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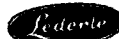
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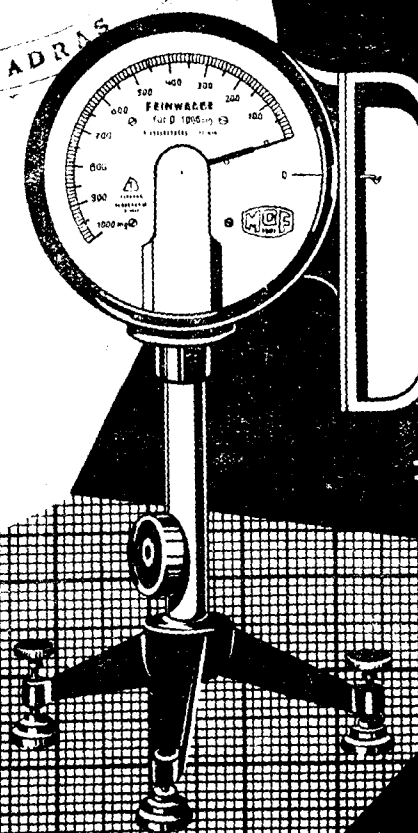
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MANUFACTURING CHEMISTS

1/153, MOUNT ROAD, MADRAS-2, INDIA.



AVAILABLE ON DOCTOR'S PRESCRIPTION

THE SUPREME TONIC RESTORATIVE

# Hall's WINE

Guaranteed free from Meat Extract.

# Ergoapiol-(Smith)

## A Menstrual Regulator . . .

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

In cases of Amenorrhea, Dysmenorrhea, Menorrhagia and Metrorrhagia.

hagia, Ergoapiol serves as a good uterine tonic and hemostatic. Valuable in obstetrics after delivery of the child.

DOSAGE: 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.

## Aimed to combat Anaemias

Acknowledged as the anti-anaemic therapy of proved merit, LIVULES contains proteolysed liver and stomach powder, iron, vitamins B-complex and C. Also available with folic acid or B12 or both; or with folic acid, B12, and intrinsic factor.

### Each capsule contains:-

|                                                                                      |                          |
|--------------------------------------------------------------------------------------|--------------------------|
| Proteolysed Liver Powder from                                                        | 3.25 G. of fresh liver.  |
| Proteolysed Stomach Powder from                                                      | 1.0 G. of fresh stomach. |
| Ferrous Sulphate Exe. B. P.                                                          | 0.1 G. (1½ gr. approx.)  |
| Vitamin B1 B. P.                                                                     | 5 mg.                    |
| Vitamin B2 (Riboflavin B. P.)                                                        | 2 mg.                    |
| Vitamin B6 B. P. C.                                                                  | 0.5 mg.                  |
| Calcium Pantothenate U. S. P.                                                        | 1 mg.                    |
| Niacinamide B. P.                                                                    | 15 mg.                   |
| Vitamin C B. P.                                                                      | 30 mg.                   |
| (Livules & Folic Acid) Folic Acid B. P.                                              | 1.5 mg.                  |
| (Livules & B12) Vitamin B12 B. P.                                                    | 5 mcg.                   |
| (Livules & Folic Acid, B12 & Intrinsic Factor) Purified Intrinsic Factor Concentrate | 10 mg.                   |

Livules with Folic Acid & B12 & Livules with Folic Acid & B12 (without iron) also available.

# LIVULES

(One more variety—  
LIVULES & Intrinsic Factor—  
recently introduced)

ALEMBIC CHEMICAL WORKS  
CO. LTD. BARODA-3.



YOU CAN PUT YOUR CONFIDENCE IN ALEMBIC.



## where PAIN is a symptom...

Therapy of the underlying causal condition is no doubt the prime consideration. However, when treatment of the basic disease does not or cannot afford prompt relief, 'ANACIN' will often alleviate the distress of pain and impart a sense of well-being.

'ANACIN' is a non-toxic and clinically dependable preparation, specially formulated to provide a prolonged period of analgesia with a single dose of 1 or 2 tablets.

### Composition

Quinine 1¼ gr. Aspirin 3 gr.  
Phenacetin 3 gr. Caffeine 1¼ gr

# ANACIN

  
ANALGESIC TABLETS

Manufactured and Distributed by:  
GEOFFREY MANNERS & COMPANY PRIVATE LIMITED, BOMBAY  
Trademark Proprietors:  
WHITEHALL PHARMACAL COMPANY, NEW YORK, U.S.A.

as in  
HEADACHE  
TOOTHACHE  
MUSCLE PAIN  
NEURALGIA  
NEURITIS  
DYSMENORRHOEA  
INFLUENZA

• Trade Mark

In piller-proof containers  
of 32 tablets and packets  
of 2 tablets each.

Protect your patient  
by prescribing  
**GLUCOSE POWDER**  
by name



**DEXTROSOL** is pure Anhydrous Dextrose, conforming to the U.S.P. and B.P. standards, its chemical formula being  $C_6H_{12}O_6$

**GLUCOVITA** EVERY 100 PARTS CONTAIN:  
Dextrose Monohydrate ..... 99.4  
(Purified glucose)  
Calcium Glycerophosphate ..... 0.2  
Calcium Phosphate ..... 0.4  
Each ounce of Glucovita is fortified with 250 I U of Vitamin-D (Calciferol)

**CORN PRODUCTS CO. (INDIA) PRIVATE LTD.**

Bombay-1 Calcutta-1

**THREE TONICS** with Vitamin B Complex and B<sub>12</sub> combines various B Complex factors with Glycerophosphates and acts as a general stimulant. Easily assimilable Phosphorus is available in this preparation and its administration regenerates nervous energy which has been lost by wasting diseases, over work, exhaustion, anxiety, etc. Potassium and Manganese, two vital elements, are available to the extent of normal daily requirement. Traces of Strychnine in combination with Glycerophosphates have been used for years as a tonic stimulant.

**THREE TONICS** besides being a dietary adjuvant is useful in the treatment of Anæmias, loss of appetite etc. It is also indicated in Neuritis, Beri-Beri, Nutritional Diarrhoea, Sprue, an invaluable dietary supplement during pregnancy etc. It is Sulpha Drugs or Antibiotics and also for patients suffering from Diabetes Mellitus

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Own **OLYMPUS** for

• SERVICE • STABILITY • SUPERIORITY

## LABORATORY MICROSCOPE

### Improved Model GB

Mechanical Tube Length 160 mm. • Graduated Draw Tube • Fixed Square Stage with Built on Graduated Mechanical Stage • Fine Adjustment of Double Lever-type without scale • Condensor N.A. 1.2, (with iris)—movement by Rack and Pinion • Triple Nose-piece • Interchangeable for Dark Field Condensor, Phase Contrast Accessories, Binocular and Monocular Attachments.

Huygen's Eyepiece 5x, & Periplan 10x, & 15x Achromatic Objectives 10x, 40x and 100x Oil Immersion. Magnification: 50x—1500x.

**Price Rs. 790/-**

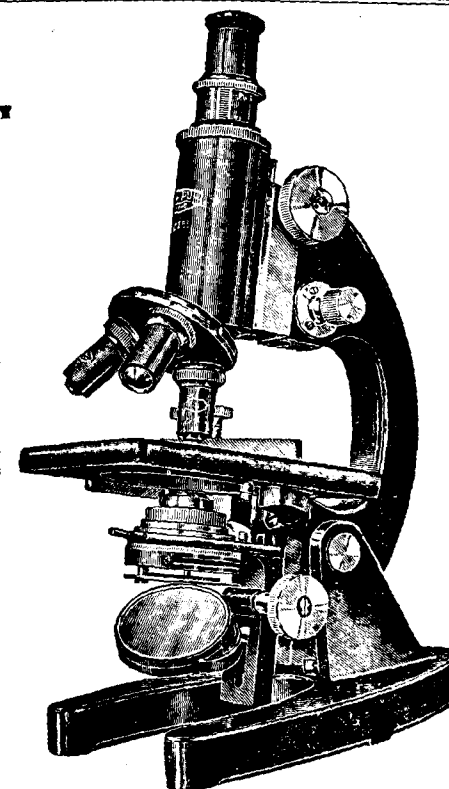
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**DARBARA SINGH & SONS,**

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166, Hornby Road, Fort,

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Also available various other models



Guaranteed

## In combating anaemias

Proteolysed Whole Liver Extract  
fortified with  
Vitamin B complex including  
Folic Acid & B<sub>12</sub>, Vit. C & Iron...



**PROLIFEX**

BENGAL IMMUNITY CO. LTD.  
CALCUTTA-13

Each tablet represents:

|                                   |          |
|-----------------------------------|----------|
| Proteolysed liver powder          | 250 mg.  |
| (Equivalent to 2 gm. fresh liver) |          |
| Stomach powder                    | 10 mg.   |
| Vitamin B <sub>1</sub>            | 2.5 mg.  |
| Vitamin B <sub>2</sub>            | 1 mg.    |
| Niacinamide                       | 10 mg.   |
| Vitamin B <sub>6</sub>            | 0.5 mg.  |
| Panthenol                         | 1 mg.    |
| Folic Acid                        | 1 mg.    |
| Vitamin B <sub>12</sub>           | 2.5 mcg. |
| Vitamin C                         | 20 mg.   |
| Ferrous Sulphate (Exsiccated)     | 100 mg.  |
| Cobalt Nitrate                    | 5 mcg.   |

In Packs of 50, 100 & 500

CALMIC LIMITED announce a  
NEW AND ORIGINAL ORGANIC-IRON TABLET  
**FERROMYN**  
(Ferrous Succinate)

*the latest and most significant advance  
towards ideal oral iron therapy*

FERROMYN is an original and logical approach to the problem of iron absorption and utilisation in the treatment of hypochromic anæmias and brings oral iron therapy a step nearer the ideal.

This new iron preparation presents Ferrous Succinate, a bivalent iron salt prepared from succinic acid, which, together with glycine is essential for the synthesis in the red bone marrow of a porphyrin (haem) containing iron.

Normal Hb. and serum iron levels were demonstrated over an average period of 24 days treatment with a group of hypochromic

anæmia patients with an average initial haemoglobin of 60%.

The controlled clinical trials with Ferromyn show an iron utilisation factor of 42% as compared with 14% Ferrous Sulphate and 28% Ferrous Gluconate.

This response was obtained with the low total average dosage of pf. 2,604 mgm. available iron.

In comparison, the controlled group treated with Ferrous Sulphate required 42 days with an average dosage of 7,568 mgm. available iron to reach the same Hb. and serum-iron value.

| AMOUNT OF AVAILABLE IRON ADMINISTERED | PREPARATION       | IRON UTILISATION COEFFICIENT |
|---------------------------------------|-------------------|------------------------------|
| 2600 mgm.                             | <b>FERROMYN</b>   | 42%                          |
| 3180 mgm.                             | FERROUS GLUCONATE | 28%                          |
| 7560 mgm.                             | FERROUS SULPHATE  | 14%                          |

FERROMYN is available in the following forms:

**FERROMYN TABLETS** Each tablet contains: Ferrous Succinate 150 mgm. Available in packs 100 and 1,000 tablets.

**ELIXIR FERROMYN 'B'** Each tea-spoonful contains: Ferrous Succinate 150 mgm. Aneurine Hydrochloride 1 mgm. Riboflavin 1 mgm. Nicotinamide 10 mgm. Available in bottles 4 oz. and 20 oz.

Manufactured in England by

**CALMIC LIMITED • CREWE • LONDON**

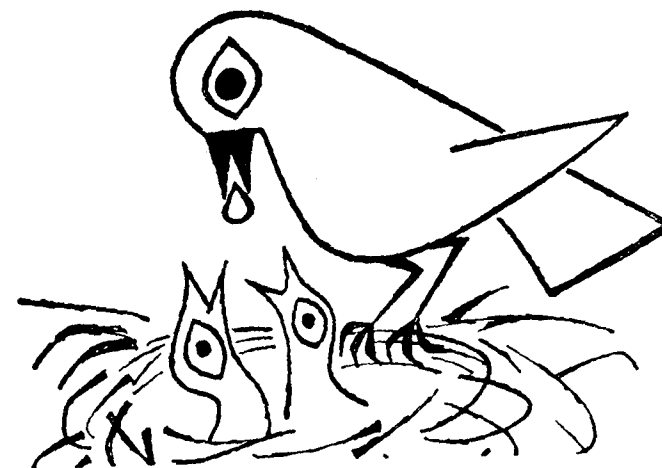
Sole Distributors of CALMIC Preparations in India:

**JUGGAT SINGH'S SON & BRO.**

Regal Cinema Building, 1st Floor, 41 Apollo Pier Rd., BOMBAY, 1

Advertisement by Courtesy of: M/s. CALMIC LTD., CREWE

*Growth needs proper care...*



**VITAMIN B COMPLEX**

with LIVER EXTRACT, Folic Acid and Vitamin B-12



SUPPLIED IN: Bottles of: 4 oz. 8 oz. and 16 oz.

Each fluid ounce contains:

Whole Liver Extract equivalent to ... 32 gms. of fresh liver, Vitamin B1 ... 10.0 mg., Vitamin B2 ... 4.0 mg., Niacinamide ... 50.0 mg., Vitamin B6 ... 1.0 mg., Vitamin B12 ... 10.0 mcgm., Cal. Pantothenate ... 5.0 mg., Methionine ... 250.0 mg., Choline Chloride ... 60.0 mg., Inositol ... 75.0 mg., Sodium Glycerophosphate ... 400.0 mg., Folic acid ... 1.5 mg.,

Deficiency of Vitamin B-Complex may remain in sub-clinical form or may manifest the deficiency syndrome of one particular Vitamin in which the total deficiency may remain submerged.

Although each component has its own function, B-Complex acts as one unit and when there is deficiency for one, usually manifestations of deficiency of other B factors also co-exist.



Manufactured by  
**DEY'S MEDICAL STORES PRIVATE LTD.**

CALCUTTA • BOMBAY • DELHI • MADRAS

# DIGEBIN

(CAPSULES)

For correcting hypo-function of the stomach and thus aiding digestion.

A rational combination of Pepsin, Papain, Diastase, Thiamine Hydrochloride, Riboflavin, Niacinamide, Betaine Hydrochloride, and Sodium Taurocholate.

**BIRLA LABORATORIES,**  
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Introducing

For the first Time in India

## ANAZID

For Tuberculosis

Isoniazid salt of Para-amino-Salicylic Acid (Chemically Combined). Effective even in resistant cases in doses of 600 mgm. per day.

3 Novel Remedies

## ACIPAS

For Rheumatic Poly-arthritis

Para-acetyl-amino Salicylic Acid. Non-toxic, reduces temperature, relieves pain abates cardiac and respiratory distresses quickly.

## SUVOCAINE

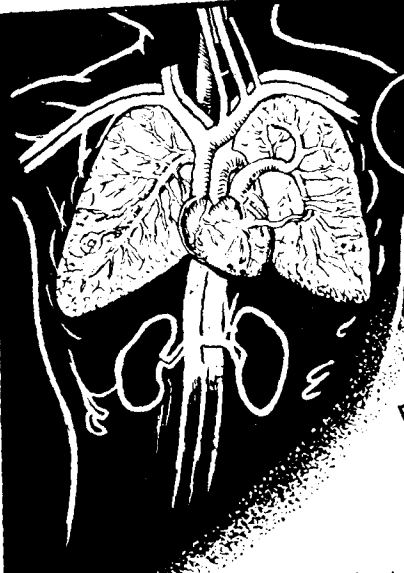
In Obstetrical local Anaesthesia

2-diethylamino-acetamidom-xylene hydrochloride. The agent of choice in pudendal block and perineal infiltration.

Products of Original Researches

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Grams: 'SULFACYL'

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## MULTIMIX

(Oral & Injectable)  
A DEPENDABLE ANTI-ASTHMATIC

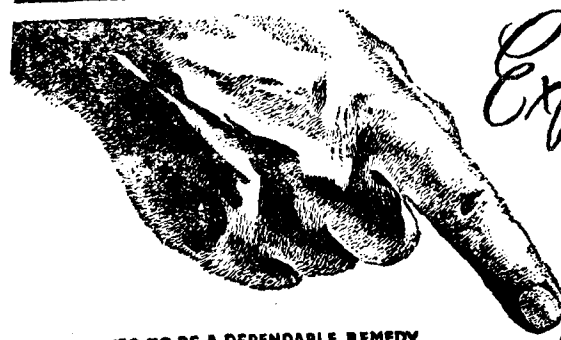
For SYNERGETIC THERAPY OF BRONCHIAL ASTHMA & SPASMODIC COUGHS

Ephedrine, Lobelia, Hyoscyamus, Grindelia, Belladonna, Sodium Iodide, Sodium Benzoate, Vasaka, Senega, Glycyrriza, Potassium Arsenate, Caffeine and Aminophylline

Telephone: 4930

Cables: Multamine

**INDO-FRENCH PHARMACEUTICAL CO., CATHOLIC CENTRE, MADRAS-1.**



*Experience Prefers*

PROVED TO BE A DEPENDABLE REMEDY THROUGH YEARS OF CLINICAL TESTS.

PLEASE CHECK UP THE NEW SCREW CAP ON QUMARESH PHIALS.

## QUMARESH

for Liver and Stomach

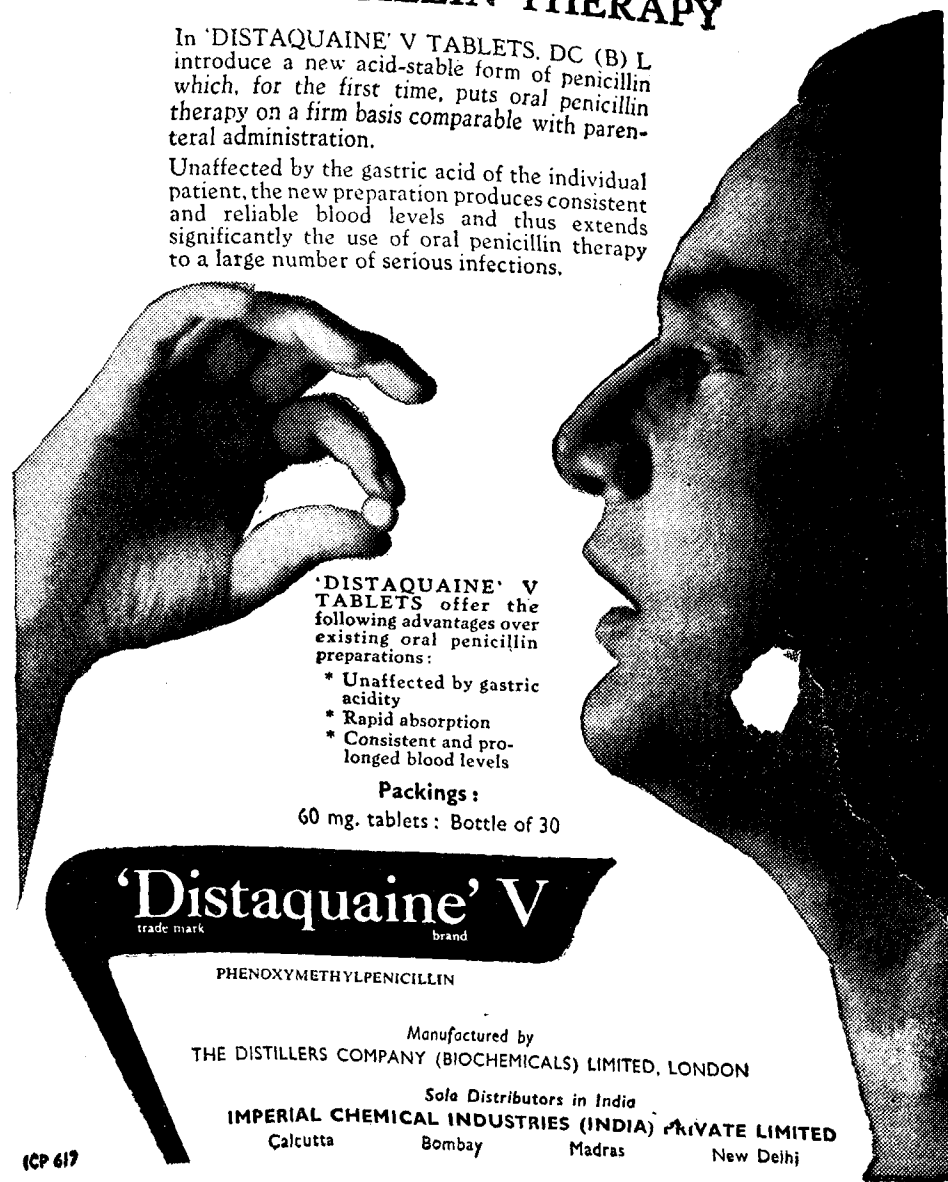
**O. R. C. L. LTD.**  
QUMARESH HOUSE, SALKIA, HOWRAH.

# a **NEW** penicillin

## an important advance in ORAL PENICILLIN THERAPY

In 'DISTAQUAINE' V TABLETS, DC (B) L introduce a new acid-stable form of penicillin which, for the first time, puts oral penicillin therapy on a firm basis comparable with parenteral administration.

Unaffected by the gastric acid of the individual patient, the new preparation produces consistent and reliable blood levels and thus extends significantly the use of oral penicillin therapy to a large number of serious infections.



'DISTAQUAINE' V TABLETS offer the following advantages over existing oral penicillin preparations:

- \* Unaffected by gastric acidity
- \* Rapid absorption
- \* Consistent and prolonged blood levels

### Packings:

60 mg. tablets: Bottle of 30

**'Distaquaine' V**  
trade mark brand

PHENOXYMETHYLPENICILLIN

Manufactured by  
THE DISTILLERS COMPANY (BIOCHEMICALS) LIMITED, LONDON

Sole Distributors in India  
**IMPERIAL CHEMICAL INDUSTRIES (INDIA) PRIVATE LIMITED**  
Calcutta Bombay Madras New Delhi

ICP 617



...for those who find  
sleep difficult, prescribe

**'SONERYL'**  
trade mark brand

BUTOBARBITONE

or

WHEN PAIN IS PRESENT

**'SONALGIN'**  
trade mark brand

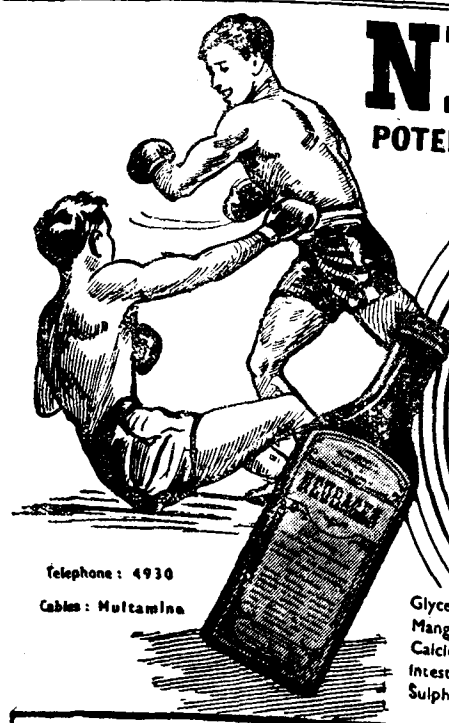
BUTOPHEN WITH CODEINE

MANUFACTURED BY  
**MAY & BAKER LTD**

M&B brand MEDICAL PRODUCTS  
Detailed information available on request

Distributed by: MAY & BAKER (INDIA) PRIVATE LTD - BOMBAY - CALCUTTA - GAUHATI - MADRAS - NEW DELHI

MA26 46 - 85



# NEURAGEN

POTENT NERVINE TONIC & REVITALISER

for  
**VIGOUR  
&  
RADIANT HEALTH**

**RECUPERATIVE  
& PICK-ME-UP**

Telephone: 4930  
Cables: Multamine

Glycerophosphate of Iron, Sodium, Calcium, Strychnine and Manganese, Vitamin B Complex Ext., Vitamin C Sodium Calcium Formoxyl, Kola Nuts Fluid Ext., Wahoo Fluid Ext., Intestinal Ferments, Papaine, Organic Copper Salt, Iron Sulphate, Manganese Sulphate in Palatable base.

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FOR OVER **80** YEARS  
Prescribed With Confidence  
by Doctors all Over the World...

## HEWLETT'S MIXTURE

WITH OR WITHOUT OPIUM IN 4 OZS. & 16 OZS. BOTTLES.

A PRINCIPAL REMEDY  
FOR

Contains:

ACID. HYDRO-  
CYAN DIL. B. P.  
TINCT. NUX.  
VOM. B. P.  
LIQ. BISMUTH.  
AND ALCOHOL  
16% V.N. AVERAGE.

INDIGESTION  
STOMACH DISORDERS  
HEART BURN  
FLATULENCY  
ACIDITY  
AND  
BOWEL COMPLAINTS

Our Other  
Products

PENICILLIN  
SKIN AND EYE  
OINTMENTS

SOLE PROPRIETORS  
**C. J. HEWLETT & SON (INDIA) LTD.**  
86, NYNIAPPA NAICK STREET, MADRAS-3

A well tried product for Primary and Secondary Amenorrhœa,  
Essential Dysmenorrhœa and Premenstrual Tension

## ERGOTAB

(Formerly known as Dr. TIBBS MENSO Tablets)

### Composition:

Quinine Hydrochloride 2gr.  
Apiol .. 1m.  
Aloes Et Myrrh .. 2gr.  
Ferri Sulph Exsiccat. 1gr.  
Ergotine ... 1gr.  
Resin Guaiacool .. 1gr.  
Pot. Perm. ... 1gr.

### Dosages:

**AMENORRHOEA SCANTY MENSES**  
Two tablets with hot water or  
tea thrice daily for five days in  
succession.

**DYSMENORRHOEA LEUCORRHOEA**  
Two tablets to be taken with hot  
water or tea three times a day for  
four days before the expected  
period.

Available with all the chemists throughout the country. For detailed literatures  
write to M/s. MOHAN BROTHERS, Manufacturing Chemists, Connaught Place,  
New Delhi. (Owner of the Trade Mark).

"EXCLUSIVE DISTRIBUTORS"

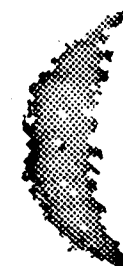
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(Ergo Tab and Dr. Tibbs Menso Tablets are one and the same.  
The change in the name is only to observe certain Drug Control Formalities).

Agility of  
an Athlete



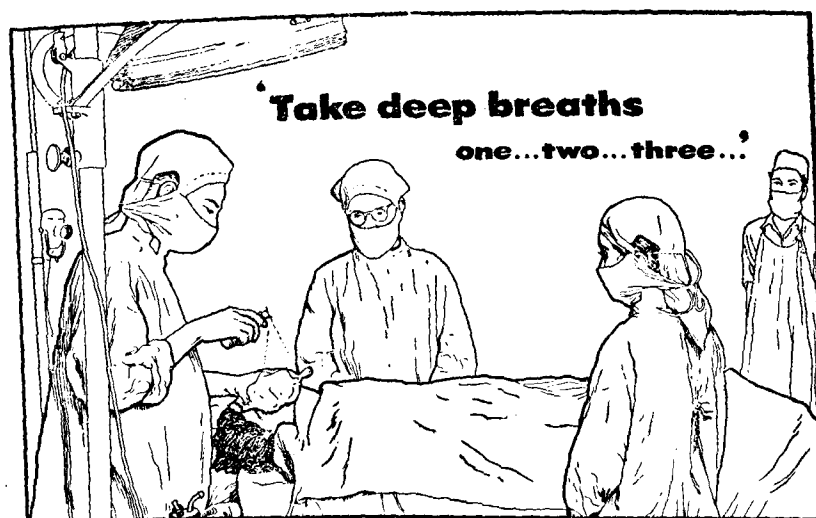
insist on  
**ADCCO'S  
COMPOUND**

**The Better Tonic**



Happy growth of physical and mental health mainly depends on  
nourishing food and regular exercises and the non-availability of same  
tells upon your health. To arrest your ever-decreasing vitality, take  
the help of ADCCO'S COMPOUND. Regular use of this better tonic  
will make you energetic, heal-  
thy, smart and active as an  
athlete brimmed with creative  
power.

**ADCCO LIMITED**  
CALCUTTA-27



All is ready for the operation.

While the anesthetist counts slowly,  
the patient drifts into unconsciousness.

No longer is surgery regarded as frightening,  
or a last resort, because of ignorance  
or superstition. All over India—even in  
the smaller towns and villages—people are  
depending on the marvels of modern  
surgery to remove pain and disease.

In every surgical operation,  
Aether plays an important part—  
soothing, healing, beneficial.  
We are proud to claim that we are  
the largest manufacturers of  
Aether Anesthetic B. P. in the East.



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HYDERABAD — DECCAN

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Intensive b-complex therapy

Injection 'PLEBEX'—this  
clinically dependable preparation,  
when administered in adequate  
dosage, relieves deficiency symptoms  
promptly and imparts a sense of well-  
being. Comprised of five crystalline  
factors of the vitamin B-Complex in  
aqueous solution, Injection 'Plebex' is  
recommended for the treatment of  
acute or chronic deficiency of one or  
more factors of the B-Complex  
whenever the oral route is uncertain.  
Where oral administration is however  
desirable, 'Plebex' Elixir and Capsules provide  
a valuable source of the B-Complex.

**Wyeth** **'PLEBEX'**  
Vitamin B-Complex  
INJECTION • ELIXIR • CAPSULES

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*Nutritive Aid*  
In Case of Malnutrition and  
Wasting Diseases

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WITH

**Creosote & Guaiacol**

Supplies

Minerals and generous amount of Vitamins

**For Vigour and Vitality**

Pulmo-Cod also prevents Seasonal Ailments,  
Cold, Cough, Bronchitis, Emetics, Summer  
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PULMO-COD**  
(Creosote & Guaiacol)

Each fluid oz. contains:  
Pancreatic hydrolysate  
of shark & Codliver Oil  
50% v/v

Vitamin A 4500 I.U.  
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Vitamin B<sub>1</sub> 3 mgs.  
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Vitamin B<sub>12</sub> 5-0 mcgs.  
Nicotinic Acid 40 mgs.  
Folic Acid 920 mcgs.  
Sodi Hypo. 120 mgs.  
Potassi Hypo. 120 mgs.  
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{ Creosote 1/3%  
{ Guaiacol 1%

Extract Wild Cherry,  
Gentian, Eucalypt, 0.7%  
Invert Sugar, Glycerine,  
Malt & Aromatics q.s.

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The antibiotic  
with the  
widest  
range of  
antibacterial  
action



**SYRUP  
&  
CAPSULES**  
SEALED  
IN BOTTLES OF  
12, 100 & 1,000

*Lepetit*  
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**RANBAXY & CO. PRIVATE LTD.** P.O. BOX 104  
NEW DELHI  
BRANCHES - BOMBAY - CALCUTTA - MADRAS - DELHI - KANPUR



THIS INJURED ARM IS PROTECTED BY A DALMAS  
ELASTIC WOUND DRESSING WHICH GIVES SECURITY  
AGAINST OUTSIDE INFECTION AND CONTAMINATION

# DALMAS

PRODUCTS

Dalmas Elastic Dressings are prepared under hygienic conditions. They reduce danger of secondary infection. Always keep Dalmas elastic dressings handy—they are an invaluable aid to rapid healing, easy to apply and perfect in protection.



**DALZO**—Dalzo Zinc Oxide plasters have proved their efficiency throughout the world. They are hygienically safe and fully antiseptic. Available in 10 yd. and 5 yd. spools, widths 1 in. to 4 in. and 3 1/4 yd. and 1 yd. spools, widths 1/2 in. and 1 in.



**DALZOFLEX BANDAGES AND DALZOFLEX STRAPPING.** For the ambulatory treatment of ulcerated legs there is no safer dressing than Dalzoflex Bandage. The strapping is recommended for securing abdominal dressings in situ. Available in 1 and 3 yd. spools. Widths from 1/2 in. to 4 in.



**DALZOBAND BANDAGES** (3 medications). An Unna's zinc paste type bandage which is always moist. Wound loosely round the affected part and covered with a Dalzoflex bandage applied spirally, size, 6 yds. x 3 1/4 in. Medications include Zinc Oxide, Ichthammol, Urethane, Calamine or Coal Tar.



**PERMALAST BANDAGES.** The efficient cotton elastic bandage, light, porous and washable. Firm support without restriction of circulation. Widths: 2 in., 2 1/2 in., 3 in., 3 1/4 in., 4 in., 6 in. Fully stretched 5 yards long.

*Enquiries should be sent to:—*  
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**DALMAS**  
Manufacturers of Medical and Surgical  
plasters for over 130 years.  
JUNIOR STREET LANCETER ENGLAND. Est. 1823.

## Prescription for Recovery

"Take  twice a day"

Wincarnis has proved extremely beneficial as a tonic after illness. It is a digestive acceptable to the weakest stomach, and palatable enough for the most reluctant appetite. Wincarnis acts as a gentle stimulant which helps the patient to renewed vitality and the more active mental condition so important in recovery.

★ Wincarnis is a blend of pure, matured red wines, strengthening elements and malt extract.

# WINCARNIS

over 25,000 recommendations  
from Medical Men

COLEMAN & CO. LTD., WINCARNIS WORKS, NORWICH, ENGLAND

A SIMPLE EQUATION!

**CALCIUM**

+

**VITAMIN C**  
(500 mg)

=

**CALCEFOP**

Calcium Saccharogluconate Expressed as  
Calcium Gluconate 1 G.  
Vitamin C 500 mg.

Per 10 cc. Ampoule  
Boxes of 6, 25, 50 and 100 Ampoules



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GENEVA  
SWITZERLAND

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**HELMACID**

the safest and most effective  
Anthelmintic against

**THREADWORMS**  
**ROUNDWORMS**

Administration is no problem at all. The tablets are small and easily swallowed; the pleasantly flavoured syrup is liked by infants and small children. Helmacid is convenient too; fasting, purging or hygienic precautions are unnecessary.

To eradicate threadworms, a 7-day course is recommended. A simple dosage scheme for infants and children is supplied with every pack. For roundworms, a single dose is often all that is required.

**HELMACID**

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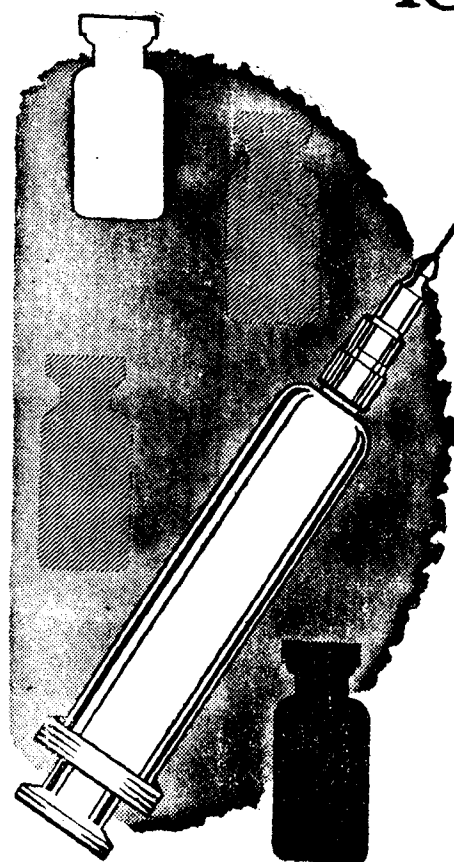
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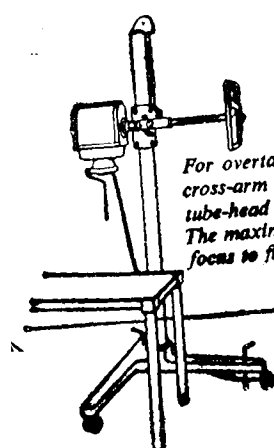
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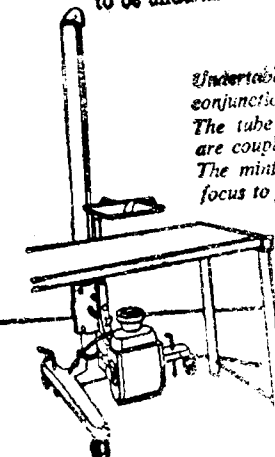
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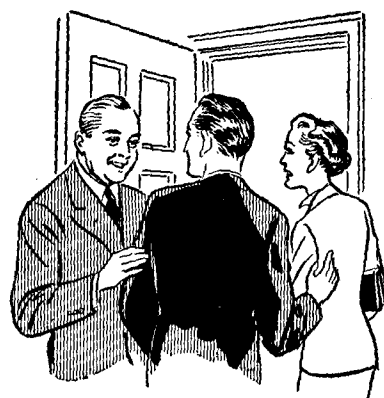
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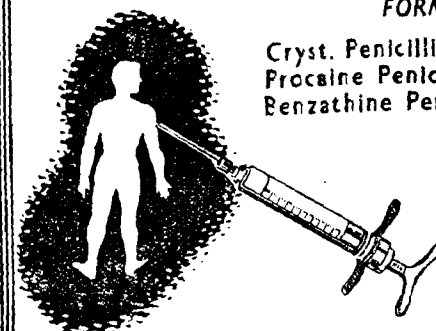
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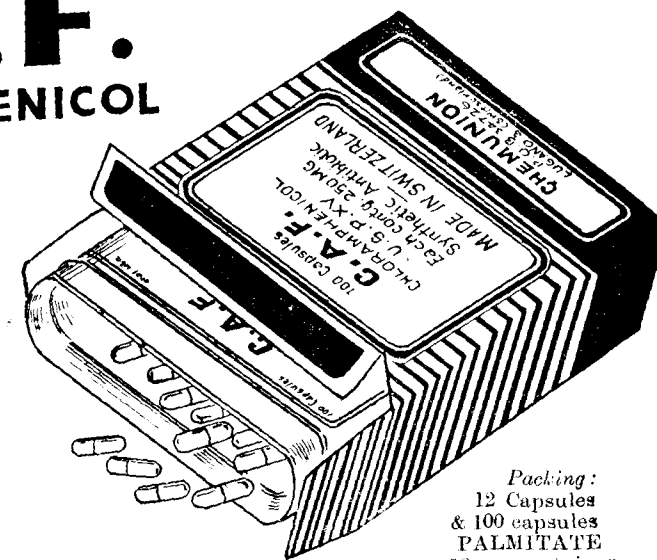


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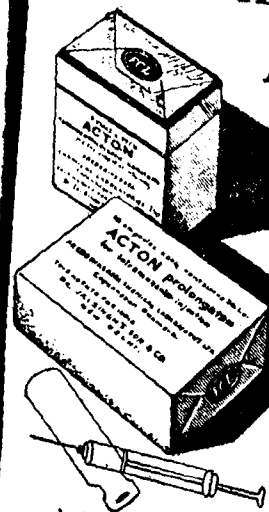
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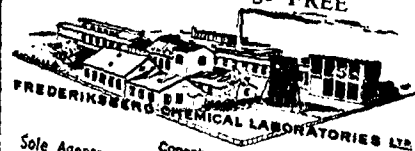
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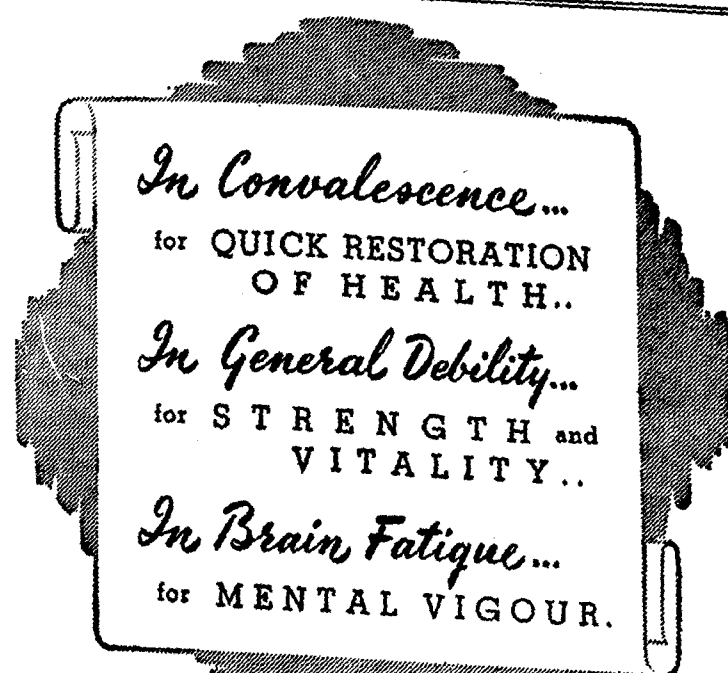
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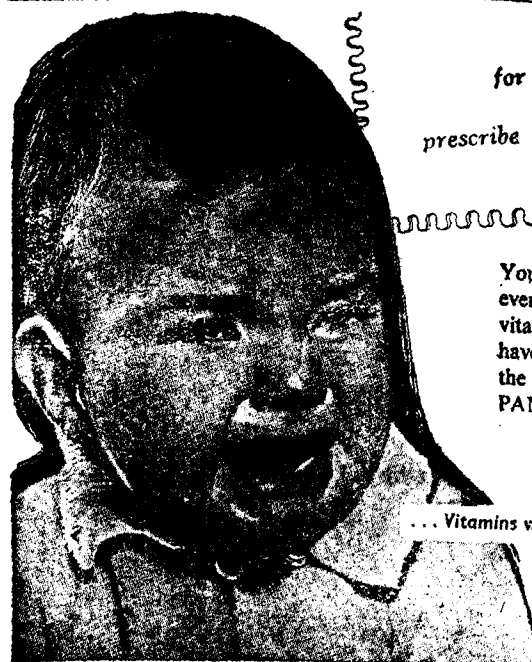
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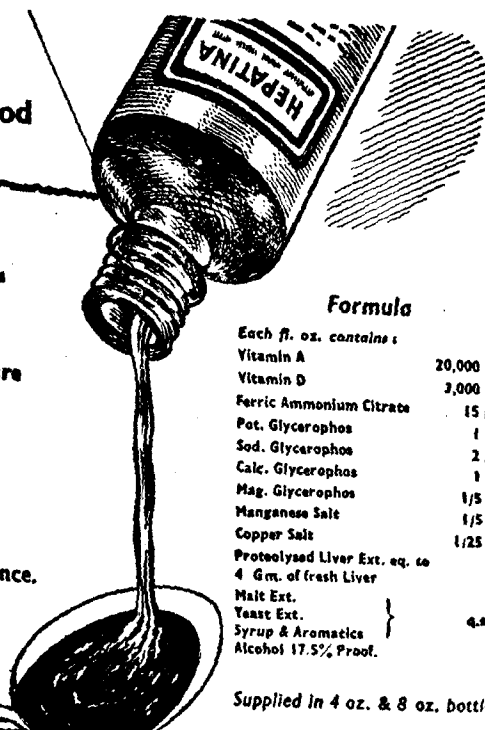
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## Original Articles

### ANTI-HISTAMINICS IN THE TREATMENT OF URÆMIA IN CASES OF CHOLERA\*

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URÆMIA happens to be numerically the second most fatal complication of the cholera syndrome, ranking next only to circulatory failure. It accounted for 20% of all deaths in Rogers' cases. (Rogers, 1921).

The underlying causes of suppression of urine and uræmia in cholera are partly renal and partly extra-renal. The extra-renal causative factors, briefly stated, are as follows:—

1. Severe shock, with consequent stagnant circulation and diminished renal blood flow. The effect of shock on kidney function has been reviewed by van Slyke (1948) and Smith (1951). That there might be a great reduction in renal blood flow and glomerular filtration (to even below 10 per cent of normal) has been shown by Lauson, Bradley and Cournard (1944).

2. Great loss of fluid and electrolytes from the blood and body fluids and the resulting hæmoconcentration. Dehydration has been shown by various workers to be associated with a great diminution in kidney function (McCance and Widdowson, 1939; McCance and Young, 1944; Smith, 1951).

3. The extreme capillary changes found in some of the organs including the kidney (Chatterjee, 1941), the pituitary, the adrenal, and other organs (Chatterjee, 1939<sup>a,b</sup>) and the bone-marrow (Chatterjee, 1946) suggest the action of some histamine-like substance or substances. Cholera vibrios can convert histidine into histamine (Chatterjee, 1939<sup>c</sup>).

\* Specially contributed to the ANTISEPTIC

4. An additional factor has been suggested as the cause in a few cases which might show hæmoglobinuria and hæmoglobinæmia by the recent work of De, Sen Gupta and Chanda (1954) who regard the intravascular hæmolysis of blood as playing an important role in the development of post-choleric uræmia. Although cases, which show hæmoglobinuria, have been clinically very rare in my experience, it is worth while to bear this in mind in dealing with a few cases one may come across.

The various changes that occur in the kidneys of cholera cases were described by Chatterjee (1941). The renal changes are essentially of a non-inflammatory and non-proliferative type and apparently completely reversible. In fact, although the renal failure in cholera is an acute and severe condition, it still appears to be more or less a temporary one. If the patient survives the acute stage of cholera with its concomitant kidney dysfunction, subsequent renal incompetence and progressive pathological changes in the nephron are extremely rare (Chatterjee, 1941).

Although the end result is the same in the acute stage of the disease in some of the cases, *viz.*, failure of the kidneys with suppression of urine, it is difficult to apportion quantitatively the exact role played by each of the above factors in individual cases of cholera where several variables come into play. It is remarkable that this very acute kidney failure of an almost specific type and clinical picture is completely reversible in character. These facts and the extreme capillary dilation of some of the internal organs mentioned previously, prompted me to use an antihistaminic (2-phenyl-benzylamino methylimidazole) drug injected intramuscularly in the kidney region of the back; and also Vitamin C intravenously in those cases where restoration of the specific gravity of the blood was not followed by urination. The results obtained in the Calcutta epidemics of 1951 and 1952 were highly encouraging (Chatterjee, 1952).

Following these studies an attempt was made in 1953 and 1954 to find out whether certain antihistaminic drugs given alone would be useful without the previous or simultaneous administration of Vitamin C. The present paper is an assessment of the work during the 1954 epidemic, and records our observations on the effect of three antihistaminics:—(1) Mepyramine maleate ('Anthisan'); (2) Chlorpromazine hydrochloride ('Largactil'); and (3) Promethazine hydrochloride ('Phenergan').

All our cases were clinical cases of cholera with a history of anuria of 5 hours' duration or more. The antihistaminics were given intramuscularly at the back in the muscles of the kidney region (Chatterjee, 1952). A series of controls were also run side by side, which received the usual treatment with different quantities of saline as advocated by Rogers, and as

ascertained mainly by the specific gravity of the blood, and the clinical features. Our initial observations in this study comprised eighty cases of clinical cholera. The three drugs Mepyramine, Chlorpromazine and Promethazine were each tried on 20 cases while 20 others served as controls. The trials were made in the order noted below:—

The first case was given Mepyramine, the second Chlorpromazine, the third Promethazine while the fourth served as a control. In our final analysis however, only those cases have been taken into consideration, which gave a positive stool culture by either or both of two consecutive stool examinations. For various reasons, it had not been possible for us to adopt the previously described and more elaborate technique of culturing the stools directly in three different selective media (Chatterjee, 1953). The stools were however, cultured on a single plate of D.E.C. medium (Panja and Ghosh, 1943) within fifteen minutes of collection by means of a boiled catheter.

As Mepyramine given alone was not found to be sufficiently effective to warrant its continued use in such a severe disease as cholera (so far as the number of cases getting relief and starting of urination was concerned) further trials were not continued beyond the first set of 20 cases. Chlorpromazine, although apparently more active, was found to depress the blood-pressure to a rather dangerous level; consequently further trials with this drug were also discontinued after the initial group of 20 cases. The study of Promethazine was, however, continued up to a total of 31 cases, 17 of which gave a positive stool culture. Controls were also continued up to a total of 31 cases alternately with Promethazine 16 of which were culture-positive.

Thus the culture-positive cases comprised: (a) Mepyramine—11 cases; (b) Chlorpromazine—11 cases; (c) Promethazine—17 cases; and (d) controls—16 cases; making a total of 55 culture positives in a total of 102 cases of clinical cholera. The results may be summarized as follows:—

GROUP A. *Mepyramine* or 'Anthisan' cases:—Of the 11 culture-positive cases, 3 died of uræmia with complete suppression of urine, giving a mortality rate of 27·2%. In the remaining 8 cases that were cured, the average urination time was found to be 12 hours after the administration of the drug. The figures for blood urea per 100 cc. of blood were:—in the 11 cases, before the onset of urination the lowest was 84 mg., highest 235 mg., average 151 mg.; after the onset of urination in 8 cases, lowest 18 mg., highest 34 mg., average 20 mg.; in the three fatal uræmia cases before death lowest 220 mg., highest 400 mg., average 210 mg., (see Table 1, p. 4).

TABLE I  
Analysis of Culture Positive Cases of Cholera

Showing the number of injections, duration of anuria before administration of drug, hour of first urination after the last injection and figures of blood urea before and after urination

| after the last injection and rigates of blood at the first |     |          |                   |   |   |                                                    |      |      |                                               |             |      |                              |                             |      |      |                                      |                        |                         |  |
|------------------------------------------------------------|-----|----------|-------------------|---|---|----------------------------------------------------|------|------|-----------------------------------------------|-------------|------|------------------------------|-----------------------------|------|------|--------------------------------------|------------------------|-------------------------|--|
| Different groups of cases                                  | No. | Per cent | No. of injections |   |   | Duration of anuria before adminis- tration of drug |      |      | Hours of first urination after last injection |             |      | No. of cases of total anuria | Blood urea before urination |      |      | Blood urea before discharge or death |                        |                         |  |
|                                                            |     |          | 1                 | 2 | 3 | Min.                                               | Max. | Avg. | Min.                                          | Max.        | Avg. |                              | Min.                        | Max. | Avg. | Min.                                 | Max.                   | Avg.                    |  |
|                                                            |     |          |                   |   |   |                                                    |      |      |                                               |             |      |                              |                             |      |      |                                      |                        |                         |  |
| Anthisan (Total cases)                                     | 11  | —        | 7                 | 4 | — | 6                                                  | 26   | 14   | 7                                             | 34          | 12   | 3                            | 84                          | 235  | 151  | —                                    | —                      | —                       |  |
| " Cured                                                    | 8   | 73       | 7                 | 1 | — | 6                                                  | 22   | 12   | 7                                             | 21          | 12   | 0                            | 84                          | 203  | 154  | 18                                   | 34                     | 20                      |  |
| " Fatal                                                    | 3   | 27       | —                 | — | — | 9                                                  | 26   | 18   | —                                             | —           | —    | 3                            | 156                         | 235  | 195  | 220                                  | 400                    | 210                     |  |
| Largactil                                                  | 11  | —        | 10                | 1 | — | 6                                                  | 35   | 26   | 5                                             | 48          | 19   | 3                            | 90                          | 170  | 122  | —                                    | —                      | —                       |  |
| " Cured                                                    | 9   | 81.8     | 9                 | — | — | 8                                                  | 27   | 25   | 5                                             | 16          | 10   | 0                            | 90                          | 150  | 120  | 14                                   | 30                     | 21                      |  |
| " Fatal                                                    | 2   | 19.2     | 1                 | 1 | — | 10                                                 | 29   | 25   | —                                             | —           | —    | 3                            | 105                         | 170  | 135  | 105                                  | 214                    | 158 (2 cases of uræmia) |  |
| Phenergan                                                  | 17  | —        | 11                | 4 | 2 | 6                                                  | 90   | 20   | 4                                             | 19          | 9    | 2                            | 43                          | 540  | 182  | —                                    | —                      | —                       |  |
| " Cured                                                    | 14  | —        | 10                | 2 | 0 | 5½                                                 | 90   | 20   | 4                                             | 19          | 9    | 0                            | 43                          | 205  | 111  | 34                                   | 158                    | 73                      |  |
| " Fatal                                                    | 3   | —        | 1                 | 1 | 1 | 6                                                  | 30   | 13   | 6                                             | 29          | 13   | 2                            | 165                         | 540  | 350  | —                                    | 540 (1 case of uræmia) | —                       |  |
| Control                                                    | 16  | —        | —                 | — | — | 3                                                  | 40   | 14   | 18                                            | 42          | 24   | 4                            | 100                         | 606  | 198  | —                                    | —                      | —                       |  |
| " Cured                                                    | 11  | —        | —                 | — | — | 4                                                  | 28   | 12   | 18                                            | 42          | 24   | 0                            | 100                         | 240  | 153  | 14                                   | 36                     | 18                      |  |
| " Fatal                                                    | 5   | —        | —                 | — | — | 3                                                  | 40   | 18   | —                                             | 38 (1 case) | —    | 4                            | 102                         | 606  | 239  | 140                                  | 660                    | 250                     |  |

GROUP B. *Chlorpromazine* or '*Largactil*' cases:—Of the 11 culture-positives treated with chlorpromazine there were 2 cases of suppression of urine, uræmia and a fatal termination (18%). One very discouraging feature with *Largactil* was the marked depression of blood-pressure. In one case (Case No. 18) the systolic blood-pressure fell by 30 mm. of Hg. from 100 mm. to 70 mm., after the administration of a 25 mg. intramuscular dose given in the kidney region. Although this particular patient survived, it was deemed advisable to reduce the dose at first to 12.5 mg. and later to 6 mg. in the adult in the subsequent cases. As there was depression of blood-pressure even with this greatly reduced dosage. *Largactil* was considered unsuitable. Foster *et al* (1954) have shown that there is a fall in blood-pressure with a rise of the pulse-rate after the administration of *Chlorpromazine* in normal volunteers. In the nine cured cases, however, the average urination time was 10 hours after the last administration of the drug. The figures for blood urea per 100 cc. of blood in the 11 culture-positive cases before the onset of urination were: minimum 90 mg., maximum 170 mg., average 122 mg.; after the onset of urination in the 9 cured cases the minimum was 14 mg., maximum 30 mg., average 21 mg., and in the two fatal cases before death the minimum was 105 mg., maximum 214 mg., average 158 mg. (see Table 1, p. 4).

GROUP C. *Promethazine* or '*Phenergan*' cases:—Of the 17 culture positive cases in this group no noticeable depression of blood-pressure was observed which could be ascribed to the drug; three died and 14 were cured. A total suppression of urine and uræmia occurred in only one of the 3 fatal cases; one case died of pulmonary oedema after the establishment of free urination and the third died of circulatory failure, also after the establishment of urination. The average urination time was found to be 9 hours in the 14 cured cases. It will be seen that there was still one case of total suppression of urine in the 17 cases, in spite of *Phenergan* treatment. I consider therefore, that a further study of combined therapy with Vitamin C and this particular antihistaminic, is needed (see Appendix) in view of the encouraging indications of combined therapy previously reported (Chatterjee, 1952). The figure for blood-urea per 100 cc. of blood in the 17 culture-positive cases before the onset of urination were:—minimum 43 mg., maximum 540 mg., average 182 mg.; 24 hours after the onset of urination in 14 cured cases the minimum was 34 mg., maximum 158 mg., average 73 mg.; in the fatal case due to uræmia before death it was 540 mg.

GROUP D. *Controls*:—Of the 16 culture-positive cases in this series, 11 were cured and 5 died. The average urination time after the administration of the usual saline transfusion was 24 hours. Of the 5 fatal cases, 4 had suppression of urine and

uræmia: the fifth died of hyperpyrexia and circulatory failure, inspite of the establishment of urination. The figures for blood urea per 100 cc. of blood in the 16 culture positive cases were:—before the onset of urination minimum 100 mg., maximum 606 mg., average 196 mg.; in the 11 cured cases after urination before discharge minimum 14 mg., maximum 36 mg., average 18 mg., and in the 4 fatal uræmia cases minimum was 140 mg., maximum 660 mg., average 250 mg., (see Table I, p. 4).

The total mortality-rate in Group D culture-positive cases was 23·6% including those due to uræmia as well as other causes. The total mortality figures of the different groups of the culture-positive cases due to all causes have been respectively: Group A 27·2%; Group B 18%; Group C 17·9%; and controls 31%. The death rate from uræmia, in the whole culture-positive group was 18·1%. (see Table II).

The uræmic deaths of the separate groups were:—Group A 27·2%, Group B 18%, Group C 9% and controls 28% (see Table II). There was no death from uræmia in the culture-negative cases.

TABLE II  
Analysis of the Fatal Cases  
Table showing the number of cases and the mortality rate of the whole group and the culture-positive group.

|             | The whole group of cases both Culture positive & Culture negative |                    |         | Number treated | Culture positive cases |          |                    |          |
|-------------|-------------------------------------------------------------------|--------------------|---------|----------------|------------------------|----------|--------------------|----------|
|             | No. of all cases                                                  | No. of fatal cases | Percent |                | Death from all causes  |          | Deaths from uræmia |          |
|             | No.                                                               | No.                | Percent |                | No.                    | Per cent | No.                | Per cent |
| Total cases | 102                                                               | 23                 | 22·3    | 55             | 13                     | 23·6     | 10                 | 18·1     |
| Anthisan "  | 20                                                                | 4                  | 20      | 11             | 3                      | 27·2     | 3                  | 27·2     |
| Largactil " | 20                                                                | 5                  | 25      | 11             | 2                      | 18       | 2                  | 18       |
| Phenergan " | 31                                                                | 6                  | 18·2    | 17             | 3                      | 17·9     | 1                  | 9        |
| Control "   | 31                                                                | 8                  | 24·2    | 16             | 5                      | 31       | 4                  | 25       |

**DOSAGE.**—*Anthisan*:—The single adult dose was 2 cc. of a 2·5% solution. Amongst the *Anthisan*-cases 7 out of 8 cured cases received a single injection while the eighth case received two. All the 3 fatal cases of uræmia received 3 injections each.

*Largactil*:—All of the 9 cured cases received one injection each. The dosage was 25 mg. in two cases; 12·5 mg. in 3 cases; 6 mg. in 4 cases; 2 injections each of 12·5 mg. were given to each of the two fatal cases.

*Phenergan*:—The single adult dose was 2 cc. of a 2·5% solution. Of the 14 cured cases 10 received a single injection,

and 2 received 2 injections each; one, two and three injections were given respectively to the 3 fatal cases.

**Discussion.**—Clinical workers on cholera must be aware of the great difficulty in assessing the value of any diuretic agent in a syndrome like that of cholera, where several variables come into play, such as the previous state of health before infection, the age of the patient, the specific gravity of the blood, the degree of disturbance of electrolytes before and after the administration of saline, and any pre-existing bowel infection (Chatterjee *et al.*, <sup>b, c</sup> 1955), which has a very important bearing on the severity of the symptoms of cholera.

Equally great are the pitfalls in the assessment of a final clinical diagnosis of cholera during the epidemic seasons, if based simply on clinical findings and signs. During the epidemic months, any case of severe vomiting and purging with circulatory collapse might be mistaken for cholera and brought in ambulance cars to the Cholera Hospital at all hours of the day and night. The initial treatment consists of emergency management of shock and dehydration, and then we promptly set to work on the diagnosis based upon the history, the clinical signs, and the specific gravity of the blood. Although for the sake of therapy, during the epidemic season a presumptive and spot-diagnosis is a practical necessity it would be extremely hazardous to regard every case admitted in the cholera-ward as a true case of cholera without rigid adherence to the examination and culture of stools, which must be done more than once. During the epidemic months of March to June, droughts with intermittent rainy weather and norwester storms are common phenomena and the hygienic conditions relating to food and water are none too good owing to the influx of a great number of refugees from Pakistan.

These hot spells with intermittent rains have a great tendency to cause various bowel infections as well as cholera to flare up (Russell and Sundara Rajan 1926–27, 1928). This period happens to coincide with the season of the ripening of the mango, the *litchie* and the jack fruits on which quite a large number of people virtually subsist during these months. The season for the rather indigestible *Hilea* fish is also during the epidemic months. One should be also on guard against food-poisoning, food-allergy and enteritis from staphylococci, salmonella, shigella and even the coliform organisms. The above list is big enough and there is also the uncharted ocean of intestinal diseases caused by virus infections—both as primary infection of the bowel and secondarily from the respiratory organs, as also the many other various bowel infections.

[During the epidemic season not a few instances have occurred where severe and atypical cases of *Entamoeba histolytica* infections were brought

in by the ambulance cars, to be confirmed later by repeated examination of stools, as persistently negative for cholera vibrio].

I wish, therefore to suggest that the positive culture of stools by the three-plate method (Chatterjee 1953) is the proper procedure for labelling any case of cholera. As a matter of fact, the above elaborate technique could not be carried out in the 1954 epidemic and stools had to be cultured on plates with one selective medium only (*see above*). Consequently, although we have rigidly followed the procedure of taking into consideration only culture-positive cases in this study, it is quite possible that a few cases may have been missed.

Amongst the reasons which led me to use the unusual method of administering the antihistaminic drugs by the intramuscular route at the back of the kidney region, may be mentioned the fact of extreme sluggishness of the peripheral circulation in the collapse stage of cholera particularly in the shrunk and shrivelled limb muscles and subcutaneous tissues. The other reason is the high toxicity of the available antihistaminic drugs by the intravenous route and the non-availability at the particular time of a safe antihistaminic which could be given intravenously in shocked cholera patients. The remarkable beneficial effects, which have been previously observed (Chatterjee 1952) were presumably obtained through some mechanism of the autonomic nervous system.

From the point of view of clinical interest the mortality in the entire group taken as a whole (both culture-positive and culture-negative cases) are given below:—

In the whole group of 102 cases the deaths amounted to 23; *i.e.*, mortality rate 22.5% from all causes; in the 20 Anthisan cases the deaths were 4; a mortality rate of 20%; in the 20 Largactil cases the deaths were 5; a mortality rate of 25%; in the 31 Phenergan cases the deaths were 6; a mortality rate of 18.2%; in the 31 Control cases the deaths were 8; a mortality rate of 24.2% (*see Table II*).

It may be mentioned that the successful *Coleus aromaticus* therapy previously reported (Chatterjee, 1953) was not available owing to the failure of our garden during the 1954 epidemic.

**Summary.**—During the 1954 epidemic in Calcutta in a series of 102 cases of cholera with total suppression of urine of more than 5 hours' duration, three different antihistaminics were tried along with suitable controls to ascertain their action in the onset of urination and relief of uræmic symptoms. Only 55 of the 102 cases were positive in stool culture at one or both of two consecutive examinations. Anthisan failed to start urination in 3 out of 11 culture-positive cases tried (27.2%); Largactil failed in 2 out of 11 of these culture-positive cases (18.1%) and Phenergan in 1 out of the 17 cases (5.9%). In the control group there was no urination in 4 cases out of 16 culture-positive cases (25%).

The average time for the starting of the urination after the last injection was:—For Anthisan 12 hours; for Largactil 10 hours; and for Phenergan 9 hours. In the control group the average time of urination was 24 hours after starting of the usual saline treatment in those cases where urinary function started.

Anthisan alone (without Vitamin C) showed no special advantage over the controls so far as the number of cures was concerned, although the average time for the onset of urination was somewhat shorter. Largactil was found to have the special drawback in cholera cases, of causing a dangerous depression of the blood-pressure. Consequently the observations were not continued beyond 20 cases with each of the latter two drugs. Phenergan seemed to be of definite help both as regard mortality rate and the earlier onset of urination. Inward reactions were not observed either in the group of 17 culture-positive cases or in any of the cases numbering 31 treated with the drug. There was failure of urination in one of the 17 cases. A combined treatment with intravenous Vitamin C and Phenergan intramuscularly in the back is suggested on the basis of my previous work (1952) (*see Appendix below*).

**Appendix.**—The work during the 1955 epidemic was a continuation of our work of 1954. The epidemic which occurred this year in Calcutta was of marked severity—the total mortality rate for the City being 32.0% for the whole season. During this epidemic a combination of antihistaminic Promethazine hydrochloride and Vitamin C was given both as a part of the treatment and as a prophylactic against uræmia. Any case in which urination did not occur within two hours after the administration of a saline transfusion, was given Promethazine intramuscularly in the kidney region, which resulted in the establishment of urination in 80% of the cases.

Cases which did not urinate within a further period of 8 hours were given Vitamin C 500 mg. intravenously. In a few cases, both the antihistaminic and the Vitamin C had to be repeated every 12 hours. As we anticipated last year, there was not a single case of uræmic death with suppression of urine in the total admissions in my ward, numbering 227 during April and May of this year. It will be interesting to note that during May, the peak month of the epidemic, the total mortality in the same group was 9 out of 180 cases or 5% in contrast to the general Cholera mortality of Calcutta amounting to 32.2% during the same period. The average time for urination after the last Phenergan injection with this combined therapy was 8 hours. Other details relating to our line of treatment, which we believe were responsible for the substantial reduction in mortality, will form the subject of a separate communication.

I wish to thank the authorities of the Chittaranjan Hospital for their co-operation; my thanks are due also to Messrs. May & Baker (India) Ltd., for the supply of the antihistaminic drugs; to Dr. R. Saha, Dr. D.K. Basu, Dr. P. K. Chakravarty and Dr. H.K. Chakravarty for their suggestions and help and to the Calcutta Corporation for furnishing me with the mortality figures relating to cholera in the city.

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## ERYTHROMYCIN: INDICATIONS FOR USE

Erythromycin is an excellent non-toxic antibiotic with a spectrum of action very similar to that of penicillin. The ease of administration and the low toxicity are tempting reasons to use the drug for all gram-positive infections. However, the fact of resistance indicates that erythromycin should be employed only when infections which are resistant to penicillin and other antibiotics present a serious, therapeutic problem. According to Kenneth Maclean of Guy's Hospital (*Practitioner*, 176: 34, 1956), the drug should be used chiefly: (1) for infections due to *Staphylococcus aureus* when the strain present has proven resistant to other antibiotics, or when the infection has failed to respond to penicillin, (2) for infection due to other gram-positive cocci if a definite contraindication to penicillin therapy exists, and (3) for diphtheria carriers in whom penicillin has failed to eradicate the organisms. Erythromycin is not indicated in the treatment of infections due to gram-negative cocci. It may occasionally be used in the treatment of brucellosis due to the *suis* and *melitensis* organisms. The recommended oral dosage is 0.3 to 0.5 grams at six-hourly intervals, making the total dose for 24 hours 1.2 to 2 grams. If parenteral administration is necessary the intravenous route is preferable; the drip method may be used: direct injection should be made over at least five minutes. If intramuscular injection is used, a large muscle must be selected. Administration of the drug should be continued for 48 hours after all evidence of the infection has disappeared. In general, toxic effects are mild, few and far between.—(*Medical Times*, April 1956).

## CHRONIC PULMONARY DISEASES AS A POSSIBLE ÆTIOLOGIC FACTOR IN LUNG CANCER

After an extensive survey of the literature dealing with pre-existing pathologic changes as etiologic factors in lung cancer, Dr. Walter Finke reports on a study of 159 patients with proved neoplastic disease of the lungs. Results of this study support the view that chronic pulmonary disease possibly may be a precipitating factor, and even though its real importance is still to be evaluated, control and prevention of these pulmonary diseases are important ends in themselves. All of the 159 patients had primary lung cancer.

An analysis of their hospital records revealed that a long-standing pulmonary ailment of some kind had pre-existed in one-third of the group. In 76 cases, information over and above that supplied by the hospital records was available, and in this group the figure for chronic pulmonary ailments rose to 60 per cent. Bronchitis and asthma were the leading disorders, but old tuberculosis accounted for a substantial number of cases. In two control groups as well as in statistics for the general population, the incidence of primary lung cancer was much lower. The number of the group who had had influenza in the years 1918 to 1920 and of pneumonia in the distant past was particularly high in the cancer group but was just about the same as that in patients with bronchopulmonary disease. In the patients with broncho-pulmonary disease, however, the rate of multiple lung-damaging episodes was only half that found in the series of 50 cases of lung cancer.—(*Intern. Rec. Med.*, Feb. '56, via *N.Y.S.J. Med.*, 1-5-1956)

CLINICAL TRIALS WITH INVENOL (BZ 55),  
AN EFFECTIVE ORAL ANTIDIABETIC DRUG\*  
(A Survey of 101 Cases)

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THE introduction of *INVENOL* as an advance in the treatment of diabetes mellitus has aroused great interest among medical men and in the public at large. This new sulpha-compound is prepared in Germany. It was studied there extensively in 1954 and 1955 under the designation "BZ 55," and then officially introduced early in 1956 for therapy in Germany and shortly thereafter in other countries. Clinical reports on its use in Germany and other countries have since been published.

A clinical evaluation of the effects of Invenol in a series of 101 patients over a period of about six months is recorded by us in this paper. A preliminary clinical report on 40 cases after the first three months' trial was submitted in July last year.

Chemically, Invenol is  $N_1$ -sulphanilyl- $N_2$ -n-butyl urea. It is a white substance slightly soluble in water and available in 0.5 g. oral tablets. It is well absorbed on oral administration and is so well retained in the body as to classify it as a "Depot-sulpha." In men and animals it exhibits a pronounced blood-sugar lowering effect. The relation of its chemical structure to its pharmacological action has been the subject of numerous investigations. It has been found that the blood-sugar lowering action remains unimpaired if p.NH<sub>2</sub> group is substituted by CH<sub>3</sub> group. It was further found that a certain hypoglycæmic effect is also noticed in substances in which the butylcarbamide group is substituted by propyl-, butyl- or amylthiodiazol or their isomers.

Selection of cases for clinical trials.—Apart from considering maturity of age as a definite point in the selection of cases for this therapy as recommended in the literature, we were particular to have a wider range of selection of cases so as to evaluate its full clinical effects. We have included in our study younger diabetics (20 years of age) and much older age groups (72 years) as also a few cases of renal glycosuria. Also cases with complications of the disease like nephropathy, neuropathy, retinopathy etc., and associated conditions like pulmonary tuberculosis, mild surgical conditions etc. were treated with this drug. The complications associated with the diabetic condition in our series are listed overleaf in Table I.

\* Specially contributed to the ANTISEPTIC

TABLE I

|                                                        |               |
|--------------------------------------------------------|---------------|
| Total number of patients with complications            | ... 70        |
| Boils, furuncle, small abscess and whitlow             | ... 4 cases   |
| Pruritus—generalised, anal and vulval                  | ... 6 "       |
| Peripheral neuritis                                    | ... 26 "      |
| Hypertension                                           | ... 10 "      |
| Retinopathy                                            | ... 5 "       |
| Nephropathy                                            | ... 7 "       |
| Active tuberculosis lesion                             | ... 2 "       |
| Miliary tuberculosis                                   | ... 1 case    |
| Pleurisy with effusion                                 | ... 1 "       |
| Urinary infection                                      | ... 4 cases   |
| Coronary insufficiency                                 | ... 2 "       |
| Kala-azar, malaria and other parasitic infections      | ... 2 "       |
| Total number of patients without obvious complications | ... 31        |
| Total                                                  | ... 101 cases |

We took particular care to avoid frank cases of diabetic ketosis or coma or cases with serious surgical complications.

Seventy-six cases in our series had been treated previously with insulin for periods varying from 15 days to 28 years; the majority of them however, had insulin only intermittently and for less than 5 years.

Mode of treatment.—A glucose-tolerance test was done in every case before commencing Invenol therapy in order to ascertain the nature and severity of the diabetic condition. In this series 53 patients were admitted in the hospital and treated with Invenol as in-patients for some time and then discharged to continue the treatment as out-patients with regular follow-up. The other 48 in this series, were treated only as out-patients. All of them were prescribed a certain definite diabetic diet according to the General Hospital Dietetic Regime (Non-vegetarian 1900 calories and Vegetarian 2100 calories) during the course of this therapy.

A post-prandial random blood-sugar estimation at a particular time with simultaneous urine examination was done every day during the first three days of the treatment, once in three days for the next ten days, and then once a week, and later on once in a fortnight. In our opinion, the random blood-sugar values give a more definite indication of the diabetic state than the fasting blood-sugar level. The urine was examined qualitatively for sugar and the results were expressed as +, ++, + + +, + + + + and so on. Sugar estimations in urine specimens were not carried out quantitatively as a routine measure, although it was done in a few cases, since the quantitative urine sugar does not furnish absolute evidence of improvement or deterioration in the diabetic condition. At the beginning of our clinical trials, frequent blood-sugar estimations were made, even more than

twice a day. But later we found that such frequent blood-sugar estimations are not absolutely necessary for clinical evaluation of the drug, apart from the fact that our patients refused to have such frequent blood examinations.

The W.B.C. counts were checked up before and during the Invenol therapy and during any infection or allergic reaction. Blood-urea, urea-clearance and blood cholesterol and liver-function tests were done when necessary in a few cases. More detailed hæmatological investigations like sternal marrow studies, platelet counts, capillary fragility tests etc., were not done, although we were on the look-out for any toxic or side-effects of the drug that would warrant such investigations. Blood level and urine level studies of Invenol were not done in any case owing to want of facilities. Finally, Invenol was also administered to three volunteers to study the effect of the drug on normal individuals; fourth hourly blood sugar estimations were made and the results recorded.

Dosage and duration of treatment.—As a routine the schedule of treatment was the same in all cases irrespective of the severity of the diabetic state as indicated by blood-sugar levels or the duration of diabetes or the age of the individual or the nature of previous insulin treatment. We administered 5 tablets (2.5g.) on the first day; three (1.5g.) on the second and third days and two (1.0g.) daily thereafter.

In a few cases with low blood-sugar levels and in renal glycosuria the drug was given in smaller doses, viz., 3 tablets on the first day, 2 on the second day, two on the third day and one tablet daily thereafter. In a few other instances where the blood-sugar levels were maintained low during treatment (lower than 80 mg.%) the dosage was reduced to one tablet daily with the continuance of the beneficial results. In certain isolated instances (in 6 of our cases) the maintenance dose was increased to three tablets daily without any appreciable beneficial results.

The maintenance dose of two tablets in most of the cases has been continued right through the clinical trials to date. Cases which did not respond to Invenol after prolonged therapy for 6 to 8 weeks, were switched on to insulin after discontinuing the oral treatment. Four cases in our present series fell out of treatment after a period varying from 15 days to 2 months owing to their own private reasons, and these have not been considered in this paper. In the first six patients of the present series, after a period of 4 months, Invenol was discontinued as an experimental measure for a period of 10 to 20 days and blood-sugar studies were made during that period. All of them had to be restarted on the drug, as their blood-sugar levels had

gone up higher than the previous levels which could be brought down to within normal limits by the same maintenance dose.

In those cases which were previously on insulin, an interval of 2 to 4 days as a rule, was given prior to Invenol therapy.

In four cases of the present series where Invenol alone was deemed to be insufficient, insulin was administered in small doses to supplement the therapy, especially where mild surgical conditions like boils, furuncles co-existed.

Therapeutic effects and clinical results.—In the majority of cases (68) the blood-sugar was definitely lowered in 48 hours' time and reached near normal levels in 4 days and remained so thereafter on a maintenance dose. The amount of sugar in the urine also came down along with lowering of blood sugar and the urine remained sugar-free on a maintenance dose of the drug. The results of therapy in such cases were classed as "Good."

In fifteen cases the blood-sugar was less responsive and came down only after a period varying from 7 to 10 days up to one month and then to high normal or near normal levels, where it was maintained. Here the urine occasionally showed the presence of sugar in small amounts. In such cases the results were classed as "Satisfactory."

In another 18 cases the blood-sugar level was little altered by this therapy, sometimes even slightly raised, and the urine continued to show the same amount of sugar indicating lack of response to the drug even after a month. These cases were classified as "No response."

In the light of the above classifications, the following grouping of patients was done according to the age-groups (Table 2) previous insulin treatment (Table 3, see p. 15) and the duration of the diabetic state (Table 4, see p. 15).

TABLE 2  
Showing the results on the basis of age-groups

| Age-group                             | Number of cases in group | Results |              |      |
|---------------------------------------|--------------------------|---------|--------------|------|
|                                       |                          | Good    | Satisfactory | Poor |
| 25 years and below                    | 3                        | 1       | —            | 2    |
| Over 25 years and below 35 years      | 4*                       | 3*      | 1            | —    |
| 35 years and above but below 60 years | 86                       | 59      | 13           | 14   |
| 60 years and above                    | 8                        | 5       | 1            | 2    |
| Total                                 | 101                      | 68      | 15           | 18   |

\* Includes one case of renal glycosuria.

It is evident from the above table that very good response to Invenol treatment was noted in the age group of 35-60 years.

In the age-group of 60 years and over, the results were about the same. The number of cases in the age-groups 25-35 years and below 25 years is too small to allow definite conclusions to be drawn. However, our clinical trials indicate that diabetics of these age groups may also respond to the treatment.

Our results are not in contra-distinction to those of others who came to the conclusion that maturity is an important factor for the clinical application of the drug and the response is poor in juvenile diabetics.

TABLE 3  
Showing the results of therapy on the basis of previous insulin treatment

|                                             | Number of cases | Results  |              |          |
|---------------------------------------------|-----------------|----------|--------------|----------|
|                                             |                 | Good     | Satisfactory | Poor     |
| *Previous insulin treatment                 | 76              | 49 (67%) | 13 (16%)     | 14 (17%) |
| No previous insulin treatment (fresh cases) | 25              | 21 (84%) | 1 (4%)       | 3 (12%)  |

(NOTE:—\*Previous insulin treatment ranged from one month to several years regularly and irregularly and so could not be classified).

It is obvious that cases which had received no previous insulin treatment responded better (84%) than cases which had had previous insulin therapy. The duration of previous insulin treatment, however, could not be a definite indication for response to this therapy. In our series, patients with more than 15 years' insulin treatment have responded just as well as those who had been on insulin only for short periods. It should, however, be noted that patients who had had no prior insulin therapy showed a better response to Invenol.

TABLE 4  
Results of therapy on the basis of duration of diabetes

| Duration of the diabetic state               | Number of cases | Good     | Satisfactory | Poor |
|----------------------------------------------|-----------------|----------|--------------|------|
| Less than 2 years                            | 37              | 28 (76%) | 2            | 7    |
| Between 2 and inclusive of 5 years' duration | 26              | 18 (77%) | 4            | 4    |
| Over 5 years and up to 28 years' duration    | 38              | 24 (63%) | 7            | 7    |

The best response to the drug was undoubtedly seen in cases with diabetes of short duration (less than 5 years). We consider however that a longer duration of the diabetic state should not be a contra-indication for the use of this drug as good results were quite often obtained even in such patients, provided there was a good amount of endogenous insulin present. Since there is no accurate method of assessing the endogenous insulin in any individual, these patients should also be given a fair trial with Invenol therapy.

The report on the clinical results will not be complete without making mention of the 4 cases of renal glycosuria which were included in the series. Invenol treatment with small doses resulted in clinical improvement and the disappearance of sugar in the urine without any hypoglycæmic symptoms.

Throughout the clinical trials, we were impressed by the qualitative and not the quantitative action of the drug in reducing blood-sugar levels. High blood-sugar levels (600-800 mg.%) as well as moderate ones (250 and 190 mg.%) were brought to normal by the same dose of the drug. In resistant cases a further increase in the dosage of Invenol was not of much help.

It was administered to three volunteers for three days in order to assess its action in non-diabetics the dosage being the same as for regular diabetics (5 tablets on the 1st day, 3 on the 2nd day and 3 on the 3rd day). In all the three volunteers, blood-sugar levels came down noticeably during the first 24 hours and still further during the second day.

TABLE 5  
Showing the blood sugar levels (mg. %) in non-diabetics after the administration of Invenol for 3 days

| Name of volunteer | First day |         |        |        | Second day |         |        |        | Third day |         |        |        |
|-------------------|-----------|---------|--------|--------|------------|---------|--------|--------|-----------|---------|--------|--------|
|                   | 7 A.M.    | 11 A.M. | 3 P.M. | 7 P.M. | 7 A.M.     | 11 A.M. | 3 P.M. | 7 P.M. | 7 A.M.    | 11 A.M. | 3 P.M. | 7 P.M. |
| P.                | 98        | 104     | 82     | 78     | 76         | 64      | 82     | 56     | 54        | *(-)    | 45     | 62     |
| C.                | 112       | 96      | 104    | 84     | 92         | 86      | 62     | 48     | 62        | 80      | 72     | 98     |
| K.                | 104       | 80      | 100    | 92     | 68         | 56      | 60     | 74     | 48        | *(-)    | 45     | 68     |

\* (-) indicates too low for estimation.

Two of the volunteers had a hypoglycæmic reaction which was relieved by the administration of glucose orally. It is concluded that Invenol definitely reduces the blood-sugar level in non-diabetics.

Insulin was used to supplement this therapy only in 4 cases, 3 of which had associated surgical conditions like boils or furuncles, chronic cystitis and unhealed amputated wound etc. It was found that the insulin requirement was thereby reduced by at least 60%. In such case, after gradual reduction of the insulin dose, it was possible to give up insulin altogether later on. These instances illustrate that this drug may also be used therapeutically with insulin in certain cases, if necessary.

Case Reports:—The following case reports from our series will be of interest:—

1. Mrs. C.B.:—70 years—had been suffering from diabetes mellitus for the last 10 years having had irregular insulin therapy, developed sensitivity skin reaction to insulin—was

subjected to this therapy. Within 2 days R.B.S. came down from 284 to 110 mg. % and continued to remain normal thereafter, with a complete absence of sugar in the urine.

V., 66 years, with history of diabetes mellitus for 2 months—had an attack of coronary thrombosis and no insulin was given to her. The G.T.T. showed a fasting 250 mg.% and a maximum of 425 mg.%. With the institution of Invenol therapy the patient's condition cleared up in a week's time and blood-sugar levels settled down to between 148 and 100 mg.%. The patient felt very much better.

3. Mr. R., aged 23 years, weighing 96 lbs. had had diabetes for 2 years and gave a history of previous irregular insulin treatment; G.T.T. blood-sugar level between 200 and 363 mg.%; he was subjected to Invenol therapy. Even at the end of a month no appreciable response was noted. R.B.S. was raised between 282 and 306 mg.% with occasional ketosis. Invenol was given up and insulin started.

4. Miss M., 48 years, with diabetes of 28 years' duration, and previous irregular insulin therapy with severe peripheral neuritis and R.B.S. 384 mg.% was subjected to Invenol therapy. R.B.S. ranged between 232 and 145 mg.% for a period of two months. With continued therapy it settled down later to 110 mg.%. This case illustrates a very much delayed response in a patient, with diabetes of 28 years' duration. The peripheral neuritis gradually improved.

5. Mr. S., aged 24, weighing 112 lbs. with diabetes of one year's duration, having regular diet and regular insulin (20 units daily before meals) received Invenol therapy. R.B.S. came down from 235 mg. % to 88 to 100 mg. % in 3 days' time and then maintained at normal levels. This is an unusual case of a young diabetic responding to this therapy. In this case, the regular restricted diet and regular previous insulin therapy probably, helped a great deal to produce such a satisfactory response to subsequent Invenol therapy.

6. Mrs. S., weighing 166 lbs. with diabetes, miliary tuberculosis and enlarged prostate and G.T.T. blood-sugar levels between 173 and 278 mg.% was given Invenol along with anti-tuberculosis treatment and treatment for the enlarged prostate. Blood sugar levels responded in 2 days and settled down to 90 to 94 mg.%. The tuberculous condition improved with anti-tubercular treatment. This case illustrates the possibility of using Invenol in diabetes associated with acute conditions like miliary tuberculosis.

7. Mr. K.A.M., aged 47 years weighing 151 lbs. with renal glycosuria of 11 months' duration—maximum 185 mg.% in G.T.T. was treated with the lower dosage schedule. R.B.S. settled down to 94-140 mg.% in a week and no hypoglycæmic reaction

was observed. The drug was then discontinued and there has been no rise in the blood-sugar levels, for the last 40 days.

8. Mrs. D. F., aged 34 a markedly obese lady weighing 162 lbs with diabetes of one year's duration and fasting level 164 mg.% and maximum 278 mg.% in G.T.T. was exhibiting very bad reactions to even small doses of insulin. The insulin reaction was sometimes mistaken for menopausal changes and the patient herself had a dread for insulin therapy. The drug was started and within a week R.B.S. settled down to 109 to 160 mg. %. The patient felt very much better and was quite happy. This is probably an ideal case in all respects for Invenol therapy.

9. Dr. C. N., weighing 210 lbs., with G.T.T. values between 210 and 400 mg.% and an active tuberculous infiltration in the apex of the left lung, was subjected to Invenol therapy. He had been previously maintained on 40 units of insulin daily. Within three days of the institution of this therapy, R.B.S. came down to 145 mg.% and urine sugar showed a progressive reduction and settled down to normal in 4 days' time. This case illustrates the value and usefulness of this therapy even in the presence of active tuberculous infection of the lung.

The *subjective improvement* noted during therapy was quite appreciable. A large majority of patients had a sense of well-being and evinced self-confidence. This sense of well-being was usually, though not always, in direct relation to the improvement of the diabetic condition. In occasional cases even when the blood-sugar response to the drug was only moderate, the patients felt much better as far as their physical condition was concerned. Polyuria and polydipsia improved in all the cases along with a reduction in blood sugar levels. Pruritus promptly disappeared in many cases after therapy. Diabetic retinopathy improved appreciably in two cases. Under-weight diabetics gained definitely in weight during this therapy while over-weight diabetics did not show much change. There seems to be an apparent increase in the carbohydrate tolerance of diabetics during the therapy although we have not progressed far enough with the investigation to confirm this point.

We found that the renal threshold for glucose during this therapy was not at all increased. On the contrary, we gained the impression that this threshold was lowered in a few cases; further observations will be necessary to confirm this finding.

On discontinuing the drug for over two weeks a recurrence of high blood-sugar levels was noted in six cases of our series, and so it would appear that the drug cannot be discontinued for long periods at a stretch, though a few days' interval in the course of the therapy may not matter much. However, with the

re-institution of the therapy the metabolism reverts to the normal balance.

*Side-effects* :—In the course of our clinical trials, we have not noted any serious side-effects. Occasionally, mild allergic skin reactions were encountered. We noted altogether two cases of urticaria, two cases of erythematous rash and six cases of itching of the skin. All these cases responded promptly to antihistamines and did not call for a further discontinuation of the drug. The W.B.C. count was not appreciably lowered in any case during therapy. We also failed to observe any changes in the differential blood-count, particularly with regard to the number of granulocytes. There were no disturbances of the liver and kidney functions during treatment. Mild hypoglycæmic symptoms were occasionally noted which required at best only oral administrations of glucose, but there was no serious hypoglycæmic reaction. From the few cases we gained the impression that during treatment with this drug severe hypoglycæmic symptoms are not likely to occur, even when rather low blood-sugar levels (as low as 40 mg.%) are present.

The *mode of action* of this new sulpha-compound with blood-sugar reducing properties is certainly a novel one for medical men in all countries. Even patients are curious to know about the action of the drug although they were not so very curious to know all about the now well-known insulin. The theory of destruction of the  $\alpha$  cells of the pancreas and consequent depressing of the effect of glucagon which is a hyperglycæmic hormone has not been held for long and it has been proved by autopsy reports that cells were quite in tact in cases subjected to Invenol for long periods. So at present, only certain possibilities regarding the mode of action of the drug have been suggested though none have been definitely proved. But the fact that the substance is therapeutically effective in selected cases, shows that it possibly supplements directly or indirectly the action of insulin. On the other hand, one particular phase of insulin action may prove to be augmented. It is extremely likely that the substance prevents the destruction of insulin either by a direct inhibition of insulinase or by a stimulation of the action of the insulinase inhibitor. These appear to be attractive theories.

Another very real possibility is that one or more enzymatic processes essential for the new formation of sugar in the liver (gluconeogenesis) are depressed, perhaps in quite an unphysiological way. If this depression due to the drug should exist and no untoward effects are produced even after several years, there should be no contra-indication at all to the therapeutic use of this drug in diabetes mellitus. It is also suggested that the rate of formation and liberation of insulin from the pancreas

may be increased in some instances. It is interesting to note in this connection that Loubatieres (1955) has obtained experimental evidence to show that these hypoglycæmic sulphonamides do liberate some pancreatic insulin. If this is confirmed by further researches, Invenol would really be an ideal antidiabetic drug.

In pursuing this study on the mode of action of these drugs, it is just possible that some extremely valuable and new information of interest to both the clinician and the research scholar might become available in connection with the factors relating to the metabolism of diabetes mellitus, which are yet to be known.

Conclusions.—The following conclusions on the clinical trials we conducted on 101 cases of diabetes, during a period of about six months, using *Invenol* would appear to be justifiable:—

1. *Invenol* undoubtedly marks a definite advance in the treatment of diabetes mellitus. We are sufficiently impressed by its definite blood-sugar reducing properties *pari passu* with the reduction of sugar in the urine. The absence of any serious toxic effects due to the drug should warrant its wider therapeutic use by physicians all over the country.

2. With a proper selection of suitable cases, the success rate with *Invenol* therapy will certainly be very high. Age seems to be a definite criterion in the selection of cases. Diabetics over the age of 35 years seem to be especially suitable. An upper age-limit seems however, to be unnecessary in our opinion for the administration of the drug. A small quantity of endogenous insulin appears to be definitely necessary for the action of *Invenol*. Excessive weight and obesity may be advantageous but not necessary for the success of the therapy. Neither the duration of diabetes nor previous insulin treatment seems to be a very important factor in the selection of cases for this therapy. Any case, no matter what the duration of diabetes and previous insulin therapy may be, is well worth a trial.

3. Cases with marked ketosis or pre-coma states or severe surgical complications must be considered unfit for this therapy at present since there is an urgent requirement for insulin in these cases and the slow action of the new drug may not be able to combat the emergency. Mild surgical complications and associated diseases like pulmonary tuberculosis or hypertension and urinary infection, do not appear to be definite contra-indications for the use of the drug to control the diabetic state. Insulin and *Invenol* may easily be administered together in necessary doses.

4. The dose of *Invenol* administered in our clinical trials appears to be quite adequate both for the mild and severe cases of diabetes. An occasional reduction in the dosage may not interfere with efficient control. An increase in the dose of the drug in severe cases did not confer any additional benefit and so is not recommended as a routine measure.

5. Although increased tolerance to foodstuffs, especially the carbohydrates has often been reported by our patients and also observed by us, we still hold that a definite diabetic regime of dieting is necessary for the proper control of the diabetic state along with *Invenol* therapy just as in the case of insulin therapy.

6. The effect of the drug as evidenced by blood and urine sugar levels often appears within the first 4 days, but sometimes it may be delayed for as long as a month. So failure of the therapy in any cases should not be gauged too early.

7. In well-controlled cases, this drug may be discontinued for short periods, say, of a few weeks. However, restarting of the drug will be necessary sooner or later. An uninterrupted maintenance treatment appears, therefore, to be the most suitable form of *Invenol* therapy.

8. The toxic effects of the drug (immediate or prolonged) observed by us have been minimal. Apart from allergic skin-reactions like urticaria and a slight hypoglycæmic reaction, no other serious toxic effects were met with so far. One point worthy of mention in our cases is that in spite of low blood-sugar values (35 to 45 mg. %) during the therapy, the patients did not exhibit any severe hypoglycæmic symptoms. It will be interesting to have the results of other observers who may be using this drug in the treatment of diabetes, reported from time to time in the medical press.

9. We noted subjective improvement in several cases, as evidenced by a sense of well-being during the treatment, which may be due partly to a psychological change in the patient's attitude who, after long periods of insulin injections would naturally be glad to take an effective oral anti-diabetic drug instead.

10. Since the action of this drug seems to be qualitative and not quantitative (as in the insulin treatment of diabetes) it would appear that the mode of action of the drug is more in the nature of an enzyme-activity inhibition or augmentation as yet undetermined. The theory that the drug can stimulate the  $\beta$  cells into producing more insulin, will if proved be an interesting finding and will prove that *Invenol* is an ideal antidiabetic drug.

Summary.—A clinical trial with a new oral antidiabetic drug, *Invenol*, was carried out in 101 cases covering a wide range of selection for the institution of the therapy.

An overall success rate with good results in 68% and satisfactory results in 15% of the cases was recorded. Nine case reports have been set out in this paper. The subjective improvement and the side-effects noted have also been recorded. Some theories on the mode of action of the drug have been stated, as also our own experience with the use of the drug.

We wish to thank Dr. C.K. Prasada Rao, M.D., Dean, Government General Hospital, Madras, for according permission and facilities for clinical trials with

this drug. We acknowledge with thanks the steady and continuous supply made by Messrs. Hoechst-Fedco Pharma (Private) Ltd., of Invenol tablets for the clinical trials.

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## INTRACRANIAL HÆMORRHAGE IN THE NEWBORN

In the newborn infant, intracranial hæmorrhage may arise from either mechanical trauma or anoxia. Differentiation by clinical observation alone is extremely difficult, although anoxic infants tend to be in better condition at birth and are less apnoeic than those injured mechanically. Mechanical trauma is more common in full-term infants, while anoxic hæmorrhage is found more often in premature infants.

Mechanical trauma may produce subdural hæmatoma with or without a visible dural tear. Subdural hæmatoma without visible dural tear may form from rupture of superior cerebral veins with hæmatoma of the convexity or from rupture of veins on the external surface with generalized hæmorrhage. Subdural hæmatoma with visible dural tear arises from rupture of the great cerebral vein of Galen with subtentorial hæmorrhage at the base of the brain, rupture of the tentorium with extension medially into the straight sinus or laterally into the transverse sinus, or rupture of the falx cerebri.

With anoxia, hæmorrhage may occur from (1) the choroid plexus into the ventricular and subarachnoid spaces or (2) the terminal vein, with local or extensive subependymal bleeding. Isolated hæmorrhages may be from the pia mater, or subependymal hæmorrhage may occur with subsequent rupture into the lateral ventricles and subarachnoid spaces.

The principal obstetric factors associated with brain injury are mal-formed and contracted pelvis, rigid maternal soft parts, precipitate or prolonged labour, abnormal presentation, high or difficult midforceps deliveries, breech extractions, and large foetal heads. Version and extraction, high mortality groups. Chief maternal complications include uterine inertia, uterine bleeding, intrapartum fever, dystocia, and hydramnios.

Infants in poor condition at birth are most likely to die from vascular accident. Initial respirations tend to be delayed until after two minutes.

Early death occurs equally often in the traumatic and anoxic groups. Most infants die within the first twenty-four hours, the largest number within the first six hours. Almost all deaths occur within the first week. —(Obst. and Gynaec. Surv., 11: 179-204, 1956 via Mod. Med., 1-9-56).

GOITRE AND MYXŒDEMA may develop during prolonged administration of large quantities of iodide. Turner, and Howard, of the University of Oklahoma, Oklahoma City, postulate that the excessive iodide interferes with the mechanism for synthesis of thyroid hormone. Symptoms of hypothyroidism disappear and the gland regresses when iodide is discontinued and desiccated thyroid or sodium L-thyroxine is given. —(J. Clin. Endocrinol., 16: 141-145, 1956).

## ÆTIOLOGY OF CHRONIC COUGH AS A SYMPTOM\*

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COUGH is a prominent symptom in various disease conditions and also occurs sometimes in normal persons. It is an important symptom as an involuntary reflex action and when it becomes chronic it is always of some significance. Cough is considered the "Watch-dog of the lungs."

Coughing is the result of a stimulation of the afferent endings of the glossopharyngeal and vagus nerves. The anatomic sites at which the cough reflex may be initiated are the pharynx, larynx, trachea, large bronchi, pleura and ear. The most sensitive zones are the larynx and the tracheal bifurcation. The cough centre is in the medulla and the motor component of the reflex consists of the muscles of inspiration and expiration.

The cough reflex presents three distinct phases viz., the inspiratory, the compressive and the compulsive phases.

Cough may be due to several causes. The common conditions in which chronic cough is a prominent symptom fall into two groups:—1. *Thoracic* comprising pulmonary, cardiac and mediastinal conditions and 2. *Extra-thoracic*.

I. The thoracic group:—A. *Respiratory conditions*:—Cough may be an important symptom in various respiratory conditions. The upper respiratory tract conditions are to some extent extra-thoracic causes, e.g., Chronic tonsillitis, chronic pharyngitis, and chronic laryngitis.

Tracheal conditions and tracheo-bronchitis often produce chronic cough. Lodgement of a foreign body in any one of these regions often produces paroxysmal coughing, followed by either collapse of the lung or inflammation and the secondary changes beyond the points of obstructions are responsible for the chronic cough. Often tracheo-bronchitis occurs as an industrial hazard, caused by certain fumes, smoke, gas etc. Even excessive smoking will produce chronic bronchitis. Chronic bronchitis and bronchiectasis due to tuberculous infection and bronchostenosis are two important causes of chronic cough. In children pertussis infection is a common cause of chronic cough. Dry bronchiectasis is often missed in the beginning. Bronchial polyps and other benign and malignant growths are also often responsible for chronic cough; early diagnosis in such cases is very essential. Pressure on the tracheal or bronchial tubes will produce chronic cough. Often torsion or abnormal angulation of the bronchi after pulmonary resection may keep on the cough. Less common

\* Based on a talk given at a symposium, 'C' ward Medical Association, Bombay on 31-8-56.  
Specially contributed to the ANTISEPTIC

conditions like tracheocele, bronchocele, and tracheopathia osteoplastica are sometimes responsible for chronic cough.

**B. Pulmonary conditions:**—We know that the lung itself is insensitive in the production of cough and that the cough is usually produced by an irritation of the bronchial system by spread of the primary lesions or pouring of the irritating material from the lesions in the bronchi.

Of the common lung conditions producing chronic cough tuberculosis stands first. Cough is a late sign of tuberculosis of the lung. As the patient starts coughing, the bronchioles are involved either by the spread of the disease or by the irritation set up by the necrotic material from the lungs. The chief mechanisms which produce cough in tuberculosis of the lung are (a) tracheal ulcers; (b) irritation by necrotic material; (c) recurrent hæmorrhage; (d) bronchial erosion by lymph nodes and (e) bronchial distortion due to fibrosis contractures. This stresses the importance—even after making a diagnosis of tuberculosis of the lung—of ascertaining the mechanism of production of cough in individual cases and then deciding on the treatment best suited for it. Some conditions require surgery for a cure. Other important pulmonary conditions producing chronic cough are chronic lung abscess, atelectasis of lung, fungus infections, sarcoidosis, fibrosis of the lung due to various diseases, including industrial hazards, chronic pneumonitis, syphilis of the lung and malignant growths. Early malignancy of the lungs must be thought of in persons over 40, having chronic cough. Besides these conditions, chronic emphysema may produce chronic cough. Pleural causes are chronic pleurisy and pleural growths.

**C. Cardiac conditions:**—Cardiac conditions can produce chronic cough by producing specific congestion in the lungs either by increasing the blood flow in the lungs or by increasing resistance somewhere. This fact is responsible for chronic cough in mitral stenosis and left ventricular failure. The other mechanism is direct pressure of the enlarging cardiac chamber or aorta on the bronchi or vagal nerve. This is often found when a huge pulmonary artery aortic aneurysm or left auricle or ventricle is pressing upon these structures. Sometimes precarditis with effusion can produce a similar pressure. Very rarely cardiac tumours and double aortic arch may produce pressure on the tracheo-bronchial tree.

**D. Mediastinal conditions:** The mediastinal structures when they get enlarged, may press upon the trachea and bronchi and produce an unproductive cough, often described as 'Brassy dry cough.' The common structures which are responsible for this are enlarged glands, mediastinal tumours of any type, and substernal thyroid enlargement. Besides this, the œsophagus

may sometimes be responsible in the production of chronic cough either by bronchial fistula or a huge enlargement in cardio-spasm. The latter condition is often associated with even atelectasis of the lung.

**II. Extra-thoracic.**—Cough reflex may be initiated by irritation of the Arnold's nerve in the ear. Similarly meningeal irritation can also produce a cough. But these causes are not frequently met with. Chronic pharyngitis, chronic laryngitis, T.B. ulcers, foreign bodies lodged in the tracheo-bronchial tree and malignancy of the larynx are the important conditions already described.

An allergic cough is often met with in practice, which may be associated with bronchial spasm or chronic bronchitis. The cough is usually loud, barking and paroxysmal. The other important conditions in places like Bombay, of ætiological importance in chronic cough, is tropical eosinophilia which is so common in Bombay that I would always like to think of it first particularly when cough is associated with breathlessness. But chronic cough may be the presenting symptom in many cases and a simple blood examination would confirm the diagnosis. Parasitic involvement, especially round worm infection is often a common cause for chronic cough in children. Paranasal sinus infections produce cough in about 25% cases. Only when we cannot find any of the above causes, will we be justified in calling it either as a habitual cough or a psychogenic one. Cough as a symptom being so common in medical practice, it is essential that no chronic cough should be treated symptomatically, without ascertaining the underlying cause in each case.

#### TREATMENT FOR TUBERCULOUS LYMPHADENITIS

Local injections of antibiotics are generally of no avail against primary or secondary cervical adenitis of tubercular origin. Oral or parenteral doses of streptomycin, isoniazide, or PAS are useful in that they serve to prevent dissemination of the disease *via* the blood; but it is seldom that such treatment has any beneficial effect on the lesions of the lymph-nodes themselves.

From results obtained with a fairly large number of children, it would seem that the antiphlogistic action of hydrocortisone can be exploited to good effect in this indication. As a general rule, 10 mg. hydrocortisone is injected into the lymph gland 2 or 3 times per week. In many cases the extent of the adenopathy diminishes within only a few days, and the surrounding tissue—which often already shows a marked tendency to fistulization—becomes normal again. The fluid obtained by puncture decreases in quantity, assuming a serous or serosanguineous appearance.

A cure may be expected within 1 to 2 months. Such relapses as may occur are less severe than the original disease and normally respond satisfactorily to renewed treatment. Should hormone therapy prove unsuccessful, it may be advisable to extirpate the lymph nodes. —(*Sem. hop. Paris.*, 32 : 135, 1956).

## MYOSPASM, MYOTONIA AND MYOCLONIA\*

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A SPASM is a sequel to excitation at any point in the spinal reflex area. The word myoclonus stands for muscle tumult or agitation. Myoclonus stands for clonic spasm and myotonus for tonic spasm.

Classification.—I. Generalised myospasm or myoclonias; II. Localised myospasms; III. Partial or fibrillary myospasms; IV. Generalised and localised tonic myospasms or myotonias.

I. GENERALISED MYOSPASMS—THE MYOCLONIAS:—1. *Paramyoclonus multiplex of Friedreich*, occurs between the ages of 40 and 50 and affects the proximal muscles, producing sudden shocklike contractions of symmetrical groups of muscles, at rates varying from 10 to 50 per minute. Different stimuli increase their intensity. Knee jerks are extremely active. The limb muscles are affected more than the trunk muscles. There is transient arrest by voluntary innervation.

Pathogenesis.—The condition is probably due to the excitability of the ventral horn cells. Attempts have been made to associate this with lesions in the cerebellum. A combination of myoclonus-epilepsy and cerebellar syndrome has been described.

TREATMENT:—Is purely empirical.

2. *Electrical chorea of Henoch*:—Occurs in children between the ages of 9 and 15. The symptoms are hastened by fright, producing lightning twitches of the muscles of the neck and shoulders not rigidly symmetrical. They become paroxysmal. No psychical abnormality can be detected and the ailment tends to become chronic.

3. *Myoclonus-epilepsy*:—In this condition there are irregular twitches of one or more parts of the body in multi-muscular groups, the symptoms affecting one or more parts of the body. A frequent incident during the process is the patient being thrown to the floor. One or both arms may be shot suddenly forward. Sometimes myoclonus may be the sole epileptic sign. In some cases the myoclonic phenomena are widespread and constant.

4. *Unverricht's familial myoclonus epilepsy*:—Several members of a family are affected. Multiple degenerative and sclerotic changes are found in the cerebral cortex, cerebellum and mid-brain. The features are continuous myoclonus during waking hours and epileptiform fits and dementia. The myoclonic twitches cease during sleep. They become intensified by voluntary movement and emotional excitement.

5. *Electrical chorea of Bergeron in hysteria*:—The chief features are:—a brief course; occurring between the ages of

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7 and 14; induced by emotion; without any interference with voluntary acts and the occurrence of abrupt jerks of the neck, shoulder, arm and the other parts of the body.

6. *Myoclonus occurs in other conditions viz.*: encephalitis, fevers like typhoid producing subsultus tendinum and multiple sclerosis.

II. LOCALISED MYOSPASMS:—1. Spasms of the ocular muscles. There may be partial oculo-motor paralysis. The condition may occur in encephalitis lethargica.

2. Spasms of the motor 5th muscles. (a) Tonic spasms known as trismus may occur in tetanus or hysteria or in disease of the temporo-mandibular joint and wisdom tooth and from myositis of Masseters. (b) Clonic spasms may occur in chills and rigors, hysteria, habit spasms in children. The treatment consists in a search for any source of irritation in the field of the trigeminal and instituting appropriate therapy.

3. *Facial spasm*:—A clonic facial spasm or facial myoclonia is the result of irritation along the course of the facial nerve. Facial spasm may be unilateral or bilateral, partial or complete, tonic, or clonic, tonico-clonic or fibrillary. The clinical varieties are:—(a) Blepharospasm; cause—(i) psychogenic, (ii) post-encephalitic parkinsonism; (b) preparalytic facial spasm, which is antecedent to facial palsy, and may occur in such lesions as compression of the nerve in extra-cerebellar tumours; and (c) post-paralytic facial spasms may be fibrillary or chronic.

4. *Spasm of the 9th, 10th and 11th groups*:—Examples of this group are: (i) laryngeal spasms or laryngismus of rickets; (ii) spasms of the spinal accessory, producing torticollis; and (iii) the glassolabial spasm of hysteria.

5. Spasms of the trunk and limbs.

6. Spasms of the respiratory musculature: Hiccup or singultus or clonic diaphragm: which (a) may be due to mechanical irritation of the phrenic nerve from enlargement of the stomach; (b) may follow operations of the colon, stomach, gallbladder and other adjoining viscera; (c) may be hysterical or psychogenic; or (d) may be of central origin produced by encephalitis or uræmia. The treatment of singultus will depend on the cause. The usual measures adopted are:—carminatives, nerve sedatives and hypnosis.

III. PARTIAL OR FIBRILLARY MYOSPASMS:—1. *Marvan's fibrillary chorea*:—This occurs after fever and is associated with shooting pains, hyperhidrosis, albuminuria, delirium and death.

2. *Myokymia of Kny and Schultze*:—The symptoms are:—a gradual onset; cramps and fibrillation.

The condition may be called myoclonus fibrillaris multiplex and is not associated with muscular atrophy. It is unaffected by rest or muscular activity and is of no serious significance.

\* Specially contributed to the ANTISEPTIC

3. *Dubini's electrical chorea*:—The condition is a meningo-radicular encephalitis with an acute febrile onset, shooting pains over the trunks and limbs, followed by the appearance of rhythmic shock-like contractions of muscles at the rate of 30 to 40 per minute. The abdominal muscles and limbs are commonly involved. The pupils become dilated; there is tachycardia and sweating. Instead of drowsiness of the ordinary encephalitis, there is insomnia. Articulation becomes indistinct. The C.S.F. shows pleocytosis. Later on, the myoclonic contractions subside and the patient passes into a phase of lethargy with ocular paralysis as in ordinary encephalitis lethargica. Coma and death may supervene.

4. *Nystagmus myoclonus of Lenoble and Aubineau*:—Is a rare congenital variety and the nystagmus is usually a later pendular variety producing involuntary jerking movements of the limbs and trunk. The nystagmus can be controlled by an effort of the will. There are other assorted congenital malformations such as hypospadias, flat foot etc.

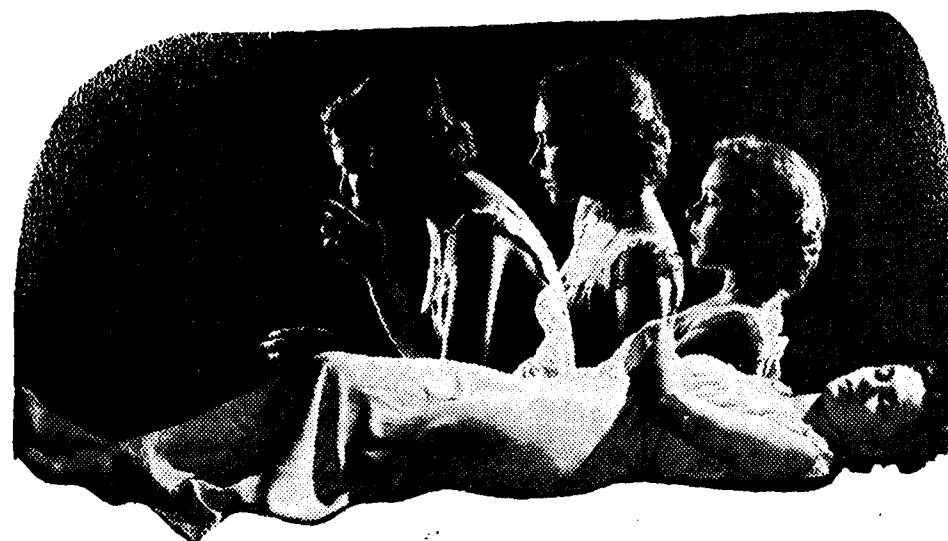
IV. TONIC SPASMS OR MYOTONIAS:—1. *Paramyotonia congenita of Eulenburg* is a familial affection involving the facial muscles. The tonic spasm is produced by cold and relieved by warmth.

2. *Myotonia congenita or Thompson's disease*:—The chief features are: (a) hypertrophy of the muscles; (b) muscular weakness; (c) myotonia; and (d) slight mental impairment. It is said that there is excessive production of acetyl-choline or the absence of destruction at the myoneural junction. The myotonic phenomena can be abolished by quinine and aggravated by prostigmine or potassium salts.

3. *Dystrophia myotonica* is a rare heredo-familial disease developing in adult life, usually occurring in males. The chief features are:—(i) muscular atrophy of the facial, sterno-mastoid and peripheral limb muscles; (ii) muscular weakness with myopathic facies; (iii) myotonia on voluntary movement; (iv) dystrophic symptoms as cataract testicular atrophy and frontal blindness. Dr. Walton and Natrass describe electrocardiographic changes indicating abnormality of the cardiac muscle.

*Cramps are painful spasms of muscles* produced by intermittent muscular contractions, caused by: (1) muscular fatigue; (2) a toxic hæmic state as in diabetes, cholera, constipation, flatulent dyspepsia, lead-poisoning, anæmias and other toxic causes; (3) disease of the blood vessels as angiospasm or pelvic tumours or pregnancy interfering with venous return. The normal muscle spasms are painless and the pain in cramps may be due to irritation on pain receptors by endogenous or exogenous toxins. Treatment consists in improving the local circulation by massage and in the use of analgesics like aspirin.

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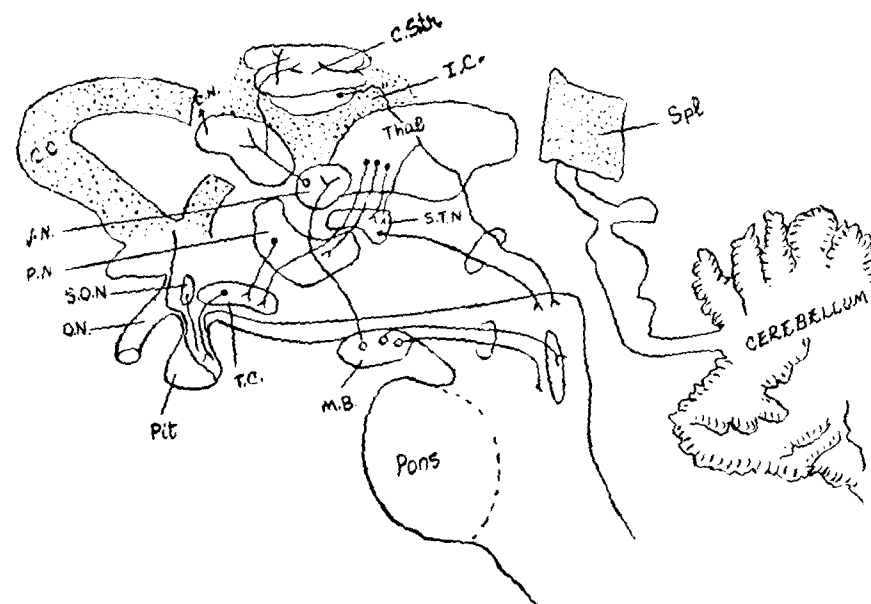
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## THE HYPOTHALAMICO-HYPOPHYSEAL MECHANISM OF NEURO-ENDOCRINE FUNCTION\*

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THE anatomy of the hypothalamic region, with its probable fibre connections is shown in the diagram below:—



## Anatomy of the Hypothalamic Region

C. Str. : Corpus striatum. I. C. : Internal capsule. C. N. : Caudate nucleus.  
 Thal : Thalamus. V. N. : Ventral nucleus of the thalamus. C. C. : Corpus callosum.  
 Spl. : Splenium. S. T. N. : Sub-thalamic nucleus. P. N. : Paraventricular nucleus.  
 S. O. N. : Supraoptic nucleus. O. N. : Optic nerve. Pit : Pituitary body.  
 T. C. : Tuber-cinereum. M. B. : Mammillary body.

The descending fibres from the subthalamic nucleus, control the sympathetic nervous system. The intimate connection between the tuber-cinereum, supra-optic nucleus and the posterior lobe of the pituitary should be noted, as they form the connections of the important hypothalamo-hypophyseal mechanism of neuro-endocrine function.

The principal masses of grey matter and fibre connections of the hypothalamus are given in the above diagram, but a great deal of additional research is needed to elucidate fully the anatomy and the physiology of this region. There is little doubt that it serves as a higher centre for control of the sympathetic nervous system. Stimulation of the subthalamic nucleus of this area produces dilatation of the pupil, exophthalmos, and widening of the palpebral fissure—convincing evidence of sympathetic activity. The rate of the heart-beat, the level of the blood-pressure and the secretion of adrenaline can likewise be modified.

\* Specially contributed to the ANTISEPTIC

It has also been shown that the rage reaction, with its widespread visceral and somatic components, depends on a reflex arc, with its centre in the ventral nucleus of thalamus. The supra-optic nucleus, tuber-cinereum and probably also the paraventricular nucleus are intimately related to the secretory activity of both the posterior and anterior lobes of the pituitary, the former through the nervous connections between the two and the latter through the effect of the neuro-secretion of the nuclei of the hypothalamus above mentioned, which enters the common blood-supply of the hypothalamus and hypophysis through the hypothalamico-hypophyseal portal system of blood vessels. Temperature regulation is in tact in the thalamic animal, but is abolished after trans-section through the diencephalon; so that function is probably controlled by this region to a significant extent. Diencephalon also controls the parasympathetic system. Stimulation of the tuber-cinereum region which is the higher centre of the parasympathetic nervous system produces vagal effects such as increased gastric secretion and motility. Cushing states that in intracranial operations fatal perforations of the stomach, or œsophagus may follow. He offers evidence that this is due to a stimulation of the diencephalon, causing disturbance of para-sympathetic activity.

**Anatomy and histology of the pituitary body.**—The pituitary body is situated in the depression known as Sella-turcica of the sphenoidal bone. It consists of an anterior lobe of glandular structure, a posterior lobe of nervous structure and stalk known as the infundibulum by which it is attached to the median eminence of the hypothalamus known as the tuber-cinereum. The anterior lobe is made up of pars-anterior, pars-tuberalis and pars-intermedia, all of which arise embryologically from Rathke's pouch from the stomodæum.

The posterior lobe is made up of the pars-nervosa, which arises from the floor of the 3rd ventricle, and is therefore of nervous origin and has a neuro-secretory function elaborating the hormone-pituitrin.

The infundibulum (stalk) is developed from the floor of the 3rd ventricle as also, the tuber-cinereum of the hypothalamus to which the stalk is attached.

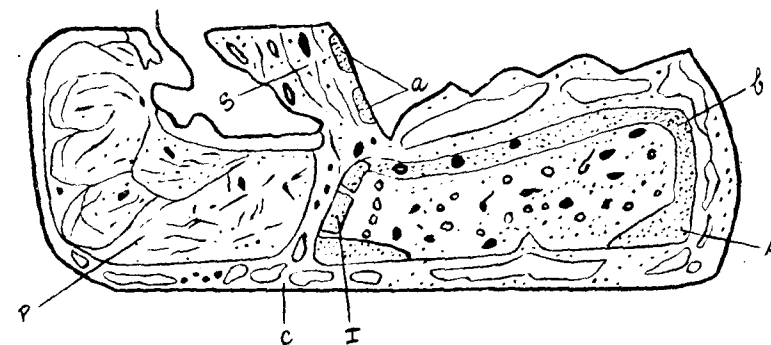
The pars-anterior or the pars-distalis of the anterior lobe is large, compact and highly vascular. It consists of cells arranged in nests or columns surrounded by connective tissue. The cells are of two kinds:—(i) chromophobe, without affinity for dyes; and (ii) chromophil, which stain readily and are subdivided according to the character of their granules into eosinophil cells which stain with eosin or acid fuchsin and basophil cells, which stain with hæmatoxylin. The functional significance and mutual relation of these various elements are not yet clear. A certain

amount of suggestive information may be derived from a study of the effects of innocent tumours (adenoma) arising from different kinds of cells. Tumours consisting of the chromophobe cells are associated with signs of hypo-pituitarism; in acromegaly, which is a condition due to hyper-pituitarism, tumours of the eosinophil cells are almost constantly present. Tumours of the basophil cells give rise to derangements of sexual and other functions.

The pars-intermedia is thin, poorly vascularized, and formed of densely backed basophil cells. Cysts of vesicles containing colloid are described in this region. It is believed generally that these are normal structures and contain the active physiological principle of the pars-intermedia. In most species, the pars-intermedia is found in the posterior lobe. Very little intermedia tissue is found in human pituitary, and what remains of it lies in the anterior lobe.

The pars-nervosa consists mainly of neuroglial elements and is highly vascular. Hyaline or colloid masses can often be found here. It is suggested that they represent the secretion of the pars-intermedia, which enters the pars-nervosa either to be absorbed in its blood vessels or to enter the C.S.F. of the 3rd ventricle.

The diagram below illustrates the structure of the human pituitary in sagittal section:



A: Pars-anterior. I: Pars-intermedia. b. (densely stippled): Region of the pars-anterior which is free from eosinophil cells. The less densely stippled region of the pars-anterior contains the eosinophil cells. P: Pars-nervosa. S: Stalk. a: Cells in the stalk resembling those at b in the anterior lobe. C: Capsule. Blood vessels are indicated in solid black. There is no pars-tuberalis.

The pituitary body and its relation to the brain stem.—The part of the pituitary, originating from the Rathke's pouch, the pars-anterior and pars-intermedia, have a glandular structure and are commonly known as the adeno-hypophysis or anterior lobe. The portion developed from the brain and fused with the adeno-hypophysis is known as the neurohypophysis. Its

two parts, the stalk or infundibulum and the expanded distal portion, the posterior lobe of the pituitary are now referred to as the neural stalk and neural lobe. The extent to which the adeno-hypophysis makes contact with the neural lobe varies considerably. It may almost entirely surround the latter. But in all instances it invests the stalk with a thin layer of tissue, which extends to the base of the brain to cover the median eminence of the tuber-cinereum. This extension of the adeno-hypophysis is called the pars-tuberalis and is seldom found in human pituitary though it is found in the cat and certain other mammals. The thin strip of tissue lining the posterior wall of the cleft, and fused with the neural lobe and which is the remnant of the posterior wall of Rathke's pouch, is known as pars-intermedia. Owing to its intimate relationship with the neural element the pars-intermedia was usually considered to be part of the posterior lobe, when this term was generally used, but when its origin from Rathke's pouch and structure are borne in mind, it should obviously be considered only as part of the adeno-hypophysis.

The remaining and much larger part of the adeno-hypophysis is called the pars-distalis or pars-anterior or pars-glandularis.

The neural lobe and stalk are composed of (a) neuroglial cells (b) fusiform cells with several processes and containing granules of a brown pigment, in their cytoplasm (pituicytes) (c) numerous nerve fibres and (d) hyaline bodies. These hyaline bodies were considered by Herring, Cushing and others to represent cells of the pars-intermedia and pars-tuberalis, which have undergone a hyaline change and are traversing the pars-nervosa and stalk to reach the 3rd ventricle. The hyaline material with which they are filled, has been considered to represent the hormone of the neural (posterior) lobe. Some doubt has been cast on this view, and many now consider these bodies as merely artefacts.

Wislocki and King have investigated the blood supply of the hypophysis in the monkey and in man; their observations would appear to show that except for a few capillary anastomoses, the blood supply of the pituitary is independent of that of the brain proper. It is derived from the *hypophyseal arteries* which are branches of the internal carotid. The circulation of the pars-distalis and pituitary stalk, is also separate from that of the neural lobe. The stalk receives its blood supply from the superior hypophyseal arteries, which form a rich plexus surrounding it; and lying between it and the thin overlying layer of the pars-tuberalis. This vascular plexus sends twigs into the substance of the stalk and extends upwards into the median eminence of the tuber-cinereum, where it anastomoses with the general capillary bed of the hypothalamus. The plexus is drained

by vessels (portal venules) which descend the stalk and empty into sinusoids of the pars-distalis. The sinusoids are also supplied with blood through the superior hypophyseal arteries. Thus, the pars-distalis is seen to receive a double vascular supply; the portal, the blood passing through two capillary beds, and the systemic. The portal has been named the hypothalamico-hypophyseal portal system by Wislocki.

*The nerve fibre connections of the hypophysis:*—The neuro-hypophysis is supplied with fibres derived from the internal carotid nerve plexus. The cell stations of the fibres are probably in the superior cervical ganglion of the sympathetic, and they reach the neural lobe along blood vessels, which descend the neural stalk. Parasympathetic innervation of the hypophysis from the great superficial petrosal nerves, which pass through the internal carotid plexus, has also been described. The most important nervous connections of the neurohypophysis are fibres originating in the hypothalamic nuclei—supraoptic, tuber-cinereum, and probably the para ventricular nuclei. These fibres, which according to one estimate, number about 50,000 descend in the neural stalk for distribution to the neural lobe. A few can be traced to the pars-intermedia, but none enters the pars-distalis. This tract of fibres, of great importance, in respect to the functions of the neural lobe, is known as the hypothalamico-hypophyseal tract. A few nerve fibres have also been described, penetrating into the pars-distalis, but they are probably vasomotor in function. The secretory function of the adeno-hypophysis, unlike that of the neural lobe, is not under direct nervous control (i.e. by secretory nerves).

The intimate relationship of the pituitary to the diencephalon with its hypothalamic centres and tuber-cinereum in the floor of the 3rd ventricle is of great importance. Non-medullated nerves pass between the hypothalamic centres and the posterior lobe, and it is probable that the secretion of the pars-intermedia passes along the infundibulum to the hypothalamus, where it may act directly on the nerve centres or may enter the 3rd ventricle. The hypothalamus and in particular the tuber-cinereum may act as a regulator of pituitary activity. Cushing remarks that if the pituitary sex hormone is the motor that sets the reproductive cycle going, the emotional self-starter is probably in the diencephalon. In the past, experimental work tended to direct attention away from the pituitary to the hypothalamus, and according to the "Hypothalamists" many symptoms which had formerly been attributed to disease of the pituitary, were, in reality caused by lesions of the diencephalon. It is better to avoid either extreme, and to regard the diencephalon and both the posterior as well as anterior pituitary as forming a single unit with reciprocal relations, the posterior pituitary secretions being under nervous control by the hypothalamic nuclei of the

anterior hypothalamic region, the hypothalamic nuclei in their turn being stimulated into activity by pituitrin, which enters the 3rd ventricle and the hypothalamico-hypophyseal tract of nerve fibres in the infundibulum or pituitary stalk and acts on the nuclei, and the anterior pituitary secretions being influenced by the level of the neuro-secretory activity of the same nuclei (supra-optic, tuber-cinereum, and para-ventricular nuclei), the neuro-secretory discharge of which the so-called hormone of the hypothalamus is absorbed into the hypothalamico-hypophyseal portal system of vessels, and thereby acts on the anterior pituitary and stimulates the formation of its hormones. The diencephalon is the most ancient part of the cerebrum which has remained almost unaltered in the course of development and it appears to contain the centres for the primitive elemental sensations of hunger and thirst. Experimental injury of the hypothalamus and particularly of the tuber-cinereum may be followed by the development of polyuria and thirst, a condition corresponding to diabetes insipidus or marked adiposity. Experimental lesions of this region are also attended by pathological sleep. The virus of epidemic encephalitis is particularly liable to attack the hypothalamic centres, and diabetes insipidus and other hypothalamic symptoms may develop as a result of this infection. Narcolepsy (periodic somnolence) is also probably hypothalamic in origin. A lesion of the posterior lobe of the pituitary, or a clamp placed on the infundibulum are certainly liable to influence the level of activity of the hypothalamic centres through the nerve paths which connect the two elements of the unit. Blocking of the passage of the pituitary secretion to the diencephalon, without interference with blood supply to the pituitary, may cause marked obesity. The polyuria of an experimental hypothalamic lesion or naturally occurring diabetes insipidus may be checked to a great extent by the use of the posterior lobe extract. In spite of the facts pointing to functional as well as structural unity of the diencephalo-hypophyseal mechanism, it seems justifiable at present to regard polyuria, adiposity and hyper-somnolence as hypothalamic symptoms, although they often occur in pituitary disease.

The control of the secretion of the adeno-hypophysis.—As already described, the pars-distalis is not under direct nervous control. Indeed, in some mammals e.g., the whale, porpoise and armadillo, etc. the pars-distalis is separated from the neural stalk by a fibrous septum, which the nerve fibres of the stalk, cannot penetrate. Furthermore, the section of the neural stalk, the only course which secretory fibres might take, often causes no noteworthy effects upon the anterior lobe function, and none, which interfere with blood supply cannot explain, though it completely extinguishes the activity of the posterior lobe and the consequent non-elaboration of its hormone, 'Pituitrin.'

Yet, there are a great many observations from which it must be concluded that the activity of the anterior lobe is subject to nervous influences. The liberation of "*Ovulation Hormone*," by the pituitary in rabbits, on sexual excitement, the release of the adreno-cortico-trophic hormones, under states of emotional stress, as shown by Long and his associates, the secretion of the thyrotrophic hormone, upon exposure to cold, and the effect of light, due to retinal stimulation upon sexual functions of birds, and of many mammals, are outstanding examples of a relationship between the output of the anterior lobe hormones, and nervous activity. It has been found by Markee and his associates, that whereas direct electrical stimulation of the pars-distalis, in the rabbit, in 15 hourly periods over a total period of 5 days failed to cause ovulation, stimulation of the tuber-cinereum for only 3 minutes, succeeded. The above observations are explained on the basis of the vascular supply to the pars-distalis. It is reasonable to presume that an almost unique vascular arrangement of this nature possesses physiological significance. The cells of the hypothalamic nuclei have every appearance of being secretory in function. There is now little doubt that these cells, as a result of impulses received from other parts of the nervous system, for example from the cerebral cortex, thalamic reticular system, the transitional cortex, the posterior hypothalamic nuclei, and other nuclei of the thalamus which send afferent impulses from the viscera to the hypothalamus, an excitatory state of the posterior hypothalamus containing sympathetic higher centres, naturally inducing a suppression of activity of these nuclei which are higher centres of the para-sympathetic nervous system as for example during emotion, exposure to cold etc., discharge a secretion into the capillary blood, which is conveyed to the sinusoids of the pars-distalis, through the hypothalamico-hypophyseal portal system of vessels.

Thus a hypothalamic hormone is brought into relation with the cells of the adeno-hypophysis, which produce the trophic hormones. In other words, the neuro-secretory cells and the portal system of vessels, serve as functioning links between the nervous system and the endocrine cells of the adeno-hypophysis. The conception of neuro-secretory cells is of course not new. The existence of such cells in the nervous system of both invertebrates (insects, molluscs, worms etc.), and vertebrates, including the human hypothalamic nuclei, has been well established. The secretion of such cells has even been demonstrated as droplets of an acidophil material, in the axons of the nerve cells. In fish also, similar material has been traced all the way along the axons from the hypothalamic cells to the hypophysis. Further evidence for the control of adeno-hypophyseal activity by means of neuro-hormones elaborated in the hypothalamus and carried to the cells which secrete the trophic hormones, may be given:—

(a) the adenohypophysis is not responsive to electrical stimulation, whereas electrical stimulation of the tuber-cinereal region of the hypothalamus is effective; (b) the effect of section of the neural stalk in abolishing control of adrenocorticotrophic hormone secretion is not constant, but Harris has shown that failure of this operation to prevent A.C.T.H. liberation in response to various states of stress, is due to rapid post-operative restoration of the hypophyseal portal circulation. If revascularization is prevented, the hypophysis remains unresponsive to hypothalamic influence; (c) grafts of hypophyseal tissue in the neighbourhood of the hypophyseal portal circulation, respond to hypothalamic stimulation, those placed in more remote situations and which therefore, are not vascularized from the hypophyseal portal vessels, do not respond.

The neuro-hypophysis and its functions.—An extract from this has been used in medicine for many years as pituitrin infundin, infundibulin etc. or as official solution of the British and U.S. pharmacopœias. Much of the knowledge regarding posterior pituitary has been gained from experiments with this relatively crude material and although it has been largely displaced by more purified fractions—Pitressin and Pitocin, an account of the whole posterior lobe extract, will first be given. The continuous activity of the uterus in the puerperal rabbit appears in the light of experimental evidence, to be due to pituitary secretion, initiated reflexly from the pelvic viscera, for the contractions undergo progressive diminution in amplitude, after interruption of the afferent pathways, by section of the pituitary stalk or of the spinal cord, above the first lumbar segment. Fisher *et al* had also previously found that after section of the hypothalamico-hypophyseal tract in cats, the expulsive moments of the uterus at term were extremely sluggish. This operation reduces almost to a vanishing point, the active principles of posterior pituitary. Very suggestive is the discovery of Cohen and Marien that the oestrogenic hormone is present in the blood, and is excreted in the urine as an inactive compound (glycuromide of oestriol), in pregnancy until just before the onset of labour when it appears in the free, active form. Expansion of melanophores in the amphibian or the erythrophores in the minnow, is most certainly a hormonal effect and also the anti-diuretic action.

The control of activity of the neurohypophysis and the source of its hormones.—While the evidence is against the adenohypophysis being under direct nervous control, the clear demonstration of nervous pathways to the neural lobe, the depletion of the posterior lobe hormones after section of the hypothalamico-hypophyseal tract, as well as other experiments in respect of the melanophore expanding and oxytocic principles leave little doubt that this part of the pituitary is directly controlled by nerves.

The current opinion as regards the source of origin of the posterior-pituitary hormones as expressed by Gelding and Oldham is that they are formed not in the pars-intermedia as formerly believed, but in the neural lobe itself, where the pressor, oxytocic, and anti-diuretic hormones are secreted. It is clear that the latter opinion must be correct, for in animals in which there is no pars-intermedia in the pituitary, *e.g.*, the whale, porpoise and chicken, there is no lack of ADH. Since the discovery of neurosecretory cells, the absence of tissue of a glandular nature from this part of the pituitary, is no obstacle to the acceptance of such a view, and as Gelding points out, the adrenal medulla is of neural origin.

Another reason for believing that the neural tissue, probably the pituicytes elaborate the post-pituitary principles, is afforded by the experiments of Fisher and his colleagues. After section of nerve fibres of the neural stalk degenerative changes confined to the posterior lobe appear, and the pressor, oxytocic and the antidiuretic principles are greatly diminished, whereas pars-intermedia contains the normal amount of melanophore-expanding principle. Detection of the posterior pituitary principles in the C.S.F. by means of oxytocic and melanophore tests, have been reported by some workers, but others have failed to confirm the observation. The recent experiments of Zondek indicate that intermedin, leaves the pituitary through the infundibular stalk. This principle was recovered from the walls of the 3rd ventricle, in the region of the autonomic centres, but from nowhere else outside the pituitary. Circumstantial evidence for the view that the posterior lobe hormone is discharged into the ventricular system has been furnished by Cushing. He found that injection of commercial pituitrin into the lateral ventricle of man produced the most striking effects, which commence within five minutes of the injection. These effects resemble closely those characteristic of parasympathetic stimulation, and are quite different from those resulting from intramuscular injection of the same. They include (a) flushing of the face and most profuse sweating; (b) fall in rectal temperature from about 99°F to 94°F; (c) nausea, vomiting and contractions of the small intestine; (d) rise in blood-pressure after an initial fall and some increase in heart rate; (e) salivation and lachrymation; (f) fall in metabolic rate within 1½ hours. These effects are not due to histamine. Similar effects have been produced by Fulton in the monkey. The intra-ventricular injection of pilocarpine, produces similar effects, and atropine being a parasympatholytic, prevents the usual results following the intra-ventricular injection of pituitrin or pilocarpine. Further, the agents have not their usual action in persons on whom the tissue of the hypothalamic region, has been destroyed by disease,

or is under the influence of an anæsthetic, such as avertin, which is believed to act upon the hypothalamus.

Cushing conceives that the secretion of the posterior lobe passes into the C.S.F. of the ventricle, and diffuses through the nervous tissue to act upon the para-sympathetic centre in the hypothalamus (tuber-cinereum). On the other hand, the secretion of the posterior lobe is controlled by impulses arising in the higher nervous centres and relayed to the gland through the hypothalamic nuclei. It is altogether likely that the osmotic pressure of the blood, which is a factor in the control of anti-diuretic hormone liberation, does not act directly upon the neural lobe, but upon the cells (osmo-receptors) of the hypothalamus (contained in the supra-optic, tuber-cinereal and para-ventricular nuclei). This conception of a nervous-hormonal synergism finds its analogy in the sympatho-adrenal system in which impulses flowing along the sympathetic, cause the liberation of adrenaline secretion, which in turn reinforces the actions of the sympathetic.

The diseases caused by the hypothalamico-hypophyseal dysfunction are:—(1) Diabetes insipidus; (2) dystrophia-adiposa-genitalis; (a) infantile (Frolich's syndrome) or juvenile type, and (b) adolescent or adult type; (3) narcolepsy; (4) catalepsy; (5) idiopathic epilepsy, either petit mal alone, or petit and grand mal combined, the convulsive seizures in the latter being of the generalized type as distinguished from focal cortical seizures of cortical origin, involving one part of the body alone or one side of the body; (6) Laurence-Biedl-Moon syndrome, and (7) Dercum's disease.

1. *Diabetes insipidus* is a condition in which large quantities of urine of very low specific gravity (1002 to 1006) and low chloride content are excreted. In an ordinary case 4 to 6 litres are excreted and in sane, many times, more. A corresponding increase in fluid-intake occurs, and there is intense thirst (polydipsia). It is due to posterior lobe deficiency, and so it is relieved by injections of pituitrin. The condition frequently accompanies tumours of the pituitary or hypothalamic region. It has been shown, however, by Bailey and Bremer, and later by others, that in animals, puncture of the hypothalamus in the region of the tuber-cinereum, without apparent injury to the pituitary causes polyuria. Diabetes insipidus also follows conditions like (epidemic encephalitis), involving a hypothalamic region. It is correct to look upon diabetes insipidus, as well as the other diseases listed under this category, as resulting from a disorder affecting the integrity of the hypophyseal-hypothalamic mechanism, rather than as always being dependent on either the pituitary or the hypothalamus exclusively. Involvement of one or other element or of the nervous connections between the two would cause the disease. Involvement of the hypothalamus

would inevitably affect the state of the pituitary, the posterior lobe secretion of which, pituitrin, again to a great extent determines the level of activity of the anterior hypothalamic nuclei (supra-optic, para-ventricular and tuber-cinereum). Fischer, Ingram and Ranson found, for example, that a lesion interrupting the supra-optico-hypophyseal tract of nerve fibres, resulted in diabetes-insipidus together with atrophy of the cells of the supra-optic nucleus and of the neural lobe of the pituitary. The atrophic posterior lobe was completely devoid of all its principles. The anterior pituitary produces a hormone, according to the theory of Haun, which antagonizes the posterior pituitary antidiuretic factor, and therefore it is, that hypophysectomy *in toto* fails to produce diabetes insipidus.

2. *Dystrophia adiposa-genitalis* is a condition in which obesity, sexual infantilism, and dwarfing, (if the condition occurs during the growing period), are the essential features. It is due to a lesion of the anterior lobe of the pituitary, which accounts for sexual immaturity and dwarfing, and of the hypothalamus or posterior pituitary. The experiments of Smith with hypophysectomised rats and of other investigators point to injury of the hypothalamus, rather than the posterior lobe, as being chiefly responsible for obesity. Marked obesity is also a feature of certain hypothalamic diseases in man, unassociated apparently with any disease of the pituitary itself.

But it stands to reason that obesity may be associated, though not apparently, with disease of the pituitary, but really with a disordered functioning of the pituitary, at times, brought about by changes in the hypothalamus, paroxysmally occurring of its own accord, due to the lowered threshold of stimulation inherently present in it, and predisposed to occur by other causes such as exposure to cold, emotion, a worried and upset mind, constipation, etc., leading to lowered pituitrin secretion and thereby a lowered activity of the neurosecretory nuclei of the anterior hypothalamus, leading also to lowered secretion of anterior pituitary hormones temporarily in the initial stages of the ailment, and if untreated, leading to a permanent underactivity of the neurosecretory nuclei, with defective functioning of both anterior and posterior lobes of the pituitary, in the later stages, with consequent lowering of their secretions, leading to permanent defects like obesity, sexual infantilism, narcolepsy, diabetes insipidus, idiopathic epilepsy, etc. *Narcolepsy* is an occasional accompaniment of the adolescent or adult type of the Frolich's syndrome and diabetes insipidus, a common one.

3. *Narcolepsy* is the term applied to a disturbance in the sleep mechanism, in which sudden attacks of an irresistible desire for sleep occur during the day time. The duration of the attacks, which resembles normal sleep, is quite brief, from a few

seconds to about twenty minutes. It is only to such sudden and brief naps and not to persistent drowsiness or to prolonged periods of pathological sleep that the term is applicable. Nocturnal sleep may be normal but is often disturbed or there may be insomnia. Sleep may overcome the subject of narcolepsy, while he is going about his usual occupation, while walking, during conversation, during a meal, driving a car, etc. There may be many attacks during the day. The condition may be a sequel to influenza or to epidemic encephalitis, involving the hypothalamus leading to over-stimulation of the anterior hypothalamic nuclei, leading to a depression of the walking centre in the posterior hypothalamus thereby causing sleep or may result from a tumour or injury in this region. In other instances, the condition appears without known cause (idiopathic narcolepsy). Though evidence is not conclusive, it is very likely that in these latter also, a disordered hypothalamic function is responsible, for other features e.g., obesity, polyuria, or impairment of the sexual functions, point to an abnormality of this region. Ephedrine sulphate (25 mg. *t.d.s.*) or benzedrine sulphate, is used with benefit, in idiopathic narcolepsy.

4. *Cataplexy* is the term given to a condition allied to and frequently associated with narcolepsy, in which the patient, as a result of some emotion—amusement, anger, fear, embarrassment or surprise—is seized with complete helplessness. The attack is brief, lasting for a few seconds or for a minute or two, at the most. Consciousness is not lost, but the muscles are completely devoid of tone and power for the time being, and if the attack supervenes while the subject is standing, his knees fail him and he sinks to the ground. The symptoms mentioned above are exactly similar to those which occur in myasthenia gravis, in which condition also, a person, who to all appearance is normal, suddenly becomes seized with a condition, in which the muscles are completely toneless and powerless, especially the muscles of the face, tongue and deglutition, though other muscles of the extremities and the rest of the body too are involved to a greater or less degree and emotion of any kind easily precipitates its occurrence. There is no abnormality of the neuro-muscular system, shown by clinical examination and no pathological lesion of the brain, muscles, or nerves has been found on *post mortem* examination. Other symptoms which occur in myasthenia gravis, are those pointing to sympathetic stimulation, and in most of the cases enlarged thymus is also found. So it is well to examine the chest in such cases by radiography, to rule out the presence of thymus in cataplexy, as well as myasthenia. The deep reflexes are lost. Cataplexy is regarded as just an exaggeration of a tendency even in normal people who may become weak with laughter, be struck "all of a heap" or transfixed, when surprised or shocked or the jaw may drop when confronted with some

unexpected occurrence. Mirth is especially liable to precipitate a cataplectic attack. Though narcolepsy occurs without cataplexy, the converse is extremely rare. This association of the two conditions at once suggests a common pathogenesis, but the muscular atonicity characterizing the cataplectic attack, cannot be explained upon any physiological basis. The cataplectic attack might most probably be due to defective functioning of the chemical changes occurring during normal neuro-muscular activity, i.e., due to a rapid destruction of the acetyl-choline formed at the muscle end plates during nervous stimulation, by the enzyme choline-esterase, and as such an anticholine esterase drug like prostigmin, given continually for some time by oral or oral and parenteral therapy combined, might serve to stabilize the neuromuscular activity and prevent cataplectic attacks.

5. *Idiopathic epilepsy*:—Either petit mal alone or combined with generalized grand mal is most probably due to a primary focus of discharge arising in the posterior hypothalamic group of nuclei in the diencephalic region, and spreading to the thalamic reticular system, initially involving only loss of consciousness and later spreading to the prefrontal areas of the cerebral cortex through the dorso-medial nucleus of the thalamus. Both cerebral hemispheres are involved and if the primary focus of discharge in the hypothalamus is of high intensity, the corpus striatum is also involved by spread from the thalamus as well as the cingulate gyrus, and the premotor area of the cerebral cortex is affected, producing sudden flexion or extension of both lower extremities, resulting in the person, who was walking at the time of occurrence, falling down, and later area of 4 or primary motor area is affected by spread from the premotor area by facilitation and convulsions of various parts of the body occur one after another, in quick succession or simultaneously till the discharge from the hypothalamic nuclei becomes normal again. The evidence for the discharge primarily occurring in the posterior hypothalamic region is the presence of visceral auræ or some special senses auræ, present just before the attack as it controls visceral sensation through the prefrontal areas and reactions to special senses stimuli through its nervous connections and signs and symptoms of tachycardia, dilatation of pupil, predisposition to attacks, when there is constipation, etc. Also the maximum voltage of discharge occurs in the midfrontal areas, of both cerebral hemispheres which are involved along with the prefrontal areas initially and then the rest of the frontal, parietal and occipital lobes. The fact that the thalamic reticular system is the primary centre of consciousness and stimulation there produces unconsciousness by means of electrodes implanted in it has also been proved by experimental evidence in animals and also during operation in human beings. That the thalamic reticular system is closely connected with hypothalamus as well as dorsomedial

nucleus of the thalamus, which is connected with the prefrontal and midfrontal areas by means of the thalamo-cortical connections, is clear from a study of the nervous pathways and tracts of connection in the C.N.S. Anything which alters the excitability of the dorso-medial nucleus of the thalamus is bound to produce cerebral dysrhythmia, by altering the normal activity of the brain. The constantly present posterior hypothalamic nuclear hyper-excitability present in these individuals, leads to a suppression of activity of the neuro-secretory cells of the anterior hypothalamic nuclei, (supra-optic, paraventricular and tuber-cinereum), which leads to lowered secretion of pituitrin, the hormone of the posterior lobe of the pituitary, as also the hormones of the anterior pituitary including sex-hormones the secretion of which is lowered on account of the defective secretion of the hypothalamic nuclei into the hypothalamico-hypophyseal portal system of vessels. The lowered secretion of pituitrin is responsible for the symptoms of polyuria and to this ailment due to lack of the anti-diuretic factor, as also impaired sexual development due to deficiency of sex hormones present in some and obesity in others, due to disturbance of fat metabolism following anterior pituitary hormonal deficiency. In view of the strong possibility of the primary focus of origin in the condition being in the hyper-excitabile posterior hypothalamic group of nuclei, containing sympathetic higher centres, with resultant diminished activity of the neuro-secretory nuclei of the anterior hypothalamus and the consequent diminished secretion of both posterior pituitary as well as certain hormones of the anterior pituitary, it is reasonable to administer to the patient in addition to the sympatholytic drugs like ergotamine or parasympathetico-mimetic drugs like prostigmin for tackling the primary root cause i.e., the posterior hypothalamic excitatory state, hormones of the posterior pituitary, pituitrin and an extract of the anterior pituitary like antuitrin or sex hormones of the ovary like oestrin or ovocyclin and testis hormones like testosterone to females and males respectively and also vitamin E, which has a correcting action on diencephalo-hypophyseal dysfunction. It is also worth while trying anti-allergic drugs also, in cases where allergy to certain types of stimuli is believed to play an important part in producing seizures in addition to the combined therapy above mentioned.

6. *Laurence-Biedl-Moon syndrome* which is a condition hitherto attributed to pituitary deficiency, is now believed to be due to involvement of the hypothalamus. The chief features are: obesity, sexual infantilism, retinitis pigmentosa, polydactylism, mental deficiency and also a familial tendency which is present also in at least 50% of cases of epilepsy. Prostigmin, Vitamin E, as well as anterior pituitary hormonal therapy by

both posterior and anterior pituitary hormones including sex hormones, might do good in this condition.

7. *Dercum's disease* (*Adiposis dolorosa*):—This usually occurs in women, after menopause. Painful, fatty, subcutaneous masses appear, especially in the arms and thighs, and there is general weakness and mental deterioration. Sugar tolerance is usually increased. The B.M.R. is low. An X-ray film of the skull may reveal alterations in pituitary fossa and visual disturbances may occur. The temperature is usually subnormal. It is alleged to be due to deficiency of the pars nervosa in adults, an essential pre-disposing cause of which may also be the lowered activity of the neuro-secretory nuclei of the anterior hypothalamus with resulting lowered production of pituitrin and anterior pituitary hormonal secretions. Hence, pituitrin, as well as prostigmin and Vitamin E might do good in these cases by restoring the normal activity of the hypothalamic nuclei.

Conclusions.—It is clear from the anatomy and physiology of the hypothalamo-hypophyseal region, and the diseases caused by dysfunction of the same, that the hypothalamus and hypophysis are synergistic in their action in both normal and abnormal functioning of the area. Except in cases of tumours arising primarily from the anterior lobe of the pituitary as such, either eosinophil or basophil or chromophobe adenomas, causing acromegaly or initial excessive and later lessened development and activity of the sex organs, with premature appearance of secondary sex characters, or signs of hypopituitarism, such as dwarfism, sexual infantilism, polyuria, and obesity, etc. respectively, according to the type of neoplasm, the rest of the diseases manifest in a few cases only, signs of hyperpituitarism initially, being due to tumours arising from the tuber-cinereum or supra-optic nuclei of the hypothalamus, which later proceed to hypopituitarism and in the rest, constituting the vast majority of cases, with signs and symptoms of hypopituitarism from the beginning, due to lesions of the anterior hypothalamic area, in front of the mammillary body, involving the tuber-cinereum, paraventricular, and supra-optic nuclei, leading to defective production of posterior pituitary hormones alone, causing diabetes insipidus, or both posterior and anterior pituitary hormones, causing narcolepsy, narcolepsy associated with D.L. Frolich's adiposo-genital syndrome either alone or combined with diabetes insipidus commonly or narcolepsy or both, and Laurence-Biedl-Moon-syndrome, etc. The above diseases may be caused by tumours arising in the diencephalic region of the brain and third ventricle, pressing on the tuber-cinereum and the adjacent nuclei of the hypothalamus, causing their defective function and atrophy or to a congenitally existing maldevelopment of the hypothalamus and the hypophysis either singly or together. The above

diseases also manifest signs of overactivity of the parasympathetic system mainly in cases of encephalitis, early in the attack, or tumours pressing on the tuber-cinereum region in the initial stages such as hyperchlorhydria, spastic constipation, bradycardia, signs and symptoms of tremor, etc., such as occur in Parkinson's disease or paralysis agitans, neurogenic bronchial asthma having vagotonia as the primary basic cause, or signs of deficient activity of the parasympathetic as hypochlorhydria, atonic constipation, tachycardia, etc. Lesions or suppressed activity of the anterior hypothalamic nuclei following the primary posterior hypothalamic nuclear hyperexcitability, present in certain individuals, (the most important cause of which may be sex-linked recessive inheritance), which consequently leads to lowered secretion of both posterior and anterior pituitary hormones, which in turn leads to still further suppression of the neuro-secretory nuclei of the hypothalamus, and the continuance of the abnormal state, unless corrected by proper combined therapy tackling nervous as well as endocrine dysfunction, also manifest either signs of sympathetic overactivity such as essential hypertension, tachycardia, diseases due to peripheral vascular spasm, such as thrombo-angiitis obliterans, Raynaud's disease, idiopathic epilepsy, emotional instability, migraine and rarely signs of deficient activity of the sympathetic in the vascular system alone, as low blood pressure, lasting for a short while, due to stimulation of the anterior part of the cingulate-gyrus, following hypothalamic overactivity, which occurs commonly during an attack of petit mal alone or combined with grand mal.

As idiopathic epilepsy usually manifests signs and symptoms of sympathetic hyper-excitability, similar to what occurs in exophthalmic goitre or Grave's disease or primary thyrotoxicosis, and symptoms of polyuria and polydipsia similar to diabetes insipidus also occur in some cases, in both conditions and a persistent enlarged thymus has been found constantly both in exophthalmic goitre, as well as myasthenia gravis, a condition allied to cataplexy, it stands to reason that the presence or otherwise of a persistent thymus is verified in all cases of idiopathic epilepsy, cataplexy, exophthalmic goitre, and diabetes insipidus by X-ray of the chest and if present, suitable measures be taken to remedy the same by deep X-ray therapy. Normally the thymus continues to enlarge and reaches its greatest dimensions about the age of two years and then gradually wastes, so that by puberty it is represented by a mass of fatty tissue. Its presence and still more its enlargement is indicated by fullness of the root of the neck, dullness over the sternum and perhaps by evidences of mediastinal pressure on the large veins and by increasing dyspnoea. A skiagram is always necessary for the ultimate diagnosis which is then often conclusive. The thymus

is also enlarged in some cases of Addison's disease, acromegaly, eunuchoidism and status thymo-lymphaticus, in which condition, sudden death occurs after some slight injury or infection in young persons in whom general swelling of the lymphoid structures is also often found. It seems possible that regression of the thymus at puberty is due to the internal secretion formed by the gonads, as is evident from the persistence of the thymus without undergoing its customary involution after castration in young animals. The possibility of incomplete differentiation of the sex glands being responsible for the non-involution of the thymus, gonodotropic and sex hormone therapy might be of definite value in diseases where its persistence commonly occurs. It is necessary to examine in all cases, manifesting symptoms of neuro-endocrine dysfunction, the specific gravity of the urine which is markedly reduced in diabetes insipidus to 1001 to 1005, as also the total output of urine per day, markedly increased to about 10 to 40 litres per day, and the same must be true of other diseases manifesting the signs and symptoms of diabetes insipidus.

So in any of the diseases manifesting symptoms due to the neuro-endocrine dysfunction above noted, pituitary hormonal therapy by means of pituitrin and sex hormones or anterior pituitary extract, Vitamin E administration which has a corrective action in hypothalamic-hypophyseal dysfunction, and anti-allergic therapy in cases which manifest symptoms of allergy, in addition to the primary basic therapy of correction of the imbalance of the autonomic nervous system and its higher centres by proper therapy according to the nature of the condition, would be the ideal method of treatment.

#### ADRENALIN OVERDOSAGE: PREVENTION, THERAPY

Freedman, Camberwell Hospitals, London, reports that overdosage with adrenalin may cause death within minutes. A 4-mg. dose given subcutaneously may be fatal; 8 mg. is probably the largest tolerated dose.

Usually, accidental adrenalin overdosage can be prevented by 4 simple precautions: (1) Concentration of adrenalin solutions for spray inhalation should be as low as compatible with therapeutic effect and should never exceed 4 mg. per cubic centimeter (0.4%). (2) Standard, commercially prepared, stable local anæsthetic-adrenalin mixtures should be used whenever possible to eliminate errors in compounding mixtures. (3) Metric units should be used in prescription to eliminate the danger of confusion between minims and centimetres. (4) Doctors and nurses must read the label on every container before using the contents.

Piperoxan should be injected as soon as possible after an overdose of adrenalin. For an adult, 15 mg. of piperoxan should be given intravenously; if 20 mg. or more of adrenalin has been given, 30 mg. is recommended. Speed is essential. Piperoxan produces few side effects; since duration of action is brief, prolonged hypotension does not occur.—(*Lancet*, 269: 575-578, 1955, via *Mod. Med.*, 1-8-'56).

# MODERN VIEWPOINTS ON THE MANAGEMENT OF PLACENTA PRÆVIA.

The cases of placenta prævia in the Vienna Frauenklinik from 1935 through 1955 are reviewed. Over-all figures, comparing the decades 1935 to 1944, and 1945 to 1954 are outlined in the following table:

|                                              | 1935 to 1944     | 1945 to 1954    |
|----------------------------------------------|------------------|-----------------|
| Number of births                             | 34,829           | 18,704          |
| Number of cases of placenta prævia           | 178              | 100             |
| Frequency of placenta prævia                 | 0.51%            | 0.53%           |
| Maternal mortality                           | 4.5% (8)         | 4.0% (4)        |
| Total foetal mortality                       | 57% (104 of 183) | 38% (39 of 103) |
| Intra-uterine foetal death                   | 7% (13 of 183)   | 9% (9 of 103)   |
| Intrapartum and postpartum foetal mortality  | 54% (91 of 170)  | 32% (30 of 94)  |
| Corrected foetal mortality (above 2,000 gm.) | 36% (43 of 118)  | 16% (12 of 75)  |

Methods of management are outlined as follows:

|                                 | No. of cases | No. of living fetuses at beginning of labour | Fro- quency (per cent) | Foetal loss (abso- lute) | Morta- lity (per cent) |
|---------------------------------|--------------|----------------------------------------------|------------------------|--------------------------|------------------------|
| 1935 to 1944 { Cesarean section | 49           | 50 (44)                                      | 29                     | 8 (2)                    | 16 (5)                 |
| { Spontaneous delivery          | 41           | 39 (32)                                      | 23                     | 14 (8)                   | 36 (25)                |
| { Operative vaginal delivery    | 88           | 81 (42)                                      | 48                     | 69 (33)                  | 84 (79)                |
| 1945 to 1954 { Cesarean section | 38           | 170 (118)                                    | 38                     | 91 (43)                  | 54 (36)                |
| { Spontaneous delivery          | 38           | 36 (35)                                      | 38                     | 3 (2)                    | 8 (8)                  |
| { Operative vaginal delivery    | 24           | 36 (31)                                      | 38                     | 7 (3)                    | 19 (10)                |
| 1935 to 1954 { Cesarean section | 100          | 22 (9)                                       | 24                     | 20 (7)                   | 91 (78)                |
| { Spontaneous delivery          | 24           | 94 (75)                                      | 30 (12)                | 32 (16)                  | 48 (28)                |
| { Operative vaginal delivery    | 278          | 264 (193)                                    | 121 (55)               | 48 (28)                  |                        |

In the first decade studied, 4 of the 8 maternal deaths were from blood loss and 4 from infection; in the second decade 4 deaths were caused by hæmorrhage. To obviate the maternal deaths, early diagnosis and an adequate blood bank are essential. The more central the placenta, the more danger is there for the mother. For better results, hospitalization should be advised early and cesarean section utilized more frequently.

Hospitalization and section increase the foetal survival also. The use of operative vaginal methods, such as the Braxton-Hicks version, extra-amniotic and intra-amniotic metreuryesis, and vaginal cesarean section, are indicated only when the foetus has succumbed. Spontaneous delivery or cesarean section is preferable otherwise.—(H. Tulzer, *Geburtsh. and Frauenh.*, 1955, 15: 610, via *Internat. Abstracts of Surgery*).

OTITIS MEDIA DURING INFANCY is most often caused by pneumococci or *Haemophilus influenzae*. Aspiration of middle-ear contents was done for 104 infants less than 2 years old. Beta hæmolytic streptococci were seldom isolated, and staphylococci were not found. The exudates were sterile in more than one-third of the patients. Mortimer, Jr., and Watterson, Jr., of Cleveland City Hospital and Western Reserve University, Cleveland, believe that antibiotics that are primarily effective against gram-positive pathogens are not adequate for otitis media in infants.—(*Modern Medicine*, August 1, 1956).

## FAMILY PLANNING\*

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OVER-POPULATION is becoming an increasingly grave and vital problem in India and is seriously interfering with the progress of the Five Year plans. Our standard of living is very low as compared with that of other nations of the world and the phenomenal increase in population is largely responsible for this state of affairs.

India records 1620 births and 1100 deaths every hour and so with each striking hour of the clock, 520 new mouths require to be fed; and during this same short period death snatches away 32 mothers and 304 infants. Imagine the tremendous mental shock to over 26,000 of families within 24 hours, and the resultant vast economic loss to India; out of a population of 35 crores and 69 lakhs only about 10 crores and 18 lakhs are self-supporting. Over 20% of these i.e., 2 crores and 3½ lakhs of workers absent themselves every day from work for various reasons.

Illiteracy amongst 84% of the population, the huge number of disabled persons including lepers, beggars, the dumb, deaf and blind and the aged and enfeebled are other liabilities. Besides un-employment, blind superstitions and fallacious dogmas exercise a strong hold over the masses.

Nature exerts a wholesome check on the population destroying the unfit in the eternal struggle for existence. The various schemes for health promotion, industrial welfare, agricultural and educational progress have no doubt been exerting their beneficial influence to some extent; still, family-planning is a necessity as that alone will offer an effective solution to the problem. Therefore, it finds a prominent place in our Second Five Year Plan.

Family planning does not simply mean birth-control but includes sex education also, whereby the married couple are enabled to derive the maximum benefit and pleasures from married life; it does not favour over-indulgence. On the other hand, it will afford ample opportunities to the couple to understand each other's needs and promptly solve sex difficulties which would otherwise become sex-disorders. It has been rightly remarked by the well-known sexologist, the late Dr. A. P. Pillay that the patients suffer from sex difficulties more than from sex-disorders. This statement is effectively supported by the fundamental law that ignorance breeds difficulties, difficulties foment disorders and disorders mar the very charm of life. Suitable sex-education is therefore, essential to every one of whatever sex, age or creed; it will help in preventing delinquency in children.

\* Specially contributed to the ANTISEPTIC

During married life, it is idle to expect long periods of continence in the average couple. Even occasional sex unions may result in a new life. Through sex education, and family planning, by spacing and limiting the number of children, the economic and social status of the family which is the basic unit, will be greatly increased. The children thus spaced could be better looked after and would also have better chances of success in life. The mothers would be spared the strain and stress of unwanted and frequent pregnancies. Married life would then be far more pleasure-giving, intimate and harmonious.

Family planning would also afford sex pleasures, even to those who would otherwise have been barred from procreating, for reasons of health (e.g. venereal and mental diseases) poor economy and low intelligence quotient. This will reduce the incidence not only of sex but also other crimes.

Greater vitality and better powers of resistance in the people will result from proper family-planning.

Adequate and proper propaganda along right lines on family-planning and control methods must form part of the educational set-up and should be given by means of films, popular lectures, leaflets, charts etc.

Amongst the various contraceptives—both natural and artificial—the safe period, coitus interruptus, diaphragm, pessary, jelly, creams, sheaths etc. are in common use. But unless the principles underlying their proper use are understood even the best among them would often fail. Surgical operations like vasectomy in the male and ovary removal in women would actually terminate fertility. Sponsors of the value of continence should realize that human nature being what it is, abstinence and sublimation of the sex-instinct are easy to preach but very difficult to practise.

There has, in recent years, been a keen awakening to the need for family planning among the people as evidenced by the fact that the response to a questionnaire, (*Jyothi* of Bombay, 4-4-1954) elicited popular opinion: (1) For family planning 87% and against 13%; (2) for sex education 76.1% against 23.9% and (3) for opening family planning clinics 85.2% and against 14.8%.

Some people have blamed contraceptives to be the cause of fertility and neurasthenia in women particularly. The charge is not really tenable.

It is perhaps fair and proper to place the following facts before the people:

1. The safe period theory has been exploded by Dr. Stieglitz of Berlin, as valueless, it has its own value under

normal circumstances; (2) the combined use of diaphragm and jelly or cream is the best method of birth-control; (3) where the wife is not co-operating the use of the sheath is to be recommended; (4) for poor persons who cannot afford to purchase the above, the use of a cotton pad or sponge with an oil or lotion of common salt or vinegar (one teaspoonful to three *paos* of water) offers a wise and practical solution; (5) resort to surgical methods without undue haste is the ideal method when performed under controlled conditions and in suitable cases; (6) the use of contraceptives should be undertaken under expert advice; (7) it must be remembered that the use of contraceptives is not meant to encourage sexual indulgence or promiscuity, which have their own serious undesirable effects. It is indeed a national crime; (8) family-planning clinics and the supply of relevant literature on the subject should be encouraged; (9) carelessness and negligence in the use of contraceptives are often responsible for the failures, that are sometimes reported; (10) it is the desire to have a son and heir, that often deters people from using contraceptives; but there can be no excuse for not resorting to them by persons who have three children, one or more of them being males.

The promiscuous and unwarranted use of all and sundry contraceptives may cause damage and hence their use must be deprecated.

Family-planning is a multipurpose social scheme of the first order, designed to prevent the calamities of over-population, ignorance and poverty. It will enable every individual and every family to have self-sufficiency, better energy and working power.

While going ahead with schemes of family-planning it is important to remember that sex is the vital force of life and that death-control by preventive and curative medicine, without adequate attention to birth-control can never succeed in the promotion of human welfare and happiness. It is the sacred duty therefore, of every citizen to understand, encourage and practice family-planning not only for his own sake but also to avert national suicide.

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BACTERÆMIA DUE TO GRAM-NEGATIVE BACILLI is usually successfully treated by the administration of streptomycin and a tetracycline compound. However, polymyxin B is preferred for infection with *Pseudomonas aeruginosa*. Spittel, Jr., Martin, and Nichols, of the Mayo Clinic and Foundation, Rochester, Minn., report that *Escherichia coli* and *Aerobacter aerogenes* are the usual infective organisms of the gram-negative group: infection usually originates in the genitourinary or gastrointestinal tract.—(*Ann. Int. Med.*, 44: 302-315, 1956, via *Modern Medicine*, August 1, 1956).

## MEDICAL TREATMENT OF MENIERE'S DISEASE

H. L. Williams suggests that persons with Meniere's disease belong to a group of patients with some inherited constitutional deficiency, a group displaying such disorders as Raynaud's disease, allergic conditions and acrocyanosis. A preferred stress or stimulus results in an abnormal reaction of the peripheral vascular bed. The hypothesis is presented that, as a result of extreme slowing of the blood stream, anoxia occurs. Vascular damage is then caused and sludging of the blood cells takes place. In addition, toxic metabolites such as histamine are released, and the collection of extracellular fluids of high protein content occurs. When this train of events occurs in the arterioles and capillaries of the *striae vasculares* of the labyrinth, a state of endolymphatic hypertension is induced, and this, in turn, may lead to the changes reported by Hallpike and Cairns. The treatment of Meniere's disease can be logically divided into that of the acute attack and that of the underlying condition. In controlling the acute attack, those drugs stimulating the adrenergic nerves or paralyzing the cholinergic nerves are successful. Atropine, one-seventy-fifth of a grain, given by the subcutaneous route will usually be effective in terminating the crisis in fifteen to thirty minutes. Epinephrine is also helpful if given as five to 10 minims of a 1 in 1000 solution, injected slowly into a vein. If taken early, ephedrine, one and a half grains, or amphetamine, five to 10 milligrammes by mouth, has also been useful. Dimenhydrinate, 250 milligrammes in five cc. of solution, for injection into a muscle, or in 15 millilitres of isotonic saline for injection into a vein, has been found to be effective in the relief of the acute attack. For control of the underlying condition, vasodilators are effective. Papaverine, four and a half to 12 or 18 grains daily by mouth, may be useful. Nicotinic acid, 100 milligrammes by mouth, or in larger dosage until an effective flush has been produced, has also been found useful. The full dosage may be taken once daily before breakfast and should be continued for from four to six weeks after the symptoms subside. Histamine also has been used as a vasodilator, being administered by the intravenous route as 2.75 milligrammes of histamine phosphate in 250 millilitres of isotonic saline, at a rate of 16 to 60 drops a minute. The rate of administration should be such that the patient has no headache and no discomfort whatsoever. The injection may be given daily for as long as may be necessary. The stomach should be protected with food and by antacids. Although there has been some diversity of conclusions as to the effect of the level of sodium in the body fluids, restriction of salt intake and the administration of ammonium chloride, six to nine grammes daily, in divided doses, are recommended. Thyroid extract and oestrogen may be helpful in some patients, and sedatives may be useful to control the tension of anxiety.—(*Arch. Otolaryng.*, Dec. 1955, via *Med. Journal of Australia*).

## PROGNOSIS FOR FOREIGN-BODY BRONCHIECTASIS

Coolley, Gushberg, Olsen, and Kirklin, of the Mayo Clinic and Foundation, report that prognosis after surgical resection for foreign body bronchiectasis is better than after operation for the primary form of disease.

Results were excellent in all of 14 patients operated upon for foreign-body bronchiectasis. Treatment consisted of pneumonectomy in 5 patients, unilobar resection in 8, and unilateral multilobar resection in 1. Empyema developed after operation in 5 patients. Postoperative atelectasis did not occur. In contrast, results were excellent in only 75% of 221 patients who were operated upon for primary bronchiectasis; postoperative atelectasis occurred in 25.8% of this group.—(*J. Thorac. Surg.*, 31: 1956 via *Med. Med.*, 1-8-1956).

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## ARTIFICIAL INSEMINATION

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AN attempt is made in this article to discuss the question of Artificial Insemination, particularly in India, which has many creeds and castes.

In our Indian society in which there are many persons having orthodox views in spite of the boasted civilization of the twentieth century, the following suggestions regarding the place of artificial insemination, will be helpful.

When is artificial insemination necessary?—1. When there is no issue after a married life of five or more years and the husband's semen is tested and found to be incapable of impregnation, while the wife is found to be fertile.

2. In some cases, where the husband is suffering from one or more hereditary diseases like diabetes mellitus, hysteria, leprosy, leucoderma, mental diseases etc., and divorce is not possible, artificial insemination is advisable in order to have healthy children.

3. Some women remain unmarried for a whole life so that they can avoid the responsibilities of married life and devote their time to social work. Such ladies may show a natural desire for motherhood and in that case the help of artificial insemination may be made available. In these cases of motherhood of unmarried ladies, society will stoutly oppose the proposal and the inherent dislike for artificial insemination from the people, will have to be faced.

4. There may also be cases in which during a married-life of ten to twelve years, one or two children may have been born, but unfortunately both die and the husband ceases to be able to impregnate due to disease or accident while the wife is capable of reproducing. In such circumstances artificial insemination for progeny is not out of place.

5. In our present civilization, there can be no bar to the re-marriage of widows; yet in some of the Hindu castes, widows who are still in the prime of their youth, are not allowed to re-marry. If artificial insemination is legalized, such widows who have no children might take advantage of this process.

Dangers of artificial insemination.—In blood transfusion procedures if the wrong type of blood is used, the receptor dies; such is not the case with artificial insemination. However 50% development of the child depends on the semen. Hence great care is necessary regarding the selection of the donor of semen. The blood of all the persons of the world can be divided into

only four different groups *viz.*, A, B, AB and O, while semen may be as of many types and varieties as there are men in this world. Of course, there is no difference in the appearance of the semen in different men, but it is capable of imparting different inherent qualities in the offspring. Hence it is important to ensure that the semen donors are not suffering from infectious diseases like gonorrhœa or syphilis, besides the disease mentioned in para 2 *supra*. Otherwise, they may be born with defects and fall an easy prey to such diseases.

In India there are many castes and creeds, hence it is imperative to ensure that the creeds of the donor and the receptor are the same, so as not to offend the sentiment and religious principles of the prospective receptors. If necessary care in this regard is not taken, there is the potential danger of reproducing hybrids as described in the *Geeta*.

Psychologically, if the semen donor is one who is given to criminal acts like stealing, robbing or even murdering, there is danger of transference of those horrible vices, to the child. Hence the semen of such donors is thoroughly unsuited for artificial insemination.

It is of the utmost importance that complete secrecy should be maintained regarding the name and identity of the semen donor. Under no circumstances should the donor and the receptor get to know each other. If such complete secrecy regarding the name of the semen donor is observed by law, the following questions are apt to arise *viz.*, (1) If boys and girls born to different women as a result of artificial insemination by a single donor, fall in love with each other and marry, can such marriages be called inter-family marriages? (2) Is there any possibility of the woman's love for her husband being transferred to the semen donor? (3) Is there any danger of creating jealousy in the husband towards the offspring born as a result of artificial insemination?

Artificial insemination and the law. Artificial insemination has been successful in animals because animals have nothing to fear like religion and creed etc. In humans, however, caste, creed, religion, heritage, etc. have all to be considered when artificial insemination is sought to be employed. Artificial insemination is not an act of debauchery and should bestow all legal rights to the child born of such procedure. Complete secrecy regarding the semen donor should be enforced by law.

Government centres for artificial insemination. At present only a very few cases are on record in Government Hospitals, in which the benefit of artificial insemination has been availed of. So far as I know, there are no special departments for artificial insemination in Government Hospitals in India. There is therefore, the need for special departments for artificial

insemination like that of blood transfusion, so that the semen donors and the receptors after thorough examination in the other departments can be directed to the department of artificial insemination. Just as blood donors are paid for donating their blood, semen donors also should be remunerated for donating their semen. Besides, there should be 'Semen banks.'

When it was announced for the first time 20 years ago that women can give birth to living children by means of artificial insemination, many persons in India were greatly astonished and even laughed at the very idea of artificial insemination. Though at present there is much awakening in society, much mass-education should be done, if artificial insemination is to be taken advantage of at all by those who need it without any difficulty or hesitation.

## THE SKIN DURING SENESCENCE

T. V. VENKATESAN, M.B., B.S., F.C.C.P., F.A.I.M., F.D.S.,  
185, New Street, Madurai

*"The moving finger having writ, moves on."*

THE aging process in skin occurs quicker due to exposure to vicissitudes of weather, the sun and the wind. Thus in a young person the so-called aging process may take place producing the sailor's skin.

The aging skin is dry, shiny and wrinkled and has a sallow appearance. Pinching shows the flaccidity and folds. The exposed areas may show increase in pigmentation. There is loss and also graying of hairs.

The histopathology of the skin.—*Epidermis*:—(1) The stratum corneum is thinner; (2) the stratum granulosum loses its layer of cells; (3) the basal layer becomes flatter; (4) the rete-malphi loses its honey-combed appearance; and (5) there is increase of pigment in the lower layers of the epidermis.

*Dermis*:—(1) Flattening of the papilla; (2) sub-papillary collagen fibres tend to degenerate and there is cloudiness in the fibrils and the ground substance and the extra-cellular spaces; (3) there is thickening of the blood vessels, and (4) there is a decrease in the number of glomus units.

*Hair*: The hair becomes grey to white due to loss of pigment in and around the cortical cells.

Physiology of the aging skin.—There is diminished circulation which produces a response even to a slight degree of chilling. Similarly excess of heat is less easily dissipated and so heat prostration is more common in old people. There is reduction of oxygen consumption and carbon dioxide diffusion. The hair becomes more coarse.

Biochemistry of aging skin.—(1) *Water*:—There is an increase in water content, though the skin is apparently dry; and there is a decrease in water loss.

(2) *Electrolytes*:—There is an increase of calcium, magnesium, potassium and sodium. The aging skin more often exhibits protein and vitamin deficiencies.

Common skin diseases during senescence.—(1) *Pruritus*:—This commonly affects the extremities but may also affect the whole body. The condition is probably due to senile atrophy. The external application of Lanoline is the best remedy. Internally serpasil is a good sedative to relieve itching. (2) *Pruritus vulvae*:—This produces extreme discomfort and the best remedy is to apply hydrocortisone ointment or fludro-cortone ointment. (3) It occurs because of a diminution in the connective tissue supporting small blood vessels. Ecchymosis in the skin and purpuric rashes. (4) *Lentigo senilis* are smooth brownish areas of pigmentation which occur on the skin. (5) *Seborrhoeic keratoses*:—raised yellowish brown scaly lesions occur on exposed parts. (6) *Senile ectasia* are tamarind-seed-sized bright red papules produced by a group of dilated arterioles in the upper dermis. (7) *Keratoses senilis* occur on the hands and face, which may lead to cutaneous horns. (8) *Cutaneous tags* are pedunculated soft growths over the neck and thorax. (9) *Malignant diseases*:—Epithelioma is more common over the senile skin. (10) *A lemon yellow degeneration* of the skin due to colloidal degeneration occurs in senile skin. (11) *Lipoid infiltrations* may occur producing xanthelasma. (12) *Leukoplakia* is a precancerous lesion occurring on the mucous membrane of the mouth. (13) *Kraurosis vulvae* is an atrophy of the vulva. (14) *Exfoliative dermatitis* is more common over the senile skin. (15) *Nutritional eczema* is more common in the aged.

Thus the aging skin is a condition which would need special study and attention. It is imperative that frequent bathing is to be avoided to prevent excessive drying and scaling. Mild soaps and starch solutions are helpful.

After bath an emollient application is a *sine qua non*.

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2. G. C. Wells.—Senile Changes in the Skin.

**INCIDENCE OF CHOLELITHIASIS** varies with race, sex, and age. The white race is apparently about 4 times as susceptible as the Negro race. Joseph A. Cunningham and Eirmon E. Hardenberge of the University of Alabama, Birmingham, find that incidence of the disease is highest—about 12 to 17%—in white females and lowest—1 to 3%—in Negro males. The frequency is about the same—6 to 10%—in white males and Negro females. Disease occurs more often with advancing age in all groups except Negro males.—(*Arch. Int. Med.* 97: 68-72, 1956 via *Modern Medicine*, August 1, 1956).

## A NEW CLINICAL TEST FOR MALDESCENDED TESTIS

DHRUBA KUMAR SEN, M.B., B.S.,

Junior Visiting Surgeon, Nilratan Sircar Medical College Hospital, Calcutta

"It should not require the peculiar talent of Sherlock Holmes to detect that there is but a solitary testicle in the scrotum," says Hamilton Baily (*Physical Signs in Clinical Surgery*, Baily, 1954). I will add neither does it need such talent to find the testis when it is situated either at the external ring or in the inguinal canal. The fact is that, at these sites the maldescended testis is readily palpable to the careful clinician. It is indeed difficult to find the testis when it is retained within the abdomen above the internal abdominal ring or at any higher level.

In about 80% of cases an inguinal hernia, usually a bubonocoele is present on the side of the maldescended testis and in such cases with a bubonocoele, the new test described below will prove to be of great value in detecting the position of the intra-abdominal testis.

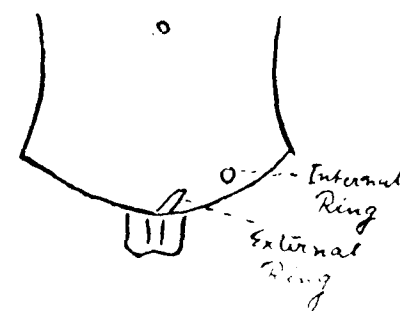


Fig. 1

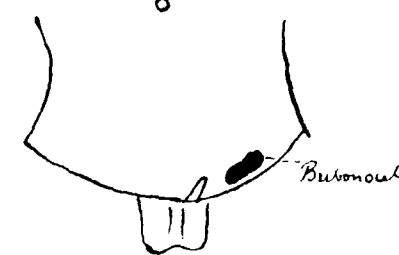


Fig. 2

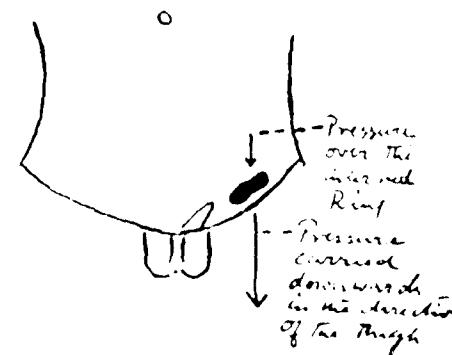


Fig. 3

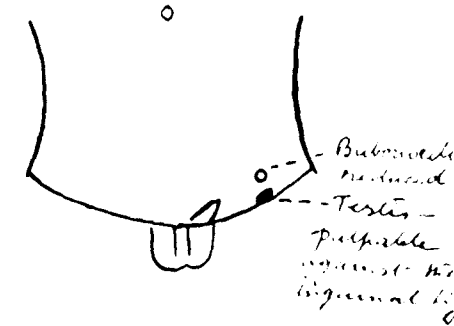


Fig. 4

The test. The patient lies on his back on the examination table. He is made to cough and the impulse on coughing (bubonocoele) is noted. The patient is made to cough again and at the zenith of the cough and when the bubonocoele appears

to be of largest size, press quickly on the internal ring with the index and the middle fingers and stop the bubonocoele from going back into the abdominal cavity. When the testis is situated intra-abdominally at or a little above the internal ring, it comes out through the ring momentarily along with the bubonocoele at the zenith of the cough. By pressing upon the internal ring at that moment both the testis and the bubonocoele are 'dislodged' into the inguinal canal. The examining fingers now displace the whole mass vertically downwards towards the thigh. This manoeuvre causes the bubonocoele to slide back into the abdominal cavity while the testis, when present, is displaced further downwards towards the thigh and against the inguinal ligament. The testis at this situation can be easily felt by the examiner's other hand. When the pressure is released, the testis immediately returns into the abdominal cavity.

This test will be positive *only* when the testis is situated at or a little above the internal ring and in the presence of a bubonocoele on the same side. A negative test indicates a much higher position of the testis inside the abdomen. (Figs. 1 to 4, see previous page).

I have elicited this test on four different patients with success and I would name it as 'Sen's Test.'

#### TREATMENT OF ACUTE SORE THROAT

Chapple, Franklin, Paulett, Tuckman, Woodall, Tomlinson, and Medonald, report that both oral penicillin and sulphamethazine are effective in the treatment of acute sore throat.

Comparable groups of patients with acute pharyngitis were treated with penicillin, sulphamethazine, or a placebo, barium sulphate. Haemolytic streptococci were recovered from throat swabs of 45% of the total of 283 patients; no specific pathogen was found in the remaining instances.

Daily dosage of penicillin was 1,200,000 units for patients 2 to 4 years of age; 1,800,000 units for patients 5 to 9 years of age; and 2,400,000 units for patients over ten years of age. In the sulphamethazine and barium sulphate groups, corresponding dosages were 2, 3, and 4 gm. daily.

Among patients receiving the placebo, 61% were still ill on the third day of treatment. Corresponding rates for those receiving sulphamethazine and penicillin were 38 and 31%, respectively. Streptococcal and non-specific infections were equally well controlled by treatment. Superiority of penicillin over sulphamethazine was greater among patients over 10 years of age than among younger children. Relapses and treatment failures were less frequent among patients given penicillin, and penicillin was more effective than sulphamethazine in eradicating *Streptococcus haemolyticus* from throat swabs. Neither penicillin nor sulphamethazine reduced the incidence of ill-effects in patients under 5 years of age. No adverse effects were observed, and resistant strains of streptococci did not develop. (B. J. Med., 1956: 705-708, 1956 via Mod. Med., 1-8-1956).

#### A CASE OF STATUS EPILEPTICUS

HARIDAS DE,

Late Senior House Physician, Campbell Hospital (Cal.), Ex-Medical Officer, Chatmohan (Pabna), Auxiliary Govt. Hospital, East Pakistan, Medical Officer, Ballarpur Collieries Company Hospital, Saste, P.O. Ballarpur, (M.P.)

EPILEPSY is a toxicopathic condition, characterized by sudden disturbances of cerebral function, which are prone to recur over long periods of time or even throughout life. In the past, epilepsy was a dreaded disease but thanks to the progress in treatment achieved within the past few years, it is now regarded with considerably less fear by patient, doctor and relative alike. The treatment of epilepsy is really one of trial and error—a trial in which the clinician must persist till he finds the drug which suits and benefits the patient most.

Early in July 1956, I was called in to see a Hindu unmarried female aged about 18 years suffering from status-epilepticus.

*Past history of the case:*—The girl was healthy, very clever and most active up to 4 years; no history of epilepsy in her family nor in the family of her maternal uncle. When she was 4 years old she suffered from high fever for about a month. Several quinine injections were given to her and was administered also by mouth by her attending physician for many days. After a month she was cured of the fever. But within a week of shedding the fever, one noon she got her first attack of fits, for which cold water was applied over her scalp and home remedies were given to her. From that date she used to get occasional fits even when she was fast asleep. She was examined by expert physicians who diagnosed it to be a case of 'Epilepsy' and prescribed Peacock's Bromides and Luminal. Since then she used to get fits once or twice a month.

*Present illness:*—Two days before my visit she got the fits very frequently, and in quick succession, without regaining consciousness between the attacks. She did not take a drop of water for 2 days. She passed urine twice only in 48 hours and did not pass any stool for two days. Her heart sounds were very weak, feeble and rapid. The respiration was also hurried. Pupils were widely dilated on both sides. She was almost unconscious. I at once diagnosed it to be a case of status-epilepticus clinically and told her relations about the grave prognosis of the case. I injected at once one ampoule Gardenal sodium 3 gr. (M & B) intramuscularly. For the heart condition I injected one amp. of Coramine (Ciba) and gave her Luminal (Bayer) gr. 1½ mixed with a little water with a help of a spoon with great difficulty. I found her temperature 99.6 F. I gave her a glycerine enema which helped to evacuate a little hard faeces.

I saw her again in the evening and found her no better. She was getting the fits frequently and was still unconscious; I told her relation to see that the patient did not hurt herself during the fits, her clothes were loosened and I showed them how her tongue could be protected by a mouth gag. I asked them to apply cold water to the face and head. I repeated another injection of Gardenal sodium and one amp. of Coramine. I advised another tablet of Luminal gr.  $1\frac{1}{2}$  to be given at night. Next morning when I again went to see her, I found to my great satisfaction that her fits were much reduced as she slept for a couple of hours in the night. She passed urine twice during the night. I injected her another ampoule of Gardenal sodium and injected her glucose solution 25 per cent 25 cc. intravenously and asked the relations to give her milk and glucose water as diet during lucid intervals. Luminal was continued twice daily. After a study of her illness I prescribed Mysoline tablets (I.C.I.) in the morning and in the afternoon, Serpasil tablet (Ciba) at noon and in the evening as her blood-pressure was found high (130 systolic and 80 diastolic) and Luminal tablet gr. iv (Bayer) at bed time. With this *regime* her recovery from status epilepticus was uneventful. For the weakness and anaemia I gave her 6 injections of Macrofolin (Glaxo). She is now regularly taking Mysoline tablets twice, Serpasil tablets twice, Luminal tablet gr.  $1\frac{1}{2}$  at bed time. As a general tonic she is taking Siotrat Liquid (AD). She is quite cheerful now and is getting fits only once in a fortnight. Her mental condition has also greatly improved.

My heartfelt thanks are due to Sri Deshmukh, Manager, Sasti Colliery for kindly according permission to report this case in the ANTISEPTIC.

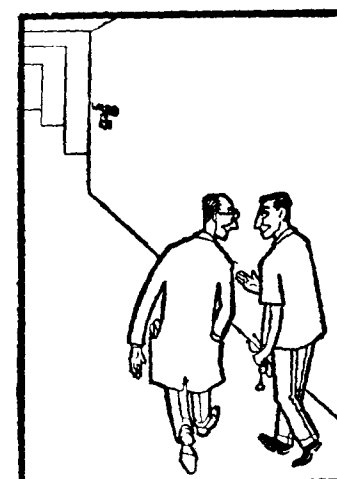
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#### TREATMENT OF PEMPHIGUS VULGARIS WITH ACTH

In 9 cases of pemphigus vulgaris, consistently good results were obtained with an ACTH gel; 8 of the 9 patients were in mortal danger at the time treatment was initiated. All reacted with prolonged remissions, during which no ACTH was required. Although these remissions were generally followed by fresh exacerbations, the latter were on each occasion effectively suppressed by a renewed course of ACTH therapy. The author has now resorted to routine maintenance therapy with small doses. Some of the patients have already been under treatment for  $4\frac{1}{2}$  years without experiencing any difficulty in tolerating this hormone.

As a general rule, treatment was begun with daily doses of 80-160 U.; in all cases, the blisters disappeared within 3 to 4 weeks at the most. The maintenance dosage—injected either daily or 3 times per week—varied between 15 and 80 U. Since no alteration in the doses is usually required, such maintenance therapy can be conducted on an out-patient (J. Amer. Med. Assoc. 160: 1011, 1956).



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# The Antiseptic

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## Editorials

### THE YEAR OF GRACE 1956

#### A Review in Retrospect

WE have just bade good-bye to the Year 1956 which has seen momentous and important world events in every field of human endeavour. The processes of democratization and liberalization were happening in a normal peaceful way without bringing great or grave upheavals in their train. Towards the end of last year, however, certain developments have taken place which have cried halt, only temporarily we hope, to such pioneering forces as were calculated to create an atmosphere favourable to the universal acceptance of "Panch Shila."

Prime Minister NEHRU stated in the Lok Sabha on the 6th of December 1956: "We are going back to a rather intense phase of the cold war. It is a dangerous and bad development. I do not personally think it is going to be a lasting development. Once we go back to the state of cold war, then you always have the hot war round the corner, if something happens. In November last, on one or two occasions we came very near a big war. .... Every word that India says should be weighed and balanced in such a way that it will not make the situation more difficult. It has been India's privilege and policy to help in joining countries, to be a bridge between them and not to break bridges that already exist." His most recent visit to America and England at this juncture, and the full and frank talks he has had with V.I.Ps. there, must result in the restoration of a peaceful atmosphere over the whole world. The joint communique on the Nehru-Ike talks stated:

"The talks confirmed the broad area of agreement between India and the United States which are bound together in strong ties of friendship deriving from their common objectives and their adherence to the highest

principles and policies of the two democracies evolved on the basis of respect for the dignity of man and of the need to improve the welfare of the individual. We are both convinced that the greater understanding of our respective policies reached at these talks will facilitate the constant efforts of India and the United States towards the achievement of peaceful and friendly intercourse among nations in accordance with the principles of the United Nations."

Notwithstanding the threats to peaceful existence and to ordered progress caused by these disquieting factors, India has, thanks to the wise and able stewardship of our NEHRUJI, been able to maintain progress in all directions during the year.

A big and bold advance on all fronts of national development is envisaged in the Second Five-Year Plan, which is designed to cover the period 1956-1961 with a total outlay of nearly 7,000 crores of rupees.

The principal objectives of the plan are:—A sizable increase in national income so as to raise the level of living in the country, rapid industrialization with particular emphasis on basic and heavy industries, a large expansion of employment opportunities and a reduction of inequalities in income and wealth and a more even distribution of economic power. The total outlay on social services will be about 950 crores of rupees, nearly twice the provision made in the First Plan. The objective of the health programmes for which about Rs. 270 crores have been allotted, is to improve the general level of health by expanding the basic health services and bringing them within the reach of the people. More specifically, the Second Five-Year Plan aims at:— (1) control of communicable diseases which affect large sections of the community; (2) improvement of environmental hygiene; (3) provision of adequate institutional facilities to serve as a base for organizing health services; (4) provision of facilities for the training of medical and health personnel and (5) family planning.

We have in our editorials referred from time to time during 1956 to the more important items in the plan and offered our suggestions for the proper utilization of the available resources. Excellent progress has been reported during the year from the several units working in different parts of the country to combat malaria, leprosy, tuberculosis, filariasis and V.D. The Employee's State Insurance Scheme has been extended to more industrial centres. The National Extension Services and the Community Projects have received considerable attention and are making steady progress in bettering the conditions of living amongst the rural population.

We are indeed very happy to be able to record our high appreciation of the hearty co-operation from our readers, contributors and advertisers but for whose continued and whole-hearted patronage it would not have been possible to report another year of steady progress for the ANTISEPTIC. We thank them all heartily and wish them a very happy and prosperous NEW YEAR.

## THE EIGHTH ALL-INDIA PÆDIATRIC CONFERENCE

(Child Welfare Programme in Health Services)  
(Contributed)

THE Eighth All India Pædiatric Conference was held on the 20th December 1956 at the Christian Medical College, Vellore with Dr. SHANTHILAL C. SHETH in the chair. A very large number of delegates from different parts of the country attended the conference which was inaugurated by Dr. U. KRISHNA RAU, M.B., B.S., M.L.A., of Madras.

Dr. KRISHNA RAU referred at the outset to the need for unity in all professional associations; thus instead of having two parallel associations for the advancement of pædiatrics in the country, it would augur well for both if they combined their efforts and worked under one banner, so as to impress those in authority with the singleness and strength of their purpose. After paying a well-deserved compliment to the unique position which the Christian Medical College Hospital at Vellore has achieved for itself in the medical world, he dwelt on the various aspects of child health stressing the need for the training of specialists in pædiatrics for teaching students and for the provision of facilities to enable all medical men right from their undergraduate days, to study the child in health and disease and in their proper home surroundings, rural and urban. He next stressed the importance of preventive work which has been found to pay excellent dividends in the case of children all over the world. The Second Five-Year Plan refers to the fact that pædiatrics is at present the weakest link in maternal and child health services and urges the necessity for improved amenities and facilities.

"It is essential to provide pædiatric training to personnel in charge of maternal and child health centres in the pædiatric departments of Medical Colleges and to equip and staff them suitably. Each pædiatric department will select six existing maternal and child health centres and augment the staff of each with a doctor trained in pædiatrics, public health nurse and other auxiliary staff. Their functions will be to take up combined preventive and curative pædiatric care of children and to attend to school health in the elementary schools of the area, in addition to the ante-natal and obstetric service already being done. Protective protein foods, essential drugs and prophylactic vaccines will also be made available to each of the centres. To begin with, it is proposed to set up at least 5 such pædiatric training centres in India. These centres will arrange for the regular training of maternal and child health personnel and also give periodic refresher courses."

He very properly considered that pædiatricians should play a large part in disseminating correct knowledge on nutrition among the people. It is needless for us to say that it would not otherwise be possible to fight the evils of gross malnutrition which is now undermining the health of the children, particularly of the vulnerable groups, viz., the growing child and the pregnant or lactating mother. It is the duty of the Government

both at the Centre and in the States to give top priority to the programmes of child welfare. The knowledge of many of the diseases prevailing among children was not complete, and there was need for detailed investigation. In the first instance, fact-finding is a necessity. We should have materials to give us sufficient information regarding statistics on elementary things such as growth studies. There was no knowledge regarding the incidence of common diseases such as diphtheria, typhoid, bowel diseases, infantile biliary cirrhosis and tuberculosis. Pædiatrics as specialists might advise the administrators on the best methods to prevent spread of these diseases. They could also give their opinion on the use of B.C.G. vaccination.

Touching on the environment of patients, Dr. KRISHNA RAU said, that if medicine was divorced from the society in which it must function, the doctor became a mere technical expert upon whom university education was wasted. Emphasizing the importance of teaching Social Preventive Medicine, he congratulated the Christian Medical College authorities on their pioneer work in taking students and doctors out to see their patients in their surroundings.

Dr. SHETH in his lucid presidential address strongly pleaded for the appointment of a "Care of Children Committee," like the Curtis Committee of England, to go into the statutory provisions and administrative arrangements for the care of children's health and make its recommendations to the Government.

Care of the child was an individual and social duty and should be attended to with all earnestness. But child-welfare activities in India were very poor and the lack of proper organizational effort in this direction for public education and professional training was only too evident. We quite agree that in any plan of pædiatric care the problem of rural areas has to be borne in mind, and that curative pædiatrics should be given the place of prime importance; but it should be the duty of every pædiatrician to give the rightful place to the preventive, public health, nutritional, organizational and nursing aspects of pædiatrics as well.

Pædiatric nursing is a specialized branch and it should be a major subject for student and undergraduate nurses. There should be a post-graduate course with pædiatric nursing as a special subject, so that the standard of nursing care of children might be raised.

In regard to pædiatric education, Dr. SHETH suggested that under-graduate students should work for two weeks in the third year and for five weeks each in the fourth and fifth years of their medical course and should have two to three months' training in pædiatrics after the qualifying examination. Ante-natal

pædiatrics and the diseases of the new-born might be taught in the obstetric wards with the co-operation of pædiatrician.

Both Dr. KRISHNA RAU and Dr. SHETH stressed the need for sustained research in pædiatrics.

We would like to impress on all medical men the basic facts that greater attention to the child, his deficiencies, and his needs will result in building up a strong and healthy nation and that the medical profession should rise to the occasion in a spirit of co-operation and carry out enthusiastically researches in every aspect of child-welfare.

### HIGHER MEDICAL EDUCATION AND MEDICAL RELIEF

ADDRESSING the members of the Coimbatore District Medical Association on the 15th Dec. 1956, Dr. A. LAKSHMANASWAMI MUDALIAR, Vice-Chancellor of the Madras University criticized the recent attempts by the Union State Governments to lower the standards of medical education and thereby the medical profession. He appealed to the members of the Medical Associations in India to view the matter seriously and express their considered views freely and frankly in regard to the proposals before Government in respect of giving higher medical education facilities and effecting reforms in medical education. The problem before those who had charge of medical education in the country was really how best under-and post-graduate medical education could be provided.

One of the greatest difficulties encountered in the reform of medical education was the provision of proper undergraduate and post-graduate courses. After independence, a number of medical colleges have been started and retired men have been appointed to be in charge of these colleges. It should be remembered that a medical college does not mean building, equipment and hostel facilities alone. We could get all these if money was available. Great importance should be attached to the recruitment of the necessary personnel who would give proper training to students in undergraduate medical education. We are strongly of the view that the necessary personnel must be recruited first before starting a new medical college. Dr. MUDALIAR was not happy at what the Indian Medical Council had achieved in the matter of legislating for proper post-graduate medical education and its needs under Indian conditions. He had visited a number of medical institutions in several foreign countries of the world in the course of his numerous itineraries. He has made a very close study of the working of nearly all such institutions. He gave it as his considered opinion based on such intimate and

extensive knowledge of medical education in the different countries, that it was absolutely necessary to have a higher standard for the development of medical science. "Recent trend in Government quarters," he said, "had upset his ideas and if that trend developed it would ruin medical education. Politicians made all sorts of suggestions and changed the atmosphere and spirit of medical education. Everything was being dictated by the Government authority."

There can be no two opinions on the question of entrusting the whole subject of medical education to an independent organization whose deliberations should not be fettered by party or political considerations and whose mature and considered advice should be accepted without any argument.

Referring to *Integrated Medicine* which is now very much to the fore in regard to Indian Medical Systems, Dr. MUDALIAR was of the opinion with which we also agree to a great extent, that if the present "integrated system of medicine" was continued the result would be the lowering of the standards of the practice of medicine, whether modern or indigenous. It would lead only to quackery. There is no justification for the use of the term "*Integrated Medicine*." It is difficult for students to undergo training in both modern and indigenous systems of medicine. The proper method of encouraging Ayurveda, Unāni or Siddha system should be to see that those who practised either one or other of these systems had a thorough grasp of that system. They must be registered under the Medical Practitioners Act.

When the Bill for the Registration of Practitioners of Integrated Medicine was discussed in the Madras Legislative Council in October last year, Dr. MUDALIAR said:—

"The only way in which we could improve the ancient system of medicine, the only way in which we could integrate the ancient system of medicine with modern system of medicine is by making those who have been trained in the modern system of medicine take a full course in the ancient system of medicine and likewise making those who have been trained in the ancient system of medicine to take a full course in the modern system of medicine as well. Even in Great Britain, there are different system of medicine. But nobody is allowed to practise any system before he had taken what was known as the basic qualification in modern medicine. Those who qualify themselves in both the modern and ancient systems of medicine can claim to have a higher qualification and I am of the view that the University can give them even a doctorate in medicine."

Nobody could have any objection to some system of sound training in Ayurveda or other Indian systems of medicine being given to doctors of modern medicine. The Madras University we are credibly informed, is prepared to give recognition to institutions started in particular systems of medicine, provided the prescribed standards are satisfied; and nobody can maintain that the modern system of medicine is perfect or is the best and that

Ayurveda deserved to be accorded only a secondary place in the order of things. The latter certainly deserves all encouragement and is luckily receiving a great deal of it. But a mix-up of two systems "will surely put back the clock of progress." Referring to the recent constitution of a Committee of seven ministers from different States "who knew nothing of medicine" to go into the question of improving Indian systems of medicine, Dr. MUDALIAR said, "this committee was constituted under political pressure in the Lok Sabha; although the Union Health Minister resisted such attempts to the last, she had finally to bow to political pressure; the idea of dealing with medical education by a set of laymen was anathema to all those who had the best interests of the medical profession at heart." He was not against the Indian systems of medicine, but what he insisted was that there should be a scientific background for the proper development of these systems.

Dr. C. S. THAKAR, President of the I.M.A., in his presidential address at the 33rd All India Medical Conference held at Trivandrum on 26th December 1956 stated:—

"The amount of research work turned out by these so-called Ayurvedic Centres of Research has been negligible and one can only express a pious hope that the liberal grant made by the Centre will enable them to achieve some substantial progress on the right lines. The Indian Medical Association is prepared to extend its full support to scientific research in indigenous systems of medicine. But the decision to set up five new Ayurvedic colleges and over 1100 dispensaries in addition to the existing 15 colleges and 255 dispensaries is, to put it mildly, unwise."

Even Dr. RAMAKRISHNA RAO, the Governor of Kerala who advocated a "philosophy of co-existence between modern and indigenous medicine was emphatically of the opinion that:—

"The indigenous systems have to be dispassionately examined and studied with the help of modern sciences, and the practitioners of modern medicine and surgery both of which had made phenomenal progress since the last war, need have no quarrel with the indigenous systems; they should take some more practical steps in this direction than merely expressing their moral support by adopting resolutions requesting Government to establish institutions of Research in the indigenous systems."

The sponsors of a shortened course of medical education to meet urgent rural needs, failed to realize that the rural population was entitled to and should not be deprived of the benefits of full-fledged modern medicine and that lip sympathy is not what the villager needs.

Dr. MUDALIAR said, "the system of providing medical aid to rural areas, that is in vogue and was very popular in Australia, may be tried in selected areas in India; even the remotest areas in the desert regions were served by a network of telephones and aerial medical units." The mobile medical van service which was planned sometime ago to carry medical relief to rural areas in many States of India does not appear to have made much

headway. But thanks to the Community Project and National Extension Services, the village population is receiving greater attention in the matter of general uplift and the provision of amenities which would certainly make for better health and a better standard of living. These two services cannot, however, solve the problem of rural medical relief in its entirety. The need for more doctors, nurses, and other auxiliary personnel, has been fully recognized by the Planning authorities and adequate budgetary provision has been made in the second plan. The success of the plans and schemes envisaged will however depend on how well and how soon they are implemented by the States. It was certainly painful reading when we were told the other day that considerable sums of money provided in the First Five Year Plan for the advancement of Public Health, came to be surrendered without being utilized, due mainly to want of active and prompt co-operation from the States. Let us hope this will not recur and that the second plan will achieve a full measure of all-round success.

### PREVENTIVE AND CURATIVE MEDICAL SERVICES

(A New Experiment in Hyderabad)

**S**PEAKING at the foundation-stone-laying ceremony at Chingleput in October 1956, the then Madras State Health Minister spoke frankly about the shortcomings of the services charged with the safeguarding of the health and providing adequate facilities for treatment of illness among the people. He had, however, nothing to say in answer to the many questions regarding what action was being taken to remedy the position. He agreed that at Chingleput there was no space for expansion and that there was need for a larger building on a sufficiently extensive site; this is true not only of the Chingleput hospital but of several others in this State, or for that matter in other States of India, many of which we are told, are outmoded; the provision of medical relief in several instances has been haphazard. Instead of simply deploring the existing state of affairs, and restating the platitude that there should be "planned development of hospital services in the future, and new medical and health institutions established in places where there is need for them," the Minister should have indicated precisely what, where and when plans would be put into execution, or at all events where a start will be made and its extent.

The greatest handicap to the expansion of the curative and preventive services has for long been the paucity of qualified medical men willing to go and work in rural areas; almost equal in magnitude is the inadequacy of qualified medical, nursing and other staff in the existing hospitals, to give proper care and attention to the greater overflow of patients admitted in

excess of available accommodation. We learn that a directive has been issued permitting hospitals to admit 25% of patients above the sanctioned bed strength and we presume this will be implemented by the appointment of additional medical and nursing staff and the provision of extra medical supplies and other equipment.

As regards health services also, there is need for considerable improvement in men and methods. In this context we would invite the attention of the authorities in Madras and other States, to the new experiment in co-operation in Hyderabad, which has blazed a new trail in this field. The health authorities in other States will do well to study the details and working of this novel venture with a view to possible adoption or adaptation to suit individual needs of their States, and relieve the pressure in overcrowded hospitals and health centres. The plan simply stated, is for a co-operative dispensary on a subscription basis, the subscription being low enough to attract people of all lower income groups, for it is assuredly for their special benefit, and the facilities offered are wide enough to take care of the everyday ailments of the people.

"Such a dispensary was finally inaugurated by the Union Deputy Minister for Health on 15th September 1956 in Nizam Bagh, a thickly populated area of the city. Established under the auspices of the State Medical Department to give speedy relief and suitable medical service to the 30,000 citizens in that area, it provides medical service to its members at a nominal monthly subscription of Rs. 2, each family being considered a member. All families who register themselves as members will be provided with a number of medical facilities, which includes out-patient treatment for males and females, X-ray examination, pathological examination and medicines *free of cost*. Home visits by doctors attached to the Dispensary are made free of charge in case of serious illness when patients are unable to attend the dispensary. At the same time all serious cases requiring in-patient treatment will be admitted in the city hospitals. Facilities are also provided for consultation of eye, ear, nose and throat specialists. It works day and night and two emergency beds have been provided, as also an ambulance car for conveying serious cases to hospitals. Doctors posted at the dispensary will visit patients' houses when required as already stated, but the medicines prescribed during such visits will have to be purchased by the patients. Government servants are to be enrolled as members free of charge on the production of certificates from heads of Departments."

This scheme is to be extended to other areas in due course. Such dispensaries, we are sure, will not only be a great boon to the citizens but will also give further impetus to the co-operative spirit among them.

This may not however solve the larger and more difficult problem of rural medical relief for obvious reasons. The progress being made in the National Extension Service and Community Project areas may provide better conditions of living which should attract young medical men to work in rural areas; it will

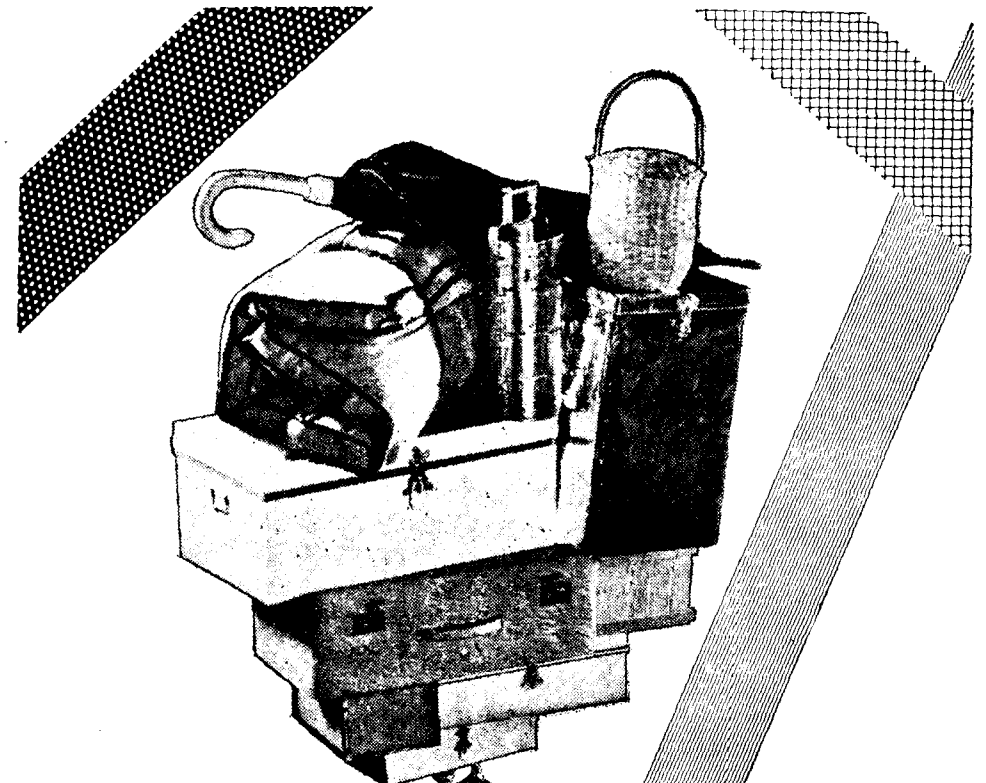
be a question of an adequate number of qualified men to take up the work. Proper planning and speedy execution will alone help in meeting the primary needs of the people.

#### LITHIUM THERAPY IN MANIA: PRACTICAL LINES OF GUIDANCE

In 69 out of 85 manic patients treated with lithium to date the manic symptoms disappeared or abated during the treatment; in 16 patients the treatment was without effect. Spontaneous variations are characteristic of manic-depressive psychoses, but in one-third of the cases the improvement is attributed to the lithium. Every psychosis with definitely manic features is an indication for treatment with lithium, but since the effect sets in rather slowly in the course of one or two weeks, it is often preferable in first time mania and in patients with infrequent brief manias to await spontaneous improvement or to use electro-shock. The treatment where Serpasil and Chlorpromazine are of undoubted therapeutic value the effect of lithium is slight or uncertain, but its effect in especially protracted or frequently recurring manias offers advantages over other forms of treatment. A tablet contains 0.3 gm. of lithium carbonate. A beginning dosage of 2 tablets two or three times daily is advised. After one or two weeks, treatment can usually be continued with a maintenance dose of 1 tablet three times daily, the final dose being determined by the effect on the psychic condition, the lithium concentration in the blood, and possible symptoms of overdosage (nausea, diarrhoea, strong tremor of the hands). A reasonable intake of salt must be insured, and the water intake must be adequate. Therapy with the substance should be discontinued if the salt elimination of the lithium concentration in the blood every two weeks is sufficient; flame photometric determination is simple and quick. Diseases of the heart and kidneys and conditions leading to low salt-intake are contra indications. No late effects have been observed on administration for over three years.—(*Med. 55*: June 17, 1956, via *J. Am. Med. Assoc.*).

#### SEVERE TOXIC EFFECTS OF AMINOPHYLLINE

Nolke describes severe toxic effects from aminophylline and theophylline suppositories in children. He reports 13 cases with four deaths. The ages of the children were from five months to six years. Most were suffering from asthma. Aminophylline suppositories were given in doses of 0.25 g. every four hours for two to twelve doses. Toxic effects occurred after two doses in 10 patients. Nausea, vomiting, dehydration, fever, restlessness, severe agitation and convulsions were observed. Three patients were given theophylline suppositories in doses of 0.12 g. (two grains), repeated every four or six hours. Toxic effects were similar to those mentioned above, as might be expected, since aminophylline is theophylline with ethylenediamine. Post-mortem examination showed pulmonary inflammation in all four children, and ulcerative oesophagitis in two. The author discusses the toxic effects of these drugs, and points out that the toxic effects are not apparently sufficiently recognized. He mentions eight other cases of intoxication due to aminophylline suppositories reported in the last two years. He states that in these recent cases the dosage was rather vague. He considers that rectal administration of theophylline or aminophylline is dangerous, and unpredictable in the result.—(*J.A.M.A.*, June 23, 1956).



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## GLEANINGS FROM THE MEDICAL PRESS

### OPHTHALMOLOGY

**Emergencies in general practice: Ocular emergencies.**—(*Br. Med. Jour.*, Dec. 10, 1955, via *Sight Saving Review*).

This paper suggests what the general practitioner can do in certain ocular emergencies before the patient can be sent to a hospital and put in the care of an eye surgeon. These conditions of sudden, unexpected onset require immediate treatment if catastrophe is to be avoided in the affected eye and often in its fellow. An acute attack of glaucoma may involve the second eye, and a penetrating injury near the ciliary body may lead to sympathetic ophthalmitis and total blindness.

In cases of vascular occlusion, the practitioner is warned that when the central retinal artery is occluded for an hour or more, vision will be lost. Vasospasm of this artery must be immediately released by dilating it and lowering the intraocular pressure. If the central retinal vein is obstructed, thrombosis may be prevented by anticoagulants.

In retinal detachment Stallard suggests that the physician instil atropine in the affected eye, occlude both eyes, and send the patient to the hospital in a recumbent position if the detachment started in the upper half of the fundus, and sitting if it started in the lower half.

**Present-day concept of diabetic retinopathy.**—(*Diabetes*, Vol. 4: p. 284, July-August 1955, via *Sight Saving Review*).

The characteristic vascular lesion of this disease is masses of minute and often hyalinized saccular aneurysms in the retinal capillaries. Diabetes in itself is associated with increasing capillary fragility, which we are not yet able to define pathologically. It is accepted today that the picture of diabetic retinopathy is not dependent on hypertension, arteriosclerosis or atherosclerosis. The retinal lesions of

the diabetic are closely related to the renal lesions described by Kimmelsteil and Wilson; both may be manifestations of the same vascular disease.

It has been suggested that both renal and retinal changes may result from an increased production of adrenocortical hormones. Other studies have shown an interrelationship between these hormones and vitamin B<sub>12</sub> deficiency in diabetes. Possibly they act together with diabetes in producing the renal and retinal lesions by means of their effect on some other deficiency or metabolic disorder.

The diabetic shows an increase in plasma lipids. Lipæmia can be produced experimentally in rabbits by alloxan or cortisone, but it is not readily elicited in rats, nor do rats develop renal or retinal aneurysms under the experimental conditions that produce these lesions in rabbits. It has been found that rats possess a high level of properdin, a newly isolated blood serum, which may play a part in their immunity to infections.

**A clinical study on the heredity of glaucoma.**—(*Bull. Soc. belge d'opht.*, 110: 255-267, June, 1955, via *Am. Journal of Ophthalmology*). 79927

The heredity of glaucoma in 162 families is suggested, at least one member of each family had glaucoma. Open-angle glaucoma and narrow-angle glaucoma formed two groups and the glaucoma following exfoliation of the lens capsule constitutes a third group. A survey of the members of the family of patients with open-angle glaucoma showed that an increased resistance to the outflow of aqueous was an early sign of the disease and preceded the rise in ocular tension. A survey of the relatives of patients with narrow-angle glaucoma confirmed the difficulties of an early diagnosis. The completeness or incompleteness in the closure of the chamber angle was the main factor in the rise of the ocular tension and depended on genetic factors, age and

sex. However, narrow-angle or open-angle glaucoma were not characteristic for a given family, as open and narrow-angle glaucoma occurred indiscriminately. Among the 14 cases of glaucoma with exfoliation of the anterior lens capsule, no family traits could be discovered.

## OBSTETRICS & GYNÆCOLOGY

**Tuberculosis and pregnancy.**—(*Dis. Chest*, 30:43-49, July 1956, via *Jour. Am. Med. Assoc.*).

Jacobs studied a series of 64 tuberculous women who received obstetric care at the Charity Hospital of Louisiana. Most of them were young Negro women receiving antibiotic therapy. It was found that pregnancy does impose an additional stress on tuberculous women, but quantitative evaluation of this stress is almost impossible. Most women, particularly those who are anxious to have children, can tolerate this stress when treated with the antibiotics currently available. To reduce this stress to the minimum, tuberculous women should be advised to defer pregnancy until the disease has been inactive at least two years if minimal, three years if moderately advanced, and five years if far advanced. Experience with a relatively small group suggests that, if this precaution is observed, even multiple pregnancies are tolerated without reactivation of the tuberculosis. To detect tuberculosis, each obstetric patient should have a chest X-ray film examination as soon as pregnancy has been discovered. When tuberculosis is found in a pregnant woman, treatment with antibiotics and rest should be started at once precisely as during the non-gravid state. Other methods of therapy should be added as needed. The patient may be assured that, with adequate therapy, she will continue to improve despite the pregnancy, may be delivered of a normal child, and will be non-infectious by the time of confinement.

**Delivery after caesarean section.**—(*Am. J. Obst. and Gynaec.*, June 1956, via *Med. J. of Australia*).

Fleming reports on 295 women who had had a previous caesarean section and were subsequently delivered, 145 by elective caesarean section and 150 after a trial of labour. It is suggested that in all cases of previous caesarean section there should be available full information as to the previous operation, with particular reference to the indications, the type of section, and any post-operative infection. The patient was admitted for observation at the thirty-seventh to thirty-eighth week. If a trial of normal labour was permitted, cross-matched, compatible blood was secured and the theatre staff was warned. X-ray placentography was considered a worthwhile procedure. Factors which influenced the performance of an elective caesarean section were (i) overdistension of the uterus, (ii) tenderness over the scar region, (iii) additional abnormalities such as fibroid tumours, an abnormal uterus, a history of myomectomy. In five cases only was there rupture of a previous scar; four of these occurred after a classical caesarean section, and one occurred after myomectomy in the anterior wall of a six-weeks gravid uterus. In the elective caesarean group of 145 patients, death of the mother occurred in two cases, and three infants were lost. In the 150 patients for whom trial of labour ensued, there were two cases of ruptured uterus, and one maternal death from postpartum hæmorrhage. Eight babies were lost. The incidence of rupture of the uterus is two in 295 cases, or 0.68%. In the trial of labour group, 118 patients were delivered vaginally; 32 sections were required. In the whole series 40% of those patients who had a previous caesarean scar were delivered vaginally.

**Uterine tamponade for postpartum bleeding.**—(*Am. J. Obst. Gynaec.*, 71: 1220-1231, 1956, via *Mod. Med.*, 15-9-1956).

Packing of the uterus and vagina with oxidized cellulose gauze is effective

in stopping severe postpartum hæmorrhage.

Intrauterine packs of oxidized cellulose effectively control bleeding from caesarean section, placenta prævia, abruptio placentæ, uterine atony, or vaginal lacerations. Any amount of the gauze necessary to produce a firm tamponade may be used in the uterus, but large amounts are not recommended for intraperitoneal use.

When exposed to blood, oxidized cellulose swells, forming a black-brown, sticky, gelatinous mass. The material packed in the uterus exudes a bubbly, frothy fluid and forms an artificial clot, exerting pressure on the placental site. Within one to three days, the uterus forces the now crumbly mahogany-coloured substance into the vagina. Usually, the material is passed spontaneously from the vagina; manual or instrumental removal is done if pressure symptoms occur.

Cause of postpartum bleeding must be discovered and corrected. The uterus should be freed of clots and massaged, and an intravenous oxytocic should be given. However, if such measures are insufficient to stop bleeding, intrauterine packs should be tried before hysterectomy is done.

Oxidized cellulose is available commercially in the form of cotton fluff, gauze squares, or strips 3 yd. long and 1 yd. wide, folded to a width of 2 in. In small quantities, oxidized cellulose is absorbable.

**Treatment of cervical cancer during pregnancy.**—(*Obst. and Gynaecol.*, 7: 522-526, 1956, via *Mod. Med.*, 15-9-56).

Prognosis of carcinoma of the cervix is as good in pregnant as in nonpregnant women if prompt and vigorous treatment is given.

Cervical carcinoma occurs in about 1 in 7,000 pregnancies. Incidence is greatest among multiparas 30 to 40 years of age.

Abortion occurs in 30 to 40% of patients. If the pregnancy goes to term, the tumour increases the risk of intrauterine infection and may inter-

fere with cervical dilatation, sometimes causing rupture of the lower uterine segment. Hæmorrhage may ensue from laceration of the tumour.

Treatment is instituted immediately on diagnosis, regardless of the duration of pregnancy. If the foetus is viable, a caesarean section is first performed.

Radium therapy is given in 2 courses of 2,400 mg. hours each, separated by an interval of two weeks; half the dosage is given intracervically and half contracervically. For patients treated early in pregnancy, hysterotomy is performed between the first and second radium treatments. Two weeks after completion of radium treatment, 2,500 to 3,000 r of deep X-ray at 250 or 400 kv. is delivered to the skin over each of the pelvic fields.

**Rupture and perforation of the uterus in association with pregnancy, labour, and the puerperium.**—(*Brit. M. J.*, 1956, 1: 65, via *Internat. Abst. Surg.*, Sep. 1956).

The clinical details of 45 cases of rupture and perforation of the uterus in association with pregnancy are described. There were 7 maternal deaths, a mortality of 15.5 per cent. Of the 7 deaths, it is considered that a fatal termination might have been avoided in 6. In these 6 cases the following errors were made: misdiagnosis within the hospital of quiet rupture as subacute bacterial endocarditis; performance of difficult version with tight uterus outside the hospital; "failed forceps" and the administration of a large dose of oxytocin outside the hospital; delayed diagnosis within the hospital in 2 cases; long transport after a motor accident.

The fate of 46 fetuses in the 45 cases was as follows: 20 survived; 22 died; there were 3 abortions and 1 miscarriage.

Classical caesarean section is no longer performed in the two hospitals mentioned, but patients bearing classical scars occasionally return for repeat section or, more rarely, with a view to vaginal delivery. The classical scar should always be regarded with sus-

picion. The lower-segment scar may also be imperfect. All women bearing scars of previous uterine operations should receive special care in pregnancy and in labour, if the latter is permitted. Although scars must always cause some concern, the authors do not subscribe to the belief "once a caesarean, always a caesarean." When vaginal delivery after previous section is contemplated, certain strict precautions should be adopted.

A combination of events conducive to rupture may develop quickly in neglected shoulder presentation.

Internal version should not be attempted unless the conditions for its safe performance are present. A bad failure of forceps delivery may cause serious trauma. Abortions should be cleared out under direct vision. The soft subinvolved puerperal uterus is easily perforated.

Hydrocephalus is a potentially dangerous complication because minor and moderate degrees of the abnormality, sufficient to cause serious difficulty in labour, are easily missed. Diagnosis, both clinical and roentgenological, is not as easy as the textbooks indicate.

Before delivery, posterior pituitary extract should be used with great care.

High multiparity provides certain problems, one of which is the possibility of spontaneous rupture of the uterus.

Brow presentation should always be considered when the foetal head fails to descend in the second stage of labour, especially in the multipara.

Precipitate labour may cause serious trauma to mother and foetus.

Women who have had plastic cervical and vaginal operations should be delivered in the hospital.

Spontaneous rupture of the vaginal and supravaginal cervix with extension into the broad ligament may occur.

The incidence of rupture and perforation of the uterus in association with pregnancy was 1 in 1,200 of all

deliveries in the service of the two hospitals.

**Functional uterine bleeding.**—(*Am. J. Obst. and Gynaec.*, June, 1956, via *Med. J. of Australia*).

Jacobs and Lindley, report 92 cases of functional uterine bleeding. The diagnosis was made on the history and the lack of pelvic findings to account for the bleeding. For all patients over thirty-five years of age a biopsy was taken and a diagnostic curette was performed. The age of the patients ranged from seven years to fifty years. Over the age of fifty years the bleeding was not regarded as functional. The endometrium was available for study in 51 cases; in 25 it was proliferative, in 11 secretory, in two menstrual, in seven hyperplastic, and in five mixed in type. Treatment was by curettage, cyclic oestrogen therapy, as recommended by Hamblen, or a combination of sedation and empirical thyroid therapy. The ultimate outcome in the patients treated by curettage and cyclic oestrogen therapy was about the same. Curettage offered better immediate results, but if the patient responded immediately to oestrogen therapy, her chances of remaining well were rather better than the curettage group. The fact that 17 of 24 patients receiving thyroid therapy and sedation were apparently cured speaks well for the fact that, given time, most of these patients will have a spontaneous cure. The authors conclude that the main problems are (i) to rule out organic pathological conditions, and (ii) to provide some means of immediate or reasonably immediate hæmostasis.

**The treatment of vesico-vaginal fistulae.**—(*Am. J. Obst. and Gynaec.*, March, 1956, via *Med. J. of Australia*).

Moir reviews and discusses the treatment in 136 consecutive cases of vesico-vaginal fistula. He considers these to be highly selected cases because of their difficulty and unusual nature, or because they had

resisted previous attempts at surgical cure. Almost one-third were attributable to obstetrical causes, either laceration during operative delivery or pressure necrosis after long labour. Over two-thirds of the cases were of gynaecological origin, and, for the most part, followed hysterectomy, colporrhaphy, radium treatment and other miscellaneous operations. The author recommends three preliminary investigations prior to operation: examination for the possibility of multiple fistulae; the performance of excretion pyelography to determine renal function; examination to exclude the presence of vesical calculus. The majority of fistulae, in this series, belonged to one of three types: true vesico-vaginal fistula arising in the trigone of the bladder and usually situated in the mid-line; fistulae due to bladder neck destruction usually following pressure necrosis at parturition; fistulae due to urethral destruction complicating difficult delivery or faulty colporrhaphy technique. The author considers that the great majority of even complicated and difficult fistulae can be repaired by simple, direct methods, through the vaginal route. Operative cure was successful in all but two of the reported cases. The size of the fistula, the presence of complete destruction of the urethra, the duration of the fistula or a history of previous attempts at surgical closure does not necessarily mean a bad prognosis for cure. Resort to transplantation of the ureters into the colon or rectum is not indicated on these grounds. Two complications of bad prognostic significance are extensive destruction of the muscle of the bladder neck, or the presence of dense fibrosis around the fistula causing it to adhere to the pubic ramus. Functional cure following operative closure was usually excellent, but residual stress incontinence was severe in four cases, and the ureters were subsequently transplanted into the rectum. The author recommends closure of a vesico-vaginal fistula by the vaginal route, unless very special reasons exist for approach by the transvesical or trans-abdominal route. Details of ope-

orative technique are discussed and illustrated. These include the position of the patient for operation, essential instruments, methods of suturing and suture material, and post-operative care. Common variations in technique to suit particular circumstances are briefly described. The author concludes that vesico-vaginal fistula is, in the majority of cases, an eminently curable lesion. Successful treatment demands gentleness of touch, infinite patience, and attention to the minutiae of technique on the part of the surgeon.

**Treatment of external endometriosis.**—(*West. J. Surg.*, May, 1956, via *Medical J. of Australia*).

Malone reviews 237 cases of external endometriosis and discusses the treatment of this disease under four broad headings: prophylactic, non-surgical, surgical, and psychosomatic. The diagnosis was established by surgical means in 82 patients and was made on the clinical findings in the remaining 155 patients. Clinical diagnosis was made on the following symptoms and findings: increasing dysmenorrhoea, menometrorrhagia, low back pain, dyspareunia, infertility, retroverted and fixed uterus, nodular and tender utero-sacral ligaments and recto-vaginal septum, and indurated adnexa. Among prophylactic measures the author mentions early marriage to ensure the protection of child-bearing, replacement of the retroverted uterus, preferably by a Smith-Hodge pessary, and the promotion of endometrial drainage. Non-surgical treatment encourages child-bearing, relieves cyclical pain with suitable analgesics, and suppresses ovarian function with hormones. The author prefers androgens to oestrogens, as there are less undesirable side-effects with the former. He considers that irradiation to ablate ovarian function has a very narrow field of application in the treatment of external endometriosis. Its chief disadvantage is that the diagnosis is not confirmed without surgical and pathological examination, and adhesions or

diseased organs cannot be treated by irradiation. Surgery has much to offer in the treatment of external endometriosis and the author emphasizes the importance of conservative surgical measures. One-third of the patients in the reported series required operation, and in 50% of these the surgical procedure was conservative. Of those patients treated conservatively, 40% later became pregnant. The following principles of surgical treatment are recommended: dilatation of the cervical canal, extirpation of endometrial implants, the freeing of adhesions, myomectomy if myomata are present, and suspension of the uterus. If there is dysmenorrhoea of a disabling nature, it may be advisable to perform presacral neurectomy. Patients of an older age group who cannot be carried on to the menopause may need radical surgical measures. The author mentions the importance of the psychosomatic approach in conservative treatment. This includes assessment of the patient as a whole, and the allaying of fear by explanation and reassurance.

**Glycosuria in pregnant diabetic patients.**—(*Arch. Int. Med.*, 97: 758-761, 1956, via *Modern Medicine*, Sept. 15, 1956).

Renal glycosuria may contribute to the occurrence of hypoglycaemic reactions and ketosis in pregnant diabetic patients.

As many as 24% of healthy pregnant women have glycosuria sometime during pregnancy; among diabetic patients, glycosuria is even more frequent. Blood-sugar levels in these patients may be normal or only slightly elevated. Cause of urinary glucose excretion during pregnancy is unknown.

In diabetic women, finding of glycosuria often leads to attempts by the patients to readjust insulin dosage on the basis of urine sugar tests. Severe insulin reactions may result from this effort. Glucose supply may be so diminished by urinary excretion that ketosis and acidosis develop.

Therapy for diabetic patients with renal glycosuria includes lowering of

the insulin dosage to prevent hypoglycaemia and provision of adequate dietary carbohydrate. Blood-sugar determinations are made frequently before and after meals to aid in regulation of the insulin dosage.

## MEDICINE AND THERAPEUTICS

**Early diagnosis of bronchial carcinoma.**—(*Munchen. med. Wchschr.*, 98: 937-941, July 13, 1956, via *Jour. of Am. Med. Assoc.*)

Knipping *et al* who reported in 1951 on early signs of bronchial cancer in 150 patients, present here observations on 180 additional patients. Early recognition is the crucial point in bronchial cancer, because long-term therapeutic results have remained unsatisfactory despite the great advances in thoracic surgery. A series of special examinations must be carried out whenever there is even the slightest suspicion of bronchial cancer. These examinations include bronchoscopy, bronchography, cytological tests, and exploratory thoracotomy. However, suspicious signs are frequent in persons of certain age groups, and those who have them often regard them as trifling and refuse to submit to the rather exhausting examinations; at any rate, they are not inclined to submit to them repeatedly, the less so since only a small proportion of those who exhibit the early suspicious signs actually have bronchial cancer. For this reason, methods are required that can be carried out without causing too much inconvenience, so that the patient will submit to them repeatedly. In patients in whom bronchial cancer seems highly probable and in whom a surgical intervention is planned, bronchoscopy and bronchography should always be employed.

The authors feel that the most important method of preliminary examination is body-section roentgenography (tomography), particularly with the improvements they have introduced. The newest form of this body-section roentgenography is

simultaneous multi-layer tomography, which is explained with the aid of a diagram. This improved method can now be employed for routine examinations. Other diagnostic methods are bronchography with the aid of either radioactive iodine-alkyl or with radioactive xenon. These methods have proved useful in routine clinical work. Another important development in the early diagnosis of bronchial carcinoma is bronchography on the basis of the visualization of the distribution of radioactive xenon in the blood vessels and air passages. This method also enabled the authors to accomplish a direct demonstration of the moving heart (*in situ* and *in vivo*) without the aid of the roentgen apparatus (angiocardiology with the aid of isotopes). They also describe further improvements and developments aimed at the development of isotope bronchography. The use of isotopes, particularly of radioactive xenon, as employed by the authors in the diagnosis of cardiac and pulmonary disorders involves no inconveniences for the patients.

**Treatment of typhoid with isoniazid.**—(*Policlinico sez. med.*, 63: 137-148, June 1956, via, *Jour. Am. Med. Assoc.*)

Conese and Colonna studied the effect of isoniazid on 41 patients with typhoid. Twenty-three patients were treated only with isoniazid. Two hundred milligrams was the maximal dose per day; it was given in divided doses of 50 mg. Treatment was continued for a few days after disappearance of the fever. Eighteen patients were treated with 200 mg. per day of isoniazid and 1.5 gm. per day of chloramphenicol. Most of the patients were young. Clinical results were very satisfactory. Splenomegaly and hepatomegaly were the last symptoms to disappear. Recurrence of the fever was noticed in only one patient. The limited number of cases does not permit the authors to formulate a hypothesis on the mechanism of action of the drug. The effect of isoniazid depends on the stage of the disease; poor results are obtained in the acute stage. Isoniazid

was chosen on account of its effect on the diencephalon-pituitary system. The synergistic action of chloramphenicol failed in only one patient.

**The blood picture in rubella: its place in diagnosis.**—(*Lancet*, 2: 66-68, July 14, 1956, via *J. Amer. Med. Assoc.*)

Hillenbrand investigated the blood-picture of patients with rubella in the Falkland Islands as well as in Britain. He found that in conjunction with lymph-node enlargement the results of routine white blood cell counts are sufficiently characteristic in rubella to permit a confident diagnosis even of subclinical infection with german measles, in which symptoms may pass unnoticed. This aid to early diagnosis can be very important when it is necessary to protect by immunization a pregnant woman who has been exposed to the infection. The lymphatic hyperplasia, mainly of the post-auricular and occipital lymph-nodes, which typically follows rubella and may persist for many months, is associated with the presence of Turk cells and plasma cells in the blood. When persistent lymph-node enlargement is associated with these blood changes, a retrospective diagnosis of rubella can be made. The fact that patients with rubella (clinical or subclinical) examined between the first and ninth days showed plasma cells or Turk cells, which nearly always persisted until the sixth week, means that a person not showing these changes is very unlikely to have had rubella. In their absence, therefore, there is no need to fear damage to the offspring of a pregnant woman or to consider the advisability of therapeutic abortion.

**Oral penicillin V therapy.**—(*Antibiotic Med. and Clin. Ther.*, June, 1956, via *Med. J. Australia*).

Wood *et al* discuss the clinical value of orally administered penicillin V. They state that orally administered penicillin is partly destroyed by acid in the gastro-intestinal tract. Phenoxymethyl penicillin

showed greater acid stability than penicillin G, and gave higher serum levels. The curative and toxic effects of penicillin G and penicillin V (phenoxymethyl penicillin) were similar. One hundred patients were treated with penicillin V given orally. Fifty-four patients received tablets containing 200,000 units of the free acid phenoxymethyl penicillin, and 46 received the benzathine salt of oral phenoxymethyl penicillin in oral suspension. A dosage of 800,000 to 1,500,000 units was given daily for streptococcal throats, pneumonia, staphylococcal impetigo and acute otitis media. The results of treatment were said to be at least comparable to the expected effects of penicillin G. Toxic effects were negligible.

## SURGERY

**The surgical treatment of achalasia of the œsophagus.**—(*N. England J. M.*, 254: 87, 1956, via *Internat. Abst. Surg.*, Sep. 1956),

About 75 per cent of the cases of achalasia were characterized by an enormous dilatation of the œsophagus above the distal segment which was capable of holding large amounts of food and liquids. The terminal segment, at operation, was very small in diameter and possessed abnormally thin muscular layers in contrast to the enormously dilated, thick-walled portion directly above it. On the basis of the series of cases reviewed, Sweet feels that a simple œsophago-plastic procedure consisting of a longitudinal incision in the atrophic lower segment plus a circumferential closure of the opening is sufficient. The procedure eliminates the narrow segment and increases the diameter of the lumen at the lower end. The resulting relief from dysphagia was complete and permanent.

Quite a different situation obtained in the remaining 25 per cent of the cases. The patients noted referred pain in the substernal area which was secondary to œsophagospasm. Although there was dilatation of the œsophagus in this second type of

achalasia, it was moderate in degree and did not assume the huge proportions characteristic of the type described initially. The lower œsophageal segment exhibited thickening due to hypertrophy of the circular muscle fibres. These patients responded very satisfactorily to a modified Heller œsophagomyotomy which consists of a longitudinal incision through the hypertrophied muscle fibres.

It has proved to be of importance that the stomach be maintained in a normal position below the diaphragm. Attention to this detail may prevent later regurgitation from the stomach into the œsophagus.

Forty-eight patients were observed in this series with an analysis of their age-range, sex, the duration of symptoms, type of operation employed, and mortality rate. Forty-six patients left the hospital in good condition; 2 died at a later date because of unrelated causes. Thirteen patients exhibited no postoperative symptoms and remained completely free of symptoms. Late postoperative symptoms consisted of transitory delay in the passage of food, regurgitation of fluid into the pharynx, varying degrees of pyrosis, dumping, and bleeding from the upper gastrointestinal tract. The majority of patients with the last complication had bleeding due to hyperæmic congestion of the gastric mucosa. Some patients with achalasia had some degree of spasticity of the antrum, pylorus, and, often of the first portion of the duodenum. Pylorospasm and the resultant delay in emptying of the stomach led to eventual impairment of nutrition, regurgitation, and contributed to the development of hyperæmic congestion of the gastric mucosa. These complications can be avoided by pyloroplasty.

For evaluation of the end results, 36 patients were studied with X-ray, fluoroscopy, and œsophagoscopy. These individuals were treated by primary resection (4 cases), secondary resection (5 cases), œsophagoplasty (20 cases), and œsophagomyotomy (7 cases). Nineteen patients showed 90 to 100 per cent improvement in their condition, 9 showed 80 to 90 per cent,

and the remainder had less than 80 per cent.

**Primary chylopericardium and its surgical treatment.**—(*Dis. Chest*, 30: 160-165, Aug. 1956, via *J. Am. Med. Assoc.*).

Naef reports a case of chylopericardium successfully treated by ligation of the thoracic duct. Up to 1954 no other case had been reported in the world literature. The diagnosis is easy to establish by chemical examination of the milky fluid aspirated from the pericardium. The aetiology is doubtful, because in this case the history revealed a definite trauma as well as an inflammatory bronchopulmonary episode. There was no mediastinal tumour as in a somewhat different case reported by Groves-Effler in

1954. From the anatomic standpoint the aetiology is extremely difficult to explain, as normal anatomy knows of no relation whatsoever between the pericardium and the thoracic duct. The treatment of chylopericardium consists in surgical exploration of the situation. It will always be extremely difficult to demonstrate and obliterate the abnormal communication, and therefore, one has to be satisfied with ligation of the thoracic duct to prevent cardiac tamponade. Local irritation of the pericardium by the chylous fluid may lead to chronic pericardial constriction and thus necessitate ultimate cardiac decortication. To prevent this future complication, the surgical treatment of chylopericardium in the acute state must be early.

## REVIEWS of BOOKS, REPORTS and PERIODICALS

**Pharmacopœia of India**—Published by the Government of India, Ministry of Health, First edition, 1955, pages 1001.

This is the first edition of the Pharmacopœia of India. The Indian Pharmacopœia Committee, its Secretary and Assistant Secretary deserve to be congratulated for their hard work. In a free and independent India it is absolutely necessary that there should be a separate Indian Pharmacopœia. Such a Pharmacopœia will have to recognize officially and prescribe standards for drugs which are commonly used by the local medical profession and will have to give recognition to substitutes for imported drugs from amongst the indigenously available material. There are a few defects here and there, but considering the fact that this is the first attempt, the Committee deserves to be congratulated on this work. The first 753 pages of this book are devoted to the various drugs and preparations. The appendices also contain valuable information relating to techniques, such as the determination of melting ranges of the refractive index of the setting point and freezing point, of the acid value, of the saponification

value etc. The last few chapters are devoted to biological essays of drugs and preparations. The index is very thorough and the printing is good. We congratulate the Indian Pharmacopœia Committee on producing such a valuable publication. We are sure it will be useful to those employed in drug manufacture and also to chemists and druggists. U.K.R.

**Textbook of Pharmacology and Therapeutics**—By B.N. GHOSH, F.R.F.P.S., F.R.S., Professor of Pharmacology, R.G. Kar Medical College, Calcutta, 1956. 656 pages. Published by Scientific Publishing Co., 85, Netaji Subhas Road, Calcutta-1. [Price Rs. 20, or 35 sh.

Pharmacology has made phenomenal progress during the last 2 decades. As a result the outlook and treatment of many diseases which were considered incurable, have changed. Drugs which were regarded as essential have been relegated to the back ground. Great advances have been made in the treatment of many diseases. There has been a re-orientation and a new approach in the teaching of pharmacology. All these have been incorporated in

this very useful book. Drugs have been classified on the basis of their pharmacologic action and therapeutic use. To enable the student to have a proper understanding of the principles of pharmacology, the physiology of the particular system has been discussed before giving the actual description of the individual drugs.

Part one deals with general considerations; part II with the pharmacology, central nervous system, heart, circulation, respiration and other systems. Part IV discusses antimalarials and other remedies including the sulphonamides. Part XV deals with Immune therapy. There are chapters on drugs influencing metabolism, vitamins etc. The last few chapters are devoted to Materia Medica, Pharmacology and Dispensing. All the drugs included in the Indian Pharmacopœia which has just been published have been included in this book and so it must be very useful to students and practitioners. The printing and general get-up are also good. We congratulate the producers on their good work.

U.K.R.

**A Concise Book of Medicine**—By DR. AKIL BOSE, 3rd Edition. 1956. Pp. 188. Thoroughly revised. Can be had of M/s. Das Gupta & Co. Private Ltd., 54/3, College Street, Calcutta-12; M/s. U. N. Dhur & Sons Ltd., 15, Bankim Chatterjee Street, Calcutta 12, and The Kothari Book Depot., Bombay 12.

In this book, Dr. Bose gives a short, concise, yet adequate and up-to-date account of clinical, systematic and therapeutic medi-

cine. The first part of the book deals with clinical medicine and gives a detailed account of case-taking in the various diseases. There is a very useful chapter on the interpretation of X-rays and their use in diagnosis. There are a few chapters devoted to physiological normals, the body constants, gastric curves, illustrations of medical bacteriology, parasitology, entomology as also some laboratory data.

Part II deals with systemic medicine and gives a description of the various diseases. Many of the subjects are treated in a tabular form so as to be useful to the students. The photographs are very illustrative. The book gives much valuable information. We congratulate the author on the novel way in which he has treated the subject and on the amount of information that he has been able to compress in a little hand book. We have nothing but praise to offer.

U.K.R.

## BOOKS RECEIVED

**Radiology of the Alimentary Tract in Infancy**—By ROY ASTLEY, M.B., M.R.C.S., D.M.R., Pp. 287. M/s. Orient Longmans (Private) Ltd., 36a Mount Road, Madras 2. Price 50 sh.

**They Did Not Pass By**—By DENIS G. MURPHY, Pp. 208. M/s. Orient Longmans (Private) Ltd., 36a Mount Road, Madras 2. Price 10/6d.

**Indian Year-book of Ophthalmology, 1955**—By Dr. VAMAN D. SATHAYE, Pp. 234, plus supplement 36 pages. 592, Narayan Peth, Poona 2.

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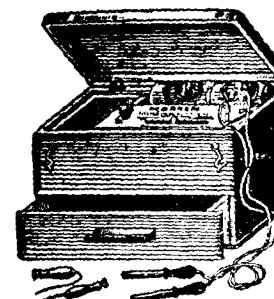
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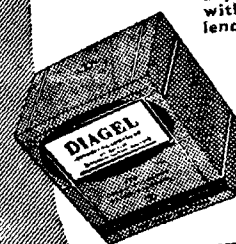
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| " oral 4oz. 2-8                        | 8-8 15-0 5gr x 1cc 100 amp           | A.G. Jap. Sup. 0-14 1-2 1-8 2-0 3-10   |                 |     |
| " B1 100mg 10cc 1-8; 50x20cc 8-12      | Aminophyllin 10 cc. 50 9-8; 10 2-4   | " ord. 0-12 0-14 1-2 1-8 2-10          |                 |     |
| " B1 & B6 10 cc. 50 mg.                | Calcium Gluconate 10%, 100amp        | Record 3-4 4-4 4-8 6-8 12-8            |                 |     |
| " B6 10cc. 50mg 2-6 100mg 4-4          | 50x10cc 10ly 7-8; 5cc 7-0; 10cc 9-0  | LuerLockBD 8-0 9-0 11-12 16-0 32-8     |                 |     |
| " B12 10cc. 100 mg 8-3;                | " Sandoz 5x10cc 5-8 10x5cc 8-12      | Jap Sup 1-8 2-4 2-12 4-8 6-8           |                 |     |
| " 200mg 4-8; 500mg x 5cc. 5-12         | " with Vit C 10x5cc 10-8             | Re. 1-0 more for side nozzle.          |                 |     |
| 1000 mg x 5cc. 9-14                    | " 5x10 cc 6-0; 50x5cc 47-0           | M. Casu Jap 2cc 2-25cc 3-2 10cc 4-2    |                 |     |
| " C 200 10A 1-2                        | Distill Water 100 amp 2cc 3-0        | Ind. 1-2 1-10 2-4 2-12 4-10            |                 |     |
| " C 5 cc 10 A 2-0; 50 A 9-8            | 5cc 3-12                             | 10-0 Lint 3-0;                         |                 |     |
| " D2 8x100 1-6                         | Emetine 1 gr 12A                     | 10-0 Needles Stainless Steel;          |                 |     |
| " E 6A 2-0; 10 cc. 1-10                | Irgapyrin 5A 7-8;                    | Eng. 3-4 Down 4-4 doz Record           |                 |     |
| " K 10A 1-8; 100A 11-12                | Milk with Iodine 5 cc 100,           | " 3-8 " 4-8 " All Glass                |                 |     |
| " AD 6 Amp. 3-0                        | Progesterone 10mg 50 10-0 6 1-8      | USA 5-0; Jap 1-8; B.D. 11-8            |                 |     |
| " A Tab. 100 4-8; 500 92-0             | 25 mg 2-2; 50 mg 3-12                | Thermometers 1min. Hicks 2-12          |                 |     |
| " AD " 100 1-10; 1000 12-8             | 10 cc 25 mg 2-4 10 mg 1-8            | Zeal Eng USA Jap. Ger. Flat            |                 |     |
| " ADE " 100 6-0; 500 27-12             | Liver Ext. TCF 10cc 2-8 B&C 3-6      | 30-12 19-8 19-8 9-0 9-0 11-8           |                 |     |
| " B Complex 100 1-5; 1000 5-0          | Normal Saline 100A 5cc 4-0           | Saline app. 300 7-8 500cc 8-8          |                 |     |
| " " forte 100 2-8; 1000 14-8           | Santonine M&B 3-8;                   | Abs. Gauge 20yd3-8 Erkameter 75-0      |                 |     |
| " " 8 forte 100 3-0 1000 22-8          | Redoxon 2cc 5 2-6; 50 16-10          | Ear or Glycerine Metal Syringe         |                 |     |
| " B1 10 mg 100 1-6; 1000 5-8           | Redoxon 5x5cc 4-0; 25x5cc 15-8       | 2oz 4-8 4oz. 5-8                       |                 |     |
| " " 25 mg 100 2-6;                     | Testosterone Prop. 6 Amp. 1cc        | F.L. or d 1-8 Sup. 2-12 doz.           |                 |     |
| " 100 mg 7-4 50mg x 100 3-0            | " 10mg 1-8; 25 mg 3-0; 50mg 3-14     | " Crocodyl finish 5-12 "               |                 |     |
| " C 50 mg 100 1-6; 1000 6-0            | " 25mg 100 20-12 50mg 50A 22-12      | " Stethoscope B.D. 25-8; Ger 9-0       |                 |     |
| " C 100mg 100 1-12; 1000 14-12         | " 10cc 25 mg. 3-0; 50 mg 5-0         | Wall Thermometer Jap. 1-8              |                 |     |
| " E 10 mg 25 1-6; 100 3-4              | Aminophyllin 100 1-6; 500 4-8        | Rubber Gloves Sup. pair 2-8            |                 |     |
| Folic Acid 15mg 10cc 2-4               | Aspirin Eng. 5-4; 1000 Ind. 3-10     | Artery Forcep 2-0 Scissors 1-8         |                 |     |
| INSULIN 10cc 20 IU 2-8 40 IU 4-8       | Camoquin 250; Strp 30-8 Pkt. 0-6-6   | Scalpel 1-0 Probe 0-6                  |                 |     |
| " P Zinc 10cc " 2-8 40 IU 4-10         | Calomel tab 1gr 100 1-0 1000 7-12    | Suture Needles St.C.&H.C. 6; 2-8       |                 |     |
| Atebrin Bayer 3 gr 25 A. 7-8           | Enterovioform 20 2-0; 100 8-12       | Scalpel Blades 6 Eng. Pkt. 1-12        |                 |     |
| Berlin 10cc 50mg 2-0; 100mg 2-8        | Ephedrine Hyd. 1gr 100 0-13 1000 4-6 | " Handle 3-12                          |                 |     |
| Penicillin G Cryst. Glaxo or Dames     | Iron Vit. B1 100 1-6; 500 5-12       | Tongue Depressor 1-0 folding 2-0       |                 |     |
| 2 5 10 laos.                           | Cibazol 20 1-10; 250 13-4            | Tooth Forcep Universal 3-14            |                 |     |
| 0-6-9 0-9-6 0-14-6                     | Influenza tab 1000 25-0; 100 3-8     | Aletis rio 15-0 Eng. 2-8               |                 |     |
| 0-7-6 0-10-9 1-0-6 Squibb              | Laxative Veg. 100 1-4 1000 7-8       | Pot. Bromide 3-6; Pot. Iodide 11-12    |                 |     |
| Procalne 20 laos 1-8-6 Gl 1-11-6       | Soda Mint 1000 1-6 How 4-0           | Silver Proteinate 1-2 Vitellin 2-0 2-2 |                 |     |
| 4 laos Pfizer 0-14-6 Rhodia 0-9-0      | Mepacrine 1000                       | Aspirin 3-10 Sod Salicylas 3-5         |                 |     |
| 4 laos Gl. 0-9-0 Ita 0-8-0 Sqb. 0-10-6 | Folic Acid 5mg 100 4-2 TCF 9-8       | Iodoform 2-0; Iodine Cryst 1-6 oz.     |                 |     |
| " 4 laos 30 laos. x 10cc 1-12          | Multivitamin 100 1-10 1000 11-0      | Calomel on 2-0 Yeastrite Tab. Lar 3-12 |                 |     |
| " tab. 12; 2 laos 2-2; 1 laos. 1-8     | Oralin 50 tab 9-4 Merles AFD 30-0    | Plastic Bag 12" 5-12                   |                 |     |
| " Oint doz. Eye 3-10 Skin 7-2          | Paludrin 1000 1 g 23-0 3 g 52-8      | Stethoscope Bag Plastic 1-4            |                 |     |
| " Lozenges 100 2-2 20 0-13             | Penobarbites Tab. 1 1/2 gr. 100 1-4  | Fountain Pen Torch Lamp. 3-0           |                 |     |
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| STREPTO-PENICILLIN DMX 1/2 G 1-1-6     | Saridon 10 1-1; 250 23-14            | Empty Gelatin Capsules:—               |                 |     |
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| " Dihydrostrepto 1gm. 0 14-6           | Sulphanilamide Powder 4-8            | 100 1-8 1-8 1-8 1-8                    |                 |     |
| Streptomycin 1 g. Pfizer 1-5-0         | " Guinadine 1000 10-8 500 5-6        | 1000 8-12 8-12 8-12 8-12               |                 |     |
| Italy 0-13 6; Gl. 0-15-9 USA 0-15-6    | " Boots 500                          | Temperature Charts 4 Hour 100 2-8      |                 |     |
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| Chloromycin Kap 11-6; Liq 10-10        | " Thiazol 500 Ind. 8-0 Boots 15-14   | Emetin Hyd. 1/2 gr. 12 H.T. 3-14       |                 |     |
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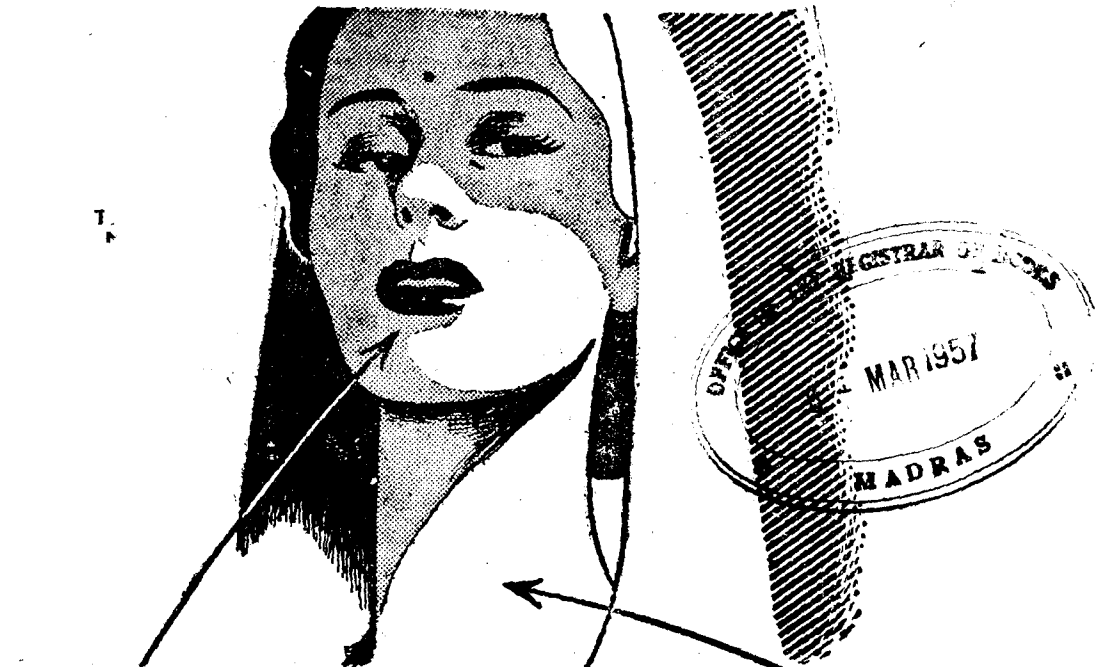
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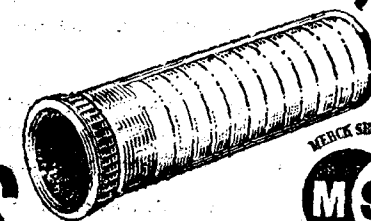
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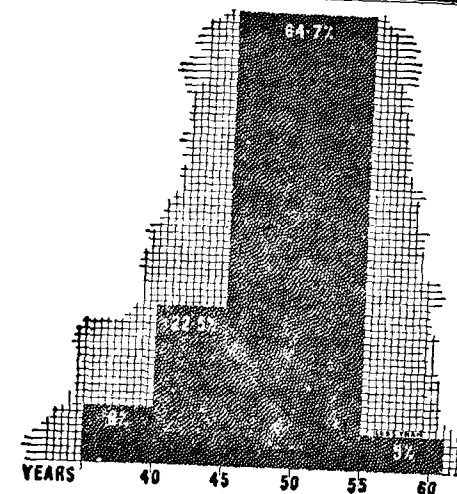
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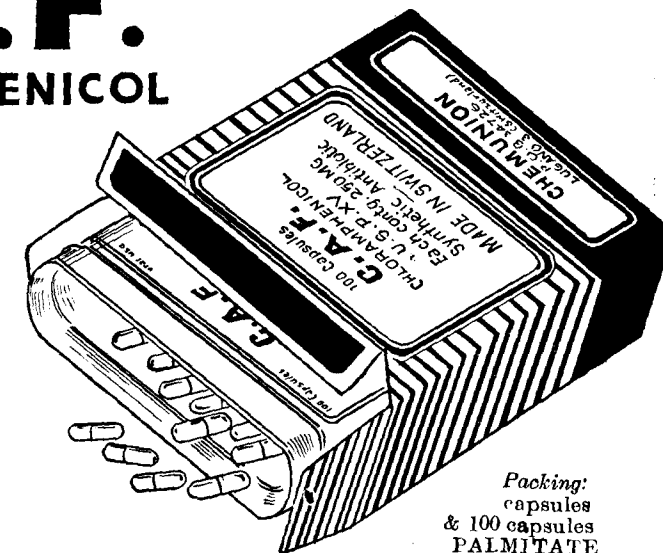
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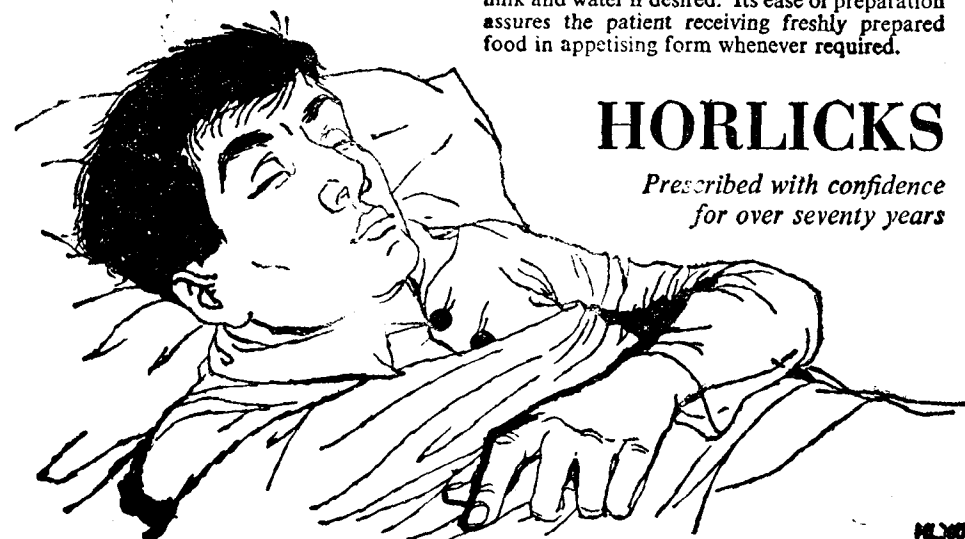
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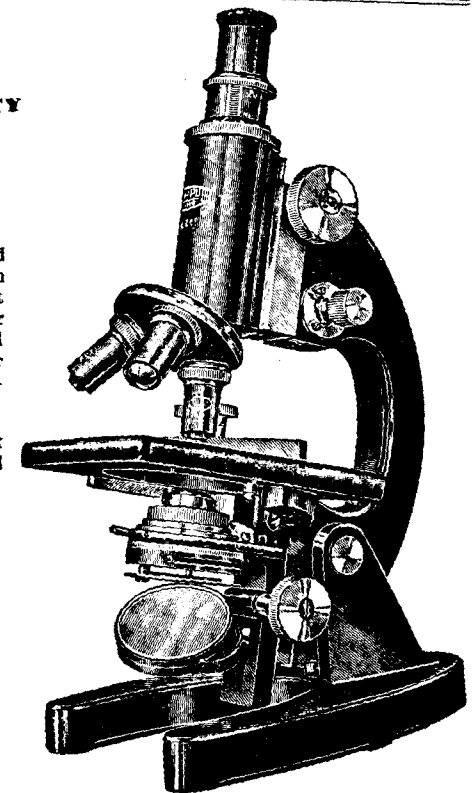
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|                            | INJECTION<br>Each 2 cc. amp.<br>supplies | TABLET<br>Each tablet<br>supplies | DROPS<br>Each cc. amp.<br>supplies |
|----------------------------|------------------------------------------|-----------------------------------|------------------------------------|
| Vitamin A                  | 8000 I.U.                                | 4000 U.S.P. Units                 | 8000 I.U.                          |
| Vitamin D                  | 1000 I.U.                                | 400 U.S.P. Units                  | 1600 I.U.                          |
| Vitamin E                  | 0.5 mg.                                  | 1 mg.                             | 0.1 mg.                            |
| Vitamin B <sub>1</sub>     | 5 mg.                                    | 4 mg.                             | 2 mg.                              |
| Vitamin B <sub>2</sub>     | 0.5 mg.                                  | 2 mg.                             | 1 mg.                              |
| Vitamin B <sub>6</sub>     | 3 mg.                                    | 1 mg.                             | 0.5 mg.                            |
| Pantoic acid               | 4 mg.                                    | 3 mg.                             | 4 mg.                              |
| Niacinamide                | 20 mg.                                   | 10 mg.                            | 20 mg.                             |
| Choline Dihydrogen Citrate | 2 mg.                                    | 2.5 mg.                           | 2 mg.                              |
| Vitamin C                  | 60 mg.                                   | 30 mg.                            | 60 mg.                             |
| Ascorbic Acid              | —                                        | —                                 | 1 mg.                              |
|                            | 6.15 mg.                                 | —                                 | —                                  |

In packs of  
4, 12 & 50

In packs of  
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tablets

In packs of  
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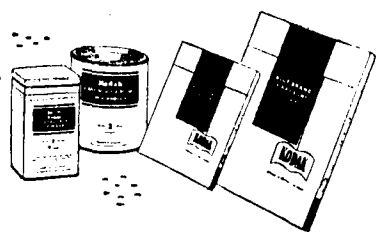
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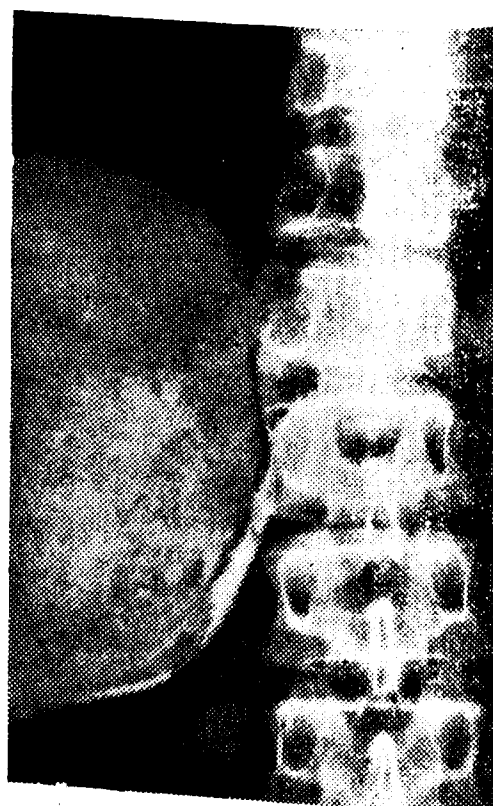
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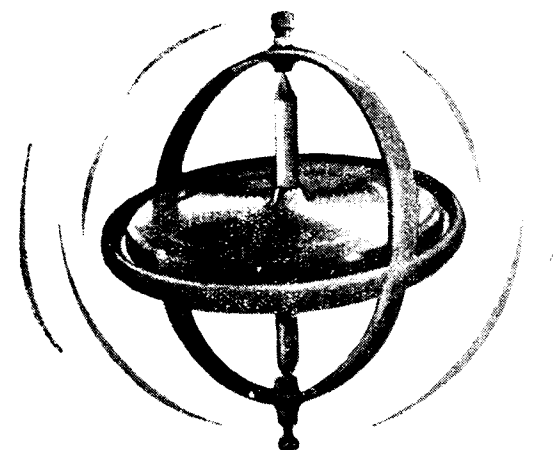
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**IN AUTONOMIC NERVOUS DISORDERS**

# Priscophen

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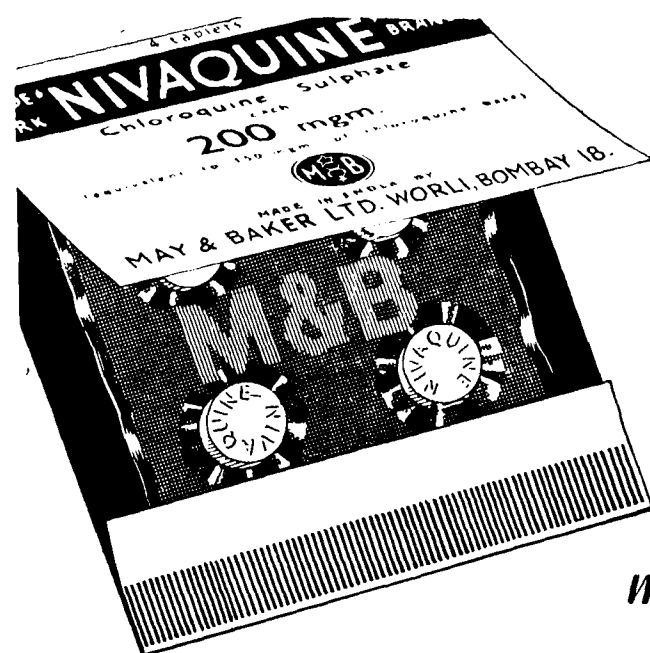


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**Indications:** Cardiac neuroses, palpitations, menopausal disturbances, fatigue, nervous instability, spastic constipation, nervous diarrhoea, travel sickness, insomnia due to over work, vascular headaches, excessive sweating and other disturbances of the autonomic nervous system.

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TABLETS OF CHLOROQUINE SULPHATE

the most rapidly effective of all antimalarials

A single dose of 4 'Nivaquine' tablets will usually control the acute malarial attack in semi-immunes within 24 hours.

PRESENTATIONS: 200 mgm. tablets (each containing the equivalent of 150 mgm. chloroquine base)  
Solution for injection in 5 c.c. ampoules (each containing the equivalent of 200 mgm. chloroquine base)



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yet another aid in fighting  
Nutritional Anæmias —

T.C.F.  
**HÆMATINIC  
LIVER  
CAPSULES**

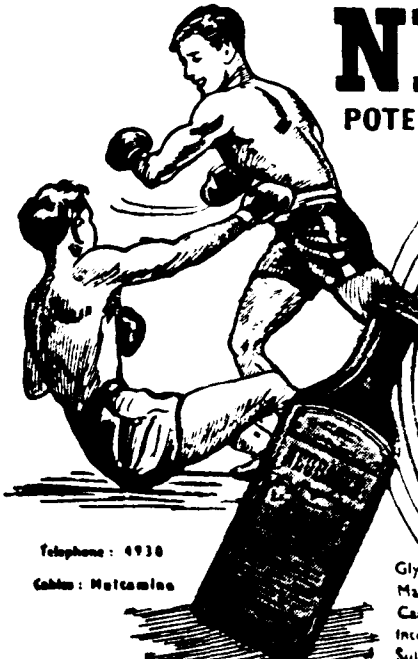
A STANDARDISED, potent  
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therapy for all nutritional anaemias.

MAIN INDICATIONS:  
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and tins of  
500 capsules

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FOR OVER **80** YEARS  
*Prescribed With Confidence  
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WITH OR WITHOUT DILUTION IN 2 OZS. & 10 OZS. BOTTLES.

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Dear Doctor,  
Is there an effective medicine for colics and vomiting in Babies? Can serious surgery be avoided in Pylorostenosis? Yes, by using.

## MYDRINDON FOR BABIES

Atropine Methylnitrate 1.10 mg. per tablet.  
in all cases of vomiting, colics, Pylorospasms and Pylorostenosis. Used by many since 15 years and respected by all who know about it. Easy to administer as every tablet represents a single effective dose. Tablets for Babies are now marked 'B'.

We also manufacture tablets of 1 mg. each for Adults now marked 'A' for Gastric and Intestinal spasms and ulcers.

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IT affords the most speedy relief yet known to Medical Science.



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## Bring the Bael to carry the Quin\*

★ IODO-CHLORO-OXYQUINOLINE to you!



The picture tells a story - the story of a new formula for the effective treatment of amoebic and bacillary dysenteries. The 'Quin' (Iodo-chloro-Oxyquinoline) is always in a hurry. It rushes through the intestinal tract and achieves very little by itself. The Standard Pharmaceutical Works have introduced Bael which forces the 'Quin' to travel very, very slowly. This ensures intimate contact of this drug with all parts of the gut. Known as *Sulpha-Quino-Bael*, this formula (see details below) provides maximum amoebicidal and bacteriostatic effect.

Each spoonful measure, as supplied inside each carton, contains:

|                          |   |       |    |
|--------------------------|---|-------|----|
| Sulphanamide             | — | 0.067 | gm |
| Sulphathiazole           | — | 0.067 | gm |
| Sulphaguanidine          | — | 0.067 | gm |
| Iodo-chloro-Oxyquinoline | — | 0.2   | gm |
| Baked Bael Powder        | — | 1.1   | gm |
| Isaphgul Powder          | — | 0.2   | gm |
| Magnesium Carbonate      | — | 0.2   | gm |

## SULPHA QUINO BAEL

Now available in Granules

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PSSQ 1



## IRON AND MOTHERHOOD

Throughout the reproductive life of a woman, there is constant drain on her iron-reserves. The demands of pregnancy and lactation, and the haemoglobin losses of menstruation and parturition, render the women especially liable to anaemia. With 'Plastules', adequate iron dosage may be administered with utmost therapeutic advantage. The inclusion of vitamin B<sub>12</sub>, folic acid, liver extract and yeast, corrects any concomitant deficiency of these important haemopoietic factors.



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Wyeth

Available in four combinations

- ★ Plain
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Packing: Bottles of 30 and 300 capsules

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METHEONINE CHOLINE INOSITOL

*to reduce fatty liver*

KIM plays an important part in the metabolism of fat. It reverses the fatty infiltration by migration of excess liver fat to the normal fat depots of the body and lowers Serum Cholesterol by excreting the excess amount with the urine.

**SYRUP**

**PLAIN AND FORTE**

Bottle of 2 oz., 4 oz., and 1 lb.

**AMPOULES**

2.5 cc x 5 and 2.5 cc x 50

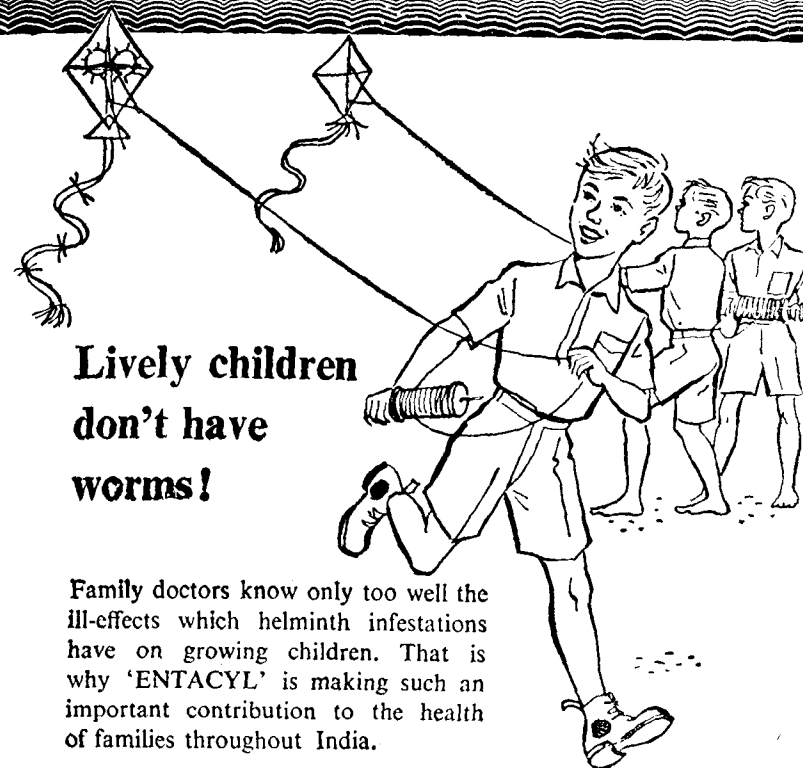
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**DI-METHIONIN** (d, l- Methionine)  
TABLETS AND AMPOULES

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Manufactured by  
**DEY'S MEDICAL STORES PRIVATE LTD.**  
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C.P.B. D.M. KIM-2-50.



**Lively children  
don't have  
worms!**

Family doctors know only too well the ill-effects which helminth infestations have on growing children. That is why 'ENTACYL' is making such an important contribution to the health of families throughout India.

*Available in two forms:*

'ENTACYL' Tablets for adults and older children

'ENTACYL' Suspension for infants and young children

*Dosage Schedule:*

**Threadworms and whipworms:**—  
1 tablet (or ¼ teaspoonful) per year of age per day up to the age of 6 years. Over 6 years of age 2 tablets (or 1 teaspoonful) three times a day. The dosage should be given from 3 to 7 days.

*One-day treatment for round-*

*worms:* 2 ¼ tablets (or 1 ¼ teaspoonfuls) per year of age up to the age of 6 years. For adults and children over 6 years, give a total dosage of 15 tablets (or 7 ¼ teaspoonfuls). The dosage should be given in a single dose or in four divided amounts during one day.

**'ENTACYL'** TRADE MARK

Tablets: Bottles of 25 and 100

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WANDER

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for the symptomatic treatment of  
BRONCHIAL ASTHMA

Combines the sedative action of allobarbitone  
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the spasmolytic action of ephedrine and xanthine  
derivatives

while extr. of Ipecacuanha improves expectoration

Tubes of 20 tablets.

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119

Cardiac specialities of preference:

## Angosedine

Coronary affections

Each dragee contains:

|                              |          |
|------------------------------|----------|
| Dihydroxypropyltheophyllinum | 100 mg.  |
| Triturate of perithrol       | 12.5 mg. |
| Adiphenine hydrochloride     | 15 mg.   |
| Phenobarbital                | 15 mg.   |
| Extract of valerian          | 30 mg.   |
| Caffeine                     | 50 mg.   |

One dragee thrice a day after meals.

## Neurocardine

Functional disorders

Each dragee contains:

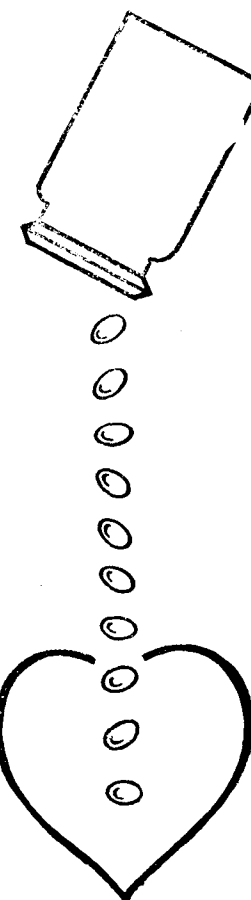
|                       |        |
|-----------------------|--------|
| Quinine hydrobromide  | 50 mg. |
| Extract of crataegus  | 30 mg. |
| Extract of valerian   | 30 mg. |
| Extract of belladonna | 5 mg.  |
| Phenobarbital         | 15 mg. |

One dragee thrice a day after meals.

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# a **NEW** penicillin

## an important advance in ORAL PENICILLIN THERAPY

In 'DISTAQUAINE' V TABLETS, DC (B) L introduce a new acid-stable form of penicillin which, for the first time, puts oral penicillin therapy on a firm basis comparable with parenteral administration.

Unaffected by the gastric acid of the individual patient, the new preparation produces consistent and reliable blood levels and thus extends significantly the use of oral penicillin therapy to a large number of serious infections.

'DISTAQUAINE' V TABLETS offer the following advantages over existing oral penicillin preparations:

- Unaffected by gastric acidity
- Rapid absorption
- Consistent and prolonged blood levels

### Packings:

60 mg. tablets: Bottle of 30

**'Distaquaine' V**

trade mark

brand

PHENOXYMETHYLPENICILLIN

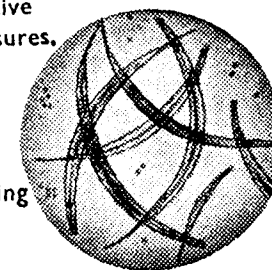
Manufactured by  
THE DISTILLERS COMPANY (BIOCHEMICALS) LIMITED, LONDON

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## Children like it... worms don't

One week's treatment with 'Antepar' Elixir is usually sufficient to eradicate threadworms. A single dose clears roundworms from the gut. Effective without fasting, purging or supporting measures. 'Antepar' acts by paralysing the worms—they are then expelled by normal peristalsis. 'Antepar', the original elixir of piperazine, is well tolerated by patients of all ages. Its pleasant taste is popular with children. Containing piperazine citrate equivalent to 500 mgm. of piperazine in each fluid drachm, 'Antepar' is supplied in bottles of 1 fl. oz., 3 fl. oz. & 16 fl. oz.



**'ANTEPAR'** Brand **ELIXIR**

BURROUGHS WELLCOME & CO. (INDIA) PRIVATE LTD.



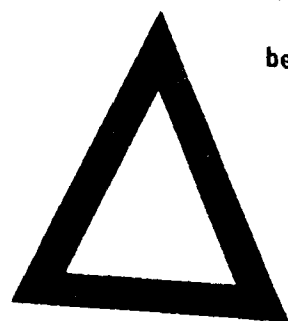
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Recent advance in anti-inflammatory  
adrenal corticotherapy

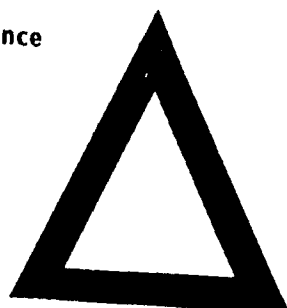
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Ensures  
regularity of action  
and  
better tolerance



**Delta -  
Cortisone**  
(PREDNISONE 2.5 mg.)

Rheumatology  
Allergies  
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(PREDNISOLONE 2.5 mg.)

5 mg. tablets according to the formula:  
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Delta-Hydrocortisone.....2.5 mg.  
VIALS OF 10 & 20 TABLETS

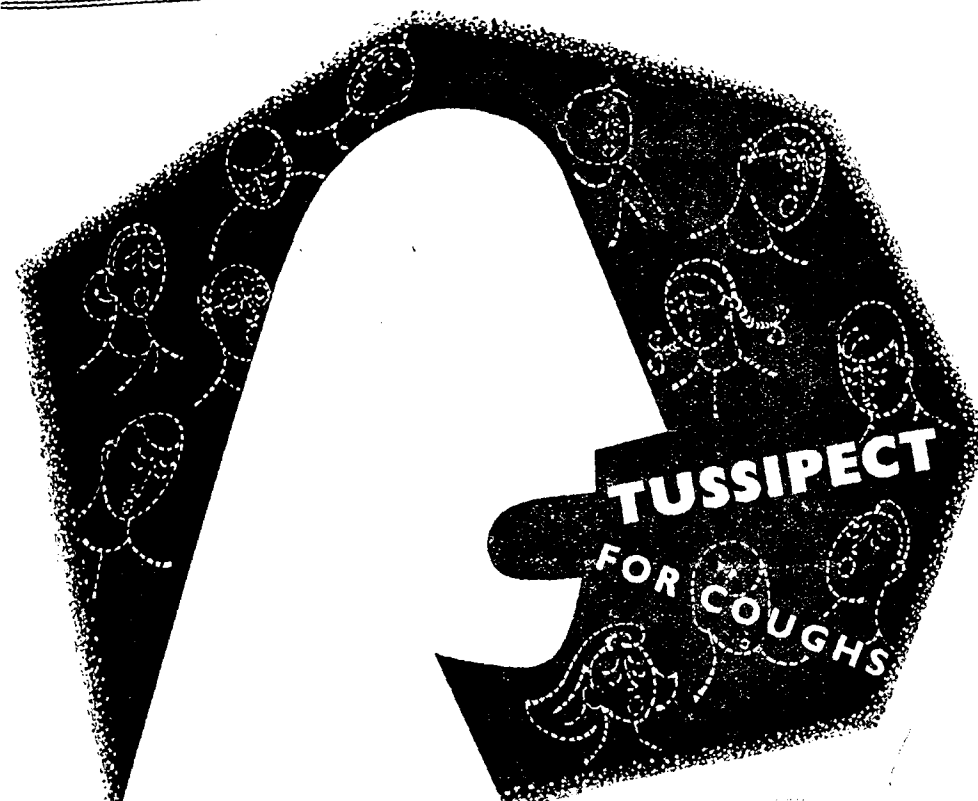
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(Prednisone)  
Vials of 15 tablets of 5 mg.  
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Laboratoires Français De Chimiothérapie  
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- \* Soothes cough.
- \* Alleviates respiratory distress.
- \* Facilitates expectoration.
- \* Increases resistance to infection.
- \* Possesses antispasmodic, antiseptic and healing properties of a high order.
- \* Well tolerated by invalids and children.

ORIGINAL  
*Beiersdorf*  
PRODUCT



**PARRY & CO., LTD.**

MADRAS · BOMBAY · CALCUTTA · NEW DELHI.



HERE  
IS  
HEALTH  
FOR  
YOUR  
BABIES!

### NAUNEHAL BABY TONIC

Useful in the following  
diseases of Children

GENERAL DEBILITY, INFANTILE  
TUBERCULOSIS, RICKETS,  
INFLAMMATION OF GUMS,  
WEAKNESS DURING CONVALE-  
SCENCE, PELLAGRA, ARTHRITIS,  
INFLAMMATION OF MOUTH,  
COLDS & CATARRH.

#### FORMULA

Each dose of 4-5 c.c. (approx.  
one teaspoonful) contains:

|                               |                |
|-------------------------------|----------------|
| Vitamin A                     | ... 2000 I. U. |
| Vitamin B1                    | ... 0.4 mg.    |
| Vitamin B2                    | ... 0.6 mg.    |
| Niacinamide                   | ... 5 mg.      |
| Vitamin C                     | ... 20 mg.     |
| Vitamin D2                    | ... 500 I. U.  |
| Calcium Glycero-<br>phosphate | ... 0.5 gr.    |
| Sodium Glycero-<br>phosphate  | ... 0.25 gr.   |
| Sucrose                       | q.s.           |

**NAUNEHAL**  
THE RICHEST TONIC FOR BABIES

**Hamdard**

DAWAKHANA (TRUST) DELHI

### NAUNEHAL GRIPE SYRUP

Useful in the following  
diseases of Children

CONSTIPATION, INDIGESTION,  
FLATULENCE, DIARRHOEA,  
DYSENTERY, TEETHING,  
ENLARGEMENT OF LIVER &  
SPLEEN, DISTURBED SLEEP,  
INFLAMMATION OF MOUTH,  
SALIVATION, ROUND WORMS  
& OTHER WORMS, EXCESSIVE  
THIRST.

#### FORMULA

Each dose of 4-5 c.c. (approx.  
one teaspoonful) contains:-

|                             |            |
|-----------------------------|------------|
| Aqua Pudina Destil-<br>lata | .. 3 min.  |
| Aqua Zira Destillata        | 3 min.     |
| Conc. Anisi Water           | .. 1 min.  |
| Aqua Anethi Conc.           | ... 1 min. |
| Aqua Menth. Pip             | ... 1 min. |
| Soda Bicarb                 | ... 2 gr.  |
| Sodii Bromidum              | ... 1 gr.  |
| Spt. Ammonia Aromat         | 1 min.     |
| Spt. Chloroformi            | ... 1 min. |
| Sucrose                     | q.s.       |



*Never a  
moment's  
worry  
although he is not  
breast-fed*

For the child who cannot be breast fed,  
Lactogen has earned a world-wide reputation as a  
safe and reliable substitute.

Prepared to resemble as closely as possible the  
formula of breast milk, it offers a well balanced and  
strictly uniform diet. By homogenization, the fat  
globules are made even smaller than those of human  
milk, facilitating digestion, while pasteurization has  
ensured the removal of pathogenic organisms.

Lactogen is also suitably fortified to  
provide adequate (but not excessive)  
intake of essential Vitamins A & D  
& Iron, based on standards recom-  
mended by the National Research  
Council, Washington.



**LACTOGEN**

*The better milk for babies*

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P.O. Box 396 Calcutta, P.O. Box 315 Bombay, P.O. Box 180 Madras

to suit your tiniest patient

# Ilotycin Drops

(Erythromycin) Ethyl Carbonate, Crystalline

*with an unexcelled antibiotic spectrum*

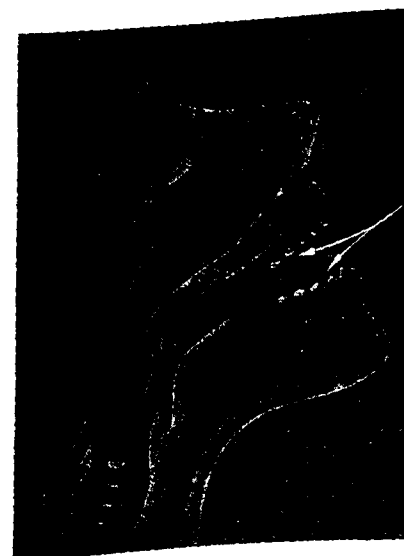
Bacterial pathogens of the respiratory tract are rapidly destroyed by the bactericidal action of 'Ilotycin.' The response is decisive and quick.

'Ilotycin' is notably safe and well tolerated. Because the coliform bacilli are resistant to the action of 'Ilotycin' the bacterial balance of the intestine is seldom disturbed. Staphylococcal superinfection of the intestine, avitaminosis and moniliasis, are not encountered.

The safety, efficacy, and convenience of this 'Ilotycin' preparation make it ideal for the treatment of respiratory infections in the infant.

*Appeals to baby for its taste-tested flavor.*

ELI LILLY AND COMPANY OF INDIA, INC.  
(Incorporated in the U.S.A. the liability of the members being limited)  
P. O. BOX 1971, BOMBAY-1.



*Concerning  
a further advance  
in the treatment of  
bucco-pharyngeal  
INFECTIONS*

Dequadin Lozenges containing a new bactericidal and fungicidal substance are rapidly effective against all the common oral pathogens including those resistant to penicillin. They do not contain any antibiotic or anaesthetic substance.

Dequadin Lozenges are indicated in the treatment of Vincent's angina, tonsillitis, sore throat, stomatitis, pyorrhœa, pharyngitis, aphthous ulcers, thrush and glossitis.

They can be used prophylactically in patients exposed to infection especially after tonsillectomy and dental extractions.

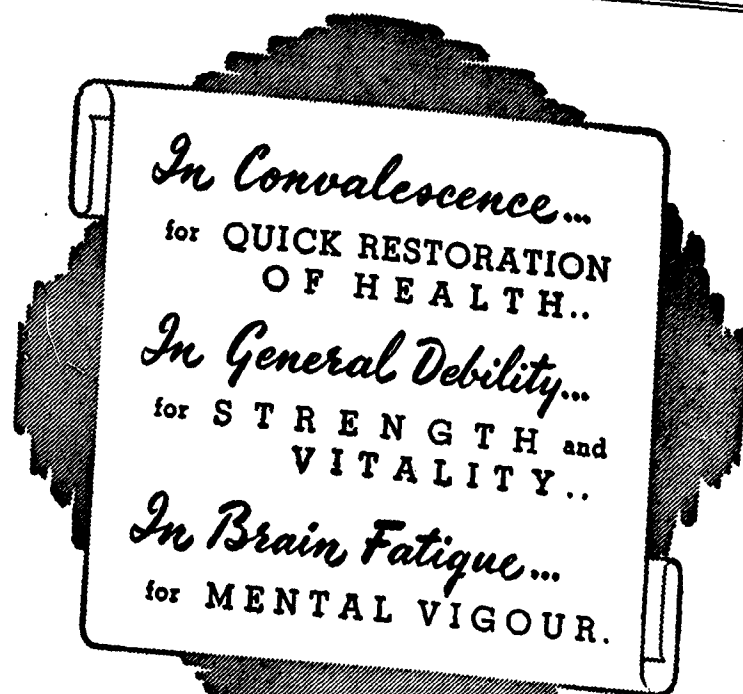
By suppressing monilial growths, Dequadin Lozenges prevent the appearance of black tongue and oral thrush. They are also rapidly effective in the treatment of oral thrush including that due to prolonged antibiotic therapy.

## DEQUADIN LOZENGES

In tubes of 20 lozenges each containing  
0.25 mg. decamethylene-bis (4-aminoquinolindinium chloride).

086/408/X

ALLEN & HANBURYS LTD  
(INCORPORATED IN ENGLAND: THE LIABILITY OF THE MEMBERS OF THE COMPANY IS LIMITED)  
CALCUTTA BOMBAY



Prescribe  
**PHOSPHOTON**  
CIPLA

The combination of Vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub> and Niacin with Extract Cola, Arrhenal, Glycerophosphates and Glutamic Acid makes Phosphoton an ideal tonic and restorative in all cases of General Debility. Glutamic Acid is well known as a brain food having regenerative effect on the central nervous system and the cerebral cortex. Phosphoton is recommended in deficiency diseases, weakness following Malaria, Influenza and other exhausting illnesses, physical exertion, mental fatigue and in operative surgery and pregnancy.



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Periods of Stress & Strain etc.

**Bivinal Forte**

With Vitamin C

(Vitamin B complex with Vitamin C)

COMPOSITION:

Each capsule contains:-

|                                          |    |         |
|------------------------------------------|----|---------|
| Vitamin B <sub>1</sub> B.P.              | .. | 10 mg.  |
| Vitamin B <sub>2</sub> (Riboflavin B.P.) | .. | 10 mg.  |
| Vitamin B <sub>6</sub> B.P.C.            | .. | 5 mg.   |
| Niacinamide B.P.                         | .. | 50 mg.  |
| Calcium Pantothenate U.S.P.              | .. | 25 mg.  |
| Vitamin C B.P.                           | .. | 150 mg. |

You can put  
your confidence  
in Alembic.

ALEMBIC CHEMICAL WORKS CO. LTD.,  
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**HEPATIC DISORDERS**

Hepatic disorders often lead to metabolic disturbances which may be corrected by supplementing specific therapy with methionine as it is the most essential amino acid for regeneration of liver parenchyma. 'Meonine'® brand di-methionine is recommended for the treatment of fatty liver, cirrhosis and toxic hepatitis. It is a useful adjuvant in the management of infectious hepatitis including amoebiasis, in burns and for administration during convalescence after acute infection and surgery.

**Meonine**

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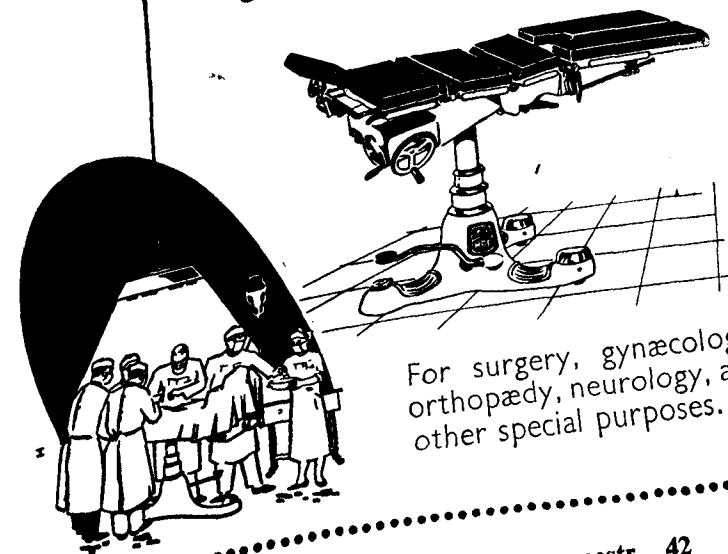
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## OPERATION - TABLES

OPERATING-TABLES

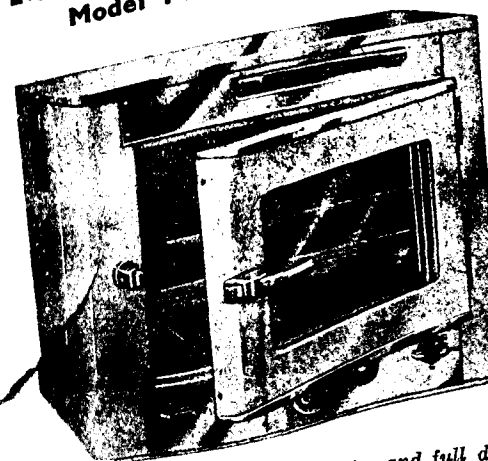


For surgery, gynæcology, orthopædy, neurology, and other special purposes.

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Model TV-10, for Sterilising, Drying and Incubating

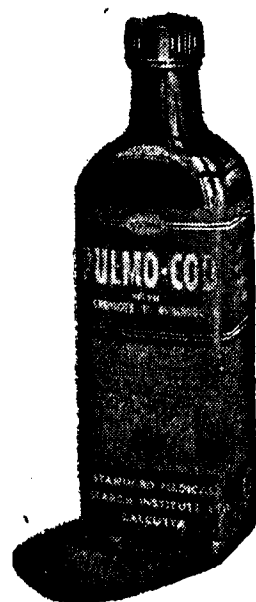


Automatic Temperature control without contact points and without relays. Its sensitive, yet sturdy, thermostat permits control within 0.5°C of the average temperature.

Electrically heated with Memmert - black - heating elements (5 years guarantee). For use on 110 volts or 220 volts AC/DC. Rapidly heating up and uniform penetration to all parts of the loaded chamber.

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*Nutritive Aid*  
In Case of Malnutrition and  
Wasting Diseases

## PULMO-COD

WITH  
**Creosote & Gualacol**

Supplies  
Minerals and generous amount of Vitamins

**For Vigour and Vitality**

Pulmo-cod also prevents Seasonal Ailments,  
Cold, Cough, Bronchitis, Rickets, Summer  
Complaints, and Bowel Irregularities  
among Children

### STADMED PULMO-COD (Creosote & Gualacol)

Each fluid oz. contains:  
Pancreatic hydrolysate  
of shark & Codliver Oil  
50% v/v

|                         |              |
|-------------------------|--------------|
| Vitamin A               | 4500 I. U.   |
| Vitamin D               | 1000-0 I. U. |
| Vitamin B <sub>1</sub>  | 3 mg.        |
| Vitamin B <sub>2</sub>  | 2 mg.        |
| Vitamin B <sub>12</sub> | 5-0 mcg.     |
| Nicotinic Acid          | 40 mg.       |
| Folic Acid              | 920 mcg.     |
| Sodi Hypo.              | 120 mg.      |
| Potassi Hypo.           | 120 mg.      |
| Calcii Hypo.            | 240 mg.      |

|            |         |
|------------|---------|
| { Creosote | 1 1/3 % |
| { Gualacol | 1 %     |

Extract Wild Cherry,  
Gentian, Eucalypt. 8.7%  
Invert Sugar, Glycerine,  
Malt & Aromatics q.s.

STADMED PRIVATE LTD.  
15, JAWPORE ROAD,  
CALCUTTA-30.

Mg L. No. DL 62 M  
DL 42 MB

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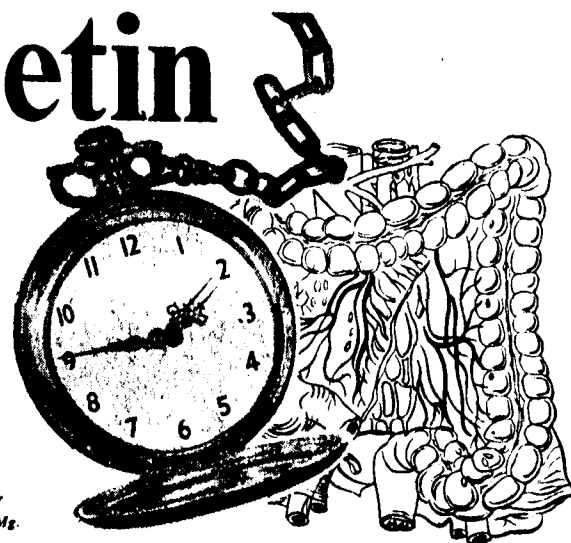
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Where Chloramphenicol is indicated doctors  
prescribe BIDRACETIN with confidence: for  
BIDRACETIN is a product of research and  
its broad antibacterial spectrum activity  
makes it the Antibiotic of choice, not merely  
in the treatment of typhus, but of many  
common infections as well. Besides, BID-  
RACETIN has the following plus factors:

- Clinical efficacy
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- Most effective by mouth.



Available in bottles of  
12 & 100 caps. of 250 Mg.

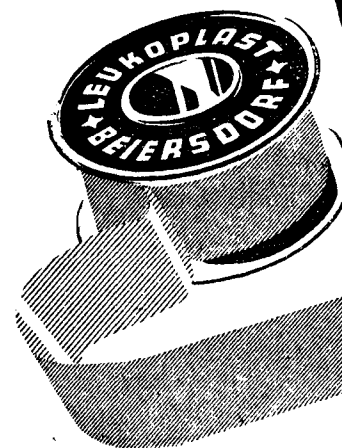


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The most useful and reliable all purpose zinc oxide adhesive  
plaster for hospital and medical use:  
is water-repellent  
possesses excellent adhesive properties  
is unaffected by long storage in the tropics  
is perfectly tolerated by normally sensitive skin

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Sole Agents for India:  
PARRY & CO. LTD. MADRAS - CALCUTTA - BOMBAY - NEW DELHI

A-E196



**Leukolastic Adhesive Bandage**  
extremely pliant, soft, and adaptable to contours of the body  
possesses excellent adhesive and keeping properties  
supplied with adhesive coating externally  
compression can be adjusted and localized easily  
provides a firm support and greatly reduces the pain

## LEUKOLASTIC

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**BETTER HEALTHY LOOK..**



**Loma**  
REGD.

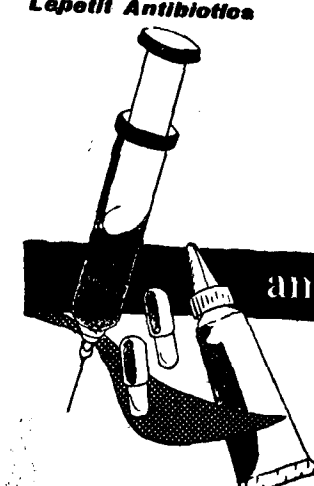
**DARKENS GREY HAIR**

...KEEPS THE GRAY COME  
...GROWS MORE DARK  
...REMOVES DANDRUFF & ITCH  
...SMELLS SWEETER



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Agents: S. NARAYAN & CO., BOMBAY - 2.

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the new broad spectrum antibiotic of widest clinical use and rapid and certain action even where other antibiotics fail

**ambramycin**

Lepetit  
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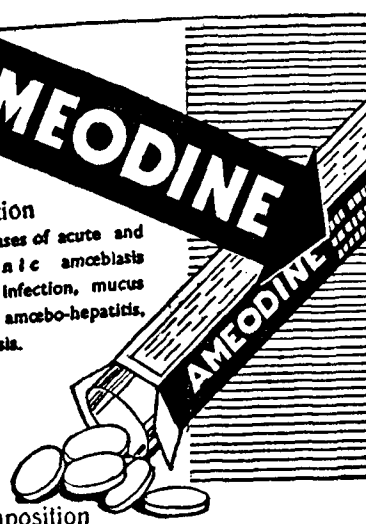
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capsules-syrup  
for injection-intramuscular  
ophthalmic ointment

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BRANCHES: BOMBAY, CALCUTTA, MADRAS, DELHI, KANPUR.

**AMEODINE**

**Indication**  
In all cases of acute and chronic amoebiasis mixed infection, mucus colitis amoebic-hepatitis, giardiasis.



**Composition**  
Each Tab. Contains -  
Iodochlorohydroxyquinoline 25 gm.  
Chloroquin Diphosphate 100 mgm.  
Ext. Belladonna Siccum 20 mgm. Vitamin B<sub>1</sub> 3 mgm. Vitamin B<sub>2</sub> 1 mgm. Vitamin C 25 mgm.

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**cough & cold!**

THE RATIONAL  
COUGH SYRUP  
WITH OR  
WITHOUT  
CODEINE  
& EPHE-  
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GUMARESH HOUSE SALKIA HOWRAH

## VITA-COD-CO

VITA-COD-CO contains products of Cod liver oil, Spleen, Liver and Pancreas with Vitamins and Minerals. These essential ingredients assist in rapidly reconstructing the body to normal. Vita-cod-co is of special value in lung affections.

PACKING :

Bottles of 8 fluid ounces

T'PHONE :  
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T'GRAM :  
'BENZOIC'  
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THIS INJURED ARM IS PROTECTED BY A DALMAS ELASTIC WOUND DRESSING WHICH GIVES SECURITY AGAINST OUTSIDE INFECTION AND CONTAMINATION

## DALMAS PRODUCTS

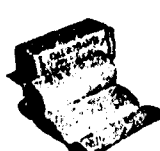
Dalmas Elastic Dressings are prepared under hygienic conditions. They reduce danger of secondary infection. Always keep Dalmas elastic dressings handy—they are an invaluable aid to rapid healing, easy to apply and perfect in protection.



**DALZO**—Dalzo Zinc Oxide plasters have proved their efficiency throughout the world. They are hygienically safe and fully antiseptic. Available in 10 yd. and 5 yd. spools, widths  $\frac{1}{2}$  in. to 4 in. and  $\frac{3}{4}$  yd. and 1 yd. spools, widths  $\frac{1}{2}$  in. and 1 in.



**DALZOFLEX BANDAGES AND DALZOFLEX STRAPPING.** For the ambulatory treatment of ulcerated legs there is no safer dressing than Dalzoflex Bandage. The strapping is recommended for securing abdominal dressings in situ. Available in 1 and 3 yd. spools. Widths from  $\frac{1}{2}$  in. to 4 in.



**DALZOBAND BANDAGES** (5 medications). An Unna's zinc paste type bandage which is always moist. Wound loosely round the affected part and covered with a Dalzoflex bandage applied spirally. size, 6 yds. x  $\frac{3}{4}$  in. Medications include Zinc Oxide, Ichthammol, Urethane, Calamine or Coal Tar.



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**DALMAS**  
Manufacturers of Medical and Surgical  
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## In Case of Diabetes DIAMELIN

will be found extraordinarily effective

Composed of:

Hyd. Prep., Stan Prep., Ferri Sesquiox.,  
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\* **DIAMELIN** is presented after prolonged experiments. It aims at not only correcting the defects of pancreas but also of the liver, nervous system, kidneys, and ductless glands which of late are also considered to be causative factors of diabetes.

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Available in packing of 50 tablets at all leading chemists @ Rs. 5-12-0 per phial.

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of quality

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A New ORAL  
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# ANAZID

(The molecular compound of P. A. S. and I.N.H.)

Indicated in early as well as chronic and resistant cases and effective in doses of 600 mgm. per day.

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Gram: 'SULFACYL'

**COMPOSITION:**  
Each Fluid Ounce  
Contains:  
Vitamin A Vitamin D  
Vitamin B<sub>1</sub> Vitamin B<sub>2</sub>

**INDICATIONS:**  
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Growing  
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nutrition (3)  
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Lactation (4)  
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Tablet  
**R.COMPOUND**  
For Arthritis, Rheumatism, Gout, &  
Allied Disorders.

Tablet  
**LEPTADEN**  
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**FAMOUS FOR OVER  
FIFTY-FIVE YEARS**  
To Regulate and Restore  
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OF THE UTERUS

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for ladies

**CONTAINS**  
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Packings: 12 oz. & 6 oz.

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is considered today by the Government and the serious minded people as India's greatest need, to raise the living standard of every common man.

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have a high degree of simplicity, dependability and acceptability.

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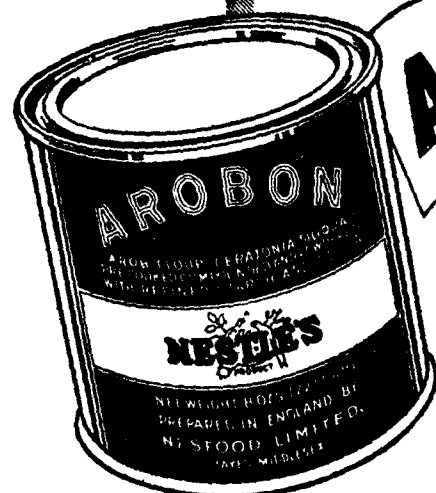
Kindly send 10% in advance along with order by Money Order or Demand Draft payable at Madras.

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For treating acute or chronic diarrhoea



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Proved highly effective for diarrhoeic and gastro-intestinal disorders amongst infants, children and adults.

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PROVED TO BE A DEPENDABLE REMEDY THROUGH YEARS OF CLINICAL TESTS.

PLEASE CHECK UP THE NEW SCREW CAP ON QUMARESH PHIALS.

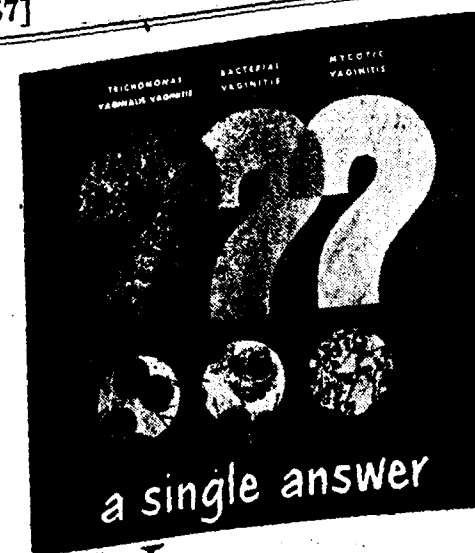
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for  
Liver  
and  
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a broad spectrum agent, free from arsenicals and mercurials, offers a suitable therapy in a safe, comfortable to use quickly soluble gelatine capsule. It's inexpensive too.

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for all types of  
anaemias which  
respond to liver  
therapy

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INTRAMUSCULAR

Parenteral

to be supplemented with  
**Elixir FOLEX-XII**

Each c. c. contains:

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|----------------------------------------------|---------|----------------------|--------|
| Liver extract deviled from 10 gms. of Liver. | 50 mg.  | Betain HCl           | 50 mg. |
| Vitamin B12                                  | 50 mcg. | Benzyl Alcohol       | 2.5 %  |
| Folic Acid                                   | 5 mg.   | Preservative: Phenol | 0.5 %  |
| Niacinamide                                  | 100 mg. |                      |        |

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**ZYMOTONE**Delightfully flavoured  
digestive and nutritive tonic

Contains:

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4 oz., 8 oz., &amp; 16 oz. Phials.

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IMPAIRED LIVER

Prescribe

**MECHOL**

A Combination of Methionine,  
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Vitamin B<sub>12</sub>

Reinforced with:—

DIASTASE &amp; PEPSIN

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Ointment

For

Dry Eczema, Psoriasis, Ring-worm  
or any dry and scaling type of  
skin-diseases.

ANTIFUNGAL  
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KERATOLYTIC.

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A UTERINE TONIC AND SEDATIVE

Each fluid ounce contains:—

|                          |           |
|--------------------------|-----------|
| Calcium Lactate          | — 15 Gra. |
| Potassium Bromide        | — 15 "    |
| Ext. Aletis Liq.         | — 10 "    |
| Ext. Ashoka Liq.         | — 15 "    |
| Ext. Lodhra Liq.         | — 15 "    |
| Ext. Ashwagandha Liq.    | — 10 "    |
| Ext. Shatavari Liq.      | — 15 "    |
| Ext. Piscid Liq.         | — 15 "    |
| Ext. Hydrast Liq. B.P.C. | — 5 "     |
| Drakehsawa               | — 2 Dr.   |
| Syrup                    | — O.S.    |
| Alcohol                  | 5% V/V.   |

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uterine tonics, and nutrients useful in the  
treatment of the common disorders of  
female reproductive system especially of  
uterus.

INDICATIONS: Irregular menstruation  
and other menstrual disorders like menorrhagia,  
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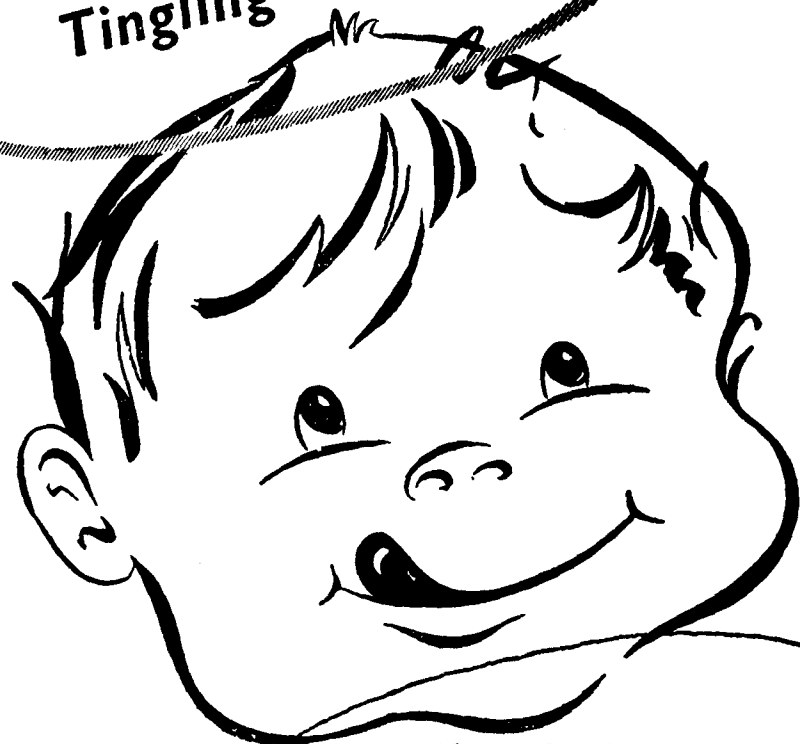
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## Original Articles

### RECENT ADVANCES IN ANÆSTHESIA\*

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In the whole context of medical science, the practice of anaesthesia itself is a 'Recent Advance' and in some of the vital aspects there has been little change over the last one hundred years. In 1851 Dr. C. R. Gillman wrote : "I prepared an article on anaesthetics in which.....I laboured to impress on those as yet unfamiliar with their use the lessons of caution and watchfulness without which I know these agents are and must be *Ministers of Death*." Only five years after ether had been used to produce clinical anaesthesia for the first time he was able to give the '*Rules for Administration of Anaesthetics*' :—

(1) "The patient should not take food immediately before the operation. (2) The mind should as far as possible be calm and composed. (3) Quiet all around is of the utmost importance—loud talking, addressing questions to the patient, etc., will all interfere with the production of the anaesthetic state. (4) As to how rapidly the patient should be hurried through the state of excitement there is a difference of opinion, and a different rule should prevail according as the agent is ether or chloroform. If ether is used the stimulation is often troublesome and the deeper states of narcosis is not readily produced. We ought therefore, to hurry the process forward, place the cupped sponge over the nose and mouth not pressing the skin, but quite near, and urge the patient to take full inspirations—let them follow each other as rapidly as is consistent with their being full and deep. (5) Care should be taken that the supply of atmospheric air is at all times adequate. There is little doubt that several of the fatal cases

\* From a post-graduate lecture delivered at Vellore.  
Specially contributed to the ANTISEPTIC

resulted from an inadequate supply of air. (6) Watch the case from the first inhalation till consciousness and sensibility have completely returned. In all operations one person should have charge of the anæsthetic, and he should think of nothing else.

In one fatal case the attendant who should have watched the patient was looking at the operation, and the man died. The person who has this charge should keep his finger on the pulse every single moment of the time—not one beat should the heart give that his finger does not take note of. The moment the pulse begins to flag or flutter, the inhalation should cease, and a puff or two of fresh air blown into his face. (He might today be subjected to the administration of oxygen!)

The degree to which the effects should be carried, it will differ in different cases. In natural labour we need ordinarily go no further than to obtund pain, and this in my opinion, can generally, be done without disturbing consciousness. In surgical operations complete relaxation of the muscles and profound sleep are generally required. This state, however, must be watched, and when the breathing is irregular or interrupted the danger is most imminent, and every means of keeping up the respiration should be resorted to. Artificial respiration is the sheet anchor in such cases, and great danger can be removed by prompt and continued artificial respiration. Much will depend on the coolness and self-possession of the operator.

(7) When the patient is allowed to emerge into consciousness anything that can startle or shock him should be avoided, and the brain quietly allowed to recover its poise. Ammonia, oxygen, galvanism, etc., have been proposed as remedies in excessive anæsthesia. They amount to nothing. Artificial respiration is the alpha and omega.

"Beyond correcting his impressions on the use of oxygen, little further can be added to his general admonitions after one hundred and three years" (Burnham, 1954); even his statement about oxygen is relevant to present day practice and mispractice. In a recent article on the 'Care of the Unconscious Patient' Mushin (1955) refers to a patient whom he was asked to see because an oxygen regulator was out of order. The man was unconscious and cyanosed; each breath was made with effort and he was obviously dying. But when his chin was held up the stertor disappeared, he became pink and within a few hours he was fully conscious. This type of incident occurs everywhere; a few weeks ago one of our anæsthetists was called to see a child who was having respiratory difficulty post-operatively and all he needed to do to correct the difficulty was to raise the child's chin. In order to be effective, oxygen must reach the alveoli. Dr. Gillman was right in saying that the essential treatment in all cases of over-dosage of any anæsthetic is artificial respiration

and for this to be effective it is essential that the patient's airway is kept free of all obstruction. So we can say that in basic principles there has been very little advance in the practice of anæsthesia during the past one hundred years. It is obvious that there have been many changes; the anæsthetist of today with an array of cylinders, tubes and syringes appears to be very different to the anæsthetist of 1851 with his 'rag and bottle.' But changes are not necessarily advances and we must look more carefully into the changes that have taken place to determine whether, and in what sense, they are really advances.

What are the essential requirements of anæsthesia? The patient asks to be free from pain and for his normal life to be disturbed as little as possible; the surgeon asks for a patient who will be unresponsive to the painful stimuli produced during surgery, who will have good muscular relaxation and whose normal physiology will be disturbed as little as possible or even restored to near-normal balance after gross disturbance due to the surgical condition. The modern surgeon may want to do extensive procedures that will take many hours to complete. Sir Clifford Allbutt (Beecher and Ford, 1955) referring to the introduction of surgical anæsthesia said: "The obvious boon of immunity from pain, precious though it was, when we look beyond the individual, was less than the boon of time." Magill (1949) has stated, "The advances made have greatly increased the scope of surgery. These advances are due partly to the discovery of new drugs partly to the use of complicated but efficient machines but largely to the realization of the need for an accurate estimation of the patient's condition." This realization of the need of a careful watch on the patient's condition is not new as we have seen from Dr. Gillman's rules and we know from the work of John Snow that some clinicians were concerned to find out what happened to the physiology of the patient when anæsthetized by these toxic drugs, but they were very few and it is only during the last twenty years that this need has become more widely recognized. If I describe some of the changes that have taken place since I gave an anæsthetic for the first time, I think, we will cover all the more recent advances. And I ask you to remember that this is not a historical survey; some of the changes that were new to me during this period had been introduced several years before.

When I was a student a patient needing major abdominal surgery was given anæsthesia by one of two basic techniques:— Either nerve-block by spinal or regional analgesia or general anæsthesia by one of several inhalation agents carried to depth sufficient to produce the relaxation needed by the surgeon. Induction was by inhalation of a vapour or a gas and, although a good induction is not unpleasant, the introduction of the short-acting barbiturates given intravenously was a great advance,

may be the biggest ever yet, from the point of view of the patient at this stage which, to him, is the most important part of the whole anæsthetic procedure. The use of pentothal and similar drugs not only gave the patient a pleasant induction but it decreased the incidence of post-operative vomiting and therefore, made the recovery period more pleasant. It has also made the anæsthetist's task very much easier than before.

But even then the maintenance of anæsthesia was by means of one or more drugs given by inhalation; nitrous oxide, ether, trilene, cyclopropane and ethylene are names that are familiar to all and need not be discussed here. Each one of them is useful in particular circumstances and not one of them, in itself, constitutes a real advance.

But the introduction of a highly volatile and explosive drug like cyclopropane necessitated a change in the method of administration which is very significant. To have a large part of the expired gases being blown out at every breath was much too extravagant and dangerous and Waters introduced the closed-circuit technique using soda-lime to absorb the carbon dioxide. Modification of his original method and the production of many different machines for this purpose have made little difference to the principles involved; and the interest in carbon-dioxide elimination that has been aroused subsequently has produced results that are applicable in many different spheres of medical practice.

One great advance, therefore, has been in the general adoption of the closed-circuit technique. But still we were maintaining anæsthesia with one or two inhalation agents to a depth sufficient for muscular relaxation when necessary. Cullen was the first to realize that the different requirements of the patient and surgeon could be met by a combination of different drugs and techniques, each one accomplishing part of the whole work done by a drug such as ether. Ether produces (1) hypnosis; the patient falls asleep; (2) it produce analgesia and therefore, prevents reflex response to painful stimuli; (3) it produces muscular relaxation chiefly by central depression. Cullen gave light anæsthesia to produce hypnosis and a nerve-block to produce both analgesia and muscular relaxation. I used this method of "balanced anæsthesia" quite often during my first years here; the pre-operative condition of our patients was often so poor that I was reluctant to give anæsthesia to a depth sufficient for relaxation for any length of time so a combination of light anæsthesia with regional or spinal nerve-block was a satisfactory alternative. But the introduction of curare into clinical anæsthesia has made possible a further development of this concept of combined or balanced anæsthesia (Little and Stephen 1954). Muscular relaxation can be produced at will by the intravenous administration of one of several relaxant drugs; the patient is kept asleep with

light anæsthesia sometimes using ether or cyclopropane but more often using nitrous oxide supplemented by intermittent doses of an analgesic such as pethidine or a hypnotic such as pentothal.

Perhaps, a few words about "relaxants" may not be out of place here. There are two main groups of relaxants: (1) those that act like curare by blocking the action of acetylcholine at the neuro-muscular junction and (2) those that act by depolarizing the muscle end-plate and preventing further contraction of the muscle by prolonging the state of depolarization.

Curare and synthetic drugs such as Callamine triethiodide ("Flaxedil") are antagonized by the anticholinesterase drugs e.g. prostigmine. Destruction of the cholinesterase allows acetylcholine to accumulate in sufficient quantities to break through the barrier and the muscle contracts.

But the usual action of drugs such as succinylcholine chloride ("Scoline" or "Anectine") is similar to the anticholinesterase effect of prostigmine and so the latter should not be given. Succinylcholine is destroyed by the pseudo-cholinesterase of the blood and the most effective way of treating prolonged apnoea is by transfusion of fresh blood.

One of these drugs given in doses sufficient to produce good abdominal relaxation will also produce a certain amount of intercostal paralysis; if respiratory exchange is inadequate the patient's respirations must be either assisted or "controlled." During assistance the reservoir bag is squeezed during each inspiration to increase the tidal volume and therefore, increase exchange of gases with subsequent improvement in oxygenation and elimination of carbon dioxide. If the intercostal muscles are partially paralysed and the respiratory centres are depressed by hypnotic and anæsthetic drugs, an attempt to assist the patient's respiration will easily cause apnoea by lowering the carbon dioxide tension in the blood (Pask 1955). This state of apnoea is often produced deliberately, especially during intrathoracic surgery; the anæsthetist continues to inflate the patient's lungs by applying pressure to the reservoir bag and then allowing the lungs to deflate. A slight degree of over-inflation increases the power of recoil due to the elasticity of the lungs. When I visited a thoracic surgical centre in 1947 the anæsthetist was not using curare or controlled respiration because he thought it was not physiological. There has been a great deal of thought and study given to this subject and now it is generally realized that intermittent positive pressure respiration (I.P.P.R.) is more physiological than spontaneous respiration than is depressed (Watrous *et al* 1951). Guedel was one of those who realized this is long ago as 1940 when he said "To one who knows respiratory physiology the apnoeic technique is safe. Passive (controlled) respiration is safer than inadequate active respiration."

Continuous positive pressure interferes with the action of the heart but if the pressure is allowed to fall to near atmospheric level at each expiration the effect of the drop in pressure from a positive level to the atmospheric, will stimulate the normal mechanism in which the pressure drops from atmospheric to a negative level. The "pump" effect on the heart is similar but it is also important that the inflation should be done slowly enough to allow the heart to beat a good many times under normal circumstances in between each pressure-peak. During normal respirations the pump effect of inspiration is applied about twenty times a minute and during I.P.P. respiration the lungs should be inflated at about 14 to 16 times a minute; certainly not faster than the average normal rate of 20.

Our present understanding of the physiological basis of I.P.P. respiration has been applied to conditions other than anaesthesia, to which I shall refer later.

Three significant advances have been made so far viz. :

(1) The intravenous administration of drugs which has made possible the use of the short-acting barbiturates during induction and relaxant and analgesic drugs during maintenance of anaesthesia; (2) the adoption of the closed-circuit technique which has made possible, in conjunction with the relaxants, the assistance or control of the patient's respirations; and (3) the practice of balanced anaesthesia by means of which the patient can be maintained at such a light level of anaesthesia that his physiology is interfered with to a minimal degree. In preserving the physiological state at a near-normal level the anaesthetist is responsible not only for the administration of the anaesthetic but also for supportive therapy such as blood transfusion or other intravenous infusions.

One of the most important duties of the anaesthetist under normal circumstances is to see that the blood-pressure of the patient does not fall to a level that will endanger the supply of oxygen to the brain or the kidney. But the danger of haemorrhage makes some surgery too hazardous to undertake and there are times when the surgeon will ask the anaesthetist to lower the blood-pressure deliberately so that he can attempt an operation that would otherwise be impossible.

Hypotensive anaesthesia using spinal nerve-block or one of the ganglion-blocking drugs such as hexamethonium or Arfonad was used extensively a few years ago. But the dangers of hypotension are too great to justify the use of this technique except when absolutely necessary. The cells of the brain and the kidney have a high oxygen-demand that may not be met if the blood-pressure is allowed to fall below 70 mm. Hg.; much work has been done during the last few years to find ways and means of lowering the oxygen requirements of the vital organs of the body

The amazing developments in cardiac surgery during the last few years have provided another reason for seeking means of reducing the oxygen requirements of the patient. Intra-cardiac surgery performed under normal conditions is limited by the fact that the circulation can be interfered with only for a very short time; therefore, it has to be done "blind" and this imposes a further limitation on the scope of the surgical treatment. Ways and means of interrupting circulation long enough for intracardiac surgery to be performed under direct vision have been under consideration in many centres. The first and obvious solution to the problem was to cut the heart out of the circulation and to provide a mechanical pump through which the circulating blood could be deviated. The technical difficulties associated with this method are obviously great; such a complicated and difficult technique is not only expansive and hazardous but is a major procedure in itself and adds materially to the magnitude and duration of the operation.

Another solution has been sought, and to a large extent found, which is based on a consideration of the oxygen-requirements of the patient. In 1950 Bigelow and his associates demonstrated that when a dog's body-temperature falls from 38°C to 20°C, its metabolism and the oxygen demands of its body are reduced to approximately 18% of normal values. They also demonstrated that hypothermia, provided it is suitably induced and does not go lower than 20°C, is a comparatively safe procedure. At this temperature dogs can survive occlusion of both the superior and inferior vena cavae for at least fifteen minutes without damage to the brain.

The principle of hypothermia has been accepted and has been applied clinically but controversy still rages concerning the best way of producing it. If the body-temperature is lowered by exposure to cold the natural defence mechanism comes into play; the animal shivers and this muscular activity causes a rise of temperature with increased oxygen-consumption and pulse-rate. Only when the defence mechanism is overcome do the body temperature and oxygen consumption fall?

If hypothermia is to be produced safely and effectively the defence mechanism must be put out of function *before* the application of cold and this can be achieved by using one or more of the following methods:—(1) deep anaesthesia, (2) curare, and (3) the new phenothiazine drugs.

The simplest method of lowering the patient's temperature is by the *surface application of cold* but this has several disadvantages:—(1) It is slow; Dogliotto (1953) has shown by experiments on guinea pigs that tolerance to hypothermia is greater when chilling and subsequent re-warming are both

carried out quickly; (2) the temperature continues to fall after the application of the cold has been withdrawn. This "over-shooting" phenomenon can cause serious trouble especially if allowance is not made for the further 2 to 3°C. fall which occurs on opening the thoracic cavity and (3) several cases of fat necrosis have been reported.

*Extra-corporeal cooling* is considered by some people to be much more effective than surface-cooling and different methods of achieving this have been attempted, most of them depending on the patient's arterial pressure for the passage of blood through a cooler before re-entering the circulation.

Extra-corporeal cooling is more difficult and involves certain risks to the patient but it has the advantages of being more rapid and controllable. The temperature is not so very likely to fall after cooling has been stopped.

Whatever be the method by which hypothermia is produced all who have used it emphasise the danger of taking the temperature below 26°C, below which level the irritability of the heart is considerable and ventricular fibrillation is very likely to occur. With this *proviso*, and taking operative precautions that are necessary to avoid air embolism after the closure of the heart, intracardiac surgery under direct vision has become a reasonably safe procedure that has already brought relief to patients who were once thought to be beyond any surgical interference.

Harold Griffiths (1955) of Montreal has said that "the modern anaesthetist must be a physician, a pharmacologist, a toxicologist, a biochemist and an electronic engineer." It is not possible to dilate here on the use of electronics in the field of anaesthetics; Some of the new, electrical devices in fairly common use are:—(1) the photo-electric cell-oximeter for estimating the oxygen saturation of the blood; (2) means for continuous pulse and blood pressure tracings; (3) the hypothermia machines with thermo-couples for keeping accurate record of the patient's temperature; (4) continuous E.C.G. record flashing across a screen like a miniature television set; and lastly (5) the automatic control of anaesthesia by the electro-encephalogram. This is of use chiefly in experimental work but has been used on humans quite successfully. Soltero and his associates (1951) at the Mayo Clinic have said, "It is not our purpose.....to propose the substitution of a complete electro-mechanical machine for a competent anaesthetist any more than one would seriously propose flight in an air liner equipped with an automatic pilot without the presence of the crew." So anaesthetists may still be needed for a few years more!

These then are the advances in the practice of surgical anaesthesia; they have also a bearing in a wider sphere than

operative surgery; much of what has been learnt in the operating room is being applied in diagnosis and therapy in other realms of medicine.

Let me remind you that arterial spasm can be relieved by sympathetic block, that the severe pain of conditions like acute pancreatitis can be relieved by selective block of the spinal nerves and that even the fits of eclampsia can be prevented or relieved by spinal-block.

But I would like to refer in greater detail to three conditions (or groups of conditions) in which the experience gained by anaesthetist in the operating room will be of help to the physicians in the wards. O'Brien (1954) says "the practising anaesthetist is not a research scientist in the strict sense, yet by nature of his training and daily experience he qualifies as a clinical cardio-respiratory physiologist" and it is this aspect of our experience that I would like to speak about at some length.

We have already seen how the use of the relaxant drugs has made necessary the widespread use of controlled or intermittent positive-pressure-respiration and this technique forms the basis of treatment in three types of conditions:—

A. *Coma* which may be caused, for example, by barbiturate poisoning, intracranial injury, or encephalitis.

As Mushin (1955) says, there are three causes of unconsciousness: natural sleep, anaesthesia and coma. Sleep differs from the other two in that the patient is roused by any sudden stimulus but "anaesthesia differs from coma only in the fact that it is to a great extent reversible and controllable by the anaesthetist"; as in the practice of surgical anaesthesia, so also in the treatment of coma, the first principle is to see that an adequate supply of oxygen is carried to the tissues. In order to do this, air or oxygen must first reach the alveoli and the patient's own respiration may be too depressed for adequate oxygenation. If the respirations are only slightly depressed an increase in the oxygen tension in the inspired air may relieve the anoxia but there is only one way of removing carbon-dioxide; that is by assisted or controlled respiration carried out as during anaesthesia.

In the past, carbon-dioxide was used in the treatment of such cases with the idea that an increase in the carbon-dioxide tension in the blood will stimulate the respiratory centre. But it has since been realized that such stimulation is only transient; an accumulation of carbon-dioxide above 7% in the inspired air has a powerfully depressant effect on the central nervous system (Mushin, 1955).

Two of the toxic effects of carbon-dioxide to be kept in mind are:—(1) that it is a narcotic; it was the first gaseous anaesthetic to be used in 1824 by Hickman for animal surgery. Ten per cent carbon-dioxide in oxygen readily induces unconsciousness in the

resting man; and that (2) it causes vaso-constriction at first but concentrations higher than 15% cause vaso-motor depression (Donald and Paton, 1955) and circulatory failure is often the cause of death in respiratory insufficiency.

Therefore, in order to maintain the patient's circulation and to hasten recovery to consciousness, it is necessary to make sure that the patient's respirations are adequate for removal of carbon-dioxide from the alveoli. These principles are also the basis for treatment in the next group.

**B. Paralysis of the intercostal muscles or the diaphragm** from acute infection or injury. This group obviously includes spinal injuries, acute poliomyelitis and other acute conditions such as diphtheria and polyneuritis. I have included tetanus also in this group although the paralysis in this case is induced deliberately as part of the treatment. Death from tetanus is thought to be due usually to the exhaustion caused by muscle spasms and a method of treatment that has been successful in many centres is based on the control of the spasms by one of the relaxant drugs. The dosage needed is often so great that the patient's intercostal and diaphragmatic movements are inadequate for ventilation, so artificial respiration must be given. In tetanus and in bulbo-spinal poliomyelitis, an added difficulty is in removing the secretions that collect in the pharynx which may cause sudden and fatal obstruction at the larynx or trachea. Therefore, the most satisfactory way of giving these patients artificial respiration by I.P.P.R. through a cuffed tracheotomy-tube. In the light of his unfortunate experiences with rabies in Israel, Wislicki (1955) suggests that the same treatment may be life-saving in this disease also. If the spasms of larynx and pharynx can be controlled by curarization there is every reason to hope that the patient may survive the acute phase.

**C. Pulmonary oedema** is another condition in which we are sometimes asked to help the physician and I think perhaps we have not been sufficiently bold in our treatment. It has been said that oxygen given under positive pressure is beneficial in this condition, which is no doubt true. But it is not easy to give it to a conscious patient; what is really needed is I.P.P.R. and for this to be carried out efficiently endotracheal intubation (Webb and Campbell, 1954) and light anaesthesia will be necessary.

A brief consideration of the factors involved in the normal balance of pressures between the alveoli and blood-stream will enable us to have a clearer understanding of the rationale of this method of treatment.

The osmotic pressure of the plasma-proteins tends to keep fluid in the pulmonary capillaries while the pressure of the circulating blood and the slight negative pressure in the alveoli at the

end of inspiration tend to "push" fluid through the capillary membrane into the alveolus. Any change in these pressures *e.g.* a raised pulmonary pressure or increase in the alveolar negative pressure due to obstruction in the respiratory passages or an increase in the permeability of the capillary membrane due to anoxia may cause pulmonary oedema.

If the slight negative pressure in the alveoli is converted into positive pressure by I.P.P.R. further passage of fluid across the capillary membrane will be prevented (Mushin 1955).

It is an interesting fact that pulmonary oedema does not occur as a complication of severe poliomyelitis or other conditions treated by I.P.P.R. Previously it was a common cause of death.

The advances that have been recorded in the field of anaesthesiology, have been made possible by one other big advance during the last ten years.

In 1893 Sir Fredric Hewitt (Beecher and Ford 1955), one of the first specialist-anaesthetists, wrote "the responsibilities involved in administering anaesthetics are not yet fully realized .....the administration is too often placed in comparatively unskilled hands.....the first step should be an educational one."

Even fifty years later, these words are still true in most parts of the world; adequate training in anaesthetics was given only in the larger medical centres in U.S.A. and Britain. But since the Second World War considerable progress has been made and the need for anaesthetists with a sound basic training and a certain amount of technical skill, has come to be recognized in all countries including India.

Let us hope that many more people will choose this speciality so that the patients may enjoy greater safety and a decreased morbidity and also in order that surgery in India may progress and reach the same high level as in other parts of the world.

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### PERNICIOUS ANÆMIA DUE TO DIETARY DEFICIENCY OF VITAMIN B<sub>12</sub>

A case of pernicious anæmia in a 60-year-old man who had refused to ingest any food of animal origin for more than eight years is described. The anæmia was caused by the dietary lack of vitamin B<sub>12</sub>. This is the first time that such a cause has been established. The diagnosis was based on observation of the characteristic morphological changes of the blood and bone marrow, a serum vitamin B<sub>12</sub> level of 70 micromicrograms per milliliter, which is in the range observed in patients with pernicious anæmia, and a characteristic hæmatological response to vitamin B<sub>12</sub> therapy. A pronounced drop in the serum iron level occurred after vitamin B<sub>12</sub> therapy until an abnormally low level was reached at a time when the red blood cell count rose to its maximum. After stabilization of erythropoiesis, the serum iron level was restored to normal in the course of the next two months. These changes were related to variations in the rate at which iron was utilized by the bone marrow for erythropoiesis.

Vitamin B<sub>12</sub> absorption, as determined by faecal elimination and urinary excretion of cobalt-60-labeled vitamin B<sub>12</sub> and hepatic deposition of cobalt-60, was shown to be normal. In addition, the potency of the intrinsic factor of the patient's gastric juice was found to be normal as determined by its capacity to produce normal absorption of vitamin B<sub>12</sub> in a patient with pernicious anæmia in remission when it was injected simultaneously with radioactive vitamin B<sub>12</sub>. The exceptional conditions that must be satisfied simultaneously for the development of pernicious anæmia caused solely by dietary deficiency of vitamin B<sub>12</sub> are exclusion from the diet of all meat, fish, fowl, dairy products, and unrefined grain with its products; these drastic dietary deficiencies must exist without simultaneously evoking other severe nutritional deficiencies or starvation; they must continue for at least two years; and the patients who become symptomatic by satisfying these three conditions must not receive ameliorative "shotgun" therapy before hospitalization. All four requirements were fulfilled by the patient reported on. The difficulty of simultaneously fulfilling them offers a plausible explanation of the rarity of this mode of causation. The chief significance of this case lies in its further substantiation of Castle's hypothesis by demonstrating that an extremely prolonged complete dietary deficiency of vitamin B<sub>12</sub> can result in the development of severe pernicious anæmia.—(*New England J. Med.*, 255: 164-169, July 26, 1956, via *J. of Am. Med. Assoc.*).

### CORTISONE in the TREATMENT of SOME LIVER CONDITIONS

Andreoli, treated with cortisone five patients with various liver conditions: two had acute hepatitis, one had common cirrhosis, and two had post-icteric cirrhosis. Three patients with acute hepatitis, two with common cirrhosis, and one with post-icteric cirrhosis were kept as control cases and received the usual treatment without cortisone. Comparing the results obtained in the two groups, the author found that cortisone had a good general effect and a marked effect on the icterus. The regression of the icterus was speedy even in cases that could not have been cured with routine treatments. In three months' time the size of the spleen and of the liver decreased markedly. Patients did not receive any collateral treatment while they were being treated with cortisone. The use of cortisone seems particularly indicated for the treatment of acute hepatitis, especially in patients who can not be cured with common routine treatments. The next best results are obtained in patients with post-icteric cirrhosis. By comparison, the effect of cortisone on common hepatitis does not seem to be pronounced. In all cases, however, the adrenal hormone succeeds in preventing progression of the condition.—(*Riforma med.*, 70: 708-712, June 23, 1956, via *Jour. of Am. Med. Assoc.*).

### CLINICAL TRIALS WITH RESERPINE IN DIABETES MELLITUS\*

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THE occurrence of permanent diabetes mellitus in conditions of marked stress and agitation associated with physical and psychical trauma has been a debated subject. Although several authors do not agree that emotional and nervous factors play a part in the ætiology of diabetes mellitus, evidence from occasional cases has accumulated to show that trauma, psychic or physical can activate or accelerate the appearance of a latent diabetes in a hereditarily predisposed individual, especially in association with infection or obesity and lack of exercise or excessive eating. If obesity may be considered as a psychosomatic problem at least in a few cases, it is clear that the origin of a diabetic state may occasionally be traced to a psychosomatic incident or accident. A small number of cases have been cited or reported in the literature during the last few decades, which point to their having an emotional or psychic or neurogenic origin. Carrasco a Spanish author (1925) cites an extraordinary case of diabetes of severe intensity appearing in a man within a few hours, as a sequel to his suffering from a double emotion. Root (1937) mentions a rare case of an obese Italian who developed symptoms of diabetes mellitus following a nervous shock. The occurrence of permanent diabetes mellitus following myocardial infarction has been documented by Goldberger in a study of 14 cases of myocardial infarcts over a period of 11 months. Shock due to severe pain has been blamed as a cause although the theory that stimulation of adrenals resulting in the alarm reaction of Selye can more than explain the precipitation of diabetes mellitus after coronary thrombosis. If the sudden stress resulting from a myocardial infarct can produce diabetes mellitus it is not surprising that continual daily stress may act as a potent factor in the precipitation of the symptoms of diabetes in a predisposed individual.

*Rauwolfia serpentina* has found a useful place in the control of stress factors and of the agitation caused by emotions and also in the treatment of mental disorders. Reserpine sedates the agitation, tension is relieved, sleep is insured, permitting integration of thought and adaptation to surroundings and it induces a general sense of well-being and euphoria.

The universal popularity of *Rauwolfia* and its derivatives in the treatment of hypertension and the very common association

\*Specially contributed to the ANTISEPTIC

## An Analysis of the Cases Studied

| No. | Name     | Age and sex | Effect on blood-sugar level | Effect on urine-sugar | Increase in weight as evidence of water-retention | Oedema                  |
|-----|----------|-------------|-----------------------------|-----------------------|---------------------------------------------------|-------------------------|
| 1   | D.       | 59, m.      | Lowered RBS 180 mg. 160 "   | Nil                   | Gain in weight                                    | + Ankles                |
| 2   | P.       | 42, m.      | Lowered RBS 380 mg. 300 "   | Lowered               | Gain in weight                                    | Nil                     |
| 3   | I. U.    | 45, f.      | Lowered RBS 560 mg. 420 "   | Nil                   | Loss in weight                                    | "                       |
| 4   | M. G.    | 13, f.      | Lowered RBS 440 mg. 400 "   | "                     | Same                                              | "                       |
| 5   | H.       | 22, f.      | Lowered RBS 440 mg. 400 "   | "                     | Slightly gain in weight                           | "                       |
| 6   | T. A.    | f.          | Lowered RBS 240 mg. 220 "   | "                     | Gain in weight                                    | "                       |
| 7   | B.       | 25, f.      | Raised RBS 320 mg. 340 "    | "                     | Loss in weight                                    | "                       |
| 8   | S. N.    | 42, m.      | Lowered RBS 180 mg. 120 "   | Lowered               | Gain in weight                                    | "                       |
| 9   | S.       | 35, m.      | Lowered RBS 210 mg. 140 "   | "                     | Gain in weight                                    | "                       |
| 10  | K.       | 29, m.      | Lowered                     | Nil                   | Nil                                               | "                       |
| 11  | V. I.    | 56, m.      | Lowered RBS 260 mg. 240 "   | Nil same              | "                                                 | "                       |
| 12  | J.       | 35, m.      | Raised RBS 210 mg. 240 "    | Same nil              | "                                                 | "                       |
| 13  | T. M.    | 39, m.      | Lowered RBS 180 mg. 160 "   | Reduced               | Increase in weight                                | Slight oedema on ankles |
| 14  | P. A. S. | 43, m.      | Same RBS 120 mg.            | Same                  | Nil                                               | Nil                     |
| 15  | T.       | 35, m.      | Lowered RBS 300 mg. 290 "   | Reduced               | "                                                 | "                       |
| 16  | M.       | 40, f.      | Lowered RBS 210 mg. 200 "   | Same                  | "                                                 | "                       |

## during the Clinical Trials

| Effect on urine-output | Effect on thirst    | Effect on blood-pressure | Psychic improvement | Side-effects                         | Complications |
|------------------------|---------------------|--------------------------|---------------------|--------------------------------------|---------------|
| Diminished             | Diminished          | Lowered                  | Yes                 | Oedema                               | Nil           |
| "                      | "                   | Slightly lowered         | Yes                 | 1. Drowsiness<br>2. Loss of appetite | "             |
| "                      | Nil                 | Nil                      | Nil                 | Nil                                  | "             |
| "                      | "                   | "                        | "                   | "                                    | Nil           |
| Slightly diminished    | Slightly diminished | "                        | "                   | "                                    | "             |
| "                      | "                   | "                        | "                   | "                                    | "             |
| "                      | "                   | "                        | "                   | "                                    | "             |
| Nil                    | Nil                 | "                        | "                   | Giddiness vomiting                   | "             |
| Diminished             | Diminished          | "                        | Yes                 | Nausea                               | "             |
| "                      | "                   | "                        | Yes                 | Nil                                  | "             |
| "                      | "                   | "                        | Yes                 | "                                    | "             |
| Reduced                | Nil                 | Lowered                  | Yes                 | "                                    | "             |
| Nil                    | "                   | Nil                      | Nil                 | "                                    | "             |
| Reduced                | Reduced             | "                        | Yes                 | "                                    | "             |
| Nil                    | Nil                 | "                        | Nil                 | "                                    | "             |
| Reduced                | Reduced             | "                        | Yes                 | "                                    | "             |
| "                      | "                   | Reduced                  | Yes                 | "                                    | "             |

## An Analysis of the Cases Studied

| No. | Name  | Age and sex | Effect on blood-sugar level | Effect on urine-sugar | Increase in weight as evidence of water-retention | Oedema  |
|-----|-------|-------------|-----------------------------|-----------------------|---------------------------------------------------|---------|
| 17  | M. N. | 32, m.      | Lowered RBS 140 mg. 120 "   | Same                  | Same                                              | Nil     |
| 18  | J. R. | 32, m.      | Same RBS 140 mg.            | Lowered sugar to nil  | Gain in weight                                    | Present |
| 19  | M. E. | 48, m.      | Lowered RBS 160 mg. 150 "   | Same                  | Nil                                               | Nil     |
| 20  | K. A. | 30, f.      | Lowered RBS 280 mg. 210 "   | Lowered               | Gain in weight                                    | Present |
| 21  | S.    | 38, m.      | Lowered RBS 290 mg. 240 "   | Same                  | Loss in weight                                    | Nil     |
| 22  | C.    | 35, m.      | Lowered RBS 130 mg. 120 "   | "                     | "                                                 | "       |
| 23  | K.    | 30, m.      | Lowered RBS 120 mg. 100 "   | "                     | Gain in weight                                    | Present |
| 24  | S.    | 48, m.      | Lowered RBS 160 mg. 140 "   | "                     | "                                                 | "       |

of hypertension with diabetes mellitus would appear to justify speculation as to whether the drug would possibly have some beneficial effect on the diabetic state as well, in view of its anti-stress properties, i.e., if stress factors have anything at all to do with diabetes; and in order to test the validity of this hypothesis of ours, a clinical trial was run on a series of twenty four selected diabetic cases using Reserpine, noting down its effect on the blood-sugar levels and on the diabetic state in general. The cases were selected irrespective of age of the patient, the duration or severity of diabetes, but with an eye to some definite psychic-trauma and stress factor being present in each case. None of these cases manifested any severe complications. A glucose-tolerance test was done in every case to establish the diabetic state prior to Reserpine administration. All the patients were admitted and treated as in-patients and were given the maximum caloric diabetic diet according to the General Hospital Diabetic-Diet-Regime and a blood-sugar estimation on specimens drawn at a particular time was done once in four days to ascertain changes in the blood-sugar level.

| Effect on urine-output | Effect on thirst | Effect on blood-pressure | Psychic improvement | Side-effects         | Complications |
|------------------------|------------------|--------------------------|---------------------|----------------------|---------------|
| Same                   | Reduced          | Nil                      | Yes                 | Nil                  | Nil           |
| Diminished             | Diminished       | "                        | Marked              | "                    | "             |
| Very much diminished   | "                | Lowered                  | Yes                 | "                    | "             |
| Same                   | Same             | Nil                      | "                   | "                    | "             |
| Diminished             | Diminished       | Nil                      | "                   | Nil except diarrhoea | "             |
| "                      | "                | "                        | "                   | Nil                  | "             |
| Nil                    | Nil              | "                        | "                   | Drowsy               | "             |
| Diminished             | Diminished       | "                        | Nil                 | Nil                  | "             |

Reserpine was continued for one month before the final results were assessed.

Dosage of Reserpine:—Two tablets of 5 mg. each thrice daily was given for about a month; no other drug, not even insulin, was given to the patients during the trial period.

The blood-sugar levels did not show any appreciable change except in two cases of juvenile diabetics who showed a definite increase, about 40 mg. of the random blood-sugar being recorded. The urinary sugar remained the same as it was prior to treatment in 17 cases in this series while, in the rest, it showed a significant reduction by the Benedict's qualitative test. The total urinary output and the frequency of micturition showed a definite reduction after Reserpine therapy in all cases except four, in which it remained unaltered. Polydipsia was also reduced *pari passu* in the reduction in the urinary output. In about 16 cases the patients noted a definite psychological well-being and improvement in their condition. The blood-pressure was little altered during the course of the therapy. No serious side-effects were noted in the patients. Drowsiness, loss of appetite,

giddiness, vomiting and nausea were noted occasionally but were not troublesome. An interesting and definite side-effect noticed in the present series was the development of oedema of the feet and ankles and a gain in weight during the course of the therapy in six cases. In one of these patients with associated hypertension a mild congestive failure was precipitated during the course of treatment when the drug was promptly discontinued.

At the end of the clinical trials we were impressed by the fact that Reserpine had no definite effect upon the blood-sugar levels and so could not serve as a blood-sugar-reducing agent, although it may be occasionally used as an adjunct to anti-diabetic treatment in a few selected cases associated with definite stress, in view of the psychological improvement produced by the drug. Whether the production of oedema and water-retention in the body as a side-effect of the drug will be a handicap in prolonged treatment with Reserpine at least in a few cases, is a matter for further investigation.

**Summary.**—(1) The relation of stress to diabetes is briefly reviewed. (2) Clinical trials on the effect of Reserpine on blood-sugar in 24 cases of diabetes are recorded.

**Acknowledgement.**—Our grateful thanks are due to M/s. Unichem Labs. for the supply of the necessary drugs etc. used in the clinical trial and to the Dean of the G. H., for according permission to us to conduct this research.

#### THE TREATMENT OF BACILLARY DYSENTERY WITH ORAL STREPTOMYCIN

Patients with bacillary dysentery had been treated with succinylsulphathiazole or phthalylsulphathiazole. In 1949, treatments were begun with streptomycin given orally. During the next five years 1474 cases of proved bacillary dysentery were treated with oral streptomycin in a dose of 1 gm. a day for children younger than 10 years and 2 gm. a day for patients over 10 years of age. Treatment was given for 5 days. The course was repeated if necessary. The causative agent in most cases was *Shigella sonnei* but *Sh. flexneri* was the causative agent in about 1/5th of the cases.

Reporting in *The Lancet* [No. 6925: 723 (1956)], Sangster indicated that the percentage of first course cures fell over the five years of the study. However, the results at the end of the study period were still better than those previously obtained with sulphonamides. Of the total number of patients, at least 80 per cent were cured by one course of treatment with streptomycin and 95 per cent by two courses. A trial in 204 patients in which streptomycin and phthalylsulphacetamide were compared showed that streptomycin was more effective and that the sulphonamide gave results comparable with those obtained with sulphonamides previously. No toxic effects were observed as a result of treatment with the antibiotic.—(*Medical Times*).

**ALLERGIC STOMATITIS** may result from sensitivity to acrylic denture material. Specific allergy is proved only by patch-testing with the liquid monomer (methyl methacrylate) of the resin, report Louis Tuff, and G. Frank Santor of Temple University, Philadelphia. Reactions which occur when the denture is strapped to the skin are nonspecific.—(*Jour. Allergy*, 27: 261-265, 1956 via *Modern Medicine*, October 1, 1956).

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## A REVIEW OF THE TREATMENT FOR PEPTIC ULCER\*

With Special Reference to Methscopolamine Bromide

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THE treatment of a patient with peptic ulcer is as much the treatment of the patient as that of the ulcer itself.

Many patients with peptic ulcer are over-anxious, over-energetic and over-conscious. They tend to worry unduly; and are very irregular in their meal times and often miss a meal—factors which predispose to ulceration.

Being a chronic and recurring disorder, the treatment (especially the dietetic part) must be continued for a very long time, almost for ever. Diet plays a most important part in the management of peptic ulcer.

Acid gastric juice which is secreted throughout the 24 hours being an essential factor in the causation and maintenance of an ulcer the more thoroughly the juice is buffered, preferably at 1 to 2 hourly intervals in the acute stage, the more quickly will nature heal the eroded surface.

It is also known that this repaired tissue is friable, and the good work done over a period of 3 to 4 weeks by a bland diet and frequent feeds can be easily undone within 24 hours by allowing a rise in the concentration of the acid gastric juice, through abstention from food or by taking forbidden articles of diet, resulting in a re-formation of the original crater.

The more thorough the initial treatment, the more sound will be the healing and the less will be liability to breakdowns.

Incomplete treatment with partial healing and repeated breakdowns produce fibrosis and the eventual mechanical disability of obstruction—cases commonly met with in daily practice. It is a sound principle to masticate the food to a soft pulp before swallowing.

*Diet*:—Considerable emphasis is laid at the present day on variations of diet contain to adequate quantities of vitamins and proteins. The diet should be served in a colourful and attractive way. A bland colourless diet may cause a smaller flow of gastric juice but it makes the diet unpalatable which many patients will refuse after a short while.

During the acute stage 2 hourly feeds of 4 to 5 ozs. of milk are given; if a pain is persistent, hourly milk feeds may be necessary and in patients with severe pain, continuous milk drip will be necessary.

When acute symptoms have subsided and the patient is ambulant, solid food is added to the diet but the 2 hourly regime

\* Specially contributed to the ANTISEPTIC

must be maintained. In the ambulant stage and even later, milk must be one of the most important articles in the diet. Egg, bread and butter, boiled and lightly cooked fish and meat, *pureed* vegetables may be added. Later on, ordinary meal times are maintained but small feeds are taken in between. Extra vitamins are usually beneficial, ascorbic acid 100 mg. per day being given to all cases. Vitamin A, D and B may be given together, along with the Vitamin C.

The diet must therefore, be sufficient in quantity and attractive in quality and appearance. The patient must be satisfied with the diet and usually a patient on an ulcer-cure diet puts on weight. Olive oil 2 to 3 teaspoonfuls daily at bed-time is very useful; besides its laxative effects, it also inhibits gastric secretion.

*Rest*:—When possible, all peptic ulcer patients should have bed-rest for 6 weeks, but this is not possible in India due to economic reasons. Although most ulcers will heal satisfactorily with ambulant treatment, healing is quicker and very complete if perfect bed-rest is enjoined along with dietetic and medicinal treatments.

*Drugs used in treatment*.—When the ulcer is causing considerable pain complete and absolute bed-rest is essential along with the continuous milk-drip. In some cases gastric lavage may relieve the pain. Not all of the many drugs advertised for the relief of stomach pain are effective. *Sedatives* are of great assistance in the initial stages of ulcer-treatments. Phenobarbitone gr.  $\frac{1}{2}$  twice or thrice daily is usually given.

*Use of antacids*:—Many are the disadvantages in using alkalis; their action is transient, there is some evidence that there is a rebound and an actual increase in acid-secretion. In many cases the alkalis do not effectively relieve the pain and there is a definite danger of alkalosis. For these reasons alkalis are not preferred.

The disadvantage of using soluble alkalis has been overcome by the development of non-absorbable antacids like colloidal aluminum hydroxide and magnesium trisilicate. The action of these substances is of short duration; they absorb acid in the stomach and release chloride in the intestines; they also absorb pepsin. They are of use in the healing stage of an ulcer to relieve symptoms and *not* to replace frequent feeds. They have a definite place in the management of peptic ulcer.

Non-absorbable antacids are undoubtedly useful; they are however, quickly neutralized and the control of inter-digestive secretion during the night becomes a difficult problem; so they are not ideal. Usually 2 to 3 teaspoonfuls, or 2 tablets are given

after each of the main meals, when necessary; they may be used more frequently.

*The belladonna group of drugs*:—Antispasmodic and antisecretory agents like belladonna undoubtedly help in the control of gastric secretion, but undesirable side-effects such as dryness of mouth, etc., occur with the high doses that are necessary for the control of both motor and secretory activities. They are particularly useful for controlling his night pain in duodenal ulcer and also to relieve pyloric spasm. Belladonna is often combined with non-absorbable antacids to secure better results. Usually one of the proprietary preparations containing belladonna is given before meals followed by non-absorbable antacids after meals. In some cases good results are obtained but failures are also often met with, particularly in cases with severe pain.

*Hexamethonium bromide*:—Hexamethonium has been used to control night-secretion in duodenal ulcer patients; there is no danger of hypotension as the patient is in bed but this is not possible during day-time. This drug has not found a place in the routine treatment of peptic ulcer, because of its many side-effects. Usually 15 to 20 mg. by injection or 25 to 50 mg. by mouth are given at bed-time.

*The newer anticholinergic drugs*:—A substance which will control both motor and secretory activities better than belladonna alkaloids and at the same time will have minimum side-effects, was sought for; and several such products are now available in the market. Clinical trials were made by me on one of such products, *e.g.*, *Methscopolamine bromide*:—It is primarily an anti-secretory agent which also possesses antispasmodic properties. It is a para-sympatholytic drug acting on the sympathetic pathways of the autonomic nervous system, acting on the post-ganglionic end plates of vagus innervation to the stomach. In effect it produces medical vagotomy. It has no action on the sympathetic nervous system.

Fifteen proved cases of peptic ulcer were treated. (10 of gastric and 5 of duodenal ulcer). All the patients showed an ulcer on X-ray films. In 4 cases of duodenal ulcer, gastric analysis was also done showing a typical high acid curve. Clinically all the patients selected, had pain more or less in relation to meals, with a duration ranging from 3 months to several years (as in one case).

On examination, tenderness was elicited either in the epigastrium or in the upper part of the umbilical region. All the patients had had dietetic treatment (Sippy diet) with non-absorbable antacids and belladonna alkaloids for 4 to 6 weeks previously. The response to those treatments was not satisfactory in most cases, as pain or acidity persisted in all cases. In 2 cases

after improvement in the 1st stage, there was a recurrence of pain in 4th week of ulcer treatment.

All 15 cases were given *Methscopolamine bromide* (2.5 mg. per tablet) by mouth, to begin with 4 tablets were given in 24 hours, half an hour before breakfast, half an hour before lunch, half an hour before the evening meal and half an hour before bed time respectively; in cases with severe pain an additional tablet was given at bed time. No other drug was given in addition, but all the patients were kept on 2 to 3 hourly milk feeds, soft rice pulp with milk during principal meals and *sandesh* (an Indian sweet) and milk for breakfast and at tea time. After 2 weeks *pureed* vegetables and boiled fish curry and a very softly cooked meat preparation was gradually added to the diet.

**RESULTS:**—The patients, (12 in the series) were very much better symptomatically within a week; pain was absent in all the cases and the acidity had almost disappeared; in fact some of the patients wanted to resume their normal diet. Clinically tenderness was much less over the epigastric region. It was not possible to repeat barium meal examination except in 2 cases, where definite healing was noticed, compared to the one done 4 weeks previously. Most of the patients in this series were ambulant and were carrying on light sedentary duties. In 3 cases complete bed-rest was strictly enforced, because of severe pain after 3 days of the commencement of therapy.

**Side-effects:**—The side-effects in this series were very few compared to belladonna alkaloids even after prolonged administration—(the minimum was 4 weeks, and the maximum was 12 weeks). Dryness of mouth in 2 cases; blurring of vision in 1 case; constipation in 4 cases; and hesitancy in urination in 1 case were all the side-effects noted.

In most cases the side-effects were markedly reduced when the dosage was reduced to 3 tablets a day. The drug can be used in all cases of peptic ulcer except where contra-indicated as in pyloric obstruction and such conditions as (a) *glaucoma*, (b) *paralytic ileus*, (c) *severe constipation*, and (d) *tendency to obstruction of the lower urinary tract*.

From the above clinical observations it would appear that *Methscopolamine bromide* produces symptomatic improvement much earlier than any other drug, even though the chances of recurrence are still there with the stoppage of the drug. For greater relief of pain and acidity its use is justified in all cases of active ulceration, as in addition to the symptomatic improvement, quick healing of ulcer is achieved, reducing the chances of chronic ulcer developing. So far nothing has been mentioned about the surgical aspects. Since this is primarily a review with reference to medical treatment, only the indications for surgery

are mentioned which are:—(1) evidence of organic pyloric stenosis; (2) repeated hæmorrhage from an ulcer; (3) repeated perforations; (4) suspicion of malignancy; (5) failure of good medical treatment carried out for at least 3 months and (6) when there are reasons to believe that the patient will not be cured permanently by medical treatment.

**Summary.**—A short review is given of the medical measures that are available for the treatment of peptic ulcer.

Diet and small meals at frequent intervals constitute a most important aspect in the management of peptic ulcer. The removal of anxieties and worries is far as possible is a very helpful adjunct and for this reason Phenobarbitone *gr. ½* twice daily is recommended.

Non-absorbable antacids and belladonna alkaloids have a definite place in the treatment. The action of antacids is however of short duration. All cases are not equally benefited with the belladonna-group of drugs. Effective doses produce unpleasant side-effects.

Recently newer anticholinergic drugs have become available and one such drug, *Methscopolamine bromide* was tried on 15 patients. It was found to be very useful for peptic ulcer patients. Symptomatic improvement was maximum when compared to other available products. So it is well worth a trial along with diet in all cases of peptic ulcer.

**Acknowledgement:**—My grateful thanks are due to the local representative of M/s. Neo-Pharma of the Upjohn division for the liberal supply of the drug (*Pamine*) used in this clinical trial.

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#### LIPOPROTEINS IN CORONARY HEART DISEASE

The prognosis with angina pectoris and myocardial infarction is significantly worse in patients with high lipoprotein atherogenic indexes.

The index is a combined measurement of Standard S<sub>10-12</sub> and Standard S<sub>12-400</sub> lipoproteins. Both classes of lipoproteins are found in higher amounts in persons with coronary disease than in healthy individuals, although elevation in one class is not invariably concomitant with elevation in the other.

When compared with a matched control group of healthy persons, individuals with myocardial infarcts are found to have significantly higher levels of lipoprotein per 100 cc. of serum. In patients with angina pectoris, lipoprotein and atherogenic index values in those with subsequent myocardial infarction are substantially elevated over those in healthy individuals. Atherogenic index values are also higher in patients dying of myocardial infarction than in patients surviving infarction.

A low-fat, low-cholesterol diet is recommended to reduce serum lipoprotein levels in ambulatory patients with coronary disease. Persons with previous myocardial infarction who adhere to the diet have fewer recurrences and a lower death-rate than those in similar circumstances who do not maintain the diet.—(*California Med.*, 84: 325-328, 1956, via *Modern Medicine*, Sept. 15, 1956).

## A NEW TREATMENT FOR RESISTANT WARTS

The basic concept in abbreviated form of this new treatment utilizes generally known clinical observations that some hyperkeratoses such as Darier's disease are related to vitamin A deficiency.

Since vitamin A is stored in the liver and gastrointestinal tract, it was reasoned that direct introduction of the vitamin into the lesion would raise the vitamin A skin level at the desired site without the need for enormous spillover dosage from the gastrointestinal tract and liver.

Oily solutions of vitamin A and other available vitamin A dispersions were used, but because of undesirable reactions a special solution was devised. In this new dispersion the surfactant concentration was kept at a minimum and alpha tocopherol was employed as an antioxidant to prevent destruction of the vitamin A in the skin. A small amount of fatty oil was incorporated as a diluent to reduce irritation and retard absorption.

This dispersion has a vitamin A activity of 50,000 units per cc. and may be ampouled and autoclaved for sterilization.

## STEINBERG'S SOLUTION FOR VERRUCAE

|                       |     |            |
|-----------------------|-----|------------|
| Vitamin A Palmitate   | ... | 2.96 gm.   |
| Alpha tocopherol      | ... | 0.40 "     |
| Sesame oil            | ... | 0.60 "     |
| Polysorbate 80 U.S.P. | ... | 10.00 "    |
| Distilled water q.s.  | ... | 100.00 cc. |

**Technique:**—The area is prepared with tincture of Merthiolate and then anaesthetized with 2% procaine or Xylocaine containing 1-100,000 epinephrine. Using a tuberculin syringe, the vitamin A dispersion is injected slowly into the base of the verruca. The needle should be left in place after the injection is completed for  $\frac{1}{2}$  minute to prevent leakage. To further prevent leakage the injection can be accomplished with 1 needle puncture by replacing the procaine syringe with the tuberculin syringe containing the vitamin A dispersion, leaving the needle *in situ*.

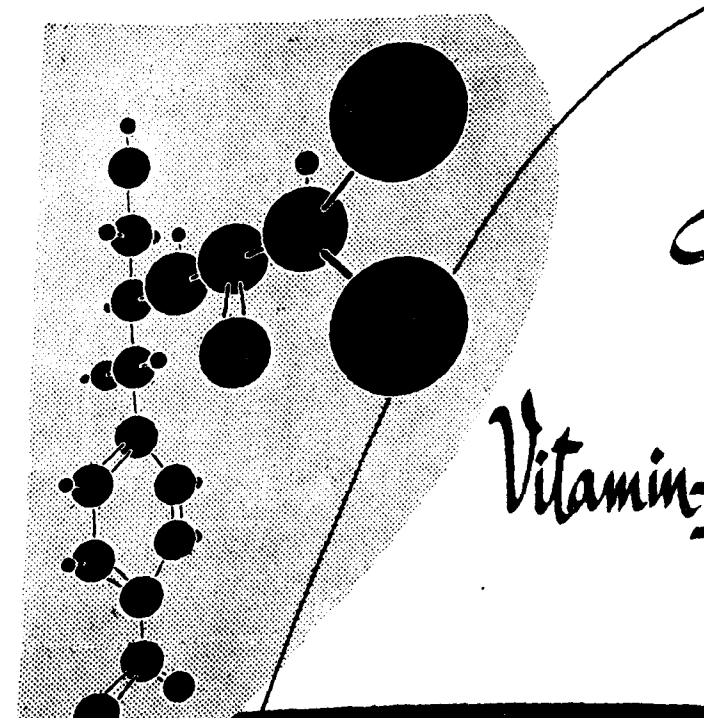
The initial dosage should not exceed 0.1 cc. per square cm. of verrucous area. The injections are given at weekly intervals and the dosage may be increased to 0.2 cc. per square cm. Care should be taken to avoid intravenous injection. Usually from 2 to 8 injections are necessary. Involution begins within a few days and after several weeks the lesions regress completely. The pupillary lines reform and no evidence of skin alteration is present. Pain usually disappears after the 1st or 2nd injection. The patient may bathe and remains ambulatory throughout the period of treatment. Only a Band-Aid is applied over the needle puncture.

In 300 cases which I treated there were only 7 failures. These failures could be accounted for by mechanical factors in the form of fibrous or keloidal barriers due to previous treatments, preventing the vitamin from diffusing through the lesion or to the unusual consistency of the verrucous area where fissures or other openings allowed the vitamin A to escape.—(Surgery, Apr. 1956, via *Current Medical Digest*, July 1956).

## FORCEPS DELIVERY—APPLICATION CHECKS

After the handles are locked satisfactorily, the application is checked. This is done in 3 ways:

1. The *posterior fontanelle* should be located, midway between the sides of the blades and one finger's breadth above the plane of the shanks.
  2. The *sagittal suture* should be perpendicular throughout its length to the plane of the shanks.
  3. The *fenestrations* of the blades should barely be felt if at all. Not more than the tip of a finger can be inserted between them and the head.
- Unless these conditions are fulfilled the application is not a true cephalic or biparietal bimalar application.—(Forceps Deliveries, via *Cur. Med. Dig.*).



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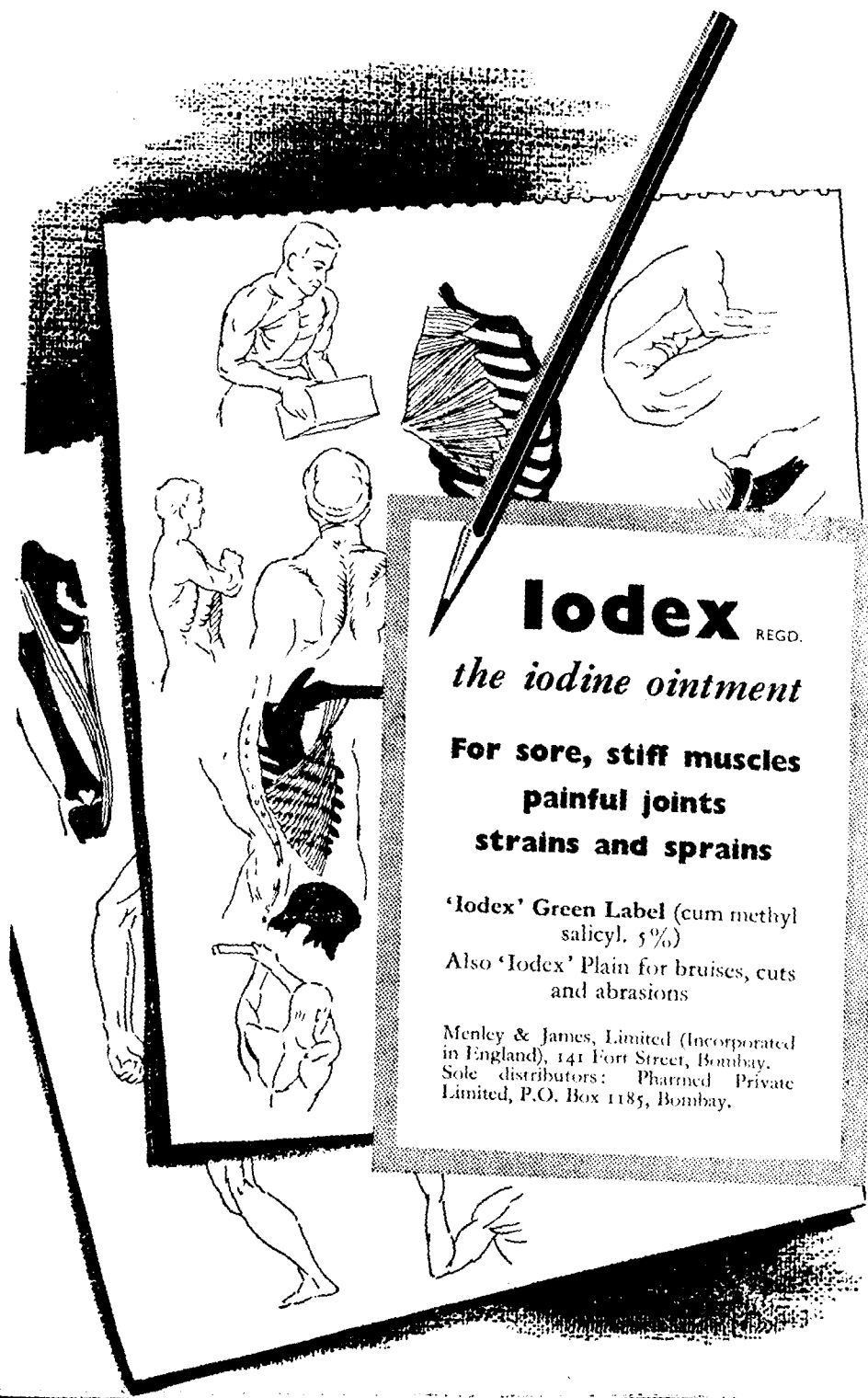
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## PERSONALITY IN PULMONARY TUBERCULOSIS AND ITS PSYCHO-DYNAMICS\*

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"Tubercle is not the cause of tuberculosis, but only one of the necessary conditions for its development."—M. Pinner.

"What happens to a patient with tuberculosis depends more on what he has in his head than what he has in his chest."—W. Osler.

FROM remote antiquity the functional unity between body and mind has been recognized by the physicians when dealing with the illnesses of their patients, but with the rapid development of the means of diagnosis and treatment of organic ailments the study of and research into emotional causes of disease came to be generally neglected. But it is only in recent times that a combined psycho-physical approach has come to be made by the physicians on a truly scientific basis, in which not only the illness from which he suffers is taken into account, but the environment in which he lives is also given equal attention.

Since many tuberculosis patients present behaviour-problems in T.B. sanatoria, many writers assume that the personality changes are caused by the disease itself. But a careful study of the total reaction of the patient to the illness will reveal the fact that it is the previous personality-trends of the patient prior to his illness which pave the way for his later attitude to the disease itself. These personality trends are in turn the aggregate of experiences and influences which he has had in the early years of his life, when his personality was elastic and impressionable. The childhood history, the family constellation and the general atmosphere of the patient's home all assume dynamic importance in determining the behaviour-patterns and general personality-reactions which he is likely to display as an adult. The patient has to fight his battle on two fronts. On the one hand he has to grapple with the problems which have remained unsolved since his early days—only to exist unnoticed within his personality; and on the other, he has to meet the inexorable demands of external environment. In this way issues relating to personality become a major contributory factor in the total situation leading to the onset of tuberculosis.

If we take an over-all view of the personality of the tuberculous patients, their inordinate need for love and affection strikes one as the outstanding feature. To achieve this primary aim their life strivings may undergo various permutations and combinations, but they all seem to cluster around one central point, i.e., the desire to be loved and cared for, the satisfaction of which alone would maintain their psychological

\* Specially contributed to the ANTISEPTIC

equilibrium. The need for affection and attention may be openly expressed, thinly veiled, well-concealed or flatly denied. So it may adopt many devious channels for its expression, involving the patients in certain typical personality-conflicts.

In a general survey of the personality-pattern of these patients we notice that at one end of the "personality scale" are individuals whose need for affection and protection is open, pressing and in certain cases almost blatant, and at the other are those who take their independence and self-sufficiency, so much for granted, that their life-plan appears to be only to drive themselves into ceaseless and strenuous work and physical toil. Between these two extremes on the scale may be found individuals to whom the admission of their need for dependence and help would constitute a serious threat to their already tenuous self-esteem, which they can only maintain by asserting their overt independence. Further distinguished from these persons are those aggressive and rebellious individuals whose masked need for dependence finds satisfaction—perhaps due to early frustrations and disappointments—through militant, sometimes anti-social behaviour. There is left yet another distinct group, viz., individuals who, on account of their conflicts over aggression, cannot make their choice between being dependent or independent, and thus continue in a state of mental stalemate with consequent inhibitions and stultification of the expression of the fundamental needs of personality. Those falling into this group may more appropriately be described as "conflict-harassed" individuals.

It is interesting to observe here that workers in other fields of study of emotional factors in chronic organic diseases have also noticed the pre-eminence of dependent personality trends in the life histories of their patients; and the conflicts connected with this outstanding personality-need in many respects are analogous to those seen in the patients suffering from tuberculosis. Alexander and his colleagues, who have recently carried out an extensive research into the emotional factors contributing to the incidence of gastro-intestinal diseases, like peptic-ulcer, duodenal ulcer, mucous colitis and allied disease entities, have noticed that the "conflict between the help-seeking and self-assertive rivalry has been found to be the nuclear conflict in some types of psychosomatic disease." Since this "nuclear conflict" invariably has its origin in the childhood situation of the patients, its solution mainly depends on the nature of the child-parent relationship which subsisted in the early days of the patients' lives. Unless a satisfactory solution had been found for this basic conflict through some healthy substitute-gratifications in the formative years of childhood, the conflict with its

strong affect of ambivalence gets repressed only to come out through circuitous routes of expression in adult life in problems of behaviour and emotional maladjustments. The personality variations which they show thus appear to be only a manifestation of difference in character-defences which they come to build up.

In a more recent work, Alexander describes analogous mechanisms of defence in his psycho-dynamic formulation of the patients suffering from the diseases of the gastro-intestinal tract: "Our analyses show that these tendencies toward over-activity, efficiency and ambitious effort are compensations to cover up the under-lying strong dependent-receptive tendencies which in turn are increased because of the fact that they are not allowed even normal expression. A vicious circle is at work here. The high claims which these individuals have regarding efficiency, activity, productivity and success lead them to make over-exertions which then stimulate the opposite, receptive of their nature, which in turn necessitates stronger and stronger over-compensations."

The case reports of 300 tuberculous patients forming the basis of the present research may be classified under 4 main headings of personality types:—

I. The overtly insecure type, comprising three sub-types: (a) the over-dependent type, (b) the leaning type, (c) the asserters of independence type.

II. The rebellious type.

III. The self-driving type.

IV. The conflict-harassed type.

The characteristic features of each one of these personality types, from the view-point of the above-mentioned two items, (i.e., childhood background and later personality) will now be examined.

I. The overtly insecure type.—A. THE OVER-DEPENDENT TYPE:—*Childhood background*:—The patients representing this type of personality were either the only children or were the youngest among the children. They were mostly delicate and frail in health and the usual childhood diseases [they suffered from were mostly prolonged, leaving them constitutionally weak. By virtue of their special position in the family constellation and their health-status, they earned for themselves special consideration from their parents and other members of the family. They were pampered by either or both the parents; they were thus at a serious disadvantage unable to cope adequately with the heavy demands made by the realities of adult life. They took their pampering and over-indulgence so much for granted. Their characteristic conflict arose when their overtly dependent needs were frustrated and they had to depend on their own resources.

Dependence created hostility in them, and this in turn created anxiety and fear of retaliation on the part of their loved ones, thus leaving them helpless and without support. A vicious circle with a difficult conflictful situation was thus set up.

*Later personality* :—Such persons enter adult life as mere “overgrown children,” with marked characteristics of an immature, emotionally retarded personality, i.e., selfishness, vanity, peevishness, intolerance of any type of frustration and active resentment of any hardship they might have to face. They mistake the realities of their later environment for realities of earlier life-situations and develop the notion that life will treat them as leniently as their parents did. These patients show a singular lack of self-drive and ambition, and being work-shy they show little or no guilt in their excessive claims on the environment. The basic “personality formula” presented by them is, “I want to be loved and mollycoddled as I was in my childhood. Let others take the responsibility for everything; anything is too much for me.” But they head towards a breakdown when they come up against hardships and difficulties they are unable to face alone, since both physically and psychologically they are ill-prepared to weather a stormy world.

A typical case of this type was that of a housewife, aged 24, who was the only child of her parents. Every attention was given to her by her parents, who however, did not get on amicably between themselves. Due to the unhappy home atmosphere the patient always felt unhappy as a child. As a grown-up girl she showed the features of a typically maladjusted girl who expended all her energies on pleasure-seeking. This girl joined as an ambulance driver in 1940 and had to work very hard. In 1942, she fell ill, and got her discharge from that post. Later, she joined the Civil Defence where she met her future husband with whom she led a very fast and hectic life. After marriage however, she realized that she did not love him. She lived under great emotional tension, but continued her reckless pursuits. Her husband went overseas and did not return until May 1944. During his absence, with her unhealthy emotional state of mind and the spell of dissipation, and self-indulgence which she had had earlier, she developed tuberculosis. Even then she could not restrain herself from pleasure-seeking and extravagance. This case typifies, the characteristic contribution which patients of this category make to the precipitation of their children's illnesses.

**B. THE LEANING TYPE :—***Childhood background* :—Not unlike<sup>a</sup> the patients with a predominantly over-dependent personality, these patients too feel a prominent need for affection and protection from others. In behaviour pattern they show themselves unduly dependent upon the parent of the opposite sex. They show feelings of being unwanted and are shut-in, reserved,

genteel and inoffensive. In their relationship to other siblings they show jealousy and inhibited aggressiveness. Due to their dependent and leaning tendencies they show personality features of shyness, emotional inhibition and general nervousness.

*Later personality* :—As adults these patients grow up as shy, self-conscious, inoffensive and inhibited individuals with marked feelings of inferiority. They constantly worry about what others think of them. They play the role of spectators rather than participants at a party. But beneath this facade of inoffensiveness and general social aloofness, lies a good deal of aggressiveness which however, remains overtly suppressed because of their prime need to lean upon the help and protection of others. They are able to sustain their psychological security system only if they have the love and support of some strong personality (usually a parent-substitute). Apart from displaying an anxious and nervous disposition—with various phobias dating back from early childhood—they are sometimes subject to spells of depression. On the one hand, these depressions are motivated by the frustration which is inevitably entailed in the excessive emotional demands they make upon others and on the other hand, they symbolize the inner struggle to keep the hatred and aggression repressed which the unfortunate circumstances of their earlier life had created, and which their strong ambivalence, with its associated feelings of guilt and anxiety, would not permit them to canalize into healthy channels of activity.

An illustrative case of this type is that of a nurse, aged 27, who was one of 7 children. When the patient was still very young, the family went to India and she was left alone in Scotland with her grandmother. She visited her parents on annual holidays in India, but, on the whole, they remained strangers to her. She felt shut in and unwanted and resented the fact that she had been singled out and left at home with a strict grandmother. “I have always felt the odd one out”; that is how she described herself as a child. The patient developed into a shy, inhibited and emotionally shut-in person, unable to express her feelings. Her father died when she was only 11 and her mother when she was 18. Shortly after the out-break of war, her brothers also died one after another. In 1940 she was engaged to a boy whom she had known since her childhood. He too died in action towards the end of 1944 and in 1945 she broke down mentally having developed tuberculosis.

The history of this patient illustrates the fact that due to lack of maturity in being self-reliant and independent, the series of traumas and painful experiences which she suffered on the deaths of her relatives one after another, proved too much for the adjustive capacities of her ego. The climax was reached when her lover died.

dictated by his parents are considered by him as alien to his fundamental personality. Patients belonging to this category show personality characteristics of the type described above.

Ontogenetically, they had had an unhappy and uncongenial environment. They were often dominated and bullied by either one or both parents. As children these patients showed characteristics of obstinacy, uncompromising negativism against the discipline and rules of conduct imposed by their parents. As one patient put it "However much my father caued me, it made no difference to me." Some of the patients in these surroundings developed a defiant and rebellious attitude against their fathers, and an air of protective solicitude towards their mothers.

*Later personality*:—Outwardly they appear happy-go-lucky but in their inter-personal relationships they are aggressive self-righteous, bossy and domineering. In their family life, they are erratic and flippant in discharging their responsibilities towards their wives and children. Some of them indulge in frequent promiscuous affairs and lead a hectic and decadent life. The following case illustrates this type:—

The patient, a fitter was the youngest of 3 children and the only son. He was spoilt by both his parents, especially by his mother. As a child he was very troublesome, given to fads, quick-tempered, constantly fighting and always up to some mischief or other. As an adult, he continued to show maladjustment in his social relationships, and was involved in frequent quarrels with other men.

The patient's father died of cancer 3 years prior to the onset of illness. Soon after his father's death he became the boss in his laundry firm. A month before his first hæmoptysis, he had a motor-bike accident. After his recovery from the accident he continued to work for about two years after his father's death but afterwards he got into bad company. He often did not get up in the morning and go to work and got involved in a theft of petrol. Because he got completely out of hand, his mother decided to remarry. He felt greatly disturbed after this incident, and after a violent scene with his step-father the patient left his mother's home. Inwardly he still pined for his mother's love and had day dreams that his mother would get re-united with him and nurse him in his illness.

It will thus be seen that his rebellious and belligerent attitude ultimately proved to be only a facade against his passive dependent wishes which got the upper hand when the frustrations in the outside world became too much for him to endure.

III. The self-driving type.—*Childhood background*:—The central point in the emotional life of these patients lies in the

rules of conduct which they were taught by their parents to observe. Originally they were spurred on by the fear of a threatening and punitive father, or by a desire to win the approval of an over-ambitious mother who made the patient the focus of her attention when she herself was frustrated in her ideal of a good husband. Here we may note two paradoxical facts in their early life-situation:—(1) the pattern of living of a stern and a slave-driving father may be unconsciously identified by them as children on account of the conflict of ambivalence towards the parent figure. This may lay the foundation for their self-frustrating and compulsive drive in their work in later life, against which they stand defenceless; (2) they may get so disappointed in their ideal of a father that all the attributes of a lazy and worthless father may be rejected in order to remain on good terms with the mother.

Those patients who lost their father at an early age were goaded on by their mothers to be self-reliant and independent, the mothers themselves setting an example of industry and diligence. Thus, these patients were prematurely loaded with heavy responsibilities at an early age, although physically and emotionally they were not sufficiently grown-up to shoulder such burden. Those patients whose mothers were deserted or divorced by their fathers, had to face the same set of circumstances. In the case of those patients whose fathers turned out to be ne'er-do-wells, drunkards or social parasites, the patients endeavoured to behave differently by exerting themselves to the utmost of their ability to remove the stigma of the unenviable conduct of their fathers. A patient having strained relations with his father said, "My father's manner was—'You must do this, you are a fool if you do this'—Although I agreed, I rebelled subconsciously against him." The patients of this type maintain a continual tussle with their fathers, and subsequently frequently kick against all types of restricting authority, yet being quite unaware that they might have assimilated many personality-trends of their fathers against whom they protest so violently. This may lead to the development of quite incompatible traits in their personality-organization producing irreconcilable conflicts in their behaviour-pattern. Deeply ingrained as is the urge in them to engage themselves in feverish activity and tiresome toil in their profession, this perfectionistic preoccupation often reaching abnormal proportions; and they abandon their extreme exertion only when their physical and mental stamina fail them completely. They do not drive themselves to work, rather are they being driven by their work.

They present a personality profile of over-conscientiousness, unlimited ambition, punctiliousness, perfectionistic trends in work-worry over financial security, inferiority complexes and self-consciousness in the social sphere. Their main conflict seems to be

between active and passive impulses focussing on immediate values, and strivings towards long-term projects, aggressivity and the need for maintaining peace. Since they cannot strike any tangible balance in their primary impulses of love and hate, as they are focussed upon their parents, they are left with personality profiles which are intra-physically split and emotionally disintegrated, despite the massive superstructure of their conscious denials and reaction-formations. Such incompatible traits in their character, invariably exert an unhealthy and deleterious effect on their health and general well-being.

**Illustrative case.**—A housewife, aged 45, lost her father in the First-World-War while she was only a child, and her mother when she was 9 years old. For years thereafter she grieved over her mother's death and then lived with her grandmother who treated her severely. If she did not do her work to her grandmother's satisfaction she was severely punished. She was a very nervous little girl. She was particularly afraid of darkness and of being alone. One of her recurrent night mares was that a huge black form smothered her. She was always afraid of water, of fire and of being suffocated.

As an obsessional self-driver this patient always worked very hard. She never allowed herself any relaxation; in fact, she was never able to relax. Her motto was: "Everything had to be as near perfect as one could do it, even to the exclusion of one's comfort."

When she got married, she had to live in a two room tenement. The difficulties of accommodation increased when she had children. In addition to this, she had to face financial strain, because her husband did not have an adequate income. She started assisting her husband in his business. According to her statement she did "an awful lot" and always did things thoroughly. By trying to be so thorough in the business and at home I knocked myself over." Ultimately the strain of her unmitigated self-driving proved so hard to bear that she started going downhill in health, and developed tuberculosis when in addition to following her hard routine at home and at her husband's office she had to attend upon her invalid daughter.

The above case illustrates the type of individual whose illness was brought on, not by exogenous causes, but by sheer pressure of her inner anxieties, the tension of which she attempted to relieve by incessant activity and self-propulsion. She suffered from a "repetition-compulsion," to repeat the earlier situation in her own home, and in relationship to her husband's business, whereby she burnt the candle at both ends.

**IV. Conflict-harassed type.**—*Childhood background:*—Since the childhood situation of the patients belonging to this category has been conflictive and unsettled, it inevitably led to

unharmonious and warped emotional development, presenting a "conflict-harassed" personality. A large majority of these patients had had an unhappy and uncongenial home-environment which bred in them the emotional conflicts and personality maladjustments of later days. Since their need for love and care were thus frustrated in this unharmonious milieu, they had strong feelings of hatred directed against their parental figures, which had to be repressed owing to their state of dependence in early days. Feelings of ambivalence thus became the key-note of their personality-constellation. The repressed hostility created in them feelings of guilt and remorse and a need for making atonement and reparation for harbouring aggressive impulses against persons whom they loved at the same time. The conflicts within their personality were not, however, confined to aggressiveness alone. Some of the patients were erotically fixated upon their parents—mostly the parent of the opposite sex. This led to an unconscious sense of shame and guilt, resulting in emotional inhibition and retardation of personality development. Due to their prominent personality characteristic of ambivalence and lack of balance in their instinctual trends they are not able to maintain a consistent and stable attitude towards their environment, and so remain caught up in the vortex of their unresolved personality conflicts. As children they were quite shy and rather inclined to be self-willed.

*Later personality:*—Unable to bring about a satisfactory solution of their childhood difficulties, these patients enter adult life with prominent emotional problems and personality maladjustments. They are quiet, serious and reserved, and although they outwardly pose as self-possessed and confident in social contacts, inwardly they remain self-conscious and harassed by feelings of inferiority. In the professional field they are conscientious and hard workers. They insist upon order and discipline in work, because being conflict-ridden, they lack these things in themselves. When in the life-situation prior to their illness their personality conflict reaches a climax and they find it difficult to canalize their pent-up feelings of aggression into healthy channels of activity, they suffer from anxiety and depression. Due to the vicious circle of dependence and defiance they take an unconsciously masochistic delight in suffering, so as to assuage their sense of guilt and remorse. Thus self-damaging and self-humiliating trends come to be the foremost characteristics of these conflict-harassed individuals.

**Illustrative cases.**—A student, aged 20, was the younger of two sons. He was born in China where his father worked as a missionary. The patient modelled himself in many ways after his mother rather than after his father. From an early age, following the pattern of his mother he showed extreme sensitivity

to pain and suffering. The mother herself had undergone several operations and bore her troubles cheerfully. The ties between the patient and his mother always remained very close; his brother was the father's favourite. The patient was brought up in a strictly religious atmosphere, but being the youngest child was especially pampered by the mother.

*Later personality* :—During the interview the patient attempted to camouflage the real nature of his emotional problems by trying to be rhetorical and over-intellectual. Only gradually did his defences break down.

The chief factors responsible for the onset of illness in the patient appear to be not externally traumatic happenings but the accentuation of his conflicts connected with sexuality which he could not hitherto solve in a satisfactory manner. The nature of these conflicts can be best assessed in the patient's own words. "When I was 15, I had a girl. I thought I was in love with her. Immorality is one of the hardest things to fight against in the world. To-day, women have lost a great deal of their modesty, as revealed particularly in their dress. Free discussion of sex is not helpful. All forms of sin are uncleanliness. I am capable of committing acts of sin, anything from theft and dishonesty to improper sexual intercourse. When I was young I used to commit petty thefts. Masturbation at 10. Very guilty. My mother understood these things. All the teachers were maiden teachers. Guilty offence to wet bed. I got into bad lot at school. Got in with older fellows. Encouraged me to display private parts to them. It was not until I was 14 that I decided that it was all wrong. When I got the disease I did wonder whether this sort of thing had brought on the trouble. I told my mother all about it. She assured me it had no bearing on the illness."

The above account given by the patient of his emotional life shows in unmistakable terms that he had been harassed by strong personality conflicts connected with his sexuality, dating back from his childhood right up till the onset of his illness. The tension produced by these conflicts seemed to have played an important role in the precipitation of his illness.

VII. The unclassifiable individuals.—To this general group belong 22 patients whose personality characteristics remain undefined and incapable of distinct classification, and so do not fit into any of the personality types which have already been described. Either their personality structure is so complicated and complex that no highlights of its features can be distinguished, or the clinical material gathered by the interview-method is too scanty to enable grouping under any specific heading. Broadly speaking, they comprise individuals suffering from gross psychological disorders, like

conversion hysteria, anxiety states, obsessional neurosis and functional psychosis. Some of them are mentally defective and anti-social characters.

*GENERAL SURVEY* :—The most fundamental features in the personality of tuberculosis patients, as we have observed in the discussion of their personality types, is their primary need to be loved and protected by others. They react with bitterness and resentment whenever the support and attention of others is withdrawn from them, or they have to put up alone with the hardships and problems of life. Concerning other cases, the basic personality needs, however, remain the same as they exist in the "Overtly Insecure Type" of patients only with this difference that the admission of these needs is incompatible with their ego-structure, hence the necessity to keep these personality traits repressed. To ward off such a contingency these individuals may either act out their conflicts in unhealthy and harmful modes of activity, e.g., compulsive overwork, perfectionism, exacting standards of living, excessive drinking and gambling, psychopathic and anti-social behaviour, or the personality itself may become the battlefield of inimical and destructive forces, resulting in a self-humiliating and self-damaging life-pattern, as is typical of "conflict-harassed" individuals. On account of their deeply involved problems of personality, the patients of the latter type who have internalized their aggressiveness present a much poorer prognosis, than the patients whose main difficulties of life arise from overwhelming and insatiable overt demands made upon them. In their reaction to illness these patients have spells of acute depression and anxiety. By way of contrast the "Overtly Insecure Type" and the "Rebellious Type" show an outgoing and extrapunitive mode of reaction, whereas the patients comprising the remaining two groups, namely, the self-driving type and the conflict-harassed type show a shut-in and intro-punitive way of meeting the external frustrations.

When we study the psycho-dynamics of depression we find that at the time when all normal avenues for the discharge of an individual's self-assertive and aggressive impulses are closed by the pressure of an externally frustrating reality, he compulsively acts out his personality-conflicts in activities which, by all standards of normal judgement, may be regarded as highly prejudicial and inimical to his general well-being and welfare. This behaviour pattern hardly seems to be "reality-dictated," as it is merely an expression of unresolved personality tensions and emotional complexes against the heavy pressure of which the individual remains defenceless. The pathological acting-out may in the end reach such proportions that in a state of lowered resistance in health he may easily fall a victim to a disease like tuberculosis.

In conclusion it may be pointed out there is no specific "tuberculous personality"; rather these patients could be grouped into a few broad headings of the most prominent personality types.

#### THE HEART IN MUSCULAR DYSTROPHY

It has been estimated that the heart is involved in 50 to 85 per cent of cases of progressive muscular dystrophy, particularly of the childhood type. The cardiac manifestations have been linked to the primary myopathy by several authors, who have suggested the term "dystrophic heart disease."

Berenbaum and Horowitz report the case of a 28-year-old man with advanced progressive muscular dystrophy who developed cardiomegaly in less than one year, a preterminal bout of congestive heart failure, and died suddenly. A post-mortem examination was not done. There was no history or clinical evidence of rheumatic, hypertensive, coronary or congenital heart disease; myocardial involvement by the dystrophic process was considered the most likely diagnosis.

Several pathologic studies have revealed lesions in the cardiac muscle identical with the lesions in the skeletal muscle. Disease of the coronary arteries has not been noted.

The clinical manifestations of dystrophic heart disease are nonspecific. Most frequently noted have been: tachycardia and arrhythmias, cardiomegaly, congestive heart failure, and nonspecific electrocardiographic abnormalities. The most frequent abnormalities in the electrocardiogram were of the P waves.

The pathologic findings in the heart are most commonly an increase of connective tissue, atrophy of muscle cells, extensive patches of myocardial fibrosis, and considerable infiltration of fat.

The authors emphasize that muscular dystrophy is not rare. It is estimated that there are well over 200,000 cases in the United States alone. The high percentage of cardiovascular complications in this group makes the problem of dystrophic heart disease an important one. It should be considered more frequently in the differential diagnosis of obscure forms of heart disease, especially those vaguely designated as "idiopathic myocarditis."—(*Am. Heart J.*, 51: 622, 1956).

#### PITUITARY NECROSIS WITH DIABETES MELLITUS

Pituitary necrosis is a relatively common and potentially dangerous complication of diabetes mellitus.

Partial pituitary necrosis occurs in about 1 of 50 persons with diabetes but in only 1 of about 550 persons in the general population. Although the lesions may not cause symptoms under ordinary circumstances, pituitary-adrenal response to stress may be inadequate. If the pituitary defect is not recognized and replacement therapy given, anaesthesia, infection, pregnancy, diabetic ketosis, or other stress may cause death from acute adrenal insufficiency.

Hypopituitarism may aggravate neurologic complications of diabetes. Reported reduction of insulin requirements in diabetic patients with pituitary necrosis would probably be eliminated if hormonal therapy were adequate. If cortisone is given orally to patients with pituitary insufficiency, blood corticoids reach a peak immediately after absorption, and need for soluble insulin is therefore increased. Labile diabetes may ensue, counterbalancing any gain from reduction in total insulin-requirement.—(*Modern Medicine*).

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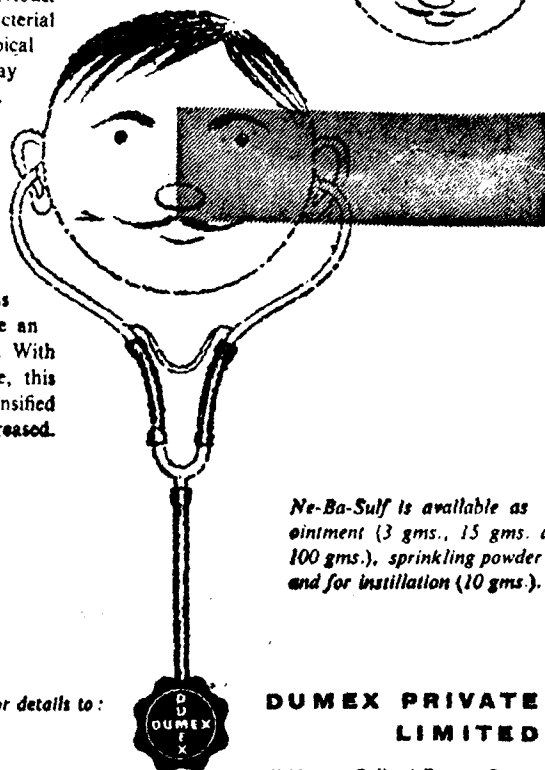
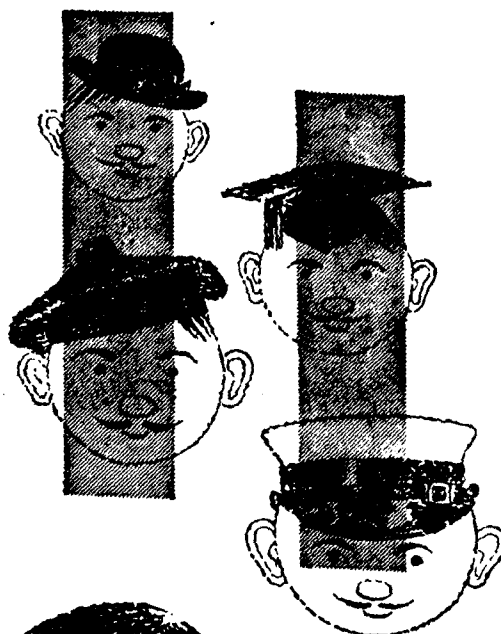
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## CHANCROID\*

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CHANCROID is an acute autoinoculable infectious disease characterized by painful ulceration usually over the genital region and often accompanied by suppurative regional adenopathy. It is usually contracted through sexual contact and the causal organism is *haemophilus ducreyi*. The disease has been recognized as an entity for centuries and has many synonyms such as 'ulcus molle cutis,' 'Ducrey's infection' and 'soft chancre.'

Ducrey (1869) described *Haemophilus ducreyi* the causative organism. Nicolas (1899) reproduced the disease experimentally in monkeys. Koch's postulates were put to the proof by Greenblatt and Sanderson (1937).

Chancroid has a world-wide distribution. Under unusual conditions such as war or mass-migration, it spreads widely and rapidly. It occurs much more commonly in men; so also is inguinal adenopathy more common in men than in women, probably due to the anatomical difference in the site of the primary lesion and in the drainage of lymphatics. Bruck isolated *H. ducreyi* from the urogenital tract of healthy women indicating that women may be carriers of the organism, a fact which may explain the cause of the low incidence of chancroid in women.

Clinically chancroid gives rise to a painful ulcer or ulcers at the site of inoculation of the germs. Being generally of venereal origin the lesion is usually on the genitalia. The incubation period varies from 1 to 3 days and its early appearance is often attributed to trauma such as a crack or an abrasion during sexual intercourse. Initially the lesion is a small crack, abrasion or an ulcer on an erythematous base. As the chancroid increases in size it becomes somewhat irregular in outline the base is soft and covered with a purulent exudate; the borders are soft and undermined, red at the periphery and yellowish at the centre. The lack of infiltration and induration has led to the term "soft chancre." It is always painful. Its auto-inoculable nature leads to a multiplicity of lesions which appear on areas in direct opposition.

The Ducrey bacillus seems to have a special predilection for the skin. In the male the lesion is often found on the prepuce, at the sulcus or frænum. Occasionally it may be intraurethral. In women it is found on the labia majora, labia minora, fourchette or clitoris. Involvement of the anus by direct extension is common in women. At this site it appears as a fissure surrounded by hypertrophic vegetations and is often mistaken for warts.

\* Specially contributed to the ANTISEPTIC

or hæmorrhoids. Lesions on the prepuce very often show œdema and give rise to secondary phimosis. Extragenital lesions are not unknown. The chancroidal ulcer may vary in size and shape according to its location, pathogenicity of the germs, resistance of the individual, duration of the lesion and hygienic habits of the person. A fresh lesion is usually small and single while older lesions are invariably multiple, large and secondarily infected.

The clinical varieties are:—(1) The small uncomplicated ulcer met with in persons of clean habits; (2) the papular type—the lesion is elevated, crusted and often associated with a warty growth, usually seen in women, and (3) phagedenic chancre—a rapidly destructive lesion spreading extensively not only on the genitals but also on the thighs and abdomen, Vincent's bacillus or *Fuso-spirochaetes* being often seen in smears from the lesion. In the pre-sulphanilamide era, this type of lesion used to be extremely resistant to local therapy and to cause vast destruction of essential organs.

Inguinal adenitis—is often a common feature in a fairly large number of patients especially of unclean habits, and is commoner in men than in women. It is precipitated by unclean habits, hard work and lack of rest. Extra-genital lesions are generally not followed by regional adenopathy. The bubo develops 1 to 2 weeks after the appearance of the ulcer. It may be prevented by the administration of sulpha drugs very early in the course of the disease. Adenitis usually occurs on the side of a chancroid or it may be bilateral. Lymph glands are enlarged and tender; periadenitis follows, and the overlying skin becomes red. In a few days the glands become soft and fluctuating and the skin on them becomes thin, shrivelled; the buboes then burst, and discharge a good amount of pus leaving a sinus. Inoculation of the skin around the sinus is quite possible and may cause the disease to spread. If not properly treated the ulceration may last for a few months, [causing extensive destruction of the tissues.

The most important symptom in chancroid is pain both at the site of the ulcer and in the adenopathy. The skin over the bubo does not become thickened and œdematous or show furrows as in the adenopathy of lymphogranuloma venereum.

Chancroid may be contracted simultaneously with other venereal diseases. It may co-exist with syphilis, gonorrhœa, lymphogranuloma venereum or granuloma inguinale. Such combinations are not unusual. The clinical picture is usually mixed and bizarre depending on the character of each disease.

Systemic changes are very mild. Where buboes and extensive ulceration are present, fever, malaise and aching may be

noticed. There is however, rapid response to specific therapy; the fever subsides, the pain becomes less, the discharges decrease and healing starts in 2 to 3 days. Glands subside rapidly if there is no softening and fluctuation. One attack does not confer immunity, against subsequent infections if exposed to *H. ducreyi*.

Clinically chancroid should always be suspected when there is a painful, purulent ulcer of short incubation, with an acute and painful adenopathy. The diagnosis must not be made on the clinical appearance alone but must be confirmed by laboratory examinations and all procedures for the exclusion of syphilis must be carried out before a diagnosis of chancroid is made.

Laboratory diagnosis.—The diagnosis of chancroid can be arrived at by different laboratory tests all of which have their limitations. No one method can be applied in all cases and the procedure suitable for each case must be selected depending on the duration, and type of the lesion. For reasons of expediency one is often tempted to make a diagnosis by exclusion only i.e. considering as chancroid a genital lesion in which a dark-field examination is negative for *T. pallida* and which responds to sulphanilamide therapy; but such temptation must be avoided as far as possible. It would not be right to call a genital lesion a chancroid simply because the dark-field examination is negative for *T. pallida*. It is equally important to exclude other venereal diseases and correlate the findings with clinical and laboratory investigations. The judicious use of appropriate procedures in the diagnosis of chancroid will rule out other venereal diseases.

The diagnostic procedures vary in their accuracy, techniques and availability. Some are direct methods such as the demonstration of the causative organism in smears and cultures, study of tissue reaction, auto-inoculation, histologic changes and intradermal test with Ducrey vaccine to detect specific immunologic changes, while other methods used in the diagnosis of other venereal diseases are indirect and are usually negative in chancroid.

*Smears for H. ducreyi*:—The actual demonstration of *H. ducreyi* in a smear from the ulcer is definite proof of the disease. Great care must be taken in the selection of the site, collection of material and preparation of smears.

The lesion should be thoroughly cleaned with saline and a smear made with a short thick platinum wire. The overhanging edge of the ulcer or undermined border of the ulcer especially advancing, is the best site for taking material for smears. The slides are prepared, dried and fixed by heat; Unna-Peppenheimer

stain is recommended. Wright's or Giemsa's stain may be used for staining instead.

The *Ducrey bacillus* is gram-negative, short, thick, with rounded ends which often stain deeply giving rise to a "safety-pin" appearance. It may be intra- or extra-cellular. Its long chains often in parallel lines suggest the typical appearance of "shoals of fish." The smears from advancing borders of an ulcer show parallel rows of bacilli while the smears from cultures give long chains. Lesions which are of more than 3 and less than 8 or 10 days' duration, are best for obtaining positive smears. Older lesions get secondarily infected with other organisms. In experienced hands this method has yielded successful results in 65 to 88 per cent of cases. In rapidly destructive lesions, superimposition of fuso-spirochaetes should be suspected and ascertained by examining smears.

*Ito-Reensteirna test or Ducrey vaccine skin-test:*—The value of this skin test in diagnosis is debatable. The test may be negative in the very early stage of the disease and become positive after some time, to remain so thereafter. The Ducrey vaccine (Lederle Laboratory) is available in 0.2 cc. or 5 cc. vials for two or fifty tests. The tube is well shaken and the required material i.e., 0.1 cc. is drawn in a tuberculin syringe and injected intradermally on the flexor aspect of the forearm. Control is not necessary. In a positive case, an erythematous papule from 7 to 12 mm. in diameter is noticed at the site within 48 hours. The test is then reported positive. In a negative case there is minimal reaction which fades away rapidly. The test is usually positive in the first or second week of the infection but occasionally after six weeks. It is almost invariably positive after the appearance of adenopathy.

*Evaluation of the test:*—A positive reaction indicates that the patient is infected with *H. ducreyi*. It does not necessarily mean that the lesion actually under observation is of a chancroidal nature as the reaction will be positive even in patients who had had chancroid years ago. The interpretation of the test is conclusive only in cases with a negative history of previous venereal disease. The test is of definite value when a negative reaction found at the onset of the disease is followed by a positive one when the test is repeated two weeks later. A negative test would indicate that the patient has not been infected with *H. ducreyi* or that if the infection has occurred, it is so recent that the patient has not developed sensitivity to the vaccine. In the latter case, the test should be repeated after 1 or 2 weeks. In some cases of chancroid where treatment is instituted immediately after the onset of infection, sensitivity does not develop and the test is often negative.

Auto-inoculation of the chancroid is one of the oldest diagnostic methods used in venereal diseases. An inoculation with material from the suspected lesion is made in the same patient representing the disease. A drop of pus from the ulcer is placed in the normal skin of the patient, and scarifications as in small-pox vaccination, are made through the drop with a sterile needle, avoiding bleeding. The area is then covered with sterile dressing. If positive, several small pustules will appear in 24 hours on the spot. In a couple of days they ulcerate and form minute chancroids which may become large and painful. *H. ducreyi* may be demonstrated in the smears made from these lesions. Sulpha-drugs are very effective, as they cure both the original lesion and the auto-inoculation. Local treatment consists of keeping the part clean and well-drained. Auto-inoculation is not meant for general use and should not be practised as a routine. This method was found to be successful in about 80 per cent of cases.

*Culture of H. ducreyi:*—Is a difficult procedure requiring special media such as defibrinated rabbit's blood or tryptine phosphate medium with fresh rabbit's blood. The colonies are characteristic in appearance and the organisms show a definite pattern in their spread. They may be in clumps or chains according as the medium used is solid or liquid. When the lesion is contaminated with other bacteria, the culture test is likely to fail in about 75 percent of cases.

*Microscopic examination of the tissue* from the ulcer is of value in the diagnosis of chancroid. The histologic changes occurring in the lesion have a distinct pattern and permit a reasonably certain diagnosis in nearly every case. This method could however seldom be used as a routine but it is the most reliable single method of diagnosis. A piece of tissue 3 mm. in diameter is removed from the ulcer with a Gaylor's forceps, processed and examined. The ulcer shows three distinct zones. The surface-zone made up of polymorphonuclear leucocytes, fibrin, red blood cells and necrotic tissue in which endothelial cells in various stages of proliferation predominate over other cellular components. Newly formed numerous blood vessels show palisading with occasional degeneration of the walls and thrombosis. The deepest zone is made up of a dense infiltration by plasma cells and lymphocytes. *H. ducreyi* may be occasionally seen in the tissue. In cases of chronic chancroidal ulceration, this method is of special value in ruling out malignancy and in confirming Ducrey's infection.

There are other methods i.e. indirect ones which must invariably be employed to help in the total evaluation of clinical and laboratory findings. Repeated negative dark-field examinations eliminate the possibility of syphilitic infection and help in

the diagnosis of chancroid. Serological tests for syphilis are negative in these cases unless there is double infection. The treponema immobilization test is negative. Frei test for lymphogranuloma venereum is also negative.

From the point of view of the general practitioner who has often to deal with these patients, the diagnostic procedures ought to be the most easy and the most practical. Of the direct methods, smears from the ulcer for *H. ducreyi* and Ito-Reens-teirna test or Ducrey skin-test may be considered feasible office procedures; others are not for routine use but may have to be used occasionally in the diagnosis and management of venereal diseases. Among the indirect methods which help to rule out other venereal diseases, the dark-field examination for *T. pallidum* and the serologic test for syphilis must always be performed. Frei test for L.V. may have to be undertaken where inguinal adenopathy is suggestive of L.V.

The prognosis in cases of chancroid is always good and a complete and rapid cure is possible in every case when proper treatment is instituted early. One attack does not confer immunity, and reinfection is quite possible. The introduction of sulphanilamides and antibiotics in therapy has greatly altered the prognosis of this disease. It has definitely shortened the course of the disease, prevented painful adenopathy, phagedenic conditions and helped in the prevention of infection.

Treatment of chancroid.—PROPHYLAXIS:—Chancroid is preventable. Immediately after intercourse the patient should wash his penis thoroughly with soap and water and then with some antiseptic lotion. If applied within an hour, a 10% aqueous solution of ephiran chloride and 2% solution of prophyline glycol are reported to afford complete protection. Sulphathiazole or sulphadiazine may be used orally as a prophylactic. Antibiotics—streptomycin, aureomycin and chloramphenicol are all effective for systemic prophylaxis against chancroidal infection.

LOCAL TREATMENT:—With the advent of the sulphanilamides, the local treatment of chancroid has altered greatly. Normal saline dressing with good drainage and proper cleanings are ordinarily quite effective. Where there is œdema, hypertonic saline should be used. Surgical intervention such as dorsal slit or circumcision if considered necessary should be undertaken a couple of days after sulpha-drug therapy. Topical applications of antibiotics or antiseptics to the lesion must not be used as they are likely to interfere in the early exclusion of syphilis. If the regional lymph nodes are tender, frequent applications of dry heat, rest in bed, together with sulpha-drugs will abort bubo-formation. If there is softening and fluctuation, the bubo must *not* be incised but only aspirated with an 18 gauge B.D. needle and a tight bandage applied. Aspiration may have to be

repeated once or twice in a few cases. Injections of antiseptics into the bubo are neither necessary nor advisable. A few injections of a good preparation of chancroid vaccine intravenously in gradually increasing doses at two-day-intervals, helps to bring about early resolution of the adenitis.

SYSTEMIC TREATMENT:—Most of the cases of chancroids can be treated in the outpatient as ambulatory. It is advisable to hospitalize those with extensive ulceration, phagedena and painful adenopathy. The administration of sulphanilamides orally is the therapy of choice, as the results are uniformly good. The average dose of 1 g. at 4 hourly intervals, four to five times a day for five days in very early cases and for 7 days in late cases with adenitis, is usually very effective. An initial dose of 1.5 to 2 g. may be given. There is no need to give the drug beyond the above limit. Sulphadiazine, sulphamerazine, Gantrisin or sulphathiazole are equally effective and do not usually cause side-effects of a severe nature; they are therefore, superior to the more recent antibiotics. The margin between the effective and the tolerated dose is quite safe. The effect of medication is often rapid and dramatic. *H. ducreyi* is not found in smears taken 48 hours after treatment; the pain decreases, the discharge subsides, the ulcer becomes clean and healing starts. Adenitis rarely develops after two days' therapy. If adenitis is already present, the glands begin to subside, but if they are fairly grown in size, the resolution is slow; softening and fluctuation may follow. The use of penicillin is *not* recommended as it is not effective at all in uncomplicated chancroid, but it is likely to mask co-existing syphilis. Sulpha-drugs may be given with penicillin in cases where a double infection such as syphilis or fuso-spirochaetes is present. Streptomycin, dihydrostreptomycin or a combination of the two is effective in chancroidal infection but does not appear to be able to prevent the formation of buboes or their subsidence and resolution. In most cases the average daily dose of 1 g. intramuscularly for about 5 days is sufficient. The oral broad-spectrum antibiotics such as aureomycin, terramycin etc., are also effective against chancroid but they need not be preferred to the cheaper sulpha-drugs; the antibiotics may upset delicate biological functions of the digestive tract and also the intestinal bacterial flora. Further they are in no way superior to the sulpha-drugs in preventing bubo-formation or its progress to suppuration. They are indicated only when there is no response to sulphanilamide, or when sensitivity and resistance are noticed. The dosages recommended is 0.5 g. four times a day for about 5 to 10 days depending on the response.

Complicated cases:—If chancroid and early syphilis are both present, penicillin should be given along with sulpha-drugs,

sing for 8 to 10 days the standard dosage i.e., 4.8 mega units of procaine penicillin for the sero-negative primary stage and 1 mega unit for the early sero-positive stage. If chancroid is associated with lymphogranuloma venereum, sulpha-drugs or the broad-spectrum antibiotics should be tried.

This treatment is also effective in chancroid, with granuloma inguinale (Donovanosis); when chancroid and gonorrhoea co-exist, sulphadiazine or sulphathiazole is useful. A single dose of 100,000 units of procaine penicillin fortified with 100,000 units of crystalline penicillin may be tried and the masking of syphilis kept in view. If fuso-spirochaetes are found, repository penicillin 800,000 units should be given daily for about 3 days.

*Follow-up*:—When the treatment is over, the patient should be kept under observation and serologic tests for syphilis carried out at stated intervals for three months.

#### RADIOACTIVE GOLD FOR PROSTATIC CANCER

The most promising results from treatment of prostatic cancer with radioactive substances have been obtained with radioactive gold. Comparable effects may be possible with radioactive yttrium chloride. Radioactive chromic phosphate has proved disappointing.

The best subjects for injection treatment are patients with local extension of the carcinoma into the seminal vesicles, periprostatic tissue, and lymph nodes, but without metastases to bone or distant organs.

Multiple needles are introduced into the perineum and then guided to portions of the tumour mass by a finger in the rectum. The size of the gland is estimated, and 2 mc. of gold per gram is injected. An indwelling catheter inserted before injection is left in place until radioactivity disappears from the urine.

Some relief may be expected in one-half of patients. Objective benefit, as estimated by rectal palpation, consists of shrinkage and softening of the prostate. Greater ease in voiding and cessation of sloughing and bleeding is associated with regression of the local tumour mass.

Urinary levels of radioactive material suggest that as much as one-third of the injected dose may be lost in the urine during the first forty-eight hours. Most of this loss occurs because injections are close to or into the urethra. Some radioactive material is undoubtedly excreted through the prostatic ducts. The irregularity of urinary loss precludes calculation of total dosage actually delivered to the prostate gland.

Study of circulating blood levels of the isotope reveals that a large amount of the material is deposited in the blood stream during the first few minutes after injection. Direct vascular injection is not likely if the needles are aspirated before injection, but rigidity of the veins as a result of the disease process may be a factor.

Few serious complications are associated with radioactive therapy. Extravasation of the radioactive material outside the prostatic capsule into the retropubic space and around the root of the penis may irritate the base of the penis or cause distressing priapism. Rectal irritation with frequent stools and bleeding may occur but usually subsides in a few days.

For patients with extensive metastases, treatment with radioactive gold is often palliative.—(*J. Urol.*, 75: 837-845, 1956, via *Modern Medicine*, August 1, 1956).

## DISEASES OF THE HUMAN SYSTEM AS MANIFEST IN THE OPTIC NERVE \*

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WE deal here with the diseases affecting the area from the optic disc onwards upto but not including the optic chiasma.

A. Diseases resulting from intra-orbital affections, congenital and acquired.

B. Diseases resulting from extra-orbital affections:—(i) Cranial affections; (ii) nasal and para-nasal affections; (iii) general metastasis; (iv) deficiency of nutrition; (v) referred (such as from teeth) and (vi) miscellaneous e.g., syndromes of (general angiomas) with that of retina—Von Hippel and Von Recklinghausen—neuro-fibromatosis of skin and optic disc; (vii) blockage by parasites in central arteries.

NOTE:—Neuritis and atrophies have not been classified separately, simply to summarize the matter as excluding primary and secondary atrophies (such as pressure atrophies); the post-neuritic atrophy is itself a late stage of neuritis.

A. 1. Congenital.—Coloboma of disc, opaque nerve fibres, holes in the disc, pigmented disc, hereditary lebers neuritis (manifested late in life), oxycephaly involving optic nerve.

2. Acquired.—Lebers neuritis, waxy disc of retinal pigmentosa, neuritis resulting from local metastasis such as from orbital cellulitis, pressure neuritis or atrophy such as result from orbital tumours (osteoma, angio-endothelioma, mixed adenoma of lachrymal gland, sub-periosteal gumma of orbit, tumours of optic nerve such as glioma or endothelioma), pressure atrophies from head injuries affecting optic foramen or osteomyelitis of the latter, atrophy due to glaucoma and injuries of orbit, nerve degeneration as hyaline and amyloid.

B. 1. Cranial affections.—Brain tumours, achromegaly, vascular lesions (aneurisms etc.), cavernous thrombosis, bony lesions such as osteomyelitis of various origins in the region of the course of intra-cranial portion of the optic nerve, inflammatory lesions of the brain and meninges, hydrocephalus causing pressure atrophy and injury of the skull.

2. Nasal and para-nasal affections.—Sinusitis, causing local metastasis or by liberating toxins (the question is yet controversial whether the nerve is affected by local metastasis or is toxic in origin), cystic growths of the antrum in advanced stage causing pressure atrophy of the nerve by encroaching upon the orbit; in the same way gummas of the antrum can affect the nerve.

3. General metastasis.—Endo-toxic, diabetic, syphilitic (neuro-retinitis, tabes, multiple sclerosis), nephritis and septic

focus of any disseminated part in the system and (1) arterial blockage by parasites and (2) predisposing by causing anæmic cachexia malaria, virus affections as neuro-myelitis optica etc.

(b) Exo-toxic-amblyopias caused by tobacco, alcohol, quinine, arsenic, lead, salicylic acid etc.

4. Deficiency of nutrition.—Anæmias, hæmorrhages, menstrual troubles etc. dietetic deficiencies.

Symptoms and differential diagnosis.—Common symptom is dimness of vision which may start from centre or from periphery varying in different varieties. In some toxic amblyopias there may be pain on moving the eye. In primary optic atrophy of tabes, diminution of the vision starts from the periphery as the affection starts from the ganglionic cells of the retina and thereby the nerve fibres are affected which are the axis cylinders of the former. Here, there is concentric contraction of the field of vision which is usually very gradual. According to some there are inflammatory exudates which are responsible for the degeneration affecting the inflammatory part of the nerve or chiasma. In retrobulbar neuritis affecting of light difference than of light minimum in contrast to glaucoma (low dark adaptation) and typical pupillary reaction (no sustained contraction to light) is worth mentioning.

In neuritis of the disc or neuritis starting from behind the eye-ball, diminution of vision usually starts from the centre. Blind spot may be enlarged, there may be a central or para-central scotoma which is first relative and afterwards absolute. Field for green colour usually is affected first of all, then for red, and then for blue, and in the later stages the scotoma is absolute, i.e. for white. This order is observed more often in tabetic atrophy than in neuritis and there is concentric contraction of the field.

In pure neuritis diminution of vision is from the start, while in choked disc due to fluid pressure from the intra-vaginal space though the disc appears to be very much swollen, the defects of vision are noticed late as nerve fibres are not inflamed in such cases and they get atrophied late by constant pressure. Here there is more of concentric gradual contraction of field and less of central colour scotoma unlike pure neuritis (Duke Elder). Here pseudoneuritis of high hyper-metropia should not be lost sight of, where there is no actual neuritis and the case improves by suitable glasses though by ophthalmoscope it gives a picture of real neuritis.

Nerve affections caused by cranial lesions:—In pituitary tumours affecting the nerve, third nerve paralysis is usually found while in other intracranial affections including tumours on other situations usually sixth nerve paralysis is found. This is an important point of difference. In the

former the upper quadrant of the field of vision is the first to be involved, then the temporal and last the nasal. At least functional, if not always organic, changes in sexual organs are nearly always present in this condition. Skeletal changes of achromegaly are also to be kept in mind. In cranial lesions besides the ophthalmoscope, perimeter or Bjerrums screen, the use of X-rays, ventriculography and angiography are sometimes of great help in localizing the lesion. In orbital tumours proptosis is the first sign to be looked for. In tumours of the nerve the proptosis is straight forward while in other tumours it is from the side of the situation of the tumour, can also be felt by putting the finger between the eye ball and bony orbit.

PROGNOSIS:—Cases of primary atrophy due to tabes are the worst to deal with as the ganglionic bipolar cells are affected whereby the nerve fibres are disseminated and degenerated, which is an irreversible loss. Nerve affections due to multiple sclerosis are reversible if handled early, as only the interstitial supporting material of the nerve fibres is involved and not the nerve fibres themselves. In intracranial pressure lesions the defect is also reversible if handled early, at least cases of papilloedema due to fluid pressure. The same thing applies to cases of orbital tumour other than those arising from the nerve tissue itself. All toxic amblyopias are reversible if handled early. Of course nerves affected by arsenic and lead are difficult to handle. Cases of neuritis are reversible so long as they have not advanced to the stage of atrophy. Nerve fibres once degenerated have not been found to regenerate.

In general the prognosis depends upon the severity of the condition and the duration of the effect.

TREATMENT:—If the cause is tackled early, the nerve affection will heal of itself. Support of general health, iodides, diuretics and diaphoretics help greatly in removing the toxins from the system in toxic cases. Antibiotics are very useful in cases of septic foci as they avert the catastrophe in difficult cases. Palliative decompression by trephining of the skull in suitable intracranial pressure cases is sometimes a boon. Even lumbar puncture sometimes helps greatly deal, in such cases but in cases of tumours near the medulla oblongata one has to think twice before doing a lumbar puncture and also in cases where atrophy has started. The role of vitamin B<sub>1</sub> in such affections is well-known. BAL if started early in affections due to arsenic will prevent serious consequences developing.

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## DISSECTING ANEURYSMS

Males are affected twice as frequently as females. The condition is most common between the ages of fifty and seventy years, although it had been reported in a male child aged three months and in a female aged 100 years. Hypertension does not appear to play a major role, although it may be a contributing cause. Medical necrosis of the aorta is the fundamental cause.

Dissecting aneurysms are no respecters of persons. Nicholls, in 1761, in reporting to the Royal Society on the death of King George II of England, gave "a minute description of what occurred on that remarkable and melancholy occasion. His Majesty was found fallen on the ground, speechless and motionless. He appeared to have just come from straining at stool." Nicholls went on to describe a dissecting aneurysm with an intimal tear which had ruptured through the right ventricle.

In the past eighteen months in some 340 autopsies at the Geelong Hospital, Dr. Plueckhahn found seven cases of dissecting aneurysm. Three of these were coroner's cases of sudden death. In three of the remaining four cases the diagnosis was made before death.

*Diagnostic signs in dissecting aneurysm of the aorta:*—Levinson, Edmeades and Griffiths, in a review of 58 cases, report the presence of an aortic diastolic murmur in 27.5% of cases. The appearance of such a murmur, with a widened supracardiac shadow, severe chest or abdominal pain and negative serological findings, is practically pathognomonic of dissecting aneurysms. There are three possible causes of the murmur: (a) an intimal split of the aorta acting as an arterio-venous shunt; (b) loosening of the commissure of the valve by the intimal split, the corresponding cusps so being allowed to drop; (c) haematoma in the aortic wall distorting the aortic ring.

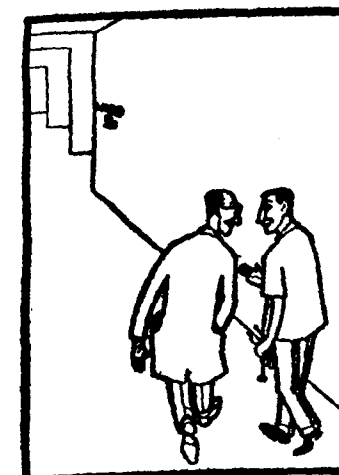
Neurological symptoms are present in approximately 20% of cases. They vary from an onset with syncope, dizziness, unconsciousness or hemiplegia to transient weakness or anaesthesia of one or more extremities.

Absent or diminished pulsation in one or other of the major peripheral arteries is noted in about 20% of cases.—(*The Medical Journal of Australia*, 3-11-1956).

## RETROPERITONEAL TUMOURS

J. A. Evans and N. Poker (*J.A.M.A.*, July 21, 1956) discuss newer radiological techniques in the diagnosis of retroperitoneal tumours. They state that special difficulties hamper the diagnosis of tumours in the space behind the posterior parietal peritoneum, above the level of the sacrum, and up to the twelfth rib and twelfth thoracic vertebra. In countering these difficulties, two of the newer radiological techniques have proved especially helpful—namely, nephrotomography and induction of retroperitoneum. The technique of nephrotomography involves the precise timing of the intravenous injection of contrast medium and the taking of tomograms at preselected levels. It has given valuable information about cysts and tumours in 195 cases in the experience of the authors. A recent improvement in retroperitoneumography involves the use of oxygen in place of air to avoid air embolism.—(*Med. J. of Australia*).

**PURULENT ENDOPHTHALMITIS** after cataract extraction may be prevented by subconjunctival injection of combined penicillin and streptomycin, reports Pearlman of the University of Illinois, Chicago. At the conclusion of extraction, 0.25 cc. of a specially prepared solution of the antibiotics is injected with a 25 to 27 gauge needle opposite the incision, usually at 6 o'clock, several millimeters from the limbus. Although post-operative chemosis and redness increased slightly, no serious allergy results.—(*Arch. Ophthalm.*, 55: 516-518, 1956 via *Mod. Med.*, 10-1-56).



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### Cases and Comments

#### A CASE OF MALFORMATION APPEARING FOR THE FIRST TIME IN THE FAMILY

K. GOVINDA MENON, B.A., M.B., B.S., M.Sc.,  
Professor of Anatomy, Madras Medical College

A FULL term still-born malformed foetus was received by me on 9-1-'56 from the Gokuldas Maternity Hospital, Rasappa Chetty Street, Georgetown, Madras.

The mother Mrs. X, aged 17 years, a primipara, was admitted to the Hospital at 4-30 p.m. on 19-12-'55. Her condition on admission was normal, full-term, breech presentation; the foetal heart was not heard. A malformed dead child was delivered at 5-25 p.m. artificially. The placenta was normal and did not require artificial removal.

The following information was elicited from the parents during a subsequent personal enquiry:—The father was aged about 27 and the mother was 17 and both belonged to the lower middle class. The child was born one year after their marriage was celebrated. Close questioning did not reveal any history of abnormality in the family on the paternal or the maternal side. The mother complained of having been subject to frightful dreams throughout the period of pregnancy, but she was not able to describe the details of the dreams. There was no history of syphilis and the blood examination of the two gave negative results. There was no history of any infective fevers or of exposure to radium or X-rays.



Fig. 1



Fig. 2

The foetus (Figs. 1 and 2) on examination was found to be abnormal in both the lower extremities. The left lower extremity was completely absent, represented only by a small button

Bunnel<sup>3</sup> thinks that congenital deformities can be the result of deficiency in diet, especially of vitamin B. The diet of the lower middle classes in South India is notoriously defective in vitamin B and there is every possibility of there being vitamin B deficiency in these parents; but if this were the cause many more cases of such deformities must have been occurring, which is not the case in South India.

There is also another factor which used to be emphasized in the early part of this century by Birnbaum, Schwalbe, Ballantine and others.<sup>1</sup> They call it maternal impressions and according to them mental impressions of the mother during pregnancy have some effect in shaping the offspring. In this case, there is the history of the mother having had frightening dreams throughout the period of her pregnancy, but the evidence collected by the workers on the subject is not sufficient to consider this as a causative factor for malformations.

Another very interesting aspect of this foetus is the mal-development of the radius on the left side with the absence of the thumb. Absence of the radius is usually<sup>2</sup>, though not always<sup>4</sup> associated with the absence of the thumb. Starr<sup>8</sup> mentions a non-articulated thumb with partial absence of the radius, but there is no reference in the available literature<sup>4</sup>, to a mal-developed radius associated with the absence of the thumb.

**Summary.**—A full term still-born malformed foetus of a primiparous mother is described. The parents are quite normal, free from syphilis with no history of infectious fevers or exposure to X-rays or radium. There was also no history of abnormalities in the family. The delivery was artificial but the placenta was normal with no bands. The mother complained of frightening dreams throughout her pregnancy.

The foetus showed the absence of the left lower extremity, partial development of the right, absence of the left thumb with maldevelopment of the left radius (a very rare abnormality) absence of the external genitalia and the anal opening and non-development of the pelvis. The nature of the internal organs is mentioned.

The probable causes of the condition are discussed and it is suggested that it may have been due to some injury to the ovum after fertilization had interfered with organization.

My thanks are due to Dr. Mrs. Kamalam of the Gokuldas Maternity Hospital for letting me have the specimen and for making the parents available to me for detailed investigation.

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## REPORT ON A CASE OF URINARY STRONGYLOIDIASIS

K. V. SUBBA RAO, M.D., D.T.M. & H. (Eng.), and EDWARD DAVID, M.B., B.S.,  
Department of Bacteriology, Andhra Medical College, Visakhapatnam.

**Introduction.**—In spite of the frequency in occurrence of Strongyloidiasis in tropical and sub-tropical countries, only brief references are found in the literature. This is due to a general misconception that *Strongyloides stercoralis* is a non-pathogenic nematode. Urinary strongyloidiasis is believed to be still more rare, in view of its vague symptomatology and varying morbidity. The first case of urinary strongyloidiasis was reported by Whitehall and Miller in 1944.

The following case which came up for laboratory investigation under one of us (K.V.S.) was of interest for its special features and brings home the importance of a thorough laboratory investigation in all cases showing vague abdominal symptomatology.

**Case report.**—A Hindu, male, aged 25, was referred for laboratory investigations with regard to frequency and urgency of urination. His present complaint started a year and a half ago, with the passing of urine every two hours, followed by a dull aching pain in the loins. He often had diurnal urgency, urinary incontinence and nocturnal diuresis. Off and on he complained of looseness of bowels with 4 or 5 motions a day with occasional streaks of mucus in the stools. The patient got easily tired and complained of inability to concentrate and also a vague pain in the precordial region. He had an attack of gonorrhoea 2 years previously and was treated with sulpha-drugs and penicillin; he believed that his present complaint started thereafter.

In view of its vague symptomatology and apparent involvement of several organs, therapy was directed to combat the ailments, using penicillin, Vitamin B<sub>12</sub>, and various other drugs with no perceptible improvement.

**Physical examination:**—Did not reveal anything definite except tenderness in the suprapubic region.

**Investigations:**—The urine was slightly cloudy, with a straw colour; sp. gr. 1014; albumin 1%; no phosphates; no sugar and no bile-salts.

**Microscopic examination** of the centrifugalized deposit showed pus cells, a few red-blood cells, and several larvæ of *Strongyloides stercoralis*. Albumin was present only when larvæ were present in the urine.

**Motion:**—Soft but well-formed, normal in colour, no ova or larvæ, no amœbæ, either vegetative or cystic forms.

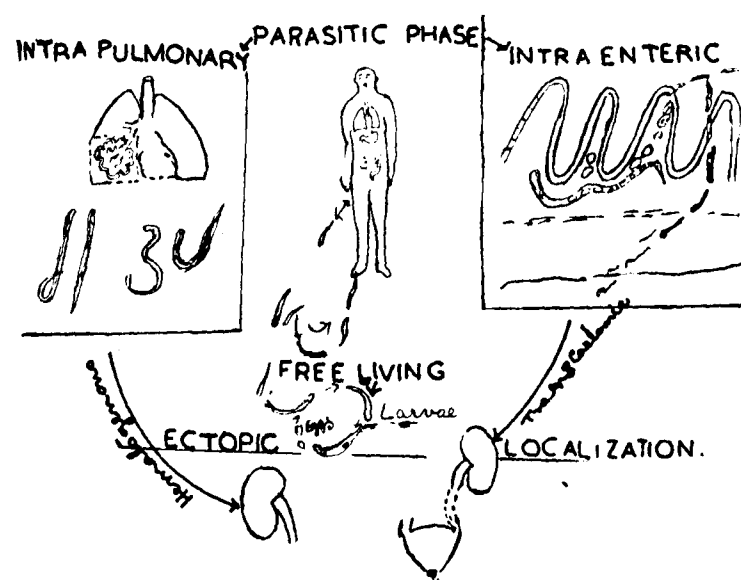
**Blood:**—Total W.B.C. 7,800 per cmm. **Differential count:**—polymorphonuclears 60%; lymphocytes 23%; eosinophils 11%;

monocytes, 5%; basophils 1%; total R.B.C. 4.2 millions per cmm.; Hb. 10.8 gms.%; E.S.R. 12 mm. per hour.

X-ray of the chest showed nil abnormal; sputum: nothing abnormal; C.S.F.: nothing abnormal.

Life cycle.—Till recently *Strongyloides stercoralis* was believed to be a non-pathogenic parasite. In view of its powers of invading not only the gut, but also other organs and the various toxic metabolites that are produced by the parasite, it is certain that the worm is pathogenic to man.

### LIFE CYCLE OF STRONGYLOIDES.



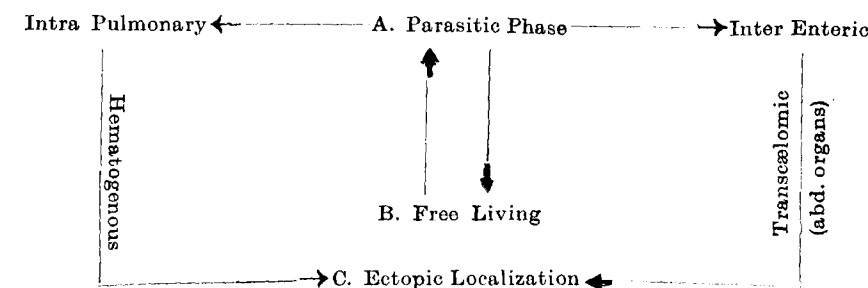
does not invade the tissues but is usually passed out of the gut. The gravid female lays its eggs, about 200 per day, in the depths of the ducts of Leiberkuhn. The eggs are hatched in a few hours and the rhabditiform larvæ which emerge are voided in the stools. Sometimes instead of passing into the gut they may penetrate deep into the wall of the gut and enter the mesenteric capillaries. Under these conditions the rhabditiform larvæ metamorphose into thin filariform ones which have greater capacity for invasion. It is during these phases of penetration into the gut, that they are liable to enter the capillaries and get swept along the blood stream to reach other organs where various ectopic localizations and manifestations might occur.

The free-living cycle is in the soil and hence need not concern us here. When environmental conditions in the soil are unfavourable, the rhabditiform larvæ change into the filariform, which enter the human host from the soil either through the skin or through

A brief description of the life-cycle of the nematode shows the possible role it may play in various clinical conditions. The adult female worm is 2.5 mm. long usually seen burrowing in the mucosa of the small intestines. The male is shorter but stouter; it

the mucous membrane. It is very tempting to suggest that sometimes, the larvæ, not only infiltrate into the wall of the gut but also pass into the peritoneal cavity and enter the various viscera of the abdomen, giving rise to ectopic localizations in the abdominal organs.

*Strongyloides stercoralis* has thus two definite life cycles:—A free-living (indirect) and a parasitic (direct), which may be either heterogenous or autogenous. The following diagrammatic representation will explain the various phases of the life cycle of this nematode (*Strongyloides stercoralis*).



Discussion.—Infestation by this worm must be regarded as a definite disease condition. Its world-wide distribution with greater prevalence in the tropical and sub-tropical countries shows that it should have a fairly high incidence. In view of the inadequacy of the surveys made of its distribution, Stoll's (1944) estimate of its world prevalence as 34.9 millions must be considered a very modest one. Kyle and Spartling (1948) described the internal auto-infection with filariform larvæ being present not only in the intestinal wall but also in many other viscera. At times the migrating larvæ fail to break out of pulmonary capillaries and gain access to the general circulation. Experimentally in the dogs, these larvæ have been demonstrated in different organs of the body, including the brain and choroid plexuses, (Yamaguchi 1925; Faust 1935). It is not unlikely that this type of erratic migration occurs in humans also. Whitehall and Miller (1944) reported a case of genito-urinary strongyloidiasis in a male patient who gave a history of abdominal discomfort after food, nocturia, urinary incontinence and diurnal urgency for urination. In the case of Redewill (1949) the urine was positive for the strongyloid larvæ while the faeces were negative. Faust and Decroat have found a generalized migration of the filariform larvæ through the bowel and mesenteric veins. The laboratory diagnosis of strongyloidiasis in 85 cases in the Charity Hospital of New Orleans (Hinman 1938) and the intense study of 100 cases by Jones revealed that the symptomatology of strongyloidiasis varies considerably but is usually associated with abdominal pain, sharply localized without any tendency to

radiate. These are usually associated with diarrhoea alternating with constipation. Wherever there is involvement of the urinary tract, definite symptoms of diurnal urgency, and frequency of micturition, are manifest.

In the present case, on close interrogation, the patient gave all the symptoms associated with strongyloidiasis and the transient albuminuria was associated with the presence of the larvæ. Taking the analogy of the localization of the bacteria in the case of pyelonephritis that a previously traumatized or damaged kidney is liable to get pyelonephritis, it is tempting to think that previous infections such as gonorrhoea or some similar infection of the genitourinary tract is liable to have an ectopic localization of these larvæ during the latter's sojourn.

**Conclusion and summary.**—Strongyloidiasis is a common infestation in tropical and subtropical countries. In view of its vague and minor symptomatology, many of these cases go undiagnosed. The constant movement of the female in the tissues, the filling of the eggs in the mucosa and the escape of the larvæ into the tissues—all these produce irritation in the parasitized areas which may lead to varying pathological conditions. During the course of ectopic localization, various organs may be invaded and lesions produced.

A case report of urinary strongyloidiasis is presented. The probable modes of invasion of the genitourinary tract by the larvæ has been outlined. It is emphasized that in every case with a vague abdominal symptomatology, a thorough repeated investigation will yield fruitful results.

**Acknowledgements:**—We wish to thank Dr. K. Satyanarayana, M.D., for referring the case to us and Mr. Edwin for the microphotographs.

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#### PULMONARY HYPERTENSION IN CONGENITAL HEART DISEASE

Keats, Kreis and Simpson (*Radiology*, May 1956) reviewed 36 cases of proved pulmonary hypertension associated with interatrial septal defects, or patent *ductus arteriosus*, in an attempt to determine whether the criteria established for the radiological detection of pulmonary hypertension in mitral valvular disease could be applied also in congenital heart disease. The only one of these criteria which proved applicable was the disproportionate narrowing of the peripheral pulmonary arteries as compared to the proximal arteries. This sign was present in 64% of the series studied. The other reported signs of right ventricular and pulmonary outflow tract enlargement occur in the presence of left-to-right shunts without pulmonary hypertension and are, therefore, unreliable as indicators of the presence of pulmonary hypertension. The degree of enlargement of the heart, the right ventricle and the pulmonary artery appears to correlate more closely with the magnitude of pulmonary blood flow.—(*M.J. of Australia*).

#### REPORT ON A CASE OF LUPUS VULGARIS

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**PATIENT**, Mrs. S., aged 37, gave a history of skin lesion of about 3 months' duration.

**Nature and extent of the lesion:**—The skin lesion, commenced as a small papule over the face and gradually spread peripherally. The lesion at the time of the examination showed a central thin scar and peripheral spread. The lesion, was distinct and elevated and when examined by pressing with a slide showed obliteration of the erythema and produced the so-called "apple-jelly nodules." A tooth-pick pressed into the nodule passed readily into and stayed in the lesion; when released it showed the involvement of the corium.

The patient gave no evidence of tuberculous focus anywhere.

**Investigations done:**—Total W.B.C. 8000; D<sub>2</sub> P 56.3 MO F 6; ESR 1 Hr. 26 mm; 2 Hrs. 42 mm.

A skin biopsy showed several tubercles with epithelioid cells, giant cells and peripheral zone of lymphocytes. These lesions were mostly found in the upper dermis. The following is a schematic representation of the biopsy made in this case.



**TREATMENT:**—The patient is under treatment for the last three weeks and is being given Isoniazid 300 mg. every day.

**Improvement noted so far:**—There is arrest in the progress of the lesion and in certain areas there is also evidence of regression.

# REPORT ON A CASE OF HYPOPYON CAUSED BY THE LOCAL USE OF CORTISONE

S. C. ROY, M.B.,  
Ophthalmic Surgeon, L. M. Hospital, Asansol

M.P., a Hindu male, aged 40 years, came on 3-11-56 with redness, pain, and photophobia of the right eye of 2 days' duration. He suffered from traumatic iritis in the same eye for two weeks, a year ago; he was cured by penicillin injections and local eye drops. He had a recurrence of the iritis with typical signs and symptoms, when he came for treatment.

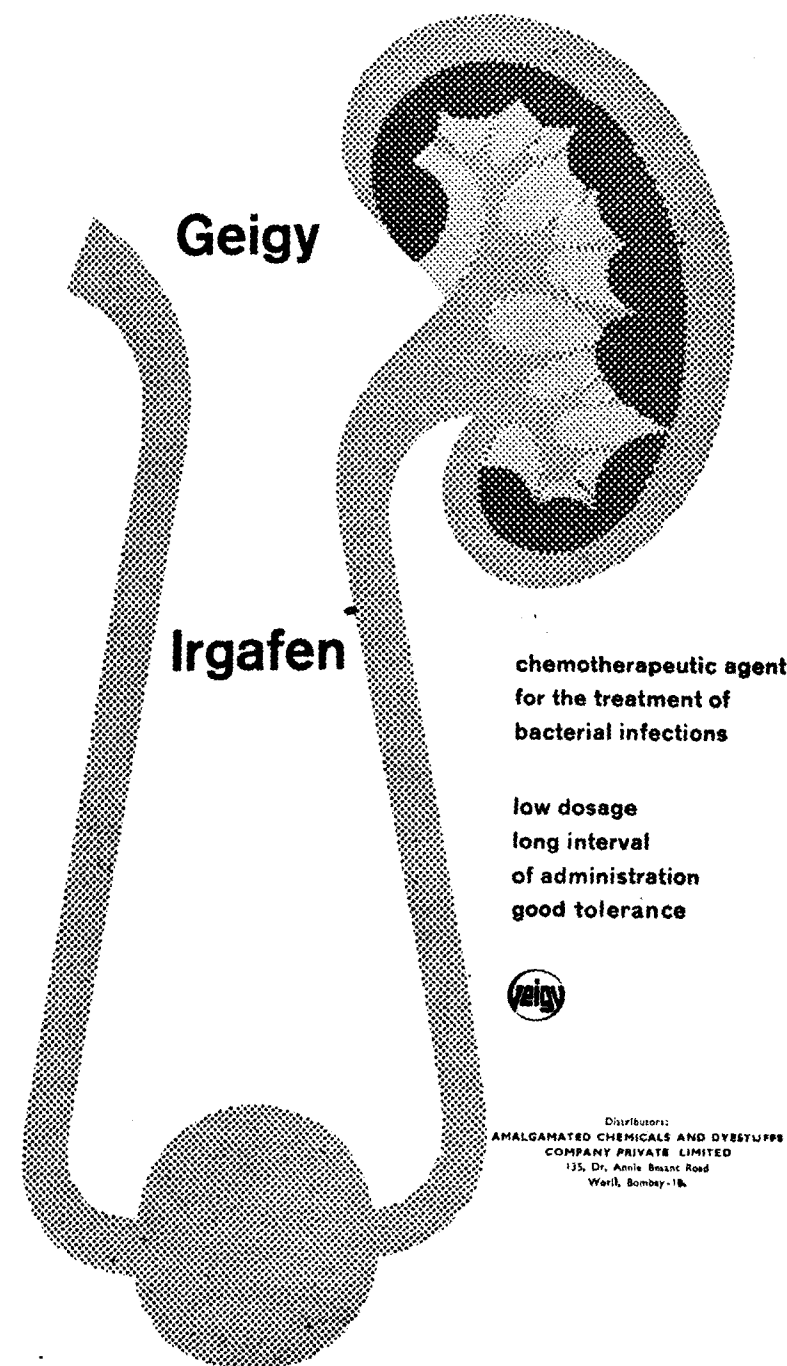
He was put on penicillin injections and local eye drops which did not produce much improvement even after 4 days. Penicillin injections were replaced by Irgapyrin injections and locally 1% cortisone eye drops were added to the usual atropine drops and used every 2 hours. When he came 2 days later, the condition of the eye was alarming. The anterior chamber was very hazy, the entire surface of the iris was covered with pus; the iris and the pupil could be seen only very faintly.

The cortisone eye drops and the Irgapyrin injections were immediately stopped. Penicillin was pushed sub-conjunctivally and systemically. During the next week he received 3 sub-conjunctival penicillin injections and 20 lac units of the drug intramuscularly.

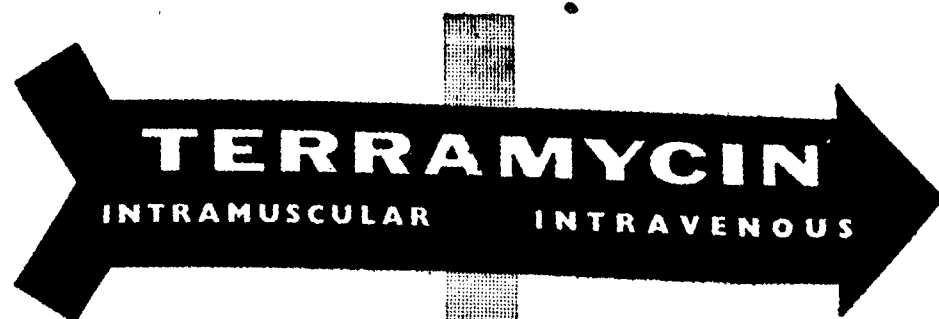
The exudates in the anterior chamber decreased but a small gelatinous mass at the centre of the pupil (the size of a pin's head) persisted without any sign of further absorption. At this stage the penicillin injections were stopped and aureomycin S.V.—2 capsules a day—were given, for a week. The eye condition showed remarkable improvement; the gelatinous exudate at the centre of the pupil disappeared leaving a clean eye. Ophthalmoscopically some dust-like spots were found on the surface of the lens. He was examined twice at intervals of a week and the eye was found normal both functionally and physically at the second examination also.

This is a case in which, simple iritis developed into a purulent one after the local application of cortisone, which is being extensively used in various kind of eye diseases. The cure in this almost hopeless case was ultimately effected by discontinuing the offending drug and resorting to more intensive use of penicillin by the sub-conjunctival and systemic routes followed by aureomycin SV.

**SATISFACTORY OBSTETRIC SEDATION** is provided by chlorpromazine (Thorazine), Seconal, and scopolamine when narcotic medication cannot be used. Norton, Weingarten, and McDonough of St. Mary's Hospital, Rochester, N.Y., report that the incidence of nausea and vomiting is reduced and neither mother nor baby is harmfully affected.—(*Am. J. Obst. Gynaec.*, 71: 1956 via *Mod. Med.*, 1-10-56).



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## Editorials

### ANNUAL MEDICAL CONFERENCES

THE country witnessed the holding of over ten conferences on medical, and allied scientific subjects during a short period of about 3 weeks ending with the 11th of January 1957.

The 33rd All India Medical Conference held at Trivandrum on the 26th December 1956 was inaugurated by Dr. B. RAMAKRISHNA RAO, Governor of Kerala, who pleaded for a programme of planned development in all national activities including the plans for the development of medical and health services. He was of the view that the conference should accept the philosophy of co-existence in the matter of Ayurveda and other systems of Indian medicine, and that we should all attempt to examine and study those systems dispassionately in the light of modern sciences.

DR. C. S. THAKAR in his presidential address, dwelt on the several important and outstanding aspects of medical education and practice in India which are engaging the attention of the profession and of the authors and implementers of the Second Five-Year Plan. After reviewing the overall achievements of the first five years, which marked a period of all-round progress with regard to health schemes, Dr. THAKAR discussed the four objectives visualized by the Second Five Year-Plan and referred to the budgetary provision of Rs. 945 crores (roughly 20 per cent of the total amount) for social services out of which Rs. 274 crores were allotted for the furtherance of the essential schemes designed to improve the health of the nation, to wit, more hospitals, greater laboratory facilities, expansion of research, control of communicable diseases like malaria, filariasis, tuberculosis, leprosy and venereal diseases all of which needed eradication. Nutrition and family planning also figure prominently in the

Second Five-Year Plan. Dr. THAKAR pleaded for a hearty co-operation by the members of the Indian Medical Association in the implementation of the various items covered by the plan. He next took stock of the working of the medical benefits under the Employees' State Insurance Scheme which was functioning in different parts of the country for periods varying from 4½ years to six months.

The defects noticed in the working of the scheme in the areas where the Panel System had been implemented were brought to the notice of the conference. The Indian Medical Association, as we are all aware, has been very vigilant and active in trying to obtain adequate medical benefits for the insured workers; if labour unions would only co-operate by bringing their requirements to the notice of the association, many difficulties could be readily solved without delay. The extension of medical care to the families of the insured workers is under the active consideration of the Union and State Governments; as the problem is a really complicated one it will necessarily therefore, have to be implemented only in stages.

The nationalization of Life Insurance Companies, which has been brought about, in such great haste, has, as we recently pointed out in a short editorial note, caused undue hardships and serious injustice to several hundred loyal and competent medical examiners who, for no fault of theirs, were abruptly thrown out of work. Dr. THAKAR drew pointed attention to the haphazard manner in which the Corporation has selected the medical examiners, without reference to any basic principles. The Indian Medical Association sought permission to be represented in the Corporation in the matter of selecting medical examiners but their request was turned down. The association has since submitted a memorandum stating its case and embodying its comprehensive scheme for the selection of medical examiners envisaging the imperative need for the Life Insurance Corporation to take the Indian Medical Association into its confidence in all such matters. We have no doubt that the Corporation will consider this memorandum favourably and render justice and fair play to the medical profession as a whole.

The President then referred to the Indian Medical Council Bill 1956, which seeks to amend the Indian Medical Council Act of 1933 and which was approved with a few minor modifications by the Rajya Sabha. It will be coming up before the Lok Sabha in the near future. Some of the provisions of the new Bill are of a highly controversial nature and the Indian Medical Association has made several representations to the Indian Medical Council and to the Union Ministry of Health stating their case *in extenso*. The Indian Medical Council has consistently declined to accept the demand of our Association for including its representative

on the Council. It is not possible to say now, if the Bill will emerge from the Lok Sabha, shorn of its undesirable and controversial features; but we always live in hopes and so let us hope for the best.

We feel it is our duty at this stage to reiterate what we have repeatedly pointed out in the past in these columns in the matter of strengthening the I.M.A. by enlarging its membership roll. It is sad to reflect that of the 70,000 doctors in the country, only 18,941 or 27 per cent have thought fit to become members of the association.

National Medical Associations in other countries of the world, like U.K., U.S.A., China, Japan, etc., count nearly all qualified medical men in the country as their members. It is only when the I.M.A. has similarly enlisted nearly all the members of the medical profession in the country in its rolls, that its legitimate rights and demands will be promptly heard, acknowledged and respected by the powers-that-be.

There is yet another point on which, for the same reason, we would like to offer a suggestion; the various specialist associations in the country—which are holding their annual conferences independently in several centres at the same time—should come together under one banner of the National Association (the I.M.A.), and act in unison for the welfare of the profession as a whole.

The 18th Annual Conference of the Association of Surgeons of India was held at Indore on the 29th December 1956 and Dr. I. J. MEHTA, who presided over it pleaded for the opening of more medical colleges with adequate staff and equipment to meet the growing demand for more and more medical men. He also pleaded for uniform pay scales for teachers working in Government Medical Colleges. In view of the shortage of trained non-clinical teachers in Medical Colleges, Dr. MEHTA appealed to Governments to relax their present rule of compulsory retirement at 55 and allow officers to work for 5 to 10 years more before a new cadre of non-clinical teachers was properly organized. We feel, however, that in permitting any such relaxation in the rules relating to superannuation, considerable circumspection should be exercised in re-appointing teachers for continued service after retirement taking due care to select only such as are absolutely physically fit and mentally quite alert.

The Third All-India Conference of Dermatologists and Venereologists was held at Madras on 29th December 1956 and the scientific session was inaugurated by Dr. V. R. KANOLKAR, Director of the Indian Cancer Research Institute, Bombay. Lt. Col. K. K. CHATTERJI, the Octogenarian Surgeon of Bengal presided over the conference. We shall be discussing the proceedings of this and other conferences in a future issue.

## THE FOURTEENTH INTERNATIONAL TUBERCULOSIS CONFERENCE

THIS conference sponsored by the International Union Against Tuberculosis, the first to be held in the East, was inaugurated by President RAJENDRA PRASAD on Monday the 7th January 1957 at Vigyan Bhavan, New Delhi. He said that with all the advances made so far in the treatment of tuberculosis there was no reason to be complacent as there was still need for a concerted drive in making the people utilize the available knowledge particularly in underdeveloped countries. Dr. P. V. BENJAMIN in his presidential address, pointed out that 30 million people in the world are suffering from tuberculosis and at least 5 million die of this fell disease every year. Though political conflicts have increased international tension during recent months, international co-operation has been steadily forthcoming in such humanitarian efforts as the control of communicable diseases, like tuberculosis, malaria, leprosy etc. Every effort at reducing the incidence and spread of these maladies must be welcomed. The associated agencies of the United Nations Organization like the WHO and UNICEF have a remarkable record of service in this direction to their credit. Ideological or other differences have not stood in the way of voluntary agencies and non-official organizations co-operating wholeheartedly in this direction.

There have been revolutionary changes in the control and treatment of tuberculosis, particularly during the last ten years and the BCG mass vaccination against tuberculosis must be considered to have progressed well in many countries of the world including our own. A mass X-ray scheme of detection to determine the incidence of tuberculosis among the people may be beyond the means of many of the underdeveloped countries, but a bold attempt in this direction has been launched in parts of our country and the results are eagerly awaited.

Dr. BENJAMIN estimates the rate of infection to vary from 72 to 77 per 1,00,000 of the population in underdeveloped countries as against 9 to 63 in the developed countries of the world. The paucity of doctors and tuberculosis clinics in the Eastern countries is indeed a serious handicap and needs must be overcome. The existing number of clinics in India is expected to be more than doubled under the Second Five-Year Plan, though the anticipated increase at the end of that plan period to about 600 clinics, would still fall short of our requirements.

Even where treatment has succeeded in checking the disease, there would be the further problem of rehabilitating the persons, for people who have been sapped of much of their vitality by the disease would not be in a position, even after being cured, to undertake strenuous work. But the very magnitude of the many problems involved calls for a sustained campaign, in order that

progressively the public health standard may be raised. The need for bettering the living conditions of the people and of raising the general standard of living, has long been recognized as a basic factor in fighting tuberculosis or for that matter, any infectious disease. This consideration would continue to be the primary and most important one in the long-term control-programme. The improvement of housing and environmental conditions is necessarily conditioned by the limited resources of the underdeveloped countries and so are also the medical facilities.

An important step forward, perhaps also a conspicuous development in the control of tuberculosis during recent times is domiciliary treatment, i.e., treatment outside hospitals and sanatoria. This has raised new hopes in the people and there was considerable unanimity of opinion on the value, importance and feasibility of ambulant and domiciliary treatment, during the discussions that were held at the Delhi International Conference. The Second Five-Year Plan provides for the expansion of existing hospitals and opening of new clinics, but not for nearly enough. It will be of advantage, therefore, to supplement the hospitals with a system of domiciliary treatment, not only because funds are not available to build enough hospitals for all who need treatment, but also because numerous cases do not really require hospitalization. Such patients will be happier, and can also make themselves useful by doing some light work if they stay at home, provided they are suitably isolated, and properly attended. Dr. RAJENDRA PRASAD emphasized the fact that nutrition, housing, and also various social factors, play a predominant part in the control of tuberculosis. Overcrowding in hospitals can be minimized and the incidence of the disease greatly lowered if people had better houses, and if adequate food can be provided to them cheaply, more plentifully and in a pure and unadulterated condition.

Housing assumes special importance in view of the fact that, as pointed out by the Union Minister of Health, RAJKUMARI AMRIT KAUR, a research project has been started to assess the value of modern anti-bacterial drugs in the domiciliary treatment of tuberculosis and is in progress. Though the Five Year-Plan provides for the development of housing, we are sorry to say, progress in this direction has been extremely slow. Apart from the fact that the laws governing accommodation in various States are such as to discourage investment in the construction and improvement of houses, building-materials and land are very dear; and Government control of building-materials has considerably added to the difficulties of private builders. These factors require to be eased and simplified to ensure better and more housing accommodation to the middle and poorer classes.

The Fourteenth International Conference provided a stimulus to the anti-tuberculosis movement in India and the Far

East. Tuberculosis workers and experts representing 64 different countries of the world who had assembled at this unique session were of the view that it was necessary to concentrate more on the tuberculosis problems of the underdeveloped countries.

There were important discussions on various aspects of tuberculosis, its control and treatment during the five-day session, at which eminent tuberculosis experts from several countries of the world took part. A short and succinct account of the discussions that took place and of the views of experts on the many important issues relating to the subject will be given in our next issue for the benefit of our readers.

## THE DRUG INDUSTRY

### Conferences of Pharmacists

Two conferences of pharmacists were held recently, one at Madras on the 31st December 1956 and the other at Calcutta on the 6th of January 1957 at which important issues were raised and the problems relating to the manufacture and control of drugs were discussed. Dr. K. VASUDEVA RAO, Chairman of the Union Drug Development Council, told pharmacists of the Madras State that South India had much leeway to make in order to achieve the requisite progress in pharmaceutical industry.

Inaugurating the first Madras State Pharmaceutical Conference at the Doveton Corrie High School, he said that necessary equipment, laboratories for research and trained personnel were the pre-requisites to progress in the manufacture of pharmaceuticals and added that India was far behind Western countries in that sphere.

Though the Madras Medical College was the first in India to start a specialized course in Pharmacy, the South was far behind North India in the manufacture of pharmaceuticals. Out of 750 manufacturing concerns in India, Madras had only 137. Lack of enterprise and of facilities for research is perhaps largely responsible for this state of affairs. The pharmaceutical industry must be controlled and worked by persons who have had the requisite training in pharmacy and who could be expected to maintain a high level of integrity, professional dignity and morality.

Dr. A. NAGARAJA RAO, the Chief Industrial Adviser to the Union Government, who presided over the Ninth Indian Pharmaceutical Congress at Calcutta on the 6th January 1957 said the Second Five-Year Plan envisaged the production in India of most of the drugs in use to-day starting from the basic chemicals wherever the quantum of demand justified economic manufacture.

In view of the great need for rapid industrial progress and the large leeway yet to be made in regard to several essential

products we agree with Dr. NAGARAJA RAO that instead of repeating work already done in the West, it might be quicker and less costly to acquire the know-how and undertake local production as soon as possible. Research organizations should also co-operate in developing new lines to catch up with advanced countries in the West.

It may be remembered that the Soviet Pharmaceutical Delegation which recently visited India suggested that there was considerable scope within this country to produce hormones and diverse vegetable products ordinarily used in medical therapeutics. This suggestion must be actively followed up and implemented. If, as it is likely, the raw material resources of our country are abundant, there will be great scope for developing export markets after meeting our entire local demands.

Dwelling on drug prices, Dr. RAO pointed out that while scope for special preparations advertised and sold on the basis of the reputation of manufacture might continue to some extent for meeting the requirements of the section that could afford to pay, it was imperative that to meet the common man's needs of essential drugs, a national formulary might have to be prepared and drugs distributed at the lowest prices, thereby benefiting the public.

We consider that in the context of establishing the pharmaceutical industry on sound lines in the future, the co-operation of the industry in achieving not only quantity but also quality production would be very essential. The setting up of a well-equipped testing and control organization owned and managed by the industry itself in co-operation with representatives of the medical profession for periodically checking-up and certifying the quality of products of manufacturers and publicizing the names of delinquents without fear or favour, would mark a definite advance in the matter of creating a healthy pharmaceutical industry.

So long as there are even a few manufacturers of doubtful reputation in the field of drugs, it will be difficult to inspire confidence in the public and the medical profession. To combat the menace of the manufacture and sale of spurious drugs, stringent measures would be necessary; special committees may be appointed in every State similar to the Eleven-Member Committee recently appointed in the Madras State. Such committees should have in our opinion on it, a knowledgeable representative of the consumer-class who would be able to place the view-points and complaints of that class before the committee.

It was indeed a welcome sign that the pharmacists from all India who had gathered at Calcutta formulated and drew up a five-year plan for the development of the industry.

Dr. AMARNATH MUKERJEE, Deputy Mayor of Calcutta, in welcoming the delegates said that the Indian pharmaceutical

industry played an important role as long as the "armamentarium" of the physician was confined to vegetable drugs and their derivatives and preparations but with the development of chemotherapeutics, synthetics and antibiotics, the entire concept had changed and it had become a very specialized industry requiring personnel having a broad technological background with knowledge of bio-chemistry, bio-physics, and pharmacology.

We would therefore, emphasize the fact that the need has now arisen for a new type of industrial scientist who would be able to carry out successfully development work connected with the pharmaceutical industry.

### DIARRHŒA IN INFANTS AND CHILDREN

Moderate or severe diarrhœa leads to incomplete digestion of food substances, diminished absorption of split foods, and excessive loss of food elements, fluids, and electrolytes.

Diarrhœa can generally be diagnosed in a child if the stools suddenly increase in number, with a greater fluid content, greenish colour, and change in odour. The child loses his appetite, cries more, and is restless. Abdominal distention is common.

The usual ætiologic agents are shigellosis, salmonellosis, and *Escherichia coli*. Other bacteria, such as *Staphylococcus aureus*, *Bacillus pyocyaneus*, and *Proteus morganii*, have appeared with greater frequency since the extensive use of antibiotics.

Overfeeding, improper feeding, sudden changes in diet, and the introduction of new foods may also precipitate diarrhœa. Constitutional factors include allergy, celiac disease, and cystic fibrosis of the pancreas. Neurogenic and emotional disturbances are sometimes implicated.

Severe diarrhœa may result in œdema, ulceration, and hæmorrhage in the intestinal mucosa. Occasionally, thrombosis of a cerebral sinus or renal vein occurs. Fatty infiltration in the liver is common.

The most severe effect of diarrhœa is metabolic disturbance. Great losses of food substance, electrolytes, and water result in hæmo-concentration, in acidosis, and, if uninterrupted, in peripheral shock and circulatory collapse.

The condition of infants and children with slight diarrhœa usually improves without special treatment. The total amount of food may be reduced, the feeding mixture diluted with water, or low-fat milk with 2 to 3% carbohydrate instead of 5% substituted. Fruits and vegetables should be excluded from the diet.

If this regimen is unsuccessful, a starvation period of six to twelve hours is recommended, after which 1 to 2 oz. of low-fat or skimmed milk formula is given every two hours. The amount of formula is increased every twelve to twenty-four hours, and three to five days is allowed for re-establishment of a full diet.

If severe diarrhœa is not controlled, the child may become febrile, and convulsions and coma may ensue. Dehydration, acidosis, and shock are hazards to life, and restoration of the circulation is the primary consideration in such instances.

For severe acidosis, Ringer's lactate solution with 5% added glucose is suitable until blood studies are completed. Blood or plasma is given to improve the circulation. Antibiotics are administered as required.—(*Paediat. Clin. North America*, 1956, pp. 137-152, via *Modern Medicine*, 1-9-1956).

### RADIOLOGY

**Malignant disease of the ovary and radiotherapy.**—(*M. J. of Australia*).

F. Ellis (*J. Fac. Radiologists*, July, 1955) reviews the cases referred to the Radiotherapy Department in Sheffield during the author's term of office there from 1930 until 1943. There were 168 cases of malignant disease. The author states that it must be realized that during that term methods were being developed and experience was being gained. A follow-up of at least ten years has been possible in most cases. The most usual classifications are made according to the degree of spread of the disease and according to the histological type of tumour. The cases were grouped into six stages: (i) one ovary alone affected, (ii) two ovaries affected, (iii) extension beyond the ovary but growth completely removable, (iv) growth only partially removable locally, (v) no removal possible owing to spread in abdomen, (vi) local recurrence after complete operation. The survival figures according to the stage of the disease are given as follows: (i) 49%, (ii) 60%, (iii) 20%, (iv) 24%, (v) 5%, (vi) 14%. Of cases not staged, in 42% the patient was alive at five years. In other words, a total of 46 out of 168 patients are alive and well, giving a total five-year survival of 27%. The author gives the surgical procedures carried out and the survival rate, and indicates in the case of the operated patients the number of survivals relative to the removal or leaving of the uterus and to the occurrence or not of rupture of the tumour. He points out that a complete operation gives manifestly better results than an incomplete one. In view of the fact that the uterus may be removed in a more advanced case so as to make the operation complete, no justifiable conclusion can be drawn regarding the desirability of hysterectomy except that leaving the uterus does not seem to make the results worse. The author has tried

to persuade gynaecologists to leave the uterus *in situ* if the removal did not make complete an otherwise incomplete removal. The object of this was to use the uterus as an applicator for radium to treat the pelvis from inside. He quotes the view of Kottmeier that intrauterine radium treatment is the best method of preventing recurrence in the pelvis. The author's radiation treatment consisted of treating the lower part of the abdomen up to the umbilicus—a dose of radiation of 3000r in a month. Also, when the uterus was not removed, radium was used in the canal and vault with a modified Stockholm dose—one application of 50 milligrammes in the uterus and 75 milligrammes in the vagina for twenty-two hours. If the uterus had been removed, radium was applied to the vaginal vault. The author shows tables to indicate that results were improved if the uterus was used for applying radium. In case of incomplete removal and complete radiation treatment, the author has shown that if the uterus was not removed, 32% of patients survived five years and 21% ten years. If the uterus was removed, then there were no five-year survivals. The author believes that intra-cavitary administration of radiation should be used in all cases of these malignant tumours except dysgerminoma, which is sensitive to small doses of radiation. The treatment is combined with X-ray therapy to the lower part of the abdomen. In all, out of 168 patients he achieved a ten-year survival rate of 23% with surgery and this form of radiotherapy.

**Radiogenic mutation (A warning).**—(Editorial, *Hawaii Medical Journal*, September - October 1956).

Damage done to individuals by injudicious exposure to ionizing radiations, in doses within the heretofore accepted limits of safety, consists principally of the small but statistically significant increase in liability to certain forms of cancer, notably thyroid cancer and leukæmias.

Damage done to an individual's descendants - to the human race, that is - by such exposure, when it occurs during the reproductive period of his or her life, consists of the increase of the normal human mutation rate. The effect of this may not be apparent for several generations to come, but we cannot on that account afford to ignore it.

B. J. Duffy, Jr., M.D., assistant professor of medicine and director of the Isotope Laboratory, Georgetown University Hospital, discusses the relationship of radio-active fall-out to this problem, and concludes that it is far less important than that of "incautiously administered X-rays."

The recently released independent conclusions of the U. S. National Academy of Sciences (*Biologic Effects of Radiation*, *Science*, 123:1157 June 29, 1956), and the Medical Research Council of Great Britain (*Hazards to Man, of Nuclear and Allied Radiation*, news summary in *Science* 124:112 July, 20, 1956) lend support to this view. They calculate the roentgens of irradiation to the gonads during the first 30 years of life as follows: from natural background radiation, 4.3r and 3r (American and British figures, respectively); from medical and dental X-rays, 3r and more than 0.67r respectively; from fall-out radiation at the present level, 0.02-0 to .5r, and 0.26r. Both groups agreed that an increase of from 30 to 80r (minimum, 5 to 15r; maximum, 150r) would be required to double the present mutation rate.

Neither report is conclusive, and both reports emphasize the need for more research. Certainly nothing in either report offers cause for alarm; indeed, on the whole, they are rather reassuring.

The important thing is that they clearly emphasize something that has not even occurred to the average physician: namely, that the possibility of permanent genetic damage is inherent in every roentgen exposure of any portion of the body, and that such damage is likely to occur if the gonads lie near the treated area and are sure to occur if they are directly exposed.

Pending the further exploration of this problem at the basic research level, the practising physician will do well to irradiate the abdominal, pelvic and perineal areas, and any areas in children, only on the basis of stringent indications and with all due precaution to avoid irradiating the gonads.

## DERMATOLOGY

Usually fatal skin disease controlled by ACTH.—(*Journal of the American Medical Association*, 24th March 1956).

Dr. Stoughton, Chicago, used the synthetic hormone for pemphigus vulgaris, a chronic and usually fatal disease of unknown origin. It causes blisters on the skin and involves the general health of the patient.

He gave corticotropin to nine patients for periods ranging from one and a half to four and a half years. All but one of the patients probably would have died of the disease if they had not received corticotropin.

Corticotropin never failed to suppress the blister formation, although it had no effect on the underlying cause of the disease. Side effects from the hormone were "surprisingly" few, Dr. Stoughton said.

All the patients had periods during which the disease process was quiet and required no corticotropin, but they also had flare-ups during which greatly increased doses were needed to control the disease.

Generally, however, dosage needs were "remarkably constant, which means treatment except for occasional hospitalization can be continued on an outpatient basis indefinitely", he said.

Adequate control of pemphigus vulgaris with corticotropin for indefinite periods of time seems entirely possible, Dr. Stoughton concluded.

Nickel dermatitis.—*July-August, 1956.*

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## GLEANINGS FROM THE MEDICAL PRESS

practice in London. In a study of 400 women patients, it was found that over 95% of them had stocking surfer dermatitis as their first manifestation of nickel sensitivity. In 19 cases the dermatitis initially was on sites in contact with the following: ear-rings, wrist-watch, brassiere clips, necklace clips, spectacle frames. The general pattern of this dermatitis may be divided into (a) the primary eruption or direct metal-contact sites and (b) the secondary eruption or areas of spread, apart from metal contact sites. The primary sites are very numerous; some of these are situated in relation to suspenders, brassiere clips, ear-rings, necklace, corsets, scissors, knitting needles, pins, hair grips, zip fasteners, brooches, spectacle frames, watches, bracelets, shoe-buckles and perambulator handles. The secondary sites are as follows:—elbow flexures, eyelids, sides of the neck and face, thighs (inner aspect) and generalized. The secondary eruption behaves like a hematogenous spread similar to the other phenomena in ring-worm and other infections. It is usually symmetrical and is related to the activity of the primary site. Nickel sensitivity induced by metal contacts at sites other than in contact with suspenders does not appear to cause a secondary eruption so easily. Nickel sensitivity can be confirmed by patch testing with 1% or 2.5% nickel sulphate solution; 5% or 10% solutions are unnecessarily strong and may give false positive results. Allergy to nickel is almost certainly permanent. Multiple contact sensitivity is not very uncommon. Patients with only primary sites affected settle down easily when metal contacts are removed. Once secondary spread has occurred, the prognosis is not so good. A high proportion of the patients had other varieties of eczema not specifically associated with their nickel-sensitivity pattern, especially on the hands.

## OBSTETRICS & GYNÆCOLOGY

Patients with four or more caesarean sections.—(*J. Am. M. Ass.*, 160:1005, 1956, via *Int. Abst. of Surgery*).

It has become common practice among obstetricians to sterilize patients who have had two or three caesarean sections, because of fear of rupture of the scar in a subsequent pregnancy or labour.

The obstetric histories of 130 patients who had had four or more caesarean sections were obtained from 20 hospitals. The period from 1936 to 1945 revealed only 14 cases of this kind, but from 1946 to 1955 there were 112.

In 42 cases, the main indication given for caesarean section was that the patient had had one or more already. Low cervical caesarean section was the operation most often done. In the 130 recent sections studied, the two kinds of anaesthesia most frequently used were spinal anaesthesia (56) and nitrous oxide and ether (24). A study of blood loss during the operation gave no evidence that subsequent sections were accompanied by any more bleeding than previous sections had been.

In this group of 130 patients having more than three caesarean sections, 87 per cent had four and five sections. Following the fifth section there is a sharp drop in incidence. The frequency of repeat pregnancies destined for caesarean section is less than that for vaginal delivery.

The majority of patients of high parity who anticipate repeat section consult an obstetrician for their care. The indications for the initial caesarean section, as well as for subsequent sections fall into generally accepted categories. Because the majority of previous operations were of low segment variety and the majority of hysterectomies followed the classical type of operations, low cervical caesarean section contributes less to weakened scar and/or rupture. Risk of prematurity of the baby is greater in patients with multiple sections. The risk of mortality, both maternal and foetal, is not increased. The distention of the uterus by an advancing pregnancy as a cause of weakened scar and/or rupture is more to be feared than labour. The danger of ruptured uterus is greatest before but near term in the absence of

labour. Hysterectomy in the multiple section patient is sometimes unnecessary and should be performed only when the uterus has been carefully judged clinically to show pathologic disease and, in the operator's opinion, cannot stand the distention of another pregnancy. Previous postoperative infection does not always cause subsequent weakness of post-section scars but does contribute to such weakness in some cases. The present day evaluation of post-caesarean scar leaves room for better clinical judgement. The capabilities and integrity of the child-bearing uterus in the patient with caesarean sections and relatively high parity have been underestimated.

**Primary cervical dystocia treated with caudal analgesia.**—(*Br. Med. Jour.*, 1: 1275, dated 2-6-'56).

Primary cervical dystocia is difficult to place in the classification of abnormal uterine action, and the causes and mechanism are not well understood. It remains one of the more difficult problems in abnormal obstetrics. The treatment usually advised is cervicotomy or caesarean section.

Ball and Chambers suggest that caudal analgesia be given a trial in cases of primary cervical dystocia before resorting to cervicotomy or caesarean section and report on 3 cases all successfully treated by them with caudal analgesia alone.

The following technique of injection was adopted in all 3 cases:—With the patient in the left lateral position, the skin was prepared and a malleable needle was inserted into the sacral canal through the posterior sacrococcygeal membrane. The needle was protected with a dressing and strapped to the skin. After aspiration to test for blood or cerebrospinal fluid, a test dose of 5 cc. of 1.5 per cent piperocaine hydrochloride was injected. As, after five minutes there was no evidence of dural puncture, the needle was connected by high-pressure tubing to a syringe and a further 30 to 40 cc. of piperocaine hydrochloride given. The patient was kept in the supine position for 15 minutes to ensure a

more even distribution of analgesia and then returned to the lateral position. Further doses of 10 to 30 cc. were repeated in half to one and half hours as required.

## SURGERY

**The syndrome of painful shoulder** (E. Vander Elst, J. Toussaint, W. Mattheiem, *Acta orthop. belg.*, 1956, 21: 509 via *Int. Abstract of Surgery*).

The numerous causes of painful shoulder (degenerative tendinitis, tendinous calcifications, arthritis) and the necessity for an early and precise diagnosis are emphasized. Frequently early diagnosis is difficult or impossible, particularly in the presence of associated trauma. In the authors' service at the Centre de Traumatologie, in Brussels, Belgium, they have had no experience with immediate surgical repair of lesions about the shoulder joint.

The prognosis should be based on a number of considerations, but in the experience of the authors the most important sign has been that of rotation movements of the shaft of the humerus. When rotation is good the prognosis is hopeful and when rotation is absent, the results are likely to be unsatisfactory.

On the authors' service, the method of treatment has been simple. All forms of physiotherapy may be judiciously employed, but most dependence has been placed upon the abduction splint. Abduction treatment is aimed at gradually overcoming the spastic contraction of the adduction muscles and, although rather simple in principle, requires several types of splint, developing progressively 25, 45, and 90 degrees of abduction. The type of splint depends upon the maximum of abduction that can be tolerated by the patient. If, for example, this maximum is 45 degrees, a 45-degree splint is applied. After from 24 to 48 hours the contracture begins to loosen, and this angle is employed as the starting point for the various active movements attempted. After 90 degrees have been achieved

abduction may be gradually increased without further increase in the splinting angle.

In the discussion, M. Verbrugge of Antwerp, speaks favourably of the use of injections of novocain and the subsequent injection of hydrocortisone in painful syndromes. He believes that they are of therapeutic value, and may actually assist in making a differential diagnosis. He believes that arthrography is not practised as much as it should be, and that all ruptures should, wherever possible, be repaired immediately; in many instances the operation should be accompanied by a resection of the acromion process. Arthrography may furnish the data necessary to make a decision. Verbrugge also approves the injection of hydrocortisone in old neglected cases of rupture. He does not recommend forceful, passive mobilization of the shoulder under anaesthesia. All passive mobilizations which produce pain should be prohibited.

## MEDICINE & THERAPEUTICS

**Antimicrobial agents in urinary infections.**—(*Medical J. of Australia*).

R. D. Herrold (*J. Urol.*, June, 1956) divides antimicrobial agents for urinary infections into two main classes: (i) those which act in an excretory capacity only; (ii) those which also act in this way, but in addition have a bactericidal effect in the tissues themselves. The author traces the history of, and indications for, the various sulphonamides and the earlier antibiotics. He states that Chloromycetin acts rather similarly to Aureomycin and Terramycin, but that it is more effective against Proteus, especially when combined with streptomycin. He has found Chloromycetin singularly free from side reactions. Polymixin B is the only effective antibiotic for urinary infections that are derived from a bacillus rather than a fungus or a streptomyces. It contains a nephrotoxic factor; hence its use is limited. However, it is safely used when only one injection per day is given, concurrently with

oral administration of Terramycin in some resistant infections, notably with *Pseudomonas*. Erythromycin, although derived from a streptomyces, is largely anti-coccal in action and is given when such infections are resistant to penicillin. Cycloserine ("Sero-mycin") is a new broad-spectrum antibiotic. While sometimes causing dizziness, it has low toxicity, no colonic side-reactions, no nephrotoxicity and no skin reactions. Since no resistance is developed to it, long-term therapy can be applied in some infections, notably pulmonary tuberculosis. Similarly, in chronic and recurrent infections of the urinary tract, cycloserine has proved valuable if continued for long periods—for example, two months or so. This drug is widely applicable, the exceptions being for infections with *Pseudomonas*, *Proteus* and *Streptococcus faecalis*. It was noted that two patients with trichomonas infection of the prostrate and urethra were cured, after four and six weeks respectively, with cycloserine. It is also noted that the best combination of agents to fight *Pseudomonas* is that of Terramycin and streptomycin; and for *Proteus* a combination of Chloromycetin and streptomycin.

**Management of obesity.**—(M. Witkin, *S. Afr. Med. Jour.*, May 19, 1956, via *Current Medical Digest*).

"Obesity" is the half-way house between health and disease. According to statistics one out of every 4 persons is overweight.

The quest for a successful treatment of obesity has always overshadowed the search for its causes. In the overweight, the "will power" to eat rich foods is mightier than the "won't" power.

To fight "dangerous curves" and to conquer the "battle of bulges" one's mental climate must change. We all realize that a slimmer waistline means a longer life-line. The over-weight loves to be told that the cause of the trouble is "glandular." No one welcomes the verdict that he eats too much. The endocrine system is seldom

at fault. The only glands involved are the salivary glands.

What harm does this extra weight do? Assuming one is 20 lb. overweight, the body has to provide a fleet of blood vessels a mile long to feed it, and the heart is forced to pump continuously extra-blood through a widely scattered territory of useless tissue. Life expectancy is thus reduced.

Rapid cures for obesity hit the headlines in newspapers and journals with remarkable regularity. We have today a glut of "diets." All are badly balanced and one-sided. There are no short cuts. No easy way is safe, and no safe way is easy. When we think of reducing we search for short cuts.

Weight reduction is the triumph of mind over platter. If the doctor gets full co-operation, the patient will lose weight as certainly as the sun rises in the east. The recruit must develop an abhorrence for succulent dishes. He must block his ears and shut his eyes to ridicule and commiseration. He must be prepared to stick to the new regime for the rest of his life. His resolve must never dissolve.

In order to reduce, one should eat less, eat slowly and masticate thoroughly; have no more than 3 meals a day and no 2nd helpings; eat nothing between meals and indulge in no nibbling and no alcohol.

Anorectics such as amphetamine may be necessary. When used with discretion they have proved a boon to the obese. They act as useful crutches and should be discarded as soon as possible.

The over-weight should never eat when he is not hungry, or when he is emotionally upset or over-tired. Allow 5 hours between meals. He should rest when tired, sleep when sleepy, dress warmly, and avoid spirits, rich soups, sauces, spices, seasonings, and salad dressings.

Weight reduction is more than a cosmetic problem. Like the iceberg, the fat visible to the naked eye is but a fraction of the internal obesity that is invisible.

### Errors in evaluation of the severity of hypertension.—(*The Am. Heart J.* 51: 776, May 1956).

Schroeder and Perry point out the necessity of carefully screening individuals to whom potent antihypertensive drugs are to be given in order to be sure that sustained hypertension is actually present.

The patients were referred to them by other physicians for control of what was believed to be severe and sustained hypertension of considerable duration. "On first consultation the blood-pressure was measured during the physical examination. A decision was then made as to whether or not the patient should enter the hospital for initiation of control of hypertension by ganglionic blocking agents and hydralazine.....So as to evaluate the effectiveness of the newer and potent chemotherapeutic agents in severe forms of hypertension, a concerted attempt was made to exclude milder cases which might respond favourably to reserpine or a combination of reserpine and hydralazine given on an out-patient basis. The individuals here discussed were considered suitable candidates for hospitalization and the use of ganglionic blocking agents, "as prior levels of blood-pressure, symptoms, and physical findings suggested to two or more independent observers that control might be necessary for prolongation of life or prevention of disability."

In 15 cases among 247 admissions to hospital an error in judgement was made in that the hypertension was considered by the referring physician and by the writers to be severe and sustained enough to warrant the use of ganglionic blocking agents. "Each patient was examined by an assistant resident physician and an intern. Orders were left that the blood-pressure be measured by nurses every four hours, day and night, and charted: this routine included both resting (or 'basal') values and those attained during normal activity. Patients were not confined to bed. All were subjected to various diagnostic procedures often new to them, such as electro-

cardiography, intravenous pyelography, studies of renal function, and the injection of drugs for specific tests. Although all were handled similarly, different nurses and members of the house staff attended them. An attempt was made to avoid psychotherapeutic influence as far as possible. Sedatives were not employed, except during a sodium amytal release test given to the 4 whose blood-pressures were elevated after two days in the hospital. The range of blood-pressure found by referring physicians in their offices, the levels found on admission to the hospital by resident physicians, and those measured by nurses every four hours were then compared."

"In all of these cases marked falls to normotensive levels occurred under the routine of the hospital. In 9, the level of blood-pressure became normal over-night. In the remainder, a more gradual decline was observed with normal levels (140 mm. Hg. systolic and 90 mm. diastolic) attained in two to six days. The mean decline from admission (physician's) to lowest (nurse's) levels was 71 mm. systolic and 31 mm. diastolic; the diastolic range was 16 to 80 mm. Seven subsequently exhibited mildly hypertensive levels before discharge. Therefore in no case could ganglionic blocking agents be used. Five of these patients, a year or more later, have required hydralazine and reserpine for control

of blood-pressure at normal or near normal levels while the remainder are taking reserpine alone.

The patients reported here were selected as carefully as possible. Yet, in spite of precautions, 6.1 per cent were erroneously considered to be in need of intensive therapy. Undoubtedly intermittent and severe hypotension would have resulted from the use of blocking agents.

These observations also emphasize the fact that any single reading of blood-pressure is at the very best an approximation subject to interpretation by various other more stringent diagnostic measures.

### Bromide intoxication.—(*Am. J. Med.*, 20: 100-106, 1956, via *Mod. Med.*, 1-8-'56).

It may be effectively treated by concurrent administration of a mercurial diuretic and ammonium chloride. Husser and Holley of the Medical College of Alabama, Birmingham, find that bromide elimination is more rapid when the ammonium rather than the sodium salt is used because of the potentiating effect of the former on diuresis. The serum bromide level decreases by about 18 mg. per cent a day when 6 gm. of ammonium chloride is given daily in divided doses together with 2 cc. of Mercurhydrin injected intramuscularly every second or third day.

### BOOKS RECEIVED

**Lymphatics Lymph and Lymphoid Tissue**—By JOSEPH MENDEL YOFFEY AND FREDERICK COLIN COURTICE. Pp. 510. Published by M/s. Edward Arnold (Publishers) Ltd., London. Distributors M/s. Orient Longmans Ltd., 36a, Mount Road, Madras-2. Price 60 sh. net.

**An Outline of Bacteriology and Immunity**—By RONALD HARE. Pp. 418. Published by M/s. Longmans, Green and Co., London, New York, Toronto. Distributors M/s. Orient Longmans Ltd., 36a, Mount Road, Madras 2. Price 35 sh. net.

**The Merck Manual**—Ninth Edition. 1956. Pp. 1888. Published by Merck & Co., Inc. Rahway, N.J., U.S.A.

**A Textbook of Gynaecology**—By MASANI. 2nd Edition. 1957. Pp. 775. Published by Popular Book Depot, Bombay 7. Price Rs. 25/-

**Pædiatrics**—By PATERSON AND McCrery. 1956. Pp. 654. Published by J. B. Lippincott Company, Philadelphia, Montreal. £5. 10s. net.

**Fight Against Tuberculosis**—By. G. GOEL. Pp. 83. Maa Saraswati Tuberculosis Hospital, Mathura, U.P.

## NEWS AND NOTES

Short refresher courses for both medical and non-medical personnel are being conducted in the Institute of Venereology, Government General Hospital, Madras. The period of training is three months and the courses are held 4 times a year beginning on 1st January, 1st April, 1st July and 1st October respectively. These courses are free for candidates sponsored by the State Governments, Local Bodies and certain recognized social and humanitarian institutions. For private candidates a fee of Rs. 30 per quarter will be charged. A uniform refundable deposit of Rs. 25 should be paid by all candidates to cover the cost of breakages. Applications may be sent to the Dean, Madras Medical College, Madras-3.

### International Congress of Occupational Health, Helsinki

The XII International Congress of Occupational Health will be held in Helsinki from July 1st to 6th, 1957. Industrial noise, evaluation of invalidity, industrial hygiene, cardiacs and work are the main subjects to be discussed. Sectional subjects will be discussed under the following three heads:—(a) General and social aspects; (b) occupational pathology and hygiene, and (c) industrial nursing.

There will also be group meetings. The official languages of the Congress are English, French, German and Spanish. A special programme will be arranged for the ladies of the Congress.

For further particulars our readers may contact:—Sri C. K. Ramachandran, Medical Service, M/s. Parry and Co. Ltd., Ranipet.

### Bengal Government's Ban on Smoking by Teenagers

Heads of educational institutions have been authorised by the State Government to seize and destroy any cigarette, cigar or *beedi* found in the possession of any person under 16 years, they find smoking within the premises of educational institutions.

The State Government have also authorised members of the Special

Constabulary to take action in respect of smoking by any such person in any street or public place.

The order which came into force from January 1, 1957 was issued with a view to preventing juvenile smoking in the State.

### Milk Colonies Second Plan Scheme

Schemes costing Rs. 17.5 crores for the development of milk industry in the country have been included in the Second Five-Year Plan.

These schemes envisage 36 co-operative milk unions for supply of milk to urban areas by procuring milk from surrounding villages; establishment of colonies for milch cattle dislodged from the Cities of Bombay, Calcutta, Delhi and Madras with large dairies for improving the milk supply to those cities; 12 co-operative rural creameries and seven milk-products factories; expansion of existing dairies; and establishment of milk boards.

### Filaria Control in Kerala

*Survey has shown the Efficacy of Control*

A survey of filariasis, of which elephantiasis is one of the manifestations, was in progress in Travancore-Cochin region of Kerala; the percentage of infection of the disease varied from taluq to taluq from about 1.7 per cent in Trivandrum, to 23.8 per cent in Shertallai. In Shertallai control measures were instituted in 1933. By 1936, an area of 42 square miles with Shertallai town as the centre was brought under control operation. To determine the efficacy of the control measures, a test survey was conducted, from which it was found that children born after the establishment of control measures, were free from the disease.

The filariasis control measures instituted in the coastal areas of Ambalapuzha Taluq in 1945, and the mosquito control measures started in Alleppey town in 1934 were being continued. A Filaria Control Unit was being established in the area as part of the National Filaria Control programme.

## NEWS AND NOTES

EB. '57]

### New System of Ear Operation

Dr. Samuel Rosen, Consulting Ear Surgeon, Mount Senai Hospital, New York, explained to members of the Indian Medical Association at Madras on 10th December '56 how he rediscovered the system of operation known as "mobilization" which had been in vogue from 1875 to 1900 in Germany, Austria, Italy and France. It had somehow been abandoned and in 1952 he brought to light the operation that he was now performing to restore hearing in cases of hereditary types of deafness due to otosclerosis.

Disclaiming any kind of personal credit to himself, Dr. Rosen explained how, having learnt clinical and surgical otology, he was trained under Dr. Lempert, the Father of Modern Surgical Otology, which enabled him to stumble on the discovery. Dr. Lempert, he said, was against any one who went beyond the old concept and when at the Convention of the American Medical Association Dr. Lempert went to see his exhibits, he had an opportunity of convincing him that it was the training he had under Dr. Lempert himself that led him to the discovery.

Dr. Rosen stated that he had demonstrated the operation in various countries including his own and the mobilization operation was being performed with great zeal and with singular success. He said that he had successfully operated on more than 1,500 cases and expressed the belief that his discovery had opened an exciting chapter in the future development of surgery of deafness. It was still in infancy and surgery to cure deafness, in his opinion, had yet to be perfected.

Narrating how he started to do this operation, Dr. Rosen pointed out that accidentally he began mobilizing the stapes and saw immediate results. "You can see in many ways this was a lucky incident and an accidental discovery." As a result of this, he said, the whole physiology of hearing might have to be re-written. He devised some instruments to do deliberately what he had done accidentally. "I love to work at it and I just keep on trying to make it better every time."

When he first revealed his discovery to his brother doctors in America, they did not believe him. "In my own hospital, I could not get a man to come and see the operation. They carried on a propaganda saying, "Do not go to see Rosen, it is not true."

It was in 1954 at a meeting of the American Academy, Dr. Rosen said, that some of them cared to see "what Rosen is doing." "I shall never forget the day these men came to the operating room and the discovery came to be acknowledged, because three of the four cases I operated on that day, improved dramatically on the table."

The operation, he explained, had been helpful to those whose deafness began within the age of 20, 30 or 40.

Explaining the broad technique, he said, the operation was done, painless and within 20 to 25 minutes, under local anaesthesia. The patient regained the sense of hearing on the operation table itself, in successful cases. The patient could leave the hospital the next day, and attend to his work a day or two thereafter, and no further special care was necessary.

He wanted to share the knowledge and experience and the technique with his colleagues in other countries and that was why he had chosen to tour 17 countries and give demonstrations.

He performed 3 operations on 8-12-56 successfully at the Stanley Hospital, Madras.

### Cobalt Therapy for Cancer

*Unit for Ahmedabad Hospital*

Seth Vadilal Sarabhai General Hospital at Ahmedabad, a municipal institution controlled by a Board of Management of which the Mayor of the City is the Chairman, placed an order with the International General Electric Company (India) (Private), Limited for a cobalt 60 beam therapy unit to be procured from Atomic Energy of Canada Limited, Ottawa.

Mr. W. J. Green, Export Sales Manager of the Atomic Energy of Canada, Limited, visited Ahmedabad along with Mr. J. A. Mehr-Homji, Manager, X-ray division, International General Electric Company (India) (Private) Limited on November 20,

1956, in order to finalize technical details. This hospital is very popular and has been raised from a 120-bed (in 1931) to 380-bed hospital (in 1956).

During the early part of 1956, the President of the Cloth Dealers' Association expressed to the then Mayor that his Association was willing to donate certain funds to the municipality to be spent in any worthwhile project of the City. The Mayor considered it desirable to utilize this fund for expansion of the Seth Vadilal Sarabhai Hospital. The idea of acquiring a cobalt 60 beam therapy unit was introduced in consultation with the International General Electric Company but at first the proposal seemed too formidable to be accomplished. However, the hospital itself decided to contribute half the cost and with the co-operative efforts of all concerned it was possible to finalize the proposals and order the first cobalt 60 unit in India. Mr. Green is now visiting other important centres in India and it is hoped that various Cancer Research institutions and prominent hospitals will interest themselves in acquiring this most modern equipment for the treatment of cancer.

We are informed that Mr. Andre A. Martin, Near-East Manager of Dr. A. Wander S.A., Berne, Switzerland,

the well-known manufacturers of Dietetic Chemical and Pharmaceutical products since 1885, arrived in Bombay in the first week of December 1956 to investigate the possibilities of manufacturing the various "WANDER" products in India and after completion of his investigations and studies in collaboration with Messrs Khatau Valabhdas and Company, left for Switzerland on 21st December '56.

#### World's Largest X-ray Machine in Operation

The largest X-ray machine in the world now in operation is for cancer treatment at the University of California Medical School in San Francisco. The giant, 70,000,000 electron volt instrument is currently being used to treat selected cancer patients on a regular continuing basis.

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Financed by the United States Atomic Energy Commission, the machine was used on humans only after five years of development and animal studies. The results which it will be able to achieve cannot be determined for several years to come.—U.S.I.S.

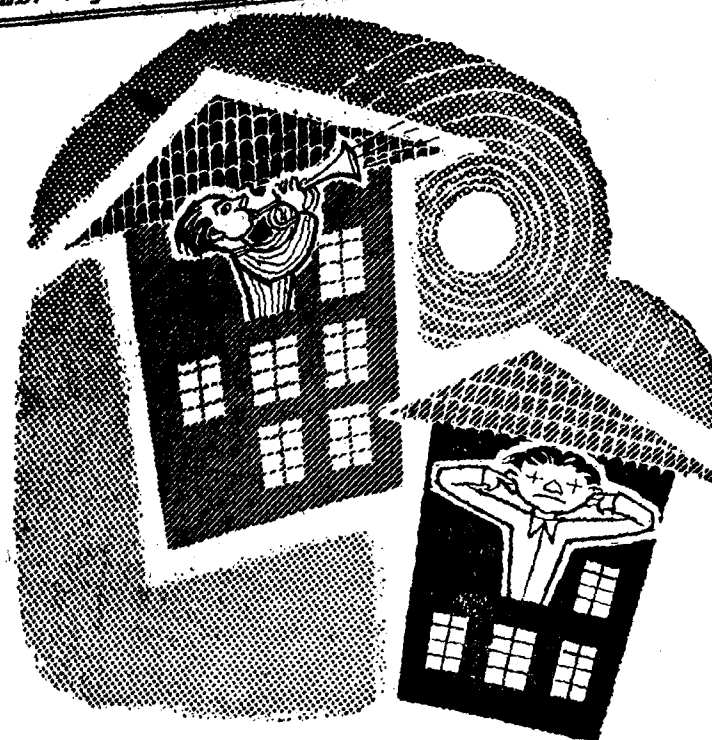
#### PREPARATIONS AND INVENTIONS

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orders and cerebral palsy. It is stated to produce muscular relaxation of greater potency and longer duration. Rapid-acting, its effect is noted in 30 to 40 minutes. It is claimed that it does not produce annoying autonomic side reactions such as nasal stuffiness, increased salivation, abdominal cramps etc. Its toxicity is supposed to be extremely low having no effect on blood, liver or kidney function. Dose is said to be one 400 mg. tablet 3 or 4 times day.

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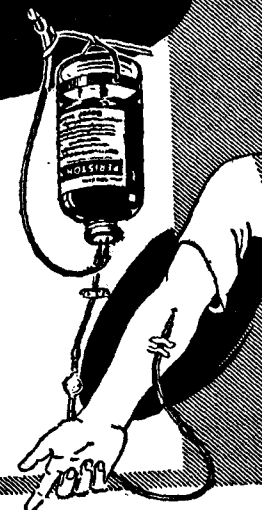
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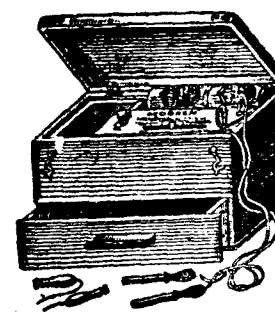
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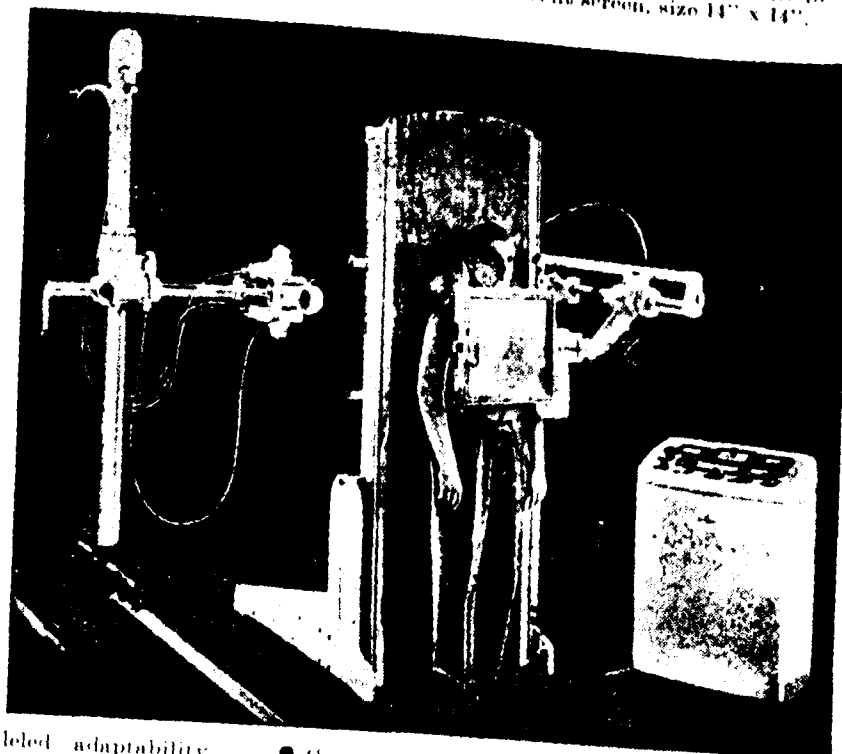
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where  
**PAIN**  
is a  
symptom...

as in  
HEADACHE  
TOOTHACHE  
MUSCLE PAIN  
NEURALGIA

DIARRHOEA  
INFLUENZA

Therapy of the underlying causal condition is no doubt the prime consideration. However, when treatment of the basic disease does not or cannot afford prompt relief, 'ANACIN' will often alleviate the distress of pain and impart a sense of well-being.

ANACIN is a non-toxic and clinically dependable preparation, specially formulated to provide a prolonged period of analgesia with a single dose of 1 or 2 tablets.

#### Composition

Quinine 114 gr. Aspirin 3 gr.  
Phenacetin 3 gr. Caffeine 114 gr

In piller-proof containers  
of 22 tablets and packets  
of 2 tablets each.  
• Trade Mark

**ANACIN**  
ANALGESIC TABLETS

Manufactured and Distributed by:  
**WANNERS & COMPANY PRIVATE LIMITED, BOMBAY**  
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For Treatment of LEPROSY

## NOVOTRONE

(Derivative of Diamino-diphenyl-sulphone)

Extremely Low Toxicity

\* High Therapeutic Value \*

Freedom from Side-effects

#### For Oral Use

Tablets of 0.5 G (7½ grs.) each.  
In bottles of 100 and 500 tablets.

#### For Parenteral Use

Boxes of 6 and 12 ampoules of 2 cc.  
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Also bottles of 25, 100 and 250 G  
granules for making solution.

\* \* \* \* \*

For mass treatment  
In Hospitals and Clinics at  
Economic cost

## NOVOPHONE

(4:4' Diamino-diphenyl-sulphone)

#### FOR ORAL USE

Mode of Issue:

NOVOPHONE (Plain)

50 and 100 mg tablets in bottles of 100 and 1000 tablets

NOVOPHONE 'Y'

(Reinforced with yeast)

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NEW

# BARDASE

3 FOLD ACTION

1 ANTISPASMODIC

*Relieves Spasm*

2

SEDATIVE

*Relaxes Nervous Tension*

3

DIGESTIVE AID

*Liquefies Starch mass*

## TABLET

**LIQUID BARDASE** combine the anticholinergic, sedative and amylolytic properties of belladonna alkaloids, phenobarbitone and TAKA-DIASE and thus represent a comprehensive therapeutic approach.

## INDICATIONS

For the relief and management of visceral and smooth muscle spasm encountered in irritable colon, peptic ulcer, ulcerative colitis, genito-urinary disturbances and dysmenorrhoea.

## PACKAGES

Tablets - Yellow sugar-coated tablets in bottles of 20 & 100; Liquid - Pleasantly flavoured liquid in bottles of 4 fl. oz.



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