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53, No. 6

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THE REGISTRAR OF JUNE 1956

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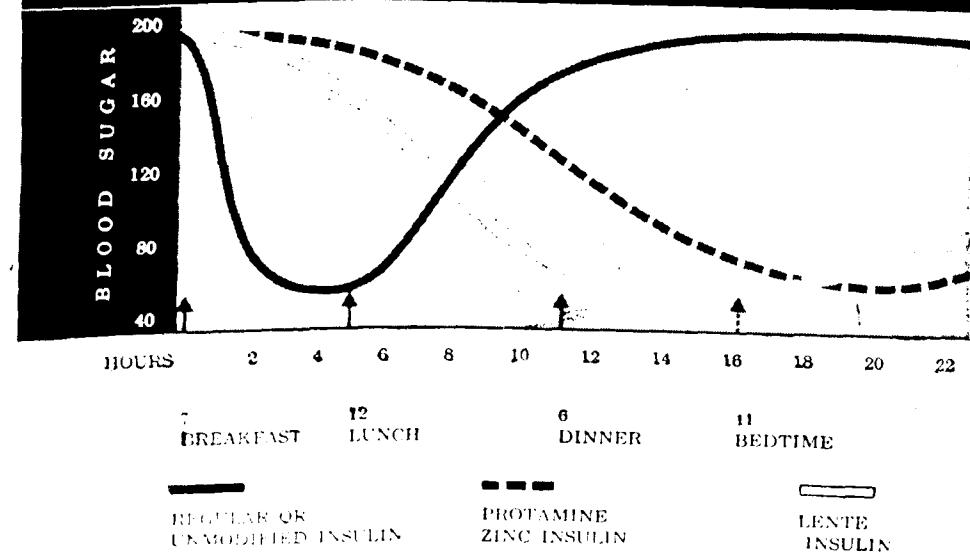
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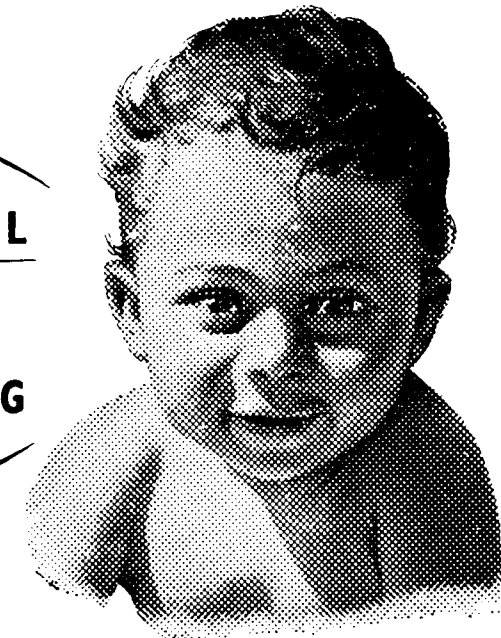
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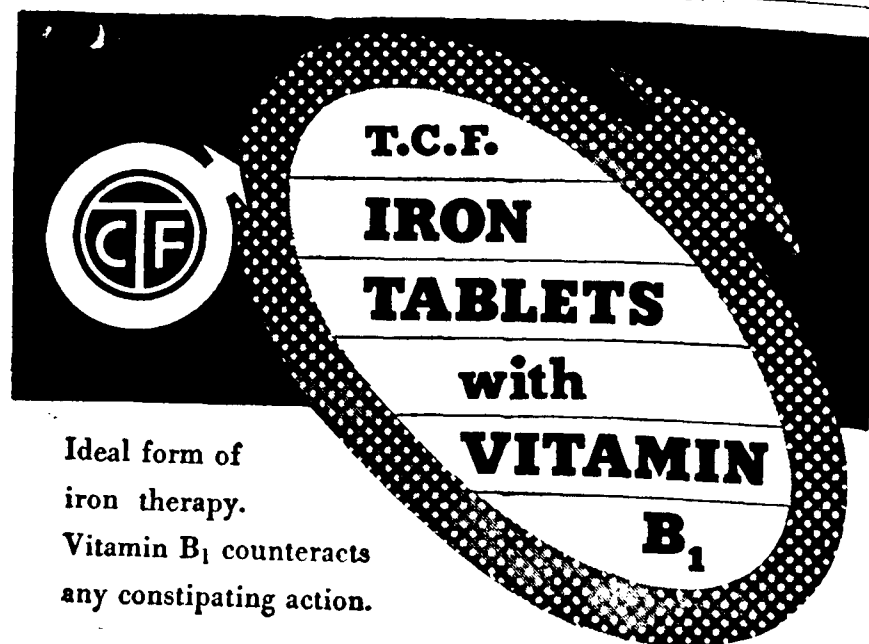
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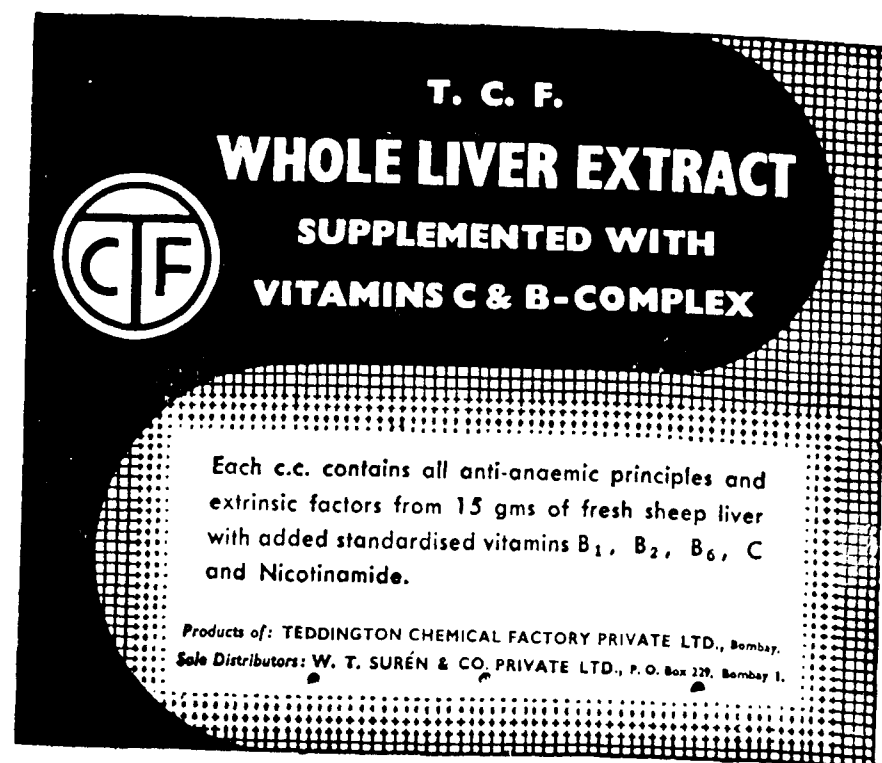


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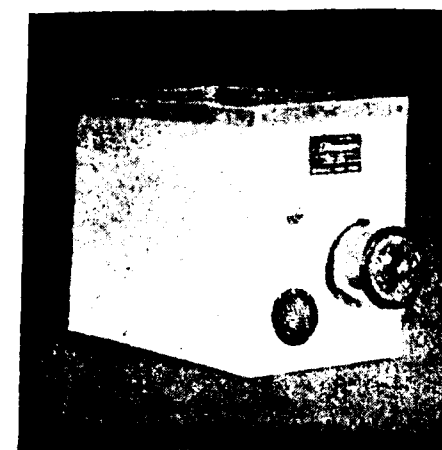
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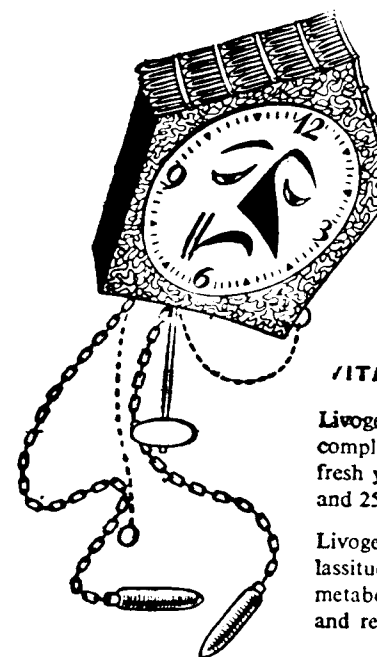
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**THERAPEUTIC PHARMACEUTICALS**

Chotani Estate, Proctor Road, BOMBAY-7.



A RUN-DOWN  
PATIENT?

It's time he had—

## LIVOGEN

with

VITAMIN B COMPLEX and VITAMIN B<sub>12</sub>

Livogen contains in each fluid ounce the natural vitamin B complex derived from 4 oz. of fresh liver, and 2 oz. of fresh yeast, together with added vitamin B<sub>1</sub> nicotinic acid, and 25 micrograms of vitamin B<sub>12</sub>.

Livogen is the rational tonic for all cases of debility, lassitude and nervous depression. It contains the essential metabolic 'activators' which create a lively interest in food, and restore natural vitality.

BRITISH DRUG HOUSES (INDIA) PRIVATE LTD., Post Box 1341, BOMBAY-1  
Branches at: Calcutta - Delhi - Madras

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 roundworms:** 2½

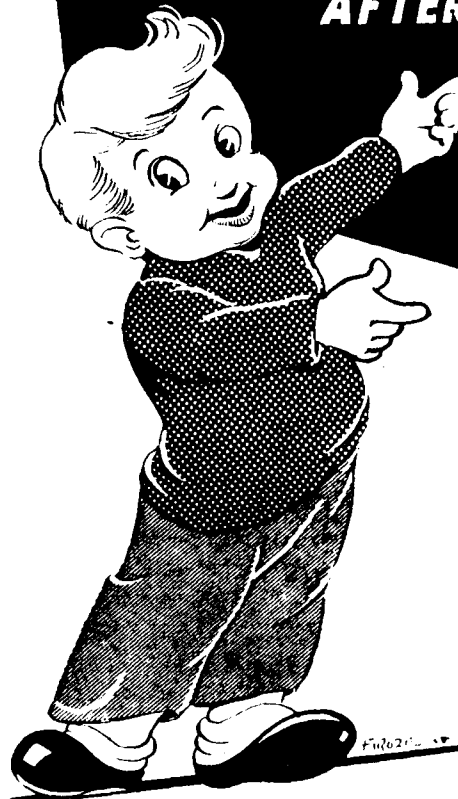
tablets (or 1 ¼ teaspoonful) per year of age up to the age of 6 years. For adults and children over 6 years, give a total dosage of 15 tablets (or 7 ½ teaspoonfuls). The dosage should be given in a single dose or in four divided amounts during one day.

**'ENTACYL'** TRADE MARK

Tablets—Bottles of 25 and 100  
Suspension—Bottles of 50 ml.

BRITISH DRUG HOUSES (INDIA) PRIVATE LTD., Post Box 1341, BOMBAY 1  
Branches at: Calcutta - Delhi - Madras

**INSIST ON . . . .**  
**ROOHAFZA**  
**NEVER AN**  
**AFTER-THIRST**



**Hamdard**  
**DAWAKHANA (TRUST) DELHI.**



## PHOSVITANON

The well-balanced Vitamin Tonic and Health Restorer with a pleasant taste

for

LOSS OF APPETITE  
 EXHAUSTION STATES  
 WEAKNESS  
 CONVALESCENCE  
 ANÆMIC CONDITIONS  
 POST-OPERATIVE PERIODS

## CITROFINAL-N

The Sodium-free diet salt

for seasoning food of any kind when a salt-free diet is indicated. Stable during cooking and baking.

Prescribe **CITROFINAL-N**

for a salt-free diet in renal and cardiac diseases associated with œdemata, in arteriosclerotic conditions, hypertension, eczema; with weight-reducing diets.

Bottle of 75 g

PRICES REDUCED!

Factory Representatives:

GERMAN REMEDIES & TRADING CO., PRIVATE LTD.,  
 P.O. Box No. 1945, BOMBAY-1

# HOMBURG

"I agree— This is a case for  
**ELEDON, Nurse**"



A wholly reliable buttermilk diet in powder form of stable composition and constant degree of acidity, ELEDON is not only an excellent specific for adults susceptible to intestinal disorders, but is highly successful in the treatment of infants and young children suffering from Diarrhoea ... Dysentery ... Pylorospasm ... and, especially Steatorrhoea and Malnutrition.



**Eledon**



Please write for literature to: NESTLÉ'S PRODUCTS (INDIA) LTD.  
P.O. Box 396 Calcutta. P.O. Box 315 Bombay  
P.O. Box 180 Madras

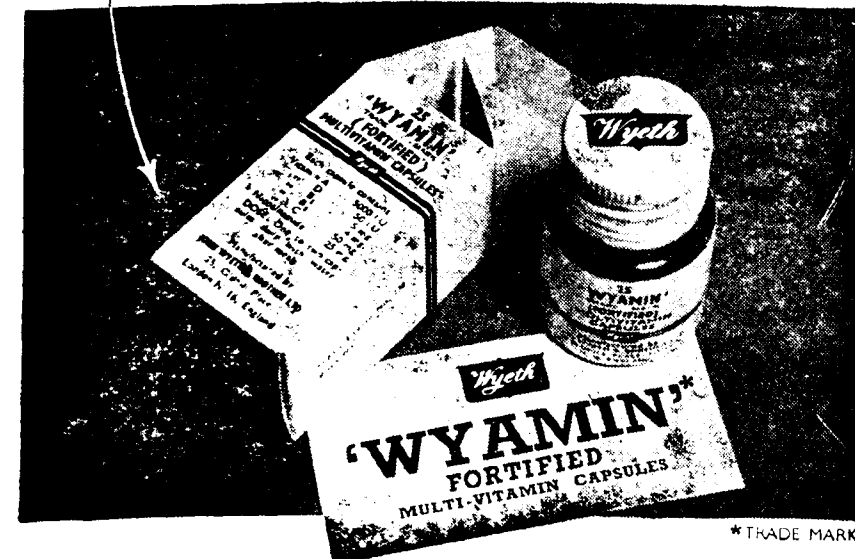
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**malnutrition...**



Numerous clinical studies have emphasized the value of supplementary vitamins in the management of malnutrition. 'Wyamin' Fortified deserves a prominent place in the treatment of nutritional deficiency conditions. It is a thoroughly reliable source of vitamins A, B<sub>1</sub>, B<sub>2</sub>, C, D and Nicotinamide in quantities especially adjusted to meet sub-tropical requirements. Presented as capsules, 'Wyamin' Fortified ensures uniform dosage and makes administration convenient.

Supplied in bottles of 25, 50 and 300 capsules



\*TRADE MARK

**JOHN WYETH & BROTHER LIMITED**  
(Incorporated with limited liability in England)  
India Branch: Magnet House, Dougall Road, Bombay 1.  
Distributors: **GEOFFREY MANNERS & CO. PRIVATE LTD.**  
Bombay . Calcutta . Madras . New Delhi

**Alembic**  
**ANTIBIOTICS PREPARATIONS**  
 (Parenteral)

**ALPROCIN**

Procaine penicillin fortified with penicillin G sodium for aqueous injection. In rubber capped vials containing the equivalent of 400,000 units of penicillin.

**DIPROCIN**

A combination of two penicillins (procaine penicillin and penicillin G sodium) with dihydrostreptomycin sulphate.

**BISTREPEN**

A combination of two penicillins and two streptomycins:—procaine penicillin, penicillin G sodium, dihydrostreptomycin sulphate, and streptomycin sulphate.

**COSTRECIN**

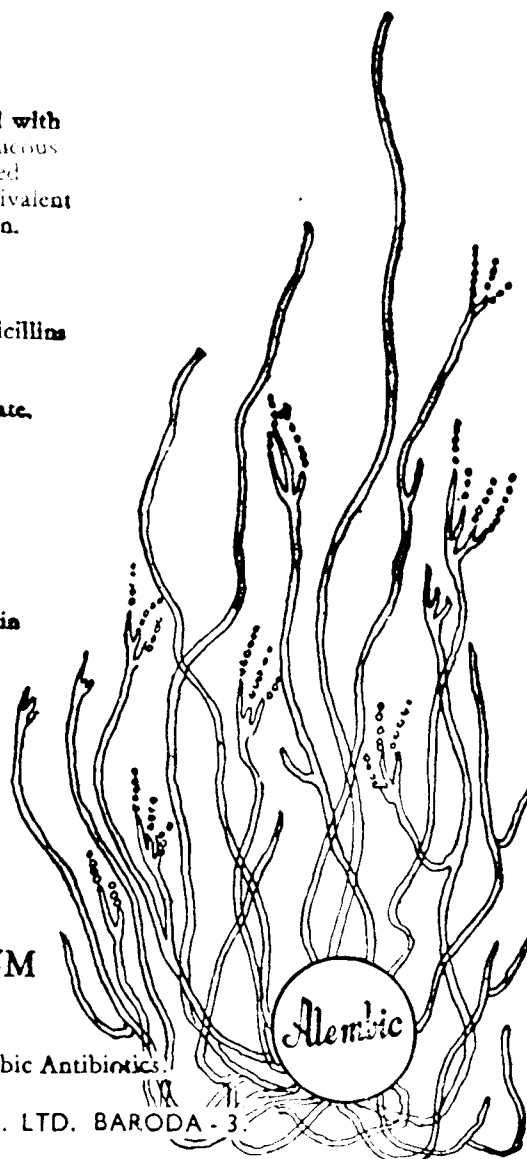
A combination of dihydrostreptomycin sulphate and streptomycin sulphate, in equal proportion.

**CRYSTALLINE  
 PENICILLIN G SODIUM**

500,000 & 1,000,000 units.

Write for complete literature on Alembic Antibiotics.

ALEMBIC CHEMICAL WORKS CO. LTD. BARODA - 3



**SYRUP  
 NEO-METHIDIN\***

Total lipotropic therapy with anti-anaemic principles and the most nutritive carbohydrate: Lævulose (for the first time for oral therapy).

| Each fl. oz. containing: |     |          |
|--------------------------|-----|----------|
| Acetyl-methionine        | ... | 4400 mg. |
| Choline chloride         | ... | 3500 mg. |
| Vitamin B <sub>12</sub>  | ... | 20 mcg.  |
| Folic acid               | ... | 5 mg.    |
| Inositol                 | ... | 50 mg.   |

In a palatable base of  
**LÆVULOSE**

Bottles of 4 and 8 ozs.

**NEO-METHIDIN\***  
**'FORTE'**

Protective and curative liver therapy for convenient intramuscular injection for children and adults.

| Each 2.5 cc. ampoule containing: |     |         |
|----------------------------------|-----|---------|
| d,l-Methionine                   | ... | 500 mg. |
| Choline chloride                 | ... | 50 mg.  |
| Inositol                         | ... | 100 mg. |
| Vitamin B <sub>12</sub>          | ... | 6 mcg.  |

Boxes of 5 and 50 ampoules.

In addition to the well-established:

**NEO-METHIDIN\***

Ampoules 10 cc. (20% d, l-Methionine per ampoule)

The first injectable methionine preparation.

Tablets (0.25 g. d, l-Methionine per tablet)

\* Trade Mark Registered



**NEO-PHARMA LIMITED**  
 Kasturi Buildings, Churchgate Reclamation,  
**BOMBAY 1**

WANDER

# Asmac

for the symptomatic treatment of  
BRONCHIAL ASTHMA

Combines the sedative action of allobarbitone  
on the nervous system with  
the spasmolytic action of ephedrine and  
xanthine derivatives  
while extr. of ipecacuanha improves expector-  
ation.

Tubes of 20 tablets.  
Bottles of 100 and 500 tablets.

Dr. A. WANDER S.A., BERNE—Switze land.

WANDER

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*Sole Importers:*

**KHATAU VALABHDAS & COMPANY**  
PHARMACEUTICAL DEPARTMENT

Indian Globe Chambers, Fort Street, Bombay-1

BRANCHES AT: Patna, Delhi, Kanpur, Madras, Madras,  
Secunderabad (Dm.) and Bangalore City.

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# CLINITEST

TRADE MARK

urine-sugar analysis set

Distinct colours for reliable readings

DOCTORS AND PATIENTS CAN BE SURE OF THE RELIABILITY AND SIMPLICITY OF 'CLINITEST' (BRAND) SETS AND REAGENT TABLETS. THE MOST DISTINCT COLOUR SCALE, THE EASILY RECOGNISABLE COLOURS OF THE TEST, GIVE PATIENTS CONFIDENCE IN THEIR READINGS, SO REDUCING THE NUMBER OF UNNECESSARY VISITS TO DOCTORS. THIS ONE-MINUTE, NO HEATING, COPPER REDUCTION TABLET TEST CAN BE MADE EASILY EVEN UNDER TRAVELLING CONDITIONS.

A VALUABLE INSTRUMENT FOR THE PRACTITIONER FOR ROUTINE SUGAR ANALYSIS, 'CLINITEST' IS THE ACCEPTED TEST FOR THE DETECTION AND CONTROL OF GLYCOSURIA.

*Approved by the Medical Advisory Committee of the Diabetic Association in  
England*

No. 2155 Complete Set, including 24 Foil-Wrapped Tablets.

No. 2157 Refill bottles (24 Foil-Wrapped Reagent Tablets).

SOLE AGENTS

**MARTIN & HARRIS LTD., CALCUTTA.**

BRANCHES : BOMBAY, MADRAS & DELHI.

Manufactured by Miles Laboratories Ltd., Bridgend, South Wales, under licence from  
Ames Company, Inc.

## *An effective Anti-Bacterial Agent*

Collosol Manganese has been widely and successfully used by the Medical profession for the successful treatment of staphylococcal conditions for over 30 years. Used alone, or in conjunction with penicillin, it is invaluable in the treatment of boils, for it lowers the relapse rate significantly. Collosol Manganese may be administered orally or by injection. Within the range of dosage recommended Collosol Manganese is *stimulating and tonic in action* and is entirely free from side effects.



**THE CROOKES LABORATORIES LIMITED** (Incorporated in England)  
COURT HOUSE · CARNAC ROAD · BOMBAY 2



# hemolon

LIVER EXTRACT INJECTABLE (CRUDE)

### COMPOSITION

Each c. c. represents Hemopoietic principles derived from 15 Grams of fresh liver and 10 mcg. of vitamin B<sub>12</sub>

### PACKING

Rubber-capped vials of 10 c.c.

ALEMBIC CHEMICAL WORKS CO. LTD., BARODA-3.  
YOU CAN PUT YOUR CONFIDENCE IN ALEMBIC



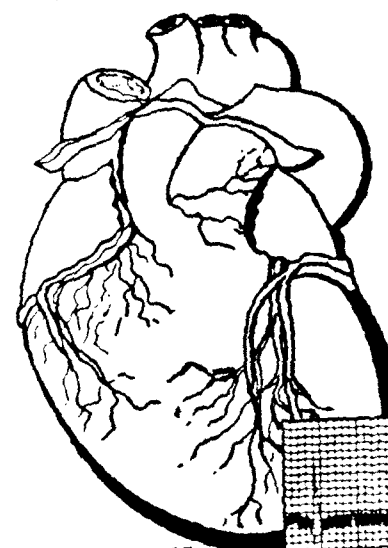
for all allergic disorders

R<sub>x</sub>  
Sandosten  
+ Calcium  
Sandoz

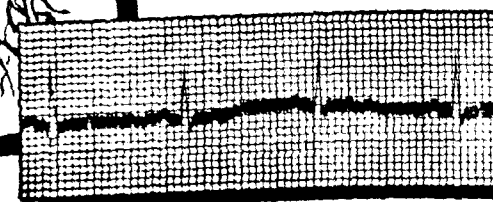
COMBINED ANTIALLERGIC ACTIONS OF  
ANTIHISTAMINE AND CALCIUM

Ampoules of  
5 c.c. and 10 c.c.

Effervescent  
Tablets



FLATTENING OF  
T WAVES INDICATING  
MYOCARDIAL DEFECT



- **Myocardial Damage**
- **Cardiac Insufficiency.**

**HERZOLAN** CIPLA  
EXTRACTUM CORDIS TOTALIS  
ORAL

"Cardiovascular diseases are caused primarily by the degeneration of heart muscle. If we replace the used up and missing active chemical constituents contained in the heart muscle responsible for normal myocardial activity, the onset of organic heart diseases could be prevented and a number of lives thus saved".

HERZOLAN is a concentrated heart muscle extract containing all the important chemicals and the essential enzyme Cytochrome C present in the heart muscle. HERZOLAN is a natural food and nourishment for the degenerating heart muscle which quickly responds to this nourishment and regains normal activity. (Ref: Abstract of World Medicine, Sept. 1950, No. 1047; Science 104.)



PACKING  
BOTTLE OF 8 OZ.

*Cipla*

B O M B A Y - 8.

"HERZOLAN"  
Exhaustive Literature  
sent on request

Cipla Sales Depot: 1,186, Mount Road, Madras

# Serpasil

Regd. Trade Mark.

## Antihypertensive

All forms of hypertension.

## Bradycardiac

Better results in cardiology when combined with digitalis; dosage of digitalis can be reduced.

## Tranquillizer

Tension, anxiety, agitation, irritability, environmental stress; hyperactive irritable infants.

Menopausal and premenstrual tension.

Emotional stabilizer in old age.

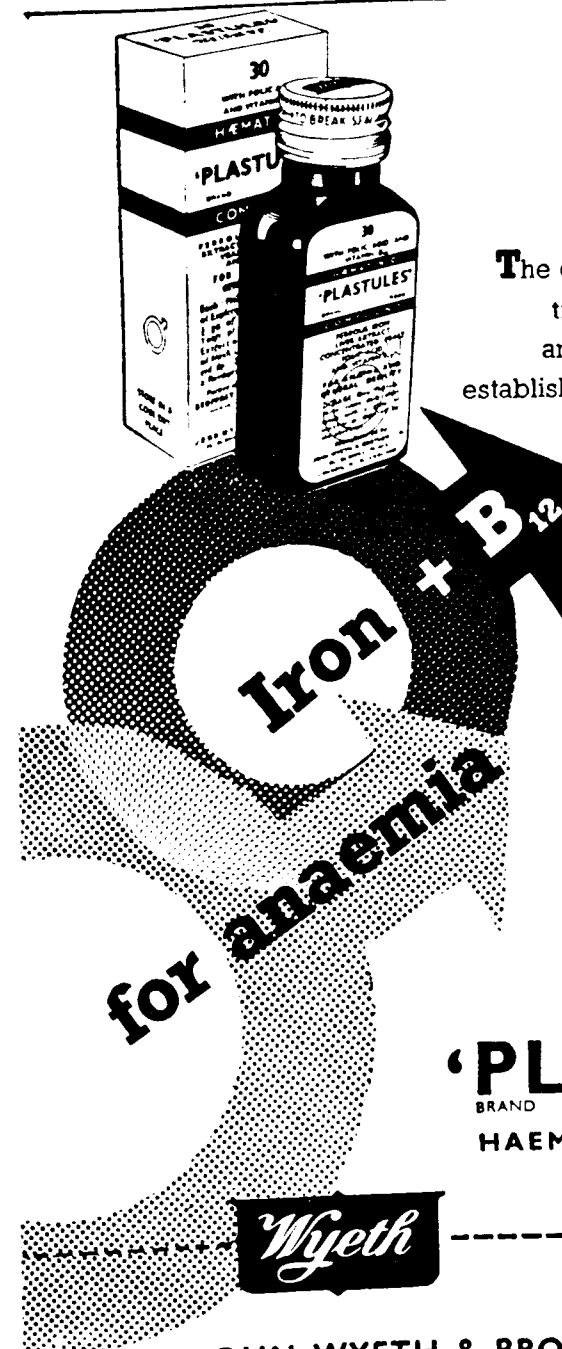
Dermatoses of emotional and psychogenic origin with uncontrollable itching.

Narcotic and alcohol withdrawal symptoms.

Nervous disorders associated with agitation and convulsions.

Mental diseases.

**CIBA** PHARMA PRIVATE LIMITED, P. O. BOX NO. 1123, BOMBAY



The efficacy of 'Plastules' in the treatment of iron-deficiency anaemias has now been well established. 'Plastules' Liver and 'Plastules' Folic Acid ensure maximum haemopoiesis in cases of delayed response. Now that vitamin B<sub>12</sub> is also being used extensively for anaemias a fourth variety of 'Plastules'—'PLASTULES' with VITAMIN B<sub>12</sub>—has been added to the well-known Wyeth range of haematinic preparations.

**'PLASTULES'**  
BRAND REGD.  
HAEMATINIC COMPOUND

**JOHN WYETH & BROTHER LIMITED**  
(Incorporated with limited liability in England)

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# Cough!

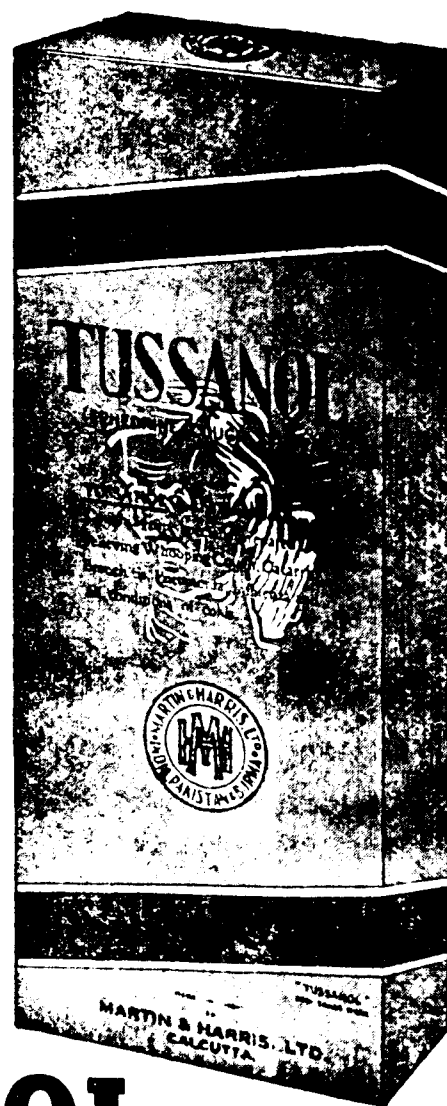
when  
diagnosis  
demands a  
cough remedy  
a majority  
of physicians  
prescribe

## TUSSANOL

(COUGH SYRUP)

THE SAFEST REMEDY FOR PATIENTS OF ALL AGES

A MARTIN & HARRIS PRODUCT



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 1 1/4 gr. Aspirin 3 gr.  
Phenacetin 3 gr. Caffeine 1/4 gr.

## ANACIN\*

ANALGESIC TABLETS

Manufactured and Distributed by:

GEOFFREY MANNERS & COMPANY PRIVATE LIMITED, BOMBAY

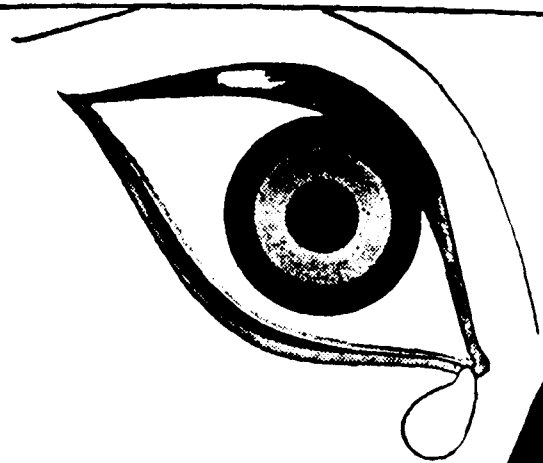
Trademark Proprietors:

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.



# OPHTHOR & OPHTHOR-H

CORTISONE AND HYDROCORTISONE OPHTHALMIC PREPARATIONS FOR  
INFLAMMATORY & ALLERGIC DISEASES OF THE EYES

OPHTHOR DROP - CORTISONE EYE DROP - 5

OPHTHOR OINT - CORTISONE EYE OINTMENT - 1.5

OPHTHOR H - HYDROCORTISONE EYE DROP



Manufactured by

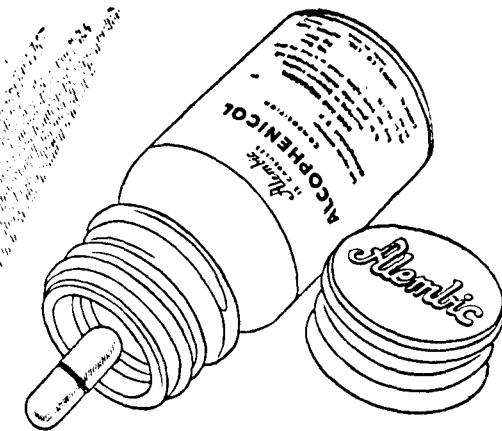
**CONTINENTAL PHARMA**

S. A. BELGO-CANADIENNE  
BRUSSELS BELGIUM

Exclusive Distributors:

**DEY'S MEDICAL STORES PRIVATE LTD.,**

CALCUTTA BOMBAY COCHIN MADRAS



# ALCOPHENICOL

CAPSULES

(CHLORAMPHENICOL B.P.)

A broad-spectrum antibiotic  
useful in...

- Salmonellosis including typhoid fever
- Shigellosis
- Pertussis
- Urinary Infections
- Pneumonias
- Brucellosis
- Typhus & Many other infections.

Each capsule contains:-  
Chloramphenicol B.P. 250 mg.  
(Bottles of 12 capsules)

ALEMBIC CHEMICAL WORKS CO. LTD., BARODA 3.  
YOU CAN PUT YOUR CONFIDENCE IN ALEMBIC.





## A BALANCED OUTLOOK



Anxine Tablets provide comprehensive symptomatic treatment of anxiety states, psychoneuroses and psychosomatic disorders

by improving mood and increasing confidence,  
by inducing gentle sedation and allaying anxiety  
and

by securing the optimal degree of muscular relaxation.

Although each of the three components of Anxine Tablets, dexamphetamine sulphate, cyclobarbitone and mephesisin, makes an important contribution to the amelioration of the symptoms of anxiety states, none is adequate alone. It is only when they are combined, in the form of Anxine Tablets, that maximum control of symptoms is achieved.

### Formula

Each Anxine Tablet

Contains:—

Dexamphetamine

sulphate 2.5 mg.

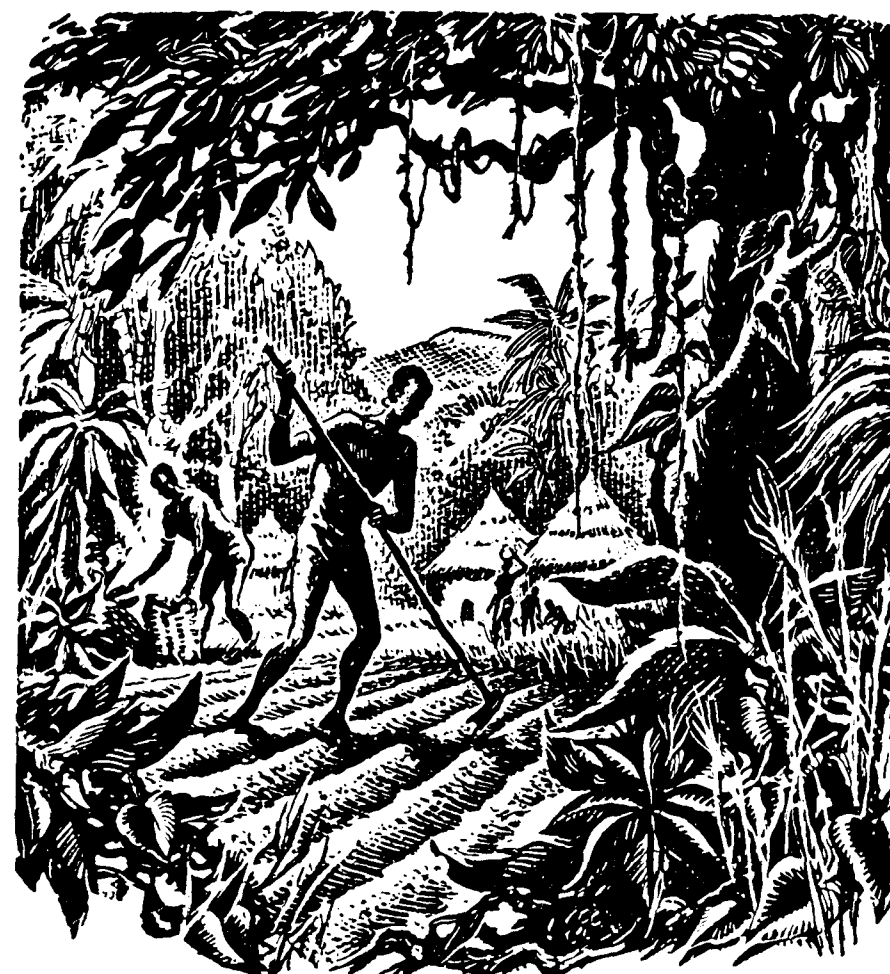
Cyclobarbitone 35 mg.

Mephesisin 120 mg.

# ANXINE

Available in bottles of 50 tablets.

**ALLEN & HANBURY LTD**  
(INCORPORATED IN ENGLAND)  
**CALCUTTA BOMBAY**



## 'Banocide' in Filariasis

The Malaria Institute of India have recommended diethylcarbamazine for mass treatment and prophylaxis in the national campaign against filaria. 'Banocide' brand diethylcarbamazine acid citrate, from extensive clinical trials and use over several years, has become established as the most effective agent against filaria yet discovered. Whether for mass populations or individual patients 'Banocide' constitutes an effective, safe and easily administered method of treatment. 'Banocide' is issued as 50 mgm. compressed product in containers of 20, 100 and 1000; and, for children, as 'Banocide' brand Syrup, 30 mgm. per c.c. in bottles of 3 fl. oz.

# 'BANOCIDE'

DIETHYLCARBAMAZINE ACID CITRATE



**BURROUGHS WELLCOME & CO (INDIA) PRIVATE LTD.,**  
P. O. BOX 290, BOMBAY.

*Doctor,  
you get*

Better Vitamin A  
absorption and  
therefore a higher  
therapeutic effect with

**Arovit Drops**

Trade Mark

One drop equivalent to  
5,000 I.U. vitamin A

For the improved treatment of

Acne  
Inner ear deafness  
Ozena  
Premenstrual tension  
Sterility in the male

Literature available on request from Voltas Limited P. O. Box 900, Bombay - 1

This new form of application (30 drops per cc) consists of a clear non-oily, non-alcoholic water-miscible solution, containing 150,000 I.U. per cc (about 82 mg vitamin A palmitate). The drops are taken in tea, coffee, fruit juice, etc., where they emulsify easily. In order to avoid any after-taste, the dose should be followed by a liquid draught.

Packings: 7.5 cc & 50 cc

F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland  
Sole Distributors for India:  
**VOLTAS LIMITED**  
Bombay, Calcutta, Madras, Cochin, New Delhi, Kanpur

## The other advantages . . .

Single-dose treatment with 'Nivaquine' brand chloroquine sulphate — the modern method of controlling the acute malarial attack within 24 hours — is so simple and so effective that the other advantages offered by this drug are sometimes overlooked.

Chloroquine is immediately active against all stages of the erythrocytic asexual parasites, and the rapidity with which parasitaemia and fever are controlled in acute infections due to *P. falciparum*, *P. vivax*, or *P. malariae*

minimizes the debility resulting from these attacks.

'Nivaquine' is economical in use, causes no discoloration of the skin, and its low toxicity and freedom from side-effects ensure that it may be given safely even to children and to pregnant patients.



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



REGISTERED BY  
**MAY & BAKER LTD**

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

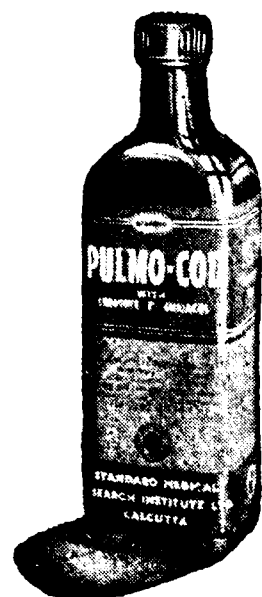
**THREE TONICS** with Vitamin B Complex and Big combines various B Complex factors with Glycerophosphates and acts as a general stimulant. Easily assimilable Phosphorus is available in this preparation and its administration regenerates nervous energy which has been lost by wasting diseases, over work, 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 Anemias, loss of appetite etc. It is also indicated in Neuritis, Beri-Beri, Nutritional Diarrhoea, Sprue, Leucorrhoea, Heartburn and vomiting in pregnancy etc. It is an invaluable dietary supplement during treatment with Sulpha Drugs or Antibiotics and also for patients suffering from Diabetes Mellitus.



**SPENCER & CO., LTD.**  
MANUFACTURING CHEMISTS  
1/153 MOUNT ROAD MADRAS-2 INDIA.

T.T. 1-5A



*Nutritive Aid*  
**In Case of Malnutrition and Wasting Diseases**

**PULMO-COD**

WITH

**Creosote & Guaiacol**

Supplies

Minerals and generous amount of Vitamin

**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 & Guaiacol)

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

Vitamin A 4500 I. U.  
Vitamin D 1000-01 U.  
Vitamin B<sub>1</sub> 3 mgs.  
Vitamin B<sub>2</sub> 2 mgs.  
Vitamin B<sub>6</sub> 5.0 mcgs.  
Nicotinic Acid 40 mgs.  
Folic Acid 920 mcgs.  
Sodi Hypo. 120 mgs.  
Potassi Hypo. 120 mgs.  
Calcii Hypo. 240 mgs.

{ Creosote 1 1/3%  
Guaiacol 1%

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

STADMED P. IVATE LTD.  
15, JAWPORE ROAD, CALCUTTA-30

M L No. DL 62 M  
DL 42 MB

**STADMED PRIVATE LTD., CALCUTTA-4**

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 u.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 Eye-piece 5x. & Pariplan 10x. & 15x Achromatic Objectives 10x, 40x and 100x Oil Immersion. Magnification: 50x-1500x.

**Price Rs. 748/-**

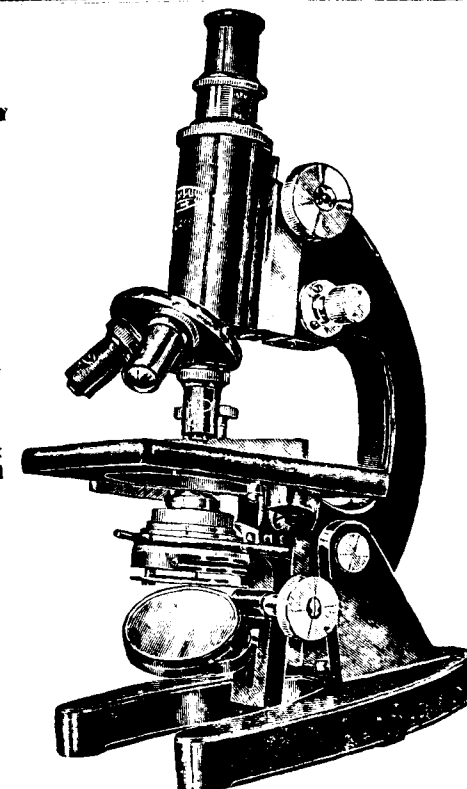
For demonstration and other particulars contact your dealers or the sole agents:-

**DARBARA SINGH & SONS,**

14, Bow Bazar Street,  
P. O. Street, Sadar Bazar,  
166, Hornby Road, Fort.

Calcutta-12  
Delhi-6  
Bombay

Also available various other models



**Guaranteed**

for promotion and regeneration of  
liver cells

**METHICOL** contains in each fl. oz.  
dl. Acetyl Methionine 5000 mg.  
Choline Dihydrogen Citrate 2400 mg.  
Folic Acid 5 mg.  
Vitamin B<sub>12</sub> 20 mcg.  
Vitamin E 1 mg.  
Extract from 4500 mg. of Dried yeast.  
Glycerine 10% with other adjuvants.

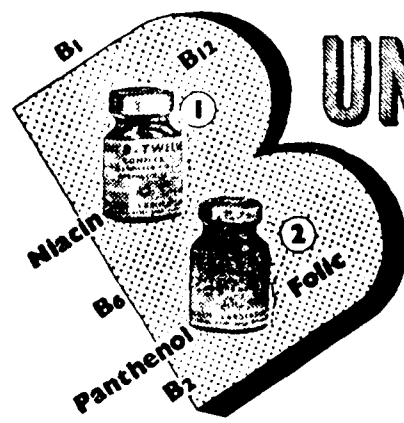
Effective in: Hepatitis-infective and amoebic, Cirrhosis of the liver, Infantile biliary Cirrhosis, Acute yellow atrophy of the liver, Jaundice, different types of liver diseases due to chemo-therapy.

**melhicol**

IN PACKS OF 2 oz & 4 oz phials



**BENGAL IMMUNITY CO., LTD. CALCUTTA-13**



## UNI-B<sub>12</sub> COMPLEX

for Anaemias & General Debility etc.

Each c.c. mixed solution ( $\frac{1}{4}$  c.c. from each)

|                               |        |                                  |         |
|-------------------------------|--------|----------------------------------|---------|
| Vitamin B <sub>12</sub> ..... | 50 ug. | Vitamin B <sub>1</sub> .....     | 25 mg.  |
| Folic Acid.....               | 5 mg.  | Niacin.....                      | 100 mg. |
| Vitamin B <sub>2</sub> .....  | 3 mg.  | Pyridoxin.....                   | 5 mg.   |
| Panthenol.....                | 10 mg. | Betain H. Citrate.....           | 25 mg.  |
| Procaine Hcl.....             | 10 mg. | Chlorobutol as preservative..... | 0.5 %   |

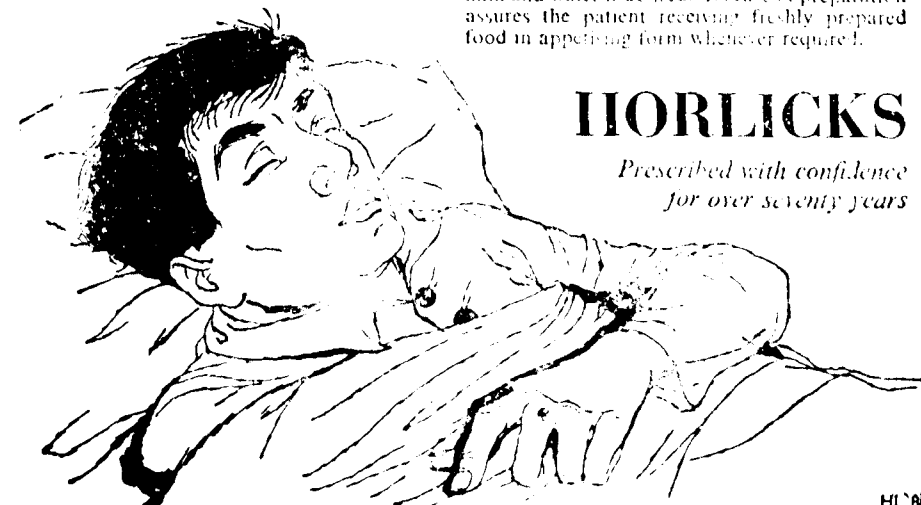
**SUPPLIED IN 2 VIALS TO ENSURE THE STABILITY.**

**UNICHEM LABORATORIES, BOMBAY 26.**

### diet in fevers

In fevers and febrile conditions Horlicks has proved itself to be an excellent form of nourishment.

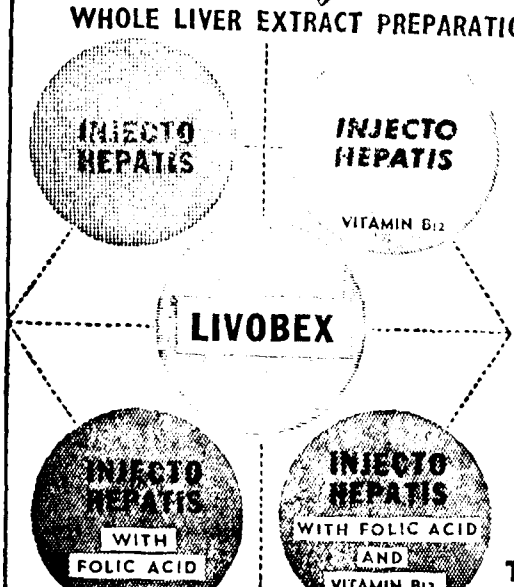
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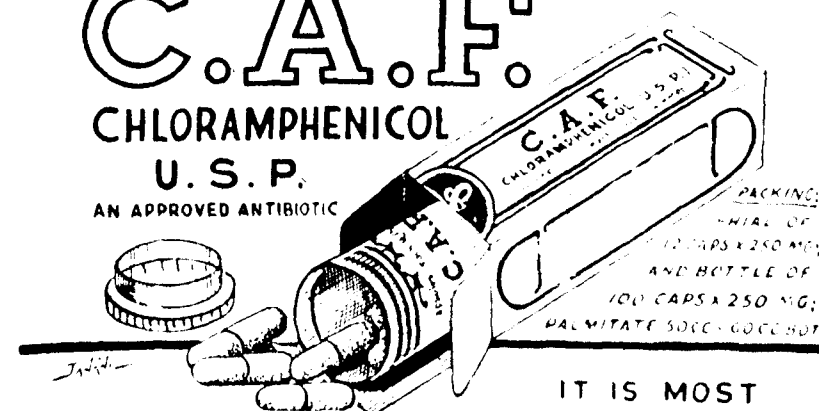
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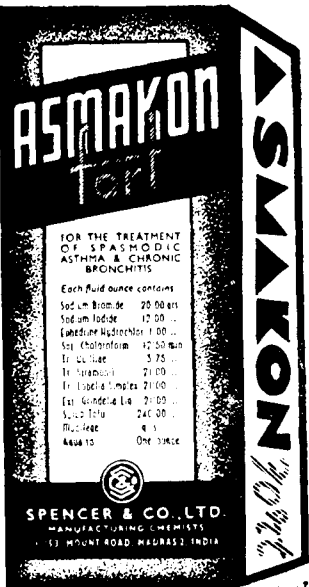
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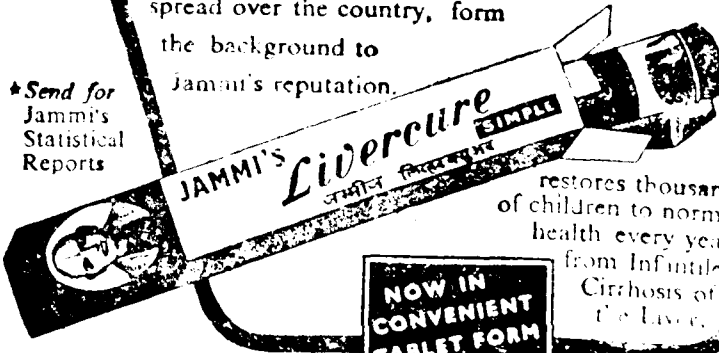
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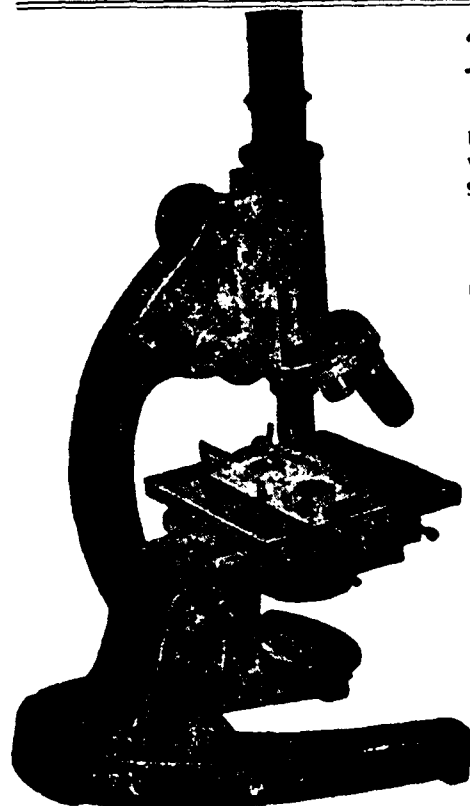
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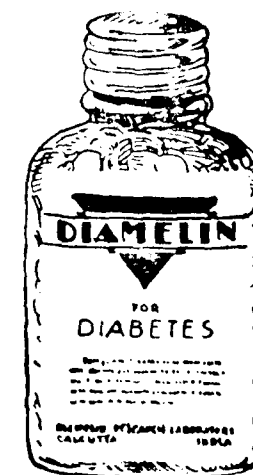
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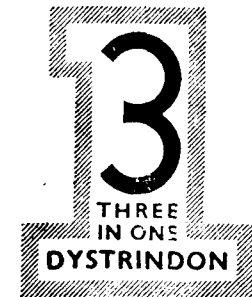
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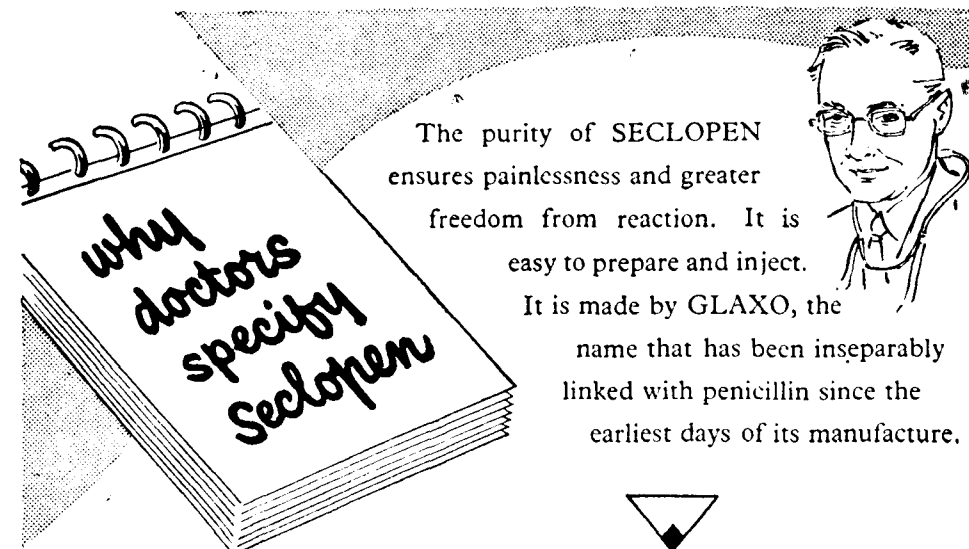
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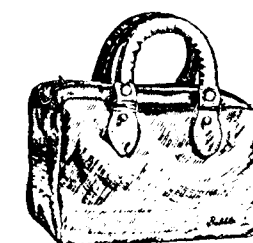
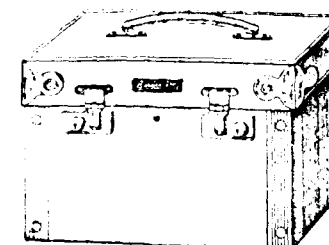
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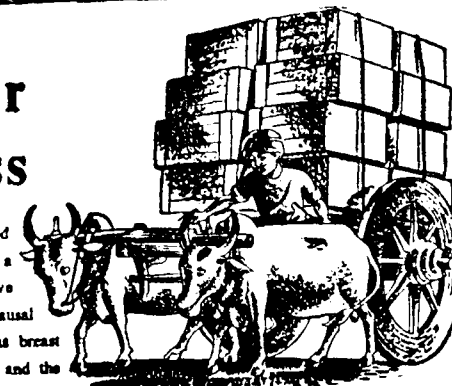
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1. "The Role of Ayurvedic Medicines in the Treatment of Diabetes Mellitus"—Indian Journal of Medical Sciences—Vol. 6, No. 2, Feb. 1952, pp-117-136.
2. "Review of Diabetic Cases Treated with Ayurvedic Medicine" "Special Therapeutic Number" of the Indian Medical Review
3. Journal of the Indian Medical Profession, Vol. 2, No. 8, pp. 870-879, November, 1955



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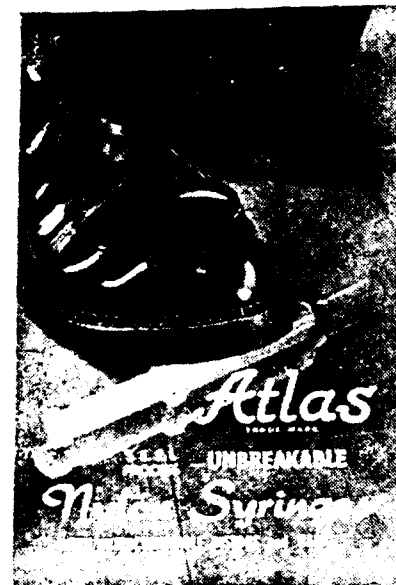
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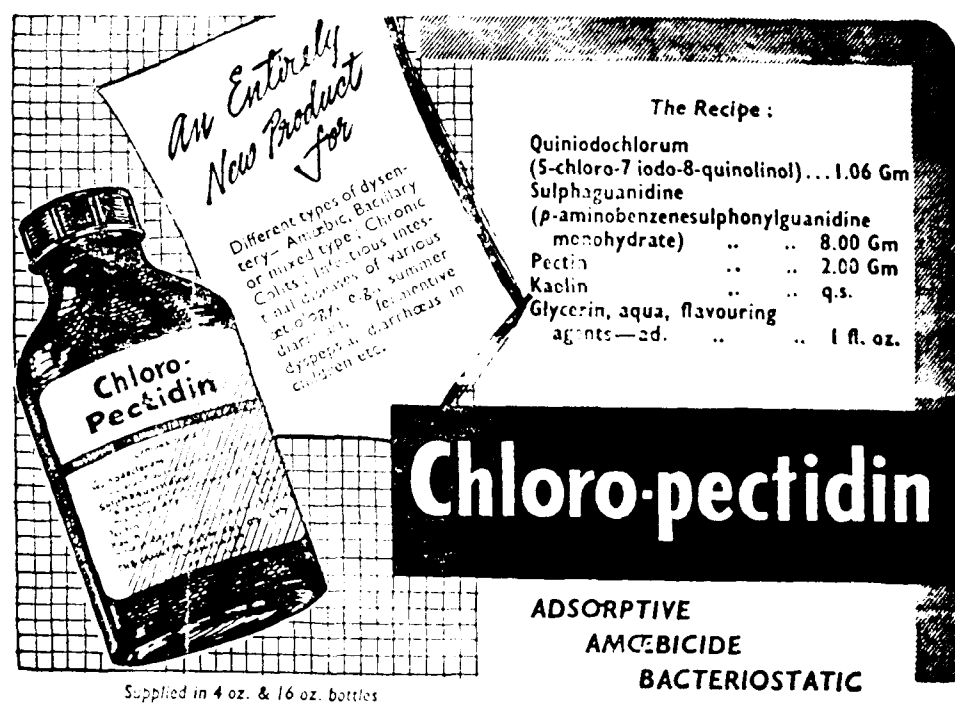
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Vol. 53

JUNE, 1956

No. 6

## Original Articles

Elizabeth Mathai Endowment Lecture, 1955-'56

### A SURVEY OF SKELETAL TUBERCULOSIS WITH PARTICULAR REFERENCE TO ITS INCIDENCE IN WOMEN AND CHILDREN\*

M. NATARAJAN, M.Ch. Orth., F.R.C.S. (Eng.),

Orthopaedic Surgeon, Stanley Hospital,

Lecturer in Orthopaedics, Stanley Medical College, Madras

THE subject I have chosen is the study of the incidence and distribution of the various skeletal tuberculous lesions in children and women and their management. The material for this study was from the cases of skeletal tuberculosis which sought treatment in the orthopaedic department of the Stanley Hospital as well as those treated in the orthopaedic section of the Tuberculosis Sanatorium, Tambaram during the years 1953 and 1954.

Tuberculosis in general is a social problem of large magnitude in our country. The incidence is very high and the mortality and morbidity are enormous enough to attract the sympathetic attention of the Union and State Governments. Tubercle bacilli are scattered extensively throughout the world and most people in their lives suffer from sub-clinical infection. An excessively large dose of infection in people with low resistance to the disease causes overt tuberculosis. The risk of exposure to infection from human beings suffering from tuberculosis is a major problem of social medicine. Bad housing and overcrowding increase exposure to infection, under-nutrition reduces bodily resistance and unemployment leads to both overcrowding and under-nutrition. The ubiquity of its aetiological

\*Specially contributed to the ANTISEPTIC.

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agent, the contrasting facts of universal human susceptibility, the readiness with which the bacilli develop resistance to drugs, its global prevalence, its insidious onset, its inexorable course, its deceptive and unpredictable behaviour, its capacity to invade bone and joint meninges, etc., all accentuate the importance of tuberculosis and elevate it to the forefront of Medicine. Tubercle bacilli show a fairly constant virulence. The great variations seen in the clinical course is due entirely to the variations in human resistance.

Although pulmonary tuberculosis has received due attention in the hands of the lay as well as medical public, the incidence and variety of skeletal tuberculosis is still not sufficiently known and appreciated. The problem has not yet been tackled due to the lack of awareness of the extent and incidence of skeletal lesion. Skeletal tuberculosis forms one of the major problems of orthopaedic work in our country but the facilities available to treat these cases are woefully inadequate. This will be obvious from the fact that, out of 200 cases of skeletal tuberculosis which sought treatment in the Orthopaedic department of the Stanley Hospital during 1953 and 1954, only 20 cases could be admitted into the T.B. Sanatorium and treated. While a good proportion of pulmonary tuberculosis cases can be given satisfactory domiciliary treatment, the skeletal tuberculosis patients cannot satisfactorily be immobilized and treated at their residences. The situation is made worse by the fact that while the largest incidence is in children, there is no special provision for treating children with skeletal tuberculosis in any of our hospitals.

Tuberculosis of bone or joint is a metastatic focus and its appearance is a proof that some pre-existing tuberculous lesion known or unknown is active and infecting the blood. Thus skeletal tuberculosis can be called a tertiary manifestation. This means there is a primary infection, a secondary general dissemination and a tertiary localization. This dissemination may leave traces of infection in other systems. Consequently no assessment of an individual case can be made until all the systems have been examined.

For clinical considerations the cases can be grouped into three types: (1) The straightforward tuberculosis of bone, nowhere near a joint, sternum, rib, metacarpals; (2) bone lesions endangering a diarthrodial joint; and (3) the spinal caries—a class by itself.

The third lesion being the most important will be considered first.

Spine.—The Hippocratic text was the first to suggest a possible relationship between spinal deformity and pulmonary disease. Treatment of the deformity was recognized to be difficult if not totally ineffectual. "The vertebrae of the spine when contracted into a hump from disease for the most part cannot be remedied more especially when the gibbosity is above the attachment of the diaphragm."

Dalechamps, a French Surgeon of the sixteenth century, re-described vertebral caries. While Hippocrates had suggested its connection with pulmonary disease Dalechamps added a very important factor by discovering its relationship to paralysis of the lower extremities. "The internal causes of vertebral displacement are cold swellings developed in the ligaments of the vertebrae. These patients are subject to disease of the kidneys and bladder and to abscesses which are difficult to cure which point in the loins and groins by sympathy and communications of these parts with the diseased ones. The legs become more slender, all the parts below lose sensation and movement but if the vertebrae are displaced in a rounded form (not sharply angulated, movement and sensation of the parts below are little or not at all affected." In this note on Galen's suggestion of vertebral caries being caused by 'tuberculæ' Dalechamps basically gave the observation on paralysis usually credited to Pott.

In the latter part of the seventeenth century there appeared in London, Richard Wiseman, the foremost British Surgeon then, whose work on surgical tuberculosis was the first important contribution to the subject since the time of the Corpus Hippocrates. During his time the tradition of the Royal Touch for scrofula was fully prevalent and the disease was termed the King's Evil. One of the Wiseman's eight surgical treatises was on King's Evil and his description of joint tuberculosis shows his remarkable insight into the pathology and clinical picture. "External accidents are the occasional cause of the King's Evil but they always suppose a pre-disposition of the body to it in which case we often see a blow compression, bruise to provide it. So also by a wrench of the hip, knee, ankle or other joint we find crude tumours to arise which are soon followed by visible symptoms of the King's Evil." Thus it was Wiseman who clarified the numerous manifestations of surgical tuberculosis and demonstrated their underlying unity.

More recently in the latter half of the nineteenth century, Hugh Owen Thomas (1843–1891) of Liverpool made the study of the skeletal tuberculosis one of his main interests in life and enunciated some basic principles on their management. He started a new era in the treatment of tuberculous joints. He demonstrated clearly how cure could be obtained by relying on the inherent power of recovery, resting the patient and providing absolute protection to the diseased joint surfaces from friction. At a time when amputation or radical excision of joints was widely practised, Thomas's treatment was a revolutionary idea and it was slow in spreading. Ultimately the good effect of prolonged immobilization was so convincing that radical operations diminished and the conservative control of skeletal tuberculosis came into favour.

The discovery of the anti-tuberculous drugs beginning with Streptomycin and followed by Para-amino-salicylic acid and

Isonicotinic acid hydrazide opened a new era in the therapy of skeletal tuberculosis. While conservative treatment is still the mainstay of the therapy, these drugs have shortened the duration of treatment, cut down the complication rate. They have also begun to change our attitude towards these diseases. In the treatment of bone and joint tuberculosis the tradition of conservatism has established certain dicta, the combined total acceptance of which will thwart our progress and condemn many patients to a prolonged convalescence which is crippling physically, mentally as well as economically. This aspect will be referred to in greater detail in the last talk.

Although tuberculosis of the spine goes by the name of Pott's disease the credit of describing it first should go to Dalechamps, the French Surgeon.

**Incidence.**—Of all the lesions in the skeletal system, the incidence in the spine is the highest. In this series of cases the spinal lesions form about 50 to 60% of the total. During a period of 2 years, out of the total of 220 cases of skeletal tuberculosis, 142 cases or 64.5% were those with spinal disease. Among the cases treated in Tambaram Sanatorium 37 out of 54, i.e., 68.5% were of spinal tuberculosis.

The incidence with reference to sex is:—Male 40; female 61; and children 41. Total 142. The incidence was much higher in the females than in males in this series.

The age incidence is given in Table I and Chart I.

| Age            | No. of cases | Percentage |
|----------------|--------------|------------|
| Below 10 years | 48           | 24.2       |
| 10-20          | 41           | 20.5       |
| 20-30          | 63           | 31.5       |
| 30-40          | 27           | 13.5       |
| 40-50          | 12           | 6.0        |
| 50-60          | 8            | 4.0        |
| 60             | 1            | 0.5        |
| Total          | 200          |            |

Of the 48 cases in the first decade 30 occurred in children below 5 years, the youngest age in which the disease occurred being in a male child one year old at the 12th dorsal and 1st lumbar vertebrae.

The largest incidence is in children and adolescents below 20 which forms about 45% of the total. The age incidence of the disease in the present series is similar to that found in Western countries 30 years ago when the disease was found commonest in childhood. Most modern authorities have shown that in Western countries the disease affects mainly young adults and is now getting less common among children.

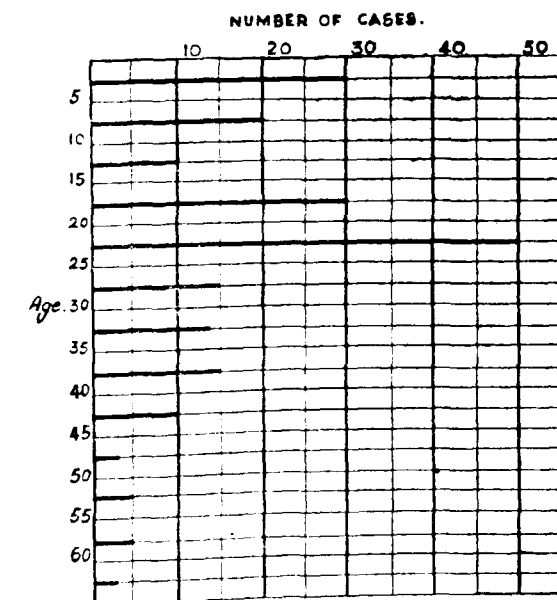


CHART I. Age distribution of 200 cases

**PATHOLOGY.**—As in tuberculosis elsewhere in the body, the tubercle is the characteristic pathologic unit and is associated with tuberculous granulation tissue, caseation necrosis, exudation and fibrosis. Typical epithelioid and Langhans giant cell-tubercles occur in the bone, the epithelioid cells being of more diagnostic significance than the Langhans giant cells. The epithelioid cells are fixed tissue cells and are phagocytic for tubercle bacilli. The lymphocytes lying in the periphery of the tubercles are delivered by the blood circulation. The differentiation into pathological types is more quantitative than qualitative.

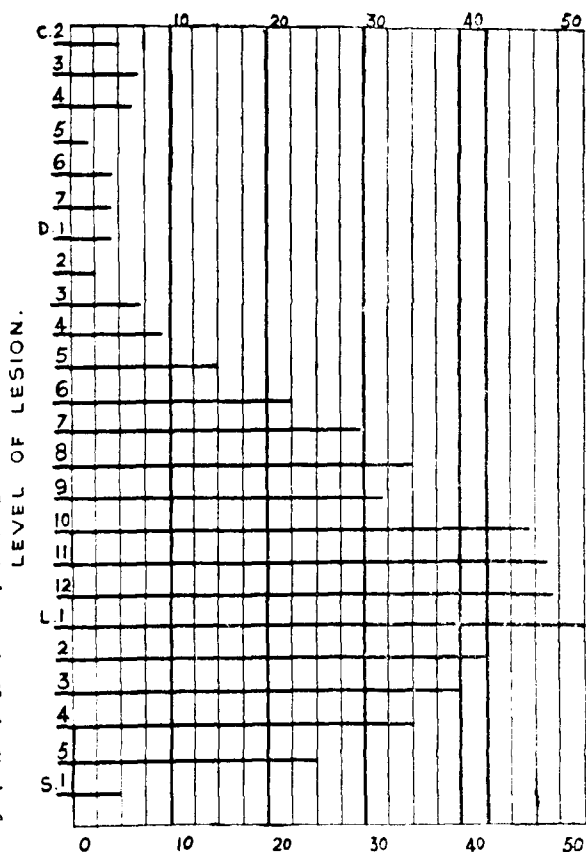


CHART II. Level of lesion in 200 cases

The incidence with reference to the site of lesion in the spine in the cases under study is shown in (Chart II below). It will be that the cervical spine is least involved. Tuberculosis is progressively more common from the top to the bottom of the spine, the highest incidence being from the 10th dorsal to the 3rd lumbar vertebra. In most cases there is involvement of two or three vertebrae as shown by the fact that in 200 cases a total of 199 vertebrae were involved.

tative. When central necrosis or caseation is predominant it is called *caseating type*. When the cellular response predominates it is called the *proliferating type* where caseation is minimal.

In the spine there is marked difference in the nature of the lesion between adults and children. In location, progress and prognosis the lesion shows a marked variation between childhood and adult spinal tuberculosis.

In children, tuberculosis of spine commences as an osteomyelitis and in adults as an epiphyseal lesion near the intervertebral disc or a periostitis beneath the anterior longitudinal ligament. The characteristic has an anatomical basis: in children, the main arterial supply to the vertebral body is a branch of the posterior spinal artery, which enters the vertebral body through the central area of its posterior wall. In the adult the main vessels to the vertebra are branches from the intercostal and lumbar arteries and entering anteriorly.

Thus the lesion in children begins as a central destruction of the vertebral body leading to early collapse and spread to adjacent vertebral bodies. In the adult the lesion remains localized to a single vertebra or disc or else spreads proximally and distally under the periosteum and anterior longitudinal ligament. Formation of cold abscess is an invariable accompaniment of lesion in the spine, the difference between cases being only in the size of the abscess and the route and site of its tracking and pointing. One of the intriguing features of the cold abscess is the complete lack of correlation between the size of the lesion and the amount of pus produced. A big destructive lesion involving two or more vertebrae may produce just a small para-vertebral abscess on either side whereas a lesion with a minimal destruction of intervertebral disc may produce an enormous abscess in the iliac fossa yielding up to 600 cc. of pus. The exact pathological basis for this phenomenon is still not understood.

**DIAGNOSIS:**—A patient with the classical symptoms described by Potts presents no difficulty in diagnosis. Pain, rigidity, gibbus and cold abscesses together in a case are symptoms which are diagnostic. Unfortunately most of our patients when first seen have all these signs and symptoms. In a series of 50 patients the average duration of symptoms before a diagnosis was made is about six months. But if we want to spot these cases early before excessive destruction of bone has taken place one must look for minimal symptoms.

**Early case.**—Any child complaining of pain in the back continuously for more than 2 weeks should have a thorough investigation including X-ray to rule out the possibility of T.B. of the spine. Any adult with a pain in the back for more than three months should have an X-ray of the spine. The delay in diagnosis is often due to two causes. In children the pain is often taken to be due to a fall

which the child sustained during play. In many instances the referred pain in the abdomen is mistaken to be caused by some abdominal condition. In one case in this series a child was treated for worms for months before the spinal lesion was spotted. In adults, the low back pain in women is often treated as of gynaecological origin or simply as fibrositis.

In children a watchful mother often spots the so-called pre-tubercular phase when the child is fretful and easily tired and then restless at night. Later the child walks with a stiff carriage and is careful about stooping.

In adult cases the onset of cord compression causing difficulty in walking is sometimes the first presenting symptom.

**DIFFICULTIES IN DIAGNOSIS:**—Very often the diagnosis of T.B. of the spine is not made because the possibility is not kept in mind when atypical manifestations are met with. A few examples will make this point clear:

Mrs. P., a woman, aged 35 years, complained of vague pain in the chest and neck and loss of weight. She was investigated for pulmonary tuberculosis and declared negative. She complained only of something like an intercostal neuralgia coming to the epigastrium. There was no rigidity of spine nor any limitation of movements. (see *Fig. 1*, p. 415). X-ray of dorsal spine revealed a definite narrowing of the intervertebral space—dorsal 5 and 6.

Mrs. C., aged 25, married, mother of 3 children, complained of low back-ache, since the birth of the last child. On the finding of tuberculous tissue in the endometrium, hysterectomy was performed. The back-ache persisted and an X-ray of the lumbar spine revealed a tuberculous lesion L<sub>3</sub> and L<sub>4</sub>.

Mrs. S., complained of sciatica and back-ache, has been treated for sciatica for three months. (see *Fig. 2*, p. 415). X-ray revealed an erosion in the lateral corner of the vertebral body which has irritated the L-4 nerve root.

Other difficulties are caused by the atypical location of the lesion. A lesion in the posterior surface of the vertebral body is often localized and is not easily visible in the X-ray. A minimal lesion causes pressure on the cord and paraplegia.

Other atypical lesions occur in:—(1) The intervertebral joint. (see *Fig. 3*, p. 416); (2) the pedicle and lamina; (3) the spinous process. (see *Fig. 4*, p. 416); and (4) the costo-vertebral joint. (see *Fig. 5*, p. 416).

Even the ordinary lesion in the vertebral body when it occurs in an old person presents difficulties in diagnosis. In the young adult and middle-aged persons although the lesion may start in the juxta-epiphyseal region, the less vascular disc gets involved more readily and undergoes collapse and disintegration, the rest of the vertebral body being affected later.

In old patients with marked senile osteoporosis the lesion in the same site leads to a collapse of the porotic vertebral body much earlier, leaving the intervertebral disc relatively intact. This appearance of collapse of vertebral body with intact disc causes great difficulty in differentiating it from a secondary malignant deposit.

As a typical example I need only remind the audience of a very distinguished elder statesman of our country whose spinal caries eluded diagnosis for a long time. The final diagnosis could be made only after a vertebral biopsy which unfortunately proved too much for the patient who succumbed shortly afterwards.

Management.—At the onset it must be categorically stated that the facilities available in our State for the satisfactory treatment of cases of skeletal tuberculosis are grossly inadequate. Every case of skeletal tuberculosis must be admitted in a tuberculosis sanatorium and treated completely till the lesion becomes quiescent.

The first step in the management of a case diagnosed to be caries spine is a careful assessment of the case. The various factors which influence prognosis are taken into consideration and then a programme of long-term treatment is laid down.

The factors to be considered in assessment are :—

1. *Age*:—Prognosis is best in children. The general resistance can be built up most readily in children and the reparative processes are also very quick. In young adults the chances of total recovery are very good with proper treatment but the time of morbidity is prolonged.

*Senile tuberculosis*:—Skeletal tuberculosis in persons above 50 is almost as bad as malignant disease as the general resistance and powers of repair are very poor and prolonged immobilization itself is harmful. Very often the clinical and radiological features of the disease are atypical and diagnosis itself is often delayed and missed.

2. *Second active lesion*:—The presence of a second active focus either in the skeleton or glands or lungs denote the need for prolonged treatment.

3. *Site of the lesion*:—The upper dorsal lesion has the worst prognosis for the following reasons :—

(a) As the limitation of spine-movements are not affected much the diagnosis is often late.

(b) The danger of paraplegia is worst in this level as the spinal canal is narrowest.

(c) The dorsal lesion in children is of a galloping type where a large number of vertebrae gets destroyed in a very short time leading to gross deformities.

The best prognosis is the lesion in the lower lumbar and lumbosacral junction. This is a relatively benign type of spinal tuberculosis. Many of these are undetected and go in for healing and

quiescence and the first X-ray reveals a lesion which has been there for two to three years.

4. *Stage of the disease*:—The assessment of the case should also be done with regard to the stage of the disease, the course of which may be divided into: (a) the stage of invasion, (b) the stage of activity, and (c) the stage of repair.

Lastly the general assessment of the resistance of the patient is done by considering:—(a) the temperature. (b) the toxæmia—loss of appetite, and (c) the loss of weight. (d) *Sedimentation rate*:—The E.S.R. is the most useful guide in assessing the activity of the disease. It is not so useful as a diagnostic test, but when taken periodically once a month serves as a useful indication of the prognosis of the condition and the effect of treatment.

5. *Presence of complications*:—(a) Paraplegia. (b) Sinuses.

PRINCIPLES OF TREATMENT:—The essential principles of treatment of spinal tuberculosis which will apply to all cases of skeletal tuberculosis are as follows:—

*General measures* to build up resistance of the body enabling it to overcome the infection.

*Local measures*:—Protecting the part from further destruction and holding it in good position of function and aiming to get a sound ankylosis.

*Chemotherapy*:—A prolonged and uninterrupted course of chemotherapy, and watching for dealing with complications.

The treatment of these cases in General Hospitals is very unsatisfactory as they cannot be kept for long periods in beds which are more urgently needed for acute cases. Admission in sanatoria and the provision of high protein diets with a liberal supply of vitamins improve the general health and increase the resistance of the body to tuberculous infection.

The sheet-anchor of our treatment lies in the provision of "enforced uninterrupted and prolonged rest" to the spine as taught by Hugh Owen Thomas in order to obtain sound fusion and permanent healing.

Of the methods of immobilization available, the plaster of paris bed is the best as it is moulded to the shape of the body and ensures perfect rest to the part. In spite of the inconvenience of sweating in summer, I still prefer the plaster bed to the Bradford frame. After a while the patients get accustomed to the bed. (see *Fig. 6*, p. 416). The plaster bed mounted on wooden supports resting on an ordinary fracture cot is the most convenient setup for the case of nursing and toilet purposes.

In enforcing prolonged immobilization of patients in sanatoria, two essential requirements must be fulfilled, *viz.*, the preservation of

mental vigour and alertness and the prevention of physical complication of prolonged recumbency. Children should have facilities for continuing the education while in plaster bed or frame and answering examination papers also, so that at the end of one year or more of treatment they do not lag behind others of their age at school. In adults there should be provision for occupational therapy which not only keeps their minds diverted but also prepares them for light jobs after recovery.

The preservation of the function of joints and muscles of the limbs and the prevention of deformities, contractures pressure sores etc., are also very important.

**Chemotherapy.**—Although the discovery of anti-tuberculous drugs has modified our approach to the disease, it has not changed the fundamental principles of treatment. Chemotherapy is a very good adjuvant but can never replace the conservative treatment of skeletal tuberculosis. The nature of the bacilli, the type of the pathological reactions in the invaded tissues and the chronic course of the disease all explain the lack of dramatic effects in the control of the disease by the drugs. But streptomycin and other drugs have certainly had a beneficial effect on the disease in the following respects.

The duration of immobilization necessary to make the lesion quiescent has certainly been reduced.

|                      | Average duration. |
|----------------------|-------------------|
| Pre-streptomycin era | 2 to 3 yrs.       |
| With chemotherapy    | 12 to 15 months.  |

Thus it will be seen that the total period of immobilization has been cut down to half. This by itself is an enormous gain. Indirectly it has also cut the complication due to very prolonged immobilization such as contractures, renal calculi, etc.

In a carefully controlled study of the effect of streptomycin alone on skeletal tuberculosis by the Public Health Service of U.S.A. the following conclusions were drawn:—

Judged by X-ray evidence alone the condition of the streptomycin-treated group was not much different from that of the control group. But on the basis of total evidences like the clinical condition of the lesion, sedimentation rate, healing of sinuses, etc., the streptomycin-group was far superior to the control, 75% of the cases being quiescent in 12 months and 83% of cases being quiescent in 15 months.

The rate of complications has been reduced. The incidence of tuberculous meningitis, miliary tuberculosis and sinuses has also been reduced.

Chemotherapy has made surgery safer in these cases. The fear of reactivation of the disease and tuberculous meningitis prevented surgeons from attempting radical surgery in tuberculous joints. Joint fusions were done long after the quiescence of the disease. With the use of streptomycin, surgery can now be undertaken much earlier. Primary wound-healing can be assured and the risk of a break-up of the lesion is much less.

The chemotherapeutic course for adult cases of skeletal tuberculosis as given in the T.B. Sanatorium, Tambaram, is as follows:—

(1) Streptomycin 1 g. a day for 10 days followed by 1 g. twice a week up to a total of 60 g.

(2) Para-amino-salicylic acid (P.A.S.)—12 g. a day in 4 divided doses.

(3) Isonicotinic acid hydrazide (I.N.H.)—150 to 200 mg. a day in three divided doses.

In cases with paraplegia the streptomycin is extended to 75 g.

As the course of streptomycin continuously extends to a period of over six months, the danger of drug-resistance is minimized by giving all the three drugs together.

As streptomycin as well as I.N.H. tends to produce a Vitamin B-complex deficiency, all these patients are given vitamin B-complex during the course of chemotherapy.

The immobilization is continued till the lesion is quiescent. The diagnosis of quiescence is as important as the diagnosis of the disease. The quiescence of a lesion is judged by the following factors:—

*General:*—The patient's general condition, gain of weight and good appetite. Three readings of E.S.R. taken at monthly intervals should be near normal and constant.

*Local:*—Complete absence of local warmth, tenderness and muscle spasm.

*Radiological:*—Sclerosis of the margins of the lesions and fusion of adjacent bodies of the vertebrae.

When the lesion is considered quiescent, the plaster bed and Bradford frame are removed and the patient is kept in an ordinary fracture bed. While in recumbency both weight-bearing and movements of spine are eliminated; in the next stage of ambulatory treatment, only the movements are prevented. A posterior spinal support is fitted and the patient gradually allowed up for increasing periods. After about one month's observation in the sanatorium the patient is discharged to continue convalescence at home.

**Toxic manifestation of chemotherapy.**—The incidence of toxicity is very low with the dosage scheme given above. The main toxic manifestation of streptomycin is the involvement of

immobilization in the ambulatory stage is impossible with a brace, a spinal fusion will be essential.

In other cases surgery is undertaken to get over a serious complication or a threat to life. The most important of these indications is surgery for the treatment of paraplegia.

Technique of spinal fusion.—The technique employed is a modified form of Hibb's spinal fusion.

After accurate localization of the level of the lesion by pre-operative X-rays with a metallic marker in the skin, the spines are exposed including one above and one below the level of the lesion. The spinous processes are excised, the laminae made raw by removing cortical bone. The big raw area thus created is packed with cancellous bone chips taken from the posterior half of the iliac crest.

Use of homogeneous bone-graft.—In the T. B. Sanatorium where a large number of ribs are removed in thoracoplasty operations, I have started using split ribs obtained from another patient as grafts for packing the raw area made in the spine. This procedure saves time and a second operative wound in the patient. Callus formation is very profuse by the use of such cancellous bone and the fusion is quicker and sounder. (see *Fig. 7*, p. 417).

Pott's paraplegia.—Paraplegia is still one of the most serious complications of T.B. of the spine. Modern chemotherapy with conservative treatment has almost eliminated completely the other complications like miliary dissemination, tuberculous meningitis, persistent multiple sinuses with secondary sepsis and amyloid disease, leaving paraplegia as the only serious and dangerous complication of the disease. Before the chemotherapeutic era, its incidence was 11% but now it is much less.

The classical work of Seddon and Butler in 1935 described the causes which produced paraplegia. Two main groups can be distinguished by their onset being early or late in relation to the activity of the disease.

1. Early onset of paraplegia associated with primary activity of the disease, which is caused by:—(a) pressure on the cord by a tense intraspinal cold abscess; (b) pressure by granuloma or tuberculous debris; (c) pressure by bony sequestra or pathological fracture dislocation; and (d) occasionally a transient edema of the cord or thrombosis of vessels supplying the cord.

2. Later onset of paraplegia—the paraplegia comes on, some years after the disease has become quiescent. This can be caused by: (a) a re-activation of the disease; (b) grossly increasing spinal deformity causing a stretching of the cord.

Sometimes paraplegia is the presenting symptom in the disease especially in adults. There may be a slight tenderness in the spine but X-ray does not reveal any bony lesion. Such cases on further

observation and repeated X-rays often reveal a disease of the inter-articular joints or pedicles or laminae.

TREATMENT:—In children, paraplegia has a very good prognosis and they all recover if given the proper immobilization and chemotherapy. The prognosis is so uniformly good that Hugh Owen Thomas welcomed the onset of paraplegia in children, as it compelled the child to be in bed with more perfect immobilization.

In adults also the basis of treatment is immobilization and general treatment. The majority of paraplegias recover by such a conservative regime of treatment.

The paraplegic patient is immobilized and chemotherapy started and a careful watch is made to spot any early sign of recovery. Stopping of involuntary spasms, control of bladder function and sensory recovery occur in that order before any motor function of muscle shows recovery. If no signs of recovery appear, one has to assess carefully the points for and against operation. The difficulty is to say how long one should wait before deciding that it will not recover by conservative treatment. Some believe that if there is no evidence of recovery in one month after immobilization surgery must be undertaken. Their view is that more waiting means more irreparable damage to the cord. Others will give conservative treatment for six months or more before deciding about surgery.

It will be reasonable to fix the time-limit somewhere between the two extremes. The general condition of the patient is an important factor to be considered but the threat to viability of the cord and dangers of severe paraplegia have to be balanced against the poor reaction of the patient. The next factor is the completeness of the paraplegia and the presence of a tense paravertebral abscess shadow in the X-ray. On the whole it might be better to operate on a few cases that would perhaps recover without operation rather than to run the serious risk of irreparable permanent damage to the cord through hesitation or delay.

Thus the indications for operation will be: (1) paraplegia increasing or remaining unimproved in spite of efficient treatment for three months; (2) paraplegia already very severe and complete with uncontrollable and exhausting involuntary spasms of legs; (3) paraplegia with very tense para-vertebral abscess as shown in X-ray picture and (4) spinal tumour syndrome where the lesion is in the posterior segment.

It must be emphasized that the immobilization of the spine must be uninterrupted before, during, and after the operation.

The operative procedures for paraplegia are:—(1) Costo-transversectomy; (2) laminectomy; and (3) antero-lateral decompression.

In his description of paraplegia, Pott wrote in 1779, "the remedy for the most dreadful disease consists in procuring a large discharge

of matter and in maintaining such discharge until the patient shall have recovered the use of his legs." Thus in giving the description of the disease, Pott also laid the foundation for the surgical drainage of the condition.

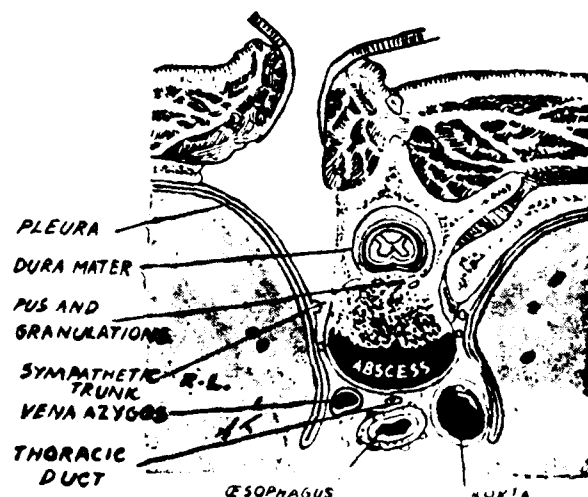


FIG. 8.

Costo-Transversectomy

1. *Costo-transversectomy*:—This is indicated when there is a tense spherical para-spinal abscess. This is a simple procedure. (Fig. 8). Through a midline incision centred at the level of the lesion, the medial 2 inches of one or two ribs, and the corresponding transverse processes of the vertebrae are excised. The cold-abscess is opened by blunt dissection, then drained and completely evacuated

of all pus and debris. The wound is partially closed with a gauze wick left in for 48 hours.

2. *Laminectomy and spinal fusion*:—This operation has a limited application in cases where the lesion is in the posterior segment of the vertebrae and when there is no obvious tense abscess shadow particularly in cases of the spinal tumour syndrome type. The pressure in these cases is due to granulation tissue or pus. Laminectomy should be followed by a spinal fusion either in the same sitting or as a second operation.

3. *Anterolateral decompression*:—This procedure also described as lateral Racho-tomy is a more severe surgical procedure. The first step is a costo-transversectomy of two ribs and corresponding transverse processes. The cold abscess is evacuated completely. The pedicles of the vertebra are nibbled off.

Using the intercostal nerves as guides, the lateral surface of the cord

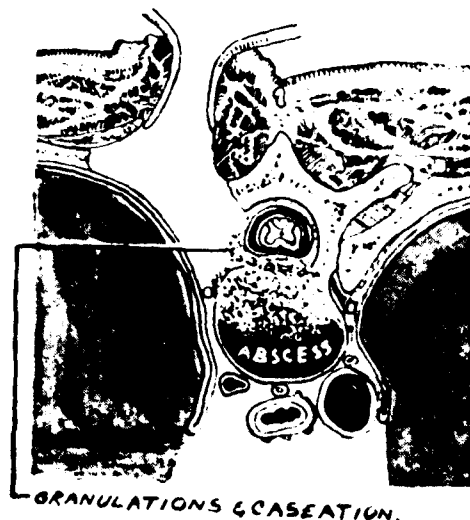


FIG. 9.

Anterolateral Decompression

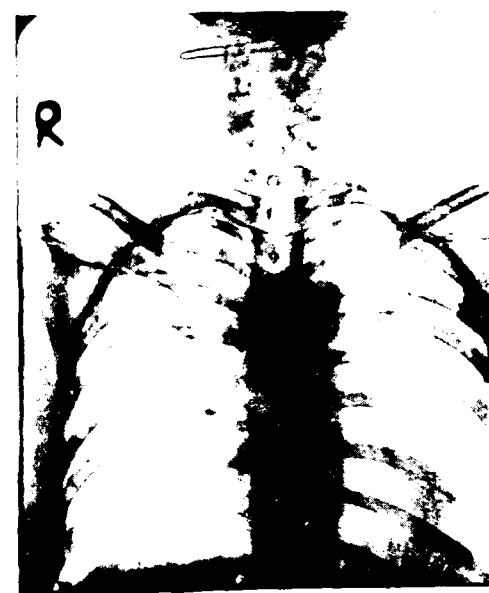


Fig. 1. A. P. and Lat. views



Fig. 1a. T. P. F. spinal spine D5 D6

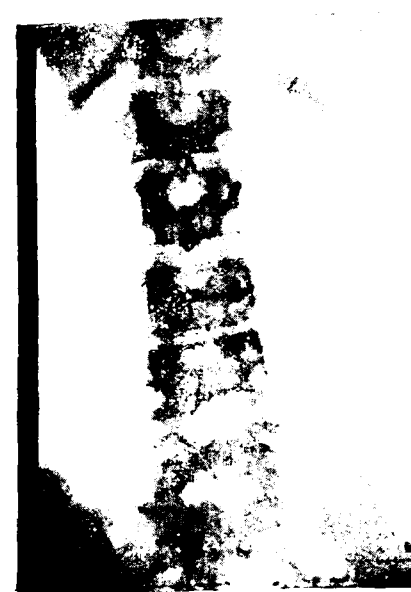


Fig. 2. A. P. and Lat. views



Fig. 2a. T.B. L3 L4



Fig. 3. L. side intervertebral articulation before treatment.



Fig. 3-a. L. side intervertebral articulation after treatment.



Fig. 4. Lumbar spine lesion in L4 spinous process.



Fig. 4. Lumbar spine lesion in L4 spinous process.



Fig. 5. Lesion in Costovertebral joint and posterior D12.



Fig. 6. Spinal lesion after thoracoplasty: Ribs from another patient.



Fig. 7-a.



Fig. 10. T.B. extra articular focus in neck of femur before treatment.



Fig. 10-a. T.B. extra articular focus in neck of femur after treatment.



Fig. 11. T.B. Hip. SE with the phenomenon of episternum formation.



Fig. 12. T.B. Hip. Brittain's arthrodesis done.

correct to say that early tuberculosis in a joint predisposes to trauma to the part. The earliest symptom of a tuberculosis hip is a limp and a sense of tiredness particularly in the latter part of the day. A child who plays about a minimal limp is more liable to slip and fall. Such a fall aggravates the pain in the joint and draws the attention of the parents who come out with the story that the joint trouble started since the time of the fall; such a sequence of events is also true of lesions in the spine and knee.

**PATHOLOGY:**—The site of the lesion in the region of the hip joint can be grouped into: (a) articular; and (b) para-articular.

The articular lesions are located in the following sites in the order of frequency:—(1) Outer half of acetabular roof. (2) Femoral head near the upper pole. (3) Femoral neck proximal part (see Fig. 10, p. 417). (4) Synovial—rare.

The para-articular focus is situated in:—(1) Greater trochanter; (2) distal part of neck of femur.

Of the two types of tissue reaction, the caseating type occurs in children causing extensive destruction of the head, acetabular roof with marked travelling acetabulum and pathological dislocation. In the adult, the reaction is of the proliferating type with slow erosion of the articular cartilages and minimal destruction.

**Infarction.**—Massive sequestra formation is a common phenomenon in a pyogenic infection of bone. In tuberculosis, the slow progress of the lesion favours the molecular type of bone destruction. Occasionally however one sees in tuberculous infection a large sequestrum enclosed in a wall of granulation tissue. (see Fig. 11, p. 417). Near the articular surface this sequestrum is wedge-shaped and when a big segment of the femoral head sequesters, the increased density and softening of the segment in the X-ray, simulates the avascular necrotic changes seen in Perthe's disease. This is caused by thrombosis of one of the big-sized arteries supplying the head of the femur.

**Abscess formation.**—The cold abscess formed inside the joint cavity distends the capsule and stretches the ligaments. There are some weak spots in the capsule which allow the abscess to perforate the capsule and reach the extra-capsular tissues and travel along fascial planes. Perforating the inferior aspect of the capsule it reaches forward and travels between the ilio-psoas and pectineus muscle and reaches the surface in the Scarpa's triangle. Travelling in various directions it may point near the lesser trochanter or under the tense-fascia lata muscle. Perforating posteriorly it may come out underneath the gluteal muscle and present near the greater trochanter. Destroying the floor of the acetabulum the abscess sometimes presents as an intra-pelvic one.

**Healing process.**—Granulation tissue is the key factor in all the stages of activity of tuberculosis in the joint. In the early

stage of joint infection two types of granulation tissue appears. One is a *non-specific sub-chondral granulation tissue* forming in the sub-chondral marrow spaces as a reaction to the presence of the joint infection. This contains lymphocytes and plasma cells but no tubercles. This is the response produced either by the endotoxins or by the presence of dead articular cartilage. The other is the *specific tuberculous granulation tissue* following the growth of the tubercle from the synovial membrane at the joint margin. This gradually destroys the articular cartilage from the periphery inwards. The removal of articular cartilage brings the two granulations together and leads to a fusion. In the early invasion stage the granulation tissue sets up a defence against the tuberculous invasion. In the active stage when the exudate and the necrotic debris have to be dealt with, it displays an absorptive function. In the healing stages the granulation tissue undergoes fibrous condensation to heal the damaged joint by fibrous ankylosis. In children this fibrous ankylosis in due course may ossify but any flare up of infection will destroy the areas of fibrous tissue.

In very rare instances tuberculous joints heal with the preservation of a useful range of motion.

**DIAGNOSIS:**—Unfortunately the vast majority of cases of T.B. of the hip in our country are easy to diagnose as they are brought to the hospital late with all the typical signs and symptoms and radiological features. By the time the diagnosis is obvious the joint is irretrievably lost. In the cases reported in this series, the average duration of symptoms before a diagnosis was made was from 6 to 8 months.

The earliest symptoms of any disease in the hip are limp and pain. Every child with such symptoms must be very carefully examined for muscle spasm, limitation of movement and an X-ray taken. A child with such minimal signs must be assumed to be having tuberculosis of the hip till it is proved to the contrary. At such an early stage the X-ray findings will be negative.

**Observation hip.**—A child showing symptoms of irritation of the hip must be labelled observation hip immobilized in bed with skin traction and the investigations done. B.S.R. and Mantoux test are done in addition to taking X-ray pictures; after three weeks the splint is removed and the child is allowed to move about. If, on resuming activity, the spasm returns the diagnosis of tuberculosis becomes almost certain. Splinting is resumed.

**Transient synovitis hip.**—This is a definite clinical entity and has been called toxic synovitis, intermittent hydro-arthritis and by various other names. The exact aetiology is not known. The synovium of the hip or knee appears to be the principal sites of involvement. Compared with synovitis of specific aetiology, this condition is transient. Septic tonsils, allergy, trauma, and mild infection have been incriminated but none has been definitely proved. According

to some, this condition is a very early stage of Perthe's disease where there is vascular embarrassment to the femoral head which, if untreated, will proceed to total avascularity and typical bony changes in the head of the femur. This condition responds well to a short period of rest in traction. Removal of septic tonsils stops further attacks of synovitis in some children.

The other affections of the hip like septic arthritis, rheumatic fever, are easily distinguished by their clinical behaviour and course.

**Deep iliac adenitis.**—One other condition which is very often mistaken for an infection of the hip is a psoas spasm due to deep iliac adenitis causing a flexion deformity of the hip with pain and limping. A child of 5 to 10 years is brought with fever, pain in the region of the hip and a flexion deformity of the hip. On careful examination it will be noticed that while any attempt to extend the hip is resisted and causes intense pain, further flexion of the hip on to the abdominal wall is painless and the child is comfortable. This sign and the presence of tender glands in the iliac fossa with negative X-ray findings clinch the diagnosis of iliac adenitis. The condition resolves completely in about two weeks by appropriate treatment of the gland infection.

**Importance of early diagnosis.**—If the difference between early and late diagnosis means a difference in end-results as wide apart as mobile joint and ankylosed joint it becomes our duty to deal with the cases as early as possible. The biopsy of deep inguinal gland gives a positive result in many cases but the procedure is not infallible. The most direct incriminating evidence can be produced only by performing synovial biopsy in such cases. While yielding a bit of synovial tissue for microscopic diagnosis of tuberculosis, the procedure has additional advantages: it relieves the tension inside the joint capsule by the escape of synovial fluid, and also produces a local hyperæmia which helps to increase the concentration in the hip of systemically administered drugs.

**TREATMENT:**—The ideal aim of treatment of a diseased joint should be the restoration of the joint to its normality in shape and function. So long as we are not able to restore full mobility to a tuberculous joint, our management of the disease can be considered only the second best. This ideal can be achieved only if the diagnosis of tuberculosis is made before there is destruction of the articular surfaces. This will show the necessity and importance of early diagnosis.

Unfortunately almost all cases of tuberculosis of the hip diagnosed have already suffered destruction of either the acetabular roof, femoral head or both, with or without pathological dislocation. In such a situation our aim in treating the cases is to obtain a sound ankylosis of the joint with minimal destruction of bone and minimal deformity. This itself is a great improvement when compared to the

pre-chemotherapeutic era, when the majority of our cases died of complications, while the few survivors had bony ankylosis in grossly deformed positions due to multiple sinuses and secondary infection.

Biological cure, by which I mean total elimination of the organism from the joint tissues, may be something unattainable as far as skeletal tuberculosis is concerned. But clinical cure of the disease with a permanently quiescent and symptomless joint should be possible if the cases are given complete treatment.

**PRINCIPLES OF TREATMENT:**—While building up the general resistance of the patient with sanatorium regime of good food, open air, etc., the joint is immobilised in the optimum position and chemotherapy given as indicated before. The treatment can be considered with reference to the different stages of the disease.

1. *Immobilization with traction:*—In early stages the destruction of the bone is minimised, by applying traction to the affected limb in Robert Jones abduction frame. Traction relieves pain by overcoming the muscle spasm and keeping apart the articular surfaces and prevents the excessive destruction of acetabular roof. This minimises the shortening of the limb. The limb is kept in a position of slight abduction, slight flexion and in neutral rotation.

2. *Immobilization without traction:*—When the active progressive stage of the disease is over, there is no further need for traction but immobilization in a plaster spica is essential till the disease becomes quiescent as judged by the clinical and radiological findings.

It is noticed that even when the full treatment is started at the early stage of invasion, the destruction process proceeds for some time before it gets arrested. In cases where the X-ray at first shows minimal lesion, a second X-ray picture taken a month or two after the beginning of treatment shows the lesion more prominently and clearly. Continuation of the treatment shows the arrest of the disease in subsequent X-ray films.

3. *Amputation with protective splinting:*—The usual end-result of such a regime of treatment is fibrous ankylosis of the joint in good position with minimal shortening. A fibrous ankylosis in a weight-bearing joint is always unsafe in the long run. Any sudden strain on the joint or a lowering of the general resistance will cause a flare-up of the disease. Even if the disease process does not flare up, the adductions and flexions will gradually cause an increasing adduction and flexion deformity of the joint. This can be prevented by prescribing a weight-relieving walking caliper splint with which the child is permitted to walk. While this splint is satisfactory as a temporary measure, the only way to stabilize the joint permanently is by surgical fusion.

Each case of T.B. of the hip is now invariably advised to have arthrodesis of the joint at the end of the period in plaster spica.

Place of surgery in T.B. of the hip.—Apart from the minor surgical procedures in relation to cold abscess, the main indications for surgery in T.B. of the hip are:—(1) Operation to protect the diseased joint permanently from re-activation—Arthrodesis. (2) Operation to correct deformities—Osteotomy. (3) Operation to equalise leg length, when there is excessive shortening. (4) Rarely as a life-saving measure—Radical excision. (5) Curetting of active lesion.

Arthrodesis of the hip joint.—The production of a mechanically sound fusion of the hip has been a difficult operative problem as the articular surfaces are at great depth. The fear of spread of infection and non-healing of the wound, kept the surgeons from entering the joint cavity. An extra-articular procedure was adopted of which the ileo-femoral arthrodesis has been the favourite method till now. In this method, a bone graft was placed between the ileum above the acetabular roof to the greater trochanter. This method suffers from a mechanical defect in that the bone graft being above the joint is under a tension strain as the weight bearing tends to adduct the joint. The graft gave way either at the upper or lower end. In children the greater trochanter being mostly cartilaginous, the graft often failed to take in its distal end.

An architecturally sounder method of ischio-femoral arthrodesis was introduced by Brittan by placing the graft under compression through an osteotomy gap into the ischium below the acetabulum. (see *Fig. 12*, p. 417). This produces better fusion particularly in children.

Para-articular arthrodesis.—As the fear of opening the joint capsule is much less now due to the availability of the anti-tuberculous drugs, one can boldly approach the joint as closely as possible in an endeavour to produce a good arthrodesis.

The method followed by me can be described as para-articular as the graft used is placed directly on the neck of the femur. After exposure of the hip-joint by a postero-lateral approach, the capsule is completely excised from superior aspect of the joint, the cortical bone is removed from the exposed part of the head and upper aspect of the neck of the femur. The greater trochanter is chiselled off at the base obliquely. The bone piece is rotated through 180° and laid on the raw surface of the neck and its tip is jammed into a groove made in the acetabular rim (see *Fig. 13*, p. 418). This contact of raw bone surfaces throws good callus and a strong bony bridge forms between the acetabulum and the trochanteric region in continuity with the neck of the femur.

The results of such a para-articular arthrodesis have been uniformly good in all the cases done so far and the post-operative period has been almost afebrile and primary healing of the wounds has resulted. This has been possible by administering pre- and post-operative course of streptomycin. Nothing original is claimed

for this method which is only a logical extension of the previous procedure influenced by the presence of the new drugs.

Operations to correct deformities.—With proper splinting and immobilization, gross deformities of the hip are not as common now as before. Occasionally we still find a case with marked flexion deformity even 60 to 90°. In such cases a subtrochanteric osteotomy is done and the deformity corrected.

CASE:—P., male, aged 14 years, was treated for T.B. of the hip at the age of 5. Flexion deformity of 90° at the hip. The boy has been walking on frames. Osteotomy done. Boy is walking erect.

I shall deal only briefly with the disease involving the knee joint.

The incidence in a series of 220 consecutive cases was 27 or about 12%, the age distribution being as under:—

| Age      | Cases | Percentage |
|----------|-------|------------|
| 1—10     | 8     | .. 29.5    |
| 11—20    | 5     | .. 18.5    |
| 21—30    | 7     | .. 26.0    |
| 31—40    | 1     | .. 3.5     |
| 41—50    | 2     | .. 7.5     |
| Above—50 | 4     | .. 15.0    |

Thus we find here again the disease mainly affects children and young adults, nearly 50% occurring in patients below 20 years.

Most observers agree that T.B. of the knee presents three different clinical types:—(1) Synovial type, (2) osseous type involving the articular surface and the (3) extra-articular osseous type.

In the late stages in most cases all the three parts are involved so that it may be impossible to decide where it originated. Microscopic foci in bone have been demonstrated in synovial types where no lesion was demonstrable in X-rays. But the important point is to distinguish between cases where synovial signs occur early and when they constitute the main pathological feature and others where demonstrable osseous foci exist perforating into the joint later.

The synovial type may present either as a hydropic form where the effusion of fluid is more marked or as the proliferating form when the synovium is infiltrated, hypertrophic and oedematous with very little synovial fluid. In this type there is not much limitation of movement although other signs like warmth, wasting joint tenderness, are present. Between the two types the proliferating type of synovial reaction is commoner. The synovial membrane is palpably thickened in these cases.

The osseous type:—The focus in the bone may be:—(a) Metaphyseal. (b) Epiphyseal.

The commonest type is the epiphyseal one where the focus starts either in the femur or tibia near the site of attachment of

the capsule and reflection of synovial membrane sometimes in the sub-chondral area. The pathological evolution is similar to that described in the hip joint. The formation of 'kissing sequestra' is quite common in the knee when wedge-shaped sequestra are seen with their bases in the articular surface. Occasionally the focus is in the patella.

**Management.**—In children—whether the lesion is synovial or osseous, the treatment should be only conservative. The response to general treatment, local immobilization in Thomas splint and chemotherapy is good. In the synovial type the joint function is almost completely restored. In the cases with destruction of articular cartilage a fibrous ankylosis is obtained. Such a joint is protected by a walking caliper for some years and only after the age of 10 the question of arthrodesis is considered if necessary.

*In adults—the synovial type* is difficult to diagnose by clinical tests alone and a routine synovial biopsy helps better to establish early diagnosis. Once the diagnosis is established conservative treatment with chemotherapy controls the lesion and the joint with a reasonable range of movement can be obtained. In addition to systemic streptomycin, intra-articular instillation of 1 g. of streptomycin once a week hastens recovery of the synovial type.

*Osseous type:*—In adults the knee is the ideal site where, with the help of chemotherapy, early surgical measures to eradicate the focus and fuse the joint can be undertaken with success. After about 3 months of constitutional treatment, immobilization and chemotherapy, an excision of the synovial membrane, articular cartilages with the diseased bone is done and an arthrodesis of knee is performed (see *Fig. 14* p. 418).

Having tried various procedures like Brittain's arthrodesis, the nailing arthrodesis using the S.P. nail etc., I found the compression method as popularised by John Charnley (see *Fig. 15*, p. 418) gave the most satisfactory fusion in the shortest time.

Arthrodesis should not be done in very young children for the following reasons:—

(1) The epiphyseal plate is so near the articular end that there is a danger of damaging the epiphyseal plate during the operation.

(2) Even if the growth plates are not damaged, when sound fusion is obtained a gradual flexion deformity develops during the course of the next few years. This deformity occurs not at the site of fusion but at the site of the still active epiphyseal plate at the lower end of femur. This is due to the action of the hamstring muscles which by the contractions produce a bending strain at the site of the epiphyseal plate.

**Extra-articular focus.**—If such cases can be diagnosed early the local focus can be controlled by surgical curetting and the joint

function can be saved. Here also a period of immobilization in Thomas splint and chemotherapy is essential before local surgical attack is undertaken.

**Sacro-iliac joint.**—One other joint which is of interest from the point of view of this survey is the sacro-iliac joint. The incidence of sacro-iliac joint disease in this series was 22 cases out of 317 or roughly 7%. The sex incidence of the sacro-iliac joint tuberculosis shows that the disease is far more common in women than in men. Thus, 17 were females (77%) and 5 were males (23%).

Five of the 17 females were in the 11 to 20 age period; 10 in the 21 to 30 and 2 were in the 31 to 40 age periods.

Of the 17 cases in females, 10 had involvement of the left side and 7 of the right side.

Thus we find that the sacro-iliac joint tuberculosis mostly affects women in the active child-bearing age-group.

The diagnosis is often difficult and late because low back-ache is so common in young women of this age-group and the trauma of repeated child-birth causes non-specific sacro-iliac arthritis and sacro-iliac strains and luxations. Radiologically also the early lesion is difficult to detect. Very often the appearance of the cold abscess is the first sign of tuberculous sacro-iliac joint.

The treatment of sacro-iliac joint tuberculosis is on the same general lines as outlined *supra*. The immobilization is best done in a plaster of paris bed which extends from the beginning of the dorsal spine down to the knees. A careful watch must be kept for cold abscess and these should be aspirated in time before they point and burst. After the lesion is definitely quiescent a sacro-iliac belt is prescribed before allowing ambulation. The problem of pregnancy with reference to this lesion has already been discussed.

**Tuberculous osteitis.**—There are certain positions where tuberculous infection is essentially an osteitis without involvement of any joint. Such lesions commonly involve: (a) the metacarpals, metatarsals and phalanges; (b) ribs and (c) sternum. The lesion in the bones of the hand and feet are common in children. The lesion starts in the medulla of the shafts of the phalanges or metacarpals, eroding the cortex from within.

Conservative treatment with immobilization and chemotherapy clears most of these. Often incision, scraping and closure hasten healing. Sometimes amputation of the digit when an unimportant one is involved eliminates the disease in the shortest time.

In the case of ribs, the best course is to resect the affected portion after a preliminary period of chemotherapy and general treatment.

I shall now refer to an uncommon type of skeletal tuberculous lesion occurring in childhood.

Multiple pseudocystic tuberculosis of bone.—Multiple pseudocyst formation is an uncommon manifestation of skeletal tuberculosis. This has been often confused with the bone lesion of sarcoidosis. The characteristic features are the predilection for childhood, the tendency for involvement of long bones symmetrically and simultaneously and to progress and regress in harmony, the rarity of joint involvement and the frequent occurrences of sinus without sequestrum formation. One such case in this series, a girl aged 8, had an early pulmonary lesion and showed the typical lesions in both hands, both elbows, ankles and feet.

This is a relatively benign manifestation in spite of the multiplicity of the lesions, there being no constitutional disturbance and the response to treatment was uniformly good.

Recent trends in the treatment of skeletal tuberculosis.—A survey of the treatment of skeletal tuberculosis reveals a certain trend of thought. The earliest attitude was that of utter helplessness when the disease was called the King's Evil. We then find a period when heroic attempts at saving the life was made mainly by amputations of the limbs or radical excisions for lesion of peripheral joints. Attempts at radical excision were followed by non-healing of wounds, infection and spread of disease to meninges ending fatally.

The importance of constitutional treatment for these conditions was recognized in the early part of this century and this led to a revolutionary change for the better as evidenced by the results. By providing absolute rest to the joint and general treatment to improve body resistance a remarkable improvement was achieved in the number of lives and limbs saved. This necessarily meant a prolonged period of immobilization which extended for 3 to 5 years in many cases with the attendant complications of wasting, contractures, renal calculi epiphyseal arrest, stunting in the physical and mental growth of children.

The advent of anti-tuberculous drugs raised hopes that we may be able to give up all conservative treatment and eradicate all lesions by the use of drugs alone. These hopes were however shattered as it soon became evident that conservative measures were still essential in the treatment and that drugs can only be adjuvants in the treatment. Disastrous results followed the reliance on drugs alone and neglect of immobilization in the management of joint-lesions. While lesions failed to become quiescent the bacilli also became resistant to the drugs.

The fact that between immobilization of the part and chemotherapy, the former is far more important and essential than the latter is brought out very well by the following case.

Case report.—Mr. K., aged 35, complained of pain in the right elbow of one month's duration. The joint was swollen, warm, with muscle spasm and marked limitation of movement. X-ray picture revealed a minimal erosion of the lateral condyle of the humerus with generalized rarefaction. At the same time he complained of some pain in the left wrist with a little soft tissue swelling on the dorsum. This was diagnosed as a tuberculous teno-synovitis. The elbow was immobilized in plaster and systemic chemotherapy started. He also had intra-articular streptomycin once a week into the right elbow. The left wrist was left alone. He had a total of 45 g. streptomycin. The right elbow improved gradually and at the end of 8 months had returned to normal with limitation only of the last 10° of extension and flexion. But the left wrist pain persisted and at this period started getting worse. X-ray picture revealed an erosion in the carpal bone and radius. This time the left wrist was immobilized in plaster and a second course of streptomycin was given. The wrist gradually improved.

This case proved to be a perfect control experiment in the same patient with the right elbow joint having immobilization and chemotherapy and the left wrist having the benefit of the systemic chemotherapy but no immobilization. While the right elbow improved and recovered completely, the left wrist actually got worse till it was also immobilized. Surgery was still an elective procedure done where the lesion was considered quiescent. This elective surgery which was previously done some years after quiescence was made safer and possible earlier, by the use of the drugs which became essential adjuvants to surgery.

Exploratory surgery with chemotherapy as adjuvant.—While life and limb saving were the aims of treatment in the earliest periods the saving of function of the joints became the aim after the drugs came into use. Attempts at earlier diagnosis were helped by exploratory surgical procedures.

Streptomycin and other drugs have helped us to undertake open biopsies of joints safely in order to establish the diagnosis early and start treatment with a view to saving the function of the joints.

Surgery as an adjuvant to chemotherapy.—While chemotherapy has been playing an adjuvant role to conservative treatment as well as elective surgery, it is becoming clear that surgery can be made to play an adjuvant role to chemotherapy in the treatment of skeletal tuberculosis.

It has been recognized that while skeletal lesions discovered in the very early stages responded very well to combined conservative means and chemotherapy the cases discovered late do not respond so well. A study of the microscopic pathology of the tuberculous lesion will explain this difference in response. While cellular response and local hyperæmia were characteristic of the early stages of

the tuberculous pathology in the later stage the characteristic picture is that of endarteritis obliterans and ischaemic necrosis together with fibrotic response surrounding the focus. It follows that ischaemic necrosis is part of the pathology of tuberculosis and unless a path-way is opened surgically, antibiotics cannot have access to the lesion.

Surgery then can play an adjuvant role to break down the barrier surrounding the tuberculous focus in bone and produce a local hyperemia and help the chemotherapeutic drugs to act on the focus. Thus we see the return of the more radical methods of local attack on the lesion helped by chemotherapy and in turn helping the chemotherapy to reach the site of lesion and exert the bacteriostatic effect on the tubercle bacilli. Thus we have reached the stage when with the full benefit of constitutional treatment and chemotherapy we approach the skeletal lesion and curette it completely.

**Curettling of the active lesion.**—In the spine the lesion is approached by costo-transversectomy in the thoracic region and transversectomy in the lumbar region. The vertebral body is approached and any para-vertebral abscess evacuated. The lesion in the vertebral body is curetted and all granulomatous tissue removed. When healthy bleeding bone is left the raw area is packed with cancellous bone piece from iliac crest bridging the adjacent vertebra. This results in a good solid anterior spinal fusion.

Such a drastic procedure has been advocated by enthusiasts like Wilkinson for all cases of T.B. of the spine. The average duration of treatment in such cases is reported to be twelve months. It appears unjustifiable to subject every patient to an operation but this curettling can certainly be done in cases which continue grumbling activity in spite of prolonged conservative treatment. A similar curettling can be done in other joints like the elbow and hip.

**Case report.**—Mr. K., male aged 30, with early lesion of the right elbow in the capitulum. After a preliminary course of streptomycin P.A.S. and I.N.H. the lesion was removed by minimal excision curettling. He now has a healed lesion with a flexion of 100° and full extension.

Wilkinson has advocated partial synovectomy and curettling of early lesions in the hip. Such a procedure in his hands has given a healed lesion with a good 90° flexion movement in the hip. The follow-up period is too short to pronounce a judgement about the curettling procedure particularly in a weight-bearing joint like the hip.

The procedure of curettling the active lesion is so diametrically opposed to the principles and practice of treatment hallowed by tradition that it can hardly be accepted on the basis of such short-term follow up. But the further development of such methods will certainly revolutionize the treatment of skeletal tuberculosis; therein lies a great danger because attempts to cure the patient by exterminating the bacilli in the local bone lesion may lead to a precarious

recovery if the constitutional treatment is neglected. With the combination of the old knowledge and the development of the new, a new chapter in the treatment of skeletal tuberculosis is opening. At this juncture it is essential to recollect once again the fact that tuberculosis is a constitutional disease of which the skeletal lesion is only a local manifestation and that tuberculosis is a special disease. The patient came to the hospital because a deep-seated tuberculous lesion became active and bacillæmic under her old house and social conditions, thus producing the skeletal focus. If we allow the patient to return to the same environment, her vitality will return to the old level, the newly acquired resistance will be lost and the lesion is likely to relapse. This only emphasises the need for a long-term rehabilitation which is well within the province of social medicine and the establishment of a Welfare State. We can only close with a note of optimism that ere long we may be able to say with the Western author that the struggle against tuberculosis has been hard, long and costly; to see the enemy in retreat, however, is one of the rare exhilarating episodes reserved for our generation.

**Acknowledgement.**—My thanks are due to Dr. C. S. Sadasivam, M.S., Superintendent, Government Tuberculosis Sanatorium, Tambaram, for permitting me to use the case records and X-ray pictures of the Orthopaedic Section of the Sanatorium. I also thank the Dean, Government Stanley Hospital, Madras, for permitting me to utilize the Hospital records and X-ray pictures in the preparation of these lectures.

#### DOES TOXAEMIA PRODUCE HYPERTENSION?

Tillman of New York studied the effect of toxæmia of pregnancy on the normotensive and hypertensive women. His findings of the study of blood pressure for 5 years preceding and four years following a normal first pregnancy in 240 women and a toxæmic first pregnancy in 137 women. He concludes: "studies of the inter-relationship of BP and toxæmia of pregnancy are subject to sources of error resulting from characteristics of the BP measurement. These characteristics are: (1) lability in normal and abnormal range, (2) the association of a temporary elevation with future sustained elevation, and (3) the lack of a universal definition of the lower limit of hypertension. The range of observation by Tillman varied from 21 months to ten years. The mean value and standard deviation of blood pressure in normal pregnancy, the mean value and standard deviation of blood pressure in toxæmia of pregnancy show no change within 1 to 4 years following pregnancy. The patient undergoing a normotensive pregnancy is essentially a normotensive person; the patient who exhibits hypertension solely in pregnancy was hypertensive even prior to pregnancy. The patient who shows the pre-eclamptic or the eclamptic form of toxæmia may be either normo or hypertensive prior to pregnancy, and the post partum BP will reflect the preparatum state. The duration and severity of the toxæmia during pregnancy are not factors in causing post-toxæmic hypertension. Toxæmia of pregnancy does not permanently exacerbate hypertension.

In the vast majority of cases, the unrecognized hypertensive state is responsible for the appearance of hypertension following the toxæmia of pregnancy. This lack of recognition results from variability of blood-pressure and the decrease of blood-pressure early in pregnancy.—(N.Y. State Jour. Med., Feb. '56).

## THE RELIABILITY OF CHOLECYSTOGRAPHY

The reliability of oral cholecystography was studied on 1,340 patients in whom cholecystographic observations were interpreted as abnormal and on whom surgical interventions were performed at the Sraffner Hospital, Stockholm, Sweden, between 1937 and 1948. Up to 1943 a Swedish proprietary preparation of iodo-phthalein sodium (Cholotrast) was used as contrast medium; during 1944 and 1945, iodo-phthalein sodium and a Swedish proprietary preparation of iodoalphonic acid (Bilitrast) were used alternately, and after 1945 iodoalphonic acid was used almost exclusively as contrast medium. The day before the examination the patient was given a fatty meal to empty the gallbladder, followed by a double dose of the medium—8 g. of iodo-phthalein sodium or 6 g. of iodoalphonic acid. The patient was then kept on a light diet, all fats being withheld. The roentgenologic examination was carried out the next morning after the patient had been given a large water enema. A preliminary roentgenogram using a 24 by 30 cm. film was first obtained to see whether the gallbladder was sufficiently filled. If so, additional roentgenograms were taken under fluoroscopic control with the patient erect, the gallbladder being compressed, and a small diaphragm employed. Whenever no filling was evident, or visualization was so poor that the presence or absence of stones was uncertain, the patient was questioned regarding his proper ingestion of the contrast medium and as to any subsequent vomiting or diarrhoea. In the latter event, he was examined again the next day after administration of a further dose of the contrast medium and tincture of opium. Attempts were also made to eliminate every other source of error. Results showed that, whenever roentgenograms of the gallbladder indicate the presence of gallstones, either directly or indirectly as defects in its contrast-filled lumen, the evidence may be relied on completely. If there is any calcification in the walls of the gallbladder it may be difficult to distinguish this from lithiasis, but the difficulty seldom occurs in practice. Failure of the gallbladder to fill with the contrast medium is almost conclusive evidence that it is diseased. Extensive injury to the liver parenchyma must be excluded, and it must be remembered that incipient hepatitis may prevent the gallbladder from filling before any sign of jaundice has developed. Other sources of error are retention of the contrast medium in the stomach, pernicious anemia, and breast-feeding. Other abnormal conditions in the biliary passages, particularly tumours of the gallbladder, biliary ducts, or head of the pancreas, also may cause defective filling. Duodenal ulcer may occasionally have the same effect. If the filling is so poor that it is impossible to state definitely whether or not stones are present, the same consideration as in the cases with no filling is warranted. If the filling is poor, but sufficient to indicate or exclude lithiasis, it need not be considered abnormal. However, if iodoalphonic acid has been given, the poor filling may sometimes denote disease of the walls of the gallbladder. Iodoalphonic acid is more likely than iodo-phthalein sodium to lead to filling of the gallbladder, regardless of whether or not its walls are diseased. Consequently there is a better chance of visualizing stones directly with the use of iodoalphonic acid. In 75% of the patients in whom the gallbladder failed to fill, the walls of the gallbladder were diseased. However, changes in the walls were present in only 25 per cent of the patients in whom stones were observed in a contrast-filled gallbladder. Normal cholecystographic findings practically always exclude disease of the gallbladder, but exceptions may occur. Collections of cholesterol flakes may be present that can form stones. A strong clinical suggestion of gallbladder disease may, therefore, occasionally warrant surgical exploration, provided all other conditions are first carefully eliminated. Sodium iodipamide (Biligradin), a new intravenous contrast medium, was not on the market before the authors' studies were completed. Although the authors consider oral contrast mediums most suitable for routine examinations, it may sometimes be advantageous to carry out examinations with sodium iodipamide (*Acta Radiol.*, 44: 185-200, Sept. 1955 via J.A.M.A.).

## TREATMENT OF HAEMORRHAGIC CHOLERA AND SEVERE HAEMORRHAGIC DIARRHOEA\*

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THE visible presence of blood is not uncommon in the cholera stools being detected in 10% of cases in the vibrio-positive series studied by Chatterjee *et al* (1955), although rice water appearance is the more usual feature. The present paper comprises a study of 58 cases of haemorrhagic stools admitted into the cholera ward during the three epidemics of 1953, 1954 and 1955. The number includes 38 cases in which the stools were positive for the comma vibrio and 20 cases in which the stools were negative. All the cases had repeated vomiting and numerous sanguinous liquid motions along with severe shock and prostration and were brought by the ambulance as cases of suspected cholera.

Amongst the first group of 38 cases besides the cholera vibrio, stool cultures in 15 cases showed the presence of active vegetative forms of *Entamoeba histolytica* in addition.

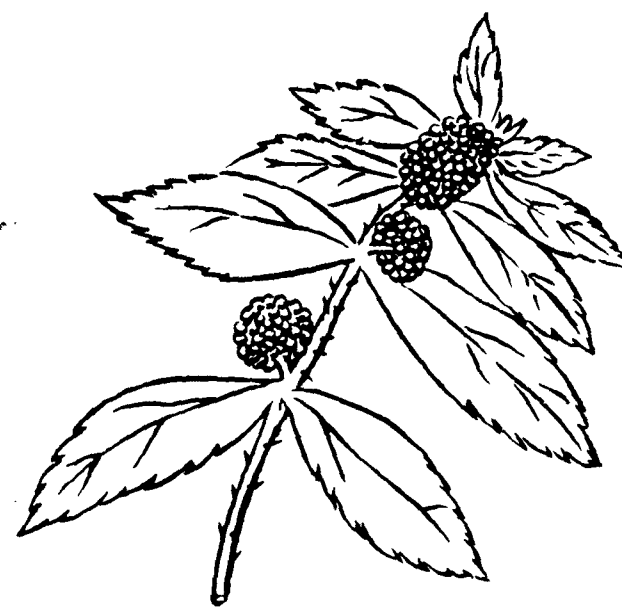


Fig. 1

The remarkable feature of all these cases was the severe symptomatology (Chatterjee *et al* 1955). Seven out of this group of 15 were given a combined treatment with terramycin (250 mg.) every four hours along with one ounce doses (t.d.s.) of the raw juice of a common Indian plant, *Colens aromaticus* (Chatterjee 1953\*, 1955). All the cases recovered. Both *Entamoeba histolytica* and the cholera vibrio were absent, 17 days after

admission. As controls, terramycin was omitted in the remaining 8 cases which were given the above dosage of *Colens aromaticus* only. The usual treatment for combating shock and dehydration was the same in both groups. The mortality rate in this control group was rather high; 3 out of 8 cases died (37%).

\*Specially contributed to the ANTISEPTIC.

This led us to the belief that *Coleus aromaticus* was not so efficacious when used alone in cholera cases showing haemorrhagic stools in contrast to its remarkable efficacy in the otherwise usual cases of cholera (Chatterjee 1953<sup>a</sup>, 1955). Regarding therapeutic efficacy



Fig. 2

terramycin when used alone in cholera was not of any significant value in the hands of the different workers (Das *et al* 1951; Konar and Sen Gupta 1951; Chatterjee 1955). Following our previous favourable experience with another common Indian herb *Euphorbia pilulifera* (Synonyms: Dudhia, Hindi; Khirki, Bengali; Amman pacharisi, Tamil; Chatterjee *et al* 1955) noted by us in haemorrhagic cases of cholera, we repeated the same in the present series.

Leaving aside the 15 cases including 8 controls, previously mentioned that were treated with *Coleus aromaticus* with or without terramycin, there remained 43 cases with haemorrhagic stools. As previously stated, 23 of these showed the presence of cholera vibrios on culture, and in four of these 23 the culture of the stools showed also *Shigella flexneri*. Of the remaining 20 vibrio-negative cases, three showed the presence of active *Entamoeba histolytica* and one of *Balantidium coli*. The usual dosage consisted of an ounce of the strained juice of the entire plant of *Euphorbia pilulifera* given with a little sugar.

Of the 43 patients belonging to both groups (culture positive and negative), thirty five cases were given 3 two-hourly doses on the first day. The rest of the cases numbering 8, which had an extremely severe haemorrhagic diarrhoea, were given four doses on the first day. In the 25 cases (58% of the combined groups), the diarrhoea and haemorrhagic stools disappeared within 24 hours.

On continuing the treatment the diarrhoea and haemorrhagic stools disappeared in 12 out of the 18 remaining cases (28% of the combined group) within 48 hours. In the remaining 6 cases, the *Euphorbia* juice had to be repeated on the 3rd day when the diarrhoea and haemorrhagic stools stopped, these comprising 14% of the total group. Thus the control of diarrhoea and haemorrhagic stools has been one of the most remarkable phenomena seen by me and could be observed in all cases whether showing cholera vibrios or not. In the culture-positive cases, the stools were examined daily both under the microscope and culturally. It was found that the cholera vibrios persisted up to the 18th day in some cases by which time most of the patients had to be discharged owing to the rush.

In order to ascertain the action of *Euphorbia pilulifera* in cases of amoebic dysentery, we administered the usual doses of the raw juice in three other cases of acute amoebiasis with bloody stools during the non-epidemic season of 1954. Although there was complete relief of clinical symptoms within 3 days, the vegetative forms of *E. histolytica* persisted even at the end of a fortnight.

In the present series, amongst the 20 cases in which stools were negative for cholera-vibrios on culture, three showed the presence of vegetative forms of *E. histolytica*. A combined tablet of Bismuth arsenillate 0.25 g. and Chloroquin 0.075 g. (1 tablet t.d.s.) was given after the acute symptoms had subsided and a free flow of the urine had been established; this usually occurred within 72 hours.

After another three days' treatment the *E. histolytica* was absent from the stools and this condition persisted at the end of ten days from the date of admission when many of these patients had to be discharged. The single patient with *Balantidium coli* could not be followed up, as he died of cerebral thrombosis although his diarrhoea had been cured. It would be interesting to mention the 4 cases which showed both the cholera vibrio and *Shigella flexneri* on stool culture. The clinical symptoms were very severe in one of these and proved fatal. The other three were comparatively mild cases and clinical cure occurred within 72 hours. This is in contrast to the severe symptomatology of the cases which showed a combined infection from cholera vibrio and *E. histolytica*, as already mentioned. The treatment for shock and dehydration as well as the other complications was common in all cases and will be described in a separate communication.

**Mortality.**—Three out of the eight cases which acted as controls for the therapy trials with Terramycin *cum* *Coleus aromaticus* died of the disease giving a mortality rate of 37% in contrast to the 7 cases which received the combined treatment and got cured.

Of the remaining 23 cases showing a positive stool culture for cholera vibrio, and treated with *Euphorbia* juice, 2 cases (8%) died; one of these died of uramia on the 4th day and the other from circulatory failure on the 3rd day. This last case also showed *B. flexneri* dysentery in the stool culture. Of the culture-negative cases (numbering 20) but with clinical symptoms of cholera, treated with the *Euphorbia pilulifera*, one died of circulatory failure 10 hours after admission although the diarrhoea had stopped while another died of cerebral thrombosis and hemiplegia 10 days after admission giving a mortality rate of 10%. This last case had shown a *balantidium* infection. It would thus appear that all diarrhoeas with haemorrhagic stools, including those showing the cholera vibrios on culture, show remarkable clinical improvement with the raw juice of *Euphorbia pilulifera*. The improvement seems to be only clinical as this vegetable juice appears to have no action on either the cholera vibrio or *E. histolytica* in the patient. For clinical interest, a short case

note of a moderately severe case admitted with the blood specific gravity of 1066 is given:

**CASE REPORT:**—Patient G. S. B., Hindu, female, aged 55 was admitted on 10-4-55, with the following: (1) history of purging, 5 times, haemorrhagic liquid motions; (2) history of vomiting—3 times; (3) eyes sunken, tongue dehydrated, with great prostration; (4) axillary temperature 98.4 F., rectal 100.2 F.; (5) specific gravity of blood 1066; (6) pulse 108 p.m., volume low, respiration 24 p.m. regular; and the (7) microscopic examination of stools showing—red blood cells in large numbers and vegetative forms of *E. histolytica* in fair numbers. *Report of stool-culture* received on the third day showed the presence of agglutinable cholera vibrios.

**TREATMENT:**—Transfusions were started by the drip method as follows: Hypertonic saline 1 pint; Isoalkaline saline 1 pint and 5% glucose in normal saline 1 pint. To check vomiting a tablet of Avomine (Chatterjee 1953<sup>b</sup>) was given after which iced 5% glucose in  $\frac{N}{4}$  saline was given to the patient to drink in any quantity desired. Three one hourly doses of the fresh juice of *Euphorbia pululifera* were given. She passed 6 more haemorrhagic stools in the hospital on the same day.

**2nd day:**—Patient looked better; tongue was fairly moist; there were three liquid motions all non-haemorrhagic although a few red cells were seen under the microscope. Pulse 80 per minute. Respiration 24 per minute. Patient passed two apparently normal stools daily, on the 3rd, 4th, 5th days. On the 6th day, the patient took voluntary discharge from the hospital. The stool however still showed the vegetative forms of *E. histolytica*. The culture report received 2 days later showed the presence of the cholera vibrio.

**Summary.**—1. Seven severe cases with haemorrhagic stools which showed the cholera vibrio and *E. histolytica* were treated using a combined therapy with terramycin and the raw juice of *Coleus aromaticus*; clinical cure was noted in all cases. Eight similar cases which did not receive terramycin served as controls; 3 of these cases died; a mortality rate of 38%.

2. Another group of 43 cases with haemorrhagic stools and severe diarrhoea was treated with the raw juice of *Euphorbia pululifera*; 23 of these cases showed the cholera vibrio in stool culture and the remaining 20 were culture negative.

3. In all cases including both the groups, diarrhoea and haemorrhagic stools were controlled within 72 hours—58% within 24 hours, 28% within 48 hours and 14% within 72 hours.

4. The action of *Euphorbia pululifera* seems to be mainly clinical as it seems to have no action on either the cholera vibrio or *E. histolytica*.

I wish to thank the authorities of Chittaranjan Hospital for their co-operation and to Dr. P. K. Chakravarty, Dr. R. K. Shah and Dr. H. K. Chakravarty for their great help during the three cholera epidemics in 1953, 1954 and 1955.

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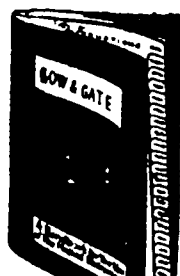
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## SOME REFLECTIONS ON STRESS AND HOW TO FIGHT IT\*

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In the modern restless world, life is geared to a fast tempo and is consequently exposed to continual stress. Since the epoch-making discoveries of Selye, stress has come to be increasingly recognized as an important factor in the causation of disease. Diseases like hyperthyroidism, hypertension, peptic ulcer, asthma, neurocirculatory asthenia, find their ultimate aetiology in the mental stress. In the treatment of disease, our best treatment will remain only palliative unless we devise ways and means to counteract stress.

It has been recognized that stress works through its influence on the mind. While doing so, it may damage the mind; and a disordered mind may remain as a constant source of stimulation of the hypothalamic centres and exhaust the nervous system. Thus, stress not only produces bodily disease but also impairs the mind, thus requiring repair and restoration to health.

We strengthen the body defences by nourishing food, physical exercise, immunization etc., but we have never seriously thought of strengthening the mind so that it may not be easily influenced by stress. It is surprising that we leave this important organ to develop its own defence. An individual who has experienced many stresses is sometimes seen to emerge with a sturdy mind, just as a person who has fought infections develops a defence in the form of immunity. If the mind is trained to face stress and resist it, the progress of disease can be stayed and in many cases prevented.

If the necessity for training of the mind is conceded, there is need for the discipline, control and education of the mind. For the execution of this task a faculty superior to the mind—the spiritual faculty or the 'Spirit'—must be invoked.

For a new approach to the problem of stress, Medicine has to look to Indian Philosophy. Our ideas about disease need reorientation. We must divest ourselves of the 'orthodox' notion of disease that has fast clung to the medical profession. Disease, to the modern medical world, is something that attacks the person from outside. We have become so obsessed by the concept of 'infection,' that it will be difficult to reconcile ourselves to the thesis that ease and disease primarily arise within the organism. Disease really denotes a fight inside us between different antagonistic forceful trends of thought and complexes. The fight between alien pathogenic agencies and the immune system plays a comparatively insignificant role in the total disease of the patient. Every bodily disease has its mental counterpart in the form of psychological reaction of the

\* Specially contributed to the ANTISEPTIC.

patient to the disease. The bodily-disease may be cured by knife or drugs but the psyche, if not attended to, may remain impaired as a result of the reactionary trauma and interfere with the total cure of the patient that is expected. Disease represents internal struggle for self-expression, self-assertion, and self-adjustment. The factors that help the organism in this fight have been ignored and even ridiculed at the present day.

We have been accustomed to seeing only two dimensions of the human being *viz.*, the body and the mind. We have been blind to the most important third dimension *viz.*, the spirit. In fact, man is an integrated unit of body, mind and spirit. Body and mind are concerned with the relation of the individual to other individuals and the surroundings, while the spirit is concerned with the relation of the individual to the universe. We are now realizing the important influence of the mind in causing disease. The spirit influences the mind and through it the body; hence the great importance of the spiritual culture in the control and cure of disease.

All living organisms respond to stress. Selye has pointed out that the basic pattern of reaction is always the same irrespective of the stress type. He calls the response as the *General Adaptation Syndrome*. A disturbance in the response-mechanism will result in various diseases which Selye groups under the name 'Diseases of Adaptation.' Selye's '*Adaptation Syndrome*' includes only the physical and physiological changes in the organism. With the development of mind in the living organism, the adaptation response is bound to be complicated by or associated with a psychical response, which is more subtle and potentially harmful by its influence over the body through the nervous system. Thus enlarging the scope of Selye's hypothesis, one may say that disease in man results from physiological and psychical maladaptation. In a healthy person physiological maladaptation is not likely; psychical maladaptation which morbidly influences the physiology is the important cause of human disease. If the psychical responses can be so modulated or influenced as to nullify or modify their effect on the human physiology, by '*the spirit*' through a better understanding of oneself in relation to the universe, the stress-produced morbidity will be largely prevented. Every attempt is made to study the target organs and the effects thereon of stress. But no effort has been made to fortify the mind against stress by a superior training or control by the higher 'spirit' centre. Such a training of mind is by a way of life which can appropriately be called a spiritual approach to medicine.

Both the clergy and the medical profession are deeply concerned with the mechanism of healing in its fullest sense. With the advance of medicine and the waning of religion, the priest has concerned himself solely with religious dogmas and does not contribute to the relief of human suffering. Now a good doctor must

combine the functions of priest and doctor. He relieves the physical suffering by proper medicines and the mental tension by soothing and reassuring talks. In my experience, more good often accrues from the latter in cases with functional disorders. By the increasing materialistic approach to medicine, the priest in the doctor is gradually dying out with the result that the stress of the patient remains unrelieved. A 'stressed' patient can find no other alleviation for him than Pot. brom and Phenobarbital. These drugs obviously do not relieve him but expose him to their toxic effects by prolonged use. He continues to worry and develops neurosis. Even the whole gamut of our materia medica does not afford him lasting relief. Medication will not solve the tension-problems associated with anxiety, despair, frustration, disappointment, but may to some extent does mask the effects. In fact all the newly discovered and undiscovered 'tranquilizer' drugs in the world will not succeed in solving the problem of 'stress.' Only a physician with a spiritual approach can do it and thus save humanity from the life-threatening stress.

To the thinking man, the realization gradually dawns that he is living in a dynamic universe, and a growing acknowledgement of a greater world of reality beyond the material, forces itself on his mind even against his wish. Worry may be described as a spasm of emotion in which the mind clings fast to a thought or obsession spasmodically. To loosen the grip a stronger and healthier idea must be introduced in the mind. Such an idea is '*Faith in God*.' As a mind accepts faith, there starts a process of change that frees all fears and tensions, with the moral and spiritual betterment of the individual.

Disease has been conceived of, as a disturbance in the cell and/or in its environment, and accordingly cellular and humoral theories of disease have been postulated. Mental processes have been known to influence both of them morbidly. If the mental processes are uncontrolled by '*the spirit*', a condition like that of a 'spinal or decerebrate animal' is produced. For example, if your neighbour hates you, you begin to hate him. Uncontrolled mental reactions very closely simulate those in animals whose higher 'spiritual' centres are not developed. A mind properly controlled by the spirit will behave differently. Just as cellular reactions are predictable, so are the reactions of the mind uncontrolled by the spirit. If the mind is trained to ignore, suppress, neutralize or modify the harmful stimuli, their disastrous effect on the body can be avoided. Hence, a physical and psychological approach alone is not enough to counteract stress and control disease, but a spiritual approach is the supreme necessity.

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## THE LEWIS BLOOD GROUPS\*

### A Summary of the Important Recent Advances

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THE Lewis-blood-group system, which was discovered by Mourant in 1946<sup>1</sup>, presents unusual serological and genetic features. Race and Sanger<sup>2</sup>, in the second edition of their monograph "Blood Groups in Man" record the extent of knowledge of this system up to the end of 1953.

The system is defined by two genes  $Le^a$  and  $Le^b$ . There are two antibodies anti- $Le^a$  and anti- $Le^b$ . The phenotypes recognised by anti- $Le^a$  alone are called  $Le(a+)$  and  $Le(a-)$ , while those recognised by both anti- $Le^a$  and anti- $Le^b$  are named  $Le(a+b-)$ ,  $Le(a-b-)$  and  $Le(a-b+)$ . These phenotypes are recognised in adults; the phenotype  $Le(a+b+)$  is recognizable only in children under the age of 18 months. This is thought to be due to the fact that the  $Le^a$  character is a Mendelian recessive.

Some anti- $Le^a$  sera contain traces of anti- $Le^b$ , usually active at lower temperatures, particularly with O and A<sub>1</sub> cells. Some pure anti- $Le^b$  sera have been described which were found to give the expected reactions only if O and A<sub>1</sub> cells were examined. This was thought to be a manifestation of epistasis, a genetical phenomenon in which one gene ( $A_1$ ) suppresses another gene ( $Le^b$ ) which is not allelomorphic to it. However, certain anti- $Le^b$  sera were found which were capable of reacting with A<sub>1</sub> cells as would be expected from their reactions with O cells. Andresen and Jordal<sup>3</sup> described a serum 'anti-X' which agglutinated all red cells except those of the phenotype  $Le(a-b-)$ .

There is an interesting relationship between the Lewis groups and ability to secrete the ABH substances. Race and Sanger<sup>2</sup> summarise the situation as under:—

$Le(a+b-)$  red cells belong to non-secretors of ABH.

$Le(a-b+)$  red cells belong to secretors of ABH.

$Le(a-b-)$  red cells usually, but not always, belong to secretors of ABH.

The  $Le^a$  and  $Le^b$  antigens are themselves secreted independently of the ABH substances; apparently all  $Le(a+)$  persons secrete  $Le^a$ , however some  $Le(a-)$  persons do so as well.  $Le(b+)$  persons secrete  $Le^b$ , and so do some  $Le(a-b-)$  persons. Many genetical theories have been presented in attempts to explain the experimental findings. The greatest difficulties lie (i) in explaining the genotype  $Le(a-b-)$ , which calls for the postulation of a third gene

allelic to  $Le^a$  and  $Le^b$ , or some more complicated theory of inheritance: the situation is also bedevilled by some doubt as to whether  $Le^b$  belongs to this system at all; (b) in understanding why some non-secretors of the ABH substances are  $Le(a-)$ ; and (c) in accounting for the fact that apparently some  $Le(a-)$  and  $Le(b-)$  persons secrete  $Le^a$  and  $Le^b$  respectively.

Recently some clarification has been forthcoming. The 'anti-X' of Andresen and Jordal is generally believed to be anti- $Le^a$ +anti- $Le^b$ . These antibodies cannot always be separated by absorption with  $Le(a+)$  or  $Le(b+)$  cells. It is now felt that this is due to these antibodies being 'polyvalent', 'linked', or 'cross-reacting'. All these expressions simply mean that the specific anti- $Le^a$  and anti- $Le^b$  receptors may sometimes be on the same antibody molecule. There is thus a fundamental similarity between the Lewis system and the ABO system in which the anti-A and anti-B receptors of group 'O' sera are sometimes on the same molecule. Wiener<sup>4</sup> has postulated that the Lewis system is basically similar to the ABO system, in that either, both or neither of two antigens ( $Le^a$  and  $Le^b$ ) may be present in the red cells and that the corresponding antibody can occur in the absence of its antigen. The preferential action of anti- $Le^b$  sera with O and A<sub>1</sub> cells now seems certainly to be due to the presence of anti-O (or H). For some unknown reason anti-O (or H) often occurs with anti- $Le^b$ .

The most spectacular advance towards complete understanding of this system has recently been provided by Sneath and Sneath<sup>5</sup>, who have demonstrated that it is possible that the Lewis antigen characteristics of red cells are passively derived by absorption from the serum. These authors feel that the Lewis system is fundamentally expressed as serum antigens: This would be in accordance with the view of Grubb<sup>6</sup> who suggested that the Lewis antigens are primarily tissue antigens.

These observations also serve to explain the ease with which the Lewis antigen can be washed off red cells<sup>2,5</sup> and also the few discrepancies observed in the correlation between Lewis blood groups and ABH secretor status. Thus it may be that  $Le(a-b-)$  persons and ABH secretors are really  $Le(a+)$  but who do not secrete the ABH substances are really  $Le(a+)$  but whose red cells have not adsorbed the  $Le^a$  substance possibly because it is not present in sufficient concentration in the serum. Similar considerations may explain the observed discrepancies between the Lewis blood group status of the red cells and the type of Lewis antigen secreted in the saliva. The correct Lewis blood group would be that indicated by saliva examination.

The Lewis antibodies are not considered to have much clinical significance<sup>7</sup>, having rarely been implicated as a cause of incompatibility reactions, and not having been known to cause haemolytic disease of the new born. Mollison and Cutbush<sup>8</sup>, however, have

\*Specially contributed to the 'ANTISEPTIC.'

demonstrated that anti-Le<sup>a</sup> is of importance as a possible cause the incompatibility reactions, because in cross-matching tests, red cells sensitised with anti-Le<sup>a</sup> may not react with certain anti-globulin sera. The importance of the Lewis anti-bodies in pre-transfusion tests has also been emphasized by Stratton<sup>11</sup> who drew attention to another peculiarity of Lewis antigen-antibody interactions. This is the ease with which agglutinated cells are dispersed. This reversal of agglutination may well be due to the fact that the reacting antigen, being adsorbed by the red corpuscle is easily eluted along with the agglutinin which is united to it.

Mohr<sup>12</sup> has shown that in all probability the Lewis and Lutheran genes are carried on the same chromosome. This fact is of profound genetical importance as it represents the first demonstration of autosomal linkage in man.

All these recent advances strengthen the usefulness of the Lewis blood group system in various spheres. The relationship of this system to clinical problems has been outlined above. The Lewis groups have been relegated to the background by anthropologists and forensic scientists largely because of the unreliability of the results obtained with samples examined some days after collection. Newer knowledge of the mode of expression of this system may enhance its anthropological and forensic value.

The association of this system with the secretion of the ABH substances has become more clear. Biochemical and serological studies should complete our understanding of the nature and inter-relationships of the antigens and antibodies constituting these systems.

This system of blood groups, though not exhibiting epistasis, as previously thought, is nevertheless of considerable genetical interest. It probably serves as an example of the pleiotropia, a genetical phenomenon in which a gene has more than one effect; the Lewis genes and those for secretion of ABH seem to be the same. Unusually, the Le<sup>a</sup> character is a Mendelian recessive, but this idea may require to be revised in course of time. The demonstration of the linkage relationship of the Lewis and Lutheran blood group systems has initiated the mapping of human autosomes. The final synthesis has not been made but it now seems to be much nearer.

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## FIFTY YEARS OF CHEMOTHERAPY AND ANTIBIOTICS\*

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**H**istorical.—“The development of chemotherapy during the present century is the most important therapeutic advance made in the history of Medicine.” The term chemotherapy was used by Ehrlich to the use of synthetic chemical substances acting specifically on infective organisms. The earliest known use of drugs to destroy parasites in the body is the action of mercury in syphilis (Marcus Cummans, 1495) and of quinine in malaria (1630).

Modern chemotherapy dates back to Ehrlich's systematic search for an effective remedy for syphilis in 1904. Towards the end of the nineteenth century Koch attempted to cure septicæmia in animals by intravenous injections of drugs and tried without success many of the disinfectants then known. This long history of failure was terminated in 1935 by the discovery of the sulphonamides. Sulphanilamides were then synthesized in 1908 and the sulphonamide dyes in 1909.

It was in 1889 that the word ‘antibiosis’ was first used. Marshall Ward (1899) applied the term ‘antibiosis’ to microbial antagonism as the converse of ‘symbiosis’. Mosse (1852) was perhaps the first to suggest the use of a micro-organism for therapeutic purposes. Flynn (1944) records that Elisha Kent Kane during his Arctic explorations (1853 to 1855) used yeast as a poultice in superficial infections occurring among the crew. Pasteur and Joubert (1877) first described clearly bacterial antagonism, while studying anthrax bacilli.

The first experimental approach to bacterial antagonism *in vivo* was made in 1887 by Emmerich who showed that an injection of streptococci from erysipelas, enabled a substantial proportion of rabbits to survive a subsequent dose of anthrax bacilli, which would otherwise have died. Although much of the biological work was excellent, only in a few cases were the investigations supported by adequate biochemical examination. During the 1930's gliotoxin was first isolated by Weindling and Emerson (1936) and in 1939 Dubos started systematic biological and chemical work on tyrothricin accompanied later by clinical trials. Antibiotic research thus received great impetus and resulted in the discovery of penicillin in 1940.

While addressing a conference on antibiotic substances Waaksman, the discoverer of Streptomycin said, “just about 5 years ago at a round table conference on the antibiotics, the sponsors failed to secure enough participants for a two-hour discussion. Today the question is to decide what could be left out and who among the

\*Specially contributed to the ANTISEPTIC,

numerous workers were able to represent the various aspects of this field of research and application!"

Thousands of plant and animal substances have been analysed for the presence of antibiotic remedies. In their "Dictionary of Antibiotics" Karel and Roach have given a description not only of every known antibiotic but of every source, plant or otherwise that has so far been studied, which number over 15,000.

In an editorial the *Br. Med. Journal* stated: "almost every known species of plant from algae and lichens through every flower, shrub and weed with which the gardener is familiar, to the most majestic of trees, has now been examined in this way—making an extract of it to find out whether it contains an antibiotic. One object of this survey has been to discover some chemotherapeutic basis for the allegedly healing properties of herbal remedies including not only those used in the middle ages and in remote parts of the world but even some of the more peculiar tinctures mentioned in the recent pharmacopœias. In this connection it is odd that this book should list *Dichorea febrifuga*, (the alkaloid from which the dichorine is described as effective in malaria) yet no mention quinine or emetine. Are these antibiotics or not?" Posing this question the article further states, "the definition of the term given in the preface is a substance derivable from living organisms and capable of adversely modifying the vital functions of specific micro-organisms." The products of bacteria and fungi undoubtedly antagonize the growth of other species with benefit to those forming them.

**Sulphonamides.**—The dye prontosil was synthesized in 1920 and its clinical action in curing a boy of peritonitis was reported by Forster in 1933. In 1935 Domagk published his clinical results on the use of this drug.

The sulphonamide group of drugs was developed with the main object of finding agents which would combat bacterial infection. It is clear that the sulphonamide drugs do not directly kill micro-organisms. Under their influence the 'toxæmia' of bacterial infections is markedly limited. It was formerly believed that the sulphonamides blocked bacterial metabolism by competing with a substance essential for the growth of bacteria *viz.*, para-amino-benzoic acid. It is now, believed that many bacteria do not need PAB and that the sulphonamide drugs act as inhibitors of essential enzyme systems which govern the normal metabolism of bacterial cells.

For effective clinical therapy, sulphonamides have to be given in doses sufficient to maintain adequate concentration of the drug. In practice, a large initial dose is required to raise the blood concentration to a suitable level, which is maintained by appropriate repetitive maintenance doses. The rate of excretion of the various sulphonamides varies with different groups and hence the interval of dosage should be adjusted accordingly. For instance, sulphadiazine should be administered every six hours and sulphamerazine every

8 hours, at the rate of 1 g. Further the drug being excreted by the kidneys, the interval may be further lengthened while treating an infection of the genito-urinary tract.

The sulphonamide drugs get detoxified in the liver and are converted in varying degrees into acetyl-compounds which are toxic and insoluble in urine. Much work has been done on acetylation, the results of which are still under evaluation.

The presence of pus or necrotic tissue interferes with the action of sulphonamides—a great disadvantage as compared with the antibiotics. Certain pure chemical substances also, *e.g.* PAB, interfere with the efficiency of these drugs. A similar inhibitory effect is produced by procaine and by nicotinic acid. Nicotinic acid is effective in checking the action of sulphapyridine.

The toxic effects of sulphonamides are many and varied which are well-known to the practising physician. Thus, cyanosis, nausea and vomiting, headache and dizziness, acidosis, fever, rash, leukopenia, agranulocytosis, leukemoid reaction, mild anæmia, hæmaturia, oliguria, crystalluria have all been recorded.

In order to avoid the toxic reactions and still obtain the maximum therapeutic effect, Lehr and others suggested that a mixture of two or three sulphonamides be given together. By this method (*e.g.* 'sulphatriad') the incidence of crystalluria is greatly reduced while the antibacterial activity is not affected.

The choice between penicillin and sulphonamides often becomes a problem. Certain pathogenic bacteria which do not respond to penicillin yield to sulphonamides. Many gram-negative bacteria (including the colon and dysentery groups, *Ducrey's* bacillus, *Hæmophilus influenzae*, and the bacillus of *Friedlander*) are amenable to sulphonamide therapy.

Of several sulpha compounds tested, those in popular use at present are:—Sulphanilamide, sulphapyridine, sulphathiazole, sulphadiazine and sulphamerazine. A combination of the last three has been found to serve much better.

**Penicillin.**—The most widely used drug of choice in general practice, to combat many bacterial infections is penicillin. No chemotherapeutic agent has been studied so thoroughly as penicillin. The story of its discovery by Fleming, Florey and chain is now quite familiar. Its place in medicine was determined in the broad clinical investigations of the National Research Council under the chairmanship of Dr. Chester A. Keefer.

Penicillin is primarily active against the gram-positive organisms; pneumococci, streptococci, staphylococci, certain of the clostridia and lactobacilli are all susceptible to the action of this drug. In the gram-negative group, meningococci and gonococci are both sensitive to penicillin, while *H. influenzae*, *E. coli*, *S. typhosi*, are all resistant to its action.

The antibacterial activity of penicillin *in vitro* is not affected by the presence of blood and serum. It has a marked treponemacidal activity and has therefore, come to be considered the drug of choice in the treatment of syphilis. Penicillin is not active against protozoa. A combination of penicillin, succinylsulphathiazole and emetine bismuth iodide has been reported to yield good results in refractory cases of amoebiasis, although the first two drugs are ineffective *in vitro*.

Procaine penicillin has now largely replaced the use of the crystalline variety and in the United States 70% of the production is in the procaine form, which has a more prolonged action, even only one injection, during 24 hours.

Following the experience with sulphonamides, during which resistant strains of organisms became a serious problem in their clinical use, it was anticipated that a similar situation might arise with the extended use of penicillin. A substantial number of strains of staphylococci are resistant to penicillin and the number of such strains is increasing. Luckily, a combination of penicillin with the broad spectrum antibiotics has to a large extent eased the problem.

Penicillin may be either bactericidal or bacteriostatic for microorganisms susceptible to it, depending on the concentration at the site of infection. The exact mechanism of the action of penicillin is not known, but it appears that its antagonistic action takes place predominantly while the organisms are actively growing and multiplying. One of the earliest effects of penicillin on staphylococcus aureus appears to be the blocking of absorption of an essential metabolite, glutamic acid, which occurs only during the period of growth and not in the resting phase.

The toxicity of penicillin as shown in the early animals as also after its extensive use has been found to be extremely low. It was clearly shown by Rake and Richardson that the so-called toxicity of penicillin decreased as the purity of the commercial preparations improved. The early indications were that penicillin produced no serious toxic effects on the nervous system. However, there is no question now, that nerve tissue is vulnerable to the action of the drug. Johnson and Walker have reported the development of convulsions in a patient following intraventricular administration of penicillin and they subsequently induced convulsions in animals by direct application of penicillin to the cerebral cortex. Peripheral neuritis also has been reported as a complication of intrathecal therapy. Instances of localised peripheral neuritis with motor and sensory disturbances have been recorded following intramuscular injections of penicillin.

Toxic reactions to oral therapy with penicillin have also been reported on numerous occasions. Cross summarizes them by stating that two common conditions following oral therapy are: discoloration of the tongue and stomatitis.

The ANTISEPTIC discussed editorially in January 1954, the alarming reactions to procaine penicillin noted in daily practice: "Recently very alarming, even fatal, reactions have been reported. Pick and Patterson (1953), Waldbott (1949) and Mayer *et al* (1953) have all reported fatal reactions to penicillin immediately after intramuscular injections. Urticaria, serum sickness, a feeling of tightness in the chest, dyspnoea etc., were predominant symptoms in these cases. It would be therefore, wise to give this drug very carefully to patients having an allergic diathesis such as bronchial asthma, urticaria etc. and also to use anti-histaminic drugs along with penicillin to avoid these untoward reactions." Personally, I have observed no fatal case of penicillin sensitivity and believe that the reactions are mostly due to the procaine radical than to the crystalline penicillin.

**Streptomycin.**—Within a year of its discovery (in 1944 by Waaksman *et al*.) its *in vivo* and *in vitro* activities were established and in spite of extremely short supplies it was found to be a safe and effective chemotherapeutic agent, and a very powerful and effective weapon against tuberculosis.

Streptomycin is effective against gram-negative organisms—and pathognomonic to mycobacteria, Brucella, Haemophilus, Salmonella and Shigella group of organisms *in vitro*. It is ineffective against fungi, viruses, and rickettsia.

The powerful suppressive action in experimental tuberculosis in guineapigs was first reported by Feldman and Hinshaw. Because of its antibacterial activity against *M. tuberculosis*, the drug was given an extensive trial; resistant strains of T.B. resulted after its use in many cases: (Youmans, Karlson, Fisher, Wolinsky, Howlett and others, also Sadusk and Swift).

From 70 to 80% of all patients receiving streptomycin for 100 to 120 days show resistant strains in their sputa. It is therefore, wise to select cases before treatment and watch for drug-resistance.

A careful study by Hawkins of the relative toxicity of dihydrostreptomycin and pure streptomycin has shown that the former affects the auditory system to a lesser extent than streptomycin. However, Maxwell Finland (*B.M.J.*, 21-11-'53) believes that "Dihydrostreptomycin tends to produce a predominantly auditory nerve damage which may be insidious in its onset and usually is irreversible, while streptomycin gives rise to predominantly vestibular dysfunction which may be recognized early and may be reversible."

The introduction of Isonicotinic acid hydrazide has further minimized the risks in streptomycin therapy. The *B.M.J.* states: "Isoniazid should no more be used alone than should streptomycin or PAS; caution is needed in giving streptomycin less often than once daily when used with isoniazid. In patients with cavities or

with more extensive disease, it is wiser to start with the well-tryed streptomycin and PAS keeping INH in reserve, in case the bacilli become resistant. When patients are desperately ill it is reasonable to give them, all the three drugs in the first place. The use of INH should be carefully timed to cover a crisis and it must not be frittered away." The British Medical Research Council conducted trials in 364 patients with pulmonary tuberculosis. Three groups were treated: Gr. I with streptomycin + Isoniazid—(SH). Gr. II with streptomycin + PAS—(SP), and Gr. III with Isoniazid alone—(H).

In general the SH patients fared rather better than the SP patients. The weight-gains were strikingly better in SH group than SP. The ESR. was also lowered more effectively by SH than by SP. treatment. The temperature and X-ray pictures, however, remained just the same in both groups. The H group of patients showed definitely less response radiologically than the SH and SP groups. Bacteriologically negative results were obtained in 67% of the SH; 55% of SP and only 37% of H. groups.

Streptomycin *cum* isoniazid (SH) was therefore, the best combination for effective treatment.

Chloromycetin or chloramphenicol.—The first of the broad-spectrum antibiotics discovered by Paul Burkholder, was shown to be active against certain gram-negative bacteria such as *B. abortus*, *E. coli*, *Salmonella schottmulleri*, and the gram-positive organism *staphylococcus aureus*. Smadel and Jackson reported on the remarkable chemotherapeutic effect of this drug on a number of rickettsiae and strains of the virus of psittacosis. It has a particularly remarkable action against the *Salmonella typhosa*, and so is unquestionably the drug of choice in this disease.

Chloramphenicol is readily and rapidly absorbed by the mouth but its distribution in the tissues is not uniform. The greatest concentration is found in the liver and kidneys; low values in the blood and spinal fluid.

Wolman (1952) reported a fatal case of aplastic anaemia and hepatitis occurring in a boy of 6 years following chloramphenicol therapy.

Finland states: "At least a significant proportion of the cases of blood dyscrasias that have been described may reasonably be attributed to this drug, but on the whole this complication is rare considering the frequency with which it is used. It should not be used repeatedly for minor indications. On the other hand in the treatment of serious and significant infectious diseases, it should be used without any hesitation."

The drug is usually given in the form of capsules containing 250 mg. each to a dose of 50 mg. per kg. of body-weight per day. When the patient becomes afebrile the dose may be reduced to 25 mg. per kg. of body-weight per day given in divided doses.

**Aureomycin.**—Discovered in 1948 by Benjamin Duggar in the Lederle laboratories aureomycin was produced and made available for commercial use even more rapidly than chloramphenicol. It is primarily a bacteriostatic agent and is bactericidal only in high concentration. It has been shown to be active against streptococci, staphylococci, certain *Salmonella*, *Brucella*, *Neisseria*, *B. subtilis*, *H. influenzae* and the viruses of psittacosis and lymphogranuloma venereum as well as rickettsiae. Although *Salmonella typhosa* is sensitive to aureomycin *in vitro*, its value in the treatment of this disease in man has not been established. It has been recently shown however, that aureomycin combined with chloramphenicol reduces the percentage of relapses considerably. Of importance to the clinician utilizing this drug is the fact that resistance of susceptible organisms to the drug develops quite slowly and so-called "dependent" strains have not yet been demonstrated. Aureomycin has a stimulating action on growth. Yodh and Vakil found it somewhat useful in 12 cases of typhoid, eight of which had bacteremia and thought a combination of this with chloramphenicol might reduce incidence of relapses.

Sainz states that aureomycin should be preferred to emetine for small children, pregnant women and persons with cardiorenal disease. Since it destroys both the cysts and the vegetative forms of *E. histolytica*, aureomycin should be an important aid in the control of the carrier state. It seems to be of value in amoebic hepatitis.

Aureomycin can be used without fear of serious toxic effects. Untoward side-reactions consist of frequency of stools, discomfort in the abdomen, epigastric distress, and vomiting.

The drug is given in the form of capsules or tablets each of 250 mg. or 50 mg. respectively and the usual dosage is 3 to 4 capsules per day for an adult.

Terramycin was discovered by John Smith *et al.* This drug is active *in vitro* as well as *in vivo*, and *Salmonella typhosa* and other organisms can be readily controlled. Antibacterial activity was shown against a wide variety of aerobic and anaerobic gram-positive and gram-negative bacteria and certain rickettsiae. The drug is bacteriostatic rather than a bactericidal. It is of doubtful value in amoebiasis; in peritonitis, it seems to be particularly useful. The most singly effective agent to date in secondary peritonitis is Terramycin, used 1 g. intravenously every 12 hours.

Terramycin is not effective in the treatment of measles, mumps, chickenpox, smallpox and trichinosis. It is not indicated in tuberculosis. It is administered usually in capsule form by the oral route. Untoward reactions are rare, only nausea, and occasionally vomiting and diarrhoea occur.

**Abuse of antibiotics.**—The promiscuous use of antibiotics for all cases really abuse, which is dangerous—since resistant strains are

likely to develop more often; there is also the possibility of super-infection taking place in the person under treatment with the antibiotic. Great circumspection has therefore, to be exercised in administering these drugs.

As the normal bacterial flora might undergo changes while the patient is taking the antibiotics these drugs should be used on fewer occasions and for shorter periods.

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#### SURGERY OF THE RHEUMATIC HAND

Notable advances in the medical and general management of rheumatoid arthritis have brought new hope to sufferers from this disabling disease, particularly in those whose condition is not far-advanced. In a recent paper, Sterling Bunnell (*Jour. Bone and Joint Surgery*, July 1955) has outlined surgical and manipulation procedures and pointed out that deformities of the hands associated with rheumatoid arthritis are not only due to joint changes but are also determined by contractures of muscles. Deformities in these cases are divided into two types—the "intrinsic-plus" position of a hand entering a coat sleeve, as compared with the claw-hand or "intrinsic-minus" position. Bunnell states that in flare-ups of the rheumatoid arthritis, the finger joints may be so distended with fluid that their ligaments become lax, and the joints are left so loose that they are an easy prey for muscle contracture. The deformities vary according to which set of muscles predominates in their contracture. The muscles are in spasm at first from irritation, but finally are fibrosed and shortened in fixed contracture. Much can be done in the early stages of mild elastic traction to maintain the position of function soon after contractures start and before the joints get fixed. Surgery should be used only in "burned-out" cases. One approach is by correcting the muscle balance and relieving the tension of the muscles. In some cases arthrodesis to restore the position of function is indicated for the wrist, for some finger joints, and even for both joints of the thumb. Tension may be relieved by tenotomy of the lateral bands or transverse aponeurosis in the fingers; this procedure allows the metacarpo-phalangeal joints to extend and the distal two joints to flex. The tension of all three sets of muscles may be relieved by shortening the metacarpals. This is best done at their bases, by removing a segment of bone and pinning them temporarily with Kirschner wires. Whenever the dislocations of the metacarpo-phalangeal joints can be reduced passively, this is the operation of choice. If, however, these dislocations, whether they are dorsal or volar, cannot be reduced, it is necessary to excise the metacarpal heads and perform arthroplasties.

The new joints should be pinned in alignment until enough fibrous tissue contracts around them and gives some amount of stability. Ulnar drift, may be relieved by the following procedure:—If the metacarpals are shortened at their bases, the metacarpophalangeal joints can be extended by tenotomy of the lateral bands and of the transverse aponeurosis. Each extensor tendon should be lifted free from the dorsal aponeurosis and transferred are sutured into a slit in the dorsal aponeurosis on the radial side of the knuckle. If arthroplasties are carried out, a similar procedure may be used: a tendon transfer of the *extensor indicis proprius* to the radial side of the lateral band of the index finger and a similar transfer for the little finger will furnish abduction to these fingers. By the use of these procedures, Bunnell has succeeded in restoring considerable function to pitifully crippled hands.—(*via Med. J. Austral.*, 3-3-'56).

#### A PRACTICAL SCHEME FOR PROVIDING MEDICAL AID TO RURAL INDIA\*

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*"A nation's health is perhaps the most potent single factor in determining the character and extent of its development and progress"*

Introduction.—"The Role of Medicine, as a social service to the community cannot be over-emphasized," said President Rajendra Prasad sometime ago. It is equally true that "no medicine however potent can be a substitute to human sympathy." It is in this spirit that this gospel of rural medical aid should be carried to the remotest parts of our country by medical personnel, who are wedded to the high ideals of the noble profession.

The problem of Public Health in our country is now dealt with at the Legislative level. Its urgency becomes obvious, from a study of the statistics periodically published. In a population of 357 millions, 75 to 90% live in about 500,000 villages; and roughly we have in all 50,000 qualified doctors, 45,000 of whom are independent practitioners, crowding the urban areas.

What is the result of this sad neglect of our rural areas? A health inventory of the nation reveals that 20 lakhs of deaths are due to malaria every year, 5,00,000 are victims of Tuberculosis, round-about 45 lakhs die of various other diseases excluding infant mortality. The story of infant mortality is a sad tale to itself; about 48% of the infants die before they complete their first decade. Maternal mortality is 2 lakhs i.e. the flower of the fair sex is sacrificed at the altar of sacred motherhood. Then we have 20 lakhs blinds resulting from infectious diseases and irritant remedies; more than 12 lakhs are afflicted with leprosy and there is the ever-increasing scourge of venereal disease to boot.

It is shocking to realize that the economic loss to the state by way of morbidity from these diseases is enormous, the figure for malaria alone being Rs. 20 crores (*Sinton*). The index of personal loss of life to individual families is given by the average expectation of life, which is very low for India, being 27 years, which fortunately is now tending to increase.

In the wake of our newly acquired freedom what has been our reaction and response to this Rural Medical Aid problem? The student of Public Health is aware that the Bhole Committee Report of 1946 drew up a scheme saddling the national exchequer to the tune of Rs. 1,000 crores, which our Government had to put into cold storage, as they were faced with other vital problems like food, housing, irrigation, industrialization, and defence to claim their

\*Specially contributed to the ANTISEPTIC.

prior attention. Our Government could ill-afford, in its present economic set-up to find this fabulous amount for Public Health; the Bhore Committee Report still remains our Bible as regards problems of Public Health and Medical Relief.

The only way to combat the problem at the present juncture is to think of cheap scientific medical aid, which is surely better than quackery, that has come to stay in India as a necessary evil. Since the victims in rural areas cannot afford to suffer till modern civilization gets into villages, till finances improve, and till times are propitious to carry very efficient medical aid to remote villages, let Government, as an emergency measure, train men and women called "Rural Health Personnel" giving about two years' training after Matriculation or School Final with small stipends if necessary. These personnel are to be recruited on the definite understanding that they will serve only in the rural areas and are eligible for pension etc., just as in the case of police officials and subordinates.

They should not be allowed to practise and will not be styled Doctors. They are to be stationed with a limited stock of essential drugs in the remote rural areas. Five to seven miles from the sphere of activity of these personnel, there must be a base hospital with beds, medical, surgical and maternity equipment with laboratory facilities etc., manned by medical graduates. This institution would supervise the work of about 5 to 10 of these "Rural Health Personnel Centres". These rural personnel ought not to treat a fever case for more than three days on their own; a blood slide taken on the first day itself may be kept or sent to the base hospital whenever necessary. Especially maternity cases and cases of enteric etc., should be moved by mobile vans to this Hospital. These are details which might be dealt with by an Expert Committee.

A cheap system like this would serve to solve this important problem without prejudice to the ideals of a uniform M.B., B.S., course or lowering the standard of medical education by having a shorter course. On the contrary we should plump for an up-grading of the present standard of the undergraduate course. This would incidentally solve the unemployment problem among medical graduates, since a good number of graduates have enlisted themselves in the Employment Exchange and 200 qualified doctors have had to leave for Burma. The proposed rural relief scheme will find employment for hundreds of matriculates in the country whose number registered with the Unemployment Exchange is legion. The whole hearted co-operation of the medical profession is required to pilot this scheme through the legislatures. This measure need be in force only till such time, as Government's finances permit to man the Rural Medical Aid scheme with a net work of medical graduates paying them adequate emoluments and making the villages attractive by providing suitable roads, transport facilities, and also social, educational, and cultural amenities.

## PREVENTIVE MEASURES AGAINST TUBERCULOSIS IN TEA ESTATES\*

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TUBERCULOSIS is a social disease, as social factors influence it most; and hence the conditions under which our people live must be satisfactorily improved. The economic condition of the people also plays a definite role in the spread of this disease and so this needs particular attention in the fight against the malady. The disease is preventable, and its prevalence and spread in our country are due to a gross disregard of the health laws. Over-crowding, lack of food, malnutrition, over-work, chronic alcoholism, and various infections, such as measles, whooping cough and diabetes, all predispose to tuberculosis.

"Tuberculosis has been assuming epidemic proportions and has been estimated to kill a person every minute in India. Next to malaria this is the biggest killer to-day and 5 lakhs of people are dying of tuberculosis every year and at least five times that number are suffering from the disease all the time" (Rajkumari Amrit Kaur).

It will be seen from the data furnished by the Tuberculosis Association of Assam, 64000 people were suffering from TB in the state. It has been estimated that about 10,000 persons die and about 50,000 persons suffer from this fell disease every year. Government alone cannot control and eradicate this scourge from India. This social evil must be fought from all angles, and every one should co-operate actively in the fight.

The tea-estates in our country are also equally concerned in this matter, and they too must shoulder a great responsibility in this national problem. In Assam, the tea-garden population comprises a tenth of the total population of the state, and the incidence of tuberculosis amongst them bears a definite relation to the incidence of the disease among the total population of the state. So in any anti-TB campaign undertaken by the State, preventive measures in tea-gardens must also be considered alongside.

The preventive measures should include: (1) B.C.G. vaccination; (2) early diagnosis of cases and their segregation; (3) a raising of the living standards of the population; (4) health education and propaganda; and (5) refresher courses for imparting the newer knowledge.

1. B.C.G. vaccination.—It has now been generally conceded that BCG inoculation is one of the major weapons to fight the

\*Specially contributed to the ANTISEPTIC.

spread of tuberculosis, although there have been differences of opinion among certain people about its efficacy. BCG vaccination is recommended for all tuberculin-negative reactors to enable them to develop some measure of immunity against the disease. But it is essential that the vaccination of all tuberculin-negative persons should be done within the shortest possible time if B.C.G. vaccination should afford real protection. In Norway T.B. is stated to have been completely rooted out by this method. The Government of India, with the help of UNICEF and WHO have started mass-scale B.C.G. vaccination amongst the tea-estate population of Assam. Supplemental vaccination should be carried out to protect the new-born who may need it, and who should not be left without this protection. B.C.G. confers the protection in about six weeks which is stated to last for many years.

2. Early diagnosis of cases and their segregation.—From the preventive point of view early diagnosis of Tuberculosis is most important. Every effort should be made to detect and diagnose the malady in its early stages so as to prevent open cases from spreading the infection. Pulmonary tuberculosis is spread amongst humans by the open cases, who throw out tubercle bacilli through their sputum; they are a real menace to children with whom they come into close contact.

Early diagnosis is possible only by radiography. So, a mass-screening of suspected people with the aid of a mobile X-ray unit would be the ideal. All cases detected should be isolated properly, and given suitable treatment. During recent years mass X-ray examinations and better medical facilities have made it possible to detect cases amongst the general population. "Such arrangements for early diagnosis and segregation of T.B. cases do not however, exist in Tea-estates; open cases of Tuberculosis remain in the family circle eating and sleeping in the same room with the other members of the family, both young and old until they die." (Major Lloyd Jones in "Standard of Medical Care for Tea Plantations in India"). It is gratifying to note that the Indian Tea Board has sanctioned Rs. 50,000 for the construction of a new T.B. Hospital attached to the Christian Hospital at Jorhat (Assam) to provide 20 beds for tea employees and 50 beds for tea-labourers. This is certainly a big step forward and will help in controlling the spread of the disease among the tea-plantation workers of Assam.

3. Improvement of living standards of the people. Poverty is largely responsible for the spread of the disease; it lowers the vitality and the resisting power of the body and renders them liable to infection. About 200 years ago England had the same problem in the matter of tuberculosis among her people. But with the improvements effected in sanitation, education, housing conditions, and mode of life the incidence of the disease fell remarkably. The

T.B. Expert Committee of the WHO advises improvement in nutrition, housing, education, occupational health, and in the standard of living of the people of the country in order to lower the incidence of the disease. The standard of living, and the housing conditions in the tea-gardens which are now far from satisfactory, should receive prompt attention from the authorities

4. Health education.—This is of supreme importance in tea areas, as well as among the general population. To make the nation healthy, the entire population should learn and observe the fundamental laws of health and hygiene. Tea-garden labourers ordinarily do not care to learn even the ABC of health laws. The importance of this preventive aspect of the disease should be brought home to them by systematic and constant propaganda, which must make them all wise about the causes for the spread of diseases, the methods for prevention, rules of diet, through posters, cinemas, radio lectures and lantern lectures. Dr. O. W. Hasselblad of the Ross Institute (India and Pakistan Branches) addressing the 6th Annual Hygiene Course held at Jorhat, stressed the need for health education among labourers in all tea estates.

5. Refresher course and newer knowledge.—Medical practitioners should undergo refresher courses in order to acquire the newer knowledge, ever accumulating, as regards tuberculosis. The Tuberculosis Association of India organizes periodical short refresher courses in different University centres to keep general practitioners in touch with up-to-date knowledge. The tuberculosis demonstration and training centres started recently in Delhi, Patna, and Trivandrum with the help of WHO, UNICEF and State Governments provide training in modern methods of tuberculosis control suited to Indian conditions with emphasis on domiciliary treatment. Medical Officers in tea gardens must also attend these courses and specialize in tuberculosis control. In every tea district there should be at least one doctor who has thus specialized and who can direct anti-T.B. campaign in the circle. The high incidence of tuberculosis amongst the workers in tea plantations is a matter of great concern to all. The President of the Assam and North Bengal Branch of the B.M.A., Colonel C. S. P. Hamilton in his presidential address in 1947 referred to the alarming increase in T.B. and entered a strong plea for better living accommodation for tea-garden labourers. The Government of Assam is opening T.B. centres in every district and town under the supervision of a T.B. specialist.

The governments, the medical profession, the INTUC and all other agencies interested in improving the health of the nation should consider sympathetically the deplorable condition of tea garden health and institute appropriate measures in tea-estates to combat this malady causing detriment to national health.

**Acknowledgement.**—My grateful thanks are due to Dr. D. N. Deb Sarma for kind help in preparing this note.

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## SALICYLATE POISONING IN CHILDREN

"Methyl salicylate (oil of wintergreen) and aspirin are salicylates which together constitute the most common cause of accidental poisoning in children. Salicylates caused 113 deaths in the United States in children under the age of 5 years during 1949 and 1950. In 1951 in the United States, 72 of 89 deaths caused by salicylates occurred in children less than 5 years of age. Twenty of the 72 deaths were caused by methyl salicylate, 31 by aspirin, and the remainder by an unspecified form of salicylate.

"Aspirin is a valuable drug in paediatrics, but because it is used so commonly the tendency is to discount the inherent danger of indiscriminate prescribing of the agent."

"TREATMENT :—The treatment of salicylism varies according to the time that elapses between ingestion of the salicylate and recourse to a physician. If the patient is seen within a few hours, the stomach should be thoroughly lavaged with water. Oxygen should be administered when salicylism is severe, to combat the tissue anoxia as well as the hyperpyrexia which may follow salicylate intoxication. To prevent hæmorrhage which may arise from hypoprothrombinæmia, synthetic vitamin K should be given; it is said that 1 mg. of vitamin K will counteract the effect of 1 gm. of salicylate. Barbiturates, paraldehyde and morphine should not be used, because they potentiate the toxic effects of salicylates. Solution of glucose should be used intravenously to counteract the ketosis, and also to provide sufficient water to prevent the dehydration which would hamper the urinary excretion of salicylate.....The initial solution to be administered intravenously up to six to eight hours after the ingestion of the salicylate should consist of equal parts of a 5 per cent solution of glucose in water and isotonic solution of sodium chloride, given at the rate of 4 to 5 cc. per kilogram of body weight per hour.....Six to eight hours after the ingestion of salicylate the solution should consist of one part of a  $\frac{1}{2}$ -molar solution of sodium lactate or bicarbonate, two parts of an isotonic solution of sodium chloride, and three parts of a 5 per cent solution of glucose in water.

The peak of the concentration of salicylate in the blood occurs two hours after ingestion. Normally, 70 per cent of the ingested salicylate is excreted within 24 hours; however, urinary excretion is diminished in the presence of dehydration and an acid urine. The recommended antipyretic dose of aspirin is 1 grain (0.065 g.) per year of age administered every four hours. Toxic effects are noted after the ingestion 1.03 grains per pound of body-weight. Death has occurred after the ingestion of 30 grains of aspirin by a 5 month old infant. A dose of 1.5 grains per pound of body-weight has been found to increase the content of salicylate in the blood to an average of 35 to 40 mg. per 100 cc. One teaspoonful of methyl salicylate equals 12 ordinary aspirin tablets in content of salicylate.

The problem of salicylate poisoning is stressed because of an alarming increase of preventable deaths caused by a common, seemingly innocuous drug.—(Proceedings of the Staff Meetings of the Mayo Clinic, 30: 417, via *Internat. Med. Dig.*, Jan. '56).

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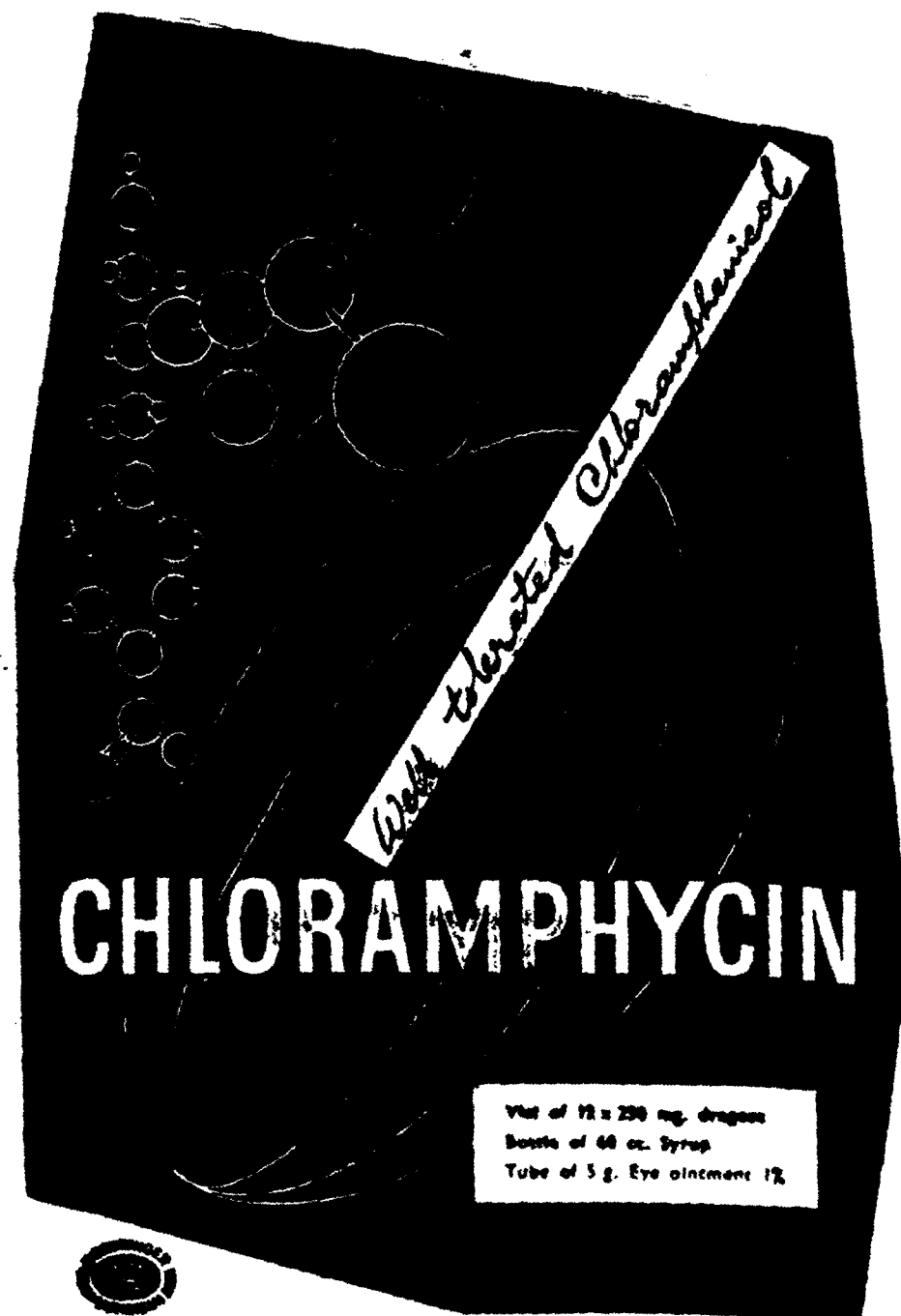
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## Editorials

### WELFARE OF CHILDREN

INAUGURATING the four-day session of the First National Conference on Child Welfare organized by the Indian Council for Child Welfare, at Delhi on the 9th May, Prime Minister Shri PANDIT NEHRU stated that child welfare schemes should be given the first place in the national development plans as, otherwise, we may be creating new problems in the future. The children of the country are not being looked after well and "this," said NEHRUJI, "makes me hang my head in shame. Though it is not possible to change the prevailing conditions overnight by magic, it is essential that every one of us should realize the extreme importance that should be attached to this problem of the welfare of children."

The Community Projects and the National Extension Service areas have so far covered over 1.5 lakhs of villages and are indeed, "of a revolutionary character which would, however, ultimately exercise a great effect on the rural life of India," provided they are worked in the right manner and in good spirit.

The Prime Minister drew the pointed attention of these projects and blocks to this most pressing problem of child welfare. Though they may not be able to handle it in an expert manner they must be able to popularize the various schemes and lay a good foundation. Child welfare in India is a big task because of the enormity of the problem. Thousands of children go without enough clothes and enough food not to talk of education and other amenities. It is estimated that today about 50% of the children in the country go to schools and the rest do not either because they cannot afford it or there are no schools in their areas. He asked the Conference to consider also the problems of the disabled, handicapped and orphaned children who had special problems that

merited the sympathy and consideration of all well-meaning citizens of India.

Mrs. INDIRA GANDHI who presided over the final session of the Conference said that as social service was essentially a voluntary function, State assistance through an autonomous body like the Central Social Welfare Board should be preferred to the formation of a Ministry of Social Welfare which, it was suggested, should be created under Government auspices. Among the many resolutions that were passed at this Conference one of the most important, to our mind, was that relating to the strengthening of parental care of children which should be considered as the most basic force in the promotion of child welfare by means of specific services like mothers' clubs, child guidance clinics and parent-teachers' associations.

Shri Dr. B. V. KESKAR, Union Minister for Information and Broadcasting who inaugurated an exhibition of juvenile literature, organized in connexion with the above conference, emphasized the need for a concerted effort to prepare adequate and suitable juvenile literature so that children's education may become easier, and more efficient. The production of suitable books for children is a distinctive field of publishing enterprise which has not so far been adequately developed in most Asian countries including India. The Government, in spite of their professed sympathy for child welfare, have done very little to encourage the production of wholesome literature for children. In this connexion we would like to stress the necessity for weaning children from the horror comics, to which they get stealthy access in spite of advice to the contrary from parents and teachers. This would be possible *only* if Government opened special Children's libraries, and arranged for "Children's Corners" in public libraries and also organized mobile libraries exclusively designed for children particularly in rural areas. This should be an effective means of encouraging the reading habit and stimulating the young minds to take a healthy interest in the world around them and beyond. It is the duty of the Government and all educational authorities to ensure that children get access to good and wholesome literature of every kind.

RAJKUMARI AMRIT KAUR, the President of the Indian Council for Child Welfare rightly laid emphasis on the need for a national blue print for child welfare work in general and a concrete plan into which all activities could be dovetailed and carried on in a more effective manner.

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*"Great occasions do not make heroes or cowards" said Canon Westcott, of Westminster, "they simply unveil them to the eyes of men. Imperceptibly, as we wake or sleep, we grow strong or weak, and at last some crisis shows us what we have become."*

## THE MADRAS STATE OPHTHALMOLOGICAL CONFERENCE

THE statement made by Dr. MEKHRI in his Presidential Address at the Madras State Ophthalmological Conference that "no very outstanding work had been done in ophthalmology in recent years, though older operations and older methods may have become improved" must have come with something of a jolt to those present at the Conference. Almost every branch of science pure and applied, has made such rapid and tremendous strides in the present generation that one would have regretfully to concur with Dr. MEKHRI that very little original work had been done by Indian Ophthalmologists. India, everyone knows, is one of the countries with the highest incidence of eye-diseases in the world and so one cannot complain that opportunities have not been plentiful. There is no doubt, that during recent years, the 'eye camps' sponsored by the Mysore State Medical and Public Health Departments have done much useful work in dealing with ocular manifestations of various kinds of deficiency diseases. But we gather the lack of adequate research facilities has stood in the way of turning the valuable findings to fruitful use. Dr. MEKHRI pleaded for the establishment of a Central Ophthalmological Research Institute with a well-equipped library, in order to enable ophthalmologists to carry out planned research and obtain training in the newer methods of diagnosis and treatment.

This suggestion should receive the highest consideration at the hands of the Planning Commission. There are a number of centres which afford training for a post-graduate Diploma in Ophthalmology but, we doubt, whether a uniform curriculum for the post-graduate course is adopted in all these centres.

The rapid industrialization of the country and the increasing tempo of life are, no doubt, adding considerably to the incidence of occupational diseases and industrial accidents and hazards. The inadequate and improper lighting of places of work is a universal limiting factor which requires immediate attention from the preventive and curative aspects. Eye-strain causes industrial fatigue ultimately resulting in manual inefficiency. It, therefore, becomes imperative that this problem is tackled as quickly and as energetically as possible. Dr. MEKHRI's suggestion to meet the situation and to make the country self-sufficient in this respect postulates the starting of institutes for the training of opticians. Optical goods with a high degree of accuracy and precision and the service of competent qualified technicians should be made available to the public which now require these aids. Then alone would it be possible to eliminate the charlatans who sell cheap and unsuitable stuff and ply their nefarious trade unhampered, taking advantage of the gullibility of the vast majority among the rural population.

Dr. MEKHRI was particularly severe in his criticism of the practice, which has lately assumed alarming proportions, of ill-equipped

and not fully competent men performing operations for cataract and other eye-conditions on a mass scale without making due provisions for the after-care of such patients and for guarding against the possibility of complications that may and do often arise. The remedy for this state of affairs would naturally be, to our mind, in the provision of efficient and qualified men in larger numbers to serve the rural poor.

This again takes us back to the vexed question of rural medical relief about which we have been writing in season and out of season and have yet to see that something *tangible* or permanent has been achieved.

### DRIVE AGAINST CANCER

CANCER, according to the latest statistics available, levies a toll of atleast two lakhs of human lives every year in India. The Government of India proposes to spend about 2½ crores of rupees in their Second Five Year Plan for combating this fell disease.

The initial step was taken on the 5th of May last when the foundation stone was laid by the Union Finance Minister, Shri C. D. DESHMUKH for the National Cancer Research Centre which will be attached to the new All India Medical Institute at New Delhi.

Welcoming the Finance Minister RAJKUMARI AMRIT KAUR, the Union Minister for Health said that Cancer was today one of the major problems of the world. Although, due to several difficulties, it had not been possible to provide adequate medical facilities for the people throughout the country, Government was striving hard and doing its best in this connection.

Cancer Research has now been taken up in every country of the world with great enthusiasm and in all seriousness and millions of dollars are being spent every year. No finality has, however, been reached; and the results of the researches have taken us no nearer to the solution of the problem of specific treatment. But enough data are being accumulated which point to the necessity of early detection of cancer cases which will certainly respond to radiological and other treatment that have been in vogue. So Shri CHINTAMAN DESHMUKH was perfectly right in calling for the widest dispersion of knowledge about the basic precautions against cancer. Medical practitioners must be kept posted not only with the basic facts about cancer but also about the "latest advances in our knowledge of the disease so that they might help, if not to diagnose, atleast to suspect in time the existence of this disease." He did not omit to advise the public who must, *pari passu*, learn to detect the earliest danger signals even without any specialized knowledge of the subject.

Stressing the need for systematic surveys on the incidence of the disease he rightly pointed out that on the one hand, medico-biological research must continue to be carried out in the laboratories, at the same time as socio-statistical surveys are systematically conducted to ascertain the incidence of the disease in the country. "From this can well start, apart from a general cancer campaign" said the Finance Minister, "also localized campaigns seeking to eradicate the practices that lead to the pre-cancerous conditions" which obtain in our households.

The National Cancer Research Centre will, we are told, serve as the nucleus for research and also as a centre for the treatment of cancer. It will have 50 beds to start with and is expected to be completed by the end of this year.

Perhaps it would not be out of place to suggest that this centre should also train technicians and nurses in large numbers, who could be sent into the country sufficiently equipped to carry out scientific surveys on the spot relating to the incidence of the disease among our men and women and teach our women how to detect early symptoms of the disease.

### GUIDED EXPERIENCE

The physician must be a student not only throughout his relatively prolonged academic training, but also henceforth, as long as he is engaged in his profession. Sir William Osler in commenting on student life said. "The hardest conviction to get into the mind of a beginner is that the education upon which he is engaged is not a college course, not a medical course, but a life course, ending only with death, for which the work of a few years under teachers is but a preparation."

That life-long qualities of a student must be essential to effective and adequate conduct on a professional level follows inevitably when one considers the change and progress currently being made in many aspects of the medical sciences. These advances are rapidly applied to the care of patients. No speciality or group in medicine is immune to the influence of progress and change. Medicine as an applied science now has far more to offer the sick than ever before....This makes failure or omission on the part of the physician potentially of greater consequence now than earlier in the history of medicine when therapeutic omissions may actually have been a blessing to the patient. Generally, it is true that powerful and effective therapeutic agents not only carry with them the capacity to do good, but may be harmful if injudiciously applied....It is an obligation tacit with the use of therapeutic thunderbolts that the physician be adequately informed concerning the limitations and dangers that their use may incur. This is but one of many reasons why the physician must accept the role of perpetual student.

Sooner or later every student must assume the initiative and responsibility for his own education if any real progress is to be made. Learning, like religion, is a personal experience. The ultimate goal of training is development of the individual's resources to such a state that he can continue on the journey unguided and unsupervised by others.—(*Qly. Bull. N.U.M.S.*, Spring, 1956).

## SURGERY

**Staphylococcal empyema.**—(Brownrigg. *Canad. M.A.J.*, 73: 787-789, Nov. 15, 1955, via *J.A.M.A.*).

Seventeen cases of pneumonia in infants and children, all caused by a penicillin-resistant micrococcus (*Staphylococcus*) were observed on the paediatric and surgical services of the St. John's General and St. Clare's Mercy Hospitals in Newfoundland, Canada. In 13 of the 17 patients the diagnosis was established clinically and adequate treatment was employed with properly selected antibiotics and drainage of empyema. Only one of these 13 patients, a 4½ month-old infant, died; autopsy confirmed the presence of empyema and bronchopleural fistula communicating with a lung abscess. In four additional infants, the presence of abscess, bronchopleural fistula, and empyema was not established clinically but was revealed by autopsy. The development of this complication was rapid but nonetheless insidious and difficult to recognize. All the patients were critically ill with respiratory distress and cyanosis, the development of fistula, pneumothorax, and empyema frequently caused little obvious change in the patient's condition. Early diagnosis and adequate treatment by a properly selected antibiotic and the prompt surgical treatment of complicating empyema with tube drainage with a closed underwater system to which suction may be added, intercostal drainage, or rib resection can bring about a dramatic reduction in mortality rate. There is no place for the employment of repeated aspiration as a method of treatment. In the author's patients, chloramphenicol was the most effective drug; *in vitro* sensitivity tests are essential to determine the drug of choice in the individual patient. Rapid change in drug sensitivity may occur. In four of the author's patients, multiple abscesses developed that were not complicated by fistula and empyema. These patients recovered, but follow-up roentgenograms showed persistent translucent areas that may have represented residual abscesses, sterilized by the

employment of antibiotics. A long follow-up period will be required to determine what sequelae, if any, will occur.

**Sympathectomy in persistent hemiplegia.**—(*J.A.M.A.*, Feb. 11, '56).

*Gifu City, Japan:*—Cervical sympathectomy is a useful procedure in selected patients with residual hemiplegia after cerebrovascular accidents, report Jiro Murakami and Eikicho Ando (Murakami Hospital).

In 31 patients whose hemiplegia showed no tendency to spontaneous improvement during several months following a stroke and who responded to a preliminary procaine block, a decided improvement resulted from sympathectomy in 22 (71 per cent). Increase in motor power and recovery of speech and improved gait, accompanied by a decrease in clumsiness of the hands, and in other neurologic symptoms, occurred successively or simultaneously.

The improvement was lasting in all except one patient whose symptoms gradually recurred over a period of 6 months. In this patient stellate ganglionectomy was performed, with renewed benefit.

The procedure used by the Japanese surgeons is resection of the lower pole of the upper cervical ganglion and its rami communicantes on the side of the cerebral lesion. This operation does not completely intercept the sympathetic innervation of the brain, but it was preferred to thoracic ganglionectomy and adventitia resection of the cervical vessels, which is a more formidable procedure, particularly in older people. Stellate ganglionectomy, although simple, was not favored because of frequent, obstinate, postoperative shoulder pain. Complications of the operation used were few, except for regular development of Horner's syndrome.

Murakami and Ando do not recommend cervical sympathectomy in the early stages of hemiplegia since spontaneous improvement is common, nor do

they now employ it when paralysis is marked, since results have been disappointing. Best results are obtained in patients without advanced cerebral arteriosclerosis, in whom a preliminary procaine block is followed by improvement in motor power and speech. (Presented at the meeting of the International College of Surgeons, Geneva, Switzerland).

**Treatment of penetrating wounds of the heart: Experimental and clinical observations.**—(*Surgery*, 37: 882, 1955 via *Int. Abst. Surg.*, Feb. '56).

In order to evaluate the operative and nonoperative treatment of penetrating wounds of the heart and pericardial tamponade, a series of experiments was performed to determine the factors influencing survival under these circumstances. More than 100 adult mongrel dogs were used.

The experiments included cardiac tamponade induced in the anesthetized animal by instilling saline solution in 20 to 25 cc. increments into the pericardial sac, and experiments conducted to determine the factors influencing survival in cardiac wounds and the effect of the myocardial damage itself upon the circulation. In experimental precordial tamponade relatively small reduction in the volume of pericardial fluid produces an immediate and strikingly favourable influence upon the circulation. The vasoconstrictor drug, norepinephrine, also proved to have a favourable effect upon the circulation through elevation of the systemic blood pressure. On the other hand, alternating positive pressure insufflation of the lungs in the presence of pericardial tamponade produced an unfavourable effect upon the circulation.

Approximately 30% of the animals wounded by a specially designed expandable blade died and 80% of these within the first 30 minutes. The majority of the dogs surviving the critical immediate period but dying in the next few hours presumably could have been saved by resuscitative measures. This suggests that patients who arrive at the hospital alive at least 30 minutes after injury have a type of cardiac wound that provides a reasonably good chance

for survival. These observations would seem to support the advocacy of the non-operative management of penetrating wounds of the heart.

Since January 1, 1951, the surgical staff at Jefferson Davis Hospital, Houston, Texas has treated penetrating wounds of the heart by nonoperative means as the method of choice. Between January 1, 1951, and October 31, 1954, 57 patients were admitted to the emergency ward with penetrating wounds of the heart. These included all patients admitted with any sign of life whatsoever, although some died immediately after admission and before any method of treatment could be instituted. Thus, among the 15 patients in whom pericardicentesis was not performed, 5 died in less than 10 minutes after arrival at the hospital. Among the 57 patients with cardiac wounds, 28 were treated by nonoperative means alone and in 11 (24.6%) cardiorrhaphy was attempted. Approximately 30% of the 57 patients died. However, the mortality rate of the group treated by operative means was five times that of the nonoperative group. It is true that the patients treated surgically were the ones with the most severe injuries, requiring more aggressive measures. On the other hand, among the 7 survivors in the operative group were 4 patients in whom thoracotomy revealed that exploration was unnecessary because the laceration had sealed off completely.

On the basis of the observations presented, nonoperative management is recommended in all cases, either as specific therapy or as a preparatory measure to emergency thoracotomy in the patients in whom response to this method of treatment is not maintained.

**Present state of the surgical treatment of chronic frontal sinusitis.**—(A. R. Bergara and A. O. Itoiz, *Arch. Otolaryngol.*, 1955, 61: 616 via *Int. Abst. of Surgery*, Feb. '56).

The most important reason for chronicity in frontal sinus disease is retention. When this is caused by extrinsic pathology it frequently yields readily to an intranasal surgical approach. Causes

of this nature include deviation of the nasal septum, hypertrophy of the middle turbinate, nasal polyposis, and constriction of the naso-frontal duct.

Causes of chronicity also are found within the frontal sinus, but these cases are more difficult to treat. Large sinuses frequently show deep diverticula, partial partition, and retention cells, and these factors favour retention with the added complication that chemotherapy and antibiotics have little effect.

In the surgical treatment of chronic frontal sinusitis the authors believe the first attempt should be an endo-nasal effort to secure good drainage. The second attempt is really two operations performed successively: first, a trans-maxillary ethmoidectomy according to the Ermiro de Lima technique, and then at once, the operation on the frontal sinus. They believe that in order to obtain adequate exposure it is necessary to mobilize the anterior wall of the frontal sinus with an osteoperiosteal flap and then to obliterate the sinus cavity with an autograft of fatty tissue taken from the anterior abdominal wall.

Local and regional anaesthesia is necessary. The incision of the skin is made in the eyebrow and undermined superiorly. After elevation of the periosteum the first trephine hole is made 3 to 4 mm. above the fronto-maxillary suture for exposure.

Through the trephine just made a curved probe is used to explore the limits of the sinus and additional trephine holes are made as near as possible to the periphery of the sinus but avoiding the orbital rim. Then a linear burr is used to link the perforations. The orbital rim is very fragile so that by applying two flat instruments through the osseous incision it is easily fractured and forms the hinge of the flap.

The mucous membrane is entirely removed and the anterior ethmoid cells are resected. The "agger-nasi" cells and cells surrounding the naso-frontal duct are removed.

Since, July 1949, the authors have not provided drainage from the sinus into the nasal fossa. It is not needed because the sinus is filled with fatty

tissue taken from the abdominal wall of the patient. The tissue is cut into small pieces but one of them should be large enough so that it can be fitted with a little pressure into the upper end of the widened naso-frontal canal, with care that it does not slip into the nasal fossa. Smaller pieces are carefully adapted to the periphery of the sinus, and with the others the rest of the cavity will be filled, but the last pieces should be inserted loosely, without pressure.

If the procedure of taking fat from the abdominal wall of the patient is to be avoided, fatty tissue obtained from a fatty tissue bank can be used. This bank is filled with material obtained in operating on a fatty tissue apron, which is later cut into pieces of about 4 by 4 by 4 cm., then washed and put into wide-mouthed bottles containing isotonic sodium chloride solution. These should then be placed in the autoclave for 5 minutes, after which they may be kept at room temperature until needed. Finally, the osteoperiosteal flap is returned to its original position and sutured.

The authors discuss other methods of obliterating a sinus, and describe several experiments illustrating the superiority of the use of free grafts of fatty tissue. They believe adipose tissue which has been boiled 5 minutes is superior to that which has not been so treated since it has suffered an osteofibrous transformation. Recently they have used with success a mixed implant formed by adipose tissue sterilized in the autoclave and a blood clot. From their observation the graft of adipose tissue was vital despite its being transplanted to a septic cavity and it resisted infection the same as any other connective tissue: with appropriate medical treatment it tended to become organized and not to be eliminated.

## OBSTETRICS & GYNAECOLOGY

**Aetiology of ectopic pregnancy: A new concept.**—(J. G. Asherman, *Obst. and Gyna.*, 6: 619-624, Dec. 1955, via *Jour. Am. Med. Assoc.*).

Of 325 women studied by the author, 251 were operated on for ectopic pregnancy at the gynaecologic and obstetric department of the Hadassah Municipal Hospital in Tel-Aviv, Israel, and 74 were private patients with various complaints and diseases who had a history of tubal pregnancy. Of these 325 patients, only one had had gonorrhoea: 4 had tubal tuberculosis; and 30 had had previous operations, 21 for ectopic pregnancy, 5 for ovarian cystectomies, one for appendicitis, one for a cause unknown, and 2 had caesarean section. Fifty-four women had been treated for primary or secondary infertility, and 181 had had one or more abortions, either spontaneous or induced. It is significant that nearly 56% of the 325 patients had had one or more curettages previous to their tubal pregnancy. Full patency or lack of anatomic changes of the fallopian tubes will not necessarily suffice to insure their normal functioning. The movements of the tubal muscles are as dependent on the hormonal as on the nervous system. Any disturbance in the neuro-endocrine balance is likely to bring about a change in the normal functioning of the tubes and may result in infertility or tubal pregnancy, depending on the severity of the disturbance. Among the 325 patients, there were 21 recurrent ectopic pregnancies, an incidence of 6.5%. The prevailing theory to the effect that ectopic pregnancy is caused by inflammatory or developmental changes in the anatomy of the tubes must be revised, although it may be correct in a certain percentage of cases. The predominant cause of ectopic pregnancy seems to be functional disturbance of the autonomic nervous system resulting from emotional conflicts and causing tubal dyskinesia. This cause is common both in ectopic pregnancy and in psychogenic infertility, explaining perhaps why both conditions occur frequently in the same woman. Before diagnosing psychogenically caused extrauterine pregnancy, one should eliminate the presence of all anatomic and endocrine disturbances as the probable causes.

**Eclampsia and its prognosis.**—(J. De Rezende, *Rev. fr. gyn. obst.*, 1955,

50: 165, via *Int. Abst. of Surgery*).

The author discusses eclampsia and its prognosis from the standpoint of a review of the literature and a repetition of his own experiences. Since, however, a portion of this material was originally published in sources which perhaps do not receive adequate notice by English language reviewers a few figures may be here included.

The author, together with Figueiredo, proposed in 1940 (*Rev. gin. obst.*, Rio, 1940, 34: 3), a classification of the toxæmias of pregnancy on the basis of the symptomatology. This grouping was suggested by that of Eden (*J. Obst. Gyn. Brit. Empire*, 1922, 29: 386) as later modified by Peckham (*Am. J. Obst.*, 1935, 29: 27).

This classification, appurtenant to the Brazilian material, consists of the following 11 divisions: (1) pulse equal to, or above 120; (2) systolic blood pressure superior to 200 mm. Hg; (3) extensive oedema; (4) massive albuminuria; (5) oliguria; (6) marked motor agitation and psychic excitation; (7) temperature above 39.5°C.; (8) icterus; (9) marked and persistent coma; (10) visual disturbances; and (11) number of crises more than 20.

The 5 last mentioned elements are considered to be of especial gravity. The condition is considered to be of benign character when none of these elements is present or when not more than one can be detected. When two are present the condition is considered as grave and when more than 4 are present it is considered as very grave. When any of the 5 last mentioned symptoms are present, the prognosis is considered to be sombre: this is what has been designated as "deviation downward," or deviation toward the bottom of the list, and presages immediate demise.

On the basis of the Eden-Peckham classification at that time the tentative figures for the Brazilian material were as follows: benign cases (25) afforded a mortality of 0; and grave cases (37) gave a maternal mortality of 27 per cent. Under the Rezende-Figueiredo classification the following figures were obtained: benign cases (41) with no

maternal deaths (foetal deaths 3); grave cases (23) with no maternal deaths (foetal deaths 7); and among the very grave cases (18) the maternal deaths amounted to 14 (foetal deaths 9).

It would require too much space to explain how this material was selected for purposes of comparison; it is merely important that it would seem to show the greater number of brackets included in the author's classification is necessary if the fate of the mother and child is to be adequately considered.

With respect to the ultimate fate of the mother the author quotes extensively from other workers (mostly English, American, French, and German), ending with the masterful report of Finnerty (*J. A. M. A.*, 1954, 154: 1075) who makes such a sharp distinction in the matter of ultimate results between those toxæmic conditions which are engrafted upon an already existing cardiovascular hypertensive disease, as shown by pre-gravid pathology of the eye grounds, and pure cases of toxæmia of pregnancy.

In this respect the author has made a study of 400 hypertensive pregnant women (6.6 per cent of 6,000 assisted at labour) of which 182 (45.5%) had pre-eclampsia and 13 (3.25 per cent) had eclampsia. In this group of hypertensive pregnancies the author includes those with the eye ground findings of cardiovascular hypertensive disease and those with the urinary findings of renal disease (nephrosclerosis). The maternal mortality in the group with the combination of hypertensive disease plus gravid toxæmia was 1.4 per cent and in the group with renal disease plus gravid toxæmia the maternal mortality was zero.

Based on his personal experience, the author notes that the incidence of recurrence of the toxæmia of pregnancy in subsequent pregnancies may be estimated at 5 per cent, and this despite adequate prenatal assistance. This figure he attributes to the persistence of the hypertensive phenomena from the previous attacks. Since the hypertension consecutive to gravid toxæmia may at times exhibit a malignant development, he believes that surgical treatment

is indicated. Surgical treatment is peculiarly efficacious and permits a new pregnancy without special danger of toxæmia (Newell and Smithwick: Pregnancy following Lumbodorsal Splanchnicectomy for Essential and Malignant Hypertension and Hypertension Associated with Chronic Pyelonephritis.—(*N. England J. M.*, 1947, 236: 851; *Surg. Gyn. Obst.*, *Internat. Abst. Surg.*, 1947, 85: 544).

**Caesarean section.**—(*Current Medical Digest*, Feb. '56).

The methods of assessing the condition of a foetus *in utero* are at present very imprecise, and therefore the decision to deliver by caesarean section in the interests of the child's life is far from easy. If the operation is delayed until labour is well advanced, the risk for both mother and child is increased: on the other hand, early caesarean section in anticipation of danger means that the operation may have been unnecessary. Although the operative risks are small, the total maternal deaths may be just as great with many operations carrying a low mortality as with few operations carrying a high mortality risk.

These problems have been examined by comparing the trends in caesarean section rates and in stillbirth and maternal mortality rates in Aberdeen primiparas. The stillbirth rates from birth trauma and unexplained intra-uterine death fell by  $\frac{1}{3}$  and the maternal mortality from difficult labour by  $\frac{1}{3}$  between the years 1938 and 1954. These reductions are attributed to (a) increased hospital confinement, (b) more extensive use of caesarean section, especially in primiparas over the age of 25, and (c) the avoidance of the effects of postmaturity by induction of labour shortly after term.

There is no doubt that recognition of the hazards of postmaturity has contributed substantially to the fall in the stillbirth rate, but the ideal practice is not easy to determine. Routine surgical induction of labour in primiparas aged 25 or over not delivered by the end of the 41st week has not had a

demonstrably better effect on the still-birth rate than a policy of induction only in cases with "clinical" evidence of postmaturity. Again, undue anxiety about the signs of foetal distress may lead to unnecessary caesarean sections.

**Therapy for cervical carcinoma.**—(*Modern Medicine*, February 1, 1956).

John L. McKelvey, and Myles G. Tompkins, University of Minnesota, Minneapolis, report that, as long as the only methods available for treatment of cervical carcinoma are irradiation and surgery, early recognition and treatment of the tumour are the most important factors in increasing survival.

Irradiation is the most effective primary therapy for uterine cervical cancer. However, for selected patients with radioresistant growths, tumours which recur or persist after radiation therapy, or coexisting disease which prohibits radiation therapy, surgical treatment is often life-saving. Of 63 patients treated surgically, disease has not recurred in 36, or 57%. Operative mortality was 6.3%. Results are best with early lesions.

Some method affording early recognition of radio-resistance, so that surgery could be performed while the extent of the tumour is slight, is needed. No accurate measure of radio-resistance is now available. When operation was done because of immediate histologic interpretation of inadequate response to irradiation, tumour was microscopically evident in only 5 of 9 specimens recovered; 4 patients had presumably unnecessary surgery. Adenocarcinoma is completely radio-resistant but may be effectively treated surgically if the lesion is localized to the cervix.

The super-radical procedure, pelvic exenteration, produced possible cure in only 1 of 9 patients. 4 operative deaths occurred. Increasing the scope of operations for extensive tumours through exenteration procedure is, therefore, not likely to increase survival significantly.

Of 5 patients treated surgically because of coexisting disease, 2 are alive three and eight years after operation respectively.

**Foetal mortality with prolonged pregnancy.**—(*Modern Medicine*, Feb. 1, 1956).

George B. Gibson, M.B., Queen's University, Belfast, Ireland, recommends watchful waiting rather than induction of labour to reduce foetal mortality with prolonged pregnancy.

Approximately 7% of pregnancies go fourteen days or more beyond the expected date of confinement. Foetal mortality among postmature infants is about double that among infants delivered at term. Intra-uterine anoxia during the first two stages of labour is apparently responsible for the increase.

Diagnosis depends on accurate estimation of the expected date of confinement. Naegle's rule is useful if the menstrual cycle is regular and not longer than twenty-eight days. If the date of quickening can be determined accurately, a pregnancy continuing for more than five months after this date may be assumed to be prolonged.

Labour should not be induced medically or surgically. If vaginal examination shows the cervix effaced and the head engaged in the pelvis, spontaneous labour should be awaited. Otherwise, the cervix should be stretched, the membranes stripped from the internal os, and a hot vaginal douche given.

Delivery should take place in the hospital and must be carefully managed. Foetal distress may be detected by auscultation of the foetal heart rate every ten minutes during the first stage and after every contraction during the second stage of labour. If distress is suspected, search for meconium staining should be made; membranes are ruptured if necessary. With distinct foetal distress, caesarean section is done immediately if forceps extraction is not feasible.

**Prevention of premature labour.**—(*Modern Medicine*, February 15, 1956).

C. V. Ward, McGill University, Montreal, states that adequate prenatal care effectively reduces incidence of premature births and increases foetal salvage.

Strenuous exercise, falls, long automobile trips, or excessive coitus must be avoided. Women who have previously had premature labours should be examined for uterine malformations, metabolic disorders, and other intercurrent diseases. Thyroid extract should be given throughout pregnancy for hypothyroid women. Oestrogen or progesterone therapy may prevent foetal loss but usually does not prolong gestation. Since the rate of prematurity increases as haemoglobin levels decline, prompt and adequate treatment of anaemia is essential.

Pregnant women must avoid contact with sources of infection, when possible, since a febrile reaction may initiate early onset of labour.

Toxaemia of pregnancy can often be prevented by proper diet, lowered fluid intake, and elimination of sodium. Such care may also prevent premature birth due to abruptio placentae, which is frequently associated with toxæmia. With premature rupture of the membranes, labour may be delayed for some time by bed-rest and sedation. Antibiotics or sulphonamides should be given to prevent intrauterine infection. Curtailment of activity may aid in preserving the membranes with breech presentation. Draining the excess fluid with a trocar may prevent premature labour with hydramnios. No way is known to prevent placenta prævia, but adequate blood replacement and bed-rest usually delay the onset of labour.

Adequacy of nutrition appears to be related to incidence of prematurity. Early births occur less often with overweight patients than with normal women; incidence of prematurity is greatest with underweight patients. If weight gain during pregnancy is normal, premature delivery is less likely.

## OPHTHALMOLOGY

**Ophthalmic use of terramycin and hydrocortisone.**—(*Medical Times*, Feb. 1956).

R. H. Dickinson (*American Journal of Ophthalmology*, 39: 839, June 1955)

reports the topical use of Terramycin and hydrocortisone singly and in combination in the treatment of 73 cases of external or anterior-segment diseases of the eye. Four preparations were used: (1) A Terramycin-polymyxin ointment, 5 mg. of Terramycin and 10,000 units of polymyxin B per gram in a white petrolatum base; (2) hydrocortisone ointment, also with a white petrolatum base, 25 mg. per gram; (3) Terramycin-hydrocortisone ophthalmic suspension in mineral oil, 5 mg. of Terramycin and 15 mg. of hydrocortisone per cc.; and (4) Terramycin-hydrocortisone ointment (white petrolatum base) with 5 mg. Terramycin and 15 mg. of hydrocortisone per gram. In 23 cases with external ocular infections or superficial injuries with possibility of infection, the Terramycin-polymyxin ointment was used; debridement when indicated was done before application of the ointment; the inflammation was promptly relieved in all but 2 of these cases; in these 2 failures the infection was "probably too deep" to be cured by topical application. Hydrocortisone ointment was used in 11 cases of allergies and non-specific inflammatory diseases, and gave prompt relief in all but 3 cases of reaction to chronic sutures after squint operations. Terramycin-hydrocortisone suspension was used in 8 cases of ocular inflammation due to infection and gave excellent results in all but one case of marginal blepharitis in a patient with parkinsonism and a poor blink reflex. The Terramycin-hydrocortisone ointment was used in 32 cases of various types of ocular inflammation with infection; and gave good results in all but 3 cases of abscessed chalazions in which the topical application apparently did not penetrate deeply enough. The author has found that Terramycin-hydrocortisone ophthalmic suspension can be employed for instillations during the day by patients who do not require eye dressings; a fistulous opening into the anterior chamber is a contra-indication to its use. The Terramycin hydrocortisone ophthalmic ointment is "particularly suited" for application at bedtime to remain in the eye all night, and for application with dressings.

**Uveitis in the contralateral eye following cataract extraction.**—(*Medical Times*, Feb. 1956).

B. Kronenberg (*American Journal of Ophthalmology*, 40: 205, Aug. 1955) reports 4 cases and reviews the literature on uveitis occurring in the unoperated eye after a cataract extraction in the other eye. This condition is observed only after extracapsular extractions. In these cases, the operated eye shows no inflammatory reaction, no reduction of vision or change in function: the unoperated eye shows marked ciliary congestion and numerous heavy keratic precipitates, which may coalesce to form a membrane. This reaction in the unoperated eye may occur within a few months after the cataract extraction in the opposite eye, or may not occur until several years after. This condition can be distinguished from sympathetic ophthalmia by the fact that there is no inflammation in the operated eye, also by the fact that in sympathetic ophthalmia the keratic precipitates are smaller and do not coalesce. The early removal of the lens of the eye affected after the cataract extraction in the opposite eye is indicated and results in a rapid improvement and useful vision. This type of uveitis following an extracapsular cataract extraction in the opposite eye, is explained as due to absorption of whatever lens matter is left in the operated eye, which sensitizes some patients to their own lens protein. The author is of the opinion that all patients in whom an extracapsular cataract extraction in one eye is indicated, should be tested for sensitivity to lens protein, and all those who show such sensitivity should be carefully watched and treatment instituted promptly if any signs of "sympathetic lens-induced uveitis" appear in the operated eye.

**Ophthalmia neonatorum.**—(Ormsby, H. L. 1955. *Canad. Med. Ass. J.*, 72: 576, via *Br. Jour. of Vener. Dis.*).

Conjunctival infections and chemical reactions in 8,418 newborn infants were noted. The first 1,703 children were treated prophylactically with two drops of Sulmefrin (a solution of 0.5 per cent

sodium sulphathiazole and 0.5 per cent. sulphadiazine) in each eye following cleansing of the infant immediately after birth. The next 1,570 children received 10 per cent sodium sulphacetamide to the conjunctival sac prophylactically. The next 3,125 children received 1% silver nitrate to the conjunctival sac, and the final 2,020 children had no treatment.

Chemical reaction in the conjunctival sac of a small percentage of the children was caused by 1% silver nitrate solution, but the incidence of staphylococcal, gonococcal, and inclusion conjunctivitis was low. When no prophylaxis was used there was a slight increase in the incidence of gonococcal conjunctivitis. The incidence of inclusion conjunctivitis was very similar to that when 1 per cent silver nitrate was used; 1 per cent silver nitrate has stood the test of time as an efficient prophylactic for gonococcal ophthalmia and has no harmful effects.

**Diagnosis and treatment of orbital tumours.**—(Foster, John, *Roy. Coll. Ann.* 17: 114-129, Aug., 1955).

Angioma is the commonest orbital tumour. Seventy per cent of the tumours arise within the orbit, 23 per cent from nearby structures, and seven per cent from distant sources. The classical symptoms are exophthalmos, oedema of the lids, defective vision with or without optic nerve changes, and diplopia. X-ray studies in 42 per cent of cases, show increased tissue density, distention of the orbit, erosion, rarefaction, fossa or dent, or dilatation of the optic canal or sphenoidal fissure. A lateral orbitotomy rather than a trans-frontal approach is advocated.

**Influence of coffee on ocular tension.**—(*Modern Medicine*, Jan. 1, 1956).

W. Leydhecker, Bonn University, Germany, believes that patients with glaucoma should avoid drinking large quantities of any fluid. However, contrary to the opinion that coffee increases ocular tension and should be forbidden, some patients may safely ingest small quantities. Provocative

tests with 0.4 gm. pure caffeine, which is approximately the amount contained in 45 gm. of coffee, should be made. If no abrupt change in ocular tension is detected, the patient is permitted to have one cup of coffee at a time.

Caffeine and water-drinking tests were done separately and on different days in a group of 164 patients with glaucomatous eyes with initial tensions below 30 mm. of mercury. Abrupt rises in ocular tensions occurred with caffeine in 7% and with water in 25.7% demonstrating that water is more harmful than caffeine in these patients.

## MEDICINE & THERAPEUTICS

### Consequence of pleural effusion. —(*Modern Medicine*, August 1, 1955).

Many patients with pleurisy recover completely. However, pleurisy with effusion is not an isolated local infection. Not infrequently, extrathoracic tuberculosis appears concurrently or subsequently and dissemination of tubercle bacilli after infection is rapid. Tuberculous lesions may also be found by liver biopsy. Therefore, acute sero-fibrinous pleurisy with effusion in a young adult with a positive tuberculin reaction and no demonstrable tubercle bacilli in sputum, gastric washings, or pleural fluid should be diagnosed and treated as tuberculous.

This form of pleurisy is apparently caused by perforation, in a tuberculin-sensitive person, of a subpleural tubercle with discharge into the pleural space of living and dead tubercle bacilli and caseo-necrotic material containing tuberculo-protein. The later course of the disease depends largely upon the infection dose. Perforation of a large, caseous lesion with persistent caseo-necrotic communications with the pleura will cause a serious disease state. Bed rest and chemotherapy are recommended to reduce the risk of subsequent relapse.

All of 141 young male adults who had primary serofibrinous pleural effusions while in military service reacted positively to intracutaneous tuberculin. None had chemotherapy for the initial illness.

The tuberculous aetiology of the original effusion was proved bacteriologically in 51 patients, 33 of whom later experienced relapse. Of 90 patients whose original fluids were not examined adequately or contained no tubercle bacilli, 59 later had active tuberculosis.

Relapse was as frequent with small effusions as with large ones. Pulmonary parenchymal lesions did not occur in areas originally obscured by fluid.

Return to normal physical activity after brief hospitalization resulted in relapse with active tuberculosis in over 90% of 66 persons. About 90% of 92 individuals had active tuberculosis within three years after onset of the original pleurisy. Extrapulmonary tuberculosis usually became evident within nine to fifteen months after onset of pleurisy.

### Barium reduction of intussusception in infancy.—(*Medical Times*, Jan. 1956).

E. J. Denenholtz and G. S. Fisher (*California Medicine*, 82: 8, Jan. 1955), report the use of barium reduction in 29 infants with intussusception; the age of the infants ranged from five to thirty-two months; 15 were less than one year of age. The duration of symptoms when the patient was first observed was from one hour to five days; in 8 cases symptoms had been present for less than twelve hours and in 10 cases from twelve to twenty-four hours; in 5 cases, more than seventy-two hours. The X-ray procedures and barium reduction were carried out in the radiologist's office, except in one instance; and the infant was not sent to the hospital unless the barium reduction was successful. The parents of the infant were instructed in methods of immobilizing the child and allowed to aid in the procedure. The barium enema was administered by means of child-sized Bardex catheter, under fluoroscopic control until the intussusception was recognized; then spot films were made during the process of reduction. Reduction was begun by elevating the enema container slowly above the table level; in most cases it was raised 3 to 3½ feet above the table, never more than 4 feet. If the barium did not enter the terminal ileum, the

patient was allowed to evacuate, and reduction procedure begun again; no more than three fillings were used in any case, and it was rarely necessary to use more than two fillings; in late cases and cases with complication, only one attempt at barium reduction was made. The barium reduction was successful in 22 of the 29 infants treated, including all in whom symptoms had been present for forty-eight hours or less; one of these patients was operated on "because of the family physician's insistence", but the intussusception was found to be reduced at operation. Early in the series 2 other patients were operated on because the radiologist was not certain that the intussusception was completely reduced, but it was found to be reduced at operation. In 5 cases barium reduction was not successful and operation was done; in these cases the duration of symptoms before barium reduction was fifty to one hundred and twenty hours; 2 of these patients died of toxæmia, complicated by peritonitis in one case. In the procedure of barium reduction of intussusception in infancy "close cooperation between the paediatrician and radiologist" is essential.

### Stomatitis: diagnosis and therapy.— (Review; *S. Clin. N. Am.*, 35: 617-627, 1955 via *Mod. Med.*, August 15, 1955).

Inflammatory oral lesions occur at all ages and in persons in both good and poor health. The lesions may be slight or severe, acute or chronic, or localized or diffuse. The aetiological factors in each case should be determined, if possible.

The erythematous, membranous, or ulcerative lesions of *bacterial stomatitis* usually occur next to the tonsil or at points of irritation. The patient commonly has foul breath, malaise, fever, and leukocytosis. To be considered causative, an organism must be found in large numbers on smear and heavy growth on culture. Darkfield studies are required in suspected syphilitic lesions, and biopsy in tuberculous ulcers and granulomas.

Gentle cleansing and frequent rinsing with an oxidizing solution are recommended. The antibiotic deter-

mined by sensitivity studies is administered until several days after the symptoms disappear. To prevent stomatitis and complicating cervical adenitis or inflammation of the salivary glands, careful attention to oral hygiene in debilitated patients is needed.

*Viral stomatitis* resembles bacterial infections of the mouth, but fails to improve with antibiotic therapy. Herpes simplex, the most common virus found, affects children and occasionally adults in an acute form with vesicle formation progressing to ulceration; cervical adenitis and sharp constitutional reaction may occur. The chronic form produces no constitutional symptoms. Herpes may be identified by complement-fixation test or inoculation of scrapings into a rabbit's cornea. Treatment is symptomatic. Repeated vaccination may reduce the tendency to recurrence.

The most common *fungous stomatitis* is thrush, caused by *Monilia* or *Candida albicans*. The condition is most frequent in young children, especially with malnutrition, poor oral hygiene, chronic hypo-parathyroidism, or after penicillin therapy. Separation of the pearl-gray pellicle leaves a shallow abrasion. Constitutional reaction is rare. The fungus is identified in scrapings examined in a hanging drop of 10% potassium hydroxide. Application of 1% aqueous gentian violet several times a day and correction of faulty oral hygiene bring prompt cure.

*Deficiencies* of riboflavin, nicotinic acid, vitamin C, or iron may produce oral inflammations that can be corrected by specific treatment. *Blood dyscrasias* such as pernicious anaemia, sprue, leukaemia, agranulocytosis, haemophilia, and purpura often cause mouth lesions.

*Food sensitivity* may produce vesicles which progress to painful, punched-out ulcers with gray exudate and narrow, hyperæmic borders. Individual lesions last seven to ten days. Recurrence is frequent. Specific diagnosis and treatment are desirable but difficult. Applications of aqueous gentian violet or tincture of benzoin may shorten the course.

Angioneurotic oedema, rapid swelling of the tissues due to an allergic reaction,

may endanger life. Epinephrine and an antihistamine should be administered promptly; tracheotomy may be necessary.

Stomatitis may be caused by *trauma, heat, or chemicals*. Leukoplakia, due to chronic irritation, is a pearl-gray or white lesion occurring in reticular striae or plaques anywhere in the mouth. Recognition of the pre-cancerous lesions calls for elimination of trauma and excision or cauterization with a ball point electrode if the condition does not disappear within two to three months.

Mercury, bismuth and gold therapy may produce swollen, bleeding gums. Bismuth may also cause grayish deposits in the gums. Lead produces deposits without inflammatory reaction.

No specific treatment is known for the mouth lesions associated with *pemphigus, erythema multiforme, and lichen planus*.

*Non specific ulcerative stomatitis* produces recurrent, painful ulcerations of the mouth and pharynx leading to cicatricidal deformities. Aureomycin gives temporary improvement but does not prevent exacerbations.

*Fordyce's disease* shows fine, pale or yellowish, hypertrophied sebaceous glands on the lips or buccal mucosa. No treatment is required.

*Black hairy tongue*, due to elongation of filiform papillae on the dorsum of the tongue, requires no therapy. The patient should be reassured.

**Toxic reactions to digitalis.**—(*Modern Medicine*, Aug. 15, '55).

F. Lowell Dunn, University of Nebraska, Omaha, believes that toxic reactions to digitalis are becoming more prevalent because of increased potency of preparations and the widespread use of (1) large single-dose techniques, (2) digitoxin, and (3) potent diuretic agents. In addition, cardiac patients are increasingly of older age groups. The purified digitalis products now available usually do not produce gastrointestinal irritation to warn of toxicity. In some instances, the toxic dose and the therapeutic dose are almost the same.

The type of preparation to be used should be selected according to the

individual's needs, availability of the patient for re-examination, and necessity of frequent readjustment of digitalis dosage because of other treatment that the patient is receiving. When digitoxin is administered, the patient should be observed closely because the rate of excretion is usually over-estimated. Digitoxin reaches full effect in six to ten hours; effects are more rapid with gitalin, digoxin, or lanatoside C.

Digitalis is especially toxic to patients with potassium deficiency. Generally, adequate food intake precludes a serious deficiency. When a deficit occurs, restoration of potassium may remove toxicity or permit higher doses.

Procaine amide, which reduces the incidence of arrhythmias caused by digitalis, is most effective if the patient is pre-treated with 5 g. of potassium chloride orally and then given procaine amide, 1 g. after one hour and 0.5 g. every three to six hours.

**Reserpine Serpasil in the treatment of hypertension.**—*Am. J. M. Sc.*, 228: 21-35, 1954. *Abst. J.A.M.A.*, 2:10-54).

Reserpine (Serpasil, a pure alkaloid of *Rauwolfia serpentina* was given orally to 62 unselected ambulatory patients with mild to severe hypertension. The initial dose of reserpine was usually 1 to 2 mg. per day given in divided doses after each meal and at bedtime. If excessive sedation occurred, the dose was temporarily decreased, and after several weeks it was again increased to the previous level. If no reduction of blood-pressure, it was increased until as much as 1.5 mg. was given four times daily or a total of 6 mg. daily to some patients in an effort to obtain maximum effectiveness. The patients were treated for 1 to 7 months. They were divided into two groups, one of which comprised 34 patients with an average diastolic pressure of more than 120 mm. Hg. before the start of the treatment, and the other comprised 28 patients with an average diastolic pressure of more than 100 but less than 200 mm. Hg. approximately half of the patients treated obtained a significant reduction in blood pressure. All but two of the patients who became normo-

tensive were from the group of patients with less severe hypertension. The patients who were treated for one to two months obtained just as good results as those who received the drug for two to seven months. There were no serious side-effects. Doses of 1 to 3 mg. of reserpine in 100 cc. of 5% dextrose in distilled water were administered intravenously to 17 patients. Thirteen of these patients demonstrated a significant reduction in blood pressure about one to four hours after administration of the drug, and half of them became normotensive. Although reserpine had a prominent sedative effect on the authors' patients, this effect diminished or disappeared after prolonged therapy without a concomitant increase in blood-pressure; some patients showed a significant blood pressure response without sedation. Reserpine, therefore, appears to lower the blood pressure through actions other than those related to its sedative properties. There was little difference between reserpine and extracts of *Rauwolfia serpentina* containing multiple alkaloids when compared as to side-effects and blood-pressure reduction in patients with hypertension.

**Smoking habits of physicians.**—(*Modern Medicine*, Aug. 1, 1955).

Leonid S. Snegireff, and Olive M. Lombard, Harvard University, Boston, report that the tendency in physicians is toward less cigarette smoking. One explanation is the growing interest in the possible relationship between cigarette smoking and lung cancer.

Smoking habits of 4,171 physicians were studied. The types of practice were combined into 3 main groups on the basis of the percentage of non-smokers. Group 1 comprised specialties with rates for not smoking that were above the average for all types (33.5%) and included physicians specializing in preventive medicine and public health, thoracic surgery, dermatology, neurosurgery, orthopaedics, paediatrics, ophthalmology, pathology, otolaryngology, thalmonology, urology, internal medicine, physical medicine, radiology, and chest diseases.

Group 2 included the general practitioners, whose rates for non-smoking were close to the average. Group 3 was comprised of specialists in anaesthesiology, industrial medicine, administration, general surgery, neurology and psychiatry, gynaecology and obstetrics, ophthalmology and otolaryngology, and proctology. Rates for non-smoking were below the average in this group.

The percentage of physicians who had never smoked, had stopped smoking, or were light smokers was significantly higher in group 1 than in either group 2 or 3. The percentage of physicians smoking cigarettes was lowest in group 1 and highest in group 3.

Among physicians who smoked, a significantly higher proportion of those in group 1 accepted the possible relationship between cigarette smoking and lung cancer than did those in groups 2 and 3.

Physicians tended to give different advice to heavy cigarette smokers; 55% of group 1, 64% of group 2, and 63% of group 3 advised reduction in cigarette smoking, and 36% of group 1, 34% of group 2, and 28% of group 3 recommended that heavy users stop smoking entirely.

## PAEDIATRICS

**The constipated infant.**—(*Current Medical Digest*, Jan. '56).

One of the most common complaints from mothers is "my baby is constipated." It is also reasonably safe to assume that many such complaints are more fantasy than fact.

When constipation does exist, it is very probable that it is caused by one of the following:—(1) Dietary deficiency; (2) nutritional deficiency; (3) anatomic defect, either congenital or acquired; or (4) functional defect.

The most common dietary deficiency producing constipation is the failure of adequate food-intake. The most striking example of constipation associated with small food-intake is that seen in the baby with pyloric stenosis at about 2 or 3 weeks of age.

Formula prescriptions high in protein, low in carbohydrate are very likely to produce dry, hard, putty-like fecal masses, which move slowly along the intestinal tract. Milk with a high fat-content likewise frequently produces large soapy curds in the intestinal tract which may interfere with normal bowel emptying.

The practice today of constructing the formula from milk, with not more than 3.5% butter fat, and added carbohydrates that furnish at least 25 to 30% of the total calories, has resulted in the production of a very digestible mixture which generally is not constipating to the artificially fed baby.

Babies with infections or those who lose their appetite from some other cause, such as hot, humid weather, for short periods of time may and will become constipated as a result of decreased food-intake.

Babies chronically ill with very poor appetites and who are finicky in their eating, such as the infant with nephritis, neoplasm, or congenital heart disease, may well develop constipation resulting from poor nutritional mixtures.

Constipation arising in the otherwise normal healthy infant may be the result of one of several anatomical defects, of which anorectal stricture or stenosis is probably the most frequent. These defects can be easily diagnosed by rectal examination. The sphincter of most infants is tight to the examining finger, but will usually relax a few moments. In the presence of stricture a tight band usually is felt 2 to 3 cm. in the rectal canal. Such a band is the result of incomplete absorption of the membrane formed by the fusion of the hind gut and the proctoderm late in fetal life. Strictures of this sort have been reported by many observers, with frequency varying from 12 to 39%. The symptom of constipation, however, was present in less than  $\frac{1}{4}$  of those with stenosis, and evidence of stricture subsided in the majority by the 6th or 7th month.

The presence of fissure-in-ano resulting from the passing of a hard stool, the injudicious use of a rectal thermometer, unlubricated tip of enema tube, or other foreign body inserted into the rectum

may easily produce constipation on a reflex basis. After a few painful defecations the infant will hold his stool rather than endure the pain involved. Thus a vicious cycle is established of further drying the stool, making it harder and more painful to pass. The older infant may recognize that the urge for a bowel movement is associated with the ingestion of food, and because of the discomfort accompanying defecation may eat less. The mother may become suspicious of a fissure, particularly when the baby's stool is streaked with fresh blood. Careful inspection of the anorectal mucosa in this situation should reveal the presence of the fissure. Functional disturbances in the enervation of the gut are responsible for extremely severe constipation in infancy. Very often the symptoms of obstruction are manifest in the 1st day or 2 of life, or in milder forms within the 1st week or two.

In the otherwise healthy, happy infant, the importance of establishing good bowel habits cannot be over-emphasized. When the baby reaches the age of 3 or 4 months and the number of stools daily have reduced to 1 or 2, the mother may be encouraged to try to stimulate a little regularity in the infant either at bath time or after his first morning meal. Laying the baby on his back on a suitable table and flexing his thighs on the abdomen, with gentle pressure being exerted on the soles of his feet, simulating the sitting position on the toilet seat, may help condition the reflex of bowel emptying. At 6 or 7 months, when baby is sufficiently strong to sit for 10 or 15 minutes on a baby toilet seat securely fastened to the family toilet and equipped with a foot rest, at a definite time after a meal, encouraging a bowel movement may be helpful. Such occasion should not be a part of the baby's playtime, and attempts at coercion should be discouraged. The above procedure is not aimed at "housebreaking" so to speak, but is merely an attempt to establish good bowel habits.

The use of enemas and suppositories should definitely be discouraged in this procedure, although occasionally the baby who is slow to respond when in this position will do so if a well lubricated rectal thermometer is gently

inserted, and after a few occasions may establish some degree of regularity.

If the stool is hard and dry, causing much straining with each attempt to pass it, the instillation of a few cc. of mineral oil into the rectum with a baby ear syringe may produce the desired effect. Mineral oil by mouth during infancy should be discouraged because of the danger of aspiration and subsequent lipoid pneumonia.

On rare occasions, a laxative may be helpful. The easiest one to use is milk of magnesia, 2 to 4 cc. added to the formula. The addition to the formula of  $\frac{1}{4}$  to 1 oz. of Karo may be necessary with some infants to keep the stool soft. Also, the addition of fruits, particularly a little prune puree or prune juice, often is extremely beneficial as well as an increased amount of cereal and vegetables in the diet.

The constipated baby with malnutrition associated with chronic disease presents a greater problem, because of the general lack of muscle tone and in particular, a lack of appetite. It is sometimes very difficult to keep his stool soft and easily moveable. Such an infant may require small amounts of laxative agents at frequent intervals, and possibly enemas, until his underlying condition is corrected. Soapsuds enemas have been widely used in this connection, but it is doubtful if the physician who prescribes such a measure has ever had one himself. They are very irritating, to say the least. A warm tap water enema of a few ozs. works quite well. A much more satisfactory medication, which is not a laxative nor is it a lubricant is that of Aerosol O. T. (Dioctyl Sodium Sulphasuccinate) which acts as a wetting agent in keeping the stool soft. This may be given by mouth in a 1% aqueous solution, 2 to 3 cc. added to the formula or fruit juices.

Methylcellulose preparation added to the baby's diet is also helpful in increasing the bulk. In unusually resistant constipation the combination of Aerosol and Methylcellulose has proved very helpful.

Constipation resulting from stricture

in the recto-sigmoid area may require rather frequent dilatations which can be easily accomplished by holding the finger in place for at least 4 or 5 minutes each time. Because of the pain created by this procedure, a local analgesic ointment, like Nupercaine, may be necessary.

Small anal fissures frequently respond very well to the instillation of a few cc. of mineral oil into the rectum with a well-lubricated tip of an ear bulb syringe. Aerosol administered either by rectum in a similar manner, using 1% aqueous solution, 2 to 4 cc., or by mouth is particularly helpful in keeping the stool soft. If the fissures do not heal spontaneously after the stool is softened, application of silver nitrate to the denuded area may be beneficial.

#### Retrolental fibroplasia in premature babies.—(*Mod. Pub. Health*, 1955).

The occurrence of blindness in premature babies has been intensively studied in recent years. Retrolental fibroplasia was first described in 1942 by Terry in the *Am. Jour. Ophthalm.* The disease chiefly affects premature babies and most commonly commences at the end of the first four weeks. The disease is bilateral and blindness occurs in a large proportion of cases due to the separation of the retina and the growth of a characteristic mass of embryonic connective tissue behind the lens. There is evidence that the cause of this condition is the use of high oxygen concentration in the incubation nursing of premature babies. The disease incidence is higher in premature babies under 4 lb. and highest in those under 3 lb. Normally the arterial blood in the foetal circulation has a comparatively low oxygen level and in any event certainly lower than the concentration of oxygen induced under incubation conditions by the unchecked use of oxygen. The period of survival of premature babies depends on the birth weight, the shortest survival period being found in those infants with the lowest birth weight.

## Reviews of Books and Periodicals

**Diet in Health**—By BHABA BANJAN SEN GUPTA, M.B., B.S. and DEBA-  
BRATA CHATTERJEE, M.B., B.S., 1956.  
Pp. 48. Price: Re. 1.

This booklet has been compiled at the request of Messrs. Calcutta Chemical Company Limited, Calcutta. Its object is to educate the lay public and medical students on a subject of primary importance and on which there have not been many authoritative pronouncements. A survey of the diets taken by the average Indian reveals that it is in most cases imbalanced and insufficient. Low economic condition and ignorance are perhaps largely responsible for this. Education of the people therefore, by disseminating scientific knowledge on this subject is very necessary. The authors should therefore, be congratulated on producing this little booklet. It begins with a preliminary chapter on proteins, carbohydrates, mineral salts and other vitamins necessary for health. The effects of cooking on the nutritive value of foods is dealt with in a small paragraph. The charts on vitamins, balanced diet, proper daily diet for members of the different professions with approximate food values in pregnancy and lactation and the chart on food values of the cereals, vegetables, nuts and foods like meat,

fish, eggs, dairy products are given in a very instructive manner. This is a very useful publication.  
U.R.R.

**German Medical Journal.** The above is an English translation of the DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT. The GEORG THIEME Verlag, Stuttgart will publish it as a monthly.

The first number (January '56) we have received contains a number of useful articles such as those on A New Anti-diabetic Principle, an Effective Oral Antidiabetic Drug, the influence of Surgical and Medical Treatment on the Life Expectancy of Hypertensive Patients etc. Separate sections are devoted to 'Questions and Answers' and to abstracts of current literature. The general get-up, illustrations and photographs are good.  
U.R.R.

### BOOK RECEIVED

**ACTH and Cortisone in General Practice**—By J. R. GOYAL, M.B., B.S., 1956 Edition, Pp 53. Medical Review of Reviews, P.O. Box 1160, Burn Bastion Road, Delhi. Price Rs. 3/-

## News and Notes

### Public Health in USSR

By the number of physicians, USSR takes now first place in the world. Whereas in the USA there is 1 physician for every 725 inhabitants, in France, Britain and the Netherlands for every 1,100 in Sweden 1,300, in Turkey 2,900 and in Iran 8,300, in the Soviet Union there is one physician for less than 700 inhabitants, and in some of its Republics for less than that number. For instance, in Azerbaijan, Georgia and Armenia one physician serves 400-500 inhabitants.

In 1955, the number of physicians was more than double the figure for 1940.

In the past five years 79,300 young physicians and 203,700 medical workers with secondary education were added to the staffs of public health establishments. 79,900 medical workers received education at mass-scale centres.—(News from Soviet Union, April 17th).

### Supply of Surgical Instruments

The Union Government have constituted two separate Committees with Sri Dr. U. Krishna Rau, M.B., B.S., M.L.A. as Chairman. One of the two Committees will assess the requirements of surgical instruments and the other

JUNE '56]

NEWS AND NOTES

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of the X-ray equipments for the whole country under the Second Five Year Plan. The preliminary meetings of the two Committees were held in New Delhi on February the 28th 1956. The members went into the whole question and after a careful consideration of all the relevant points have decided to ask the manufacturers to furnish the Committee within three months, detailed information on the possibility of their manufacturing the necessary instruments in India itself, as also the financial and technical help that they may require for this purpose.

The Surgical Instruments Committee will, we learn, meet again in Bombay in the month of June 1956, while the X-ray Equipment Committee will meet at Delhi during the same time.

### Funds for Rural Health Services

The Executive Director of the UNICEF announced last month that a million dollars (Rs. 47,50,000) will be recommended for sanction of the UN., for the development of rural health services, throughout India. She will get also 855,000 dollars towards her emergency feeding programme which she will share with Korea.

UNICEF sources state that an allocation of 25,000 dollars for fellowships at a Calcutta training centre will enable ten non-Indian doctors to take post-graduate training at the centre in Maternal and Child health.—(Bull. U.N., 11-3-'56).

### New Equipment and Technique for Blood-Protein Tests

An inexpensive and simple electrophoretic equipment and procedure for obtaining blood-protein patterns for diagnosis and prognosis has been developed at the Indian Institute of Science in Bangalore. Prof. Giri, Head of the Department of Bio-chemistry at the Institute, claims that the new technique, designated the "Agar electrophoresis" is a definite advance in electrophoresis and offered promise of development into an important analytical tool in the hands of medical men and laboratory workers. The technique is simple enough for introduction into big and

small hospitals for the examination of serum samples.

### Public Health Engineering

Mr. O. C. Hopkins, Adviser on Public Health Engineering, Ministry of Health, Government of India, met the Ministers of Health and Public Works, of Madras on 6-3-'56. Mr. Hopkins said that the Central Ministry of Health were considering a training programme in connexion with the national water supply and sanitation scheme, hoped that short-term courses for engineers in public health engineering existed in the Engineering Colleges at Roorkee and Guindy and at the All-India Institute of Hygiene and Public Health, Calcutta.

He added, "We discussed with the authorities in the various States, how best Government can put through this programme and find out how many engineering assistants could be trained. These will be utilised for implementing the national water supply and sanitation programme."

A course in Public Health Engineering is already being conducted in the Madras Engineering College at Guindy.

### The Leprosy Research Institute, Madras

Rajkumari Amrit, Minister for Health, presided over the meeting of the Governing Body of the Central Leprosy Teaching and Research Institute at Tirumani on 3-3-'56.

The meeting was attended by the Madras Minister for Health, the Director General of Health Services and the Secretary of the governing body of the Institute, the Director of Medical Services, Madras, the Director of Public Health, Madras, Dr. C. G. Pandit, Secretary, Indian Council of Medical Research, and the Secretary, Hind Kusht Nivaran Sangh.

The Governing body discussed routine matters relating to the budget for the coming year and approved the scheme for housing the Institute in a new building to be constructed at a cost of Rs. 6'34 lakhs in Tirumani. Work on the construction of the new building, which will consist of one laboratory

block and a clinical block, will commence shortly.

Rajkumari Amrit Kaur also paid a visit to the Polambakkam Leprosy Centre, accompanied by Dr. Hemerijekh.

#### Russian Paediatricians for India

An advance team of two Russian paediatricians and two interpreters came to Delhi in Feb. '56 in connection with the development of the paediatric centre at the Kalavathi Saran Children's Hospital which is now located in the premises of the Lady Hardinge Medical College, New Delhi. Another team of experts and technicians has since arrived and joined the first team.

#### Need for Ophthalmic Service in Rural Areas

Speaking at the 17th All India Ophthalmic Conference held at Aligarh on the 22nd of February last Rajkumari Amrit Kaur urged for the closest scientific and cultural cooperation among the nations of the world for the benefit of suffering humanity. She stressed the need for an ophthalmic service for the rural population in India, "Science knows no barriers", said she "neither geographical nor those of colour, race and creed." In a country with a population of 365 million people, there are only about 500 ophthalmic surgeons with post-graduate qualifications in this speciality. The need for urgent help in the treatment of eye diseases amongst village-folk is indeed very pressing and calls for prompt help.

#### Excessive use of Insecticides for Food-Preservation—Injurious

A warning to the trade, the profession and the public appears necessary in view of the findings arrived at by the Research-workers of the Central Food Technological Research Institute, Storage Section headed by Dr. S. V. Pingle to the effect that the daily use of jowar, Bengal gram, and potatoes sold in the Mysore and Bangalore bazaars now, which have been mixed with a large quantity of in-

secticides, is causing unknown diseases, to consumers which may prove fatal later on. The Institute informed the Mysore Public Health Department of the serious consequences of indiscriminate application of insecticides. Dr. Pingle said, at present insecticides nearly 200 to 400 parts per million were being applied by traders to check insect-post attacks. The persistence of the residue even after washing and cooking food grain exposed to the action of the insecticides in the doses applied was still as high as 30 per cent, which is far in excess of the permissible limits of human tolerance—which is only seven parts per million. Persons who eat food made from such articles would suffer from necrosis of the liver according to Dr. Pingle. "It took two years for the symptoms to appear and there was no cure," he said.

Fumigation by the chemical called Ethylene dibromide has proved effective in ridding godowns of insect pests and in preserving food-stuffs. The CFTRI has opened a centre in Mysore where traders could get disinfection with this new chemical at a nominal cost of one anna per bag.—(J.C.F.T.R.I., Mysore).

#### Committee for Tax Exemption

The Government of Bombay has appointed a committee under the Chairmanship of Dr. M. D. D. Gilder, M.D. (Lond.), F.R.C.S. (Eng.), M. P. for examining applications for exemption of spirituous medicinal preparations from tax under the Bombay Sales of Intoxicants Taxation Act, 1953. Dr. B. B. Yodh, M.R.C.P. (Lond.) in Vice-chairman of the Committee. The other members of the committee are Shri Bapalal G. Vaidya Shri O.H. Nazar, Ayurved Mahavidyalaya, Surat; Dr. Sarosh R. Wadia, M.B.B.S. (Bom.), M.P. (H) Lond., Shri M.Y. Lele, A.V.P., Principal, R. A. Podar, Ayurvedic College, Bombay; Dr. N. K. Dutta, M.B. (Cal.) D. Phil (Oxon), the Drug Controller to the Government of Bombay; the Director of Publication and Excise; and the Collector of Sales Tax, (Secretary).

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Edgar A. Haunz and Grand Forks, J.A.M.A., 159: 1611-1618, 1955.

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J. D. N. Nabarro and J. M. Stowers, The Medical Press, Oct. 14, 1953, P. 371

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Daniel W. Hayes, The Journal of the Louisiana State Medical Society, Vol. 106, No. 10, 387, 1954.

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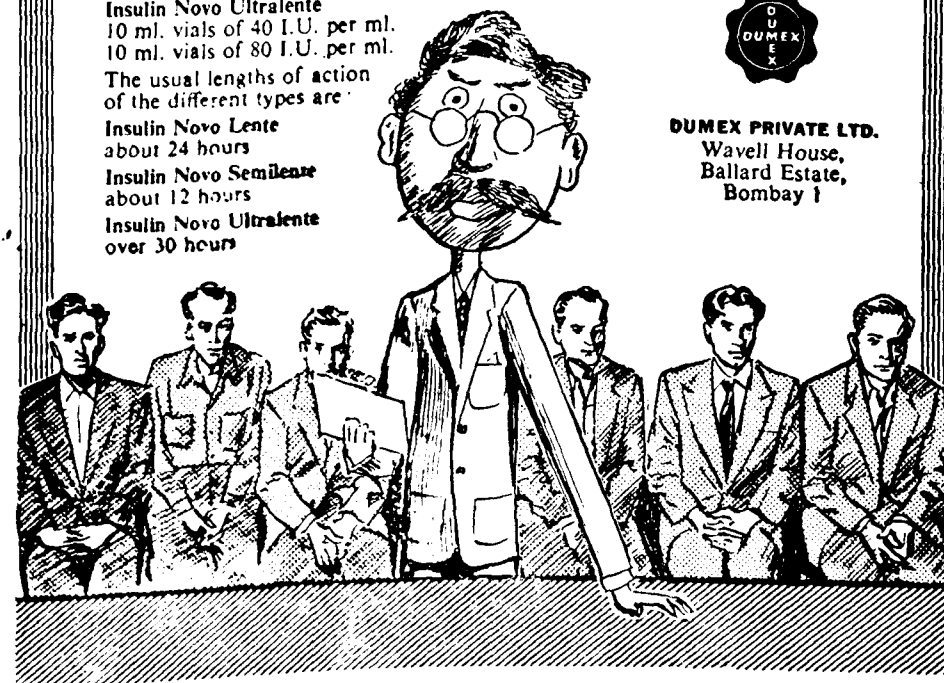
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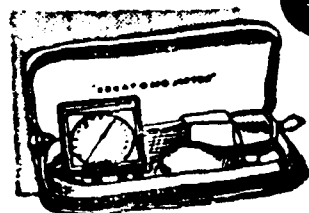


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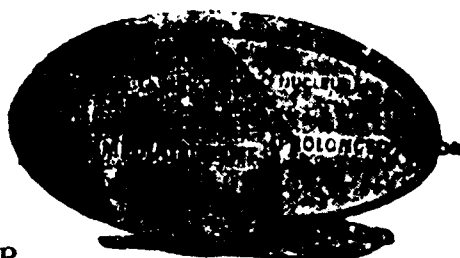
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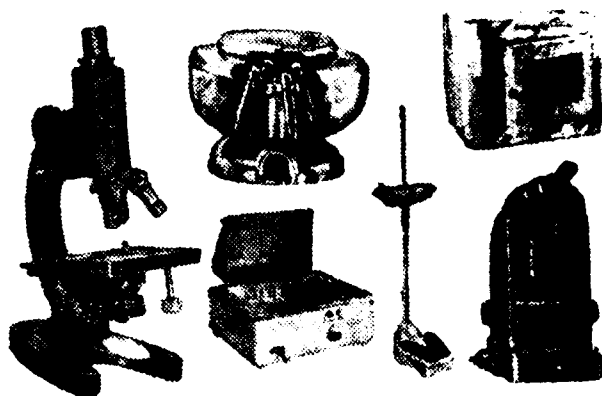
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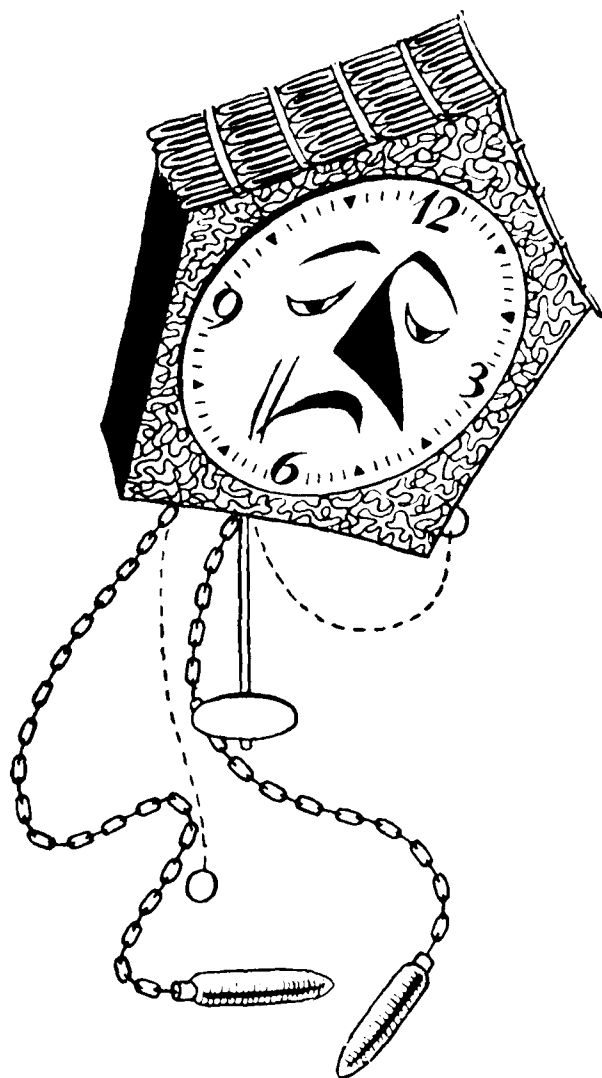
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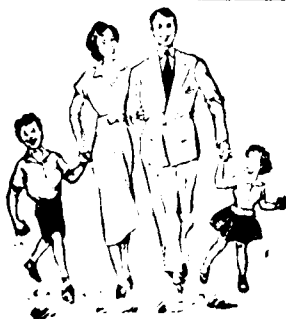
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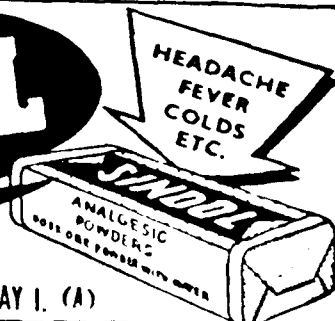
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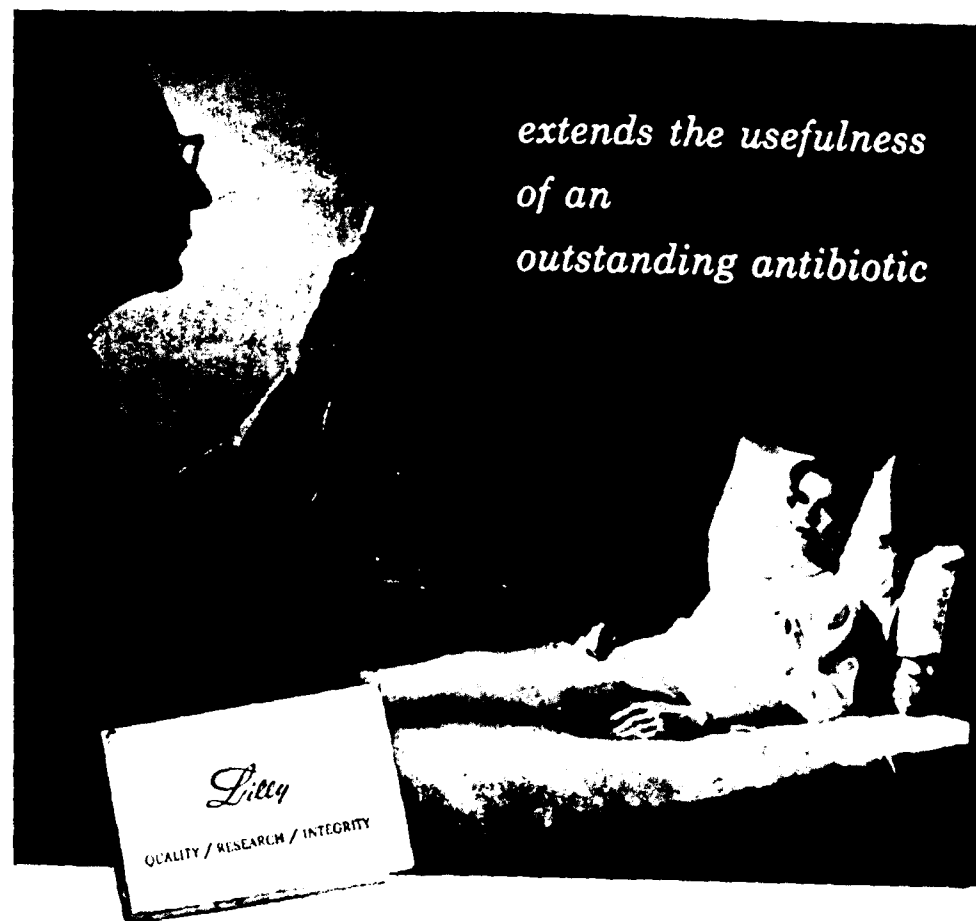
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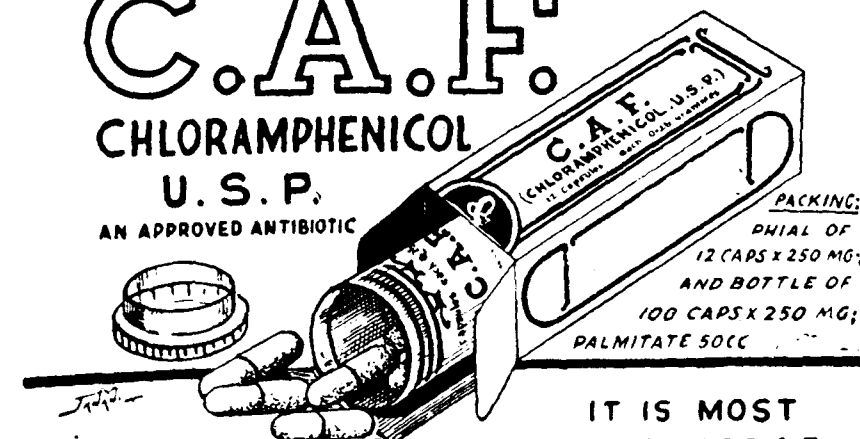
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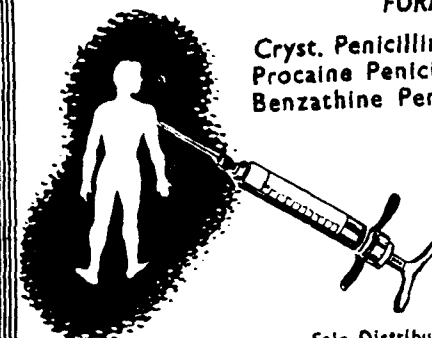
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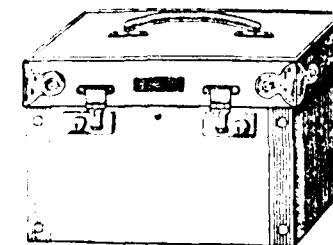
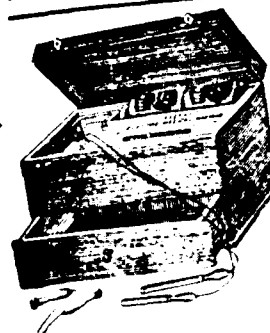
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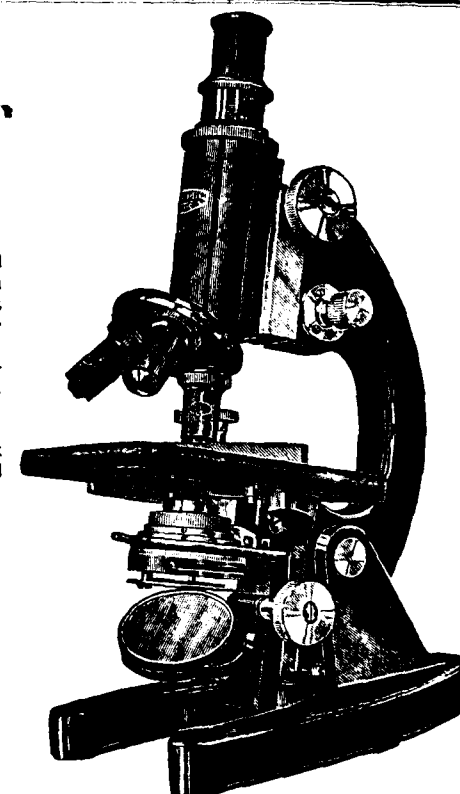
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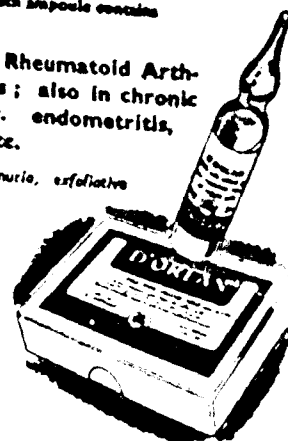
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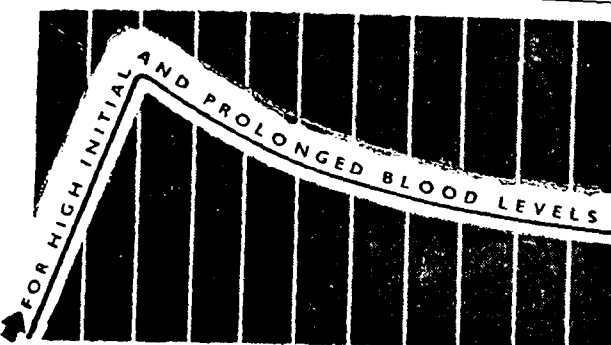
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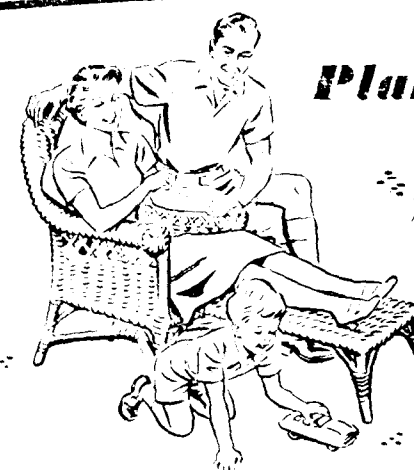
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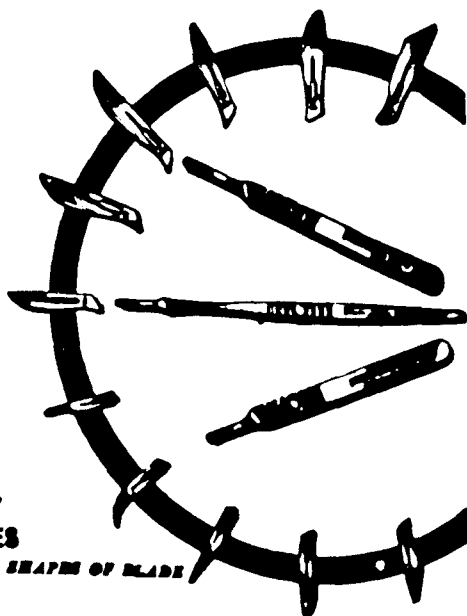
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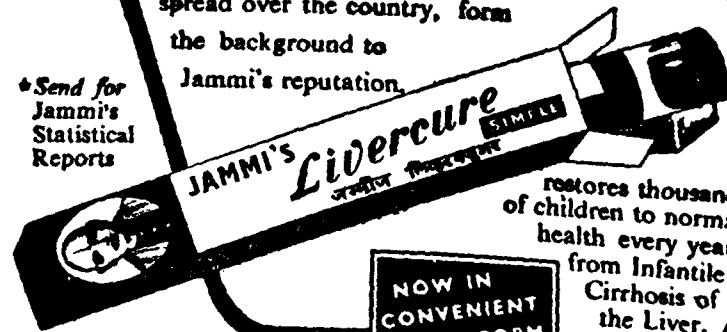
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In Case of Malnutrition and  
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WITH

**Creosote & Gualacol**

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**For Vigour and Vitality**

Pulmo-Cod also prevents Seasonal Allments,  
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(Creosote & Gualacol)

Each fluid oz. contains:  
Pancreatic hydrolysate  
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50% v/v

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| Vitamin B <sub>1</sub>  | 3 mgs.       |
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| Nicotinic Acid          | 40 mgs.      |
| Folic Acid              | 920 mcgs.    |
| Sodi Hypo.              | 120 mgs.     |
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| Calci Hypo.             | 240 mgs.     |
| { Creosote              | 1/3 %        |
| { Gualacol              | 1 %          |

Extract Wild Cherry,  
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Invert Sugar, Glycerine,  
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References:

Amer. Heart J., 1949, 37, 531.  
Brit. Heart J., 1950, 12, 54.

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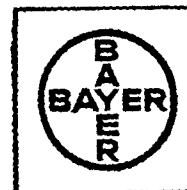


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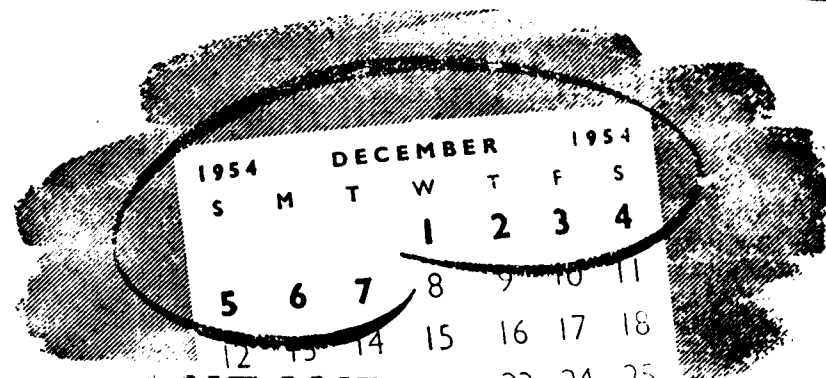
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|  | <b>BREAKFAST</b><br>followed in $\frac{1}{2}$ hr. to 1 hr. by | <b>'ALUDROX'</b><br><br>2 teaspoonfuls |
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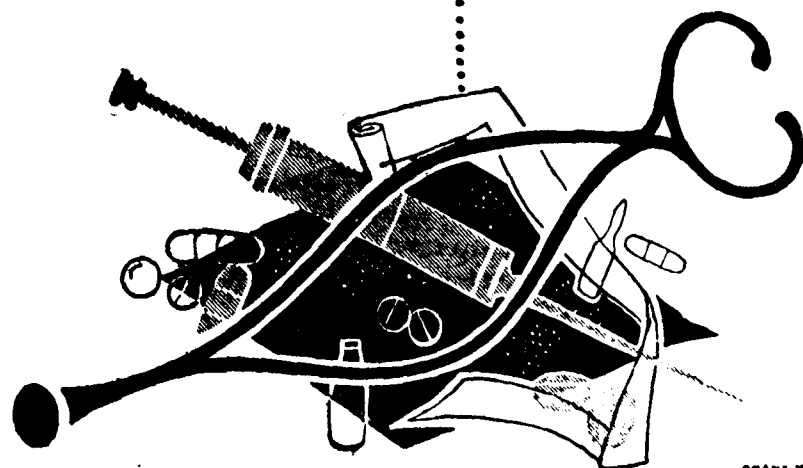
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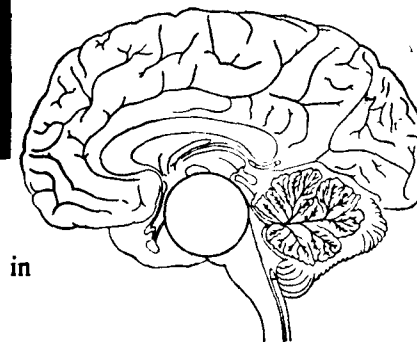
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| 2600 mgm.                                   | FERROMYN          | 42%                          |
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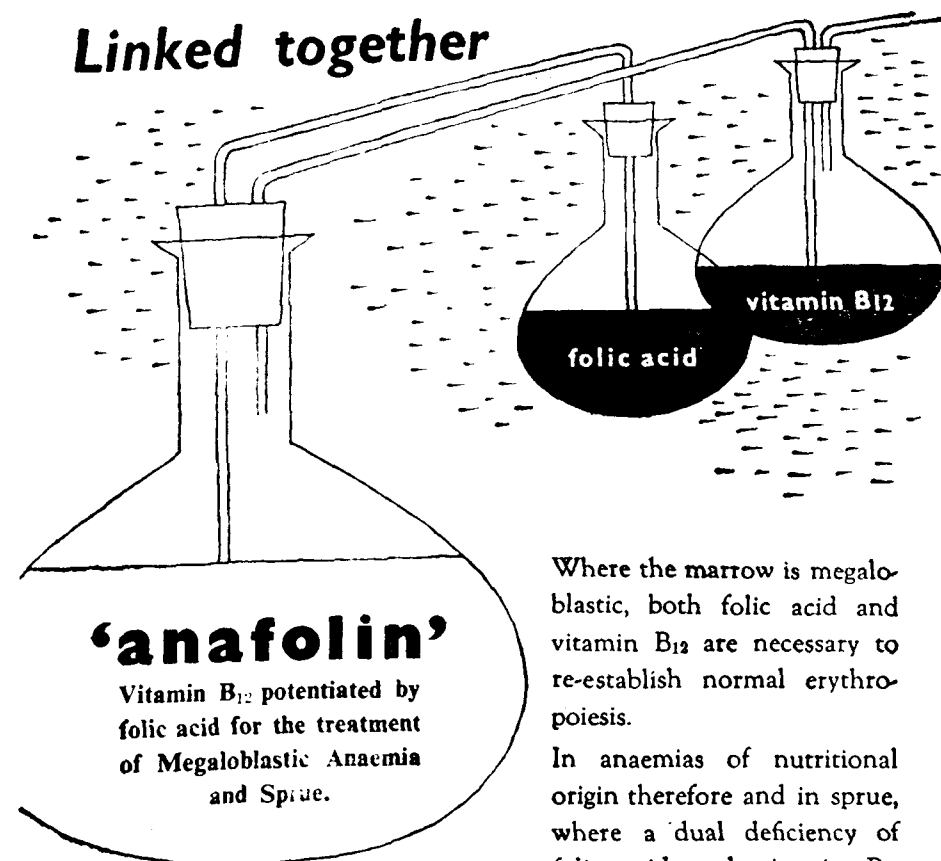
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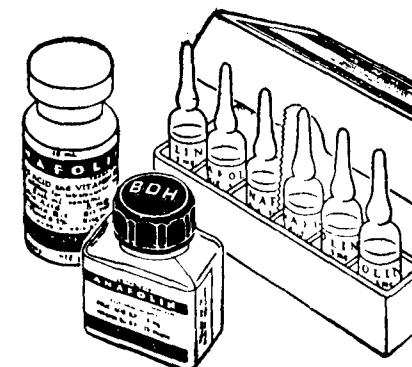
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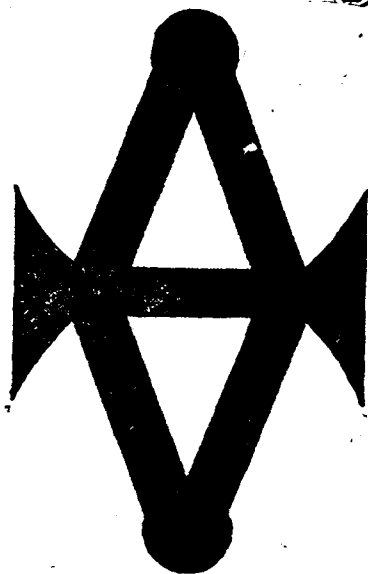
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With 'Plastules', adequate iron dosage may be administered with utmost therapeutic advantage. The inclusion of vitamin B<sub>12</sub>, folic acid, liver extract and yeast, corrects any concomitant deficiency of these important hæmopoietic factors.



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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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where  
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is a  
symptom...

as in  
HEADACHE  
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'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.

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Quinine 1/4 gr. Aspirin 3 gr.  
Phenacetin 3 gr. Caffeine 1/4 gr.

**ANACIN**  
ANALGESIC TABLETS

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

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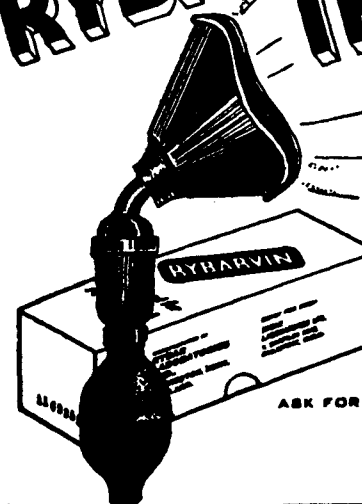
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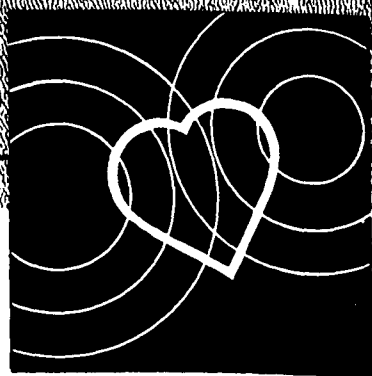
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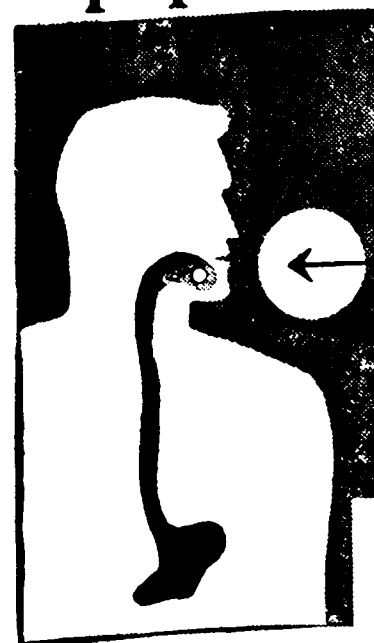
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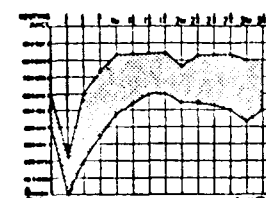
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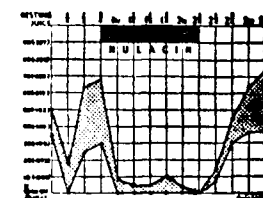
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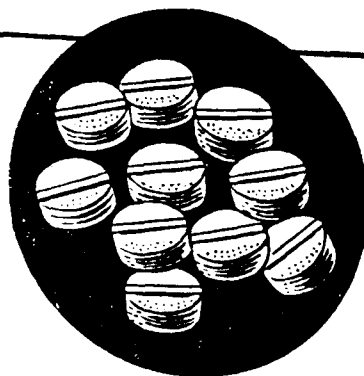
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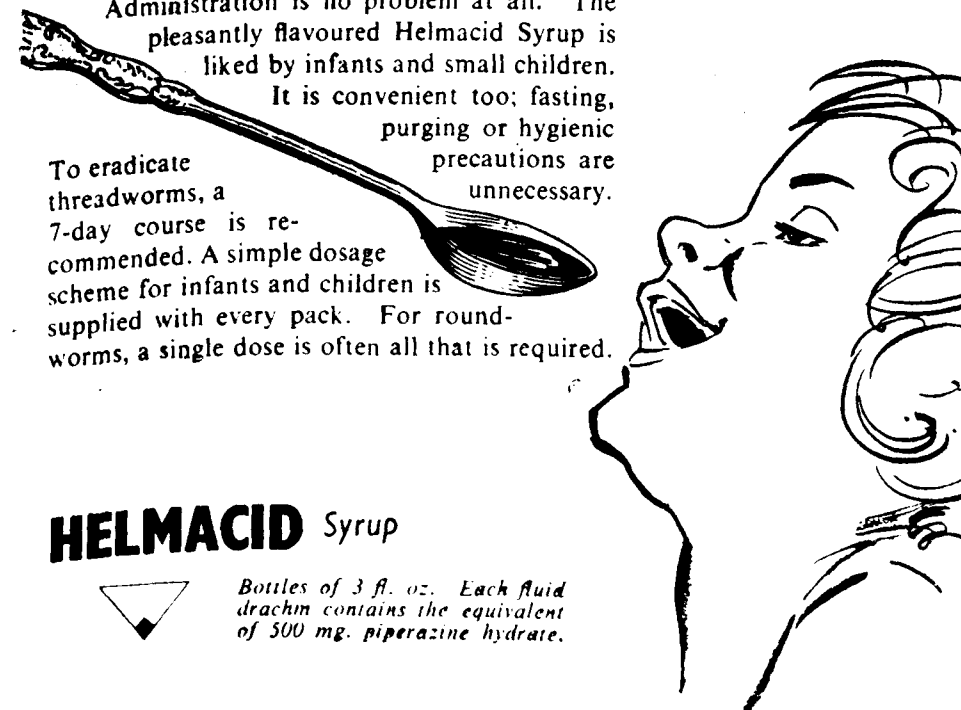
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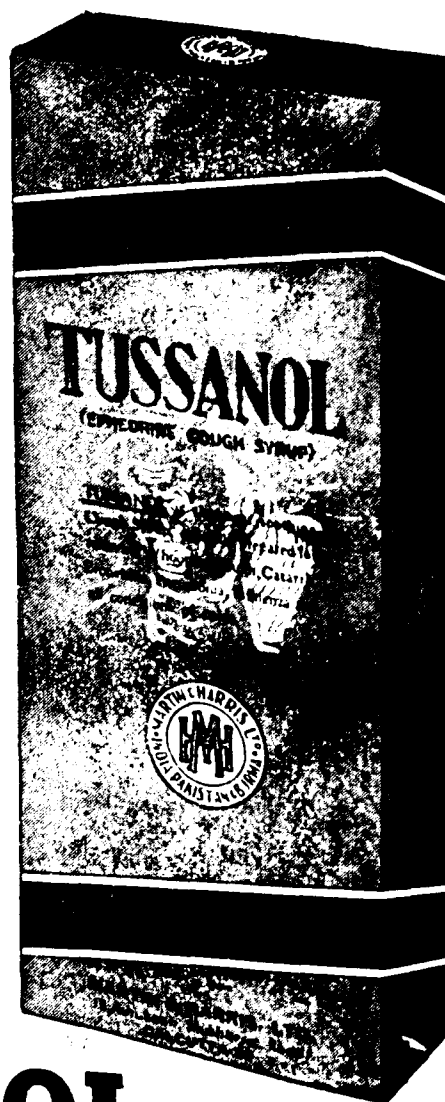
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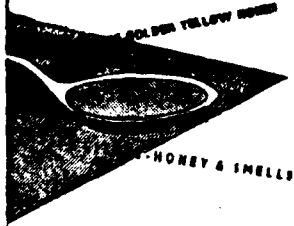
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No. 9

## Original Articles

### INFANTILE 'BILIARY' CIRRHOSIS\*

A Critical Review of the Literature on the Subject

P. KUTUMBIAH, B.A., M.D., M.R.C.P. (Lond.),

Christian Medical College, Vellore

**Nomenclature.**—The disease has been designated by different writers, at different times, by different names. Among the names that have been used the following may be mentioned:—Infantile cirrhosis (Sen, 1887); a form of biliary cirrhosis occurring in children in India (Gibbons, 1890); tropical cirrhosis, (Porter, 1904); intercellular hepatic cirrhosis, (Green-Armytage, 1926); infantile cirrhosis of the liver, (Lahiri, 1936); hypertrophic or biliary cirrhosis of the liver, (Brahmachari and Brahmachari, 1939); and subacute toxic cirrhosis of infants, (Ramachandra Rao, 1934 and Radhakrishna Rao, 1935).

Gibbons (1887) was the first to designate the disease as biliary or hypertrophic cirrhosis. Sen (1887), who was the first to describe the disease, did not agree with this name. He remarked "that the peculiar enlargement of the liver, which he had described, does not agree in symptoms or in its causation or in pathology with hypertrophic cirrhosis with which it was said to correspond." Radhakrishna Rao (1935) drew attention to the inappropriateness of this designation as applied to this disease. Based on his histopathological studies, he suggested that the condition is really a subacute toxic cirrhosis and not a "biliary" cirrhosis. He proposed "subacute toxic cirrhosis of infants" as the appropriate term to describe this condition. Ramachandra Rao (1937) commented "the so-called infantile biliary cirrhosis of this country is characterised by a progressive diffuse toxic necrosis with replacement fibrosis of the liver and is

\*Specially contributed to the 'ANTISEPTIC'

only exceptionally associated with diffuse intrahepatic chronic cholangitis as well. The justification for the use of the term 'biliary' for the uncomplicated cases of infantile biliary cirrhosis is probably only the invariable onset of toxic jaundice in the last stages and the bile staining of the liver usually observed post-mortem."

Most authorities will agree with the opinion expressed by Bhende and Deoras (1954) "that the commonly used designation, infantile biliary cirrhosis, is quite inappropriate for this condition and till its aetiology is finally settled, the non-committal name—infantile cirrhosis of the liver—is to be preferred."

**DEFINITION:**—Sen (1887) who was the first to recognise the condition as a definite clinical entity, defined the disease "as a peculiar enlargement of the liver in young children only, both male and female, without any enlargement of the spleen and associated with low fever, gradual emaciation, loss of appetite, sallow complexion and very slight jaundice but not in all." This definition obviously could refer only, if at all, to the earliest stage of the disease, when the diagnosis is very uncertain and open to question. The definition proposed by Pandalai (1934) is more comprehensive and less ambiguous. "Infantile cirrhosis of the liver is a definite disease entity of infants characterised by an insidious onset, a rather slow course, enlargement of the liver and spleen and jaundice, late ascites and an invariably fatal termination." This definition overlooks the fact that early cases of the disease may recover and death is not invariable. Brahmachari and Brahmachari (1939) define the condition as "a form of hypertrophic or biliary cirrhosis of the liver, especially affecting children in Indian cities and associated with gastrointestinal derangement and jaundice, and usually terminating fatally with ascites and anasarca. It is of an unknown origin but related to improper feeding." This definition assumes many things which subsequent studies have proved not to be correct. Though the liver is hypertrophic to begin with, definite atrophy of the liver is noted in all cases which survive to the third stage of the disease. Most authorities consider the disease as not a form of biliary cirrhosis.

**History of the disease.**—Twining (1832) described from Bengal a condition in children under four years of age, characterised by slight enlargement of the liver, coming on slowly and attended with emaciation, occasional attacks of slight fever and disorder of the digestive organs. This description may be said to apply to some cases of infantile cirrhosis of the liver. It was first mentioned as a distinct entity by Sen in a paper entitled "Enlargement of liver in children" read before the Calcutta Medical Society in 1887. Gibbons (1887, 1890 and 1891) described in detail the morbid anatomy of the disease and pointed out that the disease was biliary or hypertrophic cirrhosis.

The literature on the subject falls into three recognisable periods:

The first period is mainly concerned with the definition, clinical description, diagnosis and speculations as to the cause of the disease. During this period the epidemiology of the disease was studied and stated, the clinical features of the disease delineated and described, the aetiology of the disease critically examined and many theories as to the causation of the disease postulated.

The second period is mainly concerned with the study of morbid anatomy and the histo-pathology of the livers in this disease. Gibbons initiated these studies by his careful description of the histo-pathology in 1890. This study was revived after a lapse of 43 years by Ramachandra Rao in 1933.

The third period is mainly concerned with the experimental production of the disease in animals, the study of the histo-pathology of the liver biopsies obtained from patients suffering from the disease and the biochemistry of the disease. This work was started in 1947 and is still the main occupation of the research workers in the field.

The contents of this literature is reviewed below under appropriate headings.

**Epidemiology.—Geographical distribution:**—Mukherji (1927) recognised only two foci of the disease, viz., Bengal and Madras States. In Bengal it was mostly seen in Calcutta and the towns of the neighbouring districts. It is significant, he remarks, that no case has been reported from Assam, the hot-bed of Kala-azar. Narayanamurthi and Tirumurthi (1939) mention Madras town, Trichinopoly, Madura, Coimbatore and Tanjore for the South and for the Circars, Ganjam, East and West Godavari and Guntur, as the most effected areas in the Madras State. Sankara Iyer (1931) and Krishna Rao (1941) report that the disease was very prevalent in the Mysore State. Gan (1950) reported that the disease was fairly prevalent in Nagpur and *Madhya Pradesh*. Mukherji (1952) reported that the disease was not uncommon in Indore and Madhya Bharat, the surrounding parts of *Madhya Pradesh*, *Rajasthan* and the *Bombay State*. Seth, S.C. (1955) reported that the condition is quite common in paediatric practice in *Bombay* and seems to be common in this State.

Brahmachari and Brahmachari (1939) refute the statement frequently made that the disease does not occur in Assam and in East Bengal. They state to their knowledge the disease has occurred in these places. Mukherji (1927) asserted that the disease is not present in any place at a higher level than 1,000 feet above sea-level. This has been shown not to be correct by Krishna Rao (1941) who from Mysore writes there is no place in the state that is below 2,000 feet and yet the disease is very prevalent in the state.

Srivastava and Aikat (1954) published a clinico-pathological study of 45 cases of infantile cirrhosis of liver from Gwalior, *Madhya Bharat*.

*Influence of climatic conditions:*—Mukherji (1927) considered that high temperatures and humidity played some part in the production of the disease. Narayanamurthi and Tirumurthi (1939) observe climate does not seem to have any bearing on the production of the disease. Humidity, wet and dry seasons of the year, do not seem to increase or decrease the number of cases. All writers agree that as the disease makes an insidious onset it is difficult to say in which season of the year the disease commenced.

*Distribution according to race, religion and caste:*—Mukherji (1927) remarks that in Bengal, families of both Hindus and Mohammedans are affected. In his 292 Bengali patients, 240 were Hindus, 52 Mohammedans and only one Christian. In Madras the disease is very common in Hindus and particularly among Brahmin children. The Tamil group is more affected than the Telugu, Malayalee and Canarese group of children. In their series of 445 cases, Narayanamurthi and Tirumurthi (1939) could find no record of a case in European children. Green-Armytage (1926) is the only writer who reported cases in European and Anglo-Indian children. In his series of 63 cases there were 27 European and Anglo-Indian, 30 Hindus and 6 Mohammedans. In Bombay the condition is less common in Parsees and Muslims. In his series of 38 cases, Sheth (1955) found 92 per cent were Hindus, 5 per cent Sikhs and 3 per cent were Muslims.

*Distribution according to sex:*—In the Bengal series of 374 cases, 222 were males and 152 females. In the Madras series of 445 cases there were 272 males and 173 females. In another series of 100 cases reported by Sarma (1946) from Madras there were 66 males and 34 females. In the Gwalior series of 45 cases only 8 were females. In the Indore series of 200 cases only 13 per cent were females. In the Bombay series 58 per cent were males and 42 per cent females. Most authorities agree that the incidence is greatest in the males. Both Mukherji (1922) and Narayanamurthi and Tirumurthi (1939) state the first child of the parents and the first male authors must have copied this observation from the former without much verification. Srivastava and Aikat (1954) noted the incidence of the disease was more common in the first sibling of their series. Mukherji, S. K. (1952) noted that the maximum incidence of the disease was in the first child and incidence in the third child coming next. Both these authors do not mention the sex of the children. Ramachandra Rao, M. G. (1929) and Sankara Iyer (1931) considered that quick succession of pregnancies seems to be a predisposing factor in the production of the disease. This observation is against the idea that the disease occurs in the first child in the series. In the series of 100 cases of Sarma (1946) there were only 3 cases with the disease who were the first child of the parents. In 5 more cases

the patients were the only children of the parents. Of these five, 4 were males and one was female. So altogether the disease occurred in the first child of the parents in 7 cases only out of a hundred. In this series it occurred in the 2nd child in 5 cases, in the 3rd in 3 cases, in the 4th child in 2 cases, in the 5th child in 6 cases and in the 7th in 3 cases. These statistics do not substantiate the claim that rank in the series of children in any way predisposes the child to the disease.

*Distribution according to economic status of the patient:*—R. Ghose (1887) stated that the disease is confined to the children of the rich and middle classes only. J. N. Ghose (1887) observed that the children of the rich and poor equally suffered from this malady. Ahmed (1887) remarked that the children of the rich and the poor were equally liable. S. K. Mukherji (1922) writes the disease is seen proportionately more among the over-fed children of the rich than among ill-fed children of the poor, who cannot afford to give their babies anything else except mother's milk. Radhakrishna Rao (1934) found no typical case of the disease in 4 years of his investigation in any children of the poorer classes. Srivastava and Aikat (1954) state all their cases belonged to vegetarian families and most of them belonged to lower middle class. The general consensus of opinion is that the disease is more common among the rich and middle classes.

*Occurrence of the disease in breast-fed children and artificially-fed children:*—Dey (1887) thought that overfeeding of children with breast milk was the cause of the disease. Ghose (1887) and Gothosker (1931) and Krishna Rao (1941) believed that children fed either entirely or to a large extent on cow's milk suffered from the disease. Radhakrishna Rao (1935) found that all the children suffering from the disease were breast-fed and most of them were getting cow's milk to supplement mother's milk.

**AETIOLOGY:**—The aetiology of infantile cirrhosis of liver has always been a matter of keen speculation. Alcoholism in parents, congenital syphilis, malaria, Kala-azar, amyloid disease of liver, parasitic infection, deficiency of the anti-scorbutic vitamin, excessive carbohydrate in mother's milk, irritation of the liver by toxins and derangement of liver from overwork have all been put forward, at some time or other, as the cause of the disease. The earlier writers were more inclined to attribute the disease to unsuitable diet, over-feeding and irregularity in feeding. Irritating foods seasoned with aromatics and early administration of starch (Macanzie, 1895), early administration of starch in large quantities (Gibbons, 1890), excess of fat in cow's milk (Green-Armytage, 1926, and Mukherji, 1922), excess of sugar and deficiency of proteins (Bhattacharji, 1931) artificial feeding with all kinds of patent foods irrespective of all indications, feeding with pure cow's milk in unsuitable and large quantities and the early feeding of infants with starchy and fatty

foods (Krishna Iyengar, 1927) have all been discussed in connection with unsuitable diet, over-feeding and irregularity in feeding. Radhakrishna Rao (1934) comments "that too much stress is laid by several observers on the importance of dietetic irregularities in the causation of the disease. It is important to note that no typical case of the disease was seen in the children of poor, in whom, for want of sufficient means, the feeding is extremely unsatisfactory. Moreover, the diet of children suffering from the disease differs in no way from that of the normal children of the same age and class. It will be evident from the above observations, that dietetic irregularities alone cannot account for the causation of the disease." Prabhu (1940) was also of the same opinion. "The diet, no doubt, is more or less full of starch and considered from the nutritional point of view may be defective but in no way inferior to the diet given to infants amongst the poorest and ignorant in whom the disease is practically unknown."

It is also suggested by some authorities that deficiencies in the milk of the nursing mother may have some relation with the disease in infants. Mukherji (1922) believed that "the disease was due to deficient quantity and defective quality in the milk of the nursing mother." Forsyth (1924) reported that the greater incidence of the disease among Brahmin children was due to a high fat content of the breast milk of Brahmin women. Green-Armytage (1926) suggested that a deficiency of vitamins in the mother's milk influenced the endocrine system of the foetus in utero and thus predisposed to the disease.

We have broadly speaking four theories with regard to the cause of the disease: (1) that the disease is caused by the action of a toxin, absorbed from the gastro-intestinal tract, on cells of liver; (2) that the disease is caused by a bacterial or viral infection; (3) that the disease is caused by deficiencies in the diet of certain food factors; (4) that there are two factors concerned in the production of the disease, viz. a factor predisposing the liver cells to injury and a second precipitating, which actually causes the liver injury.

1. *Toxin as a cause of infantile cirrhosis*:—The view that toxins absorbed from the intestines may play a role in the causation of the disease was held by some of the earlier writers. Gibbons (1890) considered the condition as a peculiar form of biliary cirrhosis, the consequence of the action on the liver cells of some irritant of gastric origin which leads to degeneration of the liver cells with subsequent increase of intercellular connective tissues and later of portal sheaths. Vaidyanatha Iyer (1927) was of the opinion that whatever might have been the food, it has been found that faulty digestion is the cause, resulting in the production of toxins in the digestive tract which on passing through the blood in the liver for filtration irritate the liver cells. Ramachandra Rao (1933) suggested that a vasomotor imbalance is produced in the liver by a toxin, which precipi-

tates a vasospasm of the hepatic venous tree and vasodilatation of the portal venous tree resulting in the pathological picture of the disease. Pandalai (1934) thought that there are two factors operating:—(i) a gastrointestinal toxæmia resulting from an early faulty feeding; (ii) a congenitally insufficient liver with inadequate defence powers. Radhakrishna Rao (1935) concluded from his histopathological findings from the livers that the disease was of the nature of subacute toxæmia: the evidence was more in favour of an exogenous toxin (which is probably peculiar to India) probably dietetic, rather than endogenous or metabolic toxin. Most writers were of the opinion that the toxin was absorbed from the gastrointestinal tract of the infant. Some writers held the view that the toxins may be conveyed to the liver of the infant from the mother through the placenta. Forsyth, W. L. (1937) suggested that the cause of infantile biliary cirrhosis is a dietetic one resulting from the ingestion of *curry* stuffs and their irritant volatile oils by the pregnant mother. Such toxin is operative during the intra-uterine life and continued at the breast. Others held the view that the toxin is conveyed through the mother's milk. Green-Armytage (1926) suggested that "a nursing mother frequently suffers from pyorrhœa, anæmia or constipation resulting in, or the result of, auto-intoxication. The consequence of this is that the baby obtains a supply of milk from its mother lacking stimulating hormones, calcium, iron, phosphorus, iodine, etc. Such defects culminate in the intestinal and hepatic derangement in the infant."

Though all the above authors discuss a toxin, so far there is no evidence that any particular toxin has been incriminated.

2. *Infection as a cause of infantile cirrhosis*:—Pearse (1909) was the first to express the opinion that the disease was infective in origin. He was of opinion that the disease was a parasitic disease, "but whether microbic in origin or due to large forms, there is no evidence to show." Congenital syphilis, malaria and chronic sup-pururation have been suggested as probable causes of the disease. Castellani and Chalmers (1919) doubted whether infantile cirrhosis was not a variety of Kafa-azar. Megaw (1924) pointed out the close association between cirrhosis of the liver and bacillary dysentery. He believed the one to be the direct sequel of the other. Repeated blood examinations and serological and special tests have proved the above assumptions to be untenable. Lahiri (1936) once again raised the question of the role of infection in the ætiology of infantile cirrhosis of the liver. From the evidence derived from his experiments (described below) he concluded that infection plays an important role in the production of infantile cirrhosis. Krishna Rao, P. (1941), on very flimsy evidence, concluded that there are two factors in the ætiology of the disease, viz., cow's milk and *B. coli* infection. Cow's milk brings about the predisposing factor viz., gastrointestinal disorder and devitalisation of the liver and *B. coli* the cirrhotic changes

in the liver. Lahiri (1936) remarks "the question of the presence or absence of infection in this disease still remains unsettled; but the former possibility merits serious attention when we turn to the clinical signs and symptoms of the disease, because fever, enlargement of the spleen along with hepatic enlargement and some amount of leucocytosis is present in many cases. Bhattacharjee (1933) expressed the opinion that the so-called positive bacteriological findings are due to secondary invasions.

"It has been stated that infantile hepatic cirrhosis is due to infection with a virus. Though definite proof of this is lacking, it is possible that the acute necrosis that occurs in cases, is due to a superimposed toxæmia as a result of previous damage of the liver cell by the virus" (Chopra, 1932). Sarma (1939) found summer diarrhoea as the starting point in many of his cases of infantile cirrhosis of the liver. As the question of a viral origin of summer diarrhoea has been debated he raised the question whether infantile cirrhosis may not also be caused by a virus. Narayanamurthi and Tirumurthi (1939) also remarked on a virus factor in the aetiology of the disease. Wahi (1949) remarks "clinically infantile cirrhosis in India is often a familial disease. It may be that in the familial instances the cause is a virus infecting the mother's genital tract, the infant contracting the infection during birth. This suggestion is along the lines of recent work of Budding in which he isolated a virus identical with the virus of infantile diarrhoea from the adult genital tract. The probability that the virus may be acquired, transmitted, and maintained venereally in adults and thus serve as the original source of epidemic of diarrhoea of the new-born, must be entertained." Kutumbiah (1951) in a communication to the liver sub-committee of the I.C.M.R. based on certain histo-pathological resemblances between certain fatal cases of infective hepatitis and infantile cirrhosis, argued that in the causation of infantile cirrhosis an infection by a virus allied to I.H. or S.H. viruses may have to be seriously considered. Craig and Laning (1952) reported a group of 20 cases of hepatitis occurring early in infancy. Histologically active hepatitis having the characteristics of viral hepatitis was found in all 20 cases. In 13, in which there was a tentative diagnosis of biliary atresia, exploratory operations were performed, but in no case was the biliary tree atretic. From these data, they concluded that hepatitis having the histologic appearance of viral hepatitis is a not too frequent finding in early life and must be considered in any differential diagnosis of icterus in the neo-natal period."

3. *Deficiency of food factors as a cause of infantile cirrhosis:*—That nutritional deficiencies play a role in the production of this disease has been held by early writers. Mukherji (1922) believed that the disease was due to deficient quantity and defective quality of the milk of the nursing mother. Forsyth (1924) reported that the greater incidence of the disease among Brahmin children was due

to a high fat content of the breast milk of the Brahmin women. Green-Armytage (1926) incriminated the excess of fat in cow's milk. Bhattacharji (1931) was of opinion that the fault in diet was excess of sugar and deficiency of proteins. The chief defect was supposed to be a high fat content either in breast milk or in cow's milk and excess of carbohydrate and sugar and deficiency of proteins. These observations were merely guesses at truth and lacked scientific confirmation. Recent experimental work on cirrhosis has definitely established that certain food factors play a causative role in the production of hepatic injury. These factors are choline, cystine, and methionine. Deficiency of choline produces fatty changes, whereas deficiency of cystine and methionine produce massive necrosis. Based on this experimental evidence, Gyorgy and Goldblatt (1939) advanced the hypothesis "now that the production of an apparently nutritionally conditioned hepatic injury, with necrosis and condensation fibrosis has become possible, the question arises whether forms of toxic hepatitis and of cirrhosis of liver should be regarded as deficiency diseases rather than as toxic disorders." According to this theory infantile cirrhosis of liver is regarded as a deficiency disease in this sense. Radhakrishna Rao (1953) has been carrying out an analysis of the amino-acid composition of human milk in normal as well as in women whose children suffered from the disease with a view to finding out whether any deficiency in the aminoacids—choline, cystine and methionine—exists in the milk of mothers whose babies suffered from the disease. No conclusive evidence has so far been obtained on this matter.

4. *The theory of pre-disposing factors and precipitating factors:*—Some authorities consider that infantile cirrhosis of the liver is caused by two factors. One a predisposing factor and the other a precipitating factor. Sen (1887) suggested that possibly some constitutional predisposition or dyscrasia is inherited by the children which under any of the least exciting causes gives rise to the disease. Pandalai (1934) speaks of a congenitally insufficient liver with inadequate defensive powers. Lahiri (1936) thought the predisposing factor as a long continued dietetic error such as excess of fat in the diet and this produced devitalisation of the hepatic cells. Krishna Rao (1941) thought the predisposing factor was a gastrointestinal disorder and devitalisation of the liver by cow's milk. Wahi (1949) perhaps is nearer the truth, in assuming the predisposing factor is the absence of protective proteins in the diet of the undernourished vegetarian child and these prepare the liver to be knocked out by the precipitating factor. Sen, Pandalai, Ramachandra Rao and Radhakrishna Rao, thought the precipitating factor was dietetic errors, gastrointestinal disorders, or a toxin. Lahiri, Krishna Rao and Wahi thought the precipitating factor was an infection.

Experimental production of infantile cirrhosis of liver.—Since 1936 many attempts have been made to reproduce the disease

in experimental animals. Since the pathogenesis of the disease was not even dimly visualised and the diagnostic criteria were not properly defined, the experiments were not properly planned and carried out, and the results obtained varied widely and the interpretations offered in some cases were very wide of the mark. Working on the various theories mentioned above, experiments were devised to prove these theories. It is only very recently the studies of the liver biopsies obtained from patients suffering from the disease, have given us some definite idea as to the early changes in the disease, and some idea as to the nature of the disease. One fact has emerged from these studies, namely, whatever the disease, it is not a fatty degeneration of the liver. Necrosis of the liver cells is the most constant change to be found at every stage of the disease process and that necrosis is the primary change. In the main the experiments fall under three headings:—

(1) The study of the effect of a toxin or infection on livers rendered vulnerable by a pre-induced dietetic defect.

(2) The study of the role of nutritional factors in the production of the disease.

(3) The study of the effect of feeding rats on a diet resembling in composition, the diet actually taken by the patients suffering from the disease.

(4) The reproduction of the disease in animals by injecting them with filtered material obtained from the stools of patients suffering from the disease, or injecting the blood of an infected patient, or an emulsion of the diseased liver itself.

1. Lahiri (1936) carried out experiments on puppies. He gave a high fat diet to the puppies. Then they were given intraperitoneal injections of gradually increasing doses of colon bacilli. He thought he reproduced the earlier phases of the disease in his experimental animals. At the end of the experiment the livers of the puppies were found to be enlarged and there was continued pyrexia with gastrointestinal disorders. But the microscopic picture was far from what is seen in infantile cirrhosis of the liver. There was extensive fatty degeneration of the liver cells with round cell infiltration in many areas and along with it a proliferation of fibrous tissue in some of the lobules. The picture was one of fatty degeneration with portal cirrhosis. Forsyth's experiments with rabbits were no more illuminating. By feeding pregnant rabbits with *curry* stuffs used in hospital diet, he claimed to have produced biliary cirrhosis in the infant and the portal cirrhosis in the intra-uterine foetal livers. He considered biliary cirrhosis in the infant and the portal cirrhosis in the adult may possibly be due to this error in the diet. Rabbit is not a suitable animal for experiments on cirrhosis. Infantile cirrhosis of liver does not exclusively occur in a *curry*-eating population. We now know that infantile cirrhosis of liver is not a true biliary cirrhosis and differs essentially from the portal cirrhosis of adults.

The experiments of both Forsyth and Sunderasen (1947) emphasise the fact that a cirrhogenic toxin can pass through the placental barrier and injure the liver of the foetus. It also shows that a toxin can pass through the mammary secretion and cause necrosis of the liver of the suckling in the absence of a protective factor in the diet of the mother.

2. *Experiments for the study of the role of nutritional factors in the production of the disease*:—These experiments have been conducted to substantiate the nutritional hypothesis. It has been definitely established that the deficiency of choline, cystine and methionine in foods produce fatty and necrotic changes in the liver cells. It has been found easy to produce fatty changes in the liver in these experiments. But its attempts to produce necrotic changes has not been successful. Himsworth and Glynn (1944 and 1945) showed that when the dietary protein falls below a critical level, massive hepatic necrosis develops, which the choline content of the diet does not influence, but which a supplement of methionine can prevent. Radhakrishna Rao (1950) after repeated failures succeeded in producing necrosis of the liver with diet low in vitamin E and cystine. These experiments have confirmed the already well established facts with regard to the effect on liver cells of deficiency of these amino-acids. But they have not thrown any fresh light on the causation of the disease. One experiment of Bhaskara Menon deserves mention. He fed pregnant bitches on full term with a diet low in choline and in protein. One experimental animal delivered four healthy puppies which after nine days developed jaundice and died one after another in three days. Histological examination of the livers showed centrilobular fibrosis with thickening round the hepatic vein and irregular areas of necrosis in the liver. These lesions have a close resemblance to infantile cirrhosis of liver lesions. These experiments have to be repeated and the findings confirmed before any inference could be drawn. The possibility of a virus infection contracted independently after the delivery cannot be ruled out.

3. *The study of the effects of feeding rats on a diet resembling in composition the diet actually consumed by patients suffering from the disease*:—Patwardhan studied the effects on livers of feeding the rats on an average poor diet containing rice as the main cereal. This diet had the characteristic of being low in protein and low in fat with poor choline and methionine contents. Cystine was higher than methionine. There was definite accumulation of fat in the liver but no true cirrhosis of the liver developed even after 15 months of diet experiments. Wahi (1949) tried to reproduce the disease by feeding rats on high carbohydrate and low protein diet akin to the diet of a vegetarian Hindu in whom cirrhosis of the liver is common. There is no claim made that by this method he was able to reproduce the disease. He used two sets of rats in his experiments. One set consisted of newly weaned infant rats weighing approximately

50 grams and another consisting of adult rats weighing 100 and 150 grams. The liver of infant rats showed focal or diffuse necrosis, while the adult rats showed fatty infiltration leading to early cirrhotic changes. These experiments are only variants of the second type of experiments and have not thrown any light on the pathogenesis of the disease.

4. *The reproduction of the disease in animals by injecting them with material obtained from patients suffering from the disease:*—That infection plays a role in the production of the disease has long been known and as yet it has not been proved to be improbable. Recent literature mentions the possibility of a viral cause of liver injury in infants. The experiments of Mohanrangam *et al* (1954) on rats with the filtered material obtained from the stools of patients suffering from the disease are promising. So far the results obtained are not definite. It may be that rats are not susceptible to this disease. But it is worth pursuing with other animals if no satisfactory results are obtained with rats.

Mukherji (1922) inoculated his own child with blood obtained from a patient in the advanced stage of the disease with no results. Neither the age of the patient nor the route of the injection is mentioned. Achar (1954) tried to reproduce the disease in puppies with an emulsion of livers from patients suffering from the disease into the portal vein and also with no results.

To sum up, the result obtained so far from these experiments is disappointing. It is certain that the disease has not yet been reproduced in any laboratory animal. A fallacy underlying these experiments is the confusion between infantile cirrhosis of the liver, adult cirrhosis and the lesions produced in the liver cells by protein deficiency.

**PATHOLOGY:**—Ramachandra Rao has given a very detailed and accurate description of both the gross and microscopic anatomy of the liver in this disease. This description is quoted by Prabhu (1941) in his Elizabeth Matthai Lecture

*Gross anatomy:*—The liver in this disease is usually shrunken when seen in the autopsy room, stained green with bile, of normal shape with sharp margins and firm consistency. The capsule is thick but somewhat opaque white in colour and is free from adhesions or exudation. The capsular surface may be either smooth with indistinct lobular markings, or may be uneven, granular or flatly nodular, particularly on the under surface. The sectioned surface is also greenish in colour, with obliteration of the normal lobular pattern by a diffuse fibrosis. It presents either a smooth greyish green surface finely mottled with small scattered dark-green areas, or a finely granular surface with a diffusely spread greyish-green fibrous network enclosing small rounded islands of regenerating parenchyma in its meshes. The Glisson's capsular sheath of the

portal systems is not thickened. Even the smaller divisions of the latter can be recognized with the naked eye or with the help of the hand lens. On the other hand, the sectioned ends of the divisions of the hepatic vein are considerably curtailed and are recognized with difficulty, a change characteristically seen in hepatic fibrosis of toxic cirrhosis. The gall-bladder is enlarged, distended with colourless fluid.

*Microscopic anatomy:*—The outstanding feature of the histopathology of this condition is the diffuse replacement fibrosis, which sometimes appears to be almost interstitial in distribution. It is usually centred around partially or completely occluded thick walled sclerosed hepatic venules and forms a network of anastomosing fibrous bands. The portal systems and their fibrous contents show very little change. They appear to lie in the fibrous bands, or are crowded together in the larger nodes of the network. Regeneration islands of varying sizes formed by clusters of irregularly arranged hepatic cords are seen embedded in the meshes of the fibrous network adjoining the portal spaces. In the earlier stages, the isolated segments of the hepatic cords appear dispersed in the fine meshes of a network of almost interstitial fibrosis. Bile pigment in the form of fine granules is seen both intra and extra-cellularly, while coarser bile cylinders are also seen in the fine bile channels. Inflammatory leucocytic exudation is ordinarily very inconspicuous. Sometimes a cholangitis of the intra-hepatic branches of the bile ducts may be superimposed. The portal system including bile ducts escape appreciable changes. The fibrosis is essentially a degenerative sclerosis of the collapsed reticular frame work of the sinusoidal capillary bed of areas of parenchymal destruction. This appears to occur primarily around the branches of the hepatic venous tree, while the regenerating nodules show a periportal distribution. The hepatic venous branches show extensive, occlusive sclerosis which in the early stages appears to be of the nature of a swelling of the sub-intimal connective tissue.

Radhakrishna Rao (1935) and U. S. Rao (1941) have also published critical studies of the gross and microscopic anatomy of the livers in this disease. They follow very closely the descriptions given by Ramachandra Rao.

Krishna Rao (1941) also published a study of the histopathology of the disease. He writes, "the histopathological features of the liver and the clinical conditions of the disease satisfy all the criteria of portal cirrhosis and "infantile cirrhosis" is, therefore, undoubtedly a case of portal (or Lannec's) cirrhosis. Very few authorities agree with this conclusion.

Wahi P. N. (1949) interprets the histopathological picture differently. "The histologic development of cirrhosis is more on an infectious basis. Broad bands of fibrous tissue, patches of necrosis

cellular infiltration, complete disorganization of the liver pattern, and absence of fatty changes are outstanding in the microscopic observations. The changes are more of the nature of post-necrotic scarring leading ultimately to nodular hyperplasia rather than portal cirrhosis.

The latest contribution to the pathology of infantile cirrhosis of the liver is by Bhende and Deoras (1954). They base their conclusions on a study of the autopsy material of 9 cases of infantile cirrhosis of the liver during a period of 25 years. They write "in our opinion necrosis of the liver cells is the most constant change to be found at every stage of the disease process and that necrosis is the primary change. The invariable presence of necrosis at all stages suggests that the disease process is active all along. Such activity is probably maintained by repeated attacks of necrosis which may involve original, intact liver cells (primary necrosis) or/and the cells of regenerating nodules (secondary necrosis). Secondary necrosis in the regenerating nodules with histological changes identical with those in primary necrosis, is an invariable finding in every case. We do not think that the changes in the hepatic venous tree are primary and we are unable to say what precise role they play in the production of the hepatic lesion. The biliary tree except for proliferation of the small biliary ducts, does not show any change."

Liver biopsies.—Besides histopathological studies, we have studies of liver biopsies by many workers. V. R. Naidu and Subramaniam, V. (1949) have given a detailed histopathological study of 29 cases in various stages of the disease. They divided the course of the disease into 3 stages, stage I, II-A, II-B and III. Stage I and II-A they class as early stage. In stage II-A they describe the architectural pattern is not lost, pseudo-lobules are not seen, necrosis is diffuse and in small irregular patches, the liver cells some are normal and others are distended and vacuolated, containing lipoid material, fibroblastic activity poor, no proliferation of the bile ducts seen, cellular infiltration of the parenchyma and of the connective tissue not seen, vascular pattern not altered, regeneration not marked and bile pigment absent. In the II-B stage the architectural pattern markedly changed, pseudo-lobules are seen but are not so well marked as in the stage III, necrosis diffuse but more marked, more hypertrophic liver cells seen than in the stage II-A, fatty changes present but not marked, definite fibrotic tissue seen penetrating the pseudo-lobules, proliferation of the bile ducts present in varying degrees, cellular infiltration of the parenchyma and of the connective tissue present, vascular pattern altered but no evidence of endophlebitis, regeneration present, and bile pigment absent. In stage III, the architectural pattern is completely distorted, pseudo-lobulation marked, necrosis diffuse but more marked, a large number of liver cells distended and vacuolated a few multi-nucleated cells with one or two deep-staining nucleoli seen, fatty changes present but not very

marked, bands of connective tissue with varying degrees of collagenous fibres seen both peri-cellular and peri-lobular in distribution, condensation and proliferation of bile ducts seen but not extensive, cellular infiltration of the parenchyma and of the connective tissue present and marked, mostly lymphocytic, mononuclears, vascular pattern altered, regeneration present and bile pigment present when jaundice is marked. Culture of the biopsy specimens did not show the presence of any pathogenic or other organisms excepting in two cases where growth of *S. aureus* was seen, most probably due to extraneous contamination.

Achar (1954) found hepatic fibrosis which is often annular and pseudo-lobulation in many of his liver biopsies, especially in the well developed cases. Regarding central vein, first of all it is difficult in many of his slides to find the central vein. In a few of the biopsy slides where he has located the central vein there was no occlusion of the central vein. He did not find evidence in his biopsy slides of fibrosis or mesenchymal reaction starting round the central vein or hepatic venous tree in the first place; neither did he find the central vein or hepatic venous tree occluded as described by Radhakrishna Rao in his monograph.

Srivastava and Aikat (1954) divide the course of the disease into three stages, viz., (1) early stage, (2) well established stage, (3) very advanced and late stage, and describe the histological findings of the liver biopsies in each of these stages. In the early stage they found necrosis of liver cells with cell infiltration; condensation of the reticulum and of the portal tracts with increase of cells; minor degree of fatty change. In the well established stage they found classical diffuse hepatic fibrosis; absence of cell regeneration of any significant degree; presence of active continued cell destruction of varying degree; marked cell infiltration; extension of replacement fibrosis into pseudo-lobules; and absence of any significant fatty change. In the very advanced and late stage they found gross alteration of the structural pattern associated with diffuse hepatic fibrosis; fibrosis extending into the lobules isolating small groups and single liver cells; marked and continued cell destruction; absence of any regeneration; the connective tissue was often vascular; absence of fatty infiltration; marked areas of cell infiltration.

It will be noticed that in the liver biopsies no evidence of fibrosis or mesenchymal reaction starting round the central vein or the hepatic venous tree is found. No occlusion of the central vein or the hepatic venous tree was also noted. But in all autopsy material the thickening of the hepatic veins of varying degree with narrowing of the lumen even to the point of occlusion was noted both by Radhakrishna Rao (1935) and Srivastava and Aikat (1954). The liver biopsies confirm the findings of Bhende and Deoras (1954) in their autopsy material of a primary as well as a secondary necrosis in the liver cells.

The clinical course of the disease.—These have been described in detail by Sarma (1946) and Gan (1950). To facilitate description the disease is generally described in three stages, though clinically or pathologically, there is no sharp demarcation between one stage and the next. This description of the disease is followed by most of the writers.

*The first stage or the stage of onset of the disease:*—The healthy and active child gradually becomes dull and morose. The child may have a voracious appetite or craving for abnormal foods. The bowels are generally constipated but sometimes there may be alternate diarrhoea and constipation. Even at this stage there may be a rise of temperature. The skin loses its glossy appearance and may be muddy. Sometimes sleep is disturbed in the night. On physical examination enlargement of the liver can be noticed even at this stage. The organ is usually not tender.

*The second stage or the stage of enlargement of the liver:*—The child is irritable and peevish. Fever is more marked in this stage and is usually of an irregular, intermittent type, though rarely it may be of a low remittent type. Constipation is more marked and the stools are of a dirty whitish colour. On physical examination there may be subicteric tint of the conjunctivæ, though there is no 'overt jaundice.' The abdomen may be prominent in the right hypochondriac and epigastric regions and the liver is definitely enlarged reaching to a level of the umbilicus and sometimes even beyond it. It is not tender, is smooth on its surface and firm, with a sharply defined margin, which is thin and hard. A few prominent superficial veins on the abdominal wall may be seen even at this stage. Enlargement of the spleen may not yet become noticeable.

*The third stage or the stage of contraction of the liver:*—The child loses interest in the surroundings and towards the end may be semi-comatose. All the visible mucous membranes are icteric and in fair children the skin also may show the icteric tint. The abdomen is protuberant and in the last stages of the disease there is ascites. Superficial veins on the anterior abdominal wall are more marked. The terminal clinical picture is one of general anasarca, deep jaundice of all the visible mucous membranes and sometimes of the skin and ascites. After the onset of the ascites, it is difficult to palpate the liver and spleen due to the tense abdomen. The liver is smaller than in the previous stage, but is still palpable below the costal margin and hard with a smooth surface and a sharp edge. Sometimes petechial hæmorrhages and gastrointestinal scanty and high coloured and deeply bile-stained. The urine is typically dirty, clayish in colour and offensive. The stools are intermittent fever may also be present in this stage.

Laboratory investigations.—According to Tirumurthi and Radhakrishna Rao (1934) and Radhakrishna Rao (1934) in the first

stage of the disease examination of the urine and motion reveal nothing abnormal, while the blood may show lymphocytosis, which is only perhaps normal for that age period. In the second stage the blood shows a definite leucocytosis with preponderance of the lymphocytes. The Van den Bergh reaction is direct, delayed, while the fragility of the red blood cells is either normal or diminished. The urine shows urobilin in a fair concentration. The total fatty content of the faeces may be increased. In a few cases a low fasting blood-sugar may be found in this stage. In the third stage the blood shows slight secondary anæmia. Leucocytosis is not a common finding in this stage. The coagulation time of the blood is delayed and the fragility of the red blood cells diminished. As the jaundice grows intense, the Van den Bergh reaction becomes "direct immediate." The urea and the non-protein nitrogen may be normal. Hyperglycæmia is said to be a common feature in the second and third stages, but in all their cases in which the fasting blood-sugar was estimated, it was found to be the lower limit of the normal. Bile salts, bile-pigment and urobilin are present in the urine in high concentration. A trace of albumin is present in the urine, but it is not usual to find casts or crystals. Degenerating leucocytes and epithelial cells from the bladder may be found in the urine in the last stages. In this stage, culture of the urine may show *B. coli* or *B. faecalis* alkaligenes. The microscopic examination of the faeces is generally negative for ova of helminths, amoebæ or Charcot-Leyden crystals. The liver function tests show diminished function of the liver. The ascitic fluid is a transudate and may be deeply bile-stained. The formol-gel test (Napier) and the agglutination tests with dysenteric organisms (both of the blood serum and the ascitic fluid) are negative.

According to Krishna Rao (1941) leucocytosis is a marked feature of this disease. The differential leucocytic count shows a proportionate increase in the number of lymphocytes and a corresponding diminution in the polymorphs from 25 to 50 per cent; the large mononuclear range from 1 to 3 per cent. The Arneth count shows a definite shift to the left with an increase of mononuclear polymorphs. There is no appreciable variation in the differential count of the leucocytes according to the different stages of the disease.

He found the blood sugar level lower than normal and this was particularly so at the terminal stages of the disease.

With regard to Van den Bergh reaction he found the direct reaction negative and the indirect reaction normal. In jaundice cases the test was direct positive or showed a biphasic reaction depending upon the jaundice.

Naidu (1948) found the faecal fat was distinctly higher than the average normal (30 to 35 per cent of dry faeces) and the percentage of fat in the faeces increased with the advance of the pathological

condition. The degree of splitting of the excreted fat and hence the pancreatic efficiency was normal except in the very advanced stages of the disease. The plasma content of the cholesterol was elevated and that of lipo-phosphorus lowered in this disease. With regard to the total non-protein nitrogen and urea in plasma it was found that whilst the urea content is within normal limits even in the very advanced stages, the total N.P.N. is very much elevated in the disease.

**Liver function tests.**—Bhattacharya and Chaudhuri (1933) stress the importance of the levulose tolerance test in this disease. They found marked hepatic insufficiency by using this test in their cases. Subramanyam and Naidu (1948) have carried the thymol turbidity, the cephalin-cholesterol-flocculation and the brom-sulpholein-retention tests of liver function in different stages of the disease in their cases. They found the thymol-turbidity test runs more nearly parallel to the pathological condition than the other tests. The cephalin-cholesterol test appeared to them to be hypersensitive and the degree of flocculation is at variance with the pathological classification based on the clinical symptoms.

Srivastava and Aikat (1954) have noted the hepatic function changes as they occur in various stages of the disease. In the early stage the thymol turbidity and cephalin-cholesterol flocculation tests become positive. Serum bilirubin, urinary urobilinogen and alkaline phosphatase are within normal limits. In the well established stage thymol turbidity and cephalin-cholesterol flocculation tests are definitely increased. Serum bilirubin and urinary urobilinogen may be positive. No change is noted in alkaline phosphatase. In the very advanced stage thymol turbidity above 20 units and C.C. flocculation test—Serum bilirubin and urinary urobilinogen very much increased. No change in serum alkaline phosphatase.

**Proteins in the blood.**—The changes in the serum-protein fractions of 20 juvenile cases were studied by Radhakrishna Rao (1948). A decrease in albumin and increase in globulin without any appreciable difference in the total protein were noted by him. In other diseases the lowering in albumin is accompanied by slight decrease in total protein level also. The level of euglobulin gives an idea as to the progress of the disease.

Srivastava and Aikat (1954) found the total serum proteins were below normal in 71 per cent. of their cases. Serum albumin was below 2.5 gm. in 69 per cent and below 2 gm. in 31 per cent of their cases. Serum globulin (normal limits 2.1 to 2.5 gm.) was increased in all cases. Alteration to reversal of albumin-globulin ratio was present in about 89 per cent of their cases.

**DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS:**—These are discussed in detail by Green-Armytage (1926), Mukherji (1922), Pandalai (1934) Radhakrishna Rao (1934) and Sarma (1946). With regard to diagnosis all the writers stress the difficulty of diagnosis in the early

stages, on account of the vague and the negative laboratory findings. The irregular intermittent fever, the enlarged liver, constipation and clay-coloured stools, lymphocytosis and the sub-icteric tint of the conjunctivæ, in the second stages, are fairly typical to suggest the diagnosis of infantile biliary cirrhosis. Its diagnosis is however, quite definite in the terminal stages. The deep icterus of all the visible mucous membranes and the skin, the signs of portal obstruction (ascites, dilated veins in the anterior abdominal wall, ballooning of the umbilicus, enlarged spleen, etc.), the enlarged and hard liver, the deeply bile-stained and scanty urine, are unmistakable evidences of the last stage.

The disease has to be diagnosed from kala-azar, familial acholuric jaundice, rickets, Hanot's biliary cirrhosis, malaria, catarrhal jaundice and other forms of viral hepatitis and congenital syphilis. Passive congestion, fatty infiltration, amyloid disease, new growths and downward displacement of the liver should be remembered in the differential diagnosis of the diseases. The differentiation from kala-azar, rickets, and malaria is not difficult. The blood examination and specific serological tests, should be enough to differentiate these diseases. Hanot's cirrhosis is more chronic in its course and is generally seen in young persons rather than in infants and the crises (abdominal pain with fever, increase in the size of the liver and spleen and deepening jaundice), which are typical of the disease, are not seen in infantile biliary cirrhosis. In catarrhal jaundice the enlargement of the liver is usually slight, the organ is tender and soft, generally there is a history of high fever before the onset of jaundice, which is usually slight and diminishes gradually after the treatment. It is not so easy to differentiate this disease from other forms of viral hepatitis. It is easy to differentiate infantile biliary cirrhosis from typical cases of congenital syphilitic cirrhosis. But in occasional cases the diagnosis may be difficult. A history of syphilis in the parents and positive W.R. are not always helpful in the diagnosis of congenital syphilis. The stigmata of the disease are generally seen in the children affected with congenital syphilis. Familial acholuric jaundice may present real difficulty in diagnosis. There is no bile in the urine. The fragility of the R.B.C. is increased. The disease runs a chronic course marked by remissions and exacerbations.

Two conditions require special mention in the differential diagnosis, *viz.*, erythroblastosis foetalis and neo-natal hepatitis.

**Erythroblastosis foetalis.**—Hawkely and Lightwood (1934) suggested and gave evidence that some cases of juvenile cirrhosis are associated with erythroblastosis. Henderson (1942) from a study of 4 cases of stillborn infants with erythroblastosis and hepatic cirrhosis concluded that many cases of juvenile cirrhosis in early adulthood may be a part of or the result of erythroblastosis. The clinical findings in erythroblastosis foetalis include jaundice, œdema and

anæmia. Such manifestations may occur at birth or soon after. Hepatomegaly and splenomegaly are prominent. Hemorrhagic manifestation may be present. The presence of many nucleated R.B.C. is the rule but is not universal. A leukemoid blood picture is usual. Tribedi and Chanda (1950) report a case of a Hindu male child, four and a half years of age with low irregular fever, loss of appetite, gradual weakness, deepening yellowish colouration of the conjunctivæ and skin of one and a half months' duration. W.R. of the patient as well as of the parents was found to be negative. Father was Rh. positive, mother Rh. negative. The patient was Rh. positive. Post-mortem post-necrotic scarring was found.

Srivastava and Aikat (1954) did the Rh grouping of both mother and infant in eleven cases. All cases were Rh positive, both mother and child. Coomb's test for incomplete antibodies was negative in all cases. From these observations they concluded that Rh incompatibility has no part to play in the causation of infantile cirrhosis of liver. Moreover, from the survey of Rh grouping which is in progress in G. R. Medical College, Gwalior, it appears that the problem of iso-immunisation due to rhesus factor is very much less in the population under study as the number of Rh negative women is significantly less than what we observe in other countries." Of prime importance in establishing a diagnosis are the Rh data, which 90% of the patients will show an Rh positive father and child but an Rh negative mother. Agglutination antibodies in the maternal serum are conclusive evidence when they are demonstrated.

Neonatal hepatitis.—Craig and Landing (1952) reported a group of 20 cases of hepatitis occurring early in infancy. Histological active hepatitis having the characteristics of viral hepatitis was found in all 20 cases. In 13 in which there was a tentative diagnosis of biliary atresia, exploratory operations were performed, but in no case was the biliary tree atretic. From these data, they concluded "that hepatitis having the histological appearance of viral hepatitis is a not too infrequent finding in early life and must be considered in any differential diagnosis of icterus in the neonatal period. The disease is characterised by prolonged jaundice manifesting soon after birth. The jaundice varies in its intensity and may extend from months to years. Clinically it resembles obstructive jaundice. Apart from jaundice, vomiting is not an unusual symptom. Diarrhoea is uncommon. There is a tendency to bleed and intra-cranial hemorrhage and umbilical bleeding may occur. Anæmia is not a conspicuous feature of the disease. The abdomen is prominent and the liver is enlarged. The spleen is often palpable. Biopsy of the liver is the sure method of diagnosis. The most conspicuous and distinctive feature is the presence of multi-nucleated giant liver cells diffusely distributed throughout the lobules.

**TREATMENT:**—Green-Armytage, V. B. (1926), Pandalai, N. G. (1934), Brahmachari, U. and Brahmachari, P. (1938), Sarma, A. V. S.

(1946) and Subramaniam, V. and Naidu, V. R. (1948 and 1949), discuss the treatment in detail. All are agreed that the treatment is successful only in the early stages of the disease and of no avail in the third stage of the disease. Treatment is mainly empirical and symptomatic. This is bound to be so as long as the nature of the disease is undetermined. In the main the treatment is dietetic based on the well established fact that certain food factors like choline, cystine and methionine are essential for the proper functioning of the liver.

Green-Armytage, V. B. (1926) remarks that the treatment is successful in 70 per cent of cases provided it is started early enough and before ascites, anæmia or œdema occur. He stresses the importance of treating the mother during the anti-natal period and during lactation. The aim should be to increase the calcium, iron, iodine, etc. and also the hormone content of her milk. With regard to the feeding of the child after weaning, the absolute essential is a fat-free diet which relieves the over-worked and congested liver. He also points out the importance of a healthy wet-nurse when the mother's milk is not found satisfactory.

Pandalai, N. G. also stresses the importance of careful dieting and hygiene of the mother during pregnancy and lactation and of the infant when it is weaned.

Subramaniam, V. and Naidu, V. R. tried choline chloride in the treatment of some of their cases. They claimed good results in the early stages of the disease. They treated a number of their cases with a pepsin-proteolysed extract of the liver and spleen supplemented with choline chloride. There was no appreciable difference in the results obtained by these two methods. In stage I and stage II-A the results were good, in stage II-B the results were fair, whereas in stage III neither methods of treatment is difficult to understand.

Krishna Rao (1950) who believes that the disease is caused by two factors, viz., cow's milk and *B. coli* infection, has made this assumption the basis of his treatment. Cow's milk is substituted by any good brand of dried milk, choline in the form of mixture is 420 grains per dose—3 times a day. Subcutaneous injection of vitamin B-complex and an auto-vaccine of *B. coli*, prepared from the stools of the children suffering from the disease in divided and gradually increasing doses on alternate days from 0.1 cc. to 1 cc. per dose, (1 million organisms per cc.). The injections were continued at 1 cc. per week for two months. Later he changed the treatment to streptomycin injections  $\frac{1}{2}$  g. per day for 8 days—oral administration of vitamin B-complex and choline for 3 months and claimed good results both in early and late cases. So far there have been no reports in the medical literature about the success or failure of this treatment. There is no reason why this treatment should be any more successful than other empirical treatments as his basic assumptions have not been proved to be correct.

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## ULCERATIVE COLITIS \*

### (A HISTORICAL REVIEW)

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THE word 'Colitis' is of comparatively recent coinage, though the disease which it is meant to denote is not a new one. It has been known to occur in all ages and the symptoms were attributed to various types of dysenteries. It was not considered a separate entity, although the symptomatology was well recognized. Its pathogenesis and treatment were and continue to be shrouded in mystery. It was variously labelled 'Chronic bacillary dysentery,' 'Non-specific colitis' and 'Chronic-colitis,' from time to time.

Mention has been made of this condition in our ancient system of Hindu Medicine in which all the dysenteries and colitis were grouped together, under the heading of a common group of abdominal disorders which were further sub-divided, and dealt with in detail in the *Charaka Samhita*,<sup>1</sup> written 700 years before Christ.

Sydenham<sup>2</sup> (Father of Modern Medicine) first described the disease in 1669 and named it the 'Bloody flux.' But at that time the disease was looked upon as a regional disorder and not a systemic disease.

In 1875 Wilks and Moxon described cases of 'Chronic bloody flux' which they just believed to be a form of dysentery but which were most probably cases of ulcerative colitis.

Gemmel was the next to study cases of asylum dysentery, his description of which conforms to that of ulcerative colitis. In 1898 he described it as a specific disease, endemic as well as epidemic and he was of the opinion that a micro-organism ingested with food was probably the cause. Further, he asserted that it was fairly common and occurred under conditions similar to those that caused dysentery and that although, it was a fatal disease, it was by no means incurable.

The ætiology of the disease, has been uncertain all along and even today, no one factor can be labelled as being responsible for its causation. This does not, however, mean that the subject was neglected; on the contrary, it has received considerable attention from a number of eminent workers, though the results have so far been inconclusive.

The possibility of psychic factors being concerned in the production of colitis, has been investigated for a long time and it is now believed that there is a definite relationship between the two.

\* Specially contributed to the 'ANTISEPTIC'

Which of these may be the cause and which the effect is still however, uncertain.

Sullivan and Chandler<sup>46</sup> who were among the earliest workers, to recognize the possible role of psychogenic factors in the aetiology of ulcerative colitis, reported in 1932 that colitis was caused by psychogenic factors in 60% of cases. Then in 1938, Wittkower<sup>43</sup> observed abnormal psychological patterns in the 92.5% of the cases of colitis which he studied. His findings were however, vitiated by the absence of simultaneous controls. Alexander<sup>47</sup> was also of the opinion that emotional disturbances played a role in the aetiology of the disease. In 1948 Danielson<sup>17</sup> very emphatically stated that there was a clear-cut relationship between psychological abnormalities and ulcerative colitis, the former playing the role of precipitating factors.

Portis<sup>38</sup> in 1949 made valuable and comprehensive observations in his exhaustive articles on colitis. He suggested the possible effect of emotions on the gut, stating that in the case of emotionally hyperexcitable individuals these emotions caused an overstimulation of the parasympathetic nervous system, leading to a disturbance of the physiologic function, increased the contractions of the small intestines and hypermotility of the colon. Ulcerations might be caused by the devitalizing effect on the intestines, of a tic enzyme on the mucosa of the colon. Ulcerations lessened blood supply or due to the digestive action of the pancrea-enzyme is destroyed before it reaches the colon, but it may be lity of the bowel.

In 1951, Almy<sup>4</sup>, Grace, Wolf and Wolff<sup>48</sup> confirmed the view put forward by Portis (*loc cit*) that the stress and strain of modern life produced sustained hyperfunction of the colon; while Liium<sup>49</sup> in 1939 produced ischaemia which in its turn might cause ulceration. The findings of these workers therefore, afforded positive evidence in favour of the role of psychogenic factors in the aetiology of chronic ulcerative colitis.

In 1953, Kirsner and Palmer<sup>50</sup> studied the personality patterns of individuals who were victims to ulcerative colitis. They described most of these individuals as being 'dependent, immature, narcissistic yet hostile and aggressive individuals.' Weiss and English<sup>51</sup> who studied the psychosomatic aspects of various diseases have cited many cases of ulcerative colitis in which the psychogenic factors played a prominent role and psychotherapy was found to be of definite value in treatment.

Portis (*loc cit*) also suggested the role of lysozyme in the production of colitis and based his statement on the findings of Meyer, Gellhorn, Prudden, Lehman and Steinburg<sup>52</sup> who in 1948

studied the lysozyme titre in cases of chronic ulcerative colitis and compared it with the lysozyme titre of the colon in normal individuals. This work has added another possible factor in the aetiology of ulcerative colitis. Lysozyme is a mucolytic enzyme, which is present in small amounts normally, but the titre of which is however, found to be raised in cases of peptic ulcer and colitis. It has been suggested that lysozyme acts by bringing about a dissolution of the mucus which has a normal protective action against deleterious agents acting on the mucosa of the alimentary tract.

Infection is a major factor for consideration in the aetiology of colitis. Some of the earliest workers<sup>53</sup> were of the opinion, that colitis is only a phase of dysentery. In fact they made no differentiation between dysentery and colitis. Bargaen<sup>54</sup> was one of the earliest workers who took up the work in greater detail in 1924. He held the view that colitis was caused by a *Diplobacillus* which he detected in 80% of his cases of colitis. In 1933 Bargaen, Buie *et al.*<sup>55</sup> in an attempt to prove the streptococcal origin of ulcerative colitis reported the presence of the organisms in histological sections of the colon in experimentally produced lesions. But, Paulson, Friedenberga and Wolpor<sup>56</sup> in 1928 working under Dr. F. Boerner disagreed with Bargaen's finding, as they could find no specific data to incriminate the diplostreptococcus which therefore, had no place in the aetiology of this disease. The findings of Paulson, Friedenberga and Wolpor<sup>56</sup> were later confirmed by Torry and Montu<sup>48</sup> in 1936, Kessel<sup>57</sup> in 1935 and Rafsky and Manheim<sup>58</sup> in 1952.

In 1938 Brown and Bargaen<sup>59</sup> reported that they found no relationship between dysentery and chronic ulcerative colitis, on the basis of a sixteen-year follow-up of cases of dysentery during the course of which they observed colitis in only one out of 102 cases. The findings of these workers tally with those of Hern<sup>60</sup> who as early as 1931 noted a similarity between the chronic forms of the two diseases but did not agree with the view that ulcerative colitis is a form of bacillary dysentery. Hurst<sup>61</sup> and Felson<sup>62</sup> on the other hand, admit a definite relationship between colitis and bacillary dysentery and Hurst<sup>61</sup> in 1936 labelled ulcerative colitis as a "modified, noncontagious form of bacillary dysentery," although he could not give a satisfactory explanation for the difference in the age incidence. Felson<sup>62</sup> in 1941 reported an incidence of colitis in only 8.2% of patient who had previously suffered from bacillary dysentery. During the same year (1941) Dragstedt, Dack and Kirsner<sup>63</sup> working independently reached the conclusion that *Bacterium necrophorum* was responsible for the causation of ulcerative colitis; but this too was just a supposition. In 1951, Marshall, Kirsner and Palmer<sup>64</sup> isolated haemolytic aerobic bacteria in normal individuals as well as in patients with ulcerative colitis. Paulson<sup>65</sup> and Bockus<sup>66</sup> were the first to suggest that the normal inhabitants of the bowel may act as secondary invaders on a previously devitalized and ulcerated

mucosa and causing further damage. Paulson<sup>11</sup> put forward his view in 1933 and eight years later in 1941, Felsen<sup>12</sup> expressed the same view regarding the aetiology of colitis. In 1942 Winkelstein and Schwartzman<sup>13</sup> reiterated this fact and if proved conclusively, this would explain the presence of normal intestinal flora, found in stool and sigmoidoscopic swab cultures in many cases of ulcerative colitis.

Anderson<sup>1</sup> was among the first to suggest in 1942 the role of allergy in the production of ulcerative colitis, of which concept he is still a staunch supporter. But there is not much evidence in favour of allergy playing a role in the causation. Bockus<sup>14</sup> expressed doubts regarding the specificity of allergy in the pathogenesis of ulcerative colitis. Jones, Baggenstoss and Borgen<sup>15</sup> (1951) stressed the role of nutritional factors in the production of ulcerative colitis. But the trend of modern thought is that nutritional disturbances are only secondary and not primary to the disease. Levine, Kirsner and Klotz<sup>16</sup>, Sommers, Andersen and Warren<sup>17</sup> suggested that ulcerative colitis had in common with certain other diseases, the characteristics attributed to 'collagen diseases'; but the similarity is not striking. It was perhaps on the basis of this view that Halsted<sup>18</sup> in 1952 used ACTH in ulcerative colitis.

The disease has been classified in two ways: Borgen<sup>1</sup> in 1943 gave a clinical diagnosis, while Warren and Sommers<sup>17</sup> in 1949 gave a pathological classification. The pioneers in the field relating to the pathogenesis of colitis are Warren and Sommers<sup>17</sup> who published their earlier findings in a very comprehensive article in 1949; and have since completed their work as will be seen from the report they published in 1954<sup>19</sup>.

Brooke<sup>20</sup> in 1953 aptly summarized the prevailing views on the aetiology by stating that ulcerative colitis is not a specific disease but a pathological state resulting from infection, stress, chemical agents or some other factor causing trauma. He also drew attention to the irreparable damage done to the mucosa and stated that the weak scars that formed, may easily break down. Card<sup>21</sup> in 1952, referring to the regional distribution of the pathology, stated that the rectum and sigmoid colon are maximally affected and that tenderness over the colon, especially in the left iliac fossa was the only constant physical sign of value in the diagnosis.

Among the large volume of work on treatment we have very often heard of specific and effective treatments—only to be told later that they did not stand the test of time. The *status quo ante* remains. Dietary adjustment in these cases, was stressed by Portis<sup>22</sup> in 1949 and later by Bockus<sup>14</sup>. Dieteticians of the Mayo Clinic outlined a well-balanced and easily managed diet for these patients. Grace, Wolf and Wolff<sup>23</sup> in 1951 and Douthwaite<sup>24</sup> in 1952 reported on the effectiveness of psychotherapy and advocated the use of suitable psychotherapeutic measures as part of the treatment of colitis.

The routine use of enemas has long been advocated as being an effective and special form of local treatment and different types of retention enemata have been suggested. As early as 1931, Felsen<sup>12</sup> suggested intra-colonic oxygen, while Best<sup>25</sup> in 1938 suggested rectal instillation of Cod liver oil which would provide nutrition in addition to its soothing and lubricating effect.

The use of antibiotics is not a new suggestion, for as early as 1947 Streicher<sup>26</sup> tested the sensitivity of organisms to penicillin and suggested its use. Then in 1950, Marshall, Palmer and Kirsner<sup>27</sup> tried the effect of sulphonamide, penicillin, streptomycin and chloromycetin and came to the conclusion that it is difficult to assess the value of antibiotics in colitis.

In 1951 Strax, Marks and Wrights<sup>28</sup> published their findings on aureomycin therapy for colitis. Bierman and Jawetz<sup>29</sup> studied the effect of antibiotics on the faecal flora as such. In the meantime work had been done on the possible role of lysozyme in the production of colitis as a result of which Prudden and Meyer<sup>30</sup> published in 1950 their results on trials with Nisulfazole and Alkyl sulphate. While Bauer<sup>31</sup> and Halsted<sup>18</sup> in 1952 studied the effect of ACTH and cortisone on these cases.

The possibility of liver damage as a result of colitis has been extensively investigated. But most of these studies relate either to postmortem examination or biopsy tests. Workers assessing liver damage by the liver function tests were only able to detect mild hepatic derangement. It has not yet been established whether the liver damage, is due to malnutrition or to the toxins of the disease itself or whether it is a coincident occurrence without any particular relationship to the disease. Gyorgy<sup>32</sup> suggested that 'gastrointestinal intoxication' may lead to liver damage.

Other prominent workers in this field are Jones, Baggenstoss and Borgen<sup>15</sup>, Logan<sup>33</sup>, Comfort, Borgen and Morlock<sup>16</sup>, Cain and Cattani<sup>13</sup>, Tumen, Monaghan and Jobb<sup>49</sup>, Ross and Swarts<sup>42</sup>, Pollard and Block<sup>39</sup>, Warren Sommers<sup>51</sup>, Kimmelmanstein, Large and Verner<sup>30</sup>.

The above is a brief review of the literature relating to the state of our present knowledge of ulcerative colitis up-to-date. Future work will, we are sure, add to it and perhaps fill up the lacunae that are found therein.

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### THE USE OF NOVOCAINE BLOCK IN HYPERTENSION WITH FUNDUS CHANGES

Retrobulbar injections of 0.25 per cent novocaine (combined at times with periorbital injections) were applied in 31 patients who had changes in the fundus. The treatment was most effective in the initial stage of hypertension. The best results were obtained in patients with recent occlusions of the central retinal artery: the vision, visual fields and the central scotoma were greatly improved and there was no regression during the next one to five years. Early retinopathy also responded to the treatment. In the late stage of hypertension the novocaine injection did not change the fundus picture. The injections were given two to three times with an interval of ten days. Headaches, insomnia and nervousness were also improved. The author believes that the novocaine "blockade" acts on the pathological local changes of the retina through the central nervous system.—(*Vestnik oftal.*, 34: 17-21, March-April, 1955 via *Am. Jour. of Ophthalmol.*).

## OPHTHALMOLOGY AND QUACKERY\*

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LIKE some mocking ghost of a guilty past, quackery keeps trailing the march of science. If chemistry recognizes its spectre as alchemy, modern medicine, knows the ghost of quackery by names as varied as its many special branches. The shadow of the bone-setter or the osteopath still darkens the path of the orthopaedist. The medicine man and the witch-doctor keep dogging the physician in the dark, brown and even the white continents of the world. The eye-doctor cannot shake off the street-corner healer, not yet in India atleast. To the modern eye-doctor, ophthalmology is a scientific and fascinating study of all the branches of knowledge concerning the eye, which enables him to treat the disorders of the eye and of vision with an intellectual perception and great skill. To reach the accepted standard for the practice of ophthalmology, the ophthalmologist has to put in years of study, in getting his basic medical qualification, and then undergo a further advanced and specialized course of critical study, and adequate training under capable doctors well versed in this speciality. The quack's preparation and high-way to practice are short and easy, requiring little or no study or standards, and completely disregard the dire consequences of his empirical unscientific ministrations.

How then does this eye-quackery flourish?—The almost external and detached anatomical position of the eye from the rest of the human body, the widespread incidence of eye disorders, the many aberrations of vision, the plethora of lay literature dealing with nature-cures of visual defects, and not the least of all, the shocking credulousness even of our educated people, provide tempting material for any shrewd self-appointed healer to practise eye-craft, with a guarantee of a comfortable livelihood and a negligible threat of reprisal or punishment. Any busy street or market corner offers him ready enough space to ply his nefarious trade, his fees being anything from a few annas to tens of rupees, all that he needs being a gullible person with some affliction and a belief in his strange healing powers and nostrums. The immense natural healing forces of the human body are his greatest assets and when things go wrong, the inherent fatalism of his clients does not fail to put him beyond reproach. Is it any wonder then that quacks rush into this field where qualified doctors often fear to tread?

Quack eye-medicines and surgery.—This wide field provides prosperous occupation for many types and kinds of operators. A person or a group of persons, with office facilities in a city and with some capital resources, get up a hodge-podge formula resounding with high-falutin names of some unheard of herbs (the more difficult and more numerous the names, the better the trade) and offer it as the

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cure-all for eye afflictions of any kind! The sale of such universal healers, comforters and sight-restorers is usually effected through the mail-order business and even across the counters of reputed chemists, but the *doctors* who cook up such formulæ are never interviewable. Their lucrative obscurity is rigorously maintained under some assumed identity, which professes to have received the knowledge of the unique formula, directly from some Himalayan sage, having a pre-vision of ancient Vedas and Tantras. The credulous and neurotic elements in our city's population form the customers for such remedies, and the harm is done by their misplaced and obstinate belief in the claims made for these quack-remedies. Fortunately the illiteracy of the rural population often acts as a blessing in disguise. But though it saves some from the lure of such medicines, their illiteracy makes them victims of the machinations of yet another type of operator, who works on the street level, and is therefore, the more serious menace. His, is usually the one-man mobile unit stationed at the middle of a busy street or in a bazar corner. The mobility has self-evident advantages. Never stationed in one place long enough to experience the boomerang of curses from his victims, he moves from town to town to a slow schedule, with plenty of resourcefulness and ease to fleece misguided persons suffering from some eye affliction. His temporary street-corner shop has a certain colourful set-up. A well-spread carpet or a table before him exhibits an assorted collection of medicine bottles, complete with droppers and pipettes, filled to overflowing with coloured fluids, jars and tubes of pastes and ointments (on close scrutiny you may even find in the lot some erythromycin or cortisone!), a collection of dishes containing tidy heaps of powdered pigments, dried-up sticks of roots and tubers, intermingling with pieces of skin and hoofs and nails of some wild beast or other. Flamboyant charts of the anatomy of the eye and enterprising the person the more elaborate the picture. The more it is not unusual to find even diplomas (easily obtained for cash from some agency having a flourishing business in this trade) declaring pathy of sorts, all very impressive but absolutely meaningless and worthless certificates in some language or other. A smooth and inter-minable gift of the gab helps him to draw his clientele. Never bothered by any diagnosis, he divides his patients into three easy divisions, sore eyes, blind eyes and painful eyes, giving red pigment for the one, yellow ointment for another, or the white drops for a third. While his hit or miss tactics result in the amelioration of some of the simpler self-limiting disorders of the eye, serious conditions like glaucoma, trachoma, ulcers or cataracts deteriorate, and irreparable damage is done by the use of wrong and dangerous drugs, and very often the chance for doing good by a qualified person is lost for ever; blindness, pain or disfigurement, result in many of the victims. It is when the quack takes to 'surgery' of the eye that he

usually inflicts the maximum damage. This is done for the condition of cataract, when an opacity of the lens due to old age, appears as a white spot in the centre of the pupil and is the cause of much loss of vision. The quack makes capital out of this condition, once a willing victim gets into his clutches. The person with the white spot and blindness is exhibited to the crowd of spectators gathered round him. The self-styled surgeon then uses a speculum to keep the lids away, and then with a blunt probe, dexterously and most spectacularly pushes the opaque lens away inside the pupil. To the amazement of all sightseers (and by this time they have gathered in scores, pressing around him) the white pupil now looks black and the victim immediately admits of some vision where there was none before. The quack's success is now complete, but not so the patient's whose troubles have actually just begun with the displaced or the couched lens as it is technically known. This displaced lens eventually becomes the cause of complete loss of sight, by which time the quack-operator would have covered some long distance, inflicting injuries on several other gullible victims.

The optical quack.—He is of a less harmful but more ubiquitous kind. He is a pedlar in optical goods, with a stock of multi-coloured lenses, goggles and attractive frames. He treats defects of vision on a trial and error basis and as long as he is able to effect a 'sale', it is immaterial to him whether his customer stands to gain or lose.

The refractive defects of vision, which are not due to any pathological lesions, offer an enterprising field for yet another type of unscientific therapy, which professes to cure visual defects without the aid of glasses but only by means of suitable exercises for the eyes!

It must be stated at once that here we are dealing with a controversial subject. Treatises and books have been written for and against the success of such methods. Suffice it to say that unless one comes across a bonafide practitioner of this art of curing visual defects by naturalistic methods, it is unwise and dangerous to abide by the advice of any and every such self-styled healer.

Prevention of quackery.—We have so far considered the various types and methods of quackery in the treatment of eye disorders which are rampant in our country, which account on a cumulative basis for the colossal misery, damage and blindness that we meet with in people who have been victimized by unscrupulous quacks, whom the public, including the victims are loath to expose and bring to book. The complex problem is linked with the prevention of blindness, the spread of health education, the provision of enough qualified personnel and enough proper curative facilities for eye disease. Mere punitive legislation against quacks will not solve the problem. It is to be hoped that the proposed All India Pharmacy Act, will go a long way in eliminating, the medical atleast if not the surgical eye-quack also.

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## IDIOPATHIC EPILEPSY AND ITS PROBABLE MODE OF ORIGIN FROM SUBCORTICAL LEVEL\*

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THE most common cause of idiopathic epilepsy both major and minor, may be found in a congenitally existing predisposition to heightened activity of the hypothalamus and sympathetic chain of ganglia and the visceral ganglia in paroxysms, due to the lowering of its threshold of stimulation; this manifests its signs and symptoms mostly during the adolescent stage between the ages of 15 and 25, which is the period of active growth of the body, and marks the transition from childhood to adult life with marked alterations in the endocrine secretions and increased production of sex hormones. A lowered threshold to stimulation of hypothalamus existing inherently, is liable to manifest itself by heightened discharges occurring in it, paroxysmally of its own accord, without any extraneous or afferent stimulation and much more so, when afferent impulses from the sympathetic reach it from the body surface, special senses, and viscera, as when the skin is being stimulated by cold, olfactory stimuli affecting it through connections existing between the Rhinencephalon and the hypothalamus through the medial forebrain bundle, visceral ganglia (hypogastric mesenteric etc.) being stimulated, when there is a loaded bladder or rectum as in voluntary restraint of micturition for a long time and constipation. Stimulation of the hypothalamus either through the afferent tracts conveying sympathetic fibres reaching it, through the spinal cord, or production of increased discharges from the hypothalamus itself paroxysmally due to the lowered threshold to stimulation, inherently present in it, stimulates the large celled portion of the dorsomedial nucleus of the thalamus, which has both afferent and efferent connections with hypothalamus. The impulses from the posterior hypothalamic area reach the midline and intralaminar nuclei of the thalamus in the intermediate region by fine myelinated fibres, and through its intrathalamic connecting fibres, the impulses reach the large celled portion of the dorsomedial nucleus of the thalamus, from where it is projected by means of the cortical connections of the adjacent small celled portion of the same nucleus, to which the impulses pass, which projects it on to the prefrontal areas of the cerebral cortex (areas 8, 9, 10, 11, 12 and 45) and also to the cingulate gyrus. Due to this stimulation of areas 8 and 9, dilatation of pupils and conjugate deviation of the head and eyes to the opposite side are effected. Consciousness is lost soon after the thalamic reticular system is stimulated, according to the degree of strength of its stimulation, the occurrence and duration of the period of loss of consciousness, depending on the strength of stimuli

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reaching it from the hypothalamus, as the seat of consciousness is probably located in the thalamus, hypothalamus, and neighbouring parts of the upper brain stem.

The following opinions of leading neurologists are given in order to substantiate and support the view that the cerebral cortex is *not* the seat of consciousness and that it is seated in the thalamus, hypothalamus and neighbouring parts of the upper brain stem:—

The cerebral cortex has long been assumed to be the organ or locus of consciousness, a general preference being held for the pre-frontal areas. But Penfield and Jasper offer a fresh conception of the neural basis of consciousness—that it is seated in the thalamus, hypothalamus and neighbouring parts of the upper brain stem. They speak of these structures and their connections as the centrencephalic system, and consider the latter, rather than the cerebral cortex, as the highest level of neuronal integration. Someone or other manipulation in the region on the medial part of the thalamus, during operation, as in the instance cited by Penfield, may be followed rather suddenly by loss of consciousness, which is soon regained when the procedure which precipitated the lapse, is stopped (exactly similar to symptoms and signs of petit mal). According to this conception, it is the function of the neopallium to elaborate upon the field of consciousness for which the centrencephalic system provides a primary integrative basis. The cortex of course is essential for development of those attributes, peculiar to the brain of man—abstract thought, speech, mathematical calculation, imagination, creative ability, and all those higher mental capacities which come within the realm of intellect, and which are so variable from person to person.

(1) Experimental evidence for proof of this is clearly given in Fulton's "*Physiology of the Nervous System*":—The close functional inter-relation between the thalamus and cortex has been emphasized by the studies of Jasper and his associates. They find that the midline of the thalamus—which appears to be a continuation of the reticular system of the mid-brain—are responsible for regulating the spontaneous electrical activity of the cortex and they designate this hitherto unexplored region, the "Thalamic Reticular System." They observe that it continues to regulate spontaneous cortical activity, after they have destroyed the lateral and ventral projection nuclei—a disclosure, which harmonizes with Morison and Demsey's (1943) and Morrison and Bassett's (1945) studies on cortico-thalamic inter-relations. Jasper and others (1949) find further that when the thalamic reticular system is stimulated in conscious animals, through implanted electrodes, striking "arrest" follows in which the animal, becomes frozen in any posture which it might happen to have assumed at the time of stimulation. Stronger stimulation of the same region, caused in addition to arrest reaction, minor seizures, which consisted of twitching of the eyelids and facial

muscles, very much as in petit mal epilepsy in man. These responses were seen in both cats and monkeys. The role of the hypothalamus in conditioning, has been systematically explored by Masserman (1942). Stimulation of hypothalamus by means of an implanted electrode in the unanæsthetized, freely moving cat, elicits a fixed pattern of reaction involving pilo-erection, mydriasis, hissing, growling, lashing of the tail, clawing, biting, and running movements. These reactions cease abruptly, when the electrical stimulus ceases.

(2) Important points from the lecture delivered on 17-1-'52, by Sir Geoffrey Jefferson, M.S., F.R.S., (Emeritus Professor of Neurosurgery, University of Manchester) at one of the lectures arranged by the British Postgraduate Medical Federation and the Committee of its Central Academic Council on the scientific basis of medicine, on the organization of cortical mechanisms, emphasize the importance of the lower levels of the brain and the afferent tracts, leading to them, in the integration of the mechanism of cerebral functioning.

Nervous systems exist as communication systems, more particularly as information systems, the rest of the body existing to assist it by providing it firstly with energy required for their use and maintenance and secondly by giving us the mobility that is required for finding food, for defence, and reproduction—for maintaining ourselves and our succession in a world, an environment in which these things have to be won. The brain itself is interested in long distance control of metabolism, through the visceral brain, hypothalamus and pituitary apparatus. There is much more here, than could have been conceived of by those early experimenters, who discovered electrically stimutable areas in cortex, investigators who first obtained visible results from cortical stimulation, for all the areas of the cortex can be activated by stimulation provided that the right stimulus is used, though the results must sometimes be looked for (*e.g.*) alterations of heart rate, in B.P., respiration, blood sugar, and so forth. The Island of Reil is a good example or again results must be searched for electronically until a response in the form of altered activity is found in some distant or near cortical area.

Activity of the cerebral cortex.—The outstanding features of cortical activity are fluctuations in electric potential, in cycles per second, as recorded by E.E.G. Rhythmical activity of cerebral cortex as shown by the Alpha Rhythm at 8-15 cycles per second, is upset by attention, by interest in anything presented to the subject, as well as by drowsiness, sleep, and chemical alterations in cerebral blood flow. It is greatly altered in pathological states of depressed consciousness (Parasomnia), whether caused by injury or disease or experimentally produced. In these states, the fast-rhythm becomes slower, the fluctuations in potential more irregular, and the voltage higher. The effect is diffused symmetrically over both hemispheres and cannot be

produced by cortical injury, but is easily caused by stimulations or injuries to the brain stem or to some parts of the thalamic nuclear complex. The question of the cortex having an intrinsic rhythm of its own or whether it owes it to projection fibres from lower levels, have their advocates. No one believes that cortical speeds of discharge depend on rhythms set by a pace-maker in basal ganglia or elsewhere, though undercutting the cortex or removal of the thalamus, greatly reduces cortical activity. Intracortical spread of activity certainly occurs. The thalamus itself has its own rhythms but it is not itself responsible for every cortical wave.

[NOTE:—But it can influence and alter the nature of the cortical wave by its connections with it, rhythms of the thalamus, being influenced by various afferent stimuli received by it through the sensory tracts, viscera or special senses.]

Rhythms in cortex and thalamus are often discrepant. Thalamograms have been studied in man and animals, particularly by Williams and Parsons Smith (1950), in England by Jasper (1947) and Spiegel and Wyss in North America. We may assume that "feed-back" systems exist between cortex and thalamus. The theory of reverberating chains, have become very popular though no one has ever seen one in action. And indeed except as momentary affairs, they are doubted by neuro-physiologists.

[NOTE:—Even momentary affairs or changes play a very important role in affecting the stability of the extremely complex nervous system of human beings, especially and of the higher mammals either temporarily or permanently. Influencing of cortical activity by altering it momentarily at least, either being one of depression or excitation, due to the various afferent impulses arising in an individual during various bodily processes as digestion, peristalsis and numerous others, as well as various special senses, stimuli being conveyed through afferent channels to the brain-stem area and through thalamus and hypothalamus to the cortex, seems quite probable].

It is the view of Penfield and his colleagues that the primary disturbance in idiopathic epilepsy, has its origin in subcortical mechanism. The primary disturbance, responsible for the cortical discharge, in idiopathic epilepsy, probably lies outside the cortex. Evidence for subcortical origin of petit mal attacks, is provided by electroencephalographic studies. During such an attack, electrical potentials of the wave—spike type—appear synchronously over pre-frontal areas, as well as from other widely separated cortical areas. This suggests that the cortical discharges are initiated in a common subcortical region (centrencephalic system), connected with extensive areas of cortex. Jasper and Drooglever—Fortuyn with experiments with cats, produced electrical potentials from widespread areas of the cortex synchronously in both hemispheres, by rhythmical stimulation of a small area 2 m.m. in diameter, in the anterior part of the massa intermedia of the thalamus. The cortical potentials were of the wave spike form, characteristic of petit mal. The view that the origin of the potential changes recorded in the E.E.G.

depend upon subcortical structures, is given by Burns, from experimental evidence adduced by him. He isolated a slab of unanaesthetised cortex completely from the rest of the brain, except for its blood supply, which remained intact. The isolated tissue responded, when stimulated, but all spontaneous electrical activity, was abolished. If a narrow bridge of nervous tissue, was left connecting the slab of cortex with the rest of the brain, spontaneous electrical waves crossed the bridge and excited the otherwise isolated cortex. Division of the thalamo-cortical connections, by undercutting also abolishes or reduces the voltage of waves in the cortex and greatly alters their form. It is now generally held that while the cortex is not incapable of rhythmical electrical activity of its own, which can be influenced and altered in various ways through the usual afferent channels, namely the "resting rhythms" as ordinarily recorded, are mainly dependent on, and maintained by the activity of the neurons in the reticular formation of the brain stem and structures of the diencephalon (thalamus, hypothalamus and subthalamus)—i.e., largely those parts of the upper brain stem, which are now known as centrencephalic system.

Stimulation of various parts of the thalamus and hypothalamus was undertaken to investigate the hypothesis that the diencephalon might be the site of origin or at least of major activation of petit mal attack. From the work of Jasper with Drooglever—Fortuyn (1947) a strong suggestion that the pace-maker for the characteristic cortical discharge, seen in attacks of petit mal lay in the diencephalon, has emerged.

The importance of thalamic reticular system and effects noted by introduction of electrodes in various thalamic and subthalamic sites:—

(1) Stimulation of intra-laminar nuclei of the thalamus especially near the massa intermedia produces an arrest reaction, with stopping of normal voluntary activity engaged in by the animal, at the moment, standing as if frozen in its tracts in a fixed or crouched position, with a staring or stunned facial expression and continuing the voluntary activity engaged in, before the stimulus was applied, after the stimulus was withdrawn. Occasionally, the arrest would outlast the stimulus. Slight twitching of the lids and mouth also occur. There is no response during the arrest stage to visual or auditory stimuli.

Increase of stimulation might add turning and maintenance of abnormal fixed postures to the arrest. In some animals, generalized tonic or clonic convulsions occurred after the arrest stage, confirming the idea of H. Jackson that both grand and petit mal were but different degrees of the same condition.

(2) Rage reactions and attack, occur on stimulation of anterior hypothalamus, e.g., hysteria or psychic epilepsy.

(3) Sleep occurs on stimulation of the inferior part of the massa intermedia (cause of narcolepsy).

(4) Stimulation, deep to thalamus and anteriorly, never produced arrest, but intense searching about, closely associated with anterior temporal lobes (psychomotor epilepsy).

The existence of physiological mechanisms of sleep with an anatomical substratum similar to that in experimental animals, is highly probable. It is evident that the critical areas for arousal or wakefulness, drowsiness or coma, lies not primarily in the cortex, but in the subthalamic region and brain-stem. To have an anatomically intact cerebral cortex, is not sufficient to ensure wakefulness, the maintenance of which seems to demand the physiological integrity of much deeper structures. That this is so, is evident from the effects on consciousness of lesions of the brain stem, caused by tentorial herniation in cerebral lesions and by the seeming paradox of unconsciousness, caused by acute posterior fossa-lesions, especially hæmorrhages. Physiological blocking at this level would explain many of the paradoxes of concussion. It has been said of the cortical capillaries that if a red cell had motor power of its own, it could travel from one end of the brain to the other. How much more true must this be, of nervous impulses? But although high value must be attached to intra-cortical interplays we cannot look at them, abstracted from a continuous barrage from subcortical structures. Without this, cortex has no meaning. Amongst the more important of the newer discoveries of such integrating factors are those relating to reticular formation. The older anatomists like Bell, and the classical neurologists like H. Jackson and Todd and Marshall Hall, would have welcomed and understood them.

Morrison Dempsey (1942) had shown that stimulation of thalamus controlled the spontaneous electrical activity of the cortex, in a diffuse and wide way, and Hunter and Jasper concluded that a diffuse projection from the reticular and intralaminar nuclei ('The Thalamic Reticular System'), might be deeply involved in integration of the higher level cerebral activity such as the initiation of patterns of movement and that stimulation there, might block such movements. Existence of disease in patients with *petit mal* is rare, but is possible only in local brain disease or injury.

*Experimental evidence of hypothalamic functions and its control over the autonomic nervous system:*—1. Karplus and Kreidle were the first to furnish evidence of a sympathetic centre in the hypothalamus. Upon electrical stimulation of this region, they obtained pupillary dilatation, sweating and a rise of blood-pressure. Inhibition of intestinal movements also results. Liberation of adrenaline has also been reported to follow stimulation of the hypothalamus. By means of needle electrodes, inserted into the region of the lateral nucleus, Bronk and his colleagues have recorded impulses from the

sympathetic efferent nerves, during stimulation of the hypothalamus. On the other hand rhythmical variations in potential were produced in the hypothalamus, by stimulation of certain afferent nerves, through which reflex sympathetic responses may be elicited.

2. Beattie, Brow, and Long found that extrasystoles produced in the cat by means of chloroform anaesthesia and which had been shown by Levy to be dependent upon sympathetic impulses, were abolished by a destructive lesion placed in the posterior hypothalamic nuclei or by section of the brain behind this region.

Stimulation of the posterior hypothalamic region, on the other hand, caused extrasystoles to appear in an animal, which previously had been free from these cardiac irregularities. Animals subjected to such lesions, also showed hyperglycemia and glycosuria. Drowsiness for two or three days following the operation, was a noticeable feature in some animals. They also showed a change in behaviour being more docile and "tamer" after the operation. The nervous system of animals examined histologically sometime after lesions in the hypothalamic nuclei have been made, showed degenerating fibres, which entered the mid-brain and descended through brain stem and cord. Those in the cord entered the lateral columns of grey matter at different inter-levels down to the 3rd or 4th lumbar segment.

3. Decerebration, by a section through the mid-brain, causes a profound fall in body temperature. No such loss of temperature control follows the removal of cerebral cortex and thalamus provided the hypothalamus is left intact. It is significant that sympathetic effects *e.g.*, adrenaline liberation, erection of hair, and constriction of vessels result from exposure to cold. Moreover, Cushing calls attention to the high temperature, which frequently follows operations upon tumours in the region of the third ventricle.

4. Hess fixed electrodes in the hypothalamus of cats. After the animal had recovered from the operation, a weak electric current passed through the hypothalamus induced a state indistinguishable from normal sleep.

5. Kabit and associates, by means of electrodes, fixed at the hypothalamus, stimulated this region in the unanaesthetised animal. Pupillary dilatation, erection of hairs, inhibition of gastro-intestinal peristalsis, clawing and urination resulted. Stimulation of other parts of the brain produced none of these effects.

In recent experiments, Bard and Mount-Castle have shown that the restraining influence of higher levels of the cerebrum upon hypothalamic activity is not exerted by the neocortex, but by certain parts of the rhinencephalon (cortex of the periform lobe, amygdaloid nucleus, and hippocampal formation); and an area of the cortex on the medial aspects of the hemisphere, lying ventral to the cingular sulcus in front of and below the rostrum of the corpus callosum. This

latter area of cortex is believed to be a transitional zone between rhinencephalon and neocortex. An operation which removed the neocortex alone, leaving the rhinencephalon and the area of transitional cortex uninjured, was performed upon cats, whose behaviour in temperament had been studied for sometime previously. The manifestations of animals prepared in this way, were the reverse of those which had been subjected to complete decortication. They showed extraordinary placidity. Responses, expressive of pleasure were predominant and often exaggerated. Procedures which in a normal animal provoke resentment, anger or even rage, such as pinching the tail strongly with surgical forceps, tying the animal down on its back, strong electric shocks applied to skin evoked, no sign of resentment. The animals responded to mild nociceptive stimulation like purring or with other expressions of pleasure. An animal which before operation, resented handling or petting, became affectionate, purred, when stroked, and submitted to being tied to the animal board, as though it enjoyed the manoeuvre. Removal of those parts of the rhinencephalon mentioned above, or transitional areas of cortex, transformed animals deprived of their neocortex, i.e., abnormally placid animals into ones which upon the slightest provocation, exhibited all the signs of rage.

It is apparent from these experiments, that some part of rhinencephalon and the transitional area of cortex, exerts a restraining influence upon these hypothalamic mechanisms, governing expressions of displeasure, resentment and anger. Since the removal of the neocortex alone evokes expressions of a reverse nature, it would seem that the latter part of brain tends normally to antagonize the influence of the former part. This suggests that the temperament of an animal is normally dependent upon the balance struck between the activity of these two parts of the brain.

*The diencephalon and sleep and occurrence of attacks of grand mal in sleep:*—Several observations both clinical and experimental, point to the existence of a sleep centre in the diencephalon. Hypersomnolence is a frequent accompaniment of tumours of the structures of the floor and walls of the 3rd ventricle or of inflammatory lesions, involving the hypothalamic region. Hess claims to be able to cause sleep in animals by mild electrical stimulation of the diencephalon towards the anterior end of the cerebral aqueduct. Hess also reported that ergotamine injected directly into the 3rd ventricle, induces sleep. Ergotamine paralyzes motor and secretory fibres of the sympathetic. Since both parasympathetic and sympathetic centres, are situated only in the hypothalamus, Hess argued that the drug by suspending the activity of the sympathetic centre caused a preponderance of parasympathetic effects. Sleep, he concluded was a parasympathetic function. He also drew support for his theory from certain manifestations of parasympathetic activity, namely pupillary constriction, bradycardia, and vasodilatation which

accompany sleep. Though this observer's idea that sleep is a parasympathetic function, requires further support before it can be accepted, the evidence for the participation of hypothalamus, in the sleep mechanism, is very strong. Yet contrary to the idea that sleep is caused by excitation of some part of the hypothalamus, other investigators believe that it results from a depression of the hypothalamic activity. The hypothalamus is thus regarded as containing a waking centre, sleep following its destruction or inhibition.

[NOTE:—The occurrence of attacks of grand mal during sound sleep, lends support to the latter view, as the person in whom the sleep is initiated and maintained by the depression of the hypothalamic area, becomes subject to these attacks, due to sudden stimulation of the posterior hypothalamic nuclei containing higher centres of the sympathetic nervous system, as well as the various visceral ganglia and those of the sympathetic chain and are thereby aroused from sleep, due to a depression of the parasympathetic functioning of the anterior hypothalamic nuclei, responsible for maintaining the state of sleep, which naturally will follow the sympathetic excitatory state.]

*Cortical areas important in the causation of reactions by impulses reaching them in epilepsy:*—

1. Area 8 is called the frontal eye field. It lies in front of area 6. Stimulation of the cortex here, causes conjugate movement of the eyes to the opposite side, opening and closing of eyelids, and sometimes dilatation of pupils and lachrymation. No visual hallucinations occur in man, but an epileptiform seizure, may be provoked which spreads to the adversive field (area 6). Stimulation of area 8 in man also causes conjugate deviation of the eyes and turning of the head to the opposite side. Area 8 has depressor function. It receives fibres from the dorso-medial nucleus of the thalamus, through which it is connected with the hypothalamus. It also connects by long association tracts, both afferent and efferent with the occipital lobe (visual area 18) and with the tegmentum of the mid-brain (probably with the oculomotor nuclei).

Area 44 in the region of the posterior part of the frontal operculum in the dominant hemisphere (which is left in right handed persons) is a motor area for speech (Broca's area). Stimulation of this area in conscious patients, causes their speech to be abruptly arrested. Area 45 lying close to area 44 receives fibres from the dorso-lateral small celled part of the dorso-medial nucleus of the thalamus and stimulation of these areas for a short while, following that of areas in the orbito-frontal cortex might be the cause of temporary aphasia with difficulty in speech for a short time occurring in patients just after an attack of grand mal, even after consciousness is regained, this effect on speech, overlasting the duration of the stimulus by a short while.

Areas 9, 10, 11, 12, 13 and 14 in the prefrontal or orbito-frontal cortex, which until recent years have been thought to be inexcitable and therefore, referred to as silent or association areas, have been found now to respond to stimulation by a suitable electric current

having pulses of low frequency by responses in the autonomic nervous system and respiratory, circulatory, renal and gastrointestinal responses. After bilateral removal of these areas, B-P. is reduced, gastric secretion suppressed and gastro-intestinal movements increased. In man, suffering from intractable pain is relieved. These areas receive important fibres from the dorso-medial nucleus of the thalamus, which in turn receives impulses from the hypothalamus. These areas, especially those of the orbital surface are thought to be closely associated with emotional feeling. Their part in the scheme of cortical representation of sensation is uncertain, but they are probably concerned with visceral rather than with somatic sensations, through the hypothalamus and dorsomedial thalamic nucleus.

Area 24—The anterior part of the cingular gyrus, on the medial aspect of the hemisphere, is a powerful suppressor area. Autonomic responses following stimulation of this area are pupillary dilatation, pile-erection, acceleration of heart, and a fall in blood-pressure. Arrest of respiration in expiration, also results. The fall in B-P. during an attack of petit or grand mal is due to stimulation of this area following that of Area 8 and those of the prefrontal region. The prefrontal areas have extensive sub-cortical and cortical connections. The pathway from the hypothalamus to the cortex through the dorso-medial nucleus of the thalamus was established by stimulation of the posterior hypothalamic region and observing the action potentials in the thalamic nucleus and the cortex. The greater part of the prefrontal cortex is considered by Le Gros Clark as a projection area for the hypothalamus, just as the occipital cortex and auditory cortex are projection areas respectively, for the retina and the cochlea. The prefrontal areas are connected by efferent fibres with (a) hypothalamus, through dorso-medial nucleus of the thalamus (b) there is good evidence also for existence of a direct efferent connection with hypothalamus both in animals and man (c) with the caudate nucleus (d) nuclei of the pons (from area 10) (e) tegmentum of the midbrain.

Subsequent to stimulation of areas 8, 9, 10, 11, 12 and 24 causing the various signs and symptoms already mentioned just at the onset of an attack of petit or grand mal, coincident with or following immediately, the loss of consciousness due to stimulation of the thalamic reticular system, area 6 (premotor area) is stimulated, on account of impulses reaching it *via* corpus striatum which also is stimulated by impulses reaching it from the hypothalamus and also cingulate gyrus on the mesial aspect of the hemisphere. Stimulation of area 6 in turn facilitates stimulating of area 4, which is the motor area and only if the impulses reaching from the hypothalamus are of high intensity, areas 6 and 4 are affected.

Points from Electrical Activity of the brain as given in "Annual Physiological Review 1953 by Birger R. Kadda, Anatomical Institute, University of Oslo and Ullevaal Hospital, Department of Neurology, Oslo, Norway:—

Arduini and Terzuolo have studied cortical and subcortical components in the recruiting responses obtained by stimulation of the diffuse, thalamic, projection system, to use Starzl and Magoun's term. Positive recruited potentials and the characteristic waxing and waning of the amplitude of the responses were recorded from the subcortical white matter, after ablation of the cerebral cortex. These phenomena may thus occur at subcortical levels, and there is no need of postulating the existence of recruiting phenomena and of fluctuations of excitability primarily localised within the cerebral cortex, though this has not been disproved. According to Starzl and Magoun, the thalamic origins of this diffuse thalamic projecting system in the cat include the centromedian intralaminar, anterior, ventralis anterior and anterior reticular nuclei. These components form a functionally interconnected unit and appear to project to the cortex in a more localized fashion, than hitherto assumed, namely the associational cortex of the frontal, cingulate orbital and suprasylvian portions of the hemisphere avoiding the sensory receiving areas. However recruiting responses have also been recorded from the latter areas as olfactory bulb. A similar cortical distribution of the wave-spike complexes with optimal amplitude over the association areas in petit mal, has been demonstrated by Kadda by means of a maximum of 75 closely spaced electrodes, covering one hemisphere. Petit-mal-like attacks have been induced experimentally, not only from the thalamic midline and intralaminar nuclei, but also from anterior cingulate area. Starzl and Magoun, Kadda, summarizing the present state of knowledge of the diffuse, thalamic projection system, has drawn attention to the fact that cerebral structures, cortical and subcortical from which recruiting responses can be produced and recorded; all appear to yield inhibition of spontaneous motor movements as in petit mal epilepsy thus indicating further the functional relationship of these structures. Gestaut and Huntur in an extensive animal study of the mechanism of photic activation in petit mal, conclude that idiopathic epilepsy is a "disorder in an otherwise normal person presenting nothing more than an abnormally low threshold of thalamic synapses (or perhaps of all synapses). The periodically recurring cortical waves have been variously interpreted and Chang relates them to repetitive discharges of a cortico-thalamic reverberating circuit, a view put forward some years ago by others also, but opposed by Adrian and Bremer and Bonnet. Adrian concludes that the rhythm must be generated in the thalamus and that cortical reverberation is not essential, since it persists after destruction of the cortex. Bremer and Bonnet attribute the periodic waves to a transitory intensification of the auto-rhythmic synchronized activity of subcortical neurones in the afferent path, possibly at an infra-thalamic level.

Conclusions from the above.—(a) If the impulses from the hypothalamus are very mild, the symptoms subside with just visceral sensory, or special senses aura only or combined with pilo-erection

(b) If the impulses are more intense, consciousness is lost just for a while, with just a mild stimulation of the midline thalamic nuclei of the thalamic reticular system and is regained very quickly just after  $\frac{1}{2}$  to 2 minutes without the cerebral cortex being in the least affected and the person continues to do the work he was engaged in before the loss of consciousness occurred, after regaining consciousness in a short while, in very much the normal way. (c) If the impulses are still stronger not only is consciousness lost for a longer time, due to a more prolonged stimulation of the thalamic reticular system, but dilatation of the pupil and conjugate deviation of the eyes and head to the opposite side also occur, due to stimulation of areas 8 to 12. (d) If the impulses are of still greater magnitude, stimulation of premotor area (Area 6) occurs with its attendant signs of symptoms of adverse movements of turning of head and eyes to opposite side, accompanied by a sudden extension of flexion of contralateral limbs, which results in the person, who at the time of occurrence of the attack, was walking, falling down on the side and also showing slow generalized type of movements involving synergic groups of muscles. (e) If the impulses are still greater, area 4 is stimulated by facilitation occurring from area 6 and convulsions of various parts of the body occur one after another, till the discharge from hypothalamic nuclei becomes normal and the person regains consciousness. It is thus seen that only when impulses from the hypothalamus are of a high intensity as described in (d) and (e) that grand mal occurs and in the rest only petit mal.

**TREATMENT:**—As it is thus clearly seen from the signs and symptoms occurring in idiopathic petit and grand mal, as occurring from a generalized sympathetic excitation in the whole body with its centre of action in the hypothalamic region, the best drug for depression of the posterior hypothalamic area like, ergotamine or a para-sympathetic stimulant of the type of prostigmin, activating the thalamic excitatory state, would be the proper drugs of choice in treatment of the barbiturate group and the purely anti-convulsive drugs of the hydantoinate group, which do not tackle the fundamental root cause of the excitatory state of the posterior hypothalamus.

**CONTROL OF TETANUS CONVULSIONS** may be possible with large doses of chlorpromazine. After success in experimental infection in rabbits, R. E. Kelly, of St. Thomas's Hospital, London, and D. R. Laurence, of the University of London gave 15 mg. of the drug intravenously to a 24-year-old boy with generalized tetanus convulsions. Within ten minutes, the patient relaxed and slept. Subsequently, chlorpromazine was added to a continuous intravenous drip every two to five hours in doses determined by the severity of convulsions. During sixteen days of administration, unconsciousness was not induced and respiration was unaffected. No other drug was used until cessation of chlorpromazine therapy, when a barbiturate was given for sedation.—(*Lancet*, 270 : 118-121, 1956 via *Modern Medicine*, 1-6-1956).

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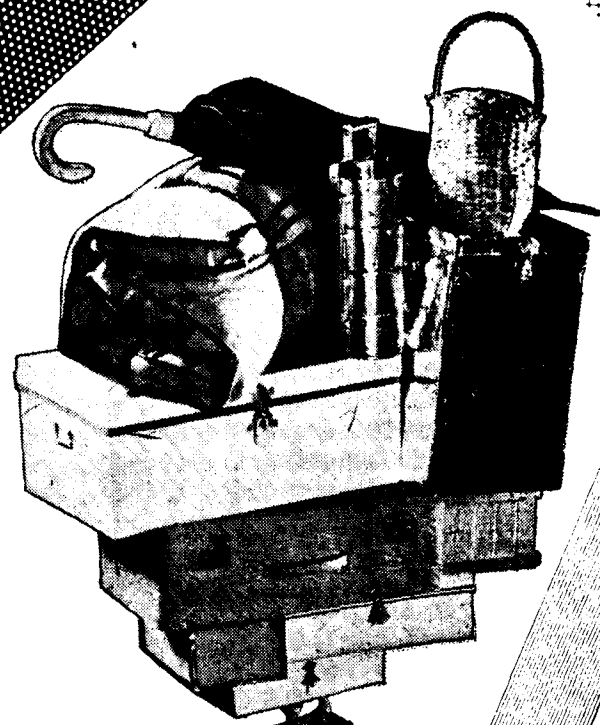
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## COMMON MEDICAL IMPAIRMENTS OF

4,000 Gurkha Personnel of the West Bengal and Calcutta Police Forces and West Bengal Fire Services : Arranged Alphabetically  
(Diseases which claimed less than 50 victims out of the total have been ignored)

B. B. DOTTO,  
Chief Medical Officer of the Police Co-operative Life  
Insurance Society, Limited, Calcutta-13

(Continued from page 593, Aug. 1956 issue of ANTISEPTIC)

### PART II

1. Alcoholic habits.—Out of the total number of applicants, 3,460 or 86.5% were used to alcoholic drinks regularly, weekly or bi-weekly. The figure is exceedingly high when compared with Indians—with the exception of Santhals—who are also being largely employed in the Police Forces during recent years. The authorities have been obliged to open rum canteens in Gurkha barracks to meet a growing demand, where drinks are sold at a very cheap rate. It is said that alcohol predisposes to disease, especially infection, and it is well-known that pneumonia is invariably fatal to alcoholics. The high percentage of alcoholics perhaps accounts for the large incidence of pneumonia among Gurkhas. Alcohol is known to shorten life and this is what does happen in the Gurkhas.

2. Anaemic appearance.—782 or 19.55% of the subjects presented an anæmic appearance. This is mainly due to mal-nourishment, vitamin deficiency, chronic malaria, dysentery and venereal diseases. Primary anæmia is quite common, mostly in a mild form. The patients have a feeling of being tired and out of sorts and catch cold very easily.

3. Arcus senilis.—67 cases were detected. Few Indian Life Assurance Companies have paid attention to this ailment. Arcus senilis has been regarded by some authorities as definite evidence of premature decay and old age and recommend acceptance with suitable extra premium, but according to the modern trend of opinion it does not act as a bar to acceptance at ordinary rates. But Arcus senilis is a positive sign of premature break-down amongst the Gurkhas, and should be declined or accepted under adequate safeguards.

4. Hard and soft chancre.—166 or 3.15% cases were detected. Serological tests were not made owing to the extra expense involved. In 97 per cent of the cases the sore appeared on the region of the genitals and in the remaining cases on the lips, tongue and breast.

5. Chronic bronchitis.—382 or 9.55% cases had chronic bronchitis—which gradually led to pulmonary tuberculosis in the

majority of cases and a few were associated with emphysema. These were mostly underweight with poor respiratory capacity.

6. Chronic eczema (Dermatitis).—52 cases: Gurkhas are usually susceptible to skin diseases due to their unclean habits—use of less water, fewer baths, etc.

7. Dysentery: (amoebic and bacillary) was detected in 208 or 5.2% cases, a large number being chronic sufferers. Here too insanitary habits and lack of precaution against infection played a large part in the spread of the disease.

8. Dyspepsia—56 cases were detected, mostly in persons aged 40 years and over all of whom were heavy smokers. 27 of the applicants were suffering from insomnia as well. It has been established that the dyspepsia and insomnia were due to heavy smoking and consequent intake of too much nicotine.

9. Enlarged spleen.—234 or 5.85% cases were detected. Usually the spleens were about one to three fingers' breadth beyond the costal margin due to frequent attacks of malaria. Constables and sepoys engaged in Indo-Pakistan borders were the worst victims.

10. Excessive smoking.—3,898 or 97.45% of the applicants smoked heavily. Mostly cheap cigarettes and 'beedies' are consumed in a chain without intermission during waking hours and this caused indigestion, irritability and sleeplessness. This habit plays a great part in the early deterioration of general health. The higher incidence of lung cancer among heavy smokers than among non-smokers is well-known, but no investigation could be made in middle-aged applicants without radiological examinations.

11. Exposure to tuberculosis through co-residence.—57 cases were detected. Gurkha subjects are accustomed to live in the same room with relations suffering from tuberculosis and the lack of proper hygienic precautions causes the disease to spread slowly but surely. Three were actually suffering at the time of the examination. The majority were in poor health and physique with low blood-pressures. It is well-known that the onset of tuberculosis is insidious, and the disease may spread extensively in the lungs, without sufficient symptoms and only disablement makes a person consult a physician. Periodic screening of the lungs, as suggested elsewhere in this paper will greatly help in the reduction of the incidence of tuberculosis.

12. Flat or barrel-shaped or pigeon chest was found in 102 or 2.55% cases. These applicants were usually susceptible to respiratory diseases and were mostly under-weight. Chronic bronchitis was found to be the cause of the barrel-shaped chest in some of the applicants.

13. Gonorrhoea was detected in 308 cases, and 206 others gave past histories; therefore, 514 or 12.85% of the applicants had been exposed. Some were chronic, some severe and some mild. Most of the victims were ex-service men. A large number of them had

undergone penicillin treatment, but the cure was not permanent due to subsequent exposures.

14. Haemorrhoids were present in 58 cases; 23 bleeding and occasional bleeding and 35 non-bleeding. 60% gave histories of heredity on the paternal or the maternal side. Perhaps want of cleanliness accounts for this malady—which ultimately causes anaemia in some victims.

15. High blood-pressure was observed in 54 cases. Some very young applicants were victims. 63% gave histories of heredity. High blood-pressure claims more victims amongst officers than among men. Officers promoted from the ranks were the worst sufferers. Some very high blood-pressures were detected in subjects who were blissfully ignorant of this serious condition and who were working as usual, occasionally complaining of sleeplessness, giddiness, headache, breathlessness on exertion, noises in the ear, irritability and palpitation of heart, particularly while in parade, route march and climbing stairs. Thus a large number of subjects were having this disease in an insidious form.

16. Hydrocele was seen in 60 cases. Trauma was the cause in a large number of cases 42 were unilateral and 18 were bilateral. Some were very large, to the extent of interfering with locomotion and the penis had almost disappeared within the swelling. Most of the victims were unwilling to undergo a surgical operation to obtain a radical cure.

17. Jaundice.—66 cases were detected. Though various causes have been assigned most of them followed an attack of malaria.

18. Low blood-pressure.—108 or 2.7% cases—mostly in young applicants—who were apparently healthy but under-weight. 37% gave histories of familial tendencies and many complained of weakness, a perpetual tired feeling, sleeplessness, headache and giddiness.

19. Malaria.—682 applicants gave past histories of one or more attacks of malaria and 409 cases were actually detected, thus 1,091 or 27.275% of the subjects were victims of severe and recurrent attacks. It was very common, being found in applicants of all ages. The malady is serious and really alarming. It is interesting to note that the incidence of malaria was far less in the fire brigade than in the police force.

20. Otorrhoea.—109 or 2.725% cases were detected. Some were mild occasional, some moderate intermittent, some moderate constant and some profuse chronic. A few resulted in partial deafness.

21. Pleurisy accounted for 108 or 2.7% cases. This disease ultimately led to pulmonary tuberculosis in the vast majority of cases due to neglect and malnutrition.

22. Pneumonia.—307 or 7.7% cases were detected or gave past histories. Some gave histories of 2 or 3 previous attacks. A good many recently cured cases appeared for examination. Pneumonia with underweight and a low blood-pressure is a very unfavourable condition, from the life assurance point of view, (*vide* alcoholic habits on p. 687).

23. Poor family history.—1,628 or 40.7% of the applicants gave very poor family histories. In some instances the applicant was the only surviving member of the family. In many instances the applicant could not state whether his parents or brothers and/or sisters were alive—who were left behind in Nepal or Indo-Nepal Borders. Death of one or both parents before maturity-age or premium-ceasing age, excluding deaths from accidents and epidemics, received particular attention in assessment.

24. Premature old age was common amongst the applicants due to a lower age having been given at the time of recruitment. This is partially due to ignorance and partially wilful in order to come under the "prescribed age." A large number of the subjects looked 5 to 7 years older than the declared age.

25. Pyorrhoea alveolaris was present in 506 or 12.65% of the applicants. The figure is very high no doubt, as such focal infection is usually the fore-runner of many diseases.

26. Ring-worm was detected in 73 applicants. This is mainly due to the unclean habits. The condition was largely seen on the body and palms of the hands and in a few in the nails.

27. Syphilis.—148 cases were detected and 256 gave past histories, making a total of 404 or 10.1%. Some were congenital. A large number of the victims were ex-service men. Serological tests could not be conducted owing to the extra expense involved.

28. Tuberculosis (family history).—127 or 3.175% gave familial histories of tuberculosis. In 70% of the cases, the parents and the wives were the victims. A few cases of doubleheredity were recorded. (*vide* "Exposure to Tuberculosis through co-residence on p. 688).

29. Under-weight.—1,056 (or 26.40%) of the applicants were under-weight. This is an alarmingly high figure and has been discussed elsewhere in this paper.

30. Varicose veins.—151 or (3%) cases were detected, mostly amongst the elderly applicants. The strain of standing for prolonged periods is a common cause for the frequency of varicose veins in constables and sepoy. It may be pointed out that the Gurkhas are mostly employed in the Armed Police, who in their normal daily routine have to stand for long periods every day e.g., Traffic constables.

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## Cases and Comments

### RESULTS OF BACTERIOLOGICAL

### EXAMINATION OF THE STOOLS OF 732 SUSPECTED CASES OF CHOLERA AT THE INFECTIOUS DISEASES HOSPITAL, MADRAS

MISS S. AROGYADOSS, M.D.,

AND

M. ANANTARAM, M.B., B.S.,

Public Health Laboratory, (Corporation of Madras)

DURING the epidemic of cholera in Madras City in the latter half of the year 1953 we made a bacteriological study of stool cultures of the suspected cases. Incidentally we collected statistics relating to age and sex in positive cases. Positive cases in three different age-groups were thus studied. The number of patients who were inoculated were noted and the predominant strain of *V. cholerae* was also noted and compared with the other strain.

For purposes of convenience in our investigation we dealt with the patients admitted daily for suspected cholera between 7 A.M. and 1 P.M., into the Infectious Diseases Hospital at Madras.

Immediately after admission, rectal swabs were taken and inoculated into one per cent alkaline peptone water and the inoculated tubes were taken to the laboratory. After incubation for about 4 hours at 37°C, loopfuls from the pellicle on the top layers of the peptone water tubes were plated out on Aronson's medium.

After about 24 hours' incubation at 37°C, the plates were examined for suspicious colonies resembling those of *V. cholerae*, which were picked up and tested by slide agglutinations using combined cholera high titre serum with a titre of 1 in 50. Positive organisms were then tested with the Ogawa and Inaba specific sera (1 in 50 titre). All the sera were obtained from the King Institute of Preventive Medicine, Guindy.

In our investigation, we found the Inaba strain to predominate (90%); while Narayana Rao *et al* had reported the Ogawa strain to be the predominant type in the previous epidemic of 1952.

Our patients were divided into three age-groups: (i) 10 years and below; (ii) 11 to 30 years and (iii) 31 years and over.

The mortality rate in the positive cases was found to be lowest being about 14.5% in the second age group *viz.*, 11 to 30 years while the mortality rates in the first and third age-groups were higher and about equal in both being 28% and 27% respectively.

An interesting observation was that two women aged 75 and 70 respectively whose stools were positive for *V. cholerae* (Inaba), survived.

There was a slight preponderance of females over males (above 10 years of age) with a corresponding higher percentage of positives. The percentage of positives was about the same in children and in females in this series.

The number of inoculated patients was 53 or 7.2%. Narayana Rao *et al* reported a percentage of only 3.1 in the previous epidemic. Five among the inoculated died (9.4%) though about 60% of the inoculated were positive. It is difficult to say how many of them had really been protected; for some had received the inoculations only on the day of the attack, some on the previous day and so on.

The youngest patient admitted was 6 months old and the youngest child showing a positive culture was 1½ years old. The oldest individual with a positive culture was a 75 year old woman.

In a total of 732 cases, about 60% were positive, the rest being negative. Out of the 436 positive cases, 90% were of the Inaba and 9% of the Ogawa types, the rest showing a mixed infection.

Our findings are given below:—

TABLE I

Showing the positive and negative results of test

| Total No. of cases | Positive Number | Positive Per cent | Negative Number | Negative Per cent |
|--------------------|-----------------|-------------------|-----------------|-------------------|
| 732                | 436             | 59.57             | 296             | 40.43             |

TABLE II

Showing the respective strains infecting

| Total No. Positive | Inaba | %     | Ogawa | %    | Mixed | %    |
|--------------------|-------|-------|-------|------|-------|------|
| 436                | 392   | 89.31 | 38    | 8.72 | 6     | 1.37 |

TABLE III

Age and sex-groups

| Group               | Total | Positives | %     |
|---------------------|-------|-----------|-------|
| Males (above 10)    | 234   | 128       | 54.7  |
| Females (above 10)  | 283   | 176       | 62.19 |
| Children (below 10) | 215   | 132       | 61.3  |

TABLE IV

Figures showing the mortality rates

| Age group          | Total | Deaths | %     | Discharge | %     | Total positive | %     | Deaths | %     |
|--------------------|-------|--------|-------|-----------|-------|----------------|-------|--------|-------|
| 10 years and below | 215   | 54     | 25.12 | 161       | 74.88 | 132            | 61.4  | 37     | 28.03 |
| 11 to 30 yrs.      | 273   | 32     | 11.71 | 241       | 88.29 | 152            | 55.67 | 22     | 14.47 |
| 30 years and over  | 244   | 57     | 23.36 | 187       | 76.64 | 152            | 62.29 | 41     | 26.98 |

TABLE V

Showing the incidence and mortality in inoculated cases

| Total No. of cases | Number inoculated | %   | Deaths among the inoculated | %   |
|--------------------|-------------------|-----|-----------------------------|-----|
| 732                | 53                | 7.2 | 5                           | 9.4 |

**Acknowledgement.**—We wish to thank the Commissioner and Health Officer of the Corporation of Madras for permitting us to publish this report. Our thanks are due to the Supdt., I. D. Hospital and its R.M.O. Dr. I. Prabhakar, M.B., B.S. for their help. We acknowledge with pleasure the assistance given to us by Dr. A. Selvaraj, M.B., B.S. Our grateful thanks are also due to Sri Dr. Y. S. Narayana Rao, M.B., B.S., D.T.M. (Cal.), D.B. (Lon.), Director of the K.I.P.M., Guindy for his helpful guidance.

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## THE PROBLEM OF RUPTURE OF UTERUS

Although cases of rupture of the uterus are frequently reported, there have been few investigations of its incidence, the relative importance of its various causes, and the influence of uterine rupture on the maternal mortality. The authors review 44 cases of rupture of the uterus that occurred in a period of 49 years at a women's clinic in which a total of 45,183 deliveries were made. Grouping the uterine ruptures into 7-year periods, the authors found that the incidence was highest during the period from 1906 to 1913 but that a new peak occurred between 1947 and 1954. The first period of high incidence coincided with a period when a narrow pelvis was frequently observed and caesarean operations were rarely done. The decreasing incidence during the subsequent periods may be partly explained by the great reduction in the number of high multiparas as a result of birth control and with this in the number of torso presentations, these being especially likely in women with many children. The decrease in forceps deliveries, versions, and other obstetrical interventions may also explain the reduction in ruptures of the uterus. The second peak in incidence coincided with the great increase in caesarean operations (cicatricial ruptures) and with the era of the frequent use of eclolics. However, only 4 of the 44 were cicatricial ruptures. Twenty eight, or nearly two-thirds of the ruptures, occurred in the clinic, whereas the other 16 women were brought to the clinic after the rupture. In this group of 16, the maternal mortality was practically 100%, whereas in those women in whom the uterus ruptured while they were in the clinic, the mortality was 50%. Fatalities from ruptured uterus accounted for 14.1% of the total maternal deaths. Although uterine ruptures accounted for 14.1% of the total maternal deaths. Although the maternal mortality at the clinic from which these records were obtained decreased during the 49-year period from 1.3% to 0.15%, the lethality and mortality of rupture of the uterus did not decrease to the same extent. The maternal lethality of uterine rupture during the first 7-year period (1906-1913) was 92% (12 of 13), and during the last 7-year period (1947-1954) it was 53% (8 of 15).—(H. Puder and H. J. Wagner, *Arch. Gynak.*, 187: 119-133, No. 2, 1955, Munich, Germany, via *J.A.M.A.*, May 5, 1956).

## A STUDY OF A FEW CASES OF YAWS IN COOCH BEHAR

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**Y**AWS is a contagious disease of non-venereal origin occurring in humid tropical areas, near the foot of hills, and characterized by muscular, lichenous rash, papillomatous frambœsia in different stages.

Though the disease can be traced to antiquity, it came to be recognized as a separate entity at the end of the 18th century. Aldo Castellani isolated the *Treponema pertenue* from unbroken lesions in 1905.

**Case report.**—CASE 1.—J. P., aged 11, Hindu, female from an interior village attended the hospital on 22-3-'55 with a punched-out ulcer under both heels with a diameter, 2 cm. of 2 years' duration. The floor of the ulcers was covered with black slough and the patient complained of pain on walking. No glandular enlargement and no history of exposure. Her general condition was good K.T. +; urine contained no albumin or sugar.

CASE 2.—G. S., aged 30, Hindu female, from a village, attended the hospital on 5-4-'55 with a punched-out ulcer 1 cm. under the right heel and a raspberry-like granulomatous growth, oval, about 2 cm. in diameter on the sole of the left great toe. Duration was 15 months. She had difficulty in walking; no history of exposure and no glandular enlargement. Her general condition was good. K.T.—negative; no albumin or sugar in the urine.

CASE 3.—R. S., aged 25, Hindu male, cultivator from a village attended the hospital on 23-8-'55 with a raw fungating papillomatous growth 3 cm. under the right heel, and a punched-out ulcer 2 cm. on the anterior part of the sole of the left foot. Duration—3 years; complained of difficulty in walking, gave no history of exposure and there was no glandular enlargement. His general condition was good. K. T.—negative. Urine—showed no albumin or sugar.

CASE 4.—A. M., aged 30, Hindu male, cultivator from an interior village attended hospital on 27-9-'55 with a pale raspberry-like growth on the palm, on its left thenar eminence 3 cm. Duration 1½ years. No history of exposure. No glandular enlargement; general condition was good. K. T.—negative. No albumin or sugar in the urine.

CASE 5.—S. S., aged 35, Hindu male, cultivator from an interior village came on 1-11-'55 with a punched-out ulcer under the right heel 2.5 cm. and one warty growth 2 cm. on the sole of the right first metatarso-phalangeal joint and raspberry-like growth 3 cm. on the anterior part of the sole of left foot. Duration 1½ years. No history of exposure. No glandular enlargement. General condition—good. K.T.—negative. Urine—normal.

SEP. '56] STUDY OF CASES OF YAWS IN COOCH BEHAR—B.C.C. 695

CASE 6.—B. R., aged 45, Hindu male, grocer from an interior village attended on 8-11-'55 with a granulomatous warty growth 3.5 cm. on the middle of the sole of his right foot. One small indurated ulcer 1.5 cm. on the sole of his left great toe. Duration 3 years. No history of exposure. No glandular enlargement. General condition—good. Urine—normal with no albumin or sugar; K. T.—negative.

CASE 7.—T. D., aged 26, Hindu male, cultivator from a village came on 8-11-'55 with a raspberry-like growth 3 cm. on the outer side of the sole of his left foot and a small warty growth 1.8 cm. on the sole of his right first metatarsophalangeal joint. Duration—4½ years. No history of exposure. No glandular enlargement. General condition—good. K.T.+. Urine contained no albumin or sugar.

**TREATMENT:**—All the seven cases were treated with acetylarsan 3 cc. intramuscularly twice a week; 10 such injections were given and the lesions dressed with eusol. The growths were treated with a paint consisting of acid salicylic gr. 40, acid benzoic gr. 30, Colloidion flexile m. l. The secondary infections in three cases were treated with Diamine penicillin—12 lacs, intramuscularly once a week for 4 injections. All the cases were cured clinically. A periodical check-up was made fortnightly for 3 months after the cure, except in case No. 6 who failed to turn up after the cure. No relapse was noted. Of the seven cases, two were females 11 and 30 years old respectively, 3 were males between 20 and 30 years, one was a male aged 35 and the other aged 45.

**Summary.**—The highest age-incidence was between 20 and 30 years, males predominating. This area is a humid one, with extremes of climate. The affected people came from the original cultivator class. The cases were chronic in nature and no seasonal prevalence was noted. The sole of the foot, was the main seat of affection except in one case where the palm was affected. No glandular enlargement was detected in any case; and no history of exposure to V. D. was elicited. Mucous membranes in no part was affected. No eye lesions were found; and no scars on the genitals. The Kahn Test in five of the cases was negative. As the cases were treated as out-patients, no cultures were made.

From my experience in the past relating to the appearance and treatment of yaws in Malaya, Chin Hills, Lushai Hills and Garo Hills area, amongst the original people of those lands I could safely state that these seven were genuine cases of yaws.

**Acknowledgement.**—My thanks are due to Dr. R. R. Roy, Surgeon Superintendent, M. J. N. Hospital, Cooch Behar for his guidance and for his kind permission to publish this paper in the ANTISEPTIC. My grateful thanks are due to Dr. B. B. Bhattacharjee, Emergency Officer, M. J. N. Hospital, Cooch Behar for his kind help in the preparation of this case report.

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# CHRONIC HOARSENESS IN EISENMENGER'S COMPLEX

C. A. AMESUR, M.S. D.L.O. (Eng.),

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THE subject of discussion is "Recurrent Laryngeal Nerve Paralysis in Heart Disease". Ten cases of rheumatic heart disease, were demonstrated at the Eighth Annual Conference of the E.N.T. Surgeons of India, by Dr. Raman.

I am reporting a very unusual case of congenital heart causing hoarseness which was brought up for discussion. S.J., a Hindu woman aged 21, consulted me on 23rd November 1945. She stated that twelve hours after the delivery of her second child five months previously, she fainted and her face became pale. After this episode, some change in her voice was noticed. The baby was duly weaned.

Three months later the voice became normal but has again become hoarse now. There was no history of diphtheria; but she had an attack of typhoid fever in 1937. Examination showed the left vocal cord in cadaveric position. I suggested that an orthodiagram be taken and thereafter the heart, aorta and the apex of the left lung be examined by a competent specialist.

Orthodiagram: Readings of the Heart

| Normal        | Diameter | on 30-11-'45 | on 13-2-'51 |
|---------------|----------|--------------|-------------|
| 11.4—14.7 cm. | Long     | 13.5 cm.     | 13.7 cm.    |
| 8.5—13.8 cm.  | Trans:   | 10.4 cm.     | 10.5 cm.    |
| 9.9—10.7 cm.  | Base:    | 12.2 cm.     | 12.3 cm.    |
| 3.9—5.7 cm.   | Aorta    | 5.6 cm.      | 6.0 cm.     |

This showed the arch of the aorta to be on the wider side of the normal diameter. Blood examination showed anaemia; Wassermann test was negative. The treatment consisted of voice-rest, diphtheria antitoxin 2,000 units plus Vit. "B" 100 mg. for two days, and then by eight further injections of Vit. "A" intramuscularly, followed by Wassermann's Valero-Foser, containing iron-formate gr. 0.03, glyceroper cc. In addition Pot. iodide was given with milk. The patient felt better for some months.

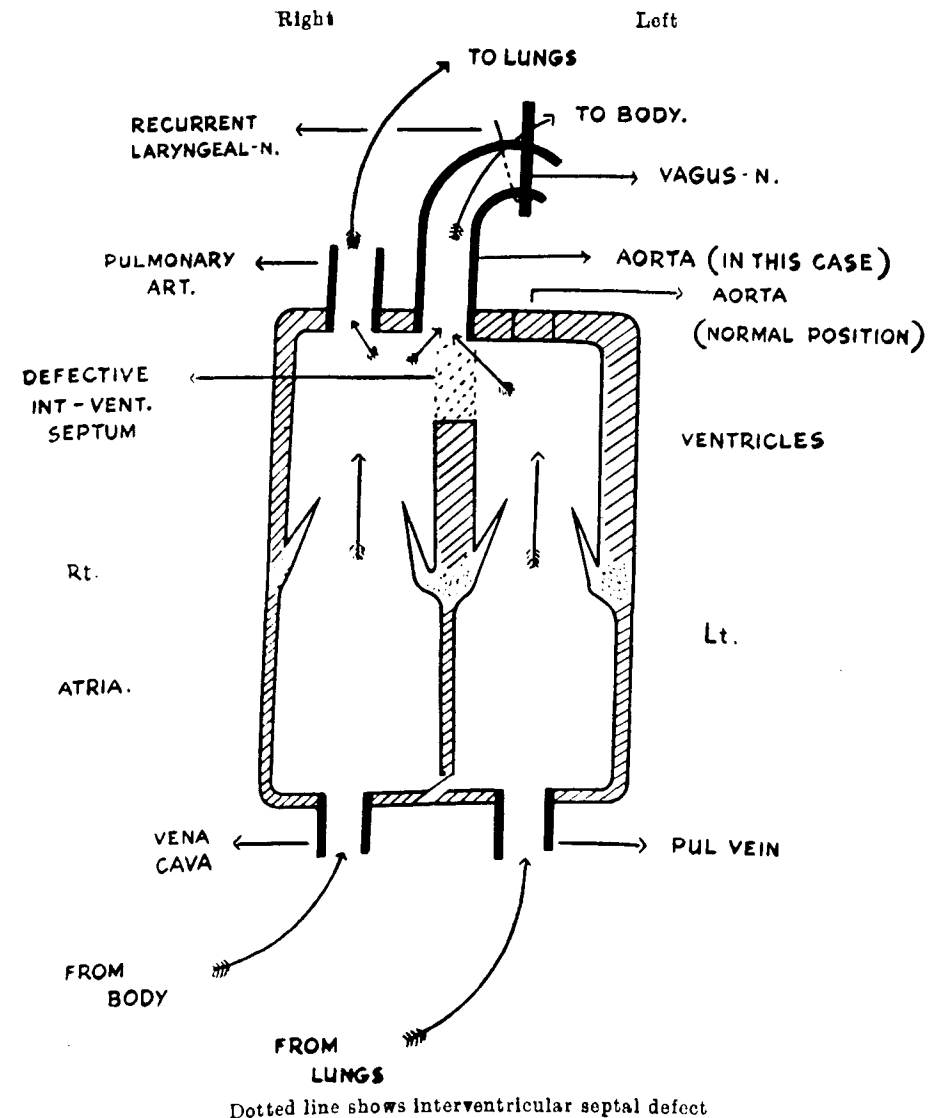
In 1946 an E.K.G. tracing was taken suggesting sinus rhythm, right axis deviation, vertical heart, (?) right ventricular strain-hypertrophy.

On 9th February 1951 the patient returned with the change in her voice. The left vocal cord was found to be the same. She was advised to consult the heart specialist again, who advised her to go to Peter Bent Hospital, in Boston (U.S.A.)

Presented at the Eighth Annual Conference of the Association of Otolaryngologists of India, held at Trivandrum on 30th December 1955.

In June 1952, the patient underwent treatment at the hands of Dr. Samuel A Levine and Dr. Lewis Dexter. In addition to the usual investigation, cardiac catheterization was done twice. The first attempt had to be given up because of severe shivering and sudden breathlessness. The second attempt was successful. It was only then that Dr. Levine and Dr. Dexter were able to diagnose the condition, as Eisenmenger's complex.

Diagrammatic representation of the heart in Eisenmenger's Complex



The patient has interventricular septal defect of the heart, there is dextroposition (over-riding) of the aorta; besides myocardial irritability due to auricular-ventricular fibrillation, for which quinine was prescribed.

She had another attack in January 1954. She is now able to sleep normally for two hours at a time but on changing the side, goes to sleep again. Her voice continues to be in the same condition.

At present attempts are being made in U.S.A. to constrict the pulmonary artery, and when this experimental stage is over, we hope something may yet be done in the way of surgical treatment of the Eisenmenger's complex.

### OPERATIVE EXCISION OF THE CHEEK FOR CANCER AND SKIN-GRAFTING REPLACEMENT

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A HINDU male, aged 15, came as out-patient to the hospital with a swelling of the left cheek and complaining of difficulty in opening his mouth. A naked-eye examination showed a slightly elevated swelling with a raised nodule at its centre. The nodule appeared to be surrounded by a depressed area and the margins of the swelling were puckered. The mass felt firm and was fixed to the maxilla. The opening and closing of the jaw was limited. A finger could not be passed between the mucosal surface of the cheek and the teeth, but a finger passed inside the mouth could not feel the presence of any suspicious induration on the tongue, tonsils, fauces or palate. The regional lymph glands appeared normal. The patient was slightly built but had not lost weight to his knowledge. He appeared anæmic but was otherwise normal on examination.

First stage of the operation.—*Excision of the cheek*:—Anæsthesia was induced with pentothal and continued with a mixture of ether and oxygen. The whole of the left cheek was excised *en masse* with the cutting point of the cautery, dividing the intervening salivary duct and blood vessels, and raising the cheek from the maxilla. The bleeding points were caught hold off and ligated. The raw cut surface showed oozing of blood which was controlled with pressure applied through a piece of gauze. The wound was packed with sterile vaseline gauze and bandaged.

The wound was opened on the fourth day and packed once again with sterile vaseline gauze. The dressings were continued for 20 days.

Second stage of the operation.—*Preparation of an artificial cheek*: (1) The scalp was infiltrated with 2% procaine with adrenaline in the area of the flap mapped out as shown in the adjoining outline diagram. The base of the flap was a line drawn horizontally forwards from the tragus of the ear to a little

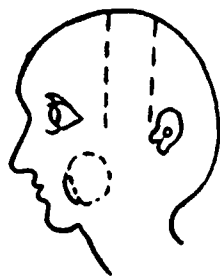


Fig. 1

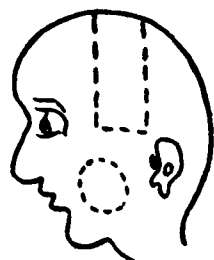


Fig. 2

outside the orbital margin. The flap was then carried upwards along two parallel lines to nearly the middle of the scalp to coincide with the line of the sagittal suture.

The flap was cut upon firmly with the scalpel, raised by blunt dissection with the handle of the scalpel from the underlying aponeurosis of the occipito-frontalis. The bleeding from the cut surface was controlled by clips fixed to the cut margins of the scalp. The bared area was temporarily packed with hot gauze.

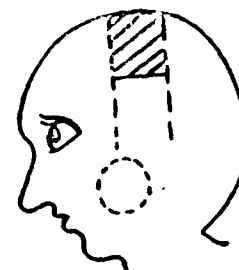


Fig. 3

(2) A piece of lint about the size of the cut cheek was then cut and an area of similar size was mapped out on the inner surface of the lower end of the right thigh. The area was anæsthetized locally and a whole flap of the thickness of the skin was cut out. This flap was bared of all fat and transferred raw surface to raw surface under the distal end of the scalp flap and carefully stitched up at the edge. The whole scalp flap was then stitched in position as also the gap created in the thigh. The flap so buried

under the scalp underwent metaplasia so as to resemble the buccal surface of the cheek.

Third stage of the operation.—*Excumation of the artificial cheek*:—After 3 weeks, the flap on the scalp was cut out precisely in the manner it was mapped out previously. The skin flap tucked under its extreme end had undergone metaplasia and was now ready to be stitched in the place of the gap caused by the excision of the cheek. The flap was reflected downwards, with its blood supply in tact at the pedicle, and stitched there with linen. The bare rectangular areas on the scalp were packed with sterile vaseline gauze and bandaged.

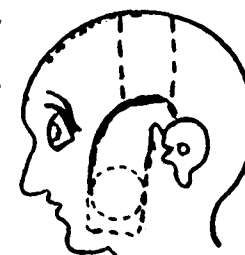


Fig. 4

Fourth stage of the operation.—*Replacement of the pedicle in situ*.

After 3 weeks the down-turned flap of the calp was divided in the contour of the cheek, straightened out and replaced over its original bed in the scalp. The whole flap was stitched in position except for the terminal  $1\frac{1}{2}$  square-cut-piece which was employed as an artificial cheek. The flap took the scalp very well because the blood supply at the pedicle was quite abundant.

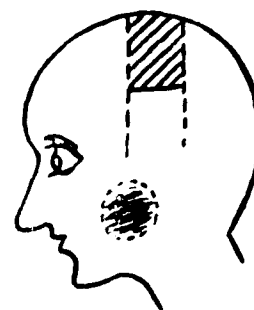


Fig. 5

Fifth stage of the operation.—A skin graft was taken from the inner surface of the left thigh and the deficit in the flap of the scalp

was filled up with it. The graft took well at places, and at others it was repeated. In the limit, the flap was well closed.

So far as the cheek was concerned, the cosmetic result was good. Unfortunately, however, granulations had by now begun to appear on the inside of the left cheek outside its periphery where obviously a cancerous process had begun to spread. Under general anaesthesia, all the upper teeth on the left side were extracted and such granulations as were visible, were cauterized. The end-result was satisfactory so far as the cheek was concerned, in that an unsightly gap had been successfully closed but in the limit cancerous infiltration would take place as also secondaries which may occur elsewhere.

#### THE INTERPOSITION OPERATION

D. W. De Carle (*West. J. Surg.*, January, 1956) discusses the advantages and limitations of the Watkins-Wertheim interposition operation for vaginal prolapse by means of a study of 29 personal operations and a review of the literature. He states that there is no unanimity among gynaecologists on whether or not this operation deserves a place in pelvic surgery. The study of 705 such operations by Zachel and Fischer (1936-1950) showed a recurrence of the pelvic abnormality in over 20% of the cases, subsequent uterine bleeding in 10 per cent, complications with fistulae in 10 per cent, and in 1 per cent to 2 per cent a subsequent fundal carcinoma. Zachel and Fischer concluded that the operation of interposition should be abandoned. On the other hand, a similar survey of this operation at the Johns Hopkins Hospital (1930-1948) suggested that the interposition operation had a definite place in gynaecological surgery. All advocates of the operation agree that there are definite limitations and contraindications as well as advantages, and that the careful choice of patients is essential. The author lists *three generally accepted indications for the operation* (i) the occurrence of a pronounced but uncomplicated cystocele; (ii) the presence of a well defined but moderate uterine prolapse; (iii) mild urinary incontinence. He considers that the first of these is by far the most important indication, and that operation in such cases gives the highest percentage of permanent cures. The age of the patient is important, and the author agrees that the *interposition operation should be limited entirely to women past the menopause*. Moreover, the uterus should be *mobile*, and indication to operation unless they can be removed by myomectomy. The author stresses the point that the operation should never be performed if there is a suspicion of uterine carcinoma or questionable adnexal abnormality. Preliminary diagnostic curettage, biopsy of the cervix and examination of the bladder are recommended. He concludes that the operation has a definite place in pelvic surgery, particularly among elderly women with severe and uncomplicated cystocele. Good results are obtained when due regard is paid to the indications and limitations of the operation. — (*M. J. Austral.*, 12-5-1956).

#### ACUTE POSTOPERATIVE PULMONARY OEDEMA

May be promptly relieved by inhalation of ethyl alcohol vapour. Ruth Weyl, M.D., of the Chicago Medical School recommends that ethanol be given whenever incipient or fulminant pulmonary oedema occurs during or after surgery. Results are usually excellent if treatment is begun early in the attack. Alcohol vapour inhalation may be combined with any other treatment and may be given safely even to patients in poor condition. — (*Modern Medicine*).

Young  
in mind  
and heart  
in spite of  
his age



Thanks to  
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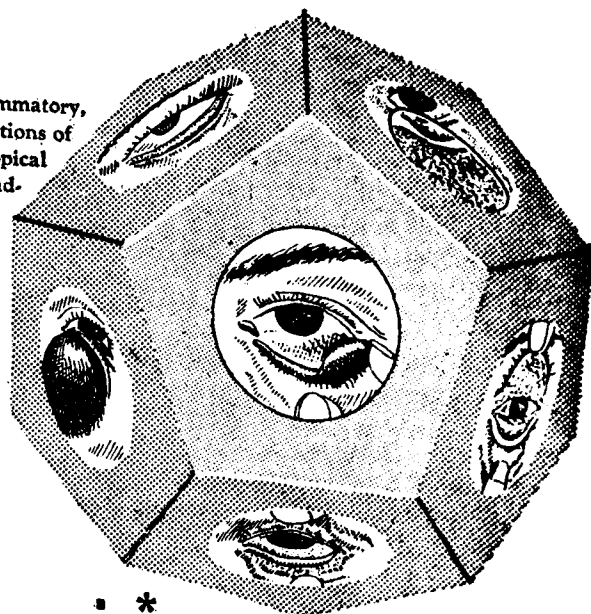
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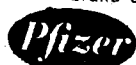
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# The Antiseptic

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## Editorials

### TOBACCO'S EFFECT ON HEALTH

THERE has been a considerable volume of writing in the medical and lay press about the relationship between smoking on the one hand and cancer of the lung and heart diseases on the other. At the 124th Annual representative meeting of the British Medical Association held in London early this year, one of the most interesting questions debated upon, was whether the members who attended the meeting may smoke or not during the proceedings. Opinions of different shades were forthcoming at this conference as to whether medical men should smoke or not and whether smoking has or has not a deleterious effect upon health. In recent years, there have been outbursts of arguments over the ill-effects of tobacco and these have torn families and provided society with conversation in its drawing rooms and after dinners.

"The Tobacco Industry Research Committee has announced an allocation of a half a million dollars to continue its support to the investigation into "Tobacco's effects on health" said a New York message dated 5th February 1956 to the Indian Press. Another message from Cincinnati under the same date had it that Dr. EARNEST L. WYNDER of "The Memorial Centre for Cancer and Allied Diseases" suggested as a result of research that cutting out smoking would reduce the lung cancer rate by 80%. Dr. EVARTS GRAHAM of St. Louis, Missouri, stated on the 27th February last that "there is not only very strong statistical evidence of a causal relationship between heavy cigarette smoking and lung cancer, but we have the additional evidence that cigarette smoke contains a factor that produces cancer in experimental animals of unrelated species." All these go to show that those against smoking are holding the field and smokers are fighting a rearguard action. A review of the medical literature gives strong evidence that cigarettes

can be reasonably expected to produce cancer of the lung. Dr. GRAHAM stated further that the statistical relationship was confirmed by twelve other independent studies in four different countries based on a total of more than 6,000 human cases of lung cancer. He came to the conclusion that there is a relationship between smoking and cancer. In the context of what has been stated above, it would be proper to review the state of our present knowledge on the subject of smoking in relation to the causation of lung-cancer and heart-disease based on a study of the published data in current medical literature.

Cancer of the lung was an extremely rare disease till about 30 years ago and ADLER in 1922 was able to collect 347 cases from the entire world literature. At the present time cancer of the lung is increasing more than cancer of any other part of the body and is found to be the most frequent form of cancer in men. Cancer of the lung represented 1.1% of all cancers in 1920, 2.2% of all cancers in 1930 and 8.3% of all cancers in 1948 and based on the number of people who are smoking today, it is predicted that in 1970, cancer of the lungs will represent 18% or approximately one out of every five persons with cancer. It has been estimated by the American Cancer Society that unless measures are promptly instituted to prevent this rapid increase, one out of every 10 or 15 men living in 1970 will have lung cancer.

It has however been suggested, perhaps in interested quarters, that cancer of the lung is not increasing but better diagnosis has made it possible to detect more cases. It is however, inconceivable that cancer of the lung was being missed at autopsies by the pathologists of a few years ago.

A Press report issued in India in April 1955 gave the information that smoking was on the increase in India and that the consumption of Indian cigarettes rose from 18,527,000,000 in 1953 to 19,776,000,000 in 1954 and that of imported cigarettes went up from 34 millions in 1953 to 54 millions in 1954. Beedi smoking in rural areas has also gone up from 114,838,000 pounds of tobacco in 1952 to 117,681,000 pounds in 1954. The same is the case with the consumption of chewing and hookah tobacco—from 260,457,000 in 1952 it rose to 264,634,000 pounds in 1954. The economic aspect of tobacco consumption involves an industry whose total business runs into crores of rupees in India and millions of dollars or pounds respectively in America and Europe. The tobacco industry has therefore, every reason to be prepared to spend large sums of money to ascertain the real position and evolve some process whereby the offending carcinogenic agent is eliminated.

A recent report in the *British Medical Journal* based on a canvass of 40,000 physicians by Doll and Hill of the British Medical Research Council revealed that among the doctors aged over 35 in Great Britain, non-smokers had an annual death-rate of 3.8 per thousand,

while those who smoked 25 or more cigarettes per day showed a death-rate of 5.2 per thousand. They noted also an increase in coronary thrombosis amongst smokers between the ages of 50 and 64 and the death-rate for coronary diseases was 95% higher among men who had always regularly smoked cigarettes than among non-smokers and 120% higher among those who were currently smoking more than 20 a day (*B.M.J.*, 1955). Thus the problems raised by the effects of smoking on the heart and arteries, are even more pressing than the publicized findings linking smoking with cancer.

In a study of arteriosclerosis, Dr. WILLIAM DOCK of the Brooklyn State University Medical Centre found that tobacco caused constriction of the blood vessels in the extremities of all the subjects he studied (*Am. J. Med.*, 2: 730) and also minor changes in the ballistocardiogram in one third and in the electrocardiogram in one half of the subjects. The cumulative effects of such changes probably contribute to the reduced life-expectancy reported by Pearl some years ago. Not only cancer of the lung but chronic sinusitis, emphysema and reduced resistance to pneumonic infections could be cited (*Science*, 87: 216). Dr. J. H. BURN of Oxford (*B.M.J.*, dated 28th July 1951) who studied the effect of smoking on the heart came to the conclusion that the smoking of even one or two cigarettes may cause constriction of the coronary arteries, thereby interfering with the nourishment to the heart muscles.

A close correlation between heart diseases and heavy smoking was reported by Dolgoff and others in *Angiology*, April 1955. The incidence of heart disease among heavy cigarette smokers was computed by them to be half as much again as those who smoked less than 10 a day.

Dr. SIGLER has made a notable survey of the smoking habits of 1520 patients in whom there was demonstrable coronary disease associated with the syndrome of angina pectoris. It was found that habitual smokers tended to develop coronary disease at a considerably earlier age than non-smokers. Of patients who smoked heavily (more than 30 cigarettes a day) 64% developed symptomatic coronary disease as compared with 29.2% among non-smokers who did so. It was also found that 35% of heavy smokers and only 6.4% of non-smokers died before the age of 50 (*N.Y. St. J. Med.*, 1-11-55). Commenting on the above the *Medical Journal of Australia* of 18-2-1956 says "the series of cases is large and the figures are convincing."

It is understandable that there are many individuals who are unwilling to accept a causal relationship between smoking and bronchogenic cancer. Obviously those concerned with the raising of tobacco, its marketing, the processing and the sale of the final product are reluctant to accept any such causal relationship. In addition, the cigarette user who has become addicted to its use, even though he might be medically trained, is reluctant to admit that

anything he does might be harmful. Because of this, there are many who will not accept the presently available evidence of the relationship between smoking and cancer. The statement frequently made is that there can be no causal relationship between smoking and lung-cancer because if there were, there would be a commensurate increase in the fatality incidence from cancer of the larynx, which is not the case. While it is true that the death-rate from cancer of the larynx has not been proportionate to the death-rate from cancer of the lung, it is equally true that cancer of the larynx has been and is increasing with the same frequency as cancer of the lung. But the cancer of the larynx is readily diagnosed when the lesion is early and can therefore, be satisfactorily treated, with resultant cure in a large percentage of cases, whereas cancer of the lung is difficult to diagnose early and because of this, the death-rate therefrom is necessarily high.

Another antagonistic argument which is frequently put forth, is that pre-cancerous lesions are found in the respiratory tract of smokers. Approximately two years ago, the department of pathology at Tulane became interested in the problem and began looking for possible pre-cancerous lesions in the blocks of bronchial wall removed from the region of the coryna and also from each main bronchus of individuals who came to autopsy. They found that there were changes in the bronchi which, on microscopic section varied according to the amount smoked. The individual who never smoked had a normal bronchial mucous membrane, the moderate smoker had changes which consisted of metaplasia and the heavy smoker had marked changes which were interpreted as pre-malignant lesions. The only reason why patients with pre-malignant lesions did not develop cancer of the lung was that they died of heart failure before lung cancer developed. This study demonstrates that cigarette-smoking is associated with pre-cancerous lesions in the bronchial mucosa and that the degree of metaplasia increases with the amount smoked.

For many years those who have been concerned with the treatment of patients with bronchogenic cancer have been impressed with the high frequency of heavy smokers among men who have had this disease. "In fact I have been so impressed by this," writes ALTON OCHSNER in *A. M. Surgeon*, 21: June 1955, "that for the last at least 5 years, I have categorically made the statement that if any man who has a pulmonary condition which might be bronchogenic cancer, if he is not a smoker, the lesion is not epidermoid cancer, either adenocarcinoma which is not produced by carcinogen but is an inflammatory lesion. In five years I have been wrong only once." The positive history of smoking at present is our best method of making a diagnosis of malignant lesion of the lung. Well over 95% of men with cancer of the lung are cigarette smokers, as contrasted with a controlled group of from 65 to 75% without cancer of the lung.

The results of the survey conducted by The American Cancer Society showed that there was a definite increase in the death-rate from all causes among individuals who smoked cigarettes as compared with those who did not smoke and this was true of all age-groups and the death-rate varied according to the amount smoked. Although the death-rate from cancer of the lung was particularly higher among smokers as compared with non-smokers, it was found that the death-rate from other cancer besides cancer of the lung was also greater among cigarette smokers than in non-smokers. As incidental finding was that the death-rate from coronary disease was definitely higher in cigarette smokers than in non-smokers. This was particularly great in the age group 60 to 65 (*Amer. Cancer Soc. Report*).

The American Cancer Study (*J.A.M.A.*, 155: 7-8-1954) showed that among heavy smokers the over-all death-rate was 75% higher than among non-smokers. The death-rate from heart disease was 95% higher than among non-smokers; the death-rate from all causes was 156% higher than among non-smokers and the death-rate from lung cancer was 400% higher than among non smokers. The study by the American Cancer Society, which was made in a completely impartial manner and which includes a large enough group of cases to be statistically significant, proves without room for any reasonable doubt that there is a causal relationship between smoking and cancer—particularly cancer of the lung, as well as a causal relationship between cigarette smoking and heart disease.

In England the British Committee on Cancer and Radiotherapy (*Lancet*, 2: 409, 28-8 '54) reported to the House of Commons that "young people should be warned of the risks apparently attendant on excessive smoking." We are also convinced that it is high time the profession urges discontinuance of smoking and that young individuals should be dissuaded from acquiring the pernicious habit.

We have endeavoured in this brief survey of the literature, to place before the profession the effects of smoking on human health with the sole object of enlightening them and through them the lay public. The medical profession has been reluctant to accept the relationship between lung-cancer, heart-disease and smoking and even if they were inclined to concede that there may be some truth in it, they have not sufficiently emphasized the evil effects; for many of them smoke and some heavily too and it is only human nature that one is unlikely to condemn or at least even discourage, what one does regularly.

PREOPERATIVE PREPARATION OF THE COLON for three days with a combination of tetracycline hydrochloride (Achromycin) and Neomycin produces an almost sterile stool. In addition to a cathartic on the first day, daily enemas, and a low-residue diet, Isidore Cohn, Jr., and Alfred B. Longacre, of Louisiana State University and Charity Hospital, New Orleans, recommend 4 tablets of the combination every hour for four hours and then every six hours for a total of 72 hours. Each tablet contains 50 mg. of Achromycin and 250 mg. of Neomycin.—(*Modern Medicine*, June 1, 1956).

## POLIOMYELITIS VACCINE: WHAT IS ITS FUTURE?

THE World Health Organization recently called together, in Stockholm, a group of scientists from nine countries to study and review the evidence about vaccination against poliomyelitis which has accumulated during the past two years. As a result of its review the group recommended that, provided a number of safeguards were introduced, countries with a high incidence of paralytic poliomyelitis should plan to bring vaccination into routine use at an early date. This recommendation can only be interpreted as a statement of faith in the safety and protective power of formalin-treated poliomyelitis-vaccine and is bound to affect the policy of health departments throughout the world.

Dr. W. L. M. PERRY, M.D., of the Department of Biological Standards, National Institute for Medical Research, London, in an interesting paper has given the background of the research on the subject.

The technique of growing monkey-kidney cells in tissue culture as the medium for the cultivation of the virus was developed by ENDERS, WELLER and ROBBINS in 1949. Within 4 years, SALK had adapted the technique to the production of polio-virus suspensions on a large scale and had worked out methods of inactivation of the suspension which, he claimed, were reliable and effective. He had also tested this suspension in a small number of children without untoward results. Thus in 1953, the National Foundation for Infantile Paralysis of the U.S.A. was convinced that there was available a vaccination against poliomyelitis, which deserved a clinical trial for its effectiveness. Thereafter, things moved rapidly. Groups of children comprising 200,000 in each were subjected to the experiments. While one group received vaccine injections, the other received injections of a sterile fluid coloured so as to resemble the vaccine but having no active ingredients. Nearly a quarter of a million children were vaccinated. This test was carried out in 1954 and a team of experts carried out a detailed evaluation of the results. Their research indicated that the vaccine had been safe, in that it had been given to 400,000 children without apparent mishap and that it had been effective in that it had prevented paralytic poliomyelitis in from 60 to 90% of the children who received it. The results of the trial were made available to the press and the public in 1955 and firms were licensed to manufacture this vaccine, which was then duly tested. Mass-vaccination was begun on April 13, 1955. On April 26, 1955 two weeks later, the first 5 cases of poliomyelitis following the injection of vaccine made by the Cutter Laboratories were reported. The mass-vaccination was therefore, temporarily suspended on May 8, 1955. This accident threw the health authorities throughout the world into a state of confusion and in many countries vaccination programmes were cancelled. On June 10, the U.S. Government issued a technical report in which the situation was reviewed. It was concluded in this report that the test carried out on the vaccine

had been insufficiently stringent and indeed live virus had since been isolated from some of the batches of vaccine concerned in the accident. New testing requirements were subsequently issued. Vaccine from other manufacturers was not implicated in any accident. The vaccination programme was resumed and has since proceeded without interruption. The pace has, however, been slow, since all vaccine had to be subjected to a series of tests which are not only more stringent and more time-consuming but which have resulted in the rejection of a higher proportion of batches as unacceptable. Nevertheless, over 10 million children have been vaccinated in the U.S.A. and in spite of careful watch no further accident has occurred. In countries like Canada, and Denmark mass-vaccination has also gone ahead without any trouble. Against this background of the Stockholm Conference, it is time that most countries started thinking of what should be their decision in the matter.

There are two implications which must be considered before any decision is taken:—The first stems from the fact that the recommendation is addressed to those countries with a high incidence of paralytic poliomyelitis. A decision of this kind must therefore, rest entirely with the health departments concerned. The second implication arises from the reservation to the main recommendation:

- (1) that the vaccine should be made from strains of poliomyelitis virus chosen to be as non-virulent as possible,
- (2) that experience and skill in production and testing of the vaccine must be assured; and
- (3) great care in diagnosis is essential, since diseases resembling poliomyelitis may be diagnosed as poliomyelitis and may consequently be regarded as "vaccine failures."

The main recommendation at Stockholm is based, upon the faith in the safety and protective power of the vaccine. The health authorities in this country are not, in any way bound to concur with this view. We must be assured that a safe vaccine is made. Many people believe that this has already been accomplished. The protective power of the vaccine should also be satisfactory. In the 1954 trial convincing evidence was available that the vaccine will protect at least 60% of those receiving it. The experience in 1955 has added little to this evidence. The health authorities must be able to find out in what age-group there is a relatively larger incidence of paralytic poliomyelitis. The experience so far obtained relates to children over 6 years and there is not sufficient evidence of protection in the younger children. Therefore, the information desired above is absolutely necessary. The problems that face the health authorities in this country and elsewhere are many. They must try and reconcile the varying facets of the situation with one another. We are sure they are fully aware of them all and that they will do their utmost to plan in such a way as to reduce the number of cases of poliomyelitis as much as possible and as quickly as possible.

# The Late Dr. P. RAMA RAU

IN the premature death at the age of 57 of Sri Rao Bahadur Dr. P. RAMA RAU the eminent radiologist of Madras, who achieved an international reputation, by dint of sheer merit, and hard work, the Medical Profession has sustained a grievous loss, the loss of an esteemed colleague and a dependable co-operator in diagnostic and curative work.

Dr. RAMA RAU set-up private practice immediately after his medical education, but later exchanged it for specialist practice in radiology for which he underwent training at the University of Vienna in 1931, where he stood first in the final examination as orientation student among medical men from all over the world. He then travelled extensively in Europe and the United Kingdom before he returned and started his X-ray institute at Madras. He was the first Indian private radiologist to possess his own radium, and his Radiological Institute in Madras is acclaimed on all hands to be one of the very best equipped of its kind in the Far East. Among his grateful patients could be reckoned people of all ranks and status from all over India, Ceylon etc.

He represented India at the Third and Fourth International Conferences of Radiology held at Paris and Zurich in 1931 and 1934 respectively. In 1937 he toured round the world visiting X-ray Institutes in U.S.A., England, Japan, China, Malaya etc. and in 1949 he again toured U.S.A. and Europe with a view to acquainting himself with the latest developments, and it was during this tour that he represented India as its delegate to the International Congress in Rheumatology held in New York.

His pioneer work in the field and his numerous valuable contributions to various medical (the ANTISEPTIC was one of them) and radiological journals, were fittingly recognized by the American College of Radiology who made him an Honorary Fellow—a distinction conferred for the first time on an Asiatic.

He was actively connected with the ANTISEPTIC, as a member of its Editorial board, during his early years, during which he rendered valuable assistance to us. He had subsequently also been evincing great interest in our journal and contributing valuable articles from time to time.

His extra-professional activities made him a very popular and prominent citizen in the City of Madras. He was an ardent Free-



mason holding a high rank in the various orders in masonry; he was a staunch supporter of the craft and seldom missed any masonic function held in the District. He was a prominent Rotarian and as President of the Madras Rotary Club he did much valuable work during the war years. He was Governor of the Rotary International in 1943 and devoted a large part of his time in spreading Rotary ideals of service, himself setting a fine example.

He was of a very genial and generous disposition and was an exceedingly popular figure (being known as 'Ramu' to his numerous friends) in the public life of Madras. He has made several endowments to the University of Madras and the University of Ceylon to further the cause of Medical education.

We offer our sincere and heartfelt condolences to the members of the bereaved family.

## INCARCERATED INGUINAL HERNIA IN INFANTS AND CHILDREN —A PREVENTABLE CONDITION

Infantile inguinal hernias occur because of failure of the embryonic processus vaginalis to become obliterated and not because of a weakness of the surrounding tissues, as is often the case with adult hernias. An inguinal mass that appears when a child cries or stands and disappears when he lies down is almost certain evidence of an inguinal hernia. The diagnosis of inguinal hernias in infants can often be made from the history alone. Seldom is the physician afforded an opportunity to visualize or palpate the bulging hernia in infants. He must rely on the history and on palpating the thickened processus vaginalis just below the external ring. Repair of inguinal hernia in infants and children as soon as the diagnosis is made is a safe, permanent, yet simple solution to a serious problem. The author lists the following reasons for advising early repair of infantile inguinal hernias: (1) Inguinal hernias seldom disappear spontaneously. (2) Incarceration in patients under one year of age is more frequent than in those at any other age. (3) An ovary may become incarcerated and become gangrenous. (4) A testicle may become gangrenous from pressure of an incarcerated hernia. (5) Parents are worried until the hernia is repaired. (6) Mortality and morbidity are lower when the operation is performed as an elective procedure. (7) The use of a truss is obsolete and often ineffective in preventing incarceration.

The frequent finding of sliding hernias in infants has not received proper emphasis. Sliding hernias often have the caecum, bladder, or fallopian tube as an integral part of the wall of the sac. In such instances the sac cannot be ligated as high as is desirable, but it is not necessary to open the abdomen through a separate incision as is advocated sometimes for similar hernias in adults. Sliding hernias in infants can be repaired by adhering to the following principles: (1) avoid cutting into the bladder, fallopian tube or caecum; (2) ligate the sac just distal to the involved viscus; and (3) if the ligated sac fails to retract inside the internal ring, suture it under the conjoined muscle. Recent advances in anaesthesia and paediatric surgical technique have not only shortened the hospital stay (two days in most instances) but have also lowered the morbidity and mortality.—(J. Ten. M.A., 49: 37-40, Feb. 1956, via J.A.M.A.).

## SURGERY

**Is biopsy safe?**—(From an editorial in *Am. Surgeon*, 21: 733, July '55).

There is increasing evidence that operations which do not completely encompass cancer but cut across it may spread cancer and accelerate the course of the disease. This tendency for cancer to be implanted and disseminated by operation is seen even in such slowly growing cancers as papillary cancer of the thyroid—a tumour which if left alone shows little tendency to distant spread. If papillary carcinomas are cut into, they often grow back as implants in subcutaneous tissue or muscle. Often these invasive recurrences cannot be removed. The tendency to distant metastasis in these cases is significantly increased.

Even needle biopsy does not appear to be safe. A papillary carcinoma of the thyroid was diagnosed by needle biopsy and removed 2 days later. Two years later it recurred as a skin nodule at the site of the needle puncture. Four years after the biopsy, the patient died of systemic metastases.

A recent report on cancer of the thyroid in which routine needle biopsy was advocated, illustrates the danger of biopsy. Despite the most radical operations, 30 per cent of the patients with papillary carcinoma of the thyroid were either dead at the end of 5 years or had had unremovable recurrences. This rate of recurrence is between 4 and 5 times as high as that usually reported following much more conservative operations. Since treatment in these cases was by the most radical type of cancer operation, it is difficult to escape the conclusion that it was the needle biopsy that disseminated the tumour and rendered it incurable.

Biopsies of abdominal cancers such as cancers of the pancreas, metastatic cancer of the liver and localized cancers of the stomach should be undertaken with the greatest caution. Cells exfoliated from these tumours or squeezed out of them may implant themselves on

peritoneal surfaces. It is this type of dissemination of cancer that gives credence to what our patients already think and tell us—that cutting into cancer spreads it and makes it grow.

Biopsy is useful in diagnosis. Employed carefully and in selected cases it may do no harm. If used indiscriminately, it may spread disease and shorten life. Even in patients with incurable cancer the surgeon has a grave responsibility. His operations, when they can do no good, at least should do no harm.

**Early ambulation**—The newer concept—A new successful experiment—(Condensed from an Editorial in *Journal of Iowa State Medical Society*, for Sept. 1955).

Within the past 15 years there has been a complete reversal in the medical profession's official attitude as regards the optimal period of hospitalization following surgery. Many factors have been responsible for this change. For one thing, doctors have been zealous, as always, in looking for ways of sparing their patients any unnecessary prolongation of disability and discomfort. And, in addition, they have sought to reduce the costs that are directly or indirectly the consequences of illness and hospitalization.

Dr. D. J. Lighthouse, of Detroit, reports upon an investigation he has conducted in early ambulation, one that he calls a "rapid recovery experiment." He has been so successful in it that he now maintains it is routinely advisable to three times in rapid succession immediately after their recovery from the anaesthetic, provided only that nurses are present to supervise the procedure.

"Every surgeon can convince himself of the value of immediate post-operative exercise if he will perform this 'rapid recovery experiment' on a patient who has undergone a major operation, e.g., cholecystectomy or gastrectomy," Dr. Lighthouse declares. "Immediately

after the patient recovers from the anaesthetic, assist him to get out of bed from the recumbent position and instruct him how to do it. Have him turn on his right side, then sit up with his feet over the edge of the bed, stand on the stool, then step down to the floor. Have him walk a few steps and then return to bed and resume recumbency for about a minute. Then repeat the procedure twice. Each of the three times that he gets out of bed, insist that he walk as many steps as possible; each time he will be able to go farther. After this exercise period (about five minutes) is completed, allow the patient to rest in the recumbent position for ten minutes, and then visit him again. You will be amazed at the improvement in his general condition."

"The surgeon should perform this experiment personally on three different patients," he contends. "By then, he should be so thoroughly convinced of its efficacy that he will be ready to adopt it as routine procedure, and to train his assistants and nurses in the management of patients during this immediate post-operative exercise."

"After this triple-rising procedure," according to Dr. Lighthouse, "most patients can get out of bed by themselves without assistance, and they are instructed that walking should be repeated frequently. If the patient is somewhat resistant or fearful, then each time he gets out of bed, have him bend over and touch the floor several times. This relieves any faintness and gives the patient confidence. If the patient should be still lagging or fearful on the day after operation, urge him to walk more rapidly or to walk up a flight of stairs. Encouragement and aggressive assistance are necessary to instil confidence in some patients, and become routine responsibilities of surgeons, interns and nurses in hospitals where early ambulation is effectively practised."

**Management of acute chest injuries.**  
—(*Texas State Journal of Medicine*, September 1955).

The central feature of acute chest injuries is the resulting disturbance of the

respiratory mechanism. An injury to the chest may cause serious respiratory disturbance without severely damaging the lungs.

Intrathoracic complications may be expected in two-thirds of all cases of multiple rib fractures. The most common complication is the "wet lung," which is a clinical term signifying the persistence of mucus, blood, serum, or fluid in the tracheobronchial tree. The chief factor in the development of wet lung is the production of abnormal amounts of interstitial and bronchial fluid under the stimulation of the trauma. Pain, dyspnoea, and excessive narcotization contribute to the condition by inhibiting the cough reflex and thus preventing removal of the fluid by an effective cough. Pneumothorax and hemothorax are also common and often serious complications of chest injuries.

Röntgenograms are essential to the recognition and proper evaluation of chest injuries. They should be repeated at intervals as a guide to the patient's progress. In the early stages of wet lung, the roentgen changes are minimal; in fact, the roentgenogram may reveal no evidence of abnormality even in the presence of considerable respiratory obstruction.

Open or sucking wounds must be closed as quickly as possible and a continuously unobstructed airway must be assured. In some cases, immediate bronchoscopy or tracheotomy may be imperative for the relief of obstruction of the air passage. If the situation is not urgent, simple measures to encourage an effective cough may suffice to clear the tracheobronchial tree. A collapsed lung must be expanded promptly. One need have no fear of too rapid removal of fluid or air from the pleural space. Skeletal fixation is seldom necessary for the control of paradoxical motion of the chest wall. A tracheotomy may be effective in such circumstances. Pain usually can be controlled by the judicious use of meperidine hydrochloride or intercostal nerve block. Provision for an adequate respiratory exchange is the fundamental objective in the management of every patient with a chest injury.

**Management of spontaneous pneumothorax.**—(*Am. Rev. Tuberc.*, 73 : 257, 1955 via G.P.).

Marrangoni and his associates analyzed 80 cases of spontaneous pneumothorax with special emphasis on 25 patients who were treated on the thoracic surgery service. These 80 patients were otherwise healthy persons who developed spontaneous pneumothorax in the absence of neoplastic disease, active tuberculosis or trauma. The authors consider that spontaneous pneumothorax usually results from a rupture of some cyst-like lesion of the lung.

Patients who have severe symptoms of tension pneumothorax, bilateral pneumothorax, a large hydro- or hæmo-pneumothorax or pneumothorax superimposed on an already seriously impaired pulmonary function are emergency problems, and all agree that they require immediate active treatment. In other patients, an aggressive form of therapy seems justified in order to speed recovery, to reduce the likelihood of recurrence, and to prevent "captive lung" in the event that expansion would not occur with conservative therapy. For these reasons, it was the practice of the present writers to treat all cases of spontaneous pneumothorax as surgical emergencies.

Fifty-five of the 80 patients were treated conservatively by one of three methods. The most common consisted of simple bed-rest. Much less commonly, repeated needle aspiration was used in addition to bed-rest. In two patients, a catheter was inserted, and simple underwater seal without active suction was utilized. The authors found these conservative methods unsatisfactory because of the long period required for re-expansion of the lung. An average of 22.5 days to 47 days was required, depending on which conservative method was used.

The current practice was used on 25 patients. Immediately after admission, the patient with spontaneous pneumothorax was taken to the operating room where a trochar and cannula were introduced into the pleural space under local infiltration anaesthesia. The second or third interspace in the ante-

rior axillary line or the fourth or fifth interspace in the mid-axillary line was used.

The trochar was withdrawn and a thoracoscope was introduced through the cannula so that the surface of the collapsed lung could be examined. The thoracoscope was then withdrawn, and the visceral and parietal pleural surfaces were thoroughly poudraged with sterile talc which was insufflated by means of a powder blower. A no. 16 French red rubber catheter was then placed through the cannula into the pleural space. The cannula was withdrawn and active waterseal suction was begun at a negative pressure of 15 to 20 cm. of water. Active suction was maintained for 24 hours, and the patient was then placed on simple waterseal drainage for an additional 24 hours. If the lung remained fully expanded and there was no fluid collection, the catheter was removed. Re-expansion occurred in a matter of minutes.

The average period of hospitalization of these patients was three days compared to an average of 43 days of hospitalization of those treated by the conservative methods. In only three patients was excisional pulmonary surgery indicated. Open thoracotomy was performed because numerous large emphysematous blebs were demonstrated. There has been no recurrence among the 25 reported patients treated by the use of talc poudrage and active waterseal catheter suction.

## OBSTETRICS & GYNÆCOLOGY

**Placenta prævia: a review of 200 cases.**—(*J. Obst. Gyn. Br. Emp.*, 62 : 497, 1955 via *Inter. Abst. Surg.*, May 1956).

A series of 200 patients with placenta prævia, who were admitted to the Royal Maternity Hospital, in Belfast, is reviewed. The patients are grouped, according to the position of the placenta, into four major categories. The first type includes those cases in which the placenta is primarily in the upper segment of the uterus with only the lower edge of the placenta extending

into the lower segment. The second type includes those cases in which the lower edge of the placenta extends as far as the internal os. The third type includes those cases in which the placenta covers the internal os when no dilatation is present. The fourth type includes those cases in which the entire lower segment is covered by the placenta.

The average onset of hæmorrhage in the first and second types, with the placenta in anterior position, was 37 weeks. In the second type, with the placenta in posterior position the average onset of hæmorrhage was 36½ weeks. In the third and fourth types the average onset was 34 weeks.

The principles of management were basically conservative, according to the technique outlined by Macafee. On admission the patients were typed, and the red cell count and hæmoglobin levels were obtained, this procedure being repeated at frequent intervals. Speculum examination was performed. Soft tissue and displacement radiographic studies were done to determine the placental site and also the presence or absence of foetal abnormality. In patients admitted after the thirty-seventh week a sterile pelvic examination in the operating room was performed after the preceding studies had been carried out.

With regard to the specific types of placenta prævia, type 1 was treated expectantly with the exception of those patients who were bleeding more than a minimal amount when rupture of the membranes was carried out. It is noteworthy that 13 of the 35 patients in this group were treated by cæsarean section for various other obstetric causes. In the type 2 placenta prævia with anterior location of the placenta, rupture of the membranes was the usual treatment selected. Again it is noteworthy that 10 of the 14 patients in this group were treated by cæsarean section for other complications. When the placenta was posterior in this type the treatment depended on whether or not the head was engaged or could be made to engage. If the head was engaged or could be made to engage, artificial rupture of the membranes was the treatment of choice. If not, cæsarean section

was the treatment of choice. In types 3 and 4 the treatment of choice was cæsarean section.

There was a gross foetal mortality of 11.9 per cent. Thirty-seven per cent of the entire group were treated by conservative measures for periods varying from 2 to 10 weeks. The foetal loss in the latter group was 16 per cent.

There were five important factors in the good results obtained by this method. The first was the co-operation of the practitioners in the area in refraining from doing pelvic examinations at home. The second was the policy of conservative treatment in those cases in which the infant was unduly premature. The third factor was the extended use of cæsarean section, particularly in the major degrees of prævia. The fourth factor was the increased accessibility of blood, and the fifth, the improved pædiatric care rendered to the infants.

**Postural shock in late pregnancy.**—(*California Med.*, 82 : 159-162, 1955 via *Modern Medicine*, May 1, 1956).

Wilkening, Knauer, and Larson of Bakersfield, Calif., report that assumption of the dorsal recumbent position may cause signs and symptoms of shock in some patients during late pregnancy.

When a pregnant woman lies supine, the enlarged, gravid uterus may compress the vena cava, causing sudden circulatory collapse, faintness, nausea, shortness of breath, pallor, perspiration, hypotension, and tachycardia. Venous pressure in the lower extremities rises, venous return to the heart and lungs is reduced, and cardiac output is decreased. Symptoms are promptly relieved when the patient assumes another position; blood transfusions and vasoconstricting drugs are not necessary.

If hypotension without obvious cause is observed during pregnancy, turning the patient to a lateral position should be tried before active treatment is begun. With shock from hæmorrhage, hypotensive drugs, or spinal anaesthesia, treatment should be given with the patient in the lateral position to eliminate postural hypotension as a complicating factor.

**Septic abortion: Diagnosis and therapy.**—(*B.M.J.*, 4950: 1239-43, 1955, via *Mod. Med.*, 1-6-'56).

Criteria of uterine sepsis are tachycardia, subinvolution and tenderness of the uterus, alterations in the lochia, and bacteriologic and hæmatologic findings. Pyrexia is an unreliable sign.

The pulse rate is rapid, usually above 110, when infection is spreading. If the uterus is empty, subinvolution is a certain manifestation of infection.

After passage of the foetus, tenderness of the uterus is a reliable indication of infection. The peritoneum is probably involved if tenderness is over the lower-abdomen and accompanied by a positive release sign. However, the abdomen is tender with threatened abortion, and a uterus contracted to expel the foetus is tender if the os is closed or rigid.

Purulent or mucopurulent lochia is significant of sepsis if the patient does not have chronic vaginal discharge.

Infection should not be diagnosed on bacteriological findings alone unless hæmolytic streptococci of Lancefield group A are detected. Bowel-derived organisms, the commonest cause of post-abortion sepsis, are usually saprophytic and become pathogenic only after retention of the necrotic products of conception and trauma. Mixed infections are common.

White cell blood count is useful in the early stages of infection and before bacteriological results are available but cannot be relied upon independently of physical signs.

Management of septic abortion depends primarily on the duration of the disease and extent of hæmorrhage and infection. Early pelvic examination, cervical swabs, catheter urine specimen, and hæmoglobin determination are essential. The necessity for investigation before therapy cannot be over-emphasized, since the result of sensitivity reactions may be the all-important factor in determining the most suitable antibiotic agent; haphazard trials of various antibiotics can endanger life.

Since severe hæmorrhage or exsanguination necessitates blood replacement, blood-grouping and cross-match

ing should be done immediately. The need for transfusion should be based more on the patient's general condition than on the hæmoglobin determination.

If the patient does not have uterine infection, chemotherapy is not required unless removal of retained products is necessary. Since retained products are always potentially infected, 1.5 gm. of Sulphatriad and 250,000 units of penicillin should be given every six hours for five days.

Sulphonamide and penicillin are required for women with local uterine infection. If coliform organisms are the sole product of cervical culture, penicillin may be discontinued. Evacuation of retained products is delayed until the drugs have been given for twenty-four to thirty-six hours, although excessive hæmorrhage necessitates immediate intervention.

The primary consideration in the management of septic abortion with invasive complications is to effect adequate control of the infection. Removal of retained products is of secondary importance unless persistent bleeding necessitates the procedure.

If combined sulphonamide and penicillin is not effective, infection is probably caused by coliform organisms or by penicillin-resistant staphylococci. Chloramphenicol is then the preferred drug, or perhaps tetracycline.

Infection is seldom a direct cause of death, but renal failure is sometimes a fatal complication of post-abortion sepsis.

**The expectant treatment of placenta prævia.**—(*Leech, Johane*, 25: 29, 1955, via *Internat. Abst. Surg.*, March 1956).

The presence of a low-lying placenta should be suspected whenever a high presenting part or malpresentation is encountered or when a painless hæmorrhage occurs after the twenty-eighth week of pregnancy. It is not infrequently possible to make a diagnosis of placenta prævia before the first warning hæmorrhage has occurred, if patients who are suspected because of a high or misplaced presenting part are subjected to roent-

genographic examination. The characteristic painless hæmorrhage of placenta prævia, which as a rule starts suddenly and stops almost as suddenly, is a major diagnostic point. Generally speaking, hæmorrhage at about the thirtieth week is more likely in first, second, and third degrees of placenta prævia. The fourth degree, strangely enough, may not manifest bleeding until the thirty-eighth or fortieth week. Pain is invariably absent unless the patient is in labour, or in the rare instances of placenta prævia associated with toxic accidental hæmorrhage.

It is of the utmost importance to distinguish the bleeding due to placenta prævia from other causes of ante-partum hæmorrhage before an expectant policy of treatment is embarked upon. When the bleeding has stopped for several days and when other clinical signs of placenta prævia are absent, it is advisable to pass a speculum with great gentleness and to inspect the vagina and cervix. It is not necessary to examine the pelvis digitally.

The object of expectant treatment of placenta prævia is to provide a definite benefit to the baby by avoiding prematurity, without harm to the mother. It is also suggested that this approach will reduce maternal mortality by following a policy of non-interference in selected cases.

The careful selection of cases for expectant treatment is all important. Usually the initial hæmorrhage in placenta prævia is not catastrophic, although there are rare exceptions. Obviously there is no place for expectant treatment when the initial hæmorrhage occurs between the thirty-seventh and fortieth weeks. There is nothing to gain and everything to lose by postponing treatment.

The ideal type of case is the one in which the initial hæmorrhage has occurred at the thirtieth week and before the thirty-sixth week in which one feels that if the pregnancy is prolonged for 4 to 6 weeks the baby's chance of survival is much greater.

In the majority of cases the bleeding occurs before the thirty-sixth week and the period of waiting can be profitably employed in not only assessing the

obstetrical problem but in treating the patient's general condition. The treatment of anæmia, for obvious reasons, is of paramount importance.

Usually the hæmorrhage in placenta prævia ceases abruptly on its own, provided the placenta is not interfered with in any way. Should it persist in any quantity, and especially over a period of 12 to 24 hours, then active treatment is indicated. On the other hand, if the losses are spaced by several days or weeks, provided none are excessive and the patient is in a fully equipped institution, the expectant treatment may be continued.

As soon as a provisional diagnosis of placenta prævia is made and (if possible) confirmed roentgenologically, the patient must be hospitalized. The majority of cases occurring before the thirty-sixth week can be carried to nearly term. The patient is confined to bed and, if bleeding is controlled with morphia (gr.  $\frac{1}{2}$ ), the hæmoglobin is estimated, and the blood is grouped. One or two weeks after the initial hæmorrhage, depending on the period of gestation and severity of the hæmorrhage, a speculum is passed gently to exclude any local cause for the bleeding in the vagina or cervix. No other examination is made if the pregnancy is of less than 36 weeks' duration. Should it be necessary to intervene before the thirty-sixth week because of hæmorrhage, or after the thirty-seventh and thirty-eighth week when the head is not engaged or is displaced, the patient is prepared for section and examined in the operating room. A vaginal examination is made under light anæsthesia. The object of this examination is primarily to determine if the presenting part could be made to enter the brim, and not to find out where the placenta is in relation to the os. It is unwise to have any preconceived idea of treatment until the vaginal examination is made. Every case should be treated individually. If the head can be made to engage easily, one is probably dealing with a Type I or II placenta prævia and treatment resolves into simple rupture of the forewaters. When the presenting part will not engage, rupture of the membranes may lead to disaster to both mother and

baby. Should bleeding occur with the onset of labour it can be controlled by artificial rupture of the membranes. If a definite posterior placenta prævia is diagnosed, and especially if this has been confirmed roentgenologically, section should be done. In multipara it is usually possible to explore the lower uterine segment, and treatment depends on the degree of placenta prævia. Palpation of the placenta through the os is a dangerous procedure. It should never be undertaken under any circumstances, except in the operating room where one is prepared to deal with any emergency. If the placenta is felt by an expert with the greatest gentleness, it is not usual to precipitate a major hæmorrhage. The more inexperienced the doctor who inserts his finger through the os, the more dangerous the practice becomes. Inexperience and roughness can account for many foetal and some maternal deaths.

Should foetal distress occur after rupture of the membranes or if the bleeding persists before labour commences, a section should be performed. If the head cannot be made to engage in the pelvis and especially if the foetal heart rate is affected by gentle attempts to engage the head, and when Types III and IV placenta prævia are diagnosed, section should be done immediately.

In the author's series of 42 cases there were 7 deaths among 42 fetuses, a foetal wastage of 16.6 per cent and the incidence of caesarean section was 40.4 per cent. There were 2 stillbirths, 4 neonatal deaths (10 per cent of live births), but no maternal deaths.

The methods of treatment were as follows: spontaneous rupture of the membranes (4), artificial rupture of the membranes (20), plugging with half-breech (1 intra-uterine death), caesarean section (17). Ten sections were done for posterior placenta prævias, two for Type III and five for Type IV.

**Isoniazid and pregnancy.**—(*Presse Med.*, 64: 45, via *J.A.M.A.*, 160: 17, 1956).

Three pregnant women with renal tuberculosis were given isoniazid alone or in combination with amino-salicylic

acid without interruption during and after their pregnancies. Their respective total doses during pregnancy were 63, 35, and 32 g. of the drug after two, four and a half, and five and a half months of pregnancy. The treatment was successful in all the patients and was sufficient to cure one of them without the aid of nephrectomy. The course of pregnancy was not affected in any way, and the children born were normal at birth and at follow-up 8½, 14, and 14 months after birth respectively.

### OTO-RHINO-LARYNGOLOGY

**Heparin in the treatment of deafness, tinnitus, and vertigo: results in 100 cases.**—(*Presse Med. Fr.*, 64: 23-29, 7-1-1956, via *J.A.M.A.*, 5-5-1956).

Heparin is suitable for the treatment of certain patients with labyrinthine disturbances because it favours resorption of exudates; disperses blood cells, thus restoring blood vessel permeability; is antianaphylactic and sympatholytic; and acts on connective tissue by altering collagen fibres (in a manner as yet poorly understood). The authors report their results in 100 patients. The treatment proved not to be dangerous, but it seemed essential that the patients be hospitalized. The best mode of administration of heparin was found to be 250 or 300 mg. a day for eight days. Deafness was immediately improved in 16% of cases, tinnitus in 59% and vertigo in 66.6%. Usually, but not always, the results are maintained during the months that follow. They are particularly good in patients who have sustained cranial injury, provided treatment is instituted early, i.e., about a month after the injury. The results of heparin therapy are even more interesting from the physio-pathological than from the clinical point of view, since they serve to separate the disorders due to lesions of the sensory cells (not amenable to therapy) from those due to involvement of vascular and connective tissue. Heparin should be tried when other treatments have lost their effect. However, it is pointless to use it in almost total deafness. Large doses

must be given. Surprising results sometimes occur in deafness, and more than half of the patients with labyrinthine disorders receive some benefit.

**Prevention of post-operative adenotonsillectomy bleeding with vitamin K and vitamin C.**—(*Annals. Otol. Rhinol. Laryngol.*, 64: Dec. 1955; via *J.A.M.A.*, April 28, 1956).

Since adequate amounts of vitamin K are essential to the normal production of prothrombin and subsequent firm clotting, and since vitamin C is necessary for firm and rapid healing, it was thought that adequate doses of each given before and after tonsillectomy and adenoidectomy might prevent both early and delayed postoperative bleeding. Two hundred children from the author's private practice were selected for the study. It was decided that both the tonsils and adenoids should be removed in each case. The ages of the patients ranged from 5 to 13 years. One-half of the group were given vitamin K and vitamin C before and after operation. The medication was prepared in soluble capsules containing 5 mg. of vitamin K and 200 mg. of vitamin C (Synkayvite-CB; each). The mother of each patient was instructed to give her child two capsules a day, one after breakfast and one after dinner for the five days preceding the operation and again for the five days after operation. If a patient was unable to swallow the large capsule, the enclosed powder was placed on jam, jelly, mashed potato, or some other food that the child enjoyed. This would be followed by milk or water to assist swallowing. Fifty of the treated patients were allowed to use, acetylsalicylic acid in gum or tablet form to relieve postoperative pain. The remaining 50 were denied the use of any salicylates, to determine the influence of this drug on post-operative bleeding, which was reduced from 14% in the untreated series to 3% in the treated group. The frequency of post-operative bleeding was not increased when acetylsalicylic acid was used by those patients who had received adequate dosage of vitamin K and vitamin C. No toxic symptoms attributable to vita-

min K or vitamin C were noted. In both the treated and the control groups, post-operative hæmorrhage from the adenoid area was much more frequent than from the tonsil areas. Although careful bleeding-time and coagulation-time studies were made, these tests failed to indicate impending bleeding in the children who suffered post-operative hæmorrhages.

### MEDICINE & THERAPEUTICS

**Oral vitamin B<sub>12</sub> in pernicious anaemia.**—(*British Medical Journal*, June 2, 1956).

Unless it is given in very large doses vitamin B<sub>12</sub> taken by mouth does not produce hæmatological remission in pernicious anaemia, but it is effective in relatively small amounts when given along with normal gastric juice, which supplies the necessary intrinsic factor. Since vitamin B<sub>12</sub>, which is now thought to be the extrinsic factor, is itself very active when given by injection, it seems that the function of the intrinsic factor is to promote the absorption of vitamin B<sub>12</sub> from the alimentary tract, possibly by making it unavailable to intestinal bacteria or preventing its destruction in some other way.

As a consequence of these recent interpretations of Castle's hypothesis, some physicians have been treating pernicious anaemia by giving vitamin B<sub>12</sub> by mouth, either alone in high doses or in combination with a source of intrinsic factor. But, though in untreated cases these methods may result in hæmatological remission, their place in routine therapy is much less well-defined. Conley and Krevans have reported on the use in maintenance treatment of large doses of oral vitamin B<sub>12</sub> without the intrinsic factor. This has the possible advantage over the intrinsic factor preparations that the crystalline material can be assayed by weight, whereas the potency of the others must necessarily be measured in terms of the response to them in patients with pernicious anaemia. These authors found that 1,000 µg. of vitamin B<sub>12</sub> as a single

tablet once a week maintained satisfactory hæmatological remission, though the concentration of the vitamin in the serum was below normal. It is necessary to give 3,000 µg. of vitamin B<sub>12</sub> to obtain a response equivalent to that produced by 40 µg. given intramuscularly. A disadvantage of the method is that the ability to absorb the vitamin differs from patient to patient.

Commercial preparations containing relatively small doses of vitamin B<sub>12</sub> together with a source of intrinsic factor (hog's stomach) are now available. Treatment with these has been reported to produce hæmatological remission in some but not all patients with pernicious anæmia in relapse: at the end of one year of maintenance-treatment with one of these preparations the hæmoglobin and red cells had fallen significantly in twelve patients, and one further patient developed signs of subacute combined degeneration. The place of prolonged maintenance therapy with these oral preparations has still, therefore, to be finally determined, and the treatment of choice for the routine management of pernicious anæmia at the present time is the intramuscular injection of vitamin B<sub>12</sub>. The oral preparations are more expensive, and careless patients might fail to take them with strict regularity.

**Comparison of cortisone and aspirin in treatment of juvenile rheumatoid arthritis.**—(B. M. Ansell, Bywaters, and Isdale, *Brit. Med. Jour.*, May 12, 1956).

In 1954 and 1955 reports were published on "a comparison of cortisone and aspirin in the treatment of early cases of rheumatoid arthritis," by a Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, A.C.T.H., and other Therapeutic Measures in Chronic Rheumatic Diseases (*British Medical Journal*, 1954, 1: 1223; 1955, 2: 695). These concerned 61 adult patients aged between 17 and 59 years admitted to six centres in England and Scotland. At the same time the committee started a similar trial in juvenile rheumatoid arthritis (Still's disease), which was

defined for this purpose as beginning before the age of 16.

Of the 25 patients taken into this trial, 22 came from this centre and 1 each from Edinburgh, Sheffield and Manchester. They have been treated and followed along the same lines to one year from the start of treatment, at first in hospital and then as out-patients with cortisone (13 patients) or with aspirin (12 patients), their allocation to one or other treatment being determined by a random order list held centrally.

The two groups of patients were almost identical at the commencement of treatment.

The polyarthritis in this juvenile group had to be of the rheumatoid type involving two or more joints and present for a period up to nine months. These patients were assessed at intervals up to the period of one year from the start of treatment, maintenance dosage at the end of the year being between 50 and 100 mg. of cortisone (mean 69 mg.) in the six patients on treatment.

Assessment showed that results during the first 13 weeks and at one year were similar to those in the adult trial except that in both groups rather more children improved than did adults. Both treatment groups improved clinically and functionally to a similar extent. X-ray films showed an increase in the number with erosions—from three to six in the cortisone group and from two to five in the aspirin group. Complications which could be ascribed to the drugs were few.

The effects of cortisone relative to those of aspirin in childhood were no different from those reported in the adult group of rheumatoid arthritis patients.

#### Hormone therapy in pulmonary tuberculosis.

At a meeting of the Tuberculosis Society in December, Favez of Leysin reported that, in tuberculous meningitis treated with streptomycin given intrathecally and cortisone, no toxic effect on the eighth cranial nerve was noted. Mannes of Brussels reported the case of a patient treated for four months with

massive doses of isoniazid without improvement, in whom hormone therapy occasioned rapid amelioration. He thinks that all patients in whom sensitivity of the tubercle bacilli has been demonstrated *in vitro* but who respond only partially to antibiotics ought to be given a preoperative course of hormone therapy. Depierre's experience with 50 patients indicates that there are three major indications for hormone therapy: prophylaxis connected with the establishment of a pneumothorax (100 mg. of hydrocortisone is injected into the pleura); severe tuberculosis of recent onset with bronchial lesions and cavitation; and fulminating cases. Breton treated 26 primary infections in children and noted good effects on the general condition, body-weight, and sedimentation rate. On the other hand, corticotherapy is not useful against hilar adenopathy, periadenitis, or disturbances of ventilation. Hydrocortisone or prednisone may be used in young children, but there is a risk of enuresis.

A new aspect of corticotherapy is its use against bronchial lesions. Morel treated three patients with bronchial tuberculosis after exeresis and one with involvement of the intermediate right bronchus during primary infection. Cortisone was administered as tampons (with chloramphenicol) or in aerosol (with neomycin). Treatment was continued for three or four months. The patients tolerated the medication well, and the functional and anatomic results were excellent. Lemenager reported treating six other such patients; they had either exudation or bronchitis with stenosis. Local therapy gave good results, both when used alone and when combined with general measures. Since certain necessary interventions are rendered impracticable by the existence of bronchial lesions, this particular feature of hormone therapy assumes especial importance. Le Tacon recommended doses smaller than those usually prescribed for cortical hormones. His experience has been with effusions following pneumothorax, which he treats with local injections of hydrocortisone. For serofibrinous pleurisy he prefers a local injection of hydrocortisone followed

a week later by puncture, evacuation of the contents, and another injection. Tuberculosis with asthmatic manifestations is amenable to hormone therapy. The minimal effective dose might be based on the temperature curve (when it stops going down, the dose may be increased). Most authors think that if hormone therapy does not take effect immediately it should be abandoned. Extreme care in giving hormones is essential in order to avoid untoward effects.

**Penicillin V.**—(*Jour. Am. Med. Assoc.*, 28-4-1956).

A group of Austrian authors have developed a method of obtaining various penicillins that differ in respect to their lateral chains. This consists in the use of "precursors," or enrichment of the culture medium with carbonic acids. One of the antibiotics thus obtained was phenoxymethyl penicillin, which is biosynthesized, with phenoxycetic acid acting as a precursor. Unlike penicillin G, this agent, called *Penicillin V*, occurs in the form of a free acid because of its great stability. The chief importance of this new penicillin is that it is acid-resistant. Serum determinations after the ingestion of 200,000 units of penicillin V show that its concentration is superior to that obtainable with penicillin G and that it remains effective for four or five hours. Thus the drug no longer has to be quintupled in amount when resistance is encountered, and the cost of oral therapy is greatly reduced.

Penicillin V also has very good diffusion, rendering it useful in the presence of such conditions as pleurisy, cholecystitis, and ascites. Satisfactory clinical results have now been reported from several countries. Micrococcic and streptococcic septicæmia and endocarditis have been treated with administration of 100 million units every four hours. Bickel and co-workers (*Schweizerische medizinische Wochenschrift*, 86: 1956) made tests to determine whether it was necessary to administer the drug after fasting in order to avoid hyperacidity, as the Austrian writers had averred. This is not the case; in fact,

it appears that it is best absorbed when given 30 minutes after a meal. Oral administration must be repeated every four hours, however, in order to assure a more or less constant blood-level.

Side-reactions to the drug seem to be about the same as those to other forms of penicillin (such as urticaria and glossitis). That no deaths due to anaphylaxis with its use have been reported does not mean this is not a possibility. Modifications of the intestinal flora must be expected. The gram-positive bacteria are apt to disappear, leaving a preponderance of resistant coliform organisms. The Swiss authors' first administrations produced diarrhoea, with decimation of the flora in general and not of any particular group. However, DeSommer has shown that oral or peritoneal administration of penicillin in guinea-pigs produces severe toxic changes that may be fatal. They are the result of destruction of all the gram-positive organisms and appearance of pathogenic coliform bacilli. Rohmer and Marie of France reported on digestive syndromes due to pathogenic coliform-bacilli in clinics and infant homes. They did not blame antibiotics, but it may be that the pathogenicity of colibacilli, like that of the micrococcus pyogenes var. aureus, is being modified under the influence of antibiotics. With proper caution, penicillin V can be administered orally, freeing the patient from the onus of frequent injections and certain sensitivity reactions.

**Lente insulin in the treatment of diabetes**—(*New England Journal of Medicine*, 253 : 722, October 27, 1955).

In the past two years lente insulin was used by Slayton *et al* in the treatment of over 300 patients. The results reported below were obtained in special studies of 57 diabetic boys attending a camp in 1954 and 43 patients observed in hospital in that year.

For the most part, capillary blood was used for the determination of blood sugar although with hospitalized patients, for technical reasons, venous blood was taken when fasting samples were desired.

**Comparison of effect of isophane (NPH) and lente insulins**—The effect of isophane (NPH) and lente insulins was compared both in day by day maintenance studies and in tests involving the determination of the blood sugar at frequent intervals over a 24 hour period. At the summer camp, with diet and physical activity as nearly uniform as possible and with the insulin dose kept at the same level, 57 boys 10 to 15 years of age were maintained for three or more days on lente and then for a comparable period on isophane insulin, or *vice versa*. The insulin dose ranged from 12 to 68 units daily and in 34 of the boys was 30 units or more daily. The diet ranged from approximately 180 to 225 gm. of carbohydrate, 85 to 120 gm. of protein, 90 to 120 gm. of fat and 1,900 to 2,500 calories daily. On certain days the blood-sugar was determined before each of the three meals and at about two hours after the evening meal. It was evident from a study of the composite values that there was no significant difference between the degree of control with the two types of insulin.

Studies were carried out to determine the behaviour of the blood sugar over a 24 hour period, first on lente and then on isophane insulin and *vice versa*.

The behaviour of the blood sugar was remarkably the same on the two types of insulin despite the fact that the fasting values were somewhat more divergent than one would have liked in an ideal study. There was some indication that the effect of the lente insulin started to diminish two to four hours earlier than that of the NPH type.

There may be minor differences in certain patients, but, in general, the physician may substitute lente insulin for NPH insulin in similar dosage with no important change in the degree of control obtained.

**Addition of unmodified insulin to lente insulin**—In the present study 40 boys were given a combination of lente and crystalline insulin in the morning before breakfast. "The doses of insulin were those appropriate for the patient concerned. Food and activity were kept

as nearly constant from day to day as practicable. On one day the two types of insulin were given by separate injections, and on another day they were placed in the same syringe and given in a single injection..... The results were not greatly different. It is true that at 9-30 a.m., two hours after insulin, the evidence of rapid insulin activity was less with the combined than with separate injections. However, by 11-30 a.m., the difference was relatively small. From then on during the rest of the 24 hours a slightly greater hypoglycemic effect was obtained with the combined injection."

From a practical standpoint, in the day by day treatment of patients generally, it has been found that good results can be obtained if lente and crystalline insulins are given in a single injection just as with isophane and crystalline insulins.

**Carbon monoxide poisoning**—(*J.A.M.A.*, 28-4-'56).

It often happens in winter that some persons suffer from drowsiness and malaise from no apparent cause. Lob and Muller (*Revue médicale de la Suisse Romande*, Austria, January, 1956) state that carbon monoxide can exert a dele-

terious effect in daily life without the patient or physician being aware of it. According to Almgren, vertigo occurs in 69 per cent of cases of carbon monoxide poisoning, insomnia in 66 per cent, affective changes in 62 per cent, cardiac symptoms in 62 per cent, apathy in 54 per cent, headache in 47 per cent, nausea and vomiting in 42 per cent, wasting in 42 per cent, memory disturbances in 40 per cent, frequency of micturition in 39%, tiredness in 32%, intolerance to alcohol in 28%, decrease in libido in 22%, anorexia in 17%, gastric symptoms in 17%, ocular disturbances in 13 per cent, and sweating in 12 per cent. The Romberg sign may be present in these patients, and there may also be ataxia, adiadochokinesia, a sensitivity hemi-syndrome, labyrinthine disturbances, disorders of convergence and accommodation, oculo-motor paralysis, narrowing of the visual field for colour, and psychosomatic complaints. The electrocardiogram may show atrioventricular block and disorders of rhythm and conduction. Signs of hyperthyroidism may be present. Usually more than one member of the family is affected, the symptoms disappear when the heating system is turned off. The carbon monoxide content of the atmosphere can be measured with apparatus having a hopcalite catalyst.

## Reviews of Books, Reports and Periodicals

**Medical Research in the Second Five Year Plan**—Memorandum on the development of Medical Research in India presented by the Director I.C.M.B. and approved by the Joint Meeting of the Scientific Advisory Board and the Governing Body of the Council held in New Delhi on 26th and 27th March 1955. (Pp. 114: Ind. Council of Med. Research, P. Block. Raisina Road, New Delhi).

This admirably well-got-up booklet of 114 pages covers the entire field of Medical Research, as it should be developed during the Second Five Year Plan. The basic principles of the plan have been lucidly outlined by Padma Shri

Dr. C. G. Pandit, the talented Director of the Indian Council of Medical Research, who has been responsible for the enormous expansion of Medical Research in India during recent years.

The plan deals with the strengthening of the facilities available for research in existing institutions in the country; the creation of new Institutes for research in specific fields; the training of research workers by a system of fellowship and by other means; providing opportunities for the maximum display of talent in challenging situations; creating a Research cadre to attract capable and promising research workers to a career in research; initiating research programmes for the

solution of the many urgent problems in medicine and public health fields and maintaining close co-operation with national and international agencies in all matters relating to research. Reference has been made to the policies that the Central and State Governments should adopt for the practical application of the knowledge gained through research, which should not be confined to Research Institutes but should also form part of the routine in Medical Colleges and Teaching Hospitals.

The nutrition policy of Governments and how they should be shaped and put into effect have been discussed as also the importance of increasing the production of protective foods in the country, by utilizing any additional agricultural resources that would have become available during the Second Five Year Plan. The Nutrition policies recommended consist in (a) protecting the vulnerable groups of the population, (b) control of specific nutritional diseases; (c) organizing nutrition work as an integral part of the State Health Departments and (d) imparting education in nutrition as part of Health Education.

Maternal and Child Health has come in for special consideration in view of the fact that research in this field has to be geared to the practical needs of a highly unsatisfactory situation. A network of maternal and child health centres throughout the country will be established in the next five years.

Drug Research holds the key to the healthy growth and development of the drug industry and the ICMR's programme is sufficiently elaborate, comprehensive and elastic to achieve considerable progress during the period.

Environmental Sanitation, which is a very wide and expansive field comprises a multitude of subjects of supreme importance to the health of the individual and of the nation. The efficiency and effectiveness of the National Water Supply and Sanitation Programmes depend largely on technical skill in the application of proven scientific methods and devices for the improvement of environmental sanitation. This has been kept boldly in view in the pro-

gramme outlined by the ICMR for the Second Five Year Plan. It is believed that a research organization will be created under the Central Government consisting of about 15 officers of various grades and disciplines with the necessary staff to engage itself in full time research on problems connected with environmental sanitation. *It would be proper and desirable that non-officials and experts with considerable experience in these problems are also included in such Organizations and Committees so that the genuine needs of the people could be brought before the Committee with suitable emphasis on the practical aspects.*

Last but by no means least comes Occupational Health which is fast assuming first-rate importance. The ICMR is giving high priority to the study of optimum thermal environmental standards; protection of industrial contaminations; human relations in industry; industrial neuroses; optimal working hours; thermal illumination and radiant energy control; disposal of industrial wastes and problems and the organization of an Industrial Health Service.

It has been possible in this necessarily cursory review, to touch only upon the barest outlines of the many and varied researches contemplated by the ICMR and approved by the Governing Body for the Second Five Year Plan period. It is indeed a very ambitious one but we are confident that with the enormous driving power and the characteristic *savoir faire* of the enthusiastic Director, most of the researches will bear good fruit during the next five years. —T.N.S.R.

**The Tuberculosis Association of India**, 22, Red Cross Road, New Delhi. Seventeenth Annual Report 1955; and Proceedings of the 17th Annual Meeting held at Delhi on 21-4-1956.

We have received the two publications mentioned above. In presenting the report on the working of the Association for 1955, Col. C. K. Lakshmanan referred to the continued steady good work which the Association was doing

under the great inspiration and sympathetic guidance of the Hon. Rajkumari Amrit Kaur, both in her capacity as Union Health Minister and as President of the Association, and also to the sustained efforts of their Technical Committee ably guided by Dr. P. V. Benjamin, who by the way, was the first proud recipient of the Sir Philip Gold Medal in June 1955 for his outstanding work in the field of tuberculosis. The report which is set out in 99 paragraphs contains a succinct and interesting account under clear-cut headings of the various activities of the Association, and its affiliated institutions in Delhi and the States as also the schemes proposed to be undertaken during the Second Five Year Plan and other recommendations calculated to intensify and improve the propaganda work. The Sixth Conference of Secretaries of the State T. B. Associations in India which met at Delhi earlier during the same week made important recommendations which are given in an appendix to the general report. Reference is made to the Fourth Commonwealth Health and Tuberculosis Conference held in London during the last week of June 1955 at which Dr. P. V. Benjamin and four other Indian representatives were present as delegates and took part in the proceedings by reading papers and taking part in the discussions.

The annual report is a very important document covering over 300 pages and contains 18 appendices (which alone take up over 270 pages).

The detailed working of (i) the sanatoria at Kasauli and Dharampore under the direct supervision and control of the T.A.I., (ii) of the New Delhi Tuberculosis Centre at Delhi and (iii) of the Lala Ram Sarup T. B. Hospital at Delhi is given in appendices 14 to 16 covering nearly a hundred pages.

The two sanatoria which function as one unit for administrative purposes really serve two different purposes quite efficiently. All patients are admitted at Kasauli; the more acutely ill and those

needing surgical treatment remain there while the ambulant cases and convalescents are moved to Dharampore. The total number of beds is 350 and all of them were fully occupied. They continued to serve also as Teaching and Training Centres for medical men, nurses and health visitors, etc., specializing in T.B. work.

The New Delhi T.B. Centre, under the able directorship of Dr. B. K. Sikhand, assisted by a team consisting of enthusiastic clinicians, a well-qualified bacteriologist and diagnosticians, continued to function quite efficiently as a diagnostic and treatment centre; in addition, its domiciliary service scheme was being maintained and even extended in association with the Care Committees that formed part of the scheme. Over 20,000 home-visits and nearly 7,000 contact examinations were made under this scheme during the year. In the well-equipped and busy laboratory of this centre, we are glad to note, there has been "an increasing load of laboratory work, consequent on the expansion of the centre's activities, which during the year included extra work in connection with the All-India X-ray Epidemiological Survey under the I.C.M.R." A total of nearly 35,000 cultural, microscopic and other special examinations were thus carried out during the year in this laboratory. Training to post-graduate doctors was also imparted at the centre. The Mehrauli Road Hospital, with 100 beds was serving the needs of that area efficiently consistent with its resources in accommodation, personnel and money. The total cost of maintaining this hospital is stated to be over Rs. 2 lakhs. Proposals for the expansion of this hospital are under way and ultimately it will have 254 beds with facilities for advanced surgery, and community service also for clinical and epidemiological research.

The report is thus an account of sustained uniform all-round progress in every branch of T.B. treatment and control, of which the Association may well be proud.

T.N.S.R.