL WORKS CO. LTD
BOMBAY B. R. A. MADRAS CALCUTTA

'NOTOAA'

Transformation of Ginger into NOTOAA Granules provides physicians with a
therapeutic agent of high potency for Acute Appendicitis.

NOTOAA contains no purgatives to make the case worse; no opium to mask the
symptoms until too late; it does not interfere with any line of treatment and does not
fail in correctly diagnosed acute cases. It is not a quack nostrum but a scientific
product.

Therefore we solicit physicians to try this medicine before resorting to the
knife. If relief is obtained you have avoided a risky operation; if no relief within half
an hour, perform the operation, if so decided.

Full Literature on request.

Bottles of 25 granules, Rs. 12 each, same as samples to Doctors Rs. 5 each if
paid in advance.

Dr. Khurshaid's

'KUSHMOL'

(The Asthmatic's Delight)

A weapon of precision. Effective from the very first dose in 98 per cent of
cases. Superior to all the drugs yet known to physicians.

Arm yourself with Kushmol and Defy Asthma.

Life-long chronic cases are cured in a few days. Bottles of 80 grs. Rs. 3-4 each.

The KUSHMOL PHARMACY, Benares City (N. India)

When writing to advertisers, please mention the "Antiseptic"

WAR AGAINST SYPHILIS**THIARSIN**

A potent organic compound of Arsenic of low toxicity
for intramuscular use in all stages of syphilis. Every
batch before issue is tested Chemically and Biologically.
Available in .075 gm., .15 gm., .30 gm., .45 gm. and
.60 gm.

THIARSIN SOLVENT

This solvent containing Chloretone, Guaiacol and
Glucose has been introduced to make the injection of
Thiarsin absolutely painless even in sufficient con-
centration. Highly useful for hypersensitive patients.
It is issued in boxes of six 5 c.c. ampoules.

BENGAL CHEMICAL AND PHARMACEUTICAL WORKS, LD.

CALCUTTA :: BOMBAY

Madras Agents:—N. DASAI GOWNDER & CO., 41, Bunder Street.

B. C. P. W.

LIVER EXTRACT

CONCENTRATED

For Intensive Parenteral Liver Therapy

Injection of 1 c.c. produces same therapeutic effect
as oral use of 1000 grms. of Fresh Liver

**Non-Toxic :: Non-Depressant
Highly Purified**

In 1 c.c., 2 c.c., 5 c.c., ampoules and 10 c.c. phials.

BENGAL CHEMICAL & PHARMACEUTICAL WORKS LD.

CALCUTTA :: BOMBAY.

Madras Agents:—N. DASAI GOWNDER & CO., 41, Bunder Street.

AN ANTICONVULSANT FOR THE TREATMENT OF EPILEPSY

KAPSEALS DILANTIN SODIUM

DILANTIN SODIUM (sodium 5,5-diphenylhydantoinate), an anticonvulsant with little or no hypnotic effect, is supplied for the treatment of epileptics not responsive to other medication. Extensive clinical use indicates that Dilantin Sodium will prevent, or greatly decrease the frequency and severity of, convulsive seizures in a majority of epileptics. However, since the significance of observed reactions to Dilantin Sodium is not fully established, patients receiving the drug should be closely observed.

Dilantin Sodium is accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Non-official Remedies

The name "Dilantin Sodium" designates the sodium salt of diphenylhydantoin. Dilantin Sodium is available as 0.1 gram (1 grain) capsules in bottles of 100.

PARKE, DAVIS & COMPANY, ROYAL OAK, MICHIGAN
The World's Largest Manufacturer of Pharmaceutical Products

Printed at the "Antiseptic" Press and Published by the Proprietor V. Krishna Rao, Madras