

The
Madras Medical Journal

THE OFFICIAL JOURNAL OF THE MADRAS MEDICAL ASSOCIATION

PUBLISHED QUARTERLY.

Vol. XX.

JANUARY—APRIL 1940.

Nos. 1 & 2.

Editor:

J. C. DAVID, M.B., B.S., PH.D. (EDIN.).

3784.

11 JUL 1940



RATES OF SUBSCRIPTION.

For Members of the Madras Medical Association on payment of an Annual Membership fee of Rs. Five only.—Free.

For non-Members including Medical Practitioners—Rs. Three per annum, post free.

For bona-fide Medical Students—Rs. Two per annum, post free.

Single Copy Twelve Annas.

Single Copy Twelve Annas.

12-144.

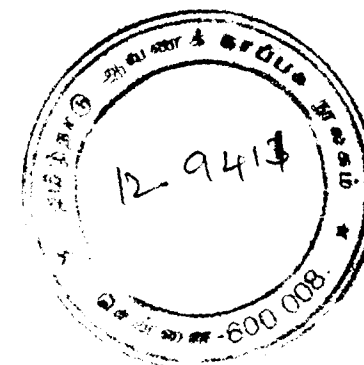
Nos. 1 & 2.

J. C. DAVID, M.B.B.S., Ph.D.

1954

P. RAMACHANDRA RAO, M.B., Ph.D.

S. K. SUNDARAM, B.A., M.D.



EDITORIAL NOTICE.

The Madras Medical Journal is issued quarterly, in January, April, July and October about 20th of the month. All Editorial communications, reports, books for review and exchange should ordinarily reach the Editor, The Madras Medical Journal, Dept. of Pharmacology, Medical College, Madras, one month prior to the date of issue of the Journal, preferably earlier. Original articles, clinical lectures, case reports, abstracts, Medical Society addresses are invited. Contributors of original articles will be supplied gratis with twenty reprints of papers, *if applications for the same are received by the Editor along with the contributions.*

BUSINESS NOTICE.

Subscription Rates.

To Members of the Madras Medical Service on payment of an Annual Membership fee of Rs. Five only—Free.

To non-Members including Medical Practitioners and others, Rs. Three per annum, post free.

To *bona-fide* Medical Students, Rs. Two per annum, post free.

Foreign 7sh. 6d., post free.

Rates of Advertisement.

	One Page.	Half Page.	Quarter Page
	Rs.	Rs.	Rs.
Single insertion ...	20	12	7
Three insertions ...	40	24	14
4 insertions ...	50	30	20
4 insertions (inside reading) 60	...	...	...

Discount of 33½ per cent will be given if advertisements are inserted for 3 complete years in advance.

All advertisement charges and subscriptions are payable in advance. Letters relating to the publication, sale and advertisement department should be addressed to :—

Dr. S. K. SUNDARAM,

Editorial Secretary,

9, Dr. Nair Road, Thyagarayanagar, Madras.

Copies of the Journal can be obtained at twelve annas each from Messrs. Gordon & Co., Ltd., Printers, 768-770, Triplicane, Madras, or at the Editor's Office, Medical College, Madras. Changes of address and complaints of non-receipt of Journals should be immediately communicated to the Secretary, to the above address. Matter for advertisement should reach the Editorial Secretary, at least ten days before the date of issue of the Journal.

THE MADRAS MEDICAL JOURNAL.

Vol. XX.

JANUARY—APRIL 1940.

Nos. 1 & 2.

CONTENTS.

	PAGE
1. BLOOD PRESSURE By Rao Bahadur Dr. M. R. Guruswami Mudaliar, B.A., M.D. & C.M. ...	1
2. HIGH BLOOD PRESSURE By Rao Bahadur Dr. M. R. Guruswami Mudaliar, B.A., M.D. & C.M. ...	16
3. URÆMIA By Rao Bahadur Dr. M. R. Guruswami Mudaliar, B.A., M.D. & C.M. ...	30
4. MALIGNANT DISEASES OF THE FEMALE GENERATIVE TRACT WITH PARTICULAR REFERENCE TO CARCINOMA OF THE CERVIX By Rao Bahadur A. Lakshmanaswami Mudaliar, M.D., F. R. C.O.G. ...	39
5. ABSTRACTS ...	58
6. ASSOCIATION AND SERVICE NOTES & NEWS ...	61

Service News and Notes.

Retirements.—The following of our members have either retired or are on leave preparatory to retirement. We wish them all a peaceful and prosperous future. May they live long to enjoy the rest they are entitled to after the arduous labours which are the lot of the medical man, especially in Government service. We trust that they will not forget the association of which all of them have been active members and some of them even enthusiastic members, and that they will continue to take the same active interest in its affairs even in their retirement:—

1. Dr. V. R. Natesa Mudaliar,
1—7—1940
2. Dr. H. Krishnan, 10—7—1940
3. Dr. P. Venkatagiri, 19—7—1940
4. Dr. P. K. Raman
Nambiar, 18—8—1940
5. Dr. S. Balavelayudham,
29—9—1940
6. Dr. T. S. Harinarayana
Pantulu, 8—10—1940
7. Dr. T. S. Tirumurthi on leave
till 30—12—1940
8. Dr. K. Gopal Rao on leave
till 24—2—1941

The following two officers have been invalided and are hence retiring before their time:—

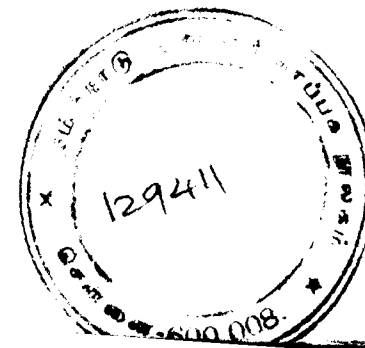
1. Dr. M. J. Santhana Krishna Pillai.

2. Dr. C. Totadri.

We trust that their health will improve by this enforced rest and that they may enjoy long years of quiet and peace.

Insurance Practice.—Government have further defined the restrictions they imposed from 1-1-40 on private practice by members of the Madras medical services. The executive committee is aware of the hardships caused by the incidental withdrawal of the privilege of insurance practice and has proposed to request the authorities to minimise our difficulties.

Annual Meeting.—We give timely notice now that **the annual meeting** along with the usual **subscription dinner** will be held in the latter part of December. It is expected that the attendance at both the functions will be large and will be characterised by the same enthusiasm that has marked them hitherto. The exact date of the meeting will be intimated later.



JL
L. S. N. R. I. M. M.

N 4020

In Dermatological Conditions

such as Acne

Eczema

Psoriasis

Urticaria

Abrasions

and other inflammations of the skin, the attention of the physician is called to the use of

Antiphlogistine



It is Osmotic
Non-irritating
Bacteriostatic
Detersive
Anti-pruritic
Repair-promoting

Sample on request

■
The
Denver Chemical
Mfg. Co.

163 Varick Street
New York

தவணைத்தாள்.

சே எண் : 129411

ப. எண் :

[illegible]

S.F. 259A-6-1,00,000-30-1-84.

The Journal of the Madras Medical Association.

PUBLISHED QUARTERLY.

Vol. XX.	JANUARY—APRIL 1940.	Nos. 1 & 2.
----------	---------------------	-------------

Blood Pressure*

BY RAO BAHADUR DR. M. R. GURUSWAMI MUDALIAR,
B.A., M.D. & C.M.

The term blood pressure includes not only arterial pressure but also intra-ventricular, intra-auricular, venous and capillary pressures. But in every-day practice it is used as equivalent to arterial pressure.

Arterial pressure may be defined as that pressure which is exerted by the blood at a given instant upon a given point of arterial wall. The factors that control blood pressure may be divided into

(A) basic or primary factors
which comprise

- (i) cardiac energy and
- (ii) peripheral resistance and

(B) secondary factors--*viz.*,

- (i) resiliency of arterial walls,
- (ii) volume of circulating blood and

- (iii) consistency of blood.

Of the two basic factors the more important is "peripheral resistance". Amount of peripheral resistance depends (a) on *general effects* due to variation in calibre of smaller arterioles and capillaries and (b) on *local effects* due to external pressure exerted by the perivascular tissue on the smaller arterioles and capillaries. The autonomic system also plays a part in these alterations of the lumen of the vessels, either through vasodilators or through vasoconstrictors, as the needs of local areas may demand. Such variation would be ineffective but for a constant head of pressure being maintained in the aorta.

The *resiliency* of aorta keeps up the pressure initiated by cardiac contraction. Let us bear in mind that the heart rests normally through diastole for about 13 hours out of 24 of the day, so that during the diastolic

period provision must be made to maintain the blood pressure at its due level. This is effected by the resiliency of the aorta and by the resistance to the outflow from arteries and capillaries. If a certain diastolic pressure were not maintained, man could not stand erect. The blood would gravitate down into lower parts of his body and death from medullary anæmia would result, unless he walked on all fours.

Volume of blood.—Total volume is one-thirteenth of body weight. At least two-thirds of this volume is required to maintain the circulation properly. With excessive loss in volume, as in hæmorrhage or cholera, blood pressure will fall.

Consistency of blood.—Increased viscosity according to Lovatt Evans and Ogawa lowers the arterial pressure as against the commonly held opinion that it raises the blood pressure. They have shown with a heart-lung preparation that increased viscosity reduces the input of the heart, which in turn diminishes the output, and that the smaller ventricular load of concentrated blood is expelled with less endocardial pressure than when it is larger and less viscous.

In peripheral circulation viscosity does play an important part, but changes in consistency and viscosity of blood are readily corrected by the tissues. The studies of Lyon suggest that the chief regulating mechanism lies not in the arterioles, but in the capillary areas.

To repeat briefly, the changes in arterial pressure may be brought about by variations in total volume of circulating blood, by variations in output from the left ventricle or by variations in the peripheral resistance. This last may be due to (a) local influences upon musculature or (b) to vasomotor intervention.

Systolic and diastolic pressures.—With the contraction of the arteries, a series of pressure waves are set up in the arteries. Each wave has a peak or crest and a base. The crest coincides with active contraction of the heart and is called the maximal or systolic pressure. The base of the wave coincides with the resting state (diastole) of the heart and is known as minimal or diastolic pressure.

Of the two pressures the diastolic is the more important because it gives the measure of the load which the arteries and aortic vales must continuously bear throughout life. The systolic pressure represents only an additional, intermittent load. The diastolic is a more definite and constant indicator not only of the cardiac energy and of the eliminatory capacity of the body, but also of peripheral resistance and of vasomotor tone. Therefore the diastolic pressure is of value both in hypo—and hyperpiesis.

Differential or pulse pressure.—44 mm. of Hg.—Any deviation from this in conjunction with the height of diastolic pressure implies either increased or diminished cardiac load.

Liair's law of arterial pressures gives a ready method of deducing diastolic pressure in any case, whether of high or of low pressures, provided there is no dissociation between systolic and diastolic pressures.

The formula is stated as

$$Mn \text{ (in mm. Hg.)} = \frac{Mx}{2} \text{ (in mm. Hg.)} + 10$$

In normal individuals pulse pressure may be stated to vary from 34 to 54 mm. of Hg., standard being 44 mm. of Hg.

As a general rule in hypopiesis pulse pressure is smaller than normal and in hyperpiesis larger than normal.

Physiological variations may be induced by

1. *Age.*—During first month of life blood pressure rises rapidly from about 40 mm. of Hg. at birth to 80 mm. of Hg. at the end of the first month. Gradually pressure rises during infancy and childhood and at about 15 years of age it stands approximately at 110 mm. of Hg. During adolescence blood pressure rises rapidly and comes to be about 120 mm. of mercury at 20 years. After physical maturity the blood pressure of healthy persons rises but little with advancing years until old age is reached. At 50 years of age it is still at 130 mm. of Hg. But although the typical blood pressure does not vary much from youth to old age, the average blood pressure in the latter shows some progressive

rise through inclusion of figures which approach the upper limit of normality. The diastolic pressure, however, does not change much between 25 and 55 years of age being 80 mm. of Hg. at 20 and but 86 mm. of Hg. at 55. Hence the rise in systolic pressure noted in the second half of life is probably associated with arteriosclerosis and is not normal.

2. *Constitution.*—Body weight has a greater influence than height. In a series of about 3,500 cases, analysed by Gager and Hurlin, which included individuals who were thin, normal and obese, the various age groups manifested pressures that were higher as the weight increased. Life assurance statistics show that with 25 per cent overweight and overpressure, the mortality rate is doubled.

3. *Sex.*—Up to puberty both sexes have equal pressure. From adolescence to 40, man has a higher systolic pressure by 8 mm. of Hg. From and after menopause woman's blood pressure becomes higher. After 50 woman's diastolic pressure is higher than man's.

4. *Exercise.*—Effect varies with the individual. Slight exercise or routine habitual exercise causes little effect on pressure. In healthy young adult strenuous exercise raises the systolic pressure, while diastolic pressure may be lowered (from the action of vasodilators). Within a few minutes the pressure resumes its original level. Athletes and men habituated to heavy work usually show pressures

below average. The better the training for a particular exercise the less the rise in pressure after it.

5. *Posture*.—Influence of posture on blood pressure is slight in normal individuals.

6 *Digestion*.—At the time of ingestion there is a slight rise in systolic and a slight fall in diastolic pressure. At the height of gastric digestion systolic pressure falls and rises again when food has passed into intestines. During fasting both pressures fall.

7. *Altitude*.—Moderate altitudes do not affect blood pressure. It is the rapidity of change in atmospheric pressure rather than the extent of it that affects blood pressure. However, when high altitudes are reached, there is a rise in systolic and a controlled fall in diastolic pressure giving an increase of pulse pressure, as observed by Schneider and Truesdell of the American School of Aviation Medicine. Increased differential pressure with increased pulse rate was held to be a form of compensation. Venous pressure was found to be reduced by altitude and capillary pressure to remain unaltered. In some men, when the oxygen pressure is reduced, the higher or psychic centres are paralysed before the vasomotor, cardiac and respiratory centres—the non-fainting type of reaction. In others the controlling centres for circulation and respiration become affected before voluntary attention and motor co-ordination are appreciably affected.

8. *Menstruation*.—Pressure rises slightly a day or two before menstruation, and falls during the period and rises again at the end.

9. *Pregnancy*.—During the early months of pregnancy there is no change in blood pressure. During the latter months of pregnancy there is rise in blood pressure probably as a result of the effect of circulating toxins in impairing the elasticity of the arterial walls and thus necessitating increased cardiac activity.

10. *Labour (parturition)*.—After normal delivery, little fall in arterial pressure is noticed in spite of anæsthetic, rapid emptying of uterus or physiological hæmorrhage. But in the presence of toxæmia, there is a notable fall in pressure at the time of labour.

11. *Emotion*.—Excitement, fear, joy, grief, anger, worry and concentration all raise systolic pressure, temporarily at all events. The diastolic pressure is not affected. When the cause persists over a long period the systolic pressure may be permanently raised.

12. *Walking and Sleeping*.—During quiet restful sleep both systolic and diastolic pressures fall, systolic to even as few as 95 mm. of Hg. in men and 90 in women. The systolic pressure drops considerably partly as a result of physical and mental repose, partly due to the lessened force of ventricular contraction and partly owing to peripheral arteriolar dilatation. During waking hours the systolic pressure rises.

If we wish to get a correct understanding about arterial pressure, it is not enough to take the systolic pressure or even the systolic and diastolic readings. A good plan is to follow Halls Dally in drawing up the complete arterial pressure picture. He notes (1) the maximal pressure (systolic), (2) the minimal pres-

sure (diastolic), (3) the differential pressure (pulse pressure), *i.e.*, difference between systolic and diastolic pressures, (4) the pulse rate and other characteristics and (5) the product of the pulse pressure multiplied by pulse rate.

The chart is made up under the following headings:—

No.	Date	Name, age, sex	Height and Weight	Diagnosis	millimeters		Differ- ential pressure	Pulse rate	PPxPR product
					280 of Hg. 1	80			
					S	D			
In a case of				arterio-sclerosis, left ventricular hypertrophy, emphysema					the product was 8,000
" "	"	"	"	cardiac dilatation, chronic bronchitis, emphysema			" "	"	8,400
" "	"	"	"	chronic myocarditis, arteriosclerosis			" "	"	9,400
" "	"	"	"	chronic bronchitis, asthma, emphysema			" "	"	4,200
" "	"	"	"	a healthy individual			" "	"	3,520
" "	"	"	"	pulmonary tuberculosis			" "	"	4,224

From the point of view of blood pressure—people may be grouped as sthenic, hyposthenic or hypersthenic. The blood pressure of the sthenic is taken as standard. The hyposthenic shows a low, the hypersthenic a high blood pressure. The hypersthenic tends to excess of tissue alkalinity, the hyposthenic towards acidity. One writer defined life as "an acid reaction in an alkaline medium". The greater the vitality the nearer the approach to "acid" type. The biological law is that "low arterial pressure, whether congenital or acquired, temporary or permanent, is always to be regarded as an expression of *low vitality*". Both high and low arterial pressures

are departures from a standard level. Metabolic imbalance lies at the root of both: in hypopiesis errors of *assimilation*, in hyperpiesis faulty *elimination*. Nutrition, vitamins and endocrines are naturally controlling factors of blood pressure. Avitaminosis depresses adrenal and thyroid glands and hence leads to low vitality and low pressure. The thyroid is said to be to the human body what the draught is to the fire and hence metabolism is raised or lowered by the state of the thyroid.

Hypopiesis—Low Blood Pressure

The subject of hypopiesis, whether congenital or acquired, is never a normal person.

Individuals who are put down as primary hypopietics because of their apparent health in spite of low blood pressure are really abnormal as they are prone to attacks of depression and as they show an extra-ordinary liability to infections of various sorts. The reactive capacity is diminished or "response to effort" is lessened.

Cases of hypopiesis fall under two heads:—

1. *Transitory*,—which include incidents, insufficiencies, infections (acute) and intoxications.
2. *Continued*,—which include conditions which are congenital, constitutional or chronic.

Hypopiesis.—Hypopiesis is a term applied to low arterial pressure in general when it is below standard limits and indicates lowered vitality, whether temporary or permanent, congenital or acquired, associated or not with organic disease. Hypotension is defined by Faught as the condition in which the systolic curve maintains an average level below the established normal level. This, however, fails to include those cases of low pressure which are transitory. Just as of high pressure, the range of low pressure varies with age, sex, physical development, occupation, temperament, sleep and muscular exercise. If one studies the figures given for upper limit of low arterial pressure by workers like Jane-

Nicholson, Bishop, Norris, Oliver and Goodman, Cornwall. Martinet, Stocks and others, one notices that they allow a margin of roughly 20 mm. of Hg., some placing the limit as low as 90 mm. of Hg., others as high as 125 mm. of Hg. For practical purposes we may adopt 110 mm. of Hg. for adult males and 105 mm. of Hg. for adult females, estimated under the standard condition of fasting for at least two hours after a meal, as upper (systolic) limit of low arterial pressure. The lower limit (diastolic) of hypopiesis is similarly taken to be 66 mm. of Hg. for males and 62 mm. of Hg. for females. The lower levels are associated with disorders of internal secretion and the higher with chronic glomerulo-hephritis.

Occurrence.—Individuals with low blood pressure present the following features: poor thin body build, light weight, narrow nostrils with frequent nasal obstruction, long neck, narrow elongated chest with sloping ribs and narrow intercostal spaces, narrow long sternum and acute epigastric angle; long diaphragm; heart narrow "pear drop" type; aortic hemicircle thin and narrow; ascending aorta narrow and long; lower abdomen lax and protruding; thoraco-lumbar curve straightened out or even convex; length of trunk predominating over breadth; urine acid: alkali ratio 1:3 or more.

The hyposthenic type is associated with errors of assimilation in youth and endocrine

deficiencies in middle and later life. Hyposthenics have a tendency to infection in general and to pulmonary infection in particular. Their arterial pressure is low, pulse pressure less than the normal 44 mm. of Hg. They have no nocturnal micturition and fatigue easily.

Signs and Symptoms.

Symptoms.—1. Lassitude and ready fatigability. 2. Headache. 3. Defective memory and concentration. 4. Insomnia. 5. Giddiness. 6. Faintness leading to convulsions and syncope. 7. Palpitation and anginiiform pain on excessive exertion. 8. Gastro-intestinal disturbances. 9. Neuralgic pains.

Physical and mental fatigue constitutes the dominant symptom of all forms of hypopiesis. Hyposthenics get up in the morning with feeling of lassitude. During the day they prefer to sit or to lie rather than to stand. On slight exertion they feel fatigued. They are unduly breathless if they go upstairs or climb hills or perform any rapid movements. On continued exertion they feel first a distress, then prostration which may continue for some days. *Mentally* they have vague anxieties and apprehensions, and cannot concentrate. Memory is weak, mental functioning slow. In advanced stages they become mental defectives. It must, however, be mentioned that some of them are brilliant in their earlier life and break down in and after middle life. So long as they live within their reserve capacity, they can lead a satis-

factory life. Insomnia of the hypopietics is peculiar. They are able to sleep in the earlier part of the night. They wake up at 2 a.m. and cannot sleep again. Even if they get snatches of broken sleep, they feel unrefreshed in the morning.

Headache.—Headache is occipital. It is more often seen in women. It occurs as pain or a sense of heavy pressure over the occipital region, occasionally spreading out laterally. It appears to correspond to a cephalalgia brought about by venous stasis of meningo-encephalitic type at the level of the straight and lateral sinuses and their effluents.

This headache alters in intensity becoming severe and paroxysmal in the recumbent posture and lessening or disappearing in the vertical position. It is often worst in the morning.

There is another type of headache which occurs on a sudden rising from recumbency or on stooping, a result of vasomotor failure of adaptation to the changed circulation.

Another variety of headache resembles the neuralgic type of migraine.

Giddiness.—This is seen both in hypopiesis and in hyperpiesis.

In the one it is due to cerebral vessels being too empty, in the other to their being too full. This symptom is seen in hypo-chondriasis, neurosis, anæmia, convalescence and in Addison's disease.

Syncope.—Fainting is due to cerebral anæmia.

Gastro-intestinal disturbance.—A sense of hollowness or emptiness referred to pit of stomach and hunger nausea are the outstanding features. They are relieved by food or pressure of a hot water bottle applied to pit of stomach.

Signs :—

(1) Pallor of skin and conjunctiva.

(2) Pulse—small, soft and often dicrotic.

(3) Vasomotor disturbances evidenced by cyanosed extremities, chilblains and varices.

(4) Delayed return of colour to skin rendered pale by pressure.

(5) Diminished ratio of titrable free to combined acid in urine.

(6) Muscular debility and flabbiness.

There are some hypopietics who show no symptoms unless some exciting causes come in, and who till then lead a quiet useful life. It is rather difficult to draw a line below which symptoms develop. The pressure zone which acts as the boundary between symptoms and no symptoms is rather a narrow one. As soon as this level is reached, a lowering of 2 or 3 mm. of Hg. pressure is enough to precipitate symptoms. Exercise and exertion, physical and mental, within their reserve, is beneficial. Avoidance of extremes of climate is essential.

Clinically the condition of low blood pressure has been noted in the following :—

I. Temporary :—

A. In association with acute conditions like

1. acute collapse and shock.

In collapse, hypopiesis is fleeting, but in shock it is more pronounced. Hypopiesis is a characteristic of both conditions. Halls Dally says, "The experimental work of the American school including W. T. Porter, Morrison and Hooker, Seelig and Joseph, Lyon and Mann has clearly demonstrated that in shock the tone of the vasoconstrictor centre is practically unaltered, and that the arterioles are maintained not in a state of dilatation but in one of constriction." Steward and Gulbric have shown that the vasomotor centre can retain its tone and reflex activity even if totally deprived of blood. Therefore, under these circumstances, a fall in arterial pressure can be accounted for by diminished output from heart. The work of Enlarger and Gasser shows that the blood becomes concentrated prior to development of grave symptoms of shock, so causing diminution in volume of circulating blood partly due to loss of plasma and partly due to jamming of the capillaries by the blood corpuscles. These result essentially in a histamine intoxication, as the result of progressive tissue malnutrition.

Biochemically, diminution of alkaline reserve of blood in shock reduces the rate of circulation, so leading to inadequate tissue

oxygenation. Experimentally and clinically hypopiesis referable to shock may be seen as a result of (a) gravity, (b) trauma, (c) hæmorrhage, (d) considerable loss of tissue fluids, (e) surgical operations and anæsthesia, (f) anaphylaxis, (g) toxic agents, (h) depressing influences of physical origin like cold or fatigue, or of psychical origin as emotion or nervous exhaustion, (i) any of the above causes in combination.

2. *Acute intoxications.*—The following agents are capable of inducing an acute and progressive depression of arterial pressure :—

(a) *by causing vascular dilatation* through their action on the vasomotor centre—
(i) through capillary depression :—general anæsthetics (chloroform); opium and morphia; chloral hydrate; snake venoms, digitalis and belladonna group of drugs in toxic doses; cannabis indica; alcohol; lupulus;

(ii) through profuse depletion from the intestines by cathartic drugs, equivalent to venesection :—croton oil, elaterium, colocynth, jalap, scammony, podophylline and calomel;

(b) *by impairment of respiratory capacity* and lowering of oxidative processes :—irritating and asphyxiating gases, e.g., chlorine; cyanogen;

(c) *by local dilatation of peripheral vessels* when

administered orally or by inhalation: the nitrite group;

(d) *from food poisoning* :—(i) from meat and fish due to products of bacillary action (toxins) or of putrefaction (ptomaines);

(ii) from edible fungi;

(e) by diffuse toxic necrosis (acute yellow atrophy) of the liver.

3. *Acute circulatory disorders :*

(a) Premature contraction—

(i) single, (ii) serial.

(b) Stokes-Adam's Syndrome (heart block).

(c) Acute carditis and tuberculous pericarditis.

(d) Acute cardiac insufficiency.

(e) Acute vassodilator crisis—(splanchnic area affected).

Paracentesis abdominis, sudden lowering of intra-abdominal pressure; abdominal crisis of tabes; sudden compression of portal or caval veins.

4. *Acute respiratory disorders, only transitory :—*

acute rhinitis, tracheitis, bronchitis;

when patients complain of chillness and shivering with subnormal temperature.

B. In association with sub-acute conditions.

II. Permanent:— (a) Congenital.

In association with chronic conditions—

1. congenital or constitutional psychasthenia (at times neurasthenic symptoms predominate and at others obsessions predominate).

In these neurasthenics symptoms are secondary to causes which induce obsession.

2. Congenital or constitutional neurasthenia—

There is undue leakage of nervous energy resulting in insomnia, profound mental and physical fatigue, heightened sensitiveness to minimal stimuli and weakening of conscious will.

3. Congenital syphilis (cardio-vascular hypoplasia, maldevelopment, defects in teeth, palate, abdomen, etc.)

(b) Acquired.

1. In association with acquired neurasthenia—

low arterial pressure, insomnia, lack of interest and concentration, defective memory, despondency, headaches, increased sensitiveness (eyes).

2. In association with insanity—

(a) states of excitement and motor restlessness and acute mania, (b) delirium tremens, (c) dementia præcox, (d) all states of mental exhaustion and (e) excited stage of G.P.I.

III. (a) In association with acute specific infectious diseases—

- (i) cholera
- (ii) enteric fever.

Huchard (1889) was the first to note the tendency of enteric fever to cause lowering of blood pressure, diastolic and compressibility of pulse, feeble first apical sound and diminution of second aortic sound. Potain observed that enteric fever causes a greater reduction in arterial pressure than does any other acute disease and that the arterial pressure does not correspond to the severity of the malady. However one has to note that the pressure rises (a) in association with active delirium, high temperature, abdominal distension and flushed face in sthenic cases; (b) at the onset of a relapse, when a slight and transitory rise is seen; (c) with inflammatory complications, e.g., cholecystitis, pleurisy.

J. D. Rolleston has reviewed the literature and his conclusions are that in enteric fever.

1. the systolic pressure was subnormal in 93.8 per cent of cases, the extent and degree of depression being in direct relation to the severity of the attack;

2. the systolic pressure of females showed a decided tendency to keep to a lower level than that of the males (contrary to diphtheria and scarlet fever);

3. 45.8 per cent of those discharged from hospital from the fifth to twenty-third week of disease whilst in hospital never

regained the normal systolic pressure for their age;

4. in the majority the systolic pressure fell below 100 mm. of mercury at some period of the disease and was higher in convalescence than in acute stage;

5. in 93.5 per cent of convalescents, readings in the recumbent or erect position were the same, and recumbent was higher than the vertical record till convalescence was firmly established;

6. intestinal hæmorrhage and myocarditis caused a considerable fall; cholecystitis and pleurisy were accompanied by a transient rise.

IV. *Diphtheria*.—Various observers have found that in mild and uncomplicated cases pressure was almost unaffected; in cases of moderate severity the depression was slight and short; while in toxic and fatal cases pressures were very low.

V. *Influenza*.—One's observation as noted in the epidemics that passed through Madras was that there was marked lowering of arterial pressure, even in uncomplicated cases, and that low blood pressure accompanied the post-influenzal depression, slow pulse being a notable feature.

VI. *Pneumonia*.—Moderate lowering of pressure occurs, probably due to the effect of toxemia upon the vasomotor centres.

VII. *Cerebrospinal fever*.—In acute cases when rash is present,

blood pressure is lowered considerably. Low arterial pressure during the first two days is of grave import.

VIII. *Malta fever*.—As the disease advances progressive lowering of both systolic and diastolic pressures occur.

IX. *Septicæmia*.—Both arterial pressures are lowered and sink very low in acute typhoid state of this infection.

X. *Erysipelas*.—In ordinary cases slight fall of blood pressure occurs; in severe cases considerable fall, probably as a result of adrenal damage. Low arterial pressure is an early and sure sign of a grave attack.

XI. *Infective endocarditis*.—This is really a septicæmia. Pressure falls to 100 mm. of mercury or less even within the first few weeks.

XII. *Acute toxæmia*.—Low arterial pressure is an early and constant symptom.

(1) *Infections of doubtful origin*—(i) typhus, (ii) tsutsugamuchi disease, (iii) scarlet fever, (iv) rheumatic fever.

(c) *Protozoal infections—malaria*.—There is a greater fall of diastolic pressure, while the systolic may or may not fall. Observations are divergent. Notwithstanding lack of agreement on the part of various observers, one salient point emerges, that the action of toxins produced by the parasite of malaria exerts an action in greater or less intensity upon the vasomotor centres.

Whether this is directly on the centre or through the damaged and inflamed adrenal is open to investigation.

(ii) *Leishmaniasis*.—A gradual reduction in blood pressure occurs.

(d) *Metazoal infections*.—(i) *trichiniasis*.—Chency of San Francisco reports an interesting man of a poorly nourished case admitted into hospital for general debility of two weeks duration. Stiffness and tenderness of neck, abdomen and limbs were present. Blood pressure of 44/18 mm. of mercury was recorded by him. 1 c.c. adrenalin raised the pressure to 110/48 mm. of Hg. which however fell to and remained at 70/42. Latter it rose to 102/64 mm. of Hg. Diagnosis was by biopsy.

(ii) *Ascariasis*.—Low blood pressure is often noticed.

(e) *Sporiochaetal infection*.—epidemic jaundice.

Syphilis.—In early acquired cardio-vascular syphilis low blood pressure results from myocardial degeneration.

In hereditary syphilis Merklen and his school believe that many cases of asthenia are due to polyglandular disturbance of luetic origin.

In neurosyphilis low blood pressure is noted in tabes and in early exaltation and excited stages of G. P. I.

IV. Chronic organic disease, acquired and persistent.

A. Chronic condition with wasting.

The cachexias :—

1. Addison's disease.

2. *Malignant disease*.—Primary stages of malignant disease are associated with high systolic and diastolic pressures. As infiltration occurs pressure steadily falls and reaches very low levels.

3. *Tuberculosis*.—The degree of decline of arterial pressure in pulmonary tuberculosis is directly dependent on the amount absorbed into the system of tuberculosis toxin. The generally held view that chronic tuberculosis is associated with low pressure is not correct. The extent of tissue involved is of far less practical importance than intensity of infection. In active and uncomplicated pulmonary tuberculosis which has not been treated the systolic pressure tends to fall while diastolic remains stationary or under-goes slight reduction.

4. *Diabetes mellitus*.—Uncomplicated diabetes in young people shows a normal or diminished blood pressure; in elderly people there is hyperpiesis, falling during sleep.

5. *Deficiency disease*.—Low blood pressure occurs in beriberi.

6. *Atrophic cirrhosis of liver*.—Permanent reduction of blood pressure takes place.

7. *Sprue*.—Both pressures are reduced.

8. *Pellagra*.—Hypopiesis has been noted.

B. In association with chronic conditions not associated with wasting—

1. (a) *status lymphaticus* (b) *myasthenia gravis*.

2. *Anæmias*—

3. *Chronic intoxications*.—(a) gastro-intestinal (histamine and cadavarine), (b) alcohol, (c) tobacco, (d) chronic arthritis and fibrositis.

The chief causes of hypopiesis in acute infective processes are :—

1. Slowing of the rate of blood flow in the arteriolo-capillary system which takes place during the febrile period.

2. Weakening of splanchnic tone by reason of toxæmia.

3. Toxic effect of infection on myocardium producing cloudy swelling or brown atrophy.

4. Depletion of certain hormones (thyroid, adrenal with resultant upset in metabolism).

Treatment

Give a preliminary injection of 1 c.c. of adrenalin (1:1000) and note of the pressure every five minutes till four consecutive readings are obtained. This will show whether the case is capable of reacting to stimuli or is not capable. If it is capable, find out the amount of reactive capacity.

(Get the blood, urine and faeces examined biochemically. Dr.

Edgar Observer's graph illustrates the three types of metabolism as revealed by their corresponding arterial pressure and urinary pictures, taken in combination.

I An average healthy type, II cellular and endocrine (katabolic) deficiency type, III suboxidation hepatic type.

The non-reacting group is a small one. All the vital processes of the body are at a very low ebb—either due to congenital deficiency, or result of infection which has depleted the system. Here the vital force is just enough to maintain life and nothing can be done for this group.

The reacting group is capable of treatment.

From the point of view of treatment, the low vitality and low reserve energy of the hypopietic is due to a low general standard of cell and tissue nutrition, congenital or acquired, which connotes a low level of metabolic processes. Where defective nutritional causes are dominant, these general measures of stimulation and support are indicated; where endocrine dyscrasia plays the major part in causation, there the exhibition of suitable endocrine products are likely to be useful.

General measures :—

1. *Mode of life*.—Moderation in all things should be the motto. The hypopietic must avoid drawing on his scanty reserves, by

well regulated living, physical and mental.

2. Diet.—(a) solids.

The diet should be nourishing, ample, easily digestible and properly balanced—proteins, fats and carbohydrates being taken in due proportions having regard to the nature of the case. Vitamins must be supplied in sufficient quantities (fresh vegetables, butter, milk, cream, etc.). Indigestion must be avoided.

(b) Fluids:

(i) Water—one pint for each five stone of body weight. Half a pint in morning and at night and the rest in divided quantities at intervals between meals.

(ii) Alcohol is best avoided, except in an emergency.

3. Rest:—

(a) Physical and mental exhaustion are met by recumbent rest in bed.

(b) Lassitude is alleviated by rest during stated hours after the chief meals and by keeping early hours of going to bed. While resting in bed, feet may be kept elevated.

Later on, massage and hydrotherapy, static electricity or ultra violet rays improve the condition.

4. Exercise is essential, but should be within the patient's power of reserve. Physical exercises recommended are stretching

and bending, combined with deep breathing, as soon as one leaves the bed in the morning, followed by a walk at a medium pace on the level at first and as improvement is established on gradually increasing slopes. These favour oxidation and counteract respiratory deficiency. Gradually increase the amount of walking exercise, but keep always short of fatigue.

5. *Change of Air*.—Holidays are helpful provided the environment is suitable. Choose a place 3,000 to 5,000 feet above sea-level. Slightly rarified air stimulates deeper breathing and augments the metabolic rate and general vitality.

Special measures—

1. Relaxation exercises and passive movements:—

By these conservation of energy is attained with a minimum expenditure of effort and beneficial results speedily appear.

2. *Deep breathing exercises*.—The three movements necessary for correct breathing are

- (1) slight forward movement of abdomen (contraction of diaphragm in descent),
- (2) full lateral and backward movement of lower set of ribs, VII-XII (further contraction of diaphragm);
- (3) full upward and forward movement of upper ribs, 1st to 5th (6th is intermediate).

The movements should glide one another in inspiration. In expiration the movements are reversed.

3. Massage and resistance exercises are specially indicated for cardio-vascular types of hypopiesis.

4. Ultra-violet radiation is unsuitable for gouty and plethoric types. Possibly U. V. radiation shifts the acid-base equilibrium of the tissues towards acidity. With patients whose morning urine has a normal ratio of 1 in 1.75 titrable acidity to ammonia fraction, it is safe; and much more so when the ratio is 1 in 3.

5. *Oxygen*.—In hypopiesis due to suboxidation in general or respiratory deficiency in particular, oxygen is very helpful. Given by inhalation, it is wasteful. Give subcutaneously by preference. 500 c.c. to 2000 c.c. are given. Absorption is hastened by hot fomentation.

6. *Hydrotherapy* is only temporary in effect. Best result is got from aerated Nacheim bath.

7. *Organotherapy*.—Thyroid $\frac{1}{8}$ to $\frac{1}{2}$ gr.,

pituitary—0.5 c.c. pituitrin daily or on alternate days,

adrenalin— $\frac{1}{2}$ to 1 c.c. as injection,

cortical extracts,

testosterone.

8. *Drugs*.—(a) Ephedrine $\frac{1}{4}$ to $\frac{1}{2}$ gr. by mouth. Rise of arterial pressure is more continuous.

(b) Caffeine sodium benzoate is specially useful in an emergency as in shock after trauma, operation and anaesthesia and in poisoning by depressants like morphine or fungi, after getting rid of the intoxication.

(c) Digitalis does not raise systolic pressure, but lowers diastolic. Therefore pulse pressure is increased. In hypopiesis, where an uncompensated heart is failing against an overload, due to cardio-vascular defects, digitalis tends to balance the arterial pressure. It should be reserved, therefore, for these cases.

(d) Strychnine has no direct action on circulatory system. Brain and spinal cord are stimulated. It is useful in cases of vasomotor failure.

(e) Ammonia is useful in cases of transient vasomotor paræsis.

(f) Symptomatic treatment.

High Blood Pressure.*

BY RAO BAHADUR DR. M. R. GURUSWAMI MUDALIAR,
B.A., M.D. & C.M.

Definition.—High blood pressure may be defined as a condition in which both the systolic and diastolic pressures are raised above normal limits. It may be temporary, intermittent, paroxysmal or permanent, and may be of renal or non-renal origin.

There is no unanimity of opinion as to what should be considered as normal for systolic or diastolic pressure. Janeway says "No fact regarding blood pressure is better established than its wide range of variation in any individual. It is therefore impossible to speak of a normal value for blood pressure, but only of certain upper and lower limits". Geoffrey Evans suggested 150 mm. of Hg. as upper limit (systolic) and 90 mm. of Hg. as lower limit (diastolic). The investigations of Symonds and Fisher on more than 100,000 insurance cases showed that the systolic pressure of healthy adults ranged around 130 mm. of Hg. and the diastolic about 85 mm. of Hg. These figures approximate to those found by Raghavachari in 232 students of the various colleges in Madras, his findings being about 120 systolic and 80 diastolic for vegetarians, 117 systolic and 83.5 diastolic for non-vegetarians (age ranging up to 29 years).

Estimation of systolic pressure alone would be misleading, *e.g.*, in cases of aortic regurgitation or of Grave's disease the systolic pressure is high and gives a very large pulse pressure.

Incidence.—After scrutinising the findings of a large number of post mortem examinations, Cabot writing about hypertensive cardio-vascular disease says, "Hypertrophy and dilatation of the heart is the commonest of all diseases of the heart," and he has found a large number of such cases without valvular disease, chronic pericarditis, or any other recognised cause of cardiac enlargement, but associated with nephritis, with arteriosclerosis, with both or with neither. Fishberg says "Essential hypertension is far more frequent than nephritic hypertension. Of 82 instances of hypertension. I studied at necropsy 72 were essential and only 10 nephritic." Major investigating in America says that there are ten million people with high blood pressure in that country, and that the condition accounts for 200,000 deaths annually. Fahr states that in men over 50 years of age, deaths due to hypertensive disease are more than those due to tuberculosis, cancer and respiratory

High Blood Pressure

diseases including pneumonia taken together, forming 23 per cent of all deaths in men and women over 50.

Clinical varieties.—Hypertension occurs in the following forms:—

A. Essential hypertension

- (a) slight or moderate—"benign"
- (b) severe and rapid—"malignant"

B. Other forms of hypertension in relation to

- (a) Constitution
- (b) Cardiac disease
- (c) Renal disease
- (d) Endocrine disorders
- (e) Increased intracranial pressure.
- (f) Obesity.

I. Essential Hypertension—

Syn. Hyperpiesia (Allbutt);
presclerosis (Huchard);

Hypertensive Cardiovascular
Disease (Janeway).

Definition.—Essential hypertension is characterised by sustained and progressive elevation of both systolic and diastolic blood-pressures, with or without symptoms; in its later stages it is associated with cardiac hypertrophy and vascular changes in the brain and kidneys, but not usually with renal insufficiency. (Halls Dally).

Etiology.—The immediate cause is unknown. It is generally

agreed that the rise in blood pressure is due to a state of functional vasoconstriction of the smooth muscle fibres of the arterioles. The precise mechanism by which this is brought about is not yet fully established. The experimental works of Pickering, Prinzmetal and Wilson show that the abnormal agent narrowing the vessels is *not primarily nervous*. Clifford Allbutt and a few others have held that *high protein diet* leads to high blood pressure. But Folin, Rosenthal, Fahr and others do not consider that high protein diet leads to high blood pressure. Thomas who investigated the blood pressure of Eskimos found that their exclusive raw flesh diet did not lead to high blood pressure. The investigation carried out by Raghavachari among students in Madras showed a slightly higher pressure among vegetarians. Hence it is reasonable to think that meat protein by itself is not really the cause of high blood pressure. Fishberg says "No convincing evidence has as yet been presented that an excess of protein in the diet results in essential hypertension or any other variety of....."

Harris writes "A comparison of pressure readings of the same patients who have been on somewhat the same quantity of beef protein and milk protein shows that the maximum pressure is actually higher in the majority of cases on milk as compared to meat protein." He further observes "In all likelihood vegetable protein is more harmful than animal. The former, as is well

* Madras University Readership Lecture, II, 1940.

known, is not a first class protein because it does not contain to a full extent the amino-acids in the quantities necessary for tissue repair. In order to supply the needs of the organism it is necessary to consume a much larger quantity of vegetable protein than animal."

Pickering writes "A comprehensive theory of the mechanism of essential, malignant and chronic nephritic hypertension must account not only for the *raised pressure* but for *internal lesions* in the smaller arteries. The presumably chemical abnormality which leads to vasoconstriction may also play some part in the genesis of the internal thickening in the smaller arteries which so often determines the course of the disease." I believe that the researches of Harris throw some light on this question. His observations show that the higher the blood pressure under high protein diet the lower the blood N. P. N. readings and vice versa. The degree of elimination of nitrogenous end-products stands in direct relation to blood pressure values. The higher the pressure the more effective the elimination of protein end-products of metabolism. Hence the high pressure is in a way protective, to throw out the nitrogenous end-products.

If we correlate the grams of nitrogen intake, the milligrammes per cent. of blood N. P. N. and grammes of urinary nitrogen, it will be found that when arterial pressure is lower the ratio of blood N. P. N. in mgs. % to gms. of

urinary nitrogen is higher, i.e., excretion is lower.

A high protein diet either effects an increase of blood pressure or an abnormal increase of blood N. P. N. Because the maximum rise which the circulatory apparatus is capable of attaining at the moment has already been attained by the intake of a small quantity of protein, a greater quantity of protein intake can only lead to an abnormal accumulation of N. P. N. in the blood.

Predisposing causes:—

Heredity and familiar tendency are prominent. There is usually a history of cerebral hæmorrhage, angina pectoris or high blood pressure in the family.

A summary of ætiological factors presented by Walker has been slightly modified by Gunewardhane and is found to be comprehensive. They are as follows:—

1. Intoxications (non-infectious)—

(a) Exogenous:—

- (1) alcohol
- (2) lead
- (3) arsenic
- (4) diet—meat, general excess, condiments, constipation.

(b) Endogenous:—

pressor bodies

2. Habits:

- (a) sedentary occupations
- (b) insufficient physical exercise.

3. Metabolic:

- (a) endocrinous (menopausal)
- (b) pregnancy
- (c) fatigue

4. Heredity and diathesis

5. Infection (past and present):

- (a) generalised systemic
- (b) focal infection with dissemination of organisms—e.g., syphilis
- (c) focal infection with dissemination of toxins.

6. Obesity

7. Psychic

8. Arteriosclerosis

9. Suprarenal hyperplasia.

High blood pressure is seen in persons of robust build, often plethoric, with broad and deep chest, big bones and a tendency to overweight. Another type is short and stocky, bull-necked, soft-muscled. Gout and diabetes are common in both these types—"musculo-digestive habitus". Partially essential hypertension coming on at the time of or after menopause is often seen in women of frail body habitus. But in women this body build is not always associated with hypertension.

Age.—High blood pressure may occur even in children. It is however not common below 30 years of age. Hutchinson observed a boy 8½ years old, whose blood pressure was 210/150 mm. of mercury. The kidneys were normal, post mortem.

Sex.—Both sexes are liable to hypertension.

Race.—Pure Chinese and primitive African negroes are said not to suffer from hypertension.

Probably the condition is dependent on a metabolic error, just as gout, diabetes and obesity are. The pressure regulating mechanism is upset. *Sedentary* habits as *overfeeding* are very largely responsible.

Endocrines.—Some cases are found with disorders of suprarenal, pituitary and sex glands. On the other hand, in the vast majority of cases of hypertension, neither clinical nor post mortem examination reveals any evidence of disease of endocrine glands.

Metabolic factors in the etiology of Essential Hypertension—

1. Protein metabolism—Pressor substances were thought to be end-products. That these produced nephritis and then hypertension is untenable.

There is no convincing evidence.

2. Fat and lipid metabolism—obesity—may be associated with low pressure.

3. Cholesterol metabolism—
In obstructive jaundice and nephrosis there is no raised pressure.

4. Carbohydrate metabolism—
Young diabetics show no high pressure.

Essential hypertension, diabetes mellitus, obesity are a triad due to some congenital peculiarity.

5. Salt metabolism—

In the majority of cases blood chloride is not elevated and in uremic patients, in spite of high tension, Na Cl is below normal.

6. Purine metabolism—

In those predisposed, gout or hypertension results.

7. Overeating.

8. Liver—

Liver extracts lower blood pressure. Major found this reduction in hypertension due to injection of methyl guanidine.

9. Nervous system—

Centre is in the medulla in the region of fovea inferior of fourth ventricle.

Pathology and morbid anatomy—

A large number of observers think that hypertension is the result of hyperactivity of—

(a) the chief controlling centre in the medulla, induced both re-

flexly and by alterations in blood chemistry, (b) subsidiary centres in the thoracic region of spinal cord and (c) the cerebral cortex. The stimulus has been attributed to augmented sensitivity of the vasomotor centres, vascular injury, interference with oxidation or arteriosclerosis of medulla. Subject to this higher control, the autonomic-endocrine system regulates the circulation. The endocrine glands like the pituitary, thyroid, adrenal or gonads act through the sympathetic by means of their hormones, pressor influences being exerted by vasopressin (posterior lobe of pituitary) and by adrenalin, while the cells of pancreas act through the vagus and depress the pressure.

Clinical picture.—The hypersthenic belong to the athletic class who show big bodies of congenital or acquired origin: large heavy body, short neck, short broad chest, horizontal ribs with wide intercostal spaces; sternum broad and short, epigastric angle obtuse; heart broad and of sessile type, resting on diaphragm; diaphragm high in position and well arched thus causing widening in the transverse diameters of the great vessels at the base of the heart; the aortic hemicircle as seen in skiagram is wider than normal; abdominal wall slightly concave. The impression of the picture is that width preponderates over length. According to Ellis these are of the "acid" group. As already mentioned the ratio of titrable acid to ammonia combined acid is between 1:1.5 and 1:2 in normal urine.

High Blood Pressure

In hypersthenics urine the ratio is 1:1 or less.

During youth hypersthenics are usually healthy, but towards middle age, owing to increasing difficulties in elimination they tend to get gout, cardiovascular defects, cerebral hæmorrhage and high arterial pressure. Pulse-pressure is higher than the normal 44 mm. of Hg.

Hypertension is among the commonest of diseases. Its onset is insidious, many subjects being unaware of any trouble for years together, or if any slight symptoms appear, ignoring them. Gunavardhane mentions a patient who came with a fainting feeling of a few seconds, duration, another of a slight transient pain over præcordium. After three to four years these showed alarming sequelæ of high blood pressure, while in the interval they led their usual life without worrying about any possibility of ill-health. Lord Horder says "To discover hypertension at the earliest possible moment was, of course, of great service to the patient. It might not be possible to change the temperament, but the patient's outlook could be modified in such a way as to diminish stresses and strains, and occasionally a man might be made a philosopher before some crippling catastrophe thrust philosophy on him." Hines has shown people with hereditary disposition to high tension are hyper-reactive to standard stimulus (immersion of hand in ice water), five times as frequently as normal people.

Essential hypertension has been classified into four groups by Kieth and Wagner.

(a) Slight to moderate increase of blood pressure; showing no symptoms, responding well to rest, and showing only slight sclerosis of retinal arteries.

(b) Moderate to severe hypertension with few or no clinical symptoms but showing moderate sclerosis of retinal arteries and occasionally venous thrombosis.

(c) Moderately severe hypertension showing angiospastic retinitis and well marked clinical symptoms.

(d) Severe hypertension showing angiospastic retinitis, oedema of optic discs and clinical symptoms.

Clinical symptoms are at first the manifestations vasoconstriction, and they are seen to be coldness in the extremities, digestive disturbances, malnutrition, breathlessness on exertion, palpitation, ready fatigability, pressure headaches, hemicrania, occasional noises in the head and defective vision. If the patient is observed for months or years, it will be found that some of these cases develop definite high blood pressure and show in addition the subjective sensations as follow in order of frequency: fulness, heaviness or throbbing in the head aggravated by mental stress, dizziness, flushing, præcordial pain, drowsiness, disinclination for effort, impaired memory and concentration, irritability, anxiety

states, neuralgia, migraine and epistaxis. Epistaxis is sometimes an early sign.

As these symptoms are identical in incidence, character frequency and duration with those found in cases of psychoneurosis with normal blood pressure, both conditions may possibly be due to similar causes and Dally thinks that "a similar causation for the two conditions is further suggested by the fact that the symptoms frequently develop with emotional upsets or environmental difficulties and subside on their removal."

Course and progress.—According to clinical course Dally divides essential hypertension into two groups—(i) slight or moderate which constitute 90 per cent of the total. Clinical manifestations are mild and renal function is not much impaired. Headache, cardiac pain and shortness of breath are accounted for by the increased blood pressure, which may be as high as 200 mm. of mercury systolic and 120 diastolic. Heart is hypertrophied. Cerebral hæmorrhage may occur causing transient paresis and aphasia. Retinal hæmorrhage may be seen. Batty Shaw says "Sometimes the paralysis affects sensory instead of motor areas, so that the patient becomes blinded without any changes being discovered in the retina or the brain." Vaquez states "Transient aphasia and fleeting paresis, specially brachial monoplegia, are frequent incidents in vascular hypertension. They appear and disappear suddenly, leaving no

traces, and may occur several months later." According to Vaquez various form of mental symptoms may be seen—*e.g.*, amnesia, mental confusion and suicidal tendency. The onset of sensory phenomena before motor paralysis was well illustrated in one of my cases:—A female patient aged 52, with blood pressure 220-140 mm. of mercury, had pricking pains in right half of tongue and diminished tactile sensation on one half of the face on 2nd October 1937. There was no albumen in her urine. After about three weeks these sensations passed off, but there was a good deal of mental confusion and inability to concentrate. She apparently recovered in four months' time. About the early part of 1938 she developed facial paralysis, and was then found to have a trace of albumen in the urine. After two years, she has recovered from these nervous manifestations but her pressure is still 180/105 mm. of mercury.

(ii) Severe, which comprise the remainder, and is usually classed as "malignant". Two main varieties occur:—one in after-middle age; the other in the young.

(a) Those of middle age, who have had high blood pressure for a long time with hypertrophy of the heart and arteriosclerosis. These might have been showing only mild symptoms. Suddenly without any obvious cause the patient becomes worse, complains of lassitude, loss of appetite, headache, giddiness and dyspnoea.

Increased frequency of micturition, especially at night indicates failure of the kidney. Albuminuric retinitis is seen. These patients are between the ages of 40 and 50 and after albuminuric retinitis patients do not live for more than 2 years.

(b) Young adults, who have been unaware of high blood pressure, may suddenly show characteristic retinitis and acute and progressive renal insufficiency. Nicturia is invariably a sign of advanced condition. Such patients can live only for a few months.

In both the groups—young and middle aged—a fore-runner of the malignant phase is seen in a persistent and steadily rising high blood pressure and rapidly advancing renal failure. A sudden fall of blood pressure in cases of hypertension is a danger sign. It is rapidly followed by cardiac asthma and heart failure.

Prognosis.—Prognosis depends on the study of blood pressure readings taken daily and on the experience of the physician. Note whether blood pressure is raised temporarily or permanently, how high it is, and whether it is rising steadily or is stationary. Take into consideration heredity, environment, constitution, body weight, age, sex, temperament and occupation in coming to a decision about prognosis. Life insurance statistics give the average normal blood pressure for different ages and sexes. A consistent elevation of 10 to 14 mm. of mercury in systolic pres-

sure or approximately 10 per cent above the average for the age, increases by 36 per cent the expected mortality. Further rises increase the risk still further. If there are signs of physical impairment—(heart, kidney, lung, etc.), the risk is still further enhanced. If the diastolic pressure is about 110 mm. of mercury, the expectation of life is at most 10 years. If systolic pressure is above 200 mm. of mercury not more than three years' outlook can be given. Gager remarks how active and free from symptoms many of these patients may be till the acute attack comes in and removes them suddenly. According to Dally "The prognosis is most favourable when high pressure is discovered fortuitously, as in examination for life assurance, or when removal of severe emotional or mental stress brings relief. It is particularly good in subjects who are leading a full life with no disturbing symptoms or cardiac disability. A marked fall in pressure as a result of rest in bed or other remedial measures is a favourable sign. The ability of women to lead a quiet life gives a better prognosis in them than in men of the same age."

Prognosis is bad in young people and when the pressure, specially the diastolic, is high. Anything above 120 mm. of mercury diastolic is a special sign of gravity. When there is degeneration of heart, arteries and kidneys as it is inevitable, the gravity depends on the extent of damage. The less tolerance to effort and the more readily

anginal pain sets in, the graver the prognosis. Gallop rhythm and pulsus alternans are warnings of imminent danger.

Death may occur, if there are no intercurrent diseases, from heart failure (45 per cent), coronary disease (15 per cent), cerebral vascular sclerosis leading to cere-

bral hæmorrhage, thrombosis and softening of brain substance (20 per cent) and terminal pericarditis, pleurisy and pneumonia (2 per cent).

The termination of high blood pressure is given in the following table by Professor Thomas of Belfast.

Observer	Cardiac failure	Cerebral hæmorrhage	Renal failure	Other causes
	per cent	per cent	per cent	per cent
Christian ...	32	25	4.5	38.5
Bell and Clawson ...	60.4	19.3	8.3	12.0
Granger ...	52	31.5	5.5	11.0
Sir T. Lewis ...	33	25	very few	less than 50

II. Other forms of hypertension—

Polycythemia hypertonica described by Gaisbock is associated with high blood pressure, increased viscosity of blood, arterio-sclerosis, nephritis and frequently cerebral hæmorrhage. Spleen is not enlarged.

Basophilic adenoma of pituitary gives rise to hypertension without renal lesion. Tumours of cortex of suprarenal (hypernephromas) or of medullary portion (phaeochromocytomas) produce hypertension, the latter paroxysmal hypertension tending to become continuous.

Menopause, natural or artificially induced, sometimes causes hypertension.

Fibromyomas of uterus also occasionally produce hypertension.

Toxaemias.—Lead poisoning, bacterial putrefaction in colon—pressor amines are absorbed—produce hypertension.

Hypertonia.—Arteriolar constriction is a dominant factor in producing hypertension.

Arterio-sclerosis is followed by hypertension in about 50 per cent of cases.

Chronic nephritis leads to hypertension.

The main points of contrast between essential hypertension and that following chronic nephritis are made clear by Prof. Thomson.

	Essential hypertension	Chronic nephritis
History	... Often family history of cardio-renal cerebral-vascular disease, common at menopause	... Sometimes previous history of acute or subacute nephritis.
Age	... Above 40	... Below 40
Heart	... Cardiac hypertrophy more marked	... Cardiac hypertrophy less marked.
Blood pressure	... Higher average. Often over 250 mm. Hg. May fluctuate with rest and other circumstances	... Raised generally, but lower average and less fluctuation. May not be raised.
Fundus	... Marked sclerosis in the retinal arteries. Arterio-venous compression striking feature. Discrete sharp-edged exudates. Oedema less common. Retinitis may be unilateral. Hæmorrhages more common	... Less sclerosis in retinal arteries. Cotton-wool patches. Oedema more common. Always bilateral. Retinal detachment commoner.
Oedema	... No oedema unless cardiac	... Oedema may occur.
Anæmia	... Generally absent	... Often present.
Polyuria	... Not obtrusive	... Marked
Albumen	... Generally present	... Inconstant and intermittent.
Urinary sediment	... Hyaline casts alone generally. Sometimes hyaline and granular. R. B. C. few in number	... Both hyaline and granular casts. Often excess of R. B. C. and epithelial cells.
Blood urea	... Under 40 mgs. per cent.	... Over 40 mgs. per cent.
Urea concentration	... Over 2 per cent.	... Under 2 per cent.
Fixation of Sp. gr.	... No.	... Yes.
Maximum Sp. gr.	... 1025 or over	... 1010 to 1020
Histology	... Afferent arterioles primarily affected. Glomeruli and tubules secondarily.	... Glomeruli primarily affected. Arterioles secondarily.
Prognosis	... Depends chiefly on cardiac condition. Relatively favourable	... Depends on degree of renal insufficiency. Grave.
Mode of death	... Cardiac failure. Cerebral hæmorrhage	... Uræmia.

Pathology.—Extensive arterio-sclerosis affecting most vessels of kidney and spleen is the prominent feature. Hyaline degeneration of the intima is the initial change, and this is followed by a secondary fatty change, leading finally to occlusion of the lumen of the arteriole. To this is superadded a gradual atrophy of the muscular layer of the arterioles involved which suffers ischæmic fibrosis. To maintain the circulation the left

ventricle hypertrophies. This is followed by dilatation of left and later of right side of heart.

Treatment.—

Treatment may be divided into—

- (a) prophylactic,
- (b) general,
- (c) symptomatic.

Prophylactic treatment applies to susceptible individuals with a hereditary history. Psychic elements play an important part in provoking or hastening a rise of blood pressure in individuals predisposed to it. Hence the physician must advise such patients to avoid emotional stress, anxiety and overexertion. A quiet life with congenial surroundings, occupation with a steady routine are to be chosen and those involving risk or anxiety must be avoided. There must be periodic holidays. Regularity in the meal time and early hours to bed must be insisted on. Bowels must kept regular. Sexual excess and overeating must be avoided. It is best to avoid tobacco and alcohol. If they can not be avoided very great moderation must be observed. Gentle exercise to keep the muscles and heart in tone and free drinking of water one hour before meals and at bed time are beneficial.

Diet.—In those that have a tendency to obesity, excess of fats and carbohydrates in food must be avoided. Small quantities of meat and fish may be allowed. Diet however should

consist largely of milk, vegetables, eggs and fruit, with enough of cereals like rice or wheat. More benefit is derived from lessening total intake of food than from mere protein restriction. Avoid under-nutrition as this will make the patient liable to succumb to infection. Let the liver and kidney be kept in good condition by occasional, weekly or fortnightly, saline purges. Weak coffee may be permitted. China tea is said to be less harmful than Indian tea. For the plethoric individual order a fasting day once a fortnight. Sleep is essential, at least eight hours a day.

With such a guarded and regulated life the probabilities are that high pressure may not set in.

If high blood pressure has set in—

In early stages the advice given for prophylaxis holds good. Find, if possible, any stimulus to the high blood pressure and counteract it. Regulation of diet, rest and exercise are essential. Correct errors of metabolism. If diastolic pressure is not more than 105 mm. of Hg. do not restrict moderate exercise. Rigid rest is harmful to non-renal cases. Moderate exercise should be encouraged. If the diastolic pressure is above 105 mm. of mercury, active exercise should be stopped and walking substituted. When this pressure goes above 120 mm of Hg. absolute rest and electrotherapy are needed. Whatever the stage, if

myocardial signs or suspicion of possible hæmorrhage is aroused, absolute rest must be enjoyed.

Psychic or endocrine influences which may be at fault must be corrected. Disturbing influences in domestic life or in occupation should as far as possible be removed. Reassurance and direct suggestions will help a good deal. If necessary give sedatives or hypnotics. This psychic and sedative treatment is specially suited for cases at menopause. Ordinarily phenobarbitol (lumin-al) $\frac{3}{4}$ gr. to $1\frac{1}{2}$ grs. *t.d.* acts as a good general sedative.

In heart failure—

Rest in bed is called for, because the heart muscle, if given a chance, is likely to respond well. *Do not use vasodilators* and do not try to reduce pressure. When blood pressure is suddenly lowered artificially by drugs, the kidney function is depressed, blood N. P. N. is increased and urinary nitrogen is diminished. Cardiac output and alkali reserve fall.

Digitalis may be given whenever there is cardiac insufficiency. Under its influence systolic and diastolic pressures are lowered and differential pressure is increased. When however fibroid degeneration of the myocardium is suspected, digitalis should be used with great hesitation.

In congestive heart failure pressure is reduced by

(a) cardiac tonics and diuretics—digitalis, theobromine and its preparations.

(b) depletives—salines, mercurials by mouth, or by injections or (if permissible) leeches.

Oxygen inhalation is good for dyspnoea.

Palpitation and restlessness are relieved by ammonium bromide gr. 10, tr. sambul m. 10, (or tr. cardamom co. $\frac{3}{32}$ p.), spts am arom. m. 10, td.

If there is arteriosclerosis avoid sudden exertion or violent emotion. General hygiene, careful dieting, calomel and saline twice a week—one grain of calomel at bed time with two drams of mag. sulph. or sodii sulph. in the morning.

If there is kidney disease—do not try to reduce pressure as a greater head of pressure is needed to maintain glomerular filtration when some of the glomeruli are damaged. Direct your treatment mainly to kidney. Restrict protein and salt, resort to diaphoretics and saline purgatives. Tepid baths and massages are useful. If uremia has set in give saline cathartics, pilocarpine, warm baths followed by rest in bed between warm blankets and hot drinks.

Physiotherapy.—This includes rest, exercise, deep breathing exercises, resistance exercises, muscular relaxation, light

massage, high frequency, diathermy, X-Rays, ultraviolet irradiation, hydro—and balneotherapy, lumbar puncture, venesection and fasting.

If kidney is not diseased, Dally advocates pure potassium sulphocyanate $2\frac{1}{2}$ grs. in aqueous solution, thrice daily after meals for the first week, but after that in reduced doses in functional cases. He claims relief in 35 per cent of cases.

In irritable or anxious patients, chloral hydras and potassium bromide 10 gr. each may be given at bed time or luminal $\frac{1}{2}$ to 1 gr. at bed time. During the last few years "pancreatic extracts" have been advocated as producing vasodilation and depressor effects. Of these *padutin* is given intramuscularly in doses of one unit twice daily for three days, then two units twice daily. It seems to give temporary relief in cases of angiospastic hypertension.

Vagotonine is another preparation which is said to augment vagal and secondarily to diminish sympathetic tones thus acting as a circulatory regulator but not as a depressor; and if there is no definite decline of pressure within two hours, the regulator mechanism is regarded as not being at fault. If the pressure falls, this treatment is continued.

Liver extract is also said to reduce pressure temporarily.

Nitrite group of drugs are used in emergency. Iodides, bromides

and bismuth subnitrate are given for vasodilatation. These are slow in action but give more lasting results. I have found guipsin useful when kidney is not badly affected. Drs. Rajagopal Naidu and Krishna Pillay have tried gold bromide in hypertension and claim some success. They gave a confection containing $\frac{1}{50}$ gr. of gold bromide with 10 grs. of garlic per dose. This is given thrice a day for ten days. Claims made for this treatment are—immediate disappearance of headache and a slow, gradual fall in systolic pressure, with a slighter fall in diastolic. From the nature of the drugs, I am inclined to think that this treatment is likely to be useful in spastic hypertension.

Mayo clinic has been using pot. sulphocyanate in the treatment of hypertension. It relieves headache. It has to be tried for about three months before being discarded. Cumulative toxic effects have to be watched for.

On the whole medical treatment of essential hypertension is, we must admit, not satisfactory. Sodium nitrite, purine derivatives like theobromine and theophyllin, iodides, tissue extracts like *padutin*, liver extracts, etc., are of very little use, really to effect permanent reduction in hypertension. Perhaps oestrogen therapy is more useful in the hypertension of menopause.

Hence one turns to surgical measures in the hope of getting better results by "extensive sympathectomy".

K. Craig summarising the experiences of various surgeons writes—

"The futility of carrying out extensive sympathectomy in cases of hypertension in which there is irreparable damage to the cardio-vascular mechanism is apparent. Nor should operation be considered in a case in which a mild and slowly progressive disease is amenable to medical treatment. Operation seems most efficacious in the definite vasospastic type of hypertension, in which sharp and brisk elevations in blood pressure occur when the hands are immersed in cold water, and in cases in which a marked fall in blood pressure is produced when pentothal sodium, sodium amytal, or a nitrite is administered. As an average rule the patient must be less than 50 years of age and the hypertension must be classed in Wagner's group (b) or (c).

The contra indications to extensive sympathectomy are congestive heart failure, angina

pectoris, marked renal insufficiency, and advanced sclerosis."

The results of this operation on 237 patients has been classified as follows:—

failure 20 per cent; temporary relief 28 per cent; fair result 28 per cent; good result 24 per cent.

The surgical treatment of essential hypertension is based on the assumption that increased arteriolar tone can be reduced by operation on the sympathetic nervous system and thus the blood pressure can be reduced. In analysing the surgical results K. Craig says "it is also necessary to keep in mind that patients who suffer from progressive hypertension face a four year mortality rate of 30 per cent in group (a), 42 per cent in group (b), 78 per cent in group (c), and 98 per cent in group (d). Although sympathectomy may not be the ideal remedy, there is much evidence that it may prevent or delay complications that all too frequently cause death in the most productive period of the patient's life."

* Uræmia.

BY RAO BAHADUR DR. M. R. GURUSWAMI MUDALIAR,
B.A., M.D. & C.M.

One hundred years ago, in 1840, this name was given to a toxic condition in some forms of kidney disease. For one hundred years various research workers all over the world have been striving to find out what brings about this toxic condition and still this "urea toxin" remains undiscovered. Some one or another at some time or other has accused almost every one of the known urinary constituents as guilty, but no incontrovertible proof has been adduced.

Urea.—The oldest theory of the causation of uræmia was retention of urea in the system. Christison demonstrated the presence of large quantities of urea in the blood in some renal patients. (Normal 30 to 40 mg. per cent in blood). The idea of urea retention was supported by the fact that in kidney failure the blood showed largest accumulations of urea, as against other urinary constituents. But Benequetin injected urea intravenously into dogs and found that it produced only diuresis and no uræmic symptoms. Hence urea must be exonerated.

Ammonium Carbonate.—Frerich modified the urea theory, stating that it is not urea by

itself that produced the uræmic symptoms, but "ammonium carbonate" which he thought was produced from urea by fermentation. When urea is broken up ammonium carbonate results. (Normal 0.1 mg. per cent in blood). He claimed that the ammoniacal smell in the breath and vomit of uræmic patients supported his view. But in renal insufficiency and uræmia it has been found that ammonia content of the blood is not elevated even though ammonia is lessened in urine. So Frerich's theory can not be maintained.

Creatinine and extractives.—Schottin advanced accumulation of creatinine and extractives in the blood. (Normal—2.5 mg. per cent). But Felty and Ritter showed that large quantities of these substances could be injected without producing symptoms of uræmia. Foster claimed that a crystalline substance could be isolated from uræmic blood and that this produced convulsion. This was not found in any other blood.

Intestinal toxins.—Becher has shown that the blood of uræmic patients contains an excess of various products of intestinal putrefaction like phenols, cresols,

aromatic oxyacids, and other aromatic bodies in addition to indican. (Normal .025 to .085 mg. per cent for indican). Becher, Litzner and Doenelke showed that, while the normal kidney was able to concentrate indican and phenol very highly, in renal insufficiency they were scarcely concentrated at all, the percentage in the blood being as high as in the urine. Rosenberg found in renal insufficiency indican up to 7 mg. per cent in blood. Becher further found *free* phenol in the serum of uræmic patients, while in normal blood it was found only in a *combined* state. In chronic renal insufficiency Becher and Rosenberg found that accumulation of indican and of other intestinal products was much greater in proportion to azotemia.

The views of Becher can not be ruled out at present and further investigation on the lines suggested by him may give good results.

Urinary unknown constituents.—Roger demonstrated that serum of uræmic patients was highly toxic. Herter showed that similar effects are produced by ligating both the ureters in dogs, *i.e.*, the serum of these dogs showed similar toxicity. Bouchard was able to separate from the normal urine a number of substances with different toxic properties—one producing drowsiness, another myosis and so on. The urine of uræmic patients was free from these toxic substances. Theoretically therefore this field of investigation is also promising.

Osmotic theory.—The blood of uræmic patients shows higher osmotic pressure than normal blood. Von Koranyi believes that this increased osmotic pressure of the body fluids interferes with the vital activity of the cells and thereby produces the symptoms of uræmia. The increased molecular concentration of the blood causes dehydration of the tissues, thus producing some of the symptoms. But such symptoms could be otherwise produced too. Further uræmic symptoms may be found in cases where there is only a very small rise of osmotic pressure.

Definition.—"At the present stage" to quote Fishberg "it seems much more probable that uræmia is a complex auto-intoxication, the variegated clinical picture being the summation of the effects of retention of various urinary constituents, largely, it would seem, end products of protein katabolism".

Occurrence.—In general terms uræmia can occur under conditions of inhibition of formation of urine or when there is obstruction to the evacuation of urine. In mechanical obstruction, uræmic symptoms are seen in their simplest form. If a large portion of the kidney—calculated as three fourths of the kidney—is suddenly put out of action, the remaining portion of kidney paranchyma is unable fully to cope with the task of eliminating the urinary constituents and a retention occurs resulting in uræmic symptoms. But in chronic diseases of

* Third University Readership Lecture, 1940.

the kidney, when there is time for adjustment, a better fight is put up by the kidney and a much larger portion than three-fourths can be put out of action and still the person may continue to live.

As mentioned in the lecture on hypertension, a protective hypertrophy of the heart enables the diminished field of filtration to meet the situation. If on the other hand the heart muscle is damaged, the head of pressure falls and the kidney fails with resultant uræmia. Similarly if an acute infection occurs, the added toxins tilt the balance against the kidney.

In chronic glomerulonephritis uræmia is common.

In acute glomerulonephritis it sometimes occurs.

In essential hypertension about 7 per cent die of uræmia.

In chronic nephrosis uremia does not occur except there be nephrotic contracted kidney.

In mercurial and other forms of necrotising nephrosis, if death occurs, it is usually due to uræmia.

Uræmia is common in bilateral pyonephrosis and in obstruction of urinary passages, *e.g.*, prostatic tumours.

It is said to occur, though rarely, in cases of acute interstitial nephritis and of subacute bacterial endocarditis.

Some writers divide uræmia into two classes—latent (asthenic) and sthenic.

Latent.—Obstruction of both ureters or of renal tubules, or removal of both kidneys causes loss of appetite, progressive weakness, increasing stupor or coma and death. No rise of blood pressure is noted. Blood urea is raised up to 0.9 per cent.

Sthenic.—In acute and chronic glomerulonephritis uræmic symptoms are epileptiform convulsions, marked rise of blood pressure, gastro-intestinal disturbance and dyspnoea.

Symptoms.—The condition may be latent or may set in suddenly. During the latent period, the earliest symptoms may be ready fatiguability—both mental and physical. Patient is unable to carry on his work, can not concentrate his attention and complains of a heavy feeling in the head. He becomes apathetic; says he feels very drowsy. Sometimes as you are talking to him he falls asleep. But he can not sleep for any length of time, he is awakened by the slightest noise. He is fretful, fidgety, constantly picking at his nose or his ear. His skin is itchy.

Some patients, however, have a clear mind till the last. Others suffer from hallucinations and delusions. Some may be melancholic. Others may be boisterous and maniacal. In such cases, unless the patient is specially examined for kidney conditions, the diagnosis of uræmia may be missed.

Along with these nervous manifestations, the patient may complain of *headache*. It is not violent; it is a dull aching pain. However, one has to remember that headache may be the result of accompanying hypertension or of cerebral arteriosclerosis and may not be really due purely to uræmia. *Vertigo* may be present.

Muscular twitchings are common. In the early stages either individual muscles or groups of muscles twitch. But there is no generalized convulsion of the whole body. In terminal stages of uræmia, generalized convulsions occur. But they are not very violent and in that way they differ from the violent convulsions (epileptiform) of non-uræmic hypertensive encephalopathy. These twitchings are associated with calcium deficiency in blood.

Reflexes.—Reflexes are increased; but Babinski's sign is not seen. These reflexes are also probably due to calcium deficiency and Chvostek's sign is present. Tetany may occasionally be seen. Peters and Selvesen do not think that these twitchings and convulsions are associated with the disturbance of either the phosphate or calcium content of serum. But in a few cases where I had the blood calcium tested, the percentage was as low as 6 instead of the normal 9 to 11 mg. per cent.

Muscular weakness of the latent period looks like pseudo-paralysis towards the later advanced stages.

Neuralgic pains.—Sometimes these may be the first signs of uræmia.

Alimentary system.—Loss of appetite, nausea and vomiting are common symptoms. Among signs—you find dryness of *mouth and tongue* and complaint of a burning sensation in the mouth and gullet. The tongue looks raw and glazed or is dry, thick and covered with foul, dark brown fur, which is very adherent. In some cases the tongue is covered with a soft greyish fur. There is an ammoniacal smell in the breath due to bacterial decomposition of salivary urea. In the later stages of uræmia, ulcers develop on the tongue and buccal mucous membrane—ulcerative stomatitis. Gums are swollen, spongy and teeth shaky. Tongue is greatly swollen. There is intense salivation. Breath is very foetid.

Gastro-intestinal symptoms are so prominent and early that the case is often mistaken for gastritis,—the patient himself saying he has dyspepsia. *Nausea* may be the only evidence of uræmia for some months. He has *anorexia* and finds the very sight of food nauseating. He has a special aversion for meat, if he has been a meat eater. *Thirst* is another prominent symptom. *Vomiting* is either copious, watery or bilious, or small and mucoid, intractable and persistent. Vomited matter smells of ammonia. Vomiting is sometimes projectile. The abdomen may be very tender. It is believed that this vomiting is nature's attempt to eliminate

the toxic substances from the body, though it may be a feeble attempt. Normally the N.P.N. content of the gastric juice is the same as in blood but in uræmia it is very much higher.

Constipation is usually seen in early stages and diarrhoea in the later stages of the disease. The diarrhoea is associated with ulceration in the colon. The solitary follicles and Peyer's patches of lower ileum, cæcum and ascending colon usually show ulceration. But the ulceration may spread even to upper part of rectum. These ulcers are said to be due to irritation by ammonia set free as the result of bacterial decomposition of urea which is being vicariously excreted through the alimentary canal. The liquid stools do contain a very large percentage of ammonia (8 gms. daily).

The whole alimentary canal from the lips to rectum seems to be specially susceptible to inflammation in uræmia.

Gougerot has described an aseptic peritonitis in cases of uræmia.

Respiratory system.—In the early stages, there are no respiratory troubles. But towards the end one meets with dyspnoea, either paroxysmal or continuous. It simulates asthmatic breathing and is often called renal asthma. Anders says that the breath sounds in this condition are characterised by dryness and harshness; but these may not always be present. Addison

pointed out that the dyspnoea of uræmia differs from that of apoplexy in that the former is quiet and silent while the latter is noisy and stertorous. It differs also from dyspnoea of diabetic coma in that there is no air-hunger.

Cheyne—Stokes breathing occurs towards the end.

On bronchoscopic examination, a peculiar grayish coating is seen in hypopharynx, larynx, trachea and bronchi. Chronic bronchitis may supervene in chronic low grade uræmia.

Circulatory system.—Usually there are hypertrophy of the heart and hypertension. In mercurial necrosis there is usually no hypertrophy. In surgical kidney hypertension is not present. If a case of chronic glomerulo-nephritis is seen towards the later stages, there may be no hypertension due to cardiac failure, but there is enlarged left ventricle. Heart failure is usually seen towards the terminal stages of kidney diseases and uræmia. Wood and White found in uræmia electrocardiographic evidence of injury to the myocardium, consisting in "changes in the T-wave of Lead II, less often abnormal rhythm, and rarely an increase in the auriculo-ventricular conduction interval or in the duration of the Q-R-S complex." Gallop rhythm is very often seen and is highly suggestive. Pulsus alternans is often found in uræmia.

Pericarditis is seen towards the late stages and is a sign of grave

warning. Probably this is an aseptic inflammation.

Skin.—Skin is dry, pale and and yellowish-brown. Becher thinks that this yellow colour is due to retention of urochromogen in chronic kidney lesions, which is converted into actual pigment by the action of light. Exposed portions of body show this discolouration.

Skin also shows numerous marks of scratching, the result of pruritus. Various forms of eruptions are also seen, first described by Huet. They are divided into two classes—

1. Erythemas of papular, vesicular, pemphigoid or hæmorrhagic types.

2. Pruritus with urticarial eczematoid, licheniform lesions.

Fever.—In uræmia the tendency is to a low fever. Occasionally however hyperpyrexia may be seen.

Emaciation.—In chronic uræmia, the emaciation is extreme. The emaciation coupled with discolouration of skin and anæmia might make one suspect malignant cachexia. Basal metabolism is not raised.

Blood.—Blood shows signs of secondary anæmia. Sometimes, however, the colour index may be nearly 1. Leucocytes are normal. Coagulation time is increased. Blood chemistry shows that there is considerable N.P.N. retention and that this varies

inversely as the hæmoglobin of blood. There is definite rise of H-ion concentration leading to great hyperpnoea and a fall of alveolar and arterial CO₂ tension.

Tissues.—Of the urinary constituents urea is found equally distributed in blood, transudates and tissues—except in fat which does not take up much urea and kidneys which retain a larger amount of urea. In an investigation by Weiss and Vaughan, approximately the same amount of urea-nitrogen was found in C.S.F., pericardial effusion, muscle and liver tissue. (Normal 200-250 mg. per cent). Total N.P.N. however is greater in tissues than in the blood. Indican which is not present normally in the tissues, is found in them in uræmia. C.S.F. urea content is the same as in blood; N.P.N. is lower than in blood.

Diagnosis.—Fishberg says "Among the symptoms which should lead to the suspicion of the possible presence of uræmia in a patient with renal disease are headache, muscular or mental weakness, somnolence, nausea and vomiting, diarrhoea, dyspnoea, pallor, emaciation, pruritus and convulsions."

If the quantity of urine passed in 24 hours is much below normal and the sp. gr. of such urine is low, you may strongly suspect uræmia. However if the kidney function is very much impaired, large quantities of pale, low sp. gr. urine may be passed.

Blood Chemistry.—The greatest aid in diagnosis is obtained

from study of blood chemistry. If the N. P. N. content of blood is normal, uræmia may be excluded. If N. P. N. is raised, it may be a case of uræmia or of essential hypertension (in which cerebral hæmorrhage has occurred or heart has failed). In cases of heart failure, coronary thrombosis and cerebral hæmorrhage sp. gr. of urine is fairly high, *i.e.*, about 1020. In uræmia it is below 1010. Diazo-reaction of blood serum if positive is an aid in the diagnosis of uræmia. This is found according to Fitz only in uræmia, but it is not an early sign. (112 mg. per cent of urea at least must be present to give a positive reaction).

Progress.—The following indicate bad prognosis—

somnolence which is deepening, truly uræmic convulsions, paroxysmal dyspnoea or sighing respiration, intractable vomiting, diminution in urinary volume, persistent hiccough, and subnormal temperature. When ulcerations are seen in alimentary tract or when pericarditis appears, the end is near.

Treatment.—Principles observed are—

1. Restrain or reform diet so as to lessen the work of the kidneys.
2. Improve the excretion by kidneys.
3. Promote extrarenal excretion.

Diet.—Restrict protein as far as possible. 20 gms. of protein

per day in adults may suffice. There is no need to restrict animal protein. This throws less strain on the kidney than vegetable protein. A number of workers have investigated this question of to give or not to give protein to people suffering from kidney lesion (uræmia), and the result is summed up by Fishberg in the following words—

“All in all, the statement seems justified that there is no convincing evidence of any difference between the various protein foods as regards nephrotoxic action or liability to produce uræmic symptoms in a patient with impaired renal function.”

The uræmic diet is built upon a basic protein-poor diet. This comprises fruit, fruit juices, vegetables, saccharose, lactose, honey, candy, corn-starch, potatoes, butter, olive oil, cream, etc. The desired amount of protein is supplied from milk, bread, cereals, eggs, meat, fish and other albuminoids. Eggs should not be given raw. As fats are difficult to digest, the calorific value must come from carbohydrates. The diet therefore should be a low-protein, medium-fat, high-carbohydrate diet.

Fluid allowed depends on the individual cases. If there is oedema or myocardial failure large quantities of fluid would be injurious, and it must be restricted. Where there is no oedema but well marked impairment of renal function, fluid must not be restricted, as it is essential to flush out the kidneys, thereby promoting removal of waste products

which the kidneys are unable to concentrate. But flushing out must not be carried too far either. Up to three pints of fluid may be given. Water is the best diuretic.

Sodium Chloride.—In acute cases restrain sodium chloride. In chronic cases moderate restriction is called for and not abstention; otherwise the fixed bases of the body will be wasted. Practically, you notice in cases of persistent uræmic vomiting, normal saline given intravenously reduces the N. P. N. of the blood and gives relief to the vomit (slow intravenous drip).

2. *Improve the excretion by kidneys.*—Apart from giving large quantities of water as already mentioned, the only other remedy that we have of improving the function of kidneys is by digitalis and strophanthin. The explanation of the efficacy of digitalisation is given by Fishberg in the following words.—“In chronic impairment of renal function the sequence of events is that the patient for a long period, sometimes many years, is unable to elaborate a concentrated urine, but wards off retention by polyuria until the heart weakens by hypertension with increasing coronary artery disease, when the urinary volume drops and uræmia ensues. In some such instances uræmia is averted by bed-rest and digitalisation.”

Salyrgan, and other powerful diuretics are not useless, but harmful.

Promote extrarenal excretion.—Nature has set the example by

inducing salivation, vomiting, diarrhoea and profuse sweating.

Except where there is already diarrhoea, saline purges should be regularly given. Not only do they eliminate waste products, but they also prevent the intestinal putrefaction which has been found to increase the uræmic manifestations.

Hot baths and hot packs with hot drinks induce sweating and at the same time combat dehydration of tissues. If the patient complains of faintness or discomfort, the sweating should be discontinued. If heart is weak and failing, do not attempt to sweat the patient.

Venesection is not useful except to relieve an engorged heart, it actually raises the N. P. N. of blood. (Explanation is that tissues have a higher percentage of retained N. P. N. than blood. When blood is withdrawn, tissue fluid replaces the lost blood, bringing with it larger amounts of N. P. N.)

Symptomatic treatment.—I should advise bromide and chloral hydras 10 gr. of each to combat sleeplessness, restlessness and headache. Avoid hypotics of the barbituric series. Codeine may be given with caution. If necessary *morphia* is given. Lumbar puncture relieves headache sometimes. Sellard states that sodium bicarbonate by neutralizing the acidosis may prove more effective than *morphia* in controlling restlessness.

Delirium of uræmia.—If *morphia* fails, try paraldehyde 3 IV

per rectum or a teaspoonful by mouth every two hours till relief.

Vomiting.—Gastric lavage may be useful. Cocaine $\frac{1}{4}$ gr. by mouth and glucose per rectum may be used too.

Pruritus.—Try morphia. If it fails give sodium bromide intravenously. It stops the itching

promptly but may give rise to bromide rash.

Muscular twitchings and spasms.—Calcium chloride or calcium gluconate intravenously stops these.

Acidotic dyspnoea is relieved by sodium bicarbonate.

Malignant Diseases of the Female Generative Tract with Particular Reference to Carcinoma of the Cervix *

BY

RAO BAHADUR A. LAKSHMANASWAMI MUDALIAR,
M.D., F.R.C.O.G.,

Principal and Professor of Obstetrics and Gynæcology, Medical College, and Superintendent, Government Hospital for Women and Children, Madras.

When I was honoured with an invitation from the Syndicate of the University of Madras to deliver the Maharajah of Travancore Curzon Endowment Lectures on a subject pertaining to Obstetrics and Gynæcology, I had little hesitation in making a choice. Realising as I do that one of the most common causes of disease, suffering and death in women is malignant disease pertaining to the female genital tract and realising further that in spite of the wide prevalence of this affection, it would appear from clinical experience that the majority of these cases are neglected, allowed to suffer or in some cases incorrectly diagnosed, I felt that no apology from me would be necessary to avail myself of this opportunity to present certain aspects of this subject and to place our experience in this hospital before the medical profession. I do so with the full confidence that thereby it would be possible to stimulate

interest in this subject in the medical profession and by so doing to educate the general public to a clearer realisation of their responsibilities in this matter.

It is unfortunate that even reasonably accurate statistics are not available in this country to give us an approximate idea as to the incidence of cancer of the genitalia in women and it would be futile on my part to attempt to assess the incidence.

The mortality in England has, of course, been correctly recorded inasmuch as every death has to be certified by a qualified doctor. It is reported that in 1934, out of every million women in England, nearly 1600 died of cancer. To present it more graphically, it may be stated, if one were in a theatre in which there were 630 women and the death rate remained unaltered,

* Being the Maharajah of Travancore Curzon Endowment Lectures delivered under the auspices of the Madras University at the Giffard School of the Government Hospital for Women and Children, Egmore, Madras, on the 26th and 28th February 1940.

one of them would die of cancer within a year. To put it slightly differently, in 1934, out of 234,000 deaths among women, 33,500 were from cancer, so that an undertaker who was responsible for the disposal of all the dead would find that 1 out of every 7 women coffined would be a woman who died of that disease. If the causes of death in women be tabulated, we find that cancer holds the second place with 14.3 per cent, heart disease coming first. In this country, it would not be an exaggeration to say that the deaths from cancer in women are no less and perhaps if one were to exclude sudden epidemics that devastate the population, cancer would still be the captain of the causes of death in women between the ages of 20 and 70.

It will thus be seen that there cannot be any doubt as to the advantage of a properly conducted propaganda for the early diagnosis of cancer. There are many who maintain that such a propaganda may probably create a sense of fear in those who have not cancer and that cancer-phobia, an unfortunate disease, may become somewhat prevalent. Most persons will, however, agree that it is better to shake the placidity of the people and even produce a little scare by judicious propaganda so that they may be better able to look after themselves and adopt those precautionary measures which are largely calculated to eradicate the disease or to bring about a cure in the early stages, if the disease is properly recognised.

The sense of self-satisfied security that all is well till it is too late will only result in a larger proportion seeking redress when nothing tangible or useful can be done or them. To this aspect, however, we shall refer at greater length at the end.

The problem is not one which concerns only the public. Let us confess that it is a problem with the medical profession even more, of better education and better sense of the responsibility that devolves upon the practitioner to recognise this condition. If every doctor would only realise that a vaginal examination should always be made, whatever the age, civil state, religion or social environments of the patient, if she seeks advice for bleeding between the periods, if every form of erosion or ulcer of the cervix which does not clear up quickly should be further investigated, if every woman who has any sort of bleeding after she has passed the menopause is carefully scrutinised and a thorough examination is made, if all those who have had traumatic lesions of the cervix or of the genitalia during child-birth were followed up in the post-natal period and preventive steps adopted, if, in fact, better midwifery and more of it were made available, and every possibility were taken to prevent those unfortunate lacerations,—if these elementary lessons could be brought home to the medical profession in general and they be put on their guard either to examine the cases thoroughly themselves or refer them to properly equipped gynaecological

clinics, much of the problems concerned with cancer would perhaps disappear. It is with that hope that I venture to present this subject and believe that it would stimulate interest in the profession and would also make the general public realise through the efforts of the family practitioners what steps to take in conditions where prompt treatment is so essential.

Malignant growths of the female genital organs may occur in any part of the female generative tract, the vulva, vagina, cervix, corpus uteri, fallopian tubes and ovaries. Among the many types of

malignant growths may be mentioned carcinomata, sarcomata, chorion—epitheliomata, endotheliomata, peritheliomata and certain of the rarer forms met with in the ovaries and occasionally elsewhere.

By far the commonest variety of malignant growths met with in the female generative tract are carcinomata and among these the commonest form of cancer is cancer of the cervix. I herewith present an analysis of 1502 cases of malignant diseases of the female generative tract treated in this hospital in a five year period showing a classification according to the situation of the cancerous growth.

TABLE I

Cancer cervix	Can-	Cancer	Can-	Cancer	Chorion	Can-	Cancer	Cancer	Total
Pre-meno-	Meno-	cer	Cancer	cer	epithe-	cer	with	with pro-	number
pausal.	pausal.	body.	vagina.	cer	lioma.	stump.	fibroids.	lapse.	of cases.
956	435	50	20	12	10	19	14	10	8
1391			1502						1502

It will be seen therefrom that 1391 out of 1502 cases were cases of cancer of the cervix.

The incidence of cervical cancer is given by Cullen as 80 per cent, Meigs as 86 per cent, Graves 78 per cent, Hofmeir as 85.2 per cent. The earlier German writers reported that cervical cancer comprised over 95 per cent of uterine cancer. My own series gives an incidence of 92.6 per cent.

We shall now take up cancer of the cervix which, as has just been stated, is about the com-

monest form of cancer in the genitals. Cancer of the cervix can occur before or after menopause. The general impression that menopausal cancer is usually cancer of the body of the uterus is not borne out by our experience in this hospital. In fact, it will be seen from the following table that menopausal cancer, i.e., cancer occurring after the menopause is far more frequent than is generally imagined, and that in this type of cancer, cancer of the cervix occurs no less frequently, in fact, much more frequently than cancer of the body of the uterus.

TABLE II.

Pre-menopausal.			Meno-pausal.	
Cauliflower growth.	Ulcerative.	Intra-cervical.	Cauliflower growth.	Crateriform ulcer.
537	369	42	88	347
	948		435	

It is possible that in some cases cancer of the body may not be recognised so easily as cancer of the cervix; but after giving due consideration to this factor, it must still be stated that cancer of the cervix dominates both in the pre-menopausal and in the meno-pausal periods of life.

The age incidence of cancer.—Speaking broadly, cervical cancer unlike cancer of the body of the uterus, is a disease of middle life and does not belong predominantly to old age. It may, however, occur at any age period. In a

study of 387 patients with cancer of the cervix at the John Hopkins Hospital, it was found that 66 per cent were between the ages of 35 and 55 years, while 18 were under 36 years of age and 29 persons past the age of 50. In our own series, as shown below, there were 10 cases of cancer between the age periods of 20 and 25, 115 between the ages of 25 and 30, 488 between 30 and 40, 335 between 40 and 50, while 8 occurred after the age of 50, among the 956 cases of pre-menopausal cancer.

TABLE III.

Years.	20—25	25—30	30—40	40—45	50—60	Total
No. of cases.	10	115	488	335	8	956
Earliest age 21 years.						

The distribution according to age in the menopausal cancer will naturally be expected, as will be seen from the following table:—

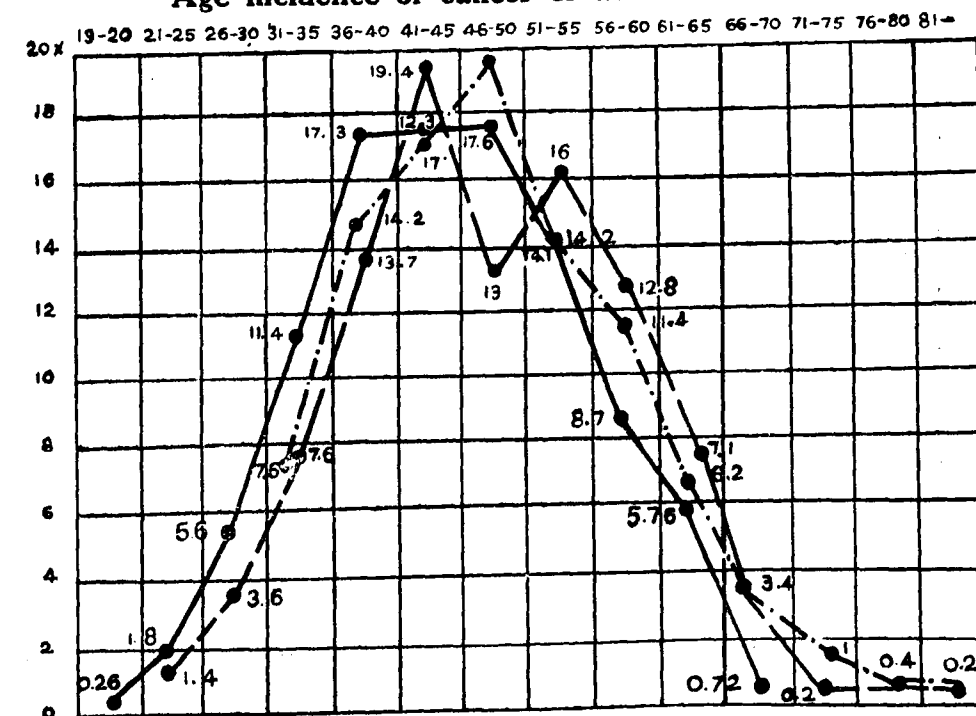
TABLE IV

Years.	30—40	40—50	50—60	60—70	About 70	Total
No. of cases	10	167	177	80	1	435
Oldest age 75 years.						

Thus 255 out of 435 cases occurred after the age of 50. The age of the oldest patient was 75 years and she developed cancer 25 years after the onset of menopause. It appears, therefore, that cancer of the cervix has its greatest incidence in the years immediately preceding and including the menopause, the menopausal period being assumed to occur between the ages of 40 and 50 years. Cancer of the corpus uteri in contrast is distinctly a disease of the meno-pausal and post-menopausal periods. In women under 20 years of age, cancer of cervix is a

rarity. The youngest patient encountered in our series was 21; while in Cullen's clinic, a 19 years, old coloured girl was admitted with an inoperable tumour. Probably, the youngest authentic case of cervical cancer is the one reported by Berkau and confirmed by Robert Mayer in a 7 months' old child in which an epidermoid cancer involved the cervix and vagina. An incidence of adenocarcinoma of the cervix is reported in a 7 year old girl. The following graph shows the age incidence of cancer of the cervix uteri according to different observers.

Age incidence of cancer of the cervix uteri



Previous pregnancy:—There is a general consensus of opinion that cancer of cervix shows a predilection for women who have borne children and that women who develop cervical cancer show a greater parity than the average group of parous women. More recent investigations would appear to show that it is not so

much the number of children that were delivered as the extent of the trauma incident to the delivery, which is the most important factor to be taken into consideration in the possible development of cancer. The following table shows the distribution in relation to parity of our 1391 cases of cancer.

TABLE V.

Parity.	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	
No. of cases	80	110	130	162	190	220	186	140	82	70	11	5	4	1
1391														

It will be noted that only 80 of this series occurred in nulliparous women and that the incidence of cancer was proportionately greater in the women who had delivered 3, 4 or 5 children. Kauffmann has stated that in his analysis, 53·7 per cent of his cancer patients gave a history of three or less pregnancies. Just what influence a previous pregnancy may have on the cervix to render it specially susceptible to cancer is difficult to state definitely, but it is the general impression of most gynaecologists, which we share, that cervical lacerations incidental to child-birth or miscarriage supply a very definite factor in the future development of cervical cancer.

The frequency with which cervical cancer is associated with myomata has been variously estimated. In our own series, there were only 10 cases which could definitely be diagnosed as cases of cancer with fibroid. This is a very low proportion but it is possible that, as most of these cases came in an advanced state

of the disease, small uterine fibroids could not be recognised by palpatory findings consequent upon the associated pelvic inflammatory condition, which involved the body of the uterus, the adnexa and the cellular tissue. At the John Hopkins Hospital, it was noted that 9 per cent of cervical cancers were associated with myomata but some of them with the small intra-mural nodules so commonly found in uteruses when carefully examined. This figure is considerably higher than that of Kaul and of Frankel who found respectively 2·4 per cent and 6·7 per cent of cervical cancer associated with myomata. It would appear that the association of myoma with cancer of the cervix uteri is more or less casual and has no particular significance.

Pathology.—Two types of cancer may definitely be recognised pathologically, the epidermoid carcinoma which is also known as squamous cell carcinoma and adeno-carcinoma. The epidermoid or squamous cell carcinoma, which is the commoner variety

may arise from any portion of the cervical canal or from its vaginal aspect. Most cervical cancers arise at the epithelial transition zone where the stratified epithelium of the vaginal portion of the cervix meets the columnar epithelium of the endocervix. The primary growth has no predilection for either the anterior or the posterior cervical lips. The cervix as a whole enlarges moderately. Later there is extension to the vaginal wall as well as anteriorly towards bladder and more deeply into the broad ligament tissues. Progress along the cervical canal into the mucous membrane of the uterus tends to be limited. These cancers necrose, ulcerate extensively and exude sero-sanguineous or bloody discharge.

Adenocarcinoma of the cervix is comparatively rare. Only 5 to 10 per cent of cervical cancers are generally adenocarcinomata. For a clearer realisation of the extent to which involvement of the neighbouring structures has occurred in cases of cancer, a classification has been adopted of cases of cancer of the cervix on the lines suggested by the League of Nations. The following table shows the nature of the cervical cancer which should be grouped under the particular head:—

League of Nations Classification

Cancer Cervix.

Group I.—The growth is strictly limited to the cervix uteri. Uterus mobile.

Group II.—Lesion spreading into one or more fornices with or

without infiltration of the parametrium adjacent to the uterus, the uterus retaining some degree of mobility.

Group III.—(a) Nodular infiltration of the parametria, on one or both sides extending to the wall of the pelvis, with limited mobility of the uterus or massive infiltration of one parametrium with fixation of the uterus.

(b) More or less superficial infiltration of a large part of the vagina with a mobile uterus.

(c) Isolated metastases in the pelvic glands, with a relatively small primary growth.

(d) Isolated metastases in the lower part of the vagina.

Generally speaking all cases not falling into Groups II or IV will be placed under Group III.

Group IV.—(a) Cases with massive infiltration of both parametria extending to the walls of the pelvis.

(b) Carcinoma involving the bladder or rectum.

(c) The whole vagina infiltrated (rigid vaginal passage) or one vaginal wall infiltrated along its whole length with fixation of the primary growth.

(d) Remote metastases.

Speaking generally we might state that Stage I includes cases of carcinoma of the cervix strictly limited to the cervix. In Stage II, there are cases in

which extension has reached the vaginal wall with or without some induration of the parametrium. The uterus is mobile. This is the so-called border line group. In Stage III, there is definite nodular infiltration by the growth of the parametric tissues with partial or complete fixation of uterus, while Stage IV consists of those cases where the carcinoma has extended much further, in some cases involving the bladder or the rectum, while in others the vagina. Portions of the true pelvis are involved or

metastasis into distant parts has already occurred. As a general rule, in trying to discriminate between these different stages, it is the practice to up-grade these cases of cancer so that a doubtful case of Stage II would be put down as Stage I and one of Stage III or IV into the stage just above so as not to raise unduly the proportion of favourable results in the less advanced grades. The following table shows the classification of our cases according to the groups mentioned:—

TABLE VI.

Group	Group I	Group II	Group III	Group IV				Total	Intra-cervical.
				(a)	(b)	(c)	(d)		
No. of cases	23	83	287	310	263 978	242	163	978	42
					1371				

Clinical cases of cancer of the cervix have been divided into two groups, the ulcerative and the proliferative. In the ulcerative group, there is excavation of the tissues. The cervix presents a moth-eaten appearance. It is the necrosis which precedes or is associated with ulceration which furnishes the tell-tale friability so important in the diagnosis of this disease. In advanced cases, the ulceration may become extreme so that a deep crateriform cup, sometimes so deep that the vaginal part of the cervix is hardly to be seen, is noted. In such advanced cases, extension has usually progressed to the vaginal walls and invasion of the recto-vaginal septum posteriorly and the blad-

der anteriorly is not uncommon. In the proliferative type, the typical cauliflower like growth may be seen, friable and occasionally fungating and bleeding readily. In between these two types there are other types that can be clinically recognised and it is important to note these types because both from the point of view of diagnosis and of prognosis, they seem to have some bearing on the lines of treatment to be adopted.

We have seen typical cases of cancer of the cervix of the ulcerating type where the ulcer is more or less limited and has not produced the deep crateriform ulcer. Secondly in some cases, it would

appear that the chief activity lay in the corroding influence of the cancerous cells so that the deep crateriform ulcer is not the result of prolonged stages of the disease but is due to the nature of cell growth which would appear to be eroding in its activity. Thirdly, there is a particular type of ulcer where the cancer is almost limited to the anterior lip of the cervix, which becomes flattened out and projects almost like a tongue like process, large and flabby with an ulcerated mass. In another variety there is a hard nodular growth which fills the whole of the vagina and does not bleed so readily, the type which may be called the cancer Botryoides. The significance of these different forms of cancer will be better appreciated when the question of treatment is discussed.

Mode of extension.—Carcinoma of the cervix extends in four ways, by continuity of tissue, by lymphatics, by the blood-stream and by implantation. Extension by continuity of tissue is the principal method and except in exceptional cases, the only method in the earlier stages of the growth. It is the insidious involvement of the contiguous tissues that makes many cervical carcinomata inoperable when first seen and it is this somewhat gradual extension outward by continuity of tissues that later causes the patient most of her suffering and ultimately death. In extension through the lymphatics, the carcinoma cells are caught in the lymph current and carried to the lymph glands.

The invasion of the lymph glands does not occur until rather late in the disease, not generally till it is extended by continuity of tissue through the cervix into the parametrium. Enlargement of the regional glands is very common in the early stages of carcinoma but this enlargement is, as a rule, not due to carcinoma cells but to the inflammatory hypertrophy that nearly always takes place in the glands draining the region that is subject to severe chronic irritation.

Extension by the blood-stream results in distant metastasis. The lungs are most frequently affected but there are many other organs that may be affected occasionally. Direct implantation of the cancer cells into healthy tissue generally occurs in operations for cancer where the cells are carried on the knife or scissors from the infiltrated area to the healthy tissue.

Symptoms.—The most important clinical evidence suggestive of cancer is hæmorrhage. It is important to emphasise that the occurrence of spontaneous hæmorrhage or any bleeding that occurs after douching, coitus or after a digital examination, should be viewed with extreme suspicion. Inter-menstrual bleeding, even if moderate, is very suggestive of malignancy, especially in patients of a cancerous age and should lead to an immediate and thorough investigation. Hæmorrhage in a woman beyond the menopause is particularly indicative of malignancy. It is true that there are other causes for hæmorrhage in

women at this period of age but it must be borne in mind that cancer of the uterus is the most serious condition which commonly causes symptoms of vaginal bleeding and a thorough investigation should therefore be made.

I cannot sufficiently emphasise at this stage the importance of examining every case of cervical polypus which causes hæmorrhage. A histo-pathological examination is absolutely necessary to decide whether a polypus that has been removed is benign or malignant and even where after such examination, the pathological report does not suggest malignancy, it is a wise precaution to keep the patient under observation and if any recurrence of bleeding occurs, to investigate her further and to examine the cervix, cervical or uterine scrapings once again.

The second symptom of importance is vaginal discharge, which may be profuse or blood-stained or offensive. It must however be mentioned that this symptom as well as pain in cases of cancer are late symptoms and should never be awaited before a definite diagnosis is made. Even hæmorrhage is a somewhat late symptom, particularly when it occurs profusely.

As for symptoms such as cachexia, anæmia, loss of weight, vesical distress, these are symptoms that should never be allowed to occur as they indicate not the presence of cancer so much as an advanced stage of the disease. One other caution, that is perhaps

unnecessary so far as the medical profession is concerned, but which should be stressed so far as the public are concerned, is that maintenance of weight and a sense of well-being are by no means guarantees against the presence of malignancy of the uterus.

Diagnosis.—The one conclusion always reached by every student of cancer statistics is that the factor which far more often than any other decides the fate of the patient is the stage at which proper treatment is begun. The term "early" as applied to cancer of the cervix is a very relative one. For practical purposes, it would be an enormous advance if the majority of cancer patients can be given the benefits of proper treatment at a stage when the cancer is confined to one lip of the cervix, when it measures not more than a centimeter or so in diameter, when there is no infiltration of the broad ligaments and when the uterus is freely mobile. If every physician could be trained to recognise cancer in this early stage, an enormous step forward would have been taken and this should be the immediate goal we should set for our profession. No one who takes the time and trouble to inspect and palpate the cervix can fail to diagnose an advanced cancer, but even the most painstaking of physicians may overlook the earlier lesions for the simple reason that his mental picture of cancer is unfortunately that of the late stages, the cauliflower growth, the necrotic ulcer or the very hard, indurated and

irregularly enlarged cervix. To enable the recognition of early stages of cancer, it is now realised that inspection has assumed a more important role than mere palpatory findings and a careful inspection particularly with certain methods of staining has come to be an invariable routine in the campaign for the early recognition of the disease. The practitioner who encounters the combination of suspicious symptoms and a suspicious cervix or who finds a suspicious cervix even without symptoms, in the course of a pelvic examination, owes it to his patients to have the diagnosis authoritatively decided, as it can be, in most cases. The contribution, therefore, which can be made to the cancer campaign by the rank and file of the profession is to develop habits of thoroughness in the examination of cervixes in women beyond 30 and, of course, in those who have observed any abnormal bleeding or discharge, to study such cervixes intensively with an eye to the picture which suggests possibility or the probability of early cancer, to pursue the diagnosis of every doubtful case unremittingly to a decision and then to see that proper treatment is begun. As has been somewhat laconically said, it is the man who has cancer on the brain who is most likely to discover cases of this disease.

Two important adjuncts are now at our disposal for the early recognition of these cases. The colposcope devised by Hinslmann gives a binocular stereoscopic view of the cervix. It enables us

to view the cervix with a magnification which ranges from 10 to 15 diameters. Viewed with this instrument, it has been stated, that early leukoplakic patches and suspicious signs can be noticed and from the suspected area located, a biopsy may be taken.

Another test which has come into vogue very largely is Schiller's test with iodine. The technique is as follows: the cervix is exposed by means of a speculum and cleaned off with cotton. Then a sufficient amount of a modified Lugol's solution containing iodine 1, potassium iodide 2, water 300, is poured into the vagina so as to cover the cervix and surrounding mucosa completely and left in contact for five minutes. The solution is then mopped up with cotton and the cervix observed for staining reaction. Normally the cervical mucosa stains a dark brown or mahogany colour. The unstained areas are regarded with suspicion. The rationale of this test is that normal mucosal epithelial cells contain glycogen and therefore combine with the iodine solution to produce the brown stain, whereas cancer cells do not contain glycogen and therefore fail to stain. Well-defined white patches with distinct borders are considered characteristic. Unfortunately, staining does not occur whenever there is a loss of mucosa, *e.g.*, in erosion. Leukoplakic areas also fail to stain. Therefore, while a failure to stain does not always mean cancer, staining does exclude its possibility. On the other hand, it must be said that the use of

Schiller's test, if differently interpreted, is of the greatest value. It definitely divides cases into two categories, the suspicious and non-suspicious and in all such suspicious cases, whether it be with the aid of Hinslmann's colposcope or with the more simple Schiller's test, a biopsy should be done. The biopsy, of course, remains the court of last appeal but it is indeed true that the colposcope and iodine test may point out areas for biopsy which would not otherwise have been suspected. Whether the biopsy is carried out by scalpel, punch or diathermy knife, the important thing is to excise the tissue at a point which is really suspicious. Unusual hardness, slight superficial granular ulcerations, the presence of a fine vegetative area, increased vascularity as manifested by bleeding on slight touch—all these must be sought for. Not infrequently wedges should be taken from more than one area in order not to miss possible malignancy. The pathologist can be expected to find cancer only when it is contained in the biopsy specimen so that a biopsy imperfectly performed or taken from a wrong area is not merely useless but actually inimical to the patient's welfare by giving a false sense of security. On the other hand, the pathologist may err if he depends for diagnosis on one or two sections from the biopsy block. For any small lesions, sections if taken from every level may show undoubted cancer. Serial sections are therefore of great importance and it is best to

section the entire block, staining sections at various levels so that the evidence of malignancy will not be missed.

Carcinoma of the cervix must be distinguished from tubercular ulcerations, erosion of the cervix, syphilitic ulceration, chancroidal ulceration, and other forms of chronic ulceration. Tubercular ulceration of the cervix is not so rare as it is stated and sometimes presents real difficulties in diagnosis. A microscopic examination may be the only decisive test but it may be mentioned that a tubercular ulcer is not hard or indurated and has a soft velvety feel about it, quite characteristic, although the worm-eaten appearance may sometimes suggest a superficial resemblance to malignancy. In syphilitic ulceration, there are usually other lesions. In any case, in a majority of such suspicious cases, a Wasserman is necessary.

Treatment.—The measures available in our attempts to attain a permanent cure of carcinoma of the cervix include:—

1. surgical therapy which involves radical operation for the removal of the uterus and adnexa with the glands,
2. radium therapy
3. roentgen radio-therapy
4. a combination of these.

At one time, surgical therapy held the field. Operation is still employed by a few but its

applicability is limited to the very few cases suitable for radical removal. The only operative procedure permissible in the treatment of this disease is a radical one. There are two important methods—Wertheim's abdominal operation and the vaginal operation of Schauta. They both aim to remove the adnexa, the entire uterus and cervix, parametrial connective tissue and at least the upper portion of the vagina in one piece. In Wertheim's abdominal operation, the regional lymph glands are also removed. Less radical operations have proved worthless. There is a considerable primary operative mortality for these radical procedures, even in the hands of those who have had the largest experience possible. The operative mortality of Wertheim was 13.8 per cent, Bonney 14 per cent, Bumm 12.6 per cent, Doderline 20 per cent, Stoeckel 19.4 per cent. In selecting the cases, it must be remembered that the growth must be early. There should be no retention of material within the uterus and the patient should be in good general condition, as regards her blood-pressure, urinary excretion, pulse rate and blood count; the bacterial flora of the cervix and vagina should be investigated before the operation and if any dangerous bacteria are present, the operation should be delayed till the vagina can be sterilized. Shock, excessive blood loss, peritonitis, and pelvic cellulitis are complications not infrequently encountered. Dysfunction of the bowel and bladder often result. Fistulae may occur.

It is not therefore a matter for surprise that opinion is gradually veering round to the view that operation is by no means the treatment of choice so far as cancer of the cervix is concerned, and in this country where unfortunately it is exceedingly rare to meet with an early case and where even in such early cases, the minimum conditions as to general health are not available, the question of operation recedes into the back-ground.

Aleck Bourne discussing the question "Is radium treatment preferable to operation" states: "It seems hardly possible to avoid coming to the conclusion that generally speaking radium can do everything that surgery can in the attempt to cure cancer of the cervix and can do it with a much lower initial mortality rate". On the precepts of "the best good for the greatest number", radium seems to be the method of choice. A similar conclusion has been arrived at by Fletcher Shaw and Daniel Dugal who report that the radical operation has been abandoned at the University of Manchester. At present America is radium-minded. It would thus seem that in many clinics operation has been virtually abandoned but there is a noticeable tendency to modify this policy in some clinics by adopting a combination of surgery and radium in at least a selected group of cases. It needs scarcely to be added that the aggregate number of cases fit for such combination of surgery and radium therapy is only a small fraction of the total number encountered.

With the exception of these limited groups, the treatment of cancer in the cervix is entirely a matter of proper radio-therapy with the combined use of radium and X-rays.

There is still considerable difference in methods, and improvements and refinements are still being devised in an effort to improve the results. The dangers of radiotherapy are real and the morbidity attending the method has been emphasised by many. In the main, however, the risks of radiotherapy in competent hands are only a small fraction of those of radical surgery, formerly so generally employed and this fact together with the fact that the results are just as good, to say the least, has established radio-therapy as the preferred treatment for the present. If only surgery or radio-therapy were to be chosen for universal adoption, there can be no question as to which would give better results and carry with it the lower mortality and morbidity, but the key-note of treatment of cervical cancer should be individualisation so that the plan of radio-therapy must be adopted to the individual cases while in some a combination of surgery and radio-therapy will be chosen as offering the patient the best chance for a cure.

Effects of radium on tissues.—As has just been stated the one most important and commonly adopted method of treatment for carcinoma is radium therapy, and it is necessary for the gynaecologist to have a clear conception of the effect of radium, the

manner of its action, the method of its use and the indications and contra-indications for radium therapy. My apology in now digressing a little, if I may, to describe in some little detail radium and its properties, is because it is fundamentally impossible to have a clear conception of radium therapy unless these primary considerations are clearly understood. When radium is applied within a cancerous mass, *e.g.*, is the centre of a carcinoma of the cervix uteri, and left there for a considerable time there are two zones of effect: (1) a zone of complete destruction of all tissues and (2) a zone of differential destruction. Within a certain distance of the radium, all tissue is devitalized and later comes away as a slough. The width of this zone varies with the dose of the radium and the method of screening. In the zone of differential destruction, only the cancer cells are killed but the tissue cells are not. Radium in its slow decomposition gives off a complicated variety of rays of which the three principal are Alpha rays, Beta rays and Gamma rays. The Alpha rays have hardly any penetrating power; hence are referred to as soft rays. They are usually all stopped by the glass of the small glass capsule in which the radium is sealed and they are of little practical importance. The Beta rays are somewhat more penetrating and must be reckoned with in their effect on tissues adjacent to the radium. The Gamma rays are deep penetrating rays. It is upon the penetrating Gamma rays that we

depend for the destruction of the cancer cell, deep in the tissues. The problem therefore, in radium treatment of an extensive carcinoma of the cervix uteri, for instance, is to give a sufficient dose of the penetrating Gamma rays to destroy the distant cancer cells throughout the pelvis without letting Beta rays cause sloughing into the rectum or bladder or ureter.

How is the problem solved?

To secure this effect, four things must be carefully considered:

1. the metal screening of the radium,
2. the situation in which the radium is placed,
3. the packing away of adjacent organs and
4. the size of the radium dose advisable in each case.

Distance screening.—In addition to these special screening materials there are other important items in the screening process. One of the items is distance. The effect of the rays diminishes rapidly with the distance from the radium. Consequently to prevent a sloughing effect in the rectal and bladder walls, it is important to push these structures away from the radium as far as possible. This is accomplished by a gauze packing. The posterior vaginal vault and the anterior vaginal vault are distended by firm packing, thus pushing away the rectum

and the bladder. This is called distance screening. The importance of screening effect is not from the gauze used but from the distance secured. When the packing is very firm, the patient may not be able to urinate and in some cases a self-retaining catheter is used.

Tissue screening.—Still another item in screening the destructive Beta rays is the mass of tissue immediately about the radium. On the other hand, in the excavating type of cancer, radium must be used with great caution as there is not enough tissue between radium and healthy tissues and occasionally this may result in sloughing and fistulae between the rectum or bladder and the vaginal wall. The dose of radium that can be safely given must be determined by a careful study of the superficial and deep conditions present in each case and the adaptation of various screening methods to these conditions.

X-rays.—Although it is not my intention to describe X-ray treatment in great detail, yet it is essential for all gynaecologists to know the elements of the subject, because the treatment of many conditions requires combined radium and X-rays to obtain the best results.

Röntgen discovered the X-rays in 1895 and Leopold Frund of Vienna first tried them for medical treatment. Speaking generally the aim has been and still is to obtain rays of the

shortest possible wave length. The higher the voltage applied to the tube, the shorter the wave length produced. At present 220,000 volts is used as a routine, and there is hope that this may be increased in the near future to 900,000 volts. In order to produce X-rays, it is necessary to detach electrons from atoms and to project these electrons at a high velocity against a piece of metal. The higher the voltage, the greater the velocity of the electrons and the shorter the wave length of the X-rays produced.

The latest discovery on this subject, the cyclotron, by Prof. E. O. Lawrence and its use for X-ray and radium therapy opens a new vista which it is at present impossible to envisage in the proper perspective. We have here a means of producing an energy approaching 6 million volts or over, and artificially producing a number of radioactive substances which when properly applied may change the whole future of X-ray and radiotherapy.

Methods of applying radium.—There are four different ways in which radium can be applied:—

(1) *Interstitial irradiation.*—Here the radium needles are implanted into the tissues to be treated. The radium is generally contained in the platinum needles as that metal has certain advantages, in that it has a very great density and therefore a thin wall forms an effective filter and it does not oxidize easily.

(2) *Surface irradiation.*—In this technique, the applicators are generally in the form of flat plaques which are placed directly on the skin or cancer tissue and usually left in position for a comparatively short time.

(3) *Cavitary method.*—The applicator is put into one of the natural cavities of the body, the vagina or the cavity of the uterus. The advantage in this method is that no tissues are disturbed but its defect at any rate in theory, is unequal distribution of the radiation. The tissues near the applicator get a very large dose compared with those at a distance.

(4) *Distance therapy (or Telecuri therapy).*—This method of treatment has been used in a few centres only as the amount of radium necessary to obtain an effect is large and cannot be within the reach of most centres. Four grams of radium are used in a small container at a great distance from the skin. Such a quantity of radium acts in much the same way as an X-ray tube. This method of treatment is termed "Radium Bomb Therapy" and this large quantity of radium is often spoken of as a "Radium Bomb."

Radiation therapy.—Radiation therapy remains unstandardized. A great many variations in the technique of applying radium are observed. It has been observed that the ordinary method of designating dosage as milligram—hours is unsatisfactory. It ignores the variables of distance, filtration and

distribution. Most of the dosages reported varied from 4000 to 8000 mgm—hours of radium although some employ a small amount of radium over a long period of time and others a large amount of over a short period of time to arrive at the same number of mgm—hours. Roentgen ray therapy with a high voltage machine (most approximate 200 K. V.) is combined with radium therapy by most. There is considerable difference of opinion whether radium should be used first and Roentgen ray therapy later or whether the process should be reversed. Those who advocate Roentgen ray therapy first, claim that the advantages of preliminary Roentgen radiation are that it makes the cervix more movable and destroys the bulk of the growth so that it is easier to find the cervical canal when radium is inserted and allow the radium to act at a greater depth. Further advantages claimed are that local sepsis is cleared out and time is given to improve the general condition of the patient. Perhaps the nature of the case should make us decide which should be adopted first. In all cases where there is a tendency to bleeding, it is much better to use radium first with a view to control a dangerous hæmorrhage that would otherwise result later.

It would be tiresome and profitless to detail the many radium techniques prescribed. The so-called Paris or Regod technique requires a small amount of radium from 70 to 80 mgms. which is distributed in the cervical canal

against the cervix in the fornices for a long period of time. The radium is left in place for several days long enough to give a dosage of 7000 to 8000 mgm. hours. The filtration is heavy, being from 1 to 1½ millimeters of platinum. Packing and radium are removed for vaginal cleansing once a day and then re-inserted. The idea behind this method is that cancer cells are most susceptible to radiation when they are in mitosis and unless the radium is constantly present over a number of days, the mitosis phase of many cells would be missed.

A second popular technique is that in use at the Radio Hemmet, Stockholm. This method requires a larger amount of radium which is distributed in the cervical canal and against the cervix, and is left in place long enough to obtain a dose of 1500 mgm—hours at one sitting which is usually for less than 24 hours. This procedure is repeated twice at weekly intervals. The total dose is usually about 4500 mgm—hours. Occasionally the total dose is given in two sittings. In the so-called American method, a very large amount of radium is used over a short period of time. In a general way, the radiation methods in vogue involve the placing of radium throughout the cervico-uterine canal against the cervix and in the lateral vaginal fornices, the amounts of radium used varying from 50 to 150 to 200 mgms. The dosage arrived varies from 4000 to 8000 mgm—hours. In some methods, the dosage is given at one sitting; in others at several sittings, usually a week

apart. The total number of hours during which the radium is in place varies, of course, with the amount of radium used. Boxes, plaques, rubes and needles are employed to distribute the radium in the desired locations. The screening varies from 1 to 2 m.m. of lead or its equivalent to 2 m.m. of platinum. There is usually a secondary filter of rubber or aluminium. In my own series, I have adopted the technique of introducing 50 mgms. of radium and keeping it for 48 hours and repeating this once or twice and then of following up with deep X-rays. Our own method of treatment has been adopted taking into consideration certain fundamental factors, the first that the majority of cases that come for treatment are fairly advanced; secondly that the general health of the patient is below par and very often the hæmoglobin is less than 50 per cent; thirdly that in the majority of cases, vaginal sepsis is the rule and care is required in the preliminary treatment of such cases. We are convinced that the large doses of radium used at some clinics will be dangerous when adopted for such patients, and I have limited the amount of radium at any single application to 50 to 60 mgms. retained for 48 hours. Even under such limitations, there are certain complications which arise which have to be carefully regarded. The patient subjected to radium treatment must be under close observation. These complications will be dealt with a little later.

Complications and mortality of radiation therapy.—That radia-

tion therapy is not without its morbidity and mortality is becoming increasingly apparent. But it must be stated that radiation *per se* is not entirely responsible as some of the complications are due to the manipulation, incidental to placing the radium and others to the relation of the growth in a vulnerable location. Complications may be divided into two groups, those due to the direct action of the radium and those arising when pre-existing inflammation is stirred up by the radiation. Among those due to the direct action of the radium may be mentioned vesico-vaginal and recto-vaginal fistulæ, cystitis, proctitis and vaginal atresia.

During the introduction of radium, the principal danger is passing the sound or dilator through the growth into the peritoneal cavity. The sound may pass without resistance into the pouch of Douglas or into the broad ligament. When such an accident is suspected, treatment should be postponed for a week. If, however, radium is inserted afterwards severe peritonitis results. The post-operative complications met with are severe bleeding, general peritonitis, septicæmia, embolism, bladder and rectal complications. One of the commonest complications is pyrexia which may be due to a septic absorption from a large sloughing growth, pelvic cellulitis, urinary infection or broncho-pneumonia. The late complications of radiological treatment are (1) Vaginitis: this causes little trouble and results in adhesions between the vaginal walls. (2) Neuritis, a

complication which appears some months after treatment as pain in the iliac fossae radiating down the legs. (3) Pelvic cellulitis due to a low grade infection which may appear any time after treatment, and cannot by examination be differentiated from recurrence. (4) Radionecrosis may appear months or years after treatment in the form of a chronic ulcer which may take many months to heal. (5) Fistulæ may appear at any time. Although some of them may be due to radio-necrosis, most of them occur in the late stages of cancer and are probably due to the extension of the growth. (6) Apart from the incidence of sepsis the most frequent complication is proctitis.

Complications of X-ray treatment.—Two main complications are the exacerbation of any sepsis and late reaction. The sepsis is probably due to a lighting up of a mild infection of the parametrium. Late reactions are fortunately rare and apparently due to over dosage from X-rays in the first instance. It is not uncommon after the daily treatment with X-rays for the patient to suffer from nausea and vomiting. Since

X-ray treatment causes leukopænia patients are more liable to infection and any minor illness such as coryza, is liable to be more severe in a treated than in a non-treated patient. Towards the end of the treatment, mild strangury of the bladder and rectal tenasmus may be troublesome but, as a rule, these rapidly improve as the reaction subsides.

Radium complications should be prevented rather than treated. Efforts should be made to clear the local infection and general health should be improved before radium is used. Douches should be given as a preliminary. The most usual causes of death following radium therapy are peritonitis, sepsis and embolism. Hæmorrhage is an occasional cause. There are certain remote consequences which may occur as a result of radium therapy. Of these late complications, injuries to the rectum and bladder form the largest group. Acute anuria occasionally results from radiation. This may be due to oedema precipitating a complete ureteral obstruction in cases in which marked partial occlusion had already taken place due to cancer.

Abstracts.

THE SULPHONAMIDES IN WOUND INFECTIONS PROPHYLAXIS AND TREATMENT.

BRITISH WAR OFFICE MEMORANDUM

(*Lancet*, 1939, ii, Nov. 4, 996 and Nov. 11, 1039).

General principles.—1. A prophylactic course should occupy about 48 hours.

2. Courses of treatment for established or developing infections should extend over 10 days, but if not effective by this time an interval of 48 hours should be allowed before continuing treatment.

3. When an injection appears to be controlled, as judged by the temperature, small doses should be continued for a further 3—5 days in order to prevent relapses.

4. A high blood concentration is to be obtained as rapidly as possible and maintained at an effective level over a period of time. Because the drugs are rapidly excreted it is necessary, in order to maintain an effective level, to administer them FOUR-HOURLY NIGHT and DAY.

Precautions.—Certain individuals are unduly sensitive to the drugs and no evidence is yet available as to whether people suffering from shock may not be even more sensitive. If patients are severely shocked, treatment with these drugs will be better suspended until the circulation,

temperature and urinary excretion have been reestablished to reasonable levels.

REACTIONS.

Mild.—

Cyanosis.—Incidence is reduced by prohibiting sulphur containing foods and especially by the avoidance of saline purges and drastic purges. Liquid paraffin is the best laxative. Cyanosis may be temporarily dispersed by giving 0.5 to 1.0 g. per day of methylene blue by mouth. Cyanosis per se should not prohibit continuance of treatment.

Acidosis.—Treat by oral administration of sodium bicarbonate.

Drug fever.—Requires to be distinguished from fever due to recrudescence of infection. If true drug fever, omit drug.

Dermatitis.—Omit drug and induce diuresis with water or simple diuretic. May be the prelude of more serious complications. Check leucocyte count, if possible.

Dizziness, headache.—If intolerable, administer fluids freely. Check leucocyte count, if severe.

Abstracts

Leucopenia.—Negligible unless rapidly progressive to below 3,000 leucocytes per c.mm.

Haematuria (M. & B. 693 only).—Administer fluids freely.

Jaundice and neuritis.—Omit drug. Induce diuresis. (See hæmolytic anæmia.)

Serious.—

Agranulocytosis.—Occurs after 10 days or more of treatment. Incidence rare. Leucocyte count only method of diagnosis. Other symptoms: headache, deterioration of condition, fever, sore throat. Treat by transfusion and Pentnucleotide.

Hæmolytic anaemia.—Occurs early (2—4 days). Incidence rare. Mortality low. Early signs jaundice, and hæmoglobinuria. Omit drug, induce diuresis, transfuse if necessary.

Dosage.—Tablets should be powdered and administered in milk or water.

Sulphanilamide.—For PROPHYLAXIS, 4 g. (8 tablets) statim, followed by 2 g. (4 tablets) in four hours' time, followed by 1 g. (2 tablets) four-hourly night and day for 48 hours.

For TREATMENT, continue on the same lines for a maximum period of 10 days. Repeat after 48 hours, if necessary; or change over to sulphapyridine (M. & B. 693). If infection appears to be controlled during the first or later courses reduce dose to 0.5 g. (1 tablet four-hourly and continue for 3-5 days after the temperature

has become normal. During the first course of treatment if no clinical effect is evident within three days a change to sulphapyridine is recommended. If some clinical effect is obvious it is worth while pursuing the full course of sulpanilamide.

Sulphapyridine (M. & B. 693).—If vomiting is troublesome split the doses and give at shorter intervals. For PROPHYLAXIS, 3 g. (6 tablets) st., 2 g. (4 tablets) in 4 hours' time, 1 g. (2 tablets) 4-hourly night and day for 48 hours. For TREATMENT, for 10 days.

Sulphapyridine (M. & B. 693) Soluble.—Of great value when swallowing is impossible or when gastric upset prevents absorption of the oral compound. It consists of a 33 per cent solution (1 g. in 3 c.cm). Injections are best made intramuscularly, but as the solution is alkaline some reaction at the site of the needle puncture is common unless care is taken to inject deeply and avoid escape into the subcutaneous tissues. The solution may also be injected intravenously if the dose is diluted with 20 c.cm. of sterile distilled water or normal saline. The drug may also be added in suitable quantity to intravenous drop transfusions of saline or blood at the rate of 1 g. per four hours. For PROPHYLAXIS and TREATMENT, 1 g. (1 ampoule) 4-hourly night and day, the prophylactic course being completed in 48 hours. The treatment course may be continued for ten days, but it is strongly recommended that a change over to the oral

compound may be effected at the earliest opportunity. The soluble compound finds its best use in the initial stages of a course of treatment and should not be regarded as a substitute for the oral compound; it should only be used for a continuous course when oral therapy is impracticable.

Modified course (if above dosage is considered too high):—

Sulpanilamide and sulphapyridine.—For PROPHYLAXIS, total of 3 g. per diem to extend over a period of 4 days, at the rate of 1 tablet (0.5 g.) every four hours. TREATMENT, first 24 hours, total dosage 4–6 g. according to severity, but in extreme cases, such as septicæmias, up to 9 g., doses should be given 4-hourly, so that half the total dose is given during the first two administrations, and the balance equally divided between the

remaining four administrations. Second 24 hours, total dosage and spacing similar to the first day. Subsequent days, dosage to be guided by the condition of the patient, reducing the administration of the drug to 2–3 g. per diem. Total period of administration not to exceed 9 days.

It is URGED that when patients who have received prophylactic or curative treatment with these drugs are transferred from one medical unit to another CLEAR INDICATIONS SHALL BE GIVEN IN THE TRANSFER DOCUMENTS as to treatment and in particular, which drug has been employed, as well as the total dosage given. Individuals who have been found to be susceptible to sulphonamide derivatives should have this fact clearly stated on their documents so that the drugs may not again be administered later.

Association and Service Notes & News.

The last general body meeting of the Association was held at 9.30 p.m. on Thursday, the 28th December 1939 with the President, Dr. Lakshmanaswamy Mudaliar in the chair. The meeting was held after the annual dinner attended by 61 members of whom 9 were from the mofussil. The President in the first instance referred to our losses and retirements and congratulated such members as had acquired titles and academic distinctions during the previous year.

The annual report which had already been circulated among the members was then passed. The following members were declared elected as a result of counting of voting papers which had been received:

President:

Dr. A. Lakshmanaswamy
Mudaliar.

Vice-Presidents:

Dr. K. Koman Nayar,
Dr. P. Kutumbiah.

Members of the Executive Committee:—

Dr. P. V. Cherian,
" J. C. David,
" N. Mangesh Rao,
" C. Raghavachari,
" R. V. Rajam,
" P. Ramachandra Rao,
" S. Ramakrishnan,
" S. K. Sundaram and
" S. Thambiah.

At a subsequent meeting of the Executive Committee held on the 28th January 1940, Drs. J. C. David and S. K. Sundaram were appointed as Honorary Secretaries and Dr. S. Ramakrishnan as Honorary Treasurer. Dr. J. C. David was to continue to edit the journal with Dr. S. K. Sundaram as the Editorial Secretary and Drs. R. Mahadevan, C. Raghavachari, R. V. Rajam, and P. Ramachandra Rao as members of the Editorial Committee.

A number of questions were raised at the general body meeting, mainly from members from Vizagapatam. They were all thoroughly discussed. Ultimately it was generally agreed that the journal should continue to be published in the present form. A proposal was made that two of the four numbers may be edited from Vizagapatam but the Vizagapatam members were not prepared to undertake the task.

In spite of the decision of the General Body that the journal should continue as a quarterly, not one article, or case report or abstract has been received from any member. The editors have therefore been forced to combine the January number with the April issue and even so there has been considerable delay. To the extent it was avoidable. The editorial staff offer their apologies for the delay.

Questions other than affecting the journal that were raised by members from Vizagapatam concerned the recent Government orders on the filling by honorary medical officers of senior service posts and on the restriction of private practice. There were many misconceptions on these questions. It was pointed out at the meeting that there was practically not one of the grievances raised that had not already been put by the Executive Committee on behalf of the Association. It was explained that at the moment members of the service had not actually suffered any serious loss as a result of Government's commitments about the honorary scheme. The Association has on the contrary been assured by the previous Government that subject to economic considerations the existing members of the service need have no fears that their legitimate interest would be jeopardised. Copies of these orders have already been circulated to members.

There were one or two points that were raised at the meeting concerning grievances of individual members. It has always been the declared policy of the Association not to take sides in disputes between members. Grievances which involved mutual interests of members of the service must be taken up by affected members themselves. No service Association can exist as an Association if it takes sides in questions involving the interest of one member or group of members against another.

There was considerable dissatisfaction among members particu-

larly from Vizagapatam on the representations made by the Committee against orders restricting private practice. It was explained at the meeting that the main difference between the position then and the approved stand taken in memorials by the Association was in the definition of consulting practice. It was hoped at the meeting that even this difference would vanish. It still exists.

Members must be aware of a note in a daily about the withdrawal by Government of the restrictions on private practice on Government servants in employment under Local bodies. A reference to the Surgeon-General fetched the actual text of the Government Order. It then became clear that the note was misleading. What Government had withdrawn was their proposal to extend to medical officers in municipal and other local bodies' employ the restrictions on private practice already imposed on their own servants, and not the latter for a section of Government medical officers.

It is now for members to decide whether further steps are called for to seek to remove the imposition of a professional introduction even for mere consultation at the medical officer's residence or consulting room; and if they are, what they should be.

Congratulations.—We offer our heartiest felicitations to Dr. T. Bhaskara Menon, M.D., M.R.C.P. (London), D.Sc. (Edin.), on the unique honour conferred on him

by the Fellows of the Royal College of Physicians, London, by electing him as one of them. The Service has every cause to be proud of the first Service recipient of this coveted fellowship.

It is our pleasant duty too to congratulate Drs. M. D. Anantachari, M.D., C. Raghavachari, M.S., F.R.C.S., and C. K. Padmanabha Menon, M.S., on the higher degrees of their own alma mater which they have earned.

Retirements.—A number of retirements are due this year. The Service has already in the first half of the year lost by

superannuation the following officers.

1. Rao Bahadur Dr. P. Krishnaswamy.
2. Dr. V. Srinivasa Rao.
3. Dr. R. Ganapathy Iyer.
4. Dr. B. Sanjiva Rao.
5. Dr. M. S. Mangapathy Naidu.
6. Dr. K. R. Sitarama Iyengar.

It is earnestly hoped that the Association has not lost them and that such of them as are already members will take a renewed interest in the affairs of the Association and give it the benefit of their mature advice in its difficult days ahead.



PNEUMONIA

As a supporting measure in all cases of pneumonia, Antiphlogistine is a great help, no matter what other means of therapy is employed.

Antiphlogistine

Sample on request

THE DENVER CHEMICAL MANUFACTURING COMPANY
163 VARICK STREET • NEW YORK CITY

19/10/26/L



Each Fluid Drachm Represents:
 Antimony Tartrate 1/160 Gr.
 Terpene Hydrate 1/8 Gr.
 Codeina Phosphate 1/8 Gr.
 Menthol 1/24 Gr.
 Syrup Tolu 15 Min.
 Syrup Vasaka Sufficient.

A palatable preparation indicated in all kinds of Cough due to acute or chronic Bronchitis, Asthma, Throat and Pulmonary Tuberculosis, Whooping Cough and many other Lung Diseases.

GLYCODIN TERP-VASAKA

**ALEMBIC CHEMICAL WORKS Co., Ltd.,
 Bombay. Baroda. Madras. Calcutta.**

Printed at MESSRS. GORDON & CO., LTD. (Gordon Press), 768-770, Triplicane High Road, Madras,
 by R. Ravaimaniokam, the Managing Director,
 Published by Dr. J. Christdoss David, M.B.B.S., Ph.D., Madras Medical Association.

The **Madras Medical Journal**

THE OFFICIAL JOURNAL OF THE MADRAS MEDICAL ASSOCIATION

PUBLISHED QUARTERLY.

Vol. XX.	JULY AND OCTOBER 1940.	Nos. 3 & 4.
----------	------------------------	-------------

Editor:

J. C. DAVID, M.B., B.S., PH.D. (EDIN.).



RATES OF SUBSCRIPTION.

For Members of the Madras Medical
 Service on payment of an Annual Member-
 ship fee of Rs. Five only.—Free.

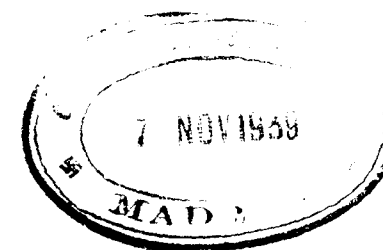
For non-Members including Medical Practi-
 tioners—Rs. Three per annum, post free.

For bona-fide Medical Students—Rs. Two
 per annum, post free.

Foreign 7sh. 6d. Post Free.

::

Single Copy Twelve Annas.



The
Madras Medical Journal.

Vol. XX.	July and October 1940.	Nos. 3 & 4.
----------	------------------------	-------------

Editor :

J. C. DAVID, M.B.B.S., Ph.D.

With the Collaboration of

R. MAHADEVAN, M.S., F.R.C.S.

C. RAGHAVACHARI, M.S., F.R.C.S. (E.)

R. V. RAJAM, M.S., M.R.C.P. (E).

P. RAMACHANDRA RAO, M.B., Ph.D.

Editorial Secretary :

S. K. SUNDARAM, B.A., M.D.

EDITORIAL NOTICE.

The Madras Medical Journal is issued quarterly, in January, April, July and October about 20th of the month. All Editorial communications, reports, books for review and exchange should ordinarily reach the Editor, The Madras Medical Journal, Dept. of Pharmacology, Medical College, Madras, one month prior to the date of issue of the Journal, preferably earlier. Original articles, clinical lectures, case reports, abstracts, Medical Society addresses are invited. Contributors of original articles will be supplied gratis with twenty reprints of papers, *if applications for the same are received by the Editor along with the contributions.*

BUSINESS NOTICE.

Subscription Rates.

To Members of the Madras Medical Service on payment of an Annual Membership fee of Rs. Five only—Free.

To non-Members including Medical Practitioners and others, Rs. Three per annum, post free.

To *bona-fide* Medical Students, Rs. Two per annum, post free.

Foreign 7sh. 6d., post free.

Rates of Advertisement.

	One Page.	Half Page.	Quarter Page
	Rs.	Rs.	Rs.
Single insertion	20	12	7
Three insertions	40	24	14
4 insertions	50	30	20
4 insertions (inside reading)	60	...	...

Discount of 33½ per cent will be given if advertisements are inserted for 3 complete years in advance.

All advertisement charges and subscriptions are payable in advance. Letters relating to the publication, sale and advertisement department should be addressed to:—

Dr. S. K. SUNDARAM,

Editorial Secretary,

9, Dr. Nair Road, Thyagarayanagar, Madras.

Copies of the Journal can be obtained at twelve annas each from Messrs. Gordon & Co., Ltd., Printers, 768-770, Triplicane, Madras, or at the Editor's Office, Medical College, Madras. Changes of address and complaints of non-receipt of Journals should be immediately communicated to the Secretary, to the above address. Matter for advertisement should reach the Editorial Secretary, at least ten days before the date of issue of the Journal.

THE MADRAS MEDICAL JOURNAL

Vol. XX.

JULY AND OCTOBER 1940.

Nos. 3 & 4.

CONTENTS.

	PAGE
1. OBSERVATIONS ON DENTAL SEPSIS—ITS RELATION TO DISEASES M. D. Ananthachari, M.D. ...	65
2. THE DIAGNOSIS OF MITRAL STENOSIS M. D. Ananthachari, M.D. ...	76
3. DIGESTIVE DISORDERS OF INFANCY AND CHILDHOOD (Lectures 1 and 2) M. B. Prabhu, M.D., M.R.C.P., M.M., S.A. ...	81
4. NICHOLAS MANUCCI (1639-1717 A. D.) A PIONEER PRIVATE PRACTITIONER OF MADRAS D. V. S. Reddy, Vizagapatam ...	100
5. ABSTRACTS FROM CURRENT MEDICAL LITERATURE ...	103
6. BRITISH EQUIVALENTS AND ALTER- NATIVES FOR FOREIGN PROPRIETARY PRODUCTS ...	130
7. EXTRACTS FROM THE REPORT OF THE CHEMICAL EXAMINER TO THE GOVERN- MENT OF MADRAS FOR 1939 ...	133
8. NOTICE (All-India Medical Conference) ...	142
9. SERVICE NEWS AND NOTES ...	143

The
Madras Medical Journal

The Journal of the Madras Medical Association.

PUBLISHED QUARTERLY.

Vol. XX.

JULY AND OCTOBER 1940.

Nos. 3 & 4

**Observations on Dental Sepsis—Its Relation to
Diseases***

M. D. ANANTHACHARI, M.D.,

Andhra Medical College, Vizagapatam.

It was the curiosity of the uninitiated which led me to enquire into the facts which prompted my colleagues to refer their patients to me for dental sepsis. It appeared to me in the short course of compulsory practice as a dentist to a large hospital, that practically all disease that 'flesh is heir to' could directly or indirectly be attributed to the so-called 'bad teeth', a condemnation made with great faith by the physician and accepted without question by the patient. In result the conclusion was irresistible that it was impossible for any one to live even a short period of the normal span of life, if so much of ill-health depended on the wholesomeness of one's

teeth. A vast majority of us are guilty of bad teeth; our lives must be a misery during the period we live and the old men we see in good health are a mystery to us as to how they managed to cheat the 'bad teeth' and live to old age. 'As there was no time for any observation, as text-book statements were gospel truths to be accepted without question, as it was easy to hang the cause of one's failure to cure one's patients to the peg of conditions not easily eradicable, it was little wonder that it took a very long time to learn by trial and error that what was thought to be cause and effect were totally unrelated. Many teeth were shed before it was realised that extraction of

* Lecture delivered before the Vizagapatam Branch of the Indian Medical Association on 23-9-39.

teeth cannot cure all conditions. Many tonsils were removed on the mere plea of their visibility and the fact of the possibility of life without them. It was soon realised by the occasional faithless patient and his all-wise doctor that one did carry on long in life and in spite of the grave and ominous prognostications foreshadowed on account of 'bad teeth'.

"It is unquestionable that unreasoning adherence to the doctrine of focal infection has perpetrated a surgical debauch from which we are now sobering" (Strecker). "Few concepts have so captured the imaginations of the medical profession for so long as the theory of focal infection" (Reimann). According to one authority, 'The time has come to examine the evidence on which this theory of focal infection has been based and whether the idea is the truth, the whole truth and nothing but the truth for whatever germ of truth there may be in it and however comforting and gratifying for the searcher after cause and effect, the whole thing has been grossly abused' (Evans 1933).

In the course of my experience, the variety of diseases that have been referred to me for the eradication of focal sepsis in the teeth (I could never understand why only the teeth) have varied from insanity and insomnia to congenital deafness and club foot. It may be adduced, as the experience of some, that removal of septic teeth has been followed by relief of pain in another part. These

spectacular results are exceptional and as scientific proof of cause and effect are no stronger than that of the familiar relief of toothache on approaching the dentist's doorstep. It is unfortunate that while weight is given to cases in which dental treatment has cured a patient here and there, the many cases where the removal of dental focal sepsis has uninfluenced the general condition for which such treatment was undertaken should remain unrecorded. 'So long as something called theory is provided as an excuse for something called practice no one seems to mind whether the theory is tenable or the practice practical. It often happens that the patient's doctor having failed to cure the condition he is facing by the accepted methods of good bedside manner, a certain amount of physic and an overwhelming confidence in nature, begins to investigate possible sources of infection. He will begin at one end of the body or other according to taste. Then floating peacefully along the alimentary canal he will cast his suspicious eye on any removable organ. Should he begin his travels on the lower or inferior extremity he will have removed such negligible things as the uterus, the colon, the appendix, gall-bladder and tonsil before he reaches the teeth. This of course gives the patient a certain respite before being fitted with dentures'. But should the thorough medico begin his pilgrimage from the oral extremity, the patient is forthwith sent to the dentist.' (Samson 1938). The dentist may

radiograph the teeth so as to postpone the moment when he is going to condemn them. The X-ray films usually throw a certain shadow of doubt on some or all the teeth and the suggestion is made that the patient should lose them though there is no certainty that the disease will be cured, as a result of such a procedure.

"In most of the cases in which the dentist's advice is sought some general condition is also present. The doctor in charge of the case, and often the patient as well, may start with a bias in favour of the view that any dental sepsis present may be the causative element in the patient's ill-health. Often, to the patient, the dental treatment presents itself as a specific treatment for his ill-health." (Pitts, 1931). This of course is unfortunate. It is as likely as not, that he will be none the better after treatment. Let me quote the following amusing incident.

Professor Laycock, an eminent Physician and at one time Professor of Medicine in the University (Edinburgh) when paying a ward visit drew the attention of the students to a patient's teeth, pointing out to them that such teeth indicated that the patient was of, what was then called 'the rheumatic diathesis.' Thereupon, the patient, much to the amusement of the class took out his dentures—dentures were seldom worn by the hospital patients in those days—and handed them to the Professor asking him whether he would like to look at them near at hand.

Let me discuss how far oral sepsis influences pathological changes in other organs of the body and the diseases which have been frequently attributed to oral sepsis.

Rheumatism and arthritis.—By rheumatism I refer to such conditions as go by the names fibrositis, fascitis, periarticular fibrosis, etc. The arthritis is usually an osteoarthritis or rheumatoid arthritis. It is a well known fact that these conditions are commoner in elderly people and in no case has any infecting organism been demonstrated in the *locus morbis* of the same nature, as the one in the focal septic area. It is often theorised that it is the toxins that are the cause of the pain in the joint and fibrous tissue. The bony articular changes in the joints could not well be attributed to the organisms of low virulence of the mouth. The changes are dystrophy, rarefaction and eburnation with production of osteophytic outgrowths. The signs of inflammation are, if any, very little, to account for the very gross anatomical changes. Could it not be possible that the same cause that induced arthritic changes in the bone ends of the articulation also produced rarefying osteitis of the alveolar margin with loss of support for the teeth and a lack of resistance to infection of gum tissue and thus produced pyorrhœa alveolaris as it produced the arthritis? Roys (1938) formulates a theory in which he places greater emphasis on an initial degeneration in the alveolar bone due to what he

terms precocious senility as the cause of pyorrhœa alveolaris. He asserts that such local causes as local irritation, mechanical stress, infection and faulty oral hygiene can produce gingivitis and not pyorrhœa without this precocious senile degeneration.

Gastric Ulcers.—Pyorrhœa alveolaris is associated so often with gastric ulcer, that it is usually taken for granted that the swallowing of pus from the pyorrhœal pockets plays a large part in the formation of the ulcer. Most of the organisms are saprophytic and the condition of the stomach in these cases is one of hyperchlorhydria. It is being increasingly realised that the cause of the stomach ulcer resides not locally but in the hypothalamus. Dodds has shown that injection of pituitary extracts causes intensive gastric hyperæmia and erosion. It has frequently been observed and remarked by Cushing that cases of brain tumour in the region of the hypothalamus have died after successful operation, of acute perforating ulcers of the stomach. Daniel T. Davis (1933) as a result of investigation on gastric ulcers concluded that the causes in many cases are mental and not physical, that the business man's worry initiates or aggravates the ulcer pain whereas a holiday causes a rapid disappearance of symptoms and healing of even long standing ulcers. He goes on to make the following interesting remarks.

"It has often been stated that all septic foci should be eradica-

ted as an essential part of medical treatment. There is really no experimental proof of this statement. For the past five years I have deliberately withheld any advice regarding attention to septic foci and since relief of symptoms and healing of craters occurred in such a high proportion of cases, most of whom come from the out-patient class, among whom oral sepsis is certainly not uncommon, it is difficult to believe that sepsis plays any part in the initiation of the peptic ulcer." Broderick's theory of pyorrhœa alveolaris is that it is due to endocrine disturbance. According to him the metabolism is upset in the direction of calcium saturation bringing about a chronic alkalosis causing a diminution of the carbon-di-oxide content of the blood leading to a deposition of tartar round the teeth which is one of the local exciting causes of pyorrhœa alveolaris. These are present in conditions of hyperchlorhydria. There is an excess of a base as a result of the passing out of the chlorine ion in the acid, and consequently, he thinks, that the association of the two conditions is not one of cause and effect, but one of common origin. Recently as a result of an enquiry into the after history of 234 out-patients in whom all teeth had been removed for various causes, Vaizey and Clarke-Kennedy (1939) question the widely accepted relation between dental sepsis and dyspepsia and rheumatism.

Pernicious anæmia.—The concept of oral sepsis accounting

for the symptoms of pernicious anæmia is due to Hunter. He postulated that without the acid barrier in the stomach the havoc caused by swallowed organisms from the mouth resulted in the production of a hæmolytic toxin to account for the blood changes and a neurotoxin to explain away the nervous symptoms. At the present day, injections of campolon or other products of liver extract are short of miraculous in the effect they produce on the blood condition, and one is surprised how long we clung with the faith of fanatics to a theory without reasoning. To-day no attempt is made to treat separately the oral condition and the existence of "bad teeth" is forgotten altogether by Wilkinson (1936) as an etiological factor. The pathogenesis of this disease has thus dramatically changed from the hæmolytic streptococcus of "focal sepsis" to deficiency of food factors and during the time it dominated treatment, served as a convenient cloak for ignorance.

The diseases that have been attributed to focal sepsis are legion. Not one of the systems have escaped attention. Diseases of the alimentary tract such as parotitis, pharyngitis, peptic ulcer, gall-bladder diseases, appendicitis have been mentioned. For diseases of the skin such as eczema and psoriasis and of the eye such as iritis, irido-cyclitis and optic neuritis, the blame has been thrown on the teeth. The most fantastic of such associations has been the claim of Cotton (1921) that an important role is

played by dental sepsis in the production of various forms of insanity.

The above list is sufficient to show that the teeth have been blamed in many of these conditions either as the chief villain of the piece or as an equally culpable accessory. "The seed having been sown, the conception of oral sepsis as an etiological factor has so impressed itself on the medical mind that hundreds of thousands of teeth have been sacrificed quite unnecessarily on the score that they were easily removable, and yet more easily replaced by prosthesis. It must be confessed that the teeth often receive short shrift largely because of the belief that the dentist can be relied on to provide adequate substitutes and because the teeth when weighed in the scales against most of the general conditions supposed to be caused by dental sepsis appear insignificant in value" (Pitts, 1921). This can be no argument. "No body would deny it possible to save a patient's life by removing his infected appendix. But because it is removable without loss of life and so could be removed when one has opened the abdomen for other reasons is no justification. When advanced surgery showed that the human body is composed of many removable parts, man was exposed to the danger of being left only with his skull and though to many it may be the least useful portion of their anatomy such a position nevertheless is precarious" (Samson 1938). "You

cannot reduce a man to his least common denominator without giving very good reasons for doing so. Text-books were written to prove that removal of removable parts, particularly if they were slightly infected, cured diseases in other parts, not so easily dispensed with. Gall-bladders were removed to cure stomachs which must stay, appendices were removed to save legs that were necessary and uterine appendages were removed to mobilise joints which were immovable. So on and so on till there was nothing left to the doctor but faith, to the surgeon hope and for the patient charity." (Samson 1938).

Dental sepsis has been mentioned as a causal factor in many diseases, on evidence bacteriological, experimental and clinical all of which have been subjected to criticism. Even the result of treatment on an empirical basis cannot be said to be unequivocal.

Let us consider this focal infection. What is it? Have we a clear conception of the condition? What is its pathology? How is it that it lurks so quietly and yet is the public enemy No. 1, it is made out to be? What conception is visualised when such terms as "bad teeth" by the lay and more pedantically "focal sepsis" by the profession are used? There are two conditions of the teeth which could be brought under focal sepsis; pyorrhœa alveolaris and apical granuloma.

Pyorrhœa Alveolaris.—This is a condition regarding the defini-

tion of which there is considerable difference of opinion. Its aliases are literally a legion, more than a hundred names having been applied to it. Briefly described, it is a condition of the gingival tissues—gum, periodontal membrane alveolar bone, whereby, on account of chronic inflammation, pus is seen exuding from the gum-margin hence the name pyorrhœa though it is quite possible that the condition may exist without discharge of any pus at all. Normally the gum is adherent to the neck of the teeth, like a purse string; when there is disease, infection and inflammation result in absorption of the bone, shallowing of the sockets with ultimate shedding of the teeth.

Apical granuloma.—This is also called apical abscess and has been recently drafted into the literature, after the advent of X-rays into dentistry. Often in X-ray pictures of teeth, there was seen a transparency of bone around apices of roots of the teeth and it was demonstrated that the transparency was due to decalcification of the bone and the formation of an abscess or of granulation tissue. The idea was readily seized upon that these covert and concealed areas were more dangerous than the overt and revealed pyorrhœa pockets. What could be more easy of comprehension than that with each movement of mastication this rubber-like cushion at the apex of the tooth would be crushed and released readily through its thin walled blood-vessels a charge of bacteria to be widely

disseminated? These are the types of focal sepsis that are so widely accused. Let us consider in detail their genius for the widespread evil that they are accused of.

Pyorrhœa is a continuous discharge of pus. How could it get into circulation for widespread systematic broadcast? The organisms or their elaborated products have to be swallowed and they have not any ready access to circulation. If they are swallowed there is the gastric barrier and the danger is only in 4 per cent of cases (Izod Bennet) the normal percentage of achlorhydrics. We are aware of so many individuals whose general health has not been affected by it in spite of long continued pyorrhœa. Have not our old people lived to a ripe age and how many of them could be pointed out as having observed oral hygiene throughout their lives? Seeing that pyorrhœa is so common, according to existing concept of focal sepsis an individual living to an old age should be a miracle. Is it not within the experience of surgeons that there are instances where the discharge of pus from the ear continues over long periods and still the individuals grow up? I have known an instance where chronic otorrhœa lasted 7 years and that individual was not any less healthy than his brother without it. Chronic sinuses of surgical origin from deep seated bone infection or those of tubercular origin are not accused of 'focal sepsis', at least so long as the discharge from them is free. Constitutional symptoms are well

marked and well known to be present if there be only a tiny quantity of pus or other septic material under tension and it is equally well known that relief of symptoms is prompt on release of this tension. For this reason the more evident and free the discharge of pus in pyorrhœa cases the less should it cause general disturbance. It might be said that the trauma of mastication may be expected to open vascular channels in the inflammatory areas for septic material to escape into circulation. Okell and Elliott (1935) have demonstrated that during extraction of teeth, there is a shower of micro-organisms into the circulation, shown by culture. This infection of blood is said to be severe when there has been considerable rocking of the teeth before extraction. But how is it that the body is not immunised to this infection, seeing that inoculation is constant and in graded doses? Why should the granulation barrier fail only in this instance? Does this not indicate that this chronic inflammatory condition of the gum tissues has persisted for reasons similar to those adduced for the non-healing of a chronic sinus? Is it not possible that the vitality of the individual may have been lowered and for that reason the normal trauma of mastication is followed by chronicity and not cure? Could it not be that the systemic disease is the cause and pyorrhœa the effect, localised to the mouth because of the constancy of the trauma during mastication? It is a well known fact that oral injuries heal rapidly and why

should the gum tissue alone be free from this property? It all shows that we are wrong in blaming the teeth whereas the fault actually lies elsewhere. Whether pyorrhœa is a local manifestation of a systemic disease or whether it is a local disease with systemic manifestations is a point on which there has been no end of argument and modern trend is towards the former view. A commission appointed by the Société de Chirurgie to investigate the matter held that the disease was not due to local causes but was rather a manifestation of constitutional disturbances (Bunting 1927).

Periapical infection or granuloma is only a radiological appearance with rarely any clinical manifestations. We have no means of knowing the nature of the pathological changes that have produced rarefaction of bone around the apex of the teeth. In as much as these areas are seen round pulpless teeth it is argued that infection must precede the destruction of bone and the formation of granulation tissue. It is hence regarded that apical rarefactions are evidence of dental sepsis. Weston Price (1924) has made a few interesting observations concerning dental granuloma in relation to infection. He considers that changes noted round the apical areas are to be regarded as expressions of the reacting characteristics of the host rather than as direct effects of invading bacteria. The granuloma should not be looked

on as a reservoir of infection but rather as a barrier to infection, a quarantine situated near the tooth itself. He has based his conclusions on elaborate experimental evidence and his point of view is at least one which deserves careful consideration.

Are we not aware of general diseases which manifest themselves in the gums—leukæmias, thrombocytopenia, granulopœnia, toxæmic states such as uræmia and diabetes, chronic poisoning with substances such as mercury, lead, phosphorous and bismuth which lead to gingivitis, ulceration, destruction and denudation of the teeth? We often overlook and lose sight of what is within the experience of every one of us that the earliest manifestation of the onset of an acute infection is a peculiar taste and feeling in the mouth and gums, long before any change could be demonstrated by gross examination. During the incubation period of many acute infective fevers there is much that is experienced by the patient and little that is manifest and demonstrable to the physician. In these cases there is some subtle change in the condition of the oral mucosa which is able to attract the notice of the patient and tells him that it is a departure from normal and when he gives expression to it we as scientific, laboratory-fed medical men are apt to scoff and put it down to the imagination of the patient. I consider that the mucous membrane of the mouth is so delicate that it is able to register humoral changes of a

general nature. If that be so is it to be wondered if pyorrhœa is mentioned as an early manifestation of a systemic disorder? If ordinary saprophytic organisms invade the skin and give rise to septic processes, do we not look for a constitutional disorder to account for it such as diabetes and albuminuria? Why then should we not think on similar lines when we find the ordinary saprophytic organisms which are in every mouth begin to invade the tissues which are known to be highly immune and extremely resistant to infection? Teleologically considered, if ordinary masticatory stress and strain were to result in definite injury and disease, there could be no animal life possible. Food that has to be bitten and chewed will be an anathema and menace to life.

Consequently the view is put forward for consideration that the disease in the mouth is an early manifestation of a disturbed mechanism by reason of which the normal immunological and resistive powers of the mucous membrane are diminished and disease process given an impetus to progress. In this connection Broderick's (1937) view is important. He considers that pyorrhœa is a manifestation of disordered ionic constitution of the body resulting either in alkalosis or excess of OH over H ions or K over Ca ion in the body when pyorrhœa is manifested or of acidity when caries is manifested. These factors are supposed to be due to changes in the controlling sympathetico-parasympathetic balance. He

explains the concomitance of pyorrhœa and peptic ulcer as being due to the same cause—the excessive stimulation of the vagus. Zondek observed that the action of endocrines is modified at the point of their action by the prevailing ionic constitution of the tissues at the point and he gives a few examples of such action. If vitamin deficiencies are associated with lack of resistance to infection particularly the mucous barriers of the body, it is understandable in the light of Zondek's observation on endocrines, how such a local manifestation as pyorrhœa can be regarded as an early indication of widespread tissue humoral ionic imbalance. We do not know how vitamins act. It might be that the enormous differences in the effective doses that are clinically recognised between one case and another are only manifestation of the differences in ionic constitution in different individuals.

The clinical course of pyorrhœa alveolaris is one of many ups and downs and the condition at any time in an expression of dominance of one or other of the two factors—tissue invasion and tissue resistance, a fight that may last through one's life-time. A period when the disease seems to have been arrested is followed by recrudescence. It has been my observation that many of the "sufferers" from the "effects" of pyorrhœa are individuals who are extremely conscious of their disability and who take considerable pains and follow as ritual the tenets of oral hygiene. I

have heard a few of them attribute the mental worry that they suffer from, to the subtle poison of pyorrhœa. Many of these cases are a psychological study. The higher the intellectual level of the patient the more acutely he becomes conscious of the fact that his mouth is septic, and the propagandic literature he avidly swallows makes him feel that his mouth is a real cesspit. He is afraid of eating and drinking with any freedom and he is soon deprived of even the desire for food which again he attributes to dyspepsia, following on his pyorrhœa. He plies his tooth brush with a vigour worthy of better results and skips from one dentifrice to another, each time to something more strongly antiseptic, with the inevitable result that the damage to his gums perpetuates the progress of his malady. The remorseless course of the disease seems to justify the radical treatment of total extraction. Is it any wonder that these patients terminate as physical and psychological wrecks? In favourable cases the extraction of the teeth may be the welcome break in the vicious circle; the mind being set at rest, the individual begins to indulge in what food his artificial denture would permit; he soon feels the effects of improved nourishment; become a sane and sound being and begins to preach his new found faith; condemns pyorrhœa as pernicious and extols extraction of teeth as a panacea. If on the contrary advice and adoption of extraction fails to cure some of the maladies which tradition in medicine has

attributed to focal sepsis, he soon becomes disillusioned and finds that the most material change is in his pass book. And strangely enough despite the persistence of the disease for which the teeth have been lost these still have faith! Such is the effect of scientific propaganda on focal sepsis! If this type of patient is reassured that his pyorrhœa is as natural as a septic wound which has not healed because of constitutional disability, that the phobia of swallowing septic organism has no basis as these very same organisms are found universally, that the God-given gastric-barrier is sufficiently safe to prevent any harm from much swallowing, he would most likely begin to take his normal food and put his teeth to physiological use with the result that he will not suffer from any dietetic deficiency, his mouth will get the benefit of physiological mastication and he will soon have the necessary feeling of well-being in the body optimistically to scoff at any harm pyorrhœa could do him.

We would do well in many of these cases, if instead of pointing to the teeth as the bane of human happiness for all time, we give the assurance that the condition is merely a sign for improving the general health. There would then be less possibility of our missing the woods in looking for the trees.

It is being increasingly realised that the mind has a very definite control over the constitution of the body and the psychological

origin of many diseases is being increasingly recognised. Peptic ulcer, ulcerative colitis, mucomembranous colic, osteo-arthritis, essential hypertension and seborrhœa are a few diseases where psychological therapy is finding favour. One is inclined to agree with Broderick (1937); "As the dermatologist is beginning to realise that urticaria and seborrhœa are not essentially diseases of the skin; as the gynæcologist is beginning to appreciate that dysmenorrhœa, menorrhagia and amenorrhœa are not exclusively diseases of the uterus or of the ovaries; as the orthopædist is beginning to understand that arthritis is not primarily a disease of the joints; as the internist now understands that gastric and duodenal ulcers and diabetes are not diseases fundamentally of the stomach and pancreas; the neurologist must see that migraine, epilepsy and melancholia do not depend mainly on brain dysfunction; the laryngologist that enlarged tonsils, adenoid growth and nasal catarrh are not diseases of the nose and throat;

the ophthalmologist that glaucoma and cataract are not diseases primarily of the eyes; so must the dentist come to understand that dental caries and pyorrhœa are not diseases of the teeth. All these conditions are symptoms of generalised disturbance based on diatheses which means when sufficiently dissected, vegetative imbalance plus some environmental strain or else end products of diseases, the consequence of long continued malfunction dependent on the same circumstance".

I should be satisfied if I have succeeded in bringing to your mind that our knowledge of many disease processes is not sufficiently profound for us to be dogmatic in asserting that 'focal sepsis' in the teeth is the cause of many pathological conditions which we are unable to cure; that in our attempts to help our patients we should view the body as a whole and not in removable parts and lastly that the influence of mind over matter should not be forgotten in our search for cause and effect.

REFERENCES.

- Broderick, F. W.—(1937) *Brit. Med. J.* i, 300.
 Broderick, F. W.—(1937) *Dent. Mag. and Oral Topics* LIV 6: 510.
 Cotton, H. A.—(1921) Quoted by Pitts, *The Science and Practice of Dental Surgery*, 1931, Vol. II Oxford Med. Public. London, p 1409.
 Davies, Daniel, T.—(1933) *Lancet*, ii, 1474.
 Izod Bennett, T.—(1925) The stomach and upper alimentary canal in health and disease quoted by Pitts.
 Jamieson Evans, J.—(1933) *Lancet*, ii, 1474.
 Oakell and Elliott.—(1935) *Lancet*, ii, 869.
 Reimann, H. A.—(1936) *Arch. Int. Med.* 58: No. 2, 356.
 Roys, Maurice.—(1918) *Dental Cosmos*, Aug 659, quoted by Bunting in *Text-Book of Operative Dentistry* by Ward, 1927, Henry Kimpton, London.
 Samson, E.—(1938) *Dental Mag. and Oral Topics*. 55: 2 and 3 p. 107 and 210.
 Srtecker, E. A.—(1935) *Practitioner's Library*, Vol. IX, 1127.
 Voizey, J. M. and Clark-Kennedy, A. E.—(1939) *Brit. Med. Jour.* i, 1263.

The Diagnosis of Mitral Stenosis

M. D. ANANTHACHARI, M.D.,

Andhra Medical College, Vizagapatam.

Of all the valvular diseases, the commonest is mitral stenosis and but for its elusiveness in diagnosis I should think that the percentage of mitral stenosis to all cardio vascular conditions should be even greater. That it trips even the most experienced in diagnosis should be within the knowledge of every one whose diagnoses have been put to the test of post-mortem verification. An investigation into why so common a disease should at all give room for failure correctly to diagnose should go a long way to help the unwary to be mindful of its presence.

There are many reasons why mitral stenosis fails to be recognised. The established disease with typical signs is one of the easiest to diagnose with certainty. Such cases are never missed and are diagnosed with the hand alone over the precordium. It is only in the very early and in the advanced and late stages that this disease is easily missed.

What then are the reasons for this? The disease may be missed because (1) no complaint is made to draw attention to the heart; (2) in the very early stages its manifestations are too inconspicuous as deviations from the

normal that crude methods of diagnosis fail to recognise them; (3) the signs and symptoms which are recognised as being abnormal are not up to known types and are therefore attributed to some other cause than mitral stenosis; (4) examination has been too inadequate; (5) in the late stages the typical signs and symptoms are overshadowed by others from such conditions as heart failure, etc.; (6) dependence is placed solely on non-clinical examinations.

Let us discuss these reasons *seriatim* and see what signs and symptoms should put one on the alert for the discovery of this condition.

(a) *Lack of history pointing to the heart.*—This should never be a reason for failure to diagnose mitral stenosis in the medical wards. A history of tonsillitis and rheumatism is so invariably associated with mitral diseases that it should be considered criminal neglect if after such a history one does not bestow careful attention to the heart.

It should be the invariable rule to examine the heart of every choreic patient.

A history of hæmoptysis or cough on slight exertion should

The Diagnosis of Mitral Stenosis

77

throw suspicion necessitating a searching examination of the heart in a very young individual.

Because an individual can or does engage himself in strenuous physical exertion, it should not be surmised that there could be nothing wrong with his heart; so perfect can the compensation be, that many cardiacs have won distinction in athletics.

Embolic phenomena such as hemiplegia, thrombosis or peripheral gangrene in young persons should arouse suspicion.

(b) *Early signs.*—There are many early signs which to the astute examiner are pointers towards a more careful examination.

A change in the first sound of the heart so that it becomes sharp and sudden in character, 'slapping' as it is frequently termed is common.

This is said to be due to the relatively small amount of blood in the ventricle on which the heart has to contract. When this sign is present the patient should be under observation for sometime until some more definite signs are forthcoming.

A systolic murmur is so rarely associated with mitral stenosis in the minds of many that the diagnosis is not made. This may happen to be the only obvious murmur either in the very early or the very late cases. If there be only a systolic murmur at the apex of a young individual, every attempt

should be made to examine him in all positions; erect, recumbent and turned to the left and after exertion, to see if any other murmur is 'brought out' by such procedures. This should invariably be done if there be a suspicious history of rheumatism. "It is the clinical experience of everybody of encountering mitral stenosis at necropsy even though one is unable to hear a diastolic murmur on careful examination. When the left ventricle is very large on account of regurgitation or other complication; the diastolic murmur of mitral stenosis may be heard only beyond the left anterior axillary line and several times the diagnosis is missed because auscultation is not carried far enough to the left" (Fishberg).

The presence of diastolic murmur near the apex or the accentuation of the pulmonary second sound as compared with the aortic second which is hardly audible should arouse suspicion of mitral stenosis.

(c) *Mitral signs attributed to some other disease.*—This ordinarily should not occur but the flint murmur of aortic insufficiency is a point in question. The distinction may not be easy especially in view of the fact that both aortic regurgitation and mitral stenosis may coexist. 'Is the rumbling apical murmur in the middle of the diastole or presystolic accentuation characteristic of mitral stenosis? A similar sound is also heard in aortic regurgitation and anæmia.

Bland, White and Jones found that out of 68 cases with mitral diastolic murmurs 28 revealed at necropsy either no deformity or at the most minimal thickening of the free edge of the mitral flaps. The writer (Fishberg) has also repeatedly heard mitral diastolic murmurs within a few months of the onset of apparently initial attacks of rheumatic fevers before sufficient time has elapsed for the development of significant mitral stenosis. Bland and his associates believe that these murmurs result, in some way as yet entirely obscure, from the dilatation of the left ventricle which was present in all their cases. But this seems scarcely compatible with the absence of similar murmurs in the left ventricular dilatation of hypertension or arteriosclerosis. To the writer (Fishberg) it would seem more likely, though as yet without proof, that the murmur may be due to early rheumatic changes in the mitral curtain which diminish their flexibility so that the auriculo-ventricular blood current sets them into audible vibration.' (Fishberg).

(d) *Inadequate examination.*—This should never be a cause of failure to diagnose when one of the 'clue' signs or symptoms is present.

(e) *Late stages of mitral stenosis.*—When ascites, gross dilatation of the heart to both right and left and dyspnoea are present it may not be possible to diagnose the original lesion of the failure as mitral stenosis. The presystolic murmur may be

absent with the onset of fibrillation and the only signs on auscultation may be a systolic murmur. But even here, if the subject is a young individual with a rheumatic history, the presence of fibrillation should be a pointer in the right direction, though absolute diagnosis may only be possible when the condition has improved under treatment. Similar reasons apply to failure to diagnose a patient who is moribund and who cannot be adequately examined.

(f) *X-ray examination of the heart.*—Sir James MacKenzie's statement whether an X-ray examination of the heart has ever thrown the slightest light on any cardiac condition is no longer tenable. On the contrary, the time has come when the heart should be as readily radiographed as the bones are when there is even a suspicion of disease with reference to them. So characteristic is the appearance of a mitral heart in the antero-posterior picture that the term 'mitralisation' has become current in medical parlance, particularly in the description of the X-ray silhouette of the heart.

The normal left border of the heart shows a depression just below the aortic knob which is occupied by the pulmonary artery, the pulmonary conus and the left auricular appendix. The contour in the area of the conus is usually concave so that this part of the heart shadow has been termed 'the waist line' of the heart. In certain conditions of right ventricular dilatation

particularly of the variety described by Kirsch as the myogenous, the right heart dilatation first manifests itself in the 'out flow' track of the ventricle; i.e., the area of the 'pulmonary conus' becomes dilated and tends to fill up the 'waist' of the heart. In addition, the associated rotation of the heart over a vertical axis in cases of right sided hypertrophy or dilatation brings the 'conus' more prominently to the 'left border' of the heart. Thus it is that the left border of the heart shadow tends to assume a straight line from the aortic knob to the apex. This is termed 'mitralisation'.

It should be remembered that this is a late sign of mitral disease since this appearance shows itself only after the effects of back pressure are manifest on the right heart. Before this can happen there are many stages which have to be passed through. The primary effect of the difficulty of the blood passing through the mitral orifice is felt in the left auricle itself. It will increase its capacity and it will be some time before the auricle 'yields' and dilates to accommodate the increased quantity of blood. This is an early stage, and if the dilatation of the left auricle can be shown on X-ray, we should have an early diagnostic aid. The left auricle in increasing in size encroaches on the retrocardiac space which fact can well be brought out by a right anterior oblique view with barium in the oesophagus.

The next stage is when the tributaries of the pulmonary

veins are dilated to accommodate the blood that is dammed back from the auricle. This may be seen in the X-ray of the lung fields as an intensification of the root shadows.

It is only at a still later stage that the right ventricle hypertrophies and dilates and shows up a mitralisation of the heart shadow.

In the very late stages or in conditions where weakness of the auricular wall leads to aneurysmal dilatation, the right border of the heart shadow is formed by the dilated left auricle.

Since mitralisation of the heart shadow can occur in many conditions other than mitral disease, confirmation can only come radioscopically from demonstration of the dilatation of the left auricle.

Thus it will be seen that the evolution of the clinically recognisable mitral stenosis is through many stages which may spread out over a period varying from a few years to practically a life time. Recognition or otherwise of the condition depends therefore on the availability of the signs at that time. Most of all, of importance is the knowledge of the fact that there is the necessity of of suspecting the disease.

In summing up, it may be said that mitral stenosis passes through the following stages, from the early to the late, clinically.

1. The earliest, with the history of rheumatic fever only and no signs or symptoms.
2. Slapping first sound at the apex, systolic murmur or an occasional localised diastolic murmur; the definite localisation of the diastolic murmur is significant.
3. Crescendo diastolic or presystolic murmur with accentuation before the systole.
4. Diastolic thrill and definite presystolic murmur at the mitral area.
5. Clinical symptoms and increased size of the left auricle.
6. Accentuation of the pulmonary second sound while the aortic is hardly audible and enlarged hilar shadows.
7. Mitralisation of the heart, shadow and enlargement of the right ventricle.
8. Dilatation (aneurysmal) of the left auricle; enlarged heart shadow.
9. Auricular fibrillation, engorgement of the veins enlargement of the liver, ascites, oedema of the feet, systolic murmur or only the second sound at the apex, etc., established heart failure of the advanced type.

THE REAL THING

A patient calls you late at night
And says that Johnny's dying;
And you must dress and hurry out—
(The day had been so trying);
But after driving miles through rain
To find it's just a belly pain,
You know darn well you can't complain—
It's not unusual.

You thought you'd splurge that New
Year's Eve;
A real celebration!
(The theatre tickets, wife's new gown,
The table reservation);
But as you donned your coat and hat
A colleague rings: "We need you stat
For operation." Well, that's that;
It's not unusual.

One day a patient saunters in,
Apparently quite healthy.
He shows a fat purse with a grin,
And seems to be quite wealthy.
Out tumble greenbacks in a flock,
The likes of which cause you a shock,
And he says: "Let me pay you, doc."
—HELL, THAT'S A MIRACLE!
(From J. A. M. A.)



Digestive Disorders of Infancy and Childhood.

M. B. PRABHU, M.D., M.R.C.P. (Ed.) M.M., S.A., London.

(From the Government Hospital for Women and Children, Madras).

LECTURE I.

The subject I have selected is "Clinical studies of digestive disorders in infancy and childhood". In these days when more and more reliance is placed on the work of the laboratories, clinical observation is tending to receive less importance. What are clinical studies except the signs that the patient exhibits, in health and illness, and which are but Nature's revelations, no less reliable than those gleaned by other methods. At the bed side, we see the reaction of the patient to disease just as in the laboratories we learn the reaction of the different tissue fluids. To the observant eye, these natural indications are as useful as the assistance derived from other sources. We are losing the habit of clinical observation. Rickets was accurately described by Glisson as early as 1650 and his original description has not been excelled to this day. The theories and findings about rickets have undergone considerable change but his description stands. In the field of Neurology the clinical signs, like Argyle—Robertson Pupil and the Babinsky's reflex have contributed invaluable,

able, may I say, indispensable assistance. To the physician, the necessary laboratory and technical aids are not always available but clinical manifestations of disease are there to help him to diagnose or understand the case.

But it should be borne in mind that the bed-side study of the patient requires the same degree of diligence as the studies in other methods. Only then will a mass of useful evidence be revealed to the physician. In the words of William Osler, philosopher and physician, "As clinical observers we study the experiments which Nature makes upon our fellow-creatures. These experiments, however, in striking contrast to those of the laboratory lack exactness, possessing as they do a variability, at once a despair and a delight, the despair of those who look for nothing but fixed laws in an art which is still deep in the sloughs of empiricism, the delight of those who find in it an expression of a universal law, transcending even scorning the petty accuracy of test tube and balance, the law that in man,

the measure of all things mutability, variability and mobility are the very marrow of his being".

Digestive disturbances are, here in South India, by far the commonest disorders of infancy and childhood. This is because during intra-uterine life, the child gets all the necessary requirements through the placenta and the digestive processes are lying dormant. At birth, all this is suddenly changed and the infant is thrown on its own resources, to take the required amount of food and digest it. Moreover, its requirements are relatively greater than in later life to meet the demands of growth and activity because we know the new-born infant requires per day 50 calories of food per pound body weight against the adult requirements of 20 calories per pound body weight. These digestive disorders are influenced by dietetic and climatic differences and in the tropics exhibit characteristics or peculiarities of their own.

These lectures are based mainly on clinical studies of children in the Government Hospital for Women and Children, Madras, where the average attendance of children is over 1000 in the In-patients and 21,000 in the Out-patients in a year.

Coming now to individual digestive disorders, let us first take into consideration the subject of *Thrush*. Who is there amongst us, who is not familiar with this disease. So common is it in infancy and so simple seems

to be its treatment with the result that this subject has not received adequate attention.

Thrush.

Is a form of stomatitis common in the new-born. It is a parasitic disease generally caused by the fungus, *Saccharomyces albicans*. It is relatively more common during the first 8 weeks of life and then the frequency decreases rapidly. It is more frequently found in hospitals than in households. It is believed that it is more common in children who are artificially fed but our experience in the Out-patient Department of the Government Hospital for Women and Children on the Children's side is that it is found as frequently in the breast-fed infants, particularly in the premature ones.

Pathology of the disease.—The spores of the fungus lodge between the epithelial cells of the mucous membrane of the tongue and cheek and gradually separate it in different layers. The disease spreads along the surface of the tongue to the inside of the lips and cheeks and frequently extends to the fauces. How it infects the infants is not yet clearly understood. It was previously thought that the fungus was present on the feeding utensils, on the nipples or on the mammae and that the child's oral cavity became infected by this. Epstein has shown that the most common source of infection is the oral cavity of the mother where the fungus is present in a latent form. It is

likely that in some cases at least, the child is infected during delivery from the fungus infection in the genital tract of the mother. Woodroffe and Hessel-tine have shown in the Chicago Lying-in Hospital a definite relationship between oral thrush in the infant and mycotic vaginitis in the mother. Thrush is sometimes present in older children and then it is associated with wasting diseases such as dysentery, typhoid and tuberculosis. The essential symptom of thrush is the appearance in the mucous membrane of the mouth of milky white patches resembling coagulated milk. They are usually dry and cannot be readily wiped off and when an attempt is made to remove them, a raw surface sometimes with a number of minute bleeding points is noticed. Associated with this there is some looseness of the bowels. The child appears weak, cries feebly, is reluctant to take breast-milk from the mother and finds it difficult to swallow it, as a result of which there may be rapid loss in weight.

Treatment.—General hygienic measures should be observed. As far as possible, all articles introduced into the child's mouth should be clean and sterile. The child should not be indiscriminately kissed on the mouth. The delicate mucous membrane of the tongue and mouth should not be cleansed too vigorously as it is thereby injured. The mouth is to be cleaned with boiled water and soft cloth.

As regards actual treatment, boro-glycerin is the usual

remedy. Holt advises cleaning the mouth with a solution of Soda Bicarb. and application of 1 per cent formalin. He is against the use of honey or syrup. On the other hand, Hahn and Junker advise against the use of Soda Bicarb. or Boro-glycerin, as these have only a surface action and because these substances stimulate the formation of mycelia. Glycerin is an irritant to the delicate raw mucous membrane of the infant's mouth and though it cleans the patch, it is likely to make the raw patch more sore than before, thereby increasing the difficulty for the child to take the breast-milk. (This is particularly so in cases of more severe type). Honey, on the other, is a demulcent. I have found Streptocide (*Sulphanilamide*—Evans) in $1\frac{1}{2}$ grain doses per day in a teaspoonful of honey, if applied frequently in 24 hours, gives highly successful results.

A new-born child, the first child of a doctor suffered from a severe type of this infection in one of the wards. It refused to take any nourishment for 24 hours and the condition was causing anxiety in spite of usual application of Boro-glycerin. The Streptocide application in honey gave good results in 12 hours and the child improved rapidly.

In cases where there is a general disturbance of nutrition, it has to be attended to in addition to the local treatment.

Vomiting.

Vomiting in infancy and childhood is comparatively far

more frequent than in later life. At birth, the infant's stomach is nearly vertical and almost cylindrical in shape with a capacity of about 1 oz. This anatomical position favours vomiting to a certain extent. The nervous system is less developed and there is less inhibition than in later life and therefore even slight stimuli are likely to produce vomiting. In the infant a disorder in any one system in the body readily tends to provoke disturbances in other systems and the alimentary system, more particularly the stomach, seems very often the earliest to be affected. Therefore vomiting is seen as an early sign in various disorders, trivial or serious.

Disturbances which cause any lowering of the general metabolic activity in children depress or reduce the tolerance of the stomach for food and the usual diet which the child has been accustomed to take may prove too rich under the changed circumstances and thus cause vomiting. (This proves often an enigma to the anxious mother—why a food which has usually agreed with the infant should now suddenly disagree?).

The causes can be clinically divided into the following groups:

- (1) physiological
- (2) congenital defects
- (3) errors in diet
- (4) errors in the mode of administration
- (5) disorders of the stomach and intestine

The Madras Medical Journal

- (6) diseases of the liver
- (7) diseases in other systems
- (8) diseases of unknown metabolic origin, and
- (9) various surgical conditions like appendicitis or intestinal obstruction which are attended with vomiting.

Let us now consider these in detail.

Physiological vomiting.—

The infants from the time of birth may bring up a little milk. This seems effortless on the part of the child and there is no retching. A small amount of milk is suddenly found in the mouth and dribbles down the sides and wets the bib. This is called "possetting" and is a physiological safety valve action on the part of the stomach.

Next cause is *Congenital defects*. The commonest here is imperforate anus where vomiting appears somewhat late. It is due to mechanical obstruction. Duodenal atresia has been mentioned as one of the causes but I have not met with any. Of the congenital causes, hypertrophic pyloric stenosis is the most well-known cause of vomiting in infancy. It is common in England. In the Great Ormond Street Hospital for Sick Children, there will be on the operation-list one or two cases of hypertrophic pyloric stenosis in a week. It is comparatively rare in this place. 4 cases were admitted into this hospital during the last seven years. In the Government General Hospital, Madras, during the years 1935, and 1936, 3866

Digestive Disorders of Infancy and Childhood

children were admitted into the In-patient Department and there is no mention of any operation done for this condition. In the Wadia Hospital for Children, Bombay, 2249 cases were treated in the In-patients and 9098 in the Out-patients in the year 1937 and there were no cases of pyloric stenosis. The disease here resembles in main, the clinical picture as described in books. I have met with six cases in all. All of them were male. Three were first-born. Vomiting began about the second week and was projectile. There was visible peristalsis of the stomach and the pylorus was palpable.

The first case was a Hindu, male child. Vomiting commenced about the second week. On careful nursing, stomach wash and regulated foods the vomiting was controlled but the food that was retained by the infant was not sufficient and the child began to lose weight. Ramsteadt's operation was done and the pyloric sphincter was found almost cartilagenous in consistency. The child improved readily.

The second one, a Hindu, 8 weeks old, had typical signs and symptoms. After ten days of medicinal treatment, the vomiting still persisted. Ramsteadt's operation was performed with good results.

The third was an English male, 3 weeks old. Medicinal treatment was done for a fortnight. Vomiting persisted. The child's weight at first remained stationary and then began to go down.

Ramsteadt's operation was done and recovery was uneventful.

The fourth was a Parsee child. Came in about the third week and the general condition was poor. Refused operation and was taken home in a low condition.

The fifth one, a Hindu child, had vomiting one week after birth. It developed icterus and occasionally had loose stools. Medicinal treatment was tried for four weeks. Child gradually became weaker and projectile vomiting persisted. Ramsteadt's operation was done but the child did well only for a few hours and then suddenly collapsed.

The sixth one, Hindu, male child, was 4 weeks old, on admission into our wards. Had pyloric stenosis. Was cured by medicinal methods (and demonstrated in one of the clinical meetings held in this place).

The drug *Eumydrine*,—*Atropine methylnitrate*—*Bayer* has been reported to be efficient in this condition. It is not available in India and we have no experience; but from the above few cases, it looks as if notwithstanding the occasional success with proper nursing and medicinal treatment, surgical assistance (Ramsteadt's operation) is the treatment of choice.

Errors in diet probably account for the largest number of cases of vomiting in infancy. Error may be one of quantity or quality. Over-feeding at the breast or at the bottle is a common cause.

Less frequently, it may be due to defect in quality. A milk with high fat content is likely to disagree and produce vomiting. In older children, food which is irritating or indigestible can bring about vomiting.

One cause usually overlooked and particularly responsible for vomiting in the bottle-fed infant is error in the mode of administration of the food. The position of the infant during feeding, the warmth of the feed, its rate of flow, the time the child has been at the bottle, the behaviour of the child during feed, all these have to be taken into account. If, for example, a child is suddenly disturbed from its sleep, it will cry and will be very irritable. If forced to take a feed, it will do so with reluctance or resistance and is mostly likely to eject it. It is essential, therefore, that in investigating the cause, the child should be fed in the presence of the physician and if there is vomiting, its time and nature should be noted.

Diseases of the stomach and intestines cause vomiting. Gastritis is not common in infancy and vomiting due to organic diseases of the stomach are less frequent than in the adult. Intestinal disturbances, on the other hand, more often cause vomiting. Probably in these cases, there is an irritant or toxic factor causing both vomiting and diarrhoea. If a child has obstinate vomiting with malaise, foul breath, furred tongue, and is constipated and has, in addition, low fever and is dull or

apathetic, early disorder of the liver, particularly jaundice may be anticipated to be subsequently confirmed by the usual triad, icterus, clay-coloured stools and bile-stained urine. Amongst nervous causes, functional disorders are oftener the cause of vomiting than organic ones. Among the organic causes are found more commonly meningitis, encephalitis and rarely cerebral tumours. Incidentally, I may mention that in about 12 cases of tubercular meningitis met with by me during the last seven years, the vomiting in all the cases was only slight and occasional. The refusal to take food was the more characteristic sign.

Diseases of the respiratory system are not an infrequent cause of vomiting, particularly in infants, because the action of coughing readily provokes vomiting. Thus it is a troublesome and persistent symptom in whooping cough, chronic bronchitis, or bronchiectasis. Sometimes, no sooner is the feed given than the child gets a bout of vomiting and brings out the whole feed so that it becomes a problem how to make the child retain the required amount of nourishment.

Fevers, and particularly eruptive fevers, are often ushered in by vomiting. Among infectious diseases, vomiting may be the only suggestive sign in early cases of whooping cough. Infrequently, vomiting may be due to cardiac diseases. Persistent vomiting in a child suffering from *chronic renal disease* denotes the

onset of uræmia. There is a type of vomiting of *unknown metabolic origin* usually known as the *cyclic* variety. It sets in suddenly and lasts for a few days. The vomiting is of the recurring type and the word "recurring" is a better term than "cyclic" since there is no regular periodicity in these attacks. It is more common in children above 3 years, particularly in the bright, intelligent and emotional. There is sometimes a family history of allergy, like asthma or migraine. After a preliminary period of 12 to 24 hours when the child is off its feed, the vomiting begins. It is persistent and severe. Even sips of water are rejected and there is marked retching, the patient getting rapidly exhausted. It is sometimes accompanied with moderate degrees of fever. On approaching the child a sweetish ethereal odour is noticed sometimes. Child is restless, alert with an anxious expression. In later stages the child lies limp and quiet. Sometimes cries from cramps in the legs and complains of severe pain in the chest due to retching, which is a marked characteristic in this disease.

Prognosis of vomiting in general.—At the outset of an illness, it is not of much significance in children. If it is noticed during the course of diseases, like enteritis, pneumonia, dysentery or cardiac disease, prognosis is less favourable. Vomiting alone, if as a result of digestive disturbances, rarely leads to fatal results.

Treatment.—Try to find out the cause and treat accordingly.

Milk generally disagrees. Glucose is specially indicated. It is given frequently and in small quantities, iced if necessary. Constipation always aggravates vomiting and if present, must be relieved by enemata. Purgatives administered by the mouth are likely to be rejected. In severe cases, glucose saline may be given per rectum. I have had no occasions to give fluids either by subcutaneous route or intravenous route to cure vomiting. Fats disagree and are likely to bring about acidosis and increase in symptoms. Cream, butter, eggs, fried products should be avoided. Carbohydrates like starch are tolerated better. Skimmed milk, rice, sago, corn flour, vegetables, weak tea or coffee with generous amount of sugar and a small amount of milk are suitable.

Drugs.—By far the best drug is calomel. It ought to be given in fractional doses, 1/6th, 1/8th grain or even 1/10th. Repeated every half hour, it will generally relieve or completely stop vomiting. Calomel is particularly suitable in cases of vomiting due to faulty diet or in the presence of other associated infections and also when the patient exhibits signs of toxæmia like fever and drowsiness. In simple cases of vomiting unattended with fever, bismuth is satisfactory, may be given in doses of 2 to 5 grains every third hour for a child one year old. Cerium oxalate once in general use for vomiting in pregnancy but now deleted from the B. P. has been found by me particularly useful in the

vomiting of infants, in 1 to 2 grain doses.

In the "cyclic" type of vomiting, the usual sedatives like Bismuth, iodine, opium, acid hydrocynic dil. are no use. Small doses of calomel followed by soda bicarb. 5 to 7 grains in syrup every two hours are satisfactory. In severe types Insulin injections 5 to 8 units with oral administration of glucose gives prompt relief.

The prophylactic treatment for recurring vomiting is to reduce the fats in the diet and increase the carbohydrates. In cases where vomiting is associated with cough, Tr. Camphor Co., Syrup Codein or Elixir of Thyme in suitable doses are indicated. Occasionally mechanical measures like stomachwash are found useful when other remedies have failed. This is very easily carried out in infants but is very difficult to carry out in the case of older children.

Chronic Constipation

Another digestive disorder is *Chronic Constipation*.—This is responsible for a certain amount of ill-health in children. These children while not appearing ill are not up to the normal standard. They are somewhat pale and flabby, have a protuberant abdomen and are capricious in their appetite. If infants, they sleep poorly and more often suffer from colicky pain in the abdomen. They strain and cry unceasingly until they pass a hard, constipated stool with slight relief. At times the colic is so severe that I have known cases where the

child almost went into convulsions.

Constipation may be due to insufficient food. It is not uncommon to find a child entirely breast-fed about 5 or 6 months old, which does not put on weight and is always constipated. On examination it is found that the child hardly gets enough nourishment from the mother and what little it gets is rapidly absorbed leaving insufficient residue. Normal motions contain about 80 per cent of water. Insufficient fluid intake associated with excessive loss in the form of perspiration in warm weather is a contributory factor. In infants the colon, particularly the sigmoid is relatively longer and therefore greater amount of water absorption takes place in infancy than in later years. Evacuation of bowels depends upon regular habits. The urge or desire for evacuation will come at accustomed intervals and if this is unattended or neglected, the bowels become sluggish and chronic constipation results. Lack of tone of the intestines, lack of tone of the abdominal muscles, as in malnutrition or rickets is a factor in bringing about constipation. Sluggish nerve stimuli is another as in hypothyroidism. Constipation may also be brought about by want of balance in the constituents of the food. Proteins tend towards alkaline, putrefying, hard stools and carbohydrates towards frothy fermenting acid stools. Fats cause loose soapy motions. Want of cellulose in the diet in older infants may

cause insufficient residue in the food and thus cause constipation. Organic causes like pyloric stenosis or achalasia of large bowels are among the rarer causes of this condition.

Treatment.—The difficulty in treating cases of chronic constipation in childhood is fully appreciated only by those who have attempted to treat the condition. A detailed enquiry must be made about food, its nature, its amount and the time and method of its administration. The nature of the stools must be examined in all cases to see whether the stools are really constipated and also to have an idea whether there is any undigested food or any abnormal constituents. In breastfed infants, test feeding is necessary to know if the child is getting enough nourishment. Enquiry must be made if the constipation as such is leading to any discomfort or inconvenience or whether in spite of constipation, the child is healthy and gaining weight. The amount of breast milk at each feed should be ascertained. If this is insufficient, steps must be taken to increase the amount of breast milk and if this is not successful, supplementary feeding must be resorted to give the child the necessary amount of nourishment. In warm weather, in between feeds, addition of water with a little sugar will help relaxation of the bowels. It is very necessary that the infant should be taught regular habits of evacuation right from the earliest months. If the child is held after each feed with its legs

drawn up, it may be trained to pass motions at regular intervals.

In the case of the artificially-fed infant, the exact amount of food the child gets must be ascertained. Very often in these infants, it is noticed that the milk given to the child is very dilute, the addition of water being so excessive that there is not enough residue left for regular evacuation of the bowels. Proportionate amount of milk must be present in the feeds. A rough guide will be that at about three months, the child should receive equal parts of milk and water and at about six months, the child should receive about two parts of milk to one of water. Addition of cereals, particularly of barley water, tends to overcome constipation in very mild cases. Since carbohydrates added to milk bring about easier evacuation, the addition of suitable carbohydrates alone to the milk is often sufficient to overcome the constipation in the early months of infancy. The carbohydrates may be either glucose or plain sugar or dextromaltose. The last is the best, but in ordinary practice, common sugar will be quite sufficient.

In case of infants after the seventh month, addition of starchy food in the form of barley flour or rice flour will tend to overcome constipation. Massage of the abdomen commencing from the right iliac fossa and working in clock-wise direction along the colon will be helpful. The custom of massage with oil—oil-bath—that is prevalent in Hindu families, is

valuable for toning up the muscles and overcoming constipation.

The child during the second year of infancy, should be given a certain amount of green vegetables, well-boiled and mashed. Fruits are particularly valuable such as grapes, prunes, apples or bananas well stewed and taken with cream and sugar. Malt is a valuable addition in the infant's dietary. Besides its promoting digestion and its nutritive value, it also tends to overcome constipation. Honey is particularly valuable as a nutritive food for infants, and more so, in these cases as it acts as a mild laxative and deserves greater notice from physicians.

Drugs.—I am taking these last because they play only a very secondary part in the treatment and it must be our aim to discontinue them at the earliest possible moment. Drastic purgatives should be avoided. A popular remedy is castor oil or any of its attractive preparations in the market but castor oil after its purgative action, has after-constipating effect. It is easy to understand that regular use of castor oil makes chronic constipation worse. In short, there is no drug so unsuitable as castor oil or its preparation in the treatment of chronic constipation. Liquid paraffin is particularly suitable. If it is given as a suspension in warm water, it acts even better. With Agar-Agar, it also forms an agreeable combination. Senna is another drug useful in the treatment of chronic constipation. The leaves are not so suitable

because the decoction is bitter to taste and the action is somewhat drastic. Senna pods are preferable; should be used as an infusion. Syrup Senna is an agreeable form to use. Rhubarb or calomel, though useful for occasional use, is not advisable in these cases. Of the saline purgatives, none is so suitable as Magnesium carbonate. It is a mild laxative and also has antacid properties and therefore suitable for infants.

Rectal suppositories may occasionally be used. They temporarily relieve the condition but in no way do they help to bring about a permanent cure.

Lastly, I have met with a small but definite group of cases of constipation which has not been described in text-books. There were six cases, all within the first 12 weeks of infancy presenting the following features. Four of the children were first-born. They were of the well-built muscular type. Constipation was somewhat obstinate, the child cried and strained and passed its stool once in two days with difficulty. But motions were neither hard nor watery; on the other hand were soft and pasty containing no undigested material. The usual treatment outlined for constipation fails in these cases. Therefore, spasm or over-action of the anal sphincter was suspected which on further examination was confirmed. The treatment for this condition is by dilatation of the anal sphincter by means of suitable Bougies. This gives permanent relief and usually one sitting should suffice.

I am very grateful to the University of Madras for having given me this opportunity of delivering these Endowment Lectures an honour and privilege which in the past has gone to more eminent and deserving people. My best thanks are due, to the Superintendents past and present of the Government Hospital for Women and Children,

Madras, who have given me all encouragement and facility to study these diseases pertaining to children and to the heads of the Departments of Bio-chemistry, Pharmacology, and Pathology for their assistance. I have also to thank my colleagues in the Childrens Department for their kind co-operation in this work.

LECTURE II.

Diarrhoea.

This complaint is very common in infancy and childhood. It accounts for the third largest group of mortality, during the first year of life. If we exclude the first four weeks of infancy when the mortality is greatest, almost entirely due to prematurity and congenital defects, the deaths from diarrhoea during the first year rank only next to those from respiratory diseases. Even here it is a moot point whether the morbidity and the malnutrition arising from diarrhoea is not, to a great extent, responsible in influencing the mortality from respiratory diseases. (Diagram 1).

Though everyone is familiar with the disease, its pathology is still imperfectly understood. A glance at the mortality reports brings out prominently the fact that the highest incidence is during the first year. Then there is a sharp decline during the second year and a sharper decline after the second year. (Chart 1). A further study shows that the

mortality is slight during the first 8 to 12 weeks of life and it is particularly high about the 4th to the 7th months and then slowly recedes. (Chart 2). It is a matter for satisfaction that the morbidity and mortality from this disease are to a great extent, preventable and going through these reports, one cannot but be struck at the steady decline in mortality rate in cities where there has been steady improvement in sanitation and health measures. (Chart 3).

The incidence of the disease has some relation to atmospheric conditions, the mortality rate rising as a rule in late summer and autumn though the total mortality rate is particularly high in the winter months. (Chart 4). Epidemics of the disease are generally in summer. This is due to more than one factor at work. The water-supply in summer time may not be as plenty and pure as at other times and we in Madras have ample experience of this.

Flies are found particularly in summer and their part in spreading the disease cannot be ignored. The role of summer heat in causing digestive disturbances has been better understood in recent years. The high temperature acts as a powerful depressant and metabolic changes are produced resulting in indigestion and diarrhoea. Rainfall is a contributing factor, the incidence of diarrhoea increasing after the rains probably on account of contamination of sub-soil water. The accompanying chart shows clearly the intimate relationship between the rainfall and mortality from the disease. (Chart 5). We can probably conclude from these charts that the mortality curve is more directly influenced by rainfall than by summer heat. The influence of summer heat is not evident immediately. As these graphs show the peaks in the mortality curves do not correspond to the peaks in the temperature curves.

The disease is almost entirely confined to infants fed on artificial food. The children brought up on breast milk entirely hardly suffer from diarrhoea, no matter how irregular the feeding might be or how poor the environmental conditions.

Bacteriology.—An enormous amount of research, bacteriological or otherwise, has been carried out but the position remains confused. In a few cases, definite bacteria, whose pathogenicity is known have been isolated. These belong to the typhoid and paratyphoid groups,

to the dysentery bacillus (Shiga) and the para-dysenteric types of Flexner-Strong and Y. The significance of unspecified bacteria such as the streptococci, pneumococci, bacillus Proteus, bacillus pyocyaneus, when found in stools in large number is uncertain. As regards the role of B. coli, it may be introduced in food. According to the investigations of Moro and others, an endogenous coli invasion in the upper small intestine takes place particularly after over feeding of nourishment rich in sugar. This endogenous infection must be considered as the biologic sub-stratum of severe forms of fermentative diarrhoea. In a large number of cases of definite infection, the ætiological agents cannot be identified.

Pathology.—It is surprising that the post mortem appearances in fatal cases are hardly sufficient to explain the cause of death. Even in severe cases, there are so few pathological changes, some congestion of superficial vessels in the bowel, congestion of Payer's patches and occasionally hæmorrhagic areas are noted. No constant, characteristic pathological condition, either macroscopic or microscopic could be established.

The new-born infant is accustomed to one form of nutrition, i.e., breast-milk and he has to learn to consume and digest other forms of milk like Cow's milk which differs from breast milk in various ways, e.g., their proteins and fats are not of the same kind. Their percentage composition

MADRAS 1938

Infantile Deaths

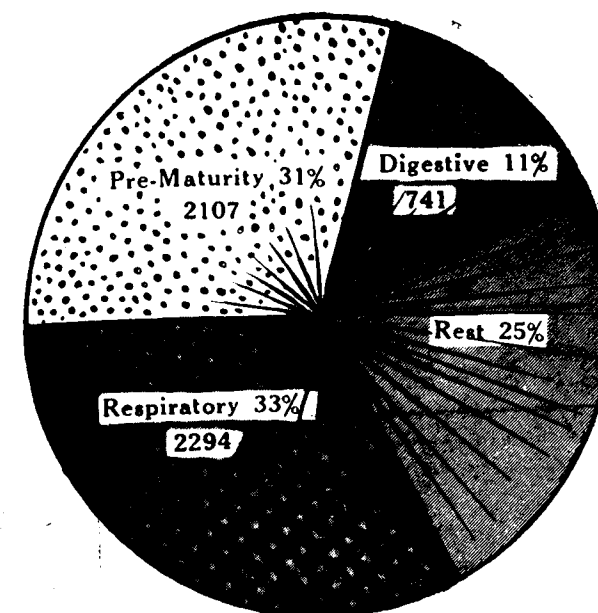


Diagram 1.

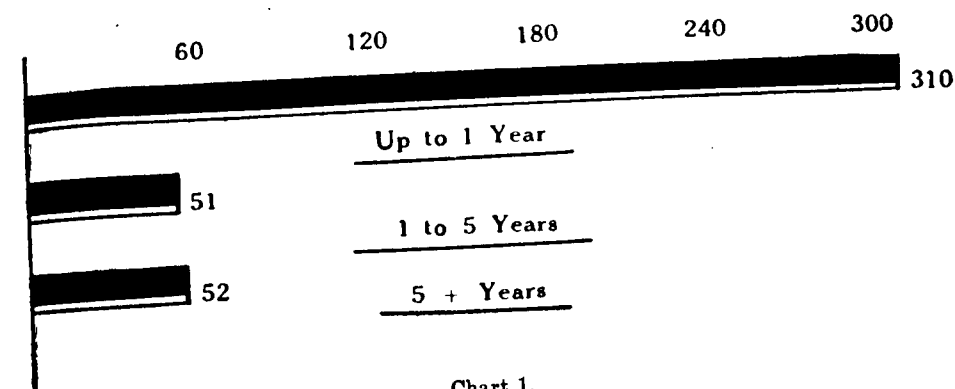
GLASGOW 1933
Mortality from Diarrhoea

Chart 1.

(The figures represent the actual number of deaths.)

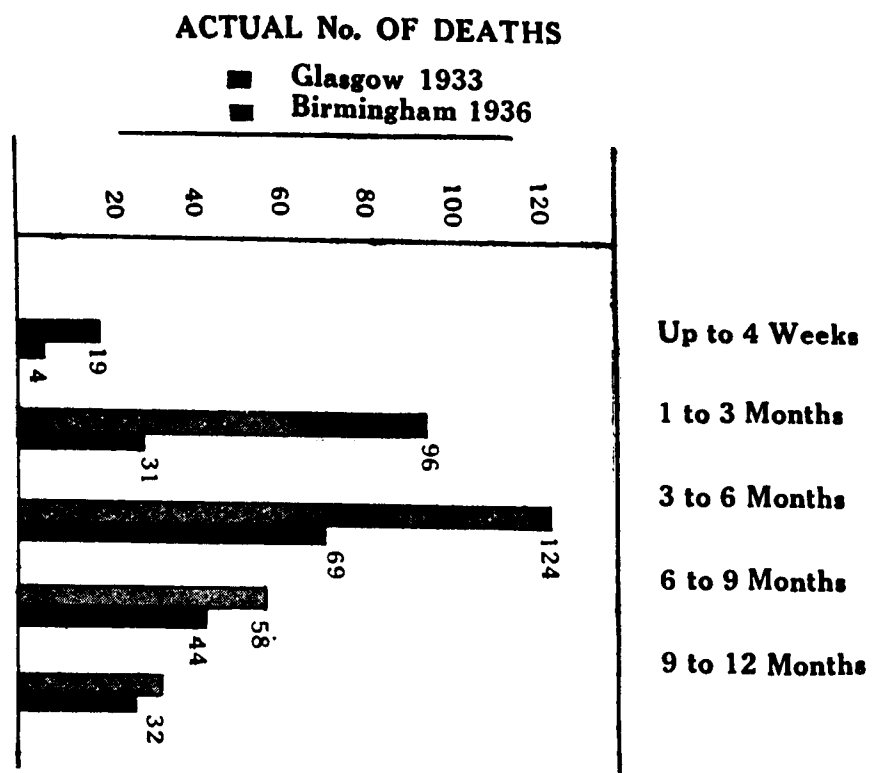


Chart 2.

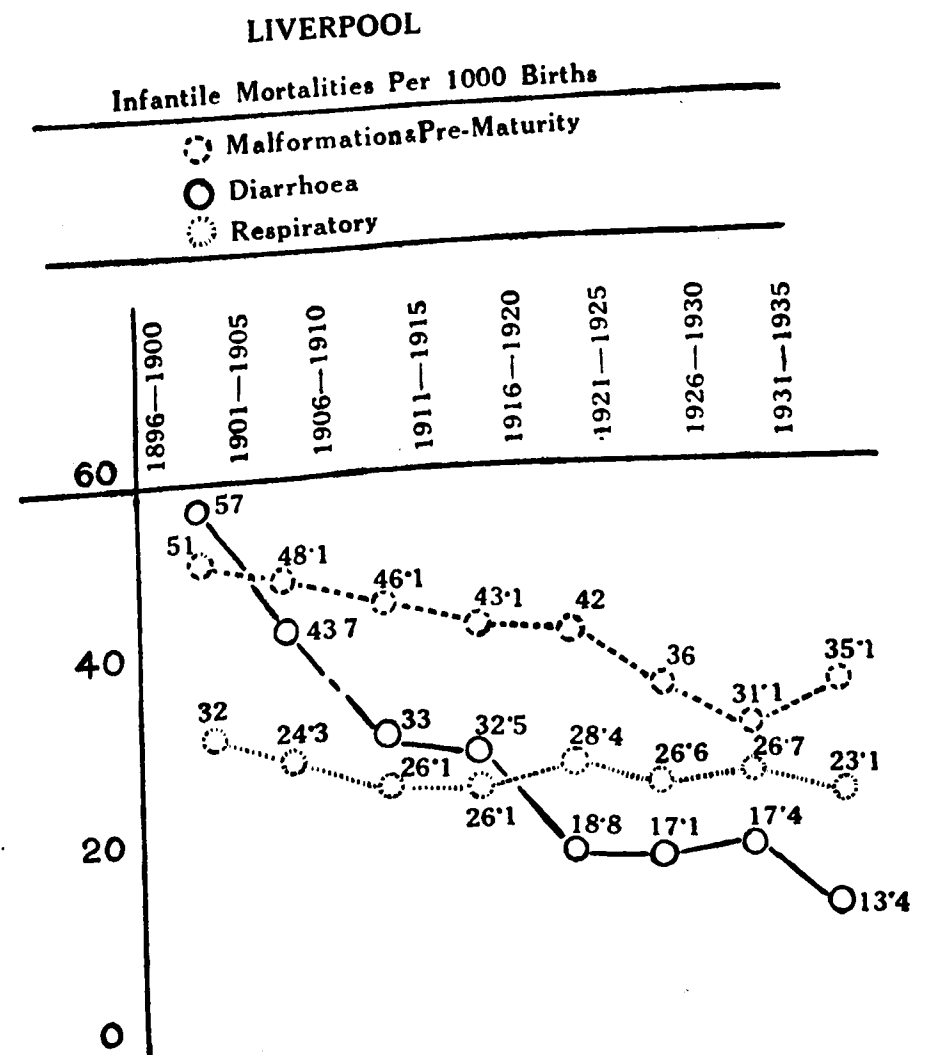


Chart 3.

Influence of public health measures on infantile mortality from

- (a) Malformations and Prematurity
- (b) Diarrhoea
- (c) Respiratory diseases

In Liverpool during forty years 1895—1935. Note the steady decline in the death rate due to Diarrhoeas.

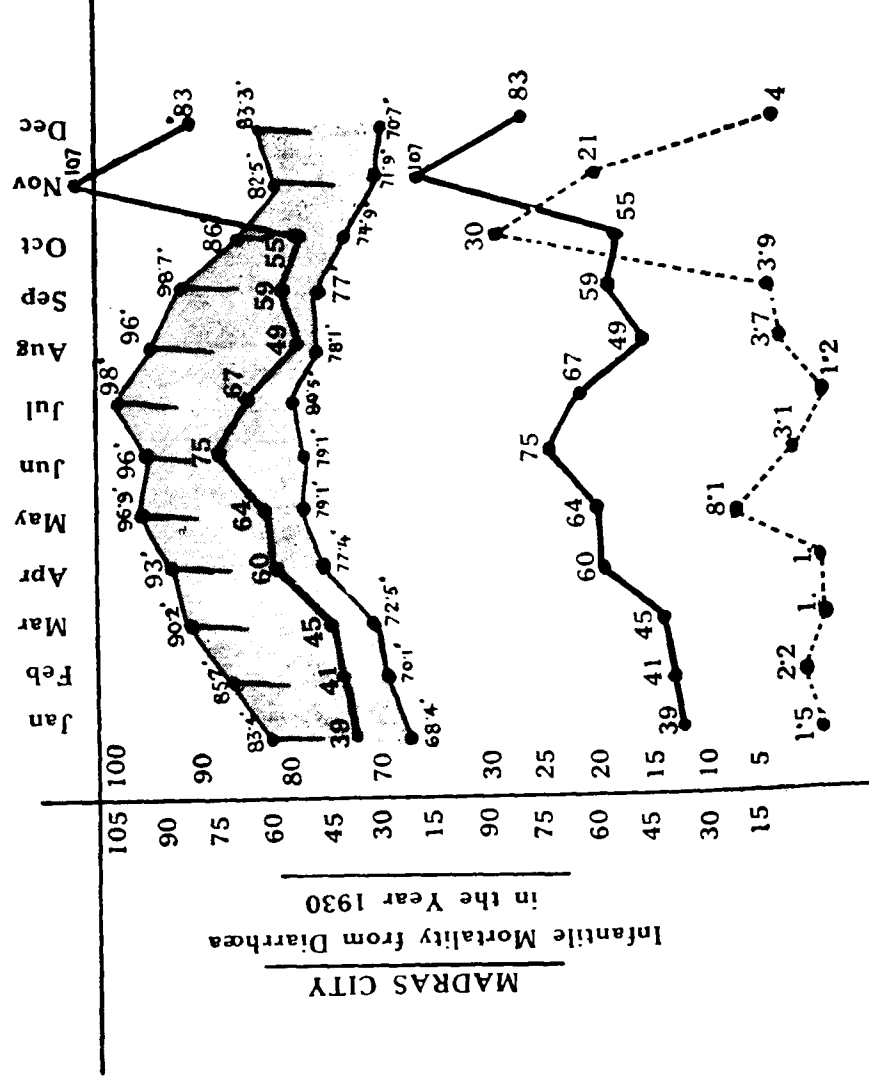


Chart 5.

The area shaded shows the monthly maximum and minimum of temperature. The graph (broken lines) shows the no. of inches of rainfall, each month. On each of the figures is superimposed a graph showing the infantile mortality from diarrhoea. Note the closer relation of the mortality curve to the rainfall than to the temperature.

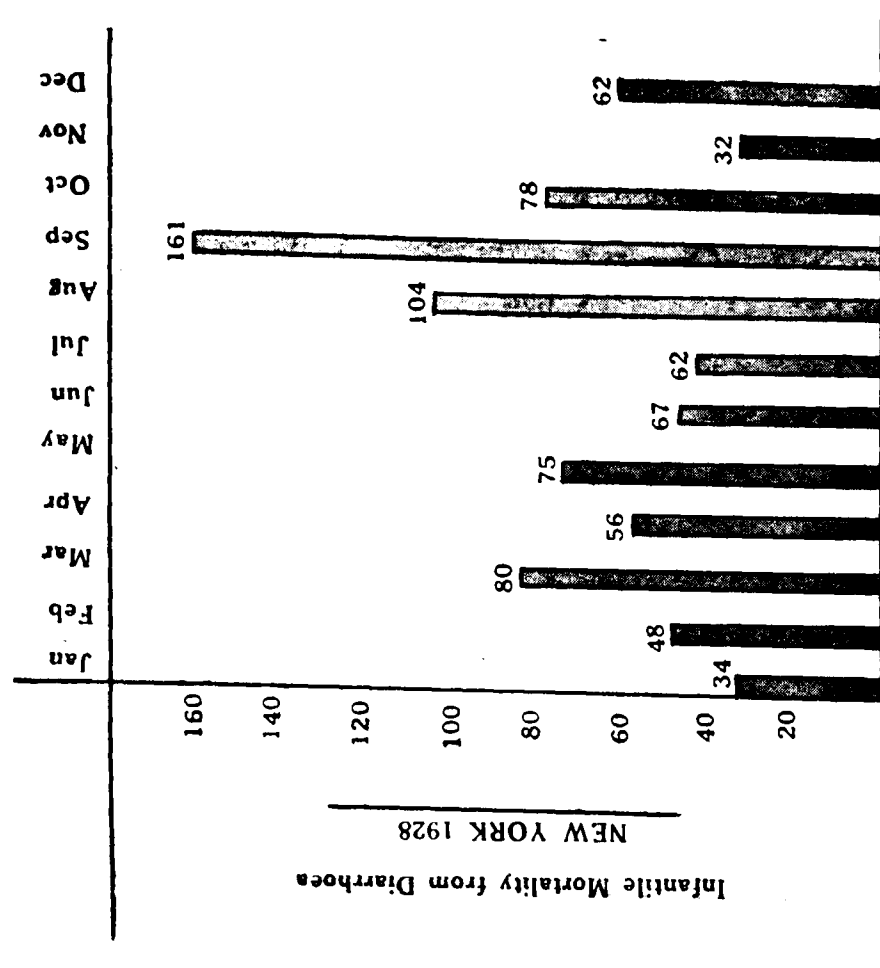


Chart 4.

Diarrhœa

also is different. There are many biological ferments in breast-milk absent in Cow's milk and therefore the infant organism has to acquire a certain degree of resistance before it can tolerate other kinds of milk than human milk. The response of the infant to variations to the thermal reactions of the body, its susceptibility to changes in the water-balance are of direct consequence in the causation of diarrhœa. Together with these, there are signs of a certain incomplete development of the central regulation especially in the first three months. There is further evidence of predominance of vegetative nervous system over the central nervous system. That is why diarrhœa in the infant have their own peculiar stamp. Finally, the helplessness toward and the dependance upon surroundings, especially nursing care, are important general factors in the pathology of the disease. The infant is entirely dependent upon his environment and in no other age period is the nursing care of such great significance in every sense of the word. The diarrhœa could be grouped as follows according to their ætiology:—(1) those due to unsuitable foods which cause irritation of the bowels with increased peristalsis and diarrhœa, (ii) those due to decomposition in the intestine as a result of which non-completely or incompletely split food appear in portions of intestine, where they ought to appear broken down into their constituents or end products, as a result of which the toxic products produced are absorbed and re-excret-

ed giving rise to diarrhœa, thirdly due to the usual coli group, the organisms becoming more pathogenic to the host, their migration to the upper part of the bowels being largely responsible for the toxic effects, lastly the child may be suffering from infection in other parts of the body and this may cause a constitutional disturbance wherein the alimentary system also suffers and gives rise to diarrhœa.

Signs and symptoms.—Clinically, the diarrhœas can be divided into two groups, the mild or the non-infective, most probably due to errors of digestion, and the severe or the infective. In the first variety, the child does not appear ill. It is the mother who appears more worried than the child. When the anxious mother is holding out the baby for inspection, the little patient unaware of the situation may be toying with the stethoscope and at the same time soiling the napkin on the mother's lap, appearing none the worse for the large broad motion it has passed. The stools contain a fair amount of fæcal matter and milk curds. There may or may not be present associated vomiting. On the other hand, in the more severe or infective type, the child appears ill. It is more or less restless and cries constantly from pain. Vomiting is often present. Motions are frequent, watery, pale, yellow or greenish and sometimes even colourless. There is hardly an undigested food in the motion. Fever is constant; in severe cases may be as high as 103 or 104°. In some of these,

toxæmic signs are prominent, the child having congested appearance, drowsy, vacant look, just like a picture of commencing pneumonia or meningitis and in addition having small frequent watery greenish or colourless stool. In others dehydration is prominent, the child is restless, cries unceasingly, eyes are sunken but bright, features pinched, hippocratic facies present, takes water readily but the motions are large, watery, and out of proportion to the fluid intake. The child shrinks rapidly as the dehydration proceeds and finally dies of exhaustion. *Cholera infantum* is a fulminating type of diarrhoea where there is marked vomiting and passage of watery colourless stools, child being rapidly prostrated; and soon turns out to be fatal. It resembles in its picture *cholera asiatica* but is not due to the cholera vibrio. The diarrhoea caused by intestinal parasites have been included in the first group for the purpose of clinical description and treatment.

Prognosis.—The prognosis in the simple variety is good. In the more serious or infective variety, it depends upon the following factors:—

- (1) Age of the patient. Younger the infant, worse is the prognosis. It is particularly fatal in the first few weeks of life.
- (2) The previous health of the child.
- (3) The season.
- (4) Presence or absence of high fever.

- (5) Presence of vomiting or otherwise.
- (6) Colour of the stools. Less the colour, worse is the prognosis.
- (7) Suppression of urine for 12 hours or more is a grave sign.
- (8) Degree of drowsiness or coma.
- (9) Presence of complications like broncho-pneumonia.

Smellie from an analysis of 500 cases of infantile diarrhoeas came to the conclusion that in infants who were never breast-fed from birth, the mortality was as high as 76.6 per cent and where the children had the benefit of breast-feeding for a month or more, the mortality was 25.9 per cent. Maitland Jones gives a mortality of 48 per cent for the infective type and these include some cases who were moribund on admission. In 1937, 65 cases of infective diarrhoea were admitted into our wards (these do not include moribund cases or those suffering from dysentery). 37 were cured, 15 improved, 2 died and 5 discharged otherwise. The discharged otherwise were those that went from bad to worse and which would have died in all probability, had they continued to stay in the hospital. If, therefore, we take the cases that died or discharged otherwise together we get a total of 13 cases giving a mortality rate of 20.5 per cent. In the Wadia Hospital for Children, Bombay, for the same year there were 213 admissions with 134 cures, 7

Diarrhoea

improved, 57 died, 14 discharged otherwise, 7 remaining giving a similar corrected mortality of 31 per cent. So we may conclude that for our South Indian condition, mortality is somewhere between 20 to 30 per cent.

Treatment.—is both prophylactic as well as curative. The prophylactic treatment is more encouraging and merits therefore greater attention from medical men and all those interested in the health and welfare of children. Breast-feeding especially in the first few weeks of life is the surest way of safeguarding infants from diarrhoea. For this, regular welfare clinics should be opened for the care of pregnant women, propaganda should be done emphasising the value of breast-milk for the growing infant. It must be brought home that breast-fed infants are far more immune to any and every kind of infection than those fed on artificial foods. It is the universal experience of all those who have anything to do with infants, that breast-milk with its defects, if any, is infinitely superior to artificial foods prepared on the best scientific lines. Emphasis has to be laid on this, lest doctors should be carried away by the idea that modern artificial foods are any day better than human milk, if they have a higher mineral content or vitamin content.

If the child has to be weaned, as far as possible, it should not be done during summer. Our Corporations and public bodies must be made alive to the fact that the

mortality from diarrhoea is to a large extent preventable, if the sanitation and public health efforts are adequate. A high mortality from diarrhoea is a blot on the administrative efforts of the health authorities.

Coming now to the curative treatment, the treatment may be divided into the following heads.

- (1) General
- (2) Dietetic
- (3) Medicinal
- (4) Specific
- (5) Treatment of complications
- (6) Treatment during convalescence.

General.—The child is taken to a well-ventilated room, all feeding vessels are properly cleaned and in a place or institution, where a large number of children are brought up, isolation is advisable. Efficient nursing goes a long way in the treatment of these cases.

Dietetic.—The diet must be of a non-irritating character to the sick infant. A common food which particularly disagrees in diarrhoea is cow's milk. The more severe the disease, the greater is the intolerance towards cow's milk. In critical cases, cow's milk even when administered in small amounts may ruin the child's chances of recovery. Why it is that cow's milk which is probably the sole substitute in the absence of breast-milk in the early months of infancy should act so deleteriously in diarrhoea

is not fully understood. Warm water, barley water, sago or arrowroot conjee, sweetened if necessary, but without milk are suitable foods. Weak tea may be used as it contains a small amount of tannin. Albumen water is particularly a suitable food in the milder types. Whey salts are believed to be irritants to the bowels; hence whey is not so preferable as the former. Glucose is easily absorbed, contains enough of calories, combats acidosis and is very popular. Treatment is often not considered complete unless glucose is prescribed and often in large amounts, especially if it is labelled as a special brand. During diarrhoea glucose is not fully absorbed from the upper part of the intestine and the unabsorbed portion increases the fermentation and definitely increases the diarrhoea and often a simple type may be converted into a more serious one on account of the indiscriminate addition of glucose. In the severe types, therefore, it is better to withhold glucose or sugar altogether and if any sweetening is necessary, sacharine is suggested. Small amounts of starch in the form of cereal water are beneficial.

Medicinal.—In mild varieties, where it is due to presence of curds, an initial purgative to get rid of the offending agent is desirable. Either castor oil, grey powder or Rhubarb may be used. These cases readily improve on this line of treatment and when 24 to 48 hours later the motions are free from irritating material, astringents may be administered,

like creta preparata, bismuth carb., catechu or acid HCl dil. It has been my experience here that creta preparata acts better than Bismuth probably on account of its antacid properties. Opium can be used cautiously. The following rule should be observed in the administration of opium in diarrhoea:

- (1) to be used cautiously and better avoided in the early weeks of life as infants do not tolerate opium and at times have an idiosyncrasy for the drug
- (2) should not be given at the onset of illness
- (3) nor if the stools contain undigested food or are offensive
- (4) nor if there is fever or toxæmia
- (5) if the child has collapsed
- (6) if the tongue is furred
- (7) if the child has suppression of urine
- (8) lastly it is not advisable to administer opium when the child is asleep.

In the severe types of diarrhoea, no initial period of starvation is advisable nor an initial purgative. The child has already been deprived of fluids and withholding them further is harmful. Water or half strength normal saline should be given in small quantities at frequent intervals. Sugar had better be avoided. Kaolin is

particularly indicated in these types. A level tea-spoon administered in 6 oz. of water gives a milky suspension which is given *ad lib.* It usually does good and no harmful effects have ever been observed.

As regards intestinal antiseptics, search is being constantly made to find the "philosopher's stone" and preparations after preparations come to the market supposed to act specifically on account of their antiseptic properties. Clinicians have not been slow to give these a trial because treatment of the severe types is always a problem and one is on the look-out for any help to simplify the treatment. But none so far have stood the test of time. One old drug which at times gives good results but which is not likely to do any harm is Liq. Hydrarg. Perchlor. in half to one minim doses, suitably diluted in a tea-spoon or two of water given every three hours. At times, the results have been very good and often, there is a definite improvement in the condition. The usual purgatives like Castor oil, grey powder, have no place in this variety because there is hardly any undigested matter found in the stools.

Specific treatment.—It is a matter for speculation if specific treatment could have any place in this disease as long as a specific cause or organism has not been identified in the large group of cases. But the use of phage prepared from the organisms usually present in these cases of diarrhoea is the only specific

line of treatment deserves our consideration. The method of administration is simple and in a small but definite percentage of cases, the results are very satisfactory and are apparent in 12 hours. Where the condition is urgent, Kaolin and half strength saline may be the better form of treatment. Marked improvement in some cases on account of the administration of phage gives this line of therapy a definite place in the treatment of diarrhoea.

Treatment of complications.—The two outstanding complications are dehydration and collapse. Fluids should be given by the mouth as often as possible. If vomiting is present sufficient amount of nourishment cannot be administered this way. In these cases, normal saline has to be given by other routes as it combats dehydration and acts as a stimulant. It also has a definite value in reducing the toxæmias probably by diluting the toxins. Rectal administration need not be considered as it will not be tolerated. Subcutaneous route is the best, 100 to 150 c.c. of normal saline injected into the sides just below the axilla drop by drop, the improvement is very noticeable and there is no other single method so certain and so useful as this. Intravenous saline is difficult in infancy and the intra-peritoneal route is not without definite risks, particularly when abdominal distension is a feature of the disease. For high fever hydro-therapy is useful and cardiac stimulants, like Coramine,

Camphor in oil may be administered if heart is failing. The blood changes of infantile gastro-enteritis are like those encountered, after removal of supra-renal cortex in animals. On experimental grounds, therefore the administration of suprarenal cortical hormone is justifiable, but the available evidence is not sufficient for a considered opinion.

There is a type of diarrhoea commonly found in older children called the nervous or the lenteric type. The child is usually about 5 to 10 years old. It is a neuro-pathic child, a product of both hereditary conditions and the environment in which it lives. Here the urge for stools sets in immediately after meals and sometimes during the course of a meal so that the child has to raise hurriedly from the table. The motions consist of half digested stool. The child does not get up at night to pass stools. This type of diarrhoea is due to increased irritability of the vagus probably a part of general nervous instability. Small doses of arsenic are considered a specific so also small doses of Dover's powder. Curiously enough, I had no occasion to treat cases purely of this type.

Lastly there is one form of acute diarrhoea of infants not very common but often overlooked. Various observers mention that 20 to 30 per cent of cases of febrile diarrhoea belong to this type. The clinical features are that the child has diarrhoea, which is the most prominent symptom and the complaint for which the treatment is sought

for. There is fever, child appears ill but not severely dehydrated. It is restless, seems to be in pain and cries constantly. The usual changes in the diet and the treatment for diarrhoea seem to bring out hardly any appreciable improvement. These are groups where the underlying cause is not in the bowels. It is not obvious and that is why it is missed. These are called the parenteral types and the infection responsible may be either a pyelitis or a middle ear infection or a septic throat or a bronchitis. In my experience, many of these cases of parenteral type have been due to pyelitis which had been overlooked. Treatment of primary condition with slight adjustment in diet speedily brings about recovery. Here I recall the instance of a child about 18 months, admitted for diarrhoea. Change in the diet, Kaolin and astringents brought no improvement whatsoever. Parents were on the point of taking the child home on account of the disappointing results. When the child was catheterised and it was noticed the urine was full of pus cells, the relations were persuaded to keep the child a little longer. The child was put on alkalis and the diarrhoea promptly improved.

Treatment during convalescence.—Treatment during convalescence is no less important. The child is very likely to have a relapse if the diet is faulty and it is particularly at this stage that a graded diet well within the tolerance of the convalescent child should receive our primary consideration because one attack

of diarrhoea confers no immunity against subsequent attack. If the diarrhoea had been severe, breast-milk if available should be tried. It is at this stage that special milk preparations like acid milk, protein milk, or peptonised milk are particularly indicated. Protein milk is the best, next being acid milk and next in merit peptonised milk. When the cow's milk is introduced in the child's diet, it should be suitably diluted so that it will agree with the infant. From observations based on successful feeding of a very large number of infants during convalescence, it is found that the fat content in the prepared milk should not be more than 1.8 per cent for our climatic conditions, if the infant is not more than 12 weeks old; otherwise any milk with higher fat content is more likely to bring about a further attack in spite of all other precautions. As tonics, iron pre-

parations are particularly beneficial not only for their astringent effects but also to combat anæmia.

I am very grateful to the University of Madras for having given me this opportunity of delivering these endowment lectures, an honour and privilege which in the past has gone to more eminent and deserving people. My best thanks are due to the Superintendents past and present of the Government Hospital for Women and Children, Madras, who have given me all encouragement and facility to study these diseases pertaining to children and to the heads of the Departments of Bio-chemistry, Pharmacology, and Pathology for their assistance. I have also to thank my colleagues in the Children's Department for their kind co-operation in this work.

SPECIAL ARTICLE

Nicholas Manucci (1639-1717 A.D.) A Pioneer Private Practitioner of Madras

D. V. S. REDDY, *Vizagapatam.*

Manucci, an Italian by birth, an adventurer by temperament and a surgeon by necessity, gravitated, in the evening of his chequered career in India, towards this comparatively quiet corner of India and finally sought refuge and settled down in this City about the year 1686. He may be rightly considered as one of the earliest of the private medical practitioners and certainly the most celebrated of the quack physicians of the early days of MADRAS. Apart from the immortality he has earned by his great book on India 'Storia do Mogor' (Moghul India), "Manucci's house" and "Manucci's garden" and "Manucci's Stones" were well-known and frequently mentioned in the conversations and records of the residents of Madras for nearly half a century after his death.

Leaving Venice, in his 14th year, and passing through many adventures on his way *via* Syria and Persia, he landed at Surat in 1656. Soon after reaching Delhi, he was appointed as an artillery man on Rs. 80 p.m. in the army of Prince Dara, and later became Captain of the artillery on Rs. 300 p.m. Subsequent to the defeat and death of Dara, he served under Raja Jai Singh, Governor of Deccan. After some

years, tiring of his position, he resigned the post and retired to the European settlement on the west coast, staying in Goa for 15 months. About 1670, he moved to Lahore and set up as a Physician. In the course of the next 7 years, he earned a moderate fortune and once more retired to the west coast. But he soon lost his money and had to try his fortune once more at the Moghul Court. Fortune favoured him, when he got an early opportunity of effecting a cure on one of the wives of Shah Alam, the eldest son of the Emperor. Thereupon he was appointed Physician to the Prince, with whom he remained for nearly a decade from 1676, wandering with the Moghul camp in the Deccan. In 1686, he got tired of the life in the Moghul service and secretly fled to the English settlement at Madras.

Among the passages in his book relating to his life at Madras, the following are of interest to the medical profession. "On my arrival at Madras, the Portuguese gentlemen who knew the zeal with which I had worked for the nation at Goa came to see me. They congratulated me on my arrival and offered their services in whatever way

Nicholas Manucci (1639-1717 A.D.)

101

would be of use to me. Such help, they would give most willingly Among the chief personages were Manuel Taxeyrs Pinto, Chief Captain, Joao da Costa Sua, Cosmo Lourenco Madeyrs, Antonia Plaha de Lima and Manuel da Silva de Menzies. I had treated them and their families gratis."

Francois Martin, Director-General of the Royal Company of France advised Manucci not to return to Europe but to marry in India, and informed the physician of a well-born lady, born in India, of good English parents—widow of Thomas Clarke—Judge and second in the Council at Madras.

Manucci also gives his old age as one of the factors which influenced him to settle down in Madras. "For as they told me having become accustomed to the climate and food of INDIA, and being already advanced in age, I should not last very long in Europe."

After due enquiries, etc., he married Mrs. Clarke in October 1686. He had a son but "God chose rather to make him an Angel in Paradise than leave him to suffer in this world."

"In this way I was fixed to a residence in the Fort St. George, where come many that knew me or heard speak of me in order to be treated. Among those who came was Rajah Champat Bundelah.

"Nor did Shah Alam fail to send in search of me in several

directions while the princess sent out one who has been my servant to seek me in Madras.'

"Very few months passed without gifts coming from the Moghul Grandees who gave me many presents and sent to me patients of title and others."

After he settled down at Madras, he conducted many negotiations with the Moghul Court and the local chiefs of the Deccan, on behalf of the English of the Fort St. George. In the first decade of the 18th century, the Council of Fort St. George granted him, in consideration of his diplomatic services, a lease of house and garden near the southern end of Broadway. During the first half of the 18th century, "Manucci's house and garden" were familiar landmarks of old Madras.

He lost his wife in 1706 and sometime before 1712, he moved to Pondicherry. He was proposing to go to Moghul Court at Lahore in 1712, at the request of Emperor Shah Alam, but the sudden death of his old patron put an end to these plans.

His career cannot be traced at Madras or Pondicherry after 1712, as no records are available. But it is believed, on the authority of an Italian Chronicle published in the middle of the 18th century, that he died in India, in 1717, as an octogenarian.

Doctor as a Servant of God.

"When I became a physician at Lahore, I baptised in 8 years

more than 1500 infants besides those I found on the road-side moribund and whom I baptised. I became so well-known that whenever medicine was asked for water would be sprinkled; that many women both Mohammadans and Hindus imagined that if their infants were sprinkled with water before they fell ill, they would never suffer from any complaint. Thus they would entrust me to sprinkle the child. But I baptised none except those infants we were bound to die. By this means I have baptized sons of persons in very good position, princes and even some of the blood Royal. With this profession of doctor, it is possible to do some service for God."

Manucci's Advice to Young Doctors.

"In this country it is incumbent on a doctor to prepare medicines, ointments and distillations—in fact, all things that appertain to apothecary's office. Many a time it is also necessary to instruct as to the fashion of preparing the patient's food. It would be a good thing to bring from Europe antidotes to poisons for frequently it happens, especi-

ally among the nobles that poison has been given.

"It is necessary to have a useful horse and one camel. On the latter are carried the requisite supplies both of drugs and other instruments."

Manucci on his own Life and Actions.

"Experience was my great teacher whereby I had acquired several secrets, in which it may be I shall allow the word to participate, for I have no heir to whom to bequeath these treasures that preserve our bodily health. But among others I may as well mention that I manufactured certain cordials regardless of expense the same being wonderful in certain complaints as many can testify. Yet, it is only a short time ago that I began to distribute these cordials, for I have no wish to imitate those who, keener for other's gold than the health of their fellowmen, make up mixtures of various things and sell them as cordials. I did not begin to sell mine until experience had taught me that the purchasers would not be cheated."

Abstracts from Current Medical Literature.

In a series of papers on **Bismuth Therapy of Syphilis** (*Am. J. Syph. Gon. and Ven. Dis.*, July 1940, Vol. 24, No. 4). Kolmer, Kast and Rule make the following observations:

1. Bismuth is excreted in urine much sooner than in stools and the determination of urinary excretion is a far better index of bismuth concentration of the blood than a determination of the total bismuth excretion in urine and faeces. It is difficult to state definitely the urinary level of bismuth required for the biological cure of syphilitic rabbits because this is in relation, not only to the amount, but also to the length of time it is sustained. In general terms it would appear that a certain minimum level of urinary excretion of bismuth is required for biologic cure, even though there is prolonged excretion, because below a minimum level the duration of excretion is apparently of much less significance.

2. That immobilisation of *S. Pallida in vitro* by bismuth indicates spirocheticidal activity is shown by the results of an experiment employing Potassium bismuth tartrate. Final dilutions of this drug with saline varying from 1:500 to 1:80,000 and seeded with 0.2 c.c. of testicular syphiloma suspension of virulent *S. Pallida* were injected into testicles of rabbits after standing for 15 minutes at room temperature.

The rabbits were observed for nine weeks to three months, when the inguinal lymph nodes of those escaping testicular infection were inoculated in the testes of fresh animals. Rabbits inoculated with 1:500 and 1:5000 final dilutions of the bismuth compound escaped infection. With citrated rabbits' blood instead of saline only the 1:500 final dilution of the bismuth compound was completely spirocheticidal, probably because the presence of the blood reduced the effects by combination with proteins.

3. According to Levaditti's theory bismuth is spirocheticidal in combination with the tissue forming *bismoxyl*, and the free or nascent bismuth which is subsequently liberated effects an organometallic combination responsible for parasiticidal effects. In an experiment, a 4% extract of rabbit's liver was prepared according to Levaditti and 3 c.c. mixed with 3 c.c. of a 4% solution of sodium tartro bismuthate in saline solution. This mixture was incubated at 37°C for 7 hours, during which a precipitate formed. The mixture was then centrifuged, the supernatant discarded, the total volume restored to 6 c.c. mixed and again centrifuged. The supernatant was discarded and the precipitate suspended in 6 c.c. of saline solution. The 6 c.c. of liver-bismuth mixture contained 0.120 g. of bismuth sodium

tartrate. $\frac{1}{10}$ c.c. of varying suspensions of precipitate with saline solution were mixed with 0.1 c.c. of a suspension of *S. Pallida* from medium sized testicular nodes from rabbits; these were kept at room temperature (27°C) and examined by dark field at the end of 15 minutes and one hour.

The compound itself produced marked immobilisation at the end of 15 minutes in a final dilution of 1:10,240 while the precipitate (bismoxyl) immobilised at 1:5,120. At the end of 1 hour, however, the final immobilising dilution of the compound was the same (1:10,240) but somewhat stronger with bismoxyl which gave immobilisation at 1:20,480. According to these results, therefore, a liver extract precipitate of bismuth sodium tartrate showed less immobilisation of *S. Pallida* than a saline solution of the compound itself at the end of 15 minutes at 27°C but distinctly more after an hour which may lend some support to the theory of Levaditti bearing upon the effects of dissociated bismuth.

4. The immobilising effects of bismuth compounds on cultures of spirochetes were studied, the cultures being 4 to 5 day growths in a freshly prepared medium of beef infusion broth (4.5 c.c.) containing 0.5 c.c. of inactivated rabbit serum. $\frac{1}{10}$ c.c. of varying dilutions of the compounds were mixed with 0.1 c.c. of culture and the mixtures examined by dark field after standing for 15 minutes

at room temperature (24–27°C.). The immobilising dilutions of six compounds varied from about 1:20 to 1:80 and were therefore much lower than those observed with spirochete in emulsions of rabbit testicular syphilomas. This was most likely due to the inactivating effects of the culture medium upon the bismuth. Exposure to 30 and 60 minutes increased the effects. Nevertheless the effects of bismuth on cultures of *S. Pallida in vitro* are very much less than upon tissue spirochetes. Similar results have been obtained with the arsenicals.

5. There is therefore no reasonable doubt but that bismuth is directly spirocheticidal both *in vitro* and *in vivo*. Whether these effects are due to the element slowly dissociated from the compound itself or after it has produced an organo bismuth complex is still an open question.

Protective value of Bismuth in Syphilis: HANZLIK, LEHMAN and VAN WINKLE (*Am J. Syph. Gon. and Ven. Dis.*, July 1940). These authors conclude from animal and human experiments that bismuth compounds injected intramuscularly act definitely as protectives against experimental syphilis in rabbits and clinical syphilis in prostitutes.

Sobisminol is effective by mouth in all stages of clinical syphilis and controlled drinking of sobisminol solution by rabbits acts as preventive of experimental syphilis.

Sobisminol orally as a protective should be comparatively safe

for human beings but should be given under supervision and controlled by frequent examinations and urinary estimations of bismuth.

A tentative outline is to begin with 3 or 6 capsules daily for one week before expected exposure. Urine is to be examined at end of first week. After exposure continue medication with 6 capsules daily for 2 weeks checking urine weekly.

Further medication with reduced dosage of sobisminol would be desirable for a period of 3 months. Medications should be stopped reduced or adjusted immediately on complaint of gastric intolerance or other systemic disturbances.

The Treatment of Delayed Menstruation with Prostigmine.

A Therapeutic test for early Pregnancy: SAMUEL SOSKIN, HANS WATCHEL AND OSCAR HECHTER, (*J. A. M. A.*, May 25, 1940). In a recent study it was found that the various component phenomena of estrus, in the rat may be classified in two categories: (1) the specific proliferative effects of estrogen and (2) those effects which are secondary to hyperæmia. The latter effects can be reproduced by non-specific hyperæmic agents, such as yohimbine. However, when they result from the action of estrogen they are due to the acetylcholine—liberating properties of this hormone, as demonstrated by Reynolds.

• 6

In view of the large proportion of the estrous phenomenon in animals which is dependent on hyperæmia, it seemed likely that the role of hyperæmia was probably even more important in the periodic menstrual bleeding of the human female. Considering the mechanism of this hyperæmia, it would presumably also be under the influence of at least the parasympathetic nervous system. This relationship of the nervous system to uterine hyperemia might readily account for the well known influence of mental, emotional and physical strain on the menstrual history of women. It thus appeared possible that cases of delayed menstruation, now generally ascribed to temporary endocrine dysfunctions, might in fact occur despite normal hormone secretion and be due to abnormally decreased vascular responsiveness. It therefore seemed worth while to attempt to treat such cases by pharmacologic rather than by endocrine means.

Methods and Results.

The mechanism of the hyperæmic action of estrogen suggested the use of acetylcholine. But, since this seemed not without danger, it was decided to potentiate the naturally occurring acetylcholine in the uterine endometrium by inhibiting the cholinesterase with prostigmine methylsulphate, a synthetic physostigmine like substance which is commercially available.

Since we proposed to use prostigmine to precipitate the menstrual flow of women in whom this function was significantly

delayed, we considered the probability that some women would present themselves in early pregnancy. Although this possibility could be ruled out by history and physical examination in more cases, it was necessary to be certain that the treatment would not disturb an early pregnancy if the diagnosis should be missed. For this purpose a series of freshly impregnated rats was used. The animals were injected on the first three successive days of pregnancy with amounts of prostigmine which varied from doses equivalent to those we wished to use on patient to large doses within the lethal range. It was seen that prostigmine did not terminate the pregnancy in a single instance, even when relatively huge amounts of the drug were given. Those animals which did not succumb to the immediate general effects of the lethal dosage went on to normal gestation periods and deliveries and bore healthy litters.

With the assurance gained from our animal experiments, we proceeded to test the effects of prostigmine on women in early pregnancy, as judged by history, physical examination and a positive Friedman (modification of the Aschheim-Zondeck) test. Table 2 shows that the pregnancies were not affected. No untoward or unpleasant, subjective or objective effects of the drug were observed.

In cases of delayed menstruation in which early pregnancy was ruled out by the history and physical examination, supplemented by

the Friedman test when necessary, prostigmine invariably precipitated the menstrual flow. The flow started as soon as half an hour after the injection in one instance. The longest interval between the last injection and the beginning of the flow was seventy-eight hours. The average time which elapsed was twenty-eight hours. In some instances the amount of flow was somewhat heavier than that usually experienced by the patient, though not alarmingly so. With one exception, all the patients reported normal menstruation at their next regular period.

We are aware of the possibility that some of our patients with delayed menstruation might have started the menstruate even if no treatment had been given or if a placebo had been employed. But the invariable nature of our results and the fact that the flow started after an average interval of only twenty-eight hours can leave no doubt that prostigmine precipitates menstruation when it would otherwise not occur. Indeed, from our experience it is possible to assure the patient treated with prostigmine that she will soon menstruate unless she is pregnant. If she fails to menstruate pregnancy may be diagnosed with the same degree of accuracy as is possible with the Friedman test.

It must be emphasized that this procedure applies only to delayed menstruation in women who have had a normal menstrual history up to the last period. It does not apply either to early or to prolonged amenorrhoea due to

endocrine dysfunction or to local organic changes. For the sake of completeness we have administered prostigmine in a considerable number of cases of the latter types, without the slightest result.

Summary and Conclusions.

1. The important role of hyperæmia in the estrous phenomenon suggested that delayed menstruation might be due to lack of vascular response rather than to endocrine dysfunction.

2. On the basis of the physiologic mechanism of estrous hyperæmia, women suffering from delayed menstruation were treated with prostigmine. Menstrual flow invariably resulted.

3. Preliminary work on animals and on human beings conclusively demonstrated that prostigmine does not initiate menstrual flow when the delay is due to early pregnancy.

4. Prostigmine has no effect on early or prolonged amenorrhoea due to endocrine dysfunction or to local organic changes.

5. The constancy of the results in menstrual delay and the lack of effect on pregnancy make it possible to use prostigmine as a combined treatment for menstrual delay and a therapeutic test for pregnancy.

Heparin. (*J.A.M.A.*, May 25th 1940. Editorial). As a result of the rapidly developing information concerning this substance during recent years, heparin,

from being a rather unique anticoagulant with limited laboratory application, has become a promising clinical adjunct. The isolation of a highly purified product has contributed to the advance in our knowledge of this substance. The rapidly accumulating information regarding heparin has recently been reviewed by the Scandinavian investigator Jorpes.

With the purified product available, organic chemists have made progress in establishing the chemical structure of the heparin molecule. Thus Charles and Todd have studied the crystalline barium salt of heparin which was isolated from heparin preparations made from beef lung, beef liver and beef intestine. All these crystalline barium salts are similar in their composition and physiologic potency. Charles and Todd, after careful observations of the chemical behaviour of heparin and on the basis of previous work, have concluded that heparin is a mucosulfuric acid in which the fundamental structural unit consists of two molecules of acetyl glucosamine and two molecules of glycuronic acid. Each unit also contains five sulfuric acid groups, which impart strongly acidic properties to heparin; physiologic inactivation follows the removal of the sulfate groupings.

The provision of highly purified preparations of heparin for experimental study encouraged clinical use of this substance.

Jorpes has attempted to demonstrate heparin directly in

the walls of the large blood vessels by the use of toluidin blue, which stains heparin strongly metachromatically. Within a few hours after large vessels have been immersed in a dilute solution of toluidin blue there results a purple staining of the vessel walls, most marked near the lumen. The old idea that heparin is localized in the vascular system thus appears in a new form. Further study in collaboration with histologists pointed to the mast cells of Ehrlich as responsible for the metachromatic purple colouration obtained with the staining dye. Strongly suggestive proof was then obtained that the granules of the mast cells of Ehrlich consist of heparin. Moreover, a rather good correlation was found between the histologically demonstrated content of mast cells of various tissues and organs and the content of heparin which they yield. There is another supporting proof for the conclusion that the metachromatic granules in the mast cells of Ehrlich consist of heparin. These cells, by virtue of their position around the capillaries and certain of the small blood vessels, apparently have the opportunity of emptying the contents of their granules directly into the blood stream.

The isolation of relatively pure heparin has led to an extensive examination of the relationship of this anticoagulant to the problem of thrombosis, particularly, by Best and his collaborators at Toronto. It was demonstrated that heparin greatly inhibits the formation of thrombi produced in

animals, by mechanical or chemical trauma to the intima of large exposed veins. The ability to produce coronary thrombosis in dogs by means of sodium ricinoleate was also greatly diminished in heparinized animals, as compared to control dogs which did not receive heparin. This successful experiments have stimulated the use of pure heparin in clinical cases of thrombosis and remarkable results have been reported at the Toronto General Hospital and in Stockholm. Heparin has been employed postoperatively with a high degree of success; pulmonary embolism or thrombophlebitis was not observed in instances in which these complications might ordinarily be expected. Although it is somewhat difficult to evaluate post-operative treatment for the prevention of thrombosis, more direct evidence of the value of heparin may be obtained in the treatment of an existent thrombus. Striking claims have been made in the Swedish clinics for the value of heparin in the treatment of thrombosis in the main trunk of the central vein of the retina, and subsequent definite return of visual acuity has been reported. Similar efficacious results with heparin are reported in vascular surgery. In recent preliminary publications in the Journal, suggestions have been made for the use of intravenous heparin drip, in conjunction with sulfapyridine, in the treatment of subacute bacterial endocarditis. The prevention of embolus formation greatly diminishes the nidus for growth of bacteria and vegetations.

Future clinical work may definitely establish the value of heparin in clinical thrombosis, coronary thrombosis, thrombosis of the large veins and thrombophlebitis. Heparin, like many other therapeutic substances, is the product of the combined efforts and interests of the physiologist, the biochemist and the clinician and has now passed from pure physiology to medicine by way of biochemistry.

Malaria simulating acute surgical diseases of Abdomen: R. A. DANIEL Jr. (*Ann. Surg.*, III, 436, March 1940). Malaria simulating acute surgical diseases of abdomen—Daniel discusses the confusing picture produced by abdominal pain, which may be a manifestation of malaria. Surgeons are familiar with the post-operative fever caused by the lighting up a chronic malarial infection. These cases sometimes occur in temperate regions.

Daniel reports nine cases of malaria simulating acute abdominal disease. Eight of the patients were encountered in a total of 266 patients with malaria admitted to the Vanderbilt University Hospital during the last thirteen years. An analysis of the cases reveals that the diagnosis of malaria was suspected and established in six cases because of the presence of leukopenia, on admission. A rise in temperature was accompanied by a leukopenia, sometime after admission, in three cases. Two patients had an unexplained chill and the parasites were found in the routine blood smear. Sudden

onset of severe abdominal pain occurred in six cases, and in three the pain was at first relatively mild and gradually increased in severity. Nausea was present in all cases and vomiting in eight. Only three patients had produced symptoms, headache and general malaise, and only three gave a history of previous attacks of similar abdominal pain. The past history of two patients was of significance in suggesting malaria as a cause of the symptoms. Chills occurred during the present illness in only three cases. The spleen of only one patient was felt, and he presented such marked abdominal tenderness and muscle spasm that neither the liver nor the spleen could be palpated until several hours after the parasites had been found and quinine was administered. The liver of only one patient could be felt. Three of the patients had a definite involuntary rigidity of the abdominal wall at the time of admission. The two patients who gave past histories of malaria had received inadequate treatment. The other patients had never had symptoms of malaria and had not received antimalarial treatment. The importance of painstaking, unhurried examination of the blood in similar cases is emphasized. Parasites are often found by the thick drop method when they are not numerous enough to be seen in the smears. Repeated examination of the blood were performed in five cases before parasites were seen. *Plasmodium vivax* was found in the blood of seven and *Plasmodium falciparum* in the blood of two patients. The usual

criteria for differentiation of malaria from the common, acute surgical diseases of the abdomen were strikingly inadequate in most of the nine cases. Leukopenia was present in eight. It may be of considerable aid in suggesting the presence of malaria. The examination of a blood smear and of thick drop led to the correct diagnosis in five. The finding of malarial parasites in the blood of patients who present characteristic signs of intraperitoneal disease does not exclude the possibility that such a disease may also be present.

Diethylstilbestrol, Synthetic Estrogenic Substance: J. A. HUET, R. J. COMTE, and A. D. HERSCHBERG, (*Gynaec. Paris* 1938, 39).

Huet and his associates employed diethylstilbestrol in forty-six cases of gynecologic disorder. The substance was found to be effective in genital infantilism, in certain forms of oligomenorrhœa and dysmenorrhœa, in functional disorders of the menopause and in a number of hypophysis-ovarian disturbances. The treatment was successful in 77 per cent of the cases of menstrual dysfunction and in 82 per cent of menopausal disturbances. In the latter it counteracted the hot flushes, the profuse sweats and the vasomotor symptoms. The untoward secondary effects of this treatment were few. In ten per cent of the cases the complications were benign. They consisted of attacks of weakness and nausea, which disappeared in the course of treatment. These complications were observed especially in women of the premenopausal and

menopausal age. In about 3 per cent of the cases total gastric intolerance existed but its symptoms were ceased when the medication was discontinued. The therapy with the synthetic estrogenic substance has advantages over that with the natural estrogens. Diethylstilbestrol is highly effective when administered by mouth; is easily handled and is relatively inexpensive. The fact that it is a powerful therapeutic agent necessitates an exact etiologic diagnosis and close clinical supervision in order to avoid disappointment. The authors recommend a dosage of 2 mg. of diethylstilbestrol daily given in two doses (morning and evening), far from meals, from the eighth to the eighteenth day, counting from the first day of the menstrual period. If an immediate menstrual flow is the object, the substance can be given in a dose of 5 mg. daily. In the presence of hypophysis-ovarian disturbance 3 mg. daily for three days is recommended, beginning with the second day of menstruation. In cases of dysmenorrhœa caused by uterine hypoplasia, 5 mg. is given on the day before the onset of the menstrual flow. In certain oligomenorrhœas the dose is reduced to 1 mg. daily for the ten days, in order to avoid too abundant hemorrhages.

Oral treatment of Trachoma with P-Aminophenylsulfanilamide: F. JASSERON AND G. MORARD. (*Presse Med. Paris*, February 28, 1940). Jasseron and Morard call attention to the oral treatment of trachoma with P-aminophenyl-sulfanilamide and point out

that in their experience this substance showed the best results in the chemotherapeutic treatment of trachoma. The authors treated nearly 200 patients. Subjective symptoms, such as pain, photophobia and lacrimation, disappeared in forty-eight hours; pannus and infiltration of the cornea were resorbed in eight days; corneal ulcers acquired epithelium in thirty-six hours; cicatrization was accelerated and clinical recovery took place weeks in 75 per cent of the cases. Secondary infections with Weeks's bacillus, diplobacilli of Morax, pneumococci and gonococci were sterilized in four days. The authors recommend for adults ingestion of 20 Gm. in thirteen days, for children aged from 8 to 12 years in Gm. in twelve days, and for children from 4 to 8 years 7 Gm. in twelve days in decreasing dosage. Limited local treatment is advised.

Sulfanilamide Derivatives in Treatment of Trachoma: L. POLEFF. (*Presse Med. Paris*, February 28, 1940). According to Poleff, subconjunctival injections were followed by intense hemorrhage at the place of injection. Repeated instillations and subconjunctival injections in five cases were not followed by sterilization of the bacterial flora of the conjunctival sac, while silver nitrate and ethoxydiamino-acridine lactate produced rapid diminution of the bacteria and general improvement. Intramuscular injections of alternated with oral administration of sulfanilamide derivatives were followed by notable decrease of bacteria in the con-

junctival sac; however, the final results were not satisfactory. Oral and intramuscular administration of sulfanilamide derivatives together with the usual treatment of trachoma produced very satisfactory results in fifteen malignant cases. Pallor and rapid loss of weight in the course of sulfanilamide therapy are symptoms of intolerance to the drug.

Sulphur and Chemotherapy: (EDITORIAL, *Lancet*, May 25, 1940). Sulphæmoglobin is less often found in the blood in significant quantities after the administration of sulfanilamide and its derivatives than methæmoglobin, but while methæmoglobin disappears within one or two days of stopping the drug sulphæmoglobin persists for from four to six weeks. During that time it immobilises part of the hæmoglobin, so that in its effect it is the equivalent of an anæmia. There is good reason, therefore, for avoiding sulphæmoglobinæmia, but there is some difference of opinion as to how this could be done. The condition is known to appear in patients receiving sulfanilamide who have much sulphuretted hydrogen or soluble sulphide in their alimentary tract. The presence of these has been thought to be due to an excess of combined sulphur in the diet, and various dietetic prohibitions have consequently been introduced. Some doctors forbid eggs, others eggs and onions, and others again prescribe a low residue diet in addition. The egg theory seems to be based on a misconception. It is true that the bacterial decomposition of egg

outside the alimentary tract gives rise to sulphuretted hydrogen, but in normal digestion the sulphur-containing amino-acids are absorbed with very little formation of sulphides. It has never been shown that eggs in the diet promote the formation of sulphæmoglobin when the intestine is normal. The same applies to other foods containing sulphur, many of which, such as cheese, contain more than eggs. Another prohibition, which is sound though not for the reason usually given, is that Epsom and Glauber's salts lead to sulphæmoglobinæmia not because the sulphates are reduced to sulphides but because they are purgatives. When purgatives are given the fluid contents of the small intestine are hurried into the colon and it is the bacterial decomposition which takes place in these liquid faeces that produce the sulphides. Certain drugs, of which phenacetin is most used, predispose to the formation of methæmoglobin, and, if even small quantities of sulphides are present, of sulphæmoglobin. Confection of sulphur administered by itself rarely results in sulphæmoglobin appearing in the blood, but if the sulphur is given with sulphanilamide sulphæmoglobin soon appears, and it appears rapidly if phenacetin is given as well. Drugs like phenacetin must therefore not be used with sulphanilamide, but aspirin is harmless in this respect. To sum up, then, when giving sulphanilamide and the like purging and phenacetin should be avoided, but there is no reason why the patient should

not have as normal a mixed diet as his condition will allow.

Chemotherapy of Infectious Diseases : EDITORIAL, *J. A. M. A.*, May 25, 1940). In 1904 Ehrlich summarized the aims of chemotherapy: "What we seek is 'specific chemotherapy', that is, we are in the search of a drug which should be capable of destroying certain parasites without at the same time causing too much damage to the host." Since the time chemotherapy has accomplished notable successes in treatment of diseases caused by protozoa and spirochaetes and more recently by other bacteria. The use of organic arsenical compounds in the treatment of syphilis, of plasmochin and atabrine in malaria, of quinoline derivatives in amebiasis and of antimony compounds in the treatment of leishmaniasis is well established. In the case of bacterial disease the problem proved to be much more difficult because the organisms are much less differentiated. Koch's failure of mercuric salts discouraged, at least temporarily, much research in this field.

The preparation in 1908 of the compound aminobenzene-sulfonamide in the course of a purely scientific research not at all concerned with problems of chemotherapy, resulted, nevertheless, in a renewed interest in the search for new chemotherapeutic agents. Horlein, Dressel and Kothe of the I. G. Farbenindustrie prepared new textile dyes from azo compounds containing sulfonamide groups.

Eisenberg demonstrated the bactericidal action of certain azo compounds in vitro and employed chrysoidin for chemotherapeutic purposes. American investigators, Heidelberger and Jacobs, linked dihydrocupreine with diazo compounds obtained from aromatic amines, including para-aminobenzenesulfonamide, and found that many of the azo compounds thus formed exhibited bactericidal properties in vitro but not in vivo. A number of azo compounds were found in the laboratories of I. G. Farbenindustrie to possess bactericidal properties in vitro. Compounds containing the sulfonamide group were found to be effective against streptococci infection in animal experiments. The chemists Kiarer and Mietzsch synthesized sulfonamide containing azo compounds, and Domagk demonstrated that one of these products was effective in preventing death in mice infected with lethal doses of streptococci. Their collaboration led to the development of a product patented as "Prontosil" and somewhat later to "Prontosil Soluble." At about the same time Truefouel and his associates in France established that a number of azo dyes prepared from para-aminobenzene-sulfonamide but of different physical and chemical properties had an antistreptococcal action like that of "Prontosil". They have advanced the hypothesis that all the active azo dyes, including "Prontosil," were reduced in the organism to sulfanilamide. This led then to the important discovery that the simple colourless compound sulfanilamide was itself highly active as a therapeutic

agent in experimental streptococcal infection. Domagk's contribution, as Heubner points out, consists in establishing the fact that of the many tested substances the derivatives of sulfonamide alone possess the property of favourably influencing streptococcal infection in the mouse, the rabbit and man.

The dramatic results obtained with sulfanilamide in many instances in a variety of streptococcal infection such as puerperal fever, meningitis, septicæmia, erysipelas, scarlet fever and osteomyelitis and in gonorrhœa are now common knowledge attested by an overwhelming literature. The new derivative sulfapyridine has been found to be strikingly effective in pneumococcal pneumonia. The most recent derivative, sulfathiazole, appears to be as effective against pneumococcal infection as sulfapyridine but is superior to both sulfapyridine and sulfanilamide against staphylococcal infection.

Empiricism, however, has definite limitations. It is realized that further knowledge can come only from understanding the mode of action of these compounds. This subject was editorially discussed in the Journal, but for more detailed exposition one should consult the reviews by Domagk, by Marshall, and a recent one by Heubner. A genuine bactericidal effect of sulfanilamide on the cocci has not been demonstrated. The effect is rather that of arrest of growth, due possibly to disturbance of metabolism or to interference

with the capsule formation of the cocci. R. L. Mayer pointed out that the frequent appearance of methemoglobin in the blood of animals and patients treated with sulfanilamide suggests the formation in the body of product of the drug responsible for the formation of methemoglobin. He advanced the hypothesis that the bactericidal effect is due not to sulfanilamide but to the same oxidative product with oxidizes hemoglobin to methemoglobin. This theory is further developed by Shaffer, who states that the probable mode of action of sulfanilamide is that the drug provides a mechanism by which the sterilising oxidation intensity of molecular antigen is applied merely at its maximum to bacteria and unfortunately also, to some extent, to host cells. The present status of our knowledge is summed up by Marshall in his review of the Pharmacology of sulfanilamide: "No satisfactory explanation of the mechanism of action has been found." There is, however, little doubt that the advent of sulfanilamide has initiated a true renaissance of bacterial chemotherapy.

In a paper on 'A Rational Approach to Research in Chemotherapy' Paul Fildes states (*Lancet*, May 25, 1940)—An *essential metabolite* is a substance or chemical group which takes an essential part in a chain of synthesis necessary for bacterial growth. A *growth factor* which must be supplied in the nutrients is an essential metabolite which the cell cannot synthesise. Nicotinic acid, for instance, is an essential metabolite for all

bacteria but a growth factor for only few.

Antibacterial substances function by *interfering* with an essential metabolite for all bacteria but a growth factor for only a few. The interference may be (1) by oxidising a substance which requires to be reduced, (2) by molecular combination forming an inactive product, or (3) by competing for an enzyme associated with the essential metabolite. It is claimed that sulphanilamide acts in (3) the essential metabolite being P-aminobenzoic acid. This substance antagonises sulphanilamide quantitatively and in very high dilutions. At the moment, therefore it is supposed that P-aminobenzoic acid is an essential metabolite for bacteria, although for technical reasons it has not yet been isolated from them nor has it yet been proved to be a *growth factor* in the absence of a bacterium which cannot synthesise it. This essential metabolite is normally associated with an enzyme, and sulphanilamide, being structurally similar to it, is capable of displacing P-aminobenzoic acid from its enzyme and stopping this essential line of metabolism.

Class (3) inhibitions require an inhibitor so closely related in formula to the essential metabolite that it can fit the same enzyme, and sufficiently unrelated to be devoid of essential metabolic activity. It is suggested that research in chemotherapy might reasonably be directed to making such modifications of Known essential

metabolites as will have these characters. It is curious to note that chemists are already proceeding on this line. In sulphapyridine, for instance, the base attached to the sulphanilamide is related to nicotinic acid, and in sulphathiazole to vitamin B₁.

Urinary Tract Infections due to B. Coli and its treatment with Sulphanilamide: L. A. RANTZ and C. S. KEEFER (*Arch. Int. Med.* May, 1940, p. 933).—In the course of this article the authors observe that to understand the action of urinary antiseptics it is necessary to review some aspects of both the pathology of pyelonephritis and the mechanisms by which infection may reach the kidney.

Pathologic investigation of renal infection has shown that there is primarily an involvement of the lymphatic system of the organ. In many instances inflammation and necrosis of the epithelium of the pelvis and calices occurs, but in addition, there is always widespread inflammation between the tubules and the glomeruli, with cellular infiltration and very often small abscesses in these areas from which bacteria may be recovered. Healing is regularly accompanied by scarring and contraction of the kidney.

The manner in which the infecting organism is able to reach the kidney and the mechanisms responsible for maintaining the disease have long been the subject of debate. It is generally agreed that obstruction to the free flow of urine predisposes this organ to infection. The principal source of

disagreement is as to whether the organism reach the kidney by way of the blood stream or ascend from the lower urinary passages. Such arguments are highly academic especially in the light of recent experimental evidence that in the presence of urinary obstruction intravenous or intraureteral injection of the colon bacillus in the rabbit will produce renal lesions practically identical with those of human pyelonephritis.

Pyelonephritis therefore is an infectious process which involves the entire kidney rather than the superficial tissues of the pelvis and to which there is a predisposition in the presence of obstruction to the free flow of urine.

In the light of these facts it is obvious that to regard the infected urinary passage as container of urine, to be sterilised by the excretion into it of a bactericidal agent is too superficial since much of the infectious process lies deep in the renal tissue, far removed from the urine. One might postulate that the drug containing urine is reabsorbed by the renal lymphatic system but this is a somewhat unlikely hypothesis. The dramatic results of the administration of sulphanilamide which frequently include sterilisation of the urine in spite of only bacteriostatic or moderately bactericidal effects in vitro suggest that the action of the drug in the patient is more complex than in the test tube.

It is certainly true that the infection in the parenchyma of the kidney must be cleared by

the same cellular and immune mechanisms responsible for the healing of inflammatory processes elsewhere in the body. The effectiveness of the therapeutic agent here is limited to that degree of bacteriostasis which it is able to exert in those concentrations in which it is brought to the tissues by the blood stream.

In view of these considerations it seems likely that an agent which in vitro exerts marked bacteriostasis or bacteriocidal effects against the organisms responsible for an infection of the urinary passages has a three-fold mode of action in the infected kidney.

Firstly, the presence of the agent in the urine inhibits the multiplication of the organism in the tubules, pelvis, ureter and bladder, and may destroy it. It is possible that those membranes in direct contact with the urine may absorb a sufficient amount of the drug for this effect to occur in their most superficial layers. The direct result of this action will be decreased production of toxin in the urinary tract, with consequent reduction of superficial inflammation, congestion and œdema and in turn, resultant relief of symptoms and decrease in obstruction to the urinary flow. Water diuresis long known to affect favourably the course of these infections, acts in a similar but less dramatic manner by washing away the organisms from these areas.

Secondly, the elimination of obstruction and the inhibition of

multiplication of the bacteria in the urine must markedly reduced the possibility of reinfection which undoubtedly occurs in the deeper renal tissues when the tubules are engorged and the organisms are multiplying freely.

Thirdly, depending on the possible relationship of the effect of the drug to its concentration in the blood, there may be direct action on the organisms in the deeper tissues, showing their multiplication and permitting the usual clearing mechanisms to operate more effectively. This action may be important in its effect on the colon bacillus, since these organisms are usually so weakly invasive that even a very slight reduction in the rate of increase of the bacteria might be adequate to enable the tissues to eliminate them.

It is then probable that final recovery from infections of the kidney results from the activity of the immunogenic mechanism of the body, which may be aided by certain chemical agents. In support of this theory are the facts that most acute renal infections are self limited and that healing is complete in the absence of obstruction even though no special therapy is instituted. Relapse in the presence of obstruction may very well be due to repeated reinfection. Chronic infection without demonstrable obstruction are extremely difficult to relieve with any drug; this fact suggests that the bacteria continue to remain viable and multiply in the tissues because of some unknown defect in the mechanism by which the

body usually removes infecting agents.

In the treatment of B. Coli infection of the urinary tract with sulphanilamide it was found that the pH of the urine seemed to produce no significant difference in the action of sulphanilamide. The concentration of the drug was, on the other hand, of the highest importance. The most striking increase in the efficacy of the drug occurred when the concentration was increased from 40 to 80 mg.; there was little demonstrable increase in the action of the drug when higher concentrations were used.

A bedside test for Sulfapyridine:
—RATISH, HERMAN D. AND BULLOWA, JESSE G. M. *Lab and Clin. Med.* 25: 654, March 1940). "It is desirable to know the concentration of sulfapyridine in the blood when treating pneumococcic pneumonias and their complications." In the writers cases treated successfully with sulfapyridine, "4 to 6 mg. per 100 c.c. were usually present in the blood. In some cases of pneumococcic meningitis 10 mg. per 100 c.c. of cerebrospinal fluid were required to effect a cure. The concentration in the cerebrospinal fluid is usually two thirds that in the blood. When the concentration is too low, larger and more frequent oral doses or parental administration may be employed."

The writers describe a simplified method for determining sulfapyridine, depending upon

the ether extraction of sulfapyridine from the blood. The test may be performed "away from the laboratory by the physician or by the nurse at the bedside, and with apparatus within the means of the smallest hospital. The test, with a simultaneous duplicate analysis, may be carried out in 10 minutes".

The following reagents and apparatus are required for the determination of sulfapyridine by the method:

"Reagents:

"1. Ether.

"2. 15 per cent trichloroacetic acid solution.

"3. 0.1 per cent solution of sodium nitrate.

"4. 1 per cent solution of Urea.

"5. A solution of a-dimethylnaphthylamine containing 1 c.c. in 250 c.c. of 95 per cent ethyl alcohol. (This reagent should be kept in dark dropping bottle).

"Apparatus:

"1. 2 c.c. Luer syringe and needle.

"2. 1 test tube of 20 c.c. capacity with round bottom, stoppered with cork and marked at 1 c.c. and 6 c.c.

1 centrifuge tube with long taper, graduated to 15 c.c. in 0.1 c.c. divisions, fitted with rubber stopper.

"3. 5 dropping bottles to contain the reagents listed above.

"4. A comparator block 2.5 inches by 4.5 inches, with 4 openings to take test tubes 100 by 12 m.m. and colour standards. (Reading is facilitated when the width of the colour band is increased by placing tubes filled with water behind the standard and the test).

"Method—Into a Luer syringe draw approximately 1.5 c.c. of venous blood. Invert the syringe with the needle still attached and deliver the blood, drop by drop, into the round bottom test tube, to the 1 c.c. mark. From the other dropping bottle add ether to the 6 c.c. mark. Insert the stopper and shake vigorously for two minutes. The fluids will rapidly separate into two layers, with the ethereal extract of sulfapyridine in the upper layer. Slowly release the stopper. Cautiously decant the ethereal extract into the centrifuge tube to the 0.5 c.c. mark and set the extraction tube aside for duplicate tests.

"By means of a dropping bottle add 15 per cent trichloroacetic acid solution to the 5 c.c. mark, place the rubber stopper over the mouth of the tube, and shake vigorously for 10 to 20 seconds. Add 0.5 c.c. of 0.1 per cent sodium nitrite solution (7 to 8 drops from a dropping bottle), bringing the solution to 5.5 c.c. mark. Again shake vigorously for 20 seconds, and add 0.5 c.c. of 1 per cent urea solution dropwise from a dropping bottle. Finally add a-dimethylnaphthylamine to the 8.5 c.c. mark from its dropping bottle, close the tube with the rubber stopper, and invert once or twice. The white

opalescence is soon replaced by a purplish-red colour. After five minutes the colour is fully developed and the tube may be compared with standards in the comparator block.

"All values of this ether extraction method lie within 75 to 95 per cent of those obtained by the Marshall method, using a photocolorimeter."

"The quantitative estimation of sulfapyridine depends upon the formation of a purplish-red azo dye. This diazotization may be completed in approximately one minute and the full colour developed in five minutes."

"The rate of colour formation after coupling with a-dimethylnaphthylamine, the comparative action of ammonium sulfamate and urea on the destruction of the excess nitrite, and the value of trichloroacetic acid and paratoluenesulfonic acid as media for the reaction, were studied. With a photoelectric colorimeter results were obtained which indicated that either group of reagents may be used. Urea and trichloroacetic acid are recommended because they are cheaper and more readily obtainable.

"(Note.—While ether does not extract sulfapyridine from watery solutions or urine as efficiently as it does from blood, it extracts sulfapyridine well from cerebrospinal fluid.)

"Preparation of colour standards.—Colour standards may be readily prepared using phenol red. They are calibrated so that the

value of sulfapyridine obtained from the sample corresponds to the true value. Dissolve 0.0075 Gm. of phenol red in 100 c.c. of distilled water. To a series of 5 tubes, add 3.9 c.c. of fifteenth molar potassium dihydrogen phosphate (KH_2PO_4) and 6.1 c.c. of fifteenth molar secondary, sodium phosphate (Na_2HPO_4). Then follow with 0.2 c.c. of normal sodium hydroxide (Na_2HPO_4) and phenol red as indicated. The volume of the phenol red should increase progressively in the different test tubes.

Amount of Phenol red.	Amount of Sulfapyridine (true value) Indicated.
0.22 c.c. 0.30 c.c.	Concentrations up to 4 mg. per cent. Concentrations up to 7 mg. per cent (usual in blood of recovered pneumococcal pneumonia patients).
0.46 c.c. 0.62 c.c.	Concentrations up to 10 mg. per cent. Concentrations up to 12.5 mg. per cent (desirable in blood of meningitis patients).
0.86 c.c.	Concentrations up to 15 mg. per cent.

"The Phenol red solutions are transferred to test tubes 100 by 12 m.m. and sealed. The value of each tube should be marked on or permanently attached to it. The standards should be protected from direct sunlight. New standards should be prepared every six months".

The effect of various Antacids on the Hydrogen Ion Concentration of the Gastric Contents—KIRSNER, JOSEPH B. and PALMER, WALTER L. (*Am. J. Dig. Dis.*, March 1940). "There is an increasing amount of evidence to indicate that acid gastric juice plays a significant role in the pathogenesis and nonhealing of gastroduodenal ulcer. The important problem of ulcer therapy, therefore, seems to be that of controlling the reaction of the gastric contents. Alkalies have been used extensively for this purpose but there is very little

evidence as to the degree of neutralization actually obtained. The purpose of this study was to appraise the in vivo neutralizing effect of a group of commonly used antacids."

"The neutralizing influence of various commonly used antacids was investigated in a total of 290 experiments performed on 25 patients with healing duodenal ulcer. The hydrogen ion concentration of the gastric contents removed hourly was determined by the glass electrode method. Control studies were made with a general diet and with hourly feedings of a 3-ounce mixture of milk and cream. The alkalies were administered hourly; they included calcium carbonate and sodium bicarbonate in varying amounts, calcium carbonate alone, aluminium hydroxide, tricalcium phosphate and magnesium trisilicate. The effect

of atropine on gastric acidity when given alone and in conjunction with various antacids, was also studied."

From this study the following observations were made:

"1. The gastric acidity is slightly and temporarily reduced by the administration of food.

"2. The higher the protein and fat content of the milk preparations, the greater was the neutralization of the acid but, at best, this effect was not marked.

"3. Of the various antacids studied calcium carbonate in 2.0 or 4.0 Gm. amounts hourly is the most effective neutralizer of gastric acidity.

"4. Tricalcate, tribasic calcium phosphate and magnesium trisilicate.....are progressively less effective, in the order named, in maintaining adequate neutralization.

"5. Aluminium hydroxide exerted relatively little influence on the gastric juice ph although the neutralizing capacity of 30 c.c. doses was appreciable.

"6. Atropine sulphate, given orally in four 1 mg. doses daily, had no influence on the ph of the gastric contents, although the volume of secretion was apparently reduced.

"7. The gastric acidity was most completely controlled by the use of atropine combined with calcium carbonate or with calcium

carbonate and sodium bicarbonate. The ph values obtained conform to the 'proteolytic' neutralization level of Hollander. Atropine permits also the effective use of smaller amounts of alkali.

"8. The effectiveness of atropine is due apparently to the resultant diminution in the volume of gastric secretion and the prolongation of gastric emptying time.

"9. The influence of an anti-acid on the gastric acidity depends not only upon its individual neutralizing capacity, but also upon the particular chemical reaction involved, the volume of gastric secretion, and the emptying time of the stomach."

Studies in Iron transportation and Metabolism: C. V. MOORE, W. R. ARROWSMITH, J. WELCH AND V. MINNOWITCH. (*J. Clin. Invest.*, September 1939). These authors have demonstrated that:

1. Absorption of iron from the gastro-intestinal tract was reflected directly by an increase in serum iron and not through an intermediate rise in the iron of the thoracic duct lymph.

2. The disappearance of i. v. injected soluble iron salts from the blood stream occurred slowly during a period of hours.

3. The height of the serum iron increase following the ingestion of iron was directly proportional to the quantity given up to the point at which intestinal irritation was great enough to interfere materially with intestinal motility.

4. When identical amounts of ferrous sulphate were given to any subject in hæmatological equilibrium the serum iron curves produced closely paralleled each other.

5. Water soluble, highly ionised ferrous salts produced comparable increases in serum iron values when given in proportionate amounts to patients with either an achlorhydria or normal gastric acidity. These findings suggest that the ease of ionisation of ferrous salts under those conditions of acidity or alkalinity present in the gastro-intestinal tract, is the important factor in determining their relative rates of absorption. The nature of the anion, except as it influences this factor would seem to be relatively unimportant.

6. In the majority of cases the serum iron absorption curves were higher following the ingestion of ferrous than of ferric salts. When ferric salts were given along with relatively large amounts of either cevitamic acid or sodium formaldehyde sulphonylate the serum iron responses were uniformly as good as those produced by ferrous salts of the same anion. These two reducing agents were likewise capable of increasing the rise obtained after ferrous preparations. Iron is thus shown to be largely absorbed in the ferrous form.

7. Difference in gastric acidity exerted no measurable effect on the serum iron absorption curves following the oral administration

of ferrous or ferric salts. It is suggested that the largeness of the doses led to a sufficient acidity.

8. No increase in serum iron was obtained following administration of the insoluble ferrous and ferric phosphate.

9. When subjects were permitted to take food just prior to or immediately following, the ingestion of iron salts there was observed frequently, not constantly, a smaller rise in the serum iron than occurred under fasting conditions.

10. Bile pigments, chlorophyll and its derivatives, the secondary anæmia liver fraction, and gastric mucin under the condition of these experiments failed to alter the height or character of the serum iron absorption curves produced by ferrous sulphate.

11. Patients with an iron deficiency anæmia frequently showed evidence of greater absorption of iron before therapy than after they had been adequately treated. On the other hand, patients with Addisonian anæmia in relapse showed no demonstrable increase in their already higher than normal serum iron values when ferrous salts were given orally; following a liver induced remission however, normal absorption curves were readily obtained. The intestinal mucosa may under certain circumstances and within certain limits assimilate or reject iron according to the body's need. They do not however constitute conclusive evidence for this hypothesis.

From the data thus presented, the following picture of iron absorption may tentatively be constructed. When ingested iron reaches the stomach, it is subjected to the influences of the prevailing acidity. The free hydrochloric acid normally present apparently has two functions: (1) to ionise and dissolve iron not already present in solution nor in an ionised state; (2) to delay the formation of insoluble and undissociated iron compounds. Since these form at a pH above 5.0 the change to them would tend to occur to some degree, at least, in the stomachs of patients with achlorhydria. When the iron is delivered to the duodenum, it is subjected to two influences: the alkaline intestinal juices and certain reducing agents. The latter tend to reduce any trivalent iron to the ferrous form before the change to non-ionisable salts has occurred. Iron is absorbed from the intestinal tract largely, if not entirely, as the ferrous iron. The degree to which ferric salts are assimilated would seem to depend upon the capacity of the intestinal contents to reduce them. It is the consensus of opinion that absorption takes place largely in the upper portion of the small intestines. When iron is absorbed it passes directly into the blood plasma and is not to any extent collected by the intestinal lymph channels.

Interpretation of the Glucose Tolerance Test. The necessity of a standard preparatory diet; CONN, JEROME W. (*Am. J. Med. Sci.* 199; 555, April 1940). "It has long

been known that starvation or restriction of carbohydrate in the diet of animals or man results in a marked decrease in the ability to utilize carbohydrate. Ingestion of a test dose of glucose, under these conditions produces hyperglycemia, glycosuria and a marked delay in clearing the blood of absorbed glucose. Although most investigators are fully aware of this phenomenon, the knowledge has not been applied in clinical medicine.

"The purpose of this report is to emphasize how much the composition of the previous diet may affect the glucose tolerance test and its interpretation. Since in mild or questionable cases of diabetes mellitus or in the differential diagnosis between non-diabetic and diabetic glycosuria, the glucose tolerance test becomes of major diagnostic importance, one must eliminate any influence which the previous dietary may have had upon the results".

Early in his work the writer observed that the presence of undernutrition per se was important in determining the degree to which carbohydrate tolerance would be diminished by restriction of carbohydrate in the diet. He, therefore, "chose as subjects for study three malnourished but otherwise normal patients, three normally nourished men (medical students) and three normally nourished women (dietitians). All nine subjects were between the ages of 19 and 25. All were fed a standard preparatory diet (300 Gm. CHO, 80 Gm. P and 3,000 Cal) for three days before

the initial glucose tolerance test was done. (Glucose, 1.75 Gm. per Kg. of body weight, given orally in the postabsorptive state was used as the test dose. Blood sugar was done by the Benedict method). All gave the normal response. They were then fed a diet containing 20 Gm. of carbohydrate, 50 Gm. of protein and 1,600 calories for five days following which the glucose tolerance test was repeated. Thus, the effect upon the normal carbohydrate tolerance of a short period of sharp carbohydrate restriction was observed".

In addition, data were studied on three patients wrongly diagnosed as diabetics. "In these, the effect upon diminished carbohydrate tolerance of a short period of normal carbohydrate intake was observed."

The following results were obtained. "A remarkable delay in clearing the blood of absorbed glucose is produced in normally nourished people by five-day period of dietary restriction. Qualitatively the response is the same in the undernourished individuals. The degree of response to the same restriction, however, is much greater in the undernourished group. Since, initially, both groups responded to three days of normal dietary by giving a normal glucose tolerance curve, it must be concluded that the existence of undernutrition makes the individual more susceptible to short periods of carbohydrate restriction."

"The additional three cases... indicate how an erroneous diag-

nosis of diabetes mellitus can be made, when the important factor of previous carbohydrate restriction is neglected. The first patient had been diagnosed and treated for diabetes with diet and insulin before coming to the University Hospital. The second had been considered to have mild diabetes and the third was said to have had diabetes for 20 years."

The first case was found to be malnourished but otherwise normal individual. This case demonstrated with what magnitude glucose tolerance will be affected by changes in the preparatory dietary carbohydrate.

In the second case, a male patient aged 72, two points are worthy of mention: "(1) What following long-standing undernutrition and carbohydrate restriction, it may require more than five days of high carbohydrate feeding to effect complete return of normal carbohydrate tolerance (2) The final curve, which was considered normal, reached a peak of 184 mg. per 100 c. c. in the first hour. "This is higher than any of the curves, on the other subjects following the preparatory diet. It has been shown, however, that normal old people exhibit a somewhat lower tolerance for carbohydrate than young people. This probably accounts for the difference.

The third case demonstrated "how a patient with renal glycosuria can be misdiagnosed as a diabetic when the glucose tolerance test is done after a period of carbohydrate restriction continuous glycosuria, because of a

low renal threshold, resulted in the prescription of a diet limited in carbohydrate. A glucose tolerance test, under these conditions, revealed a diabetic type of response. Thus, the usual criteria for the diagnosis of diabetes mellitus were satisfied. A glucose tolerance test after adequate carbohydrate preparation, however, disclosed normal carbohydrate tolerance and renal glycosuria. In this case malnutrition was not a factor. The original abnormal response was the result of previous carbohydrate restriction.

"Discussion.—It has been shown repeatedly that restriction of dietary carbohydrate in the normal individual results in a significant decrease in the rate of utilization of glucose. Yet it is not customary to scrutinize the antecedent dietary of the patient before interpreting the glucose tolerance test. The experiments reported here show again how greatly the normal rate of glucose utilization can be depressed by sharply limiting the intake of carbohydrate for several days prior to the test. In addition, it is found that when undernourished individuals, exhibiting normal carbohydrate tolerance, are subjected to the same restriction, a more marked delay in the utilization of glucose results."

"Claims have been made that the glucose tolerance test is a poor indicator of the ability of the organism to dispose of carbohydrate.... Much of the confusion arises from the lack of a standardized preparatory period

prior to the performance of the actual test." In order to obtain more standardized and comparable glucose tolerance tests, the writer has modified the procedure "by insisting that a standard preparatory diet be eaten for at least three days before the test is done. This diet is made up of 300 Gm. of carbohydrate, 80 Gm. of protein and, at least, maintenance calories. In cases in which it is known beyond question that the dietary of the preceding few days has been adequate for maintenance and abundant carbohydrate, one need not prepare the patient. When one encounters a diabetic type of glucose tolerance test with a fasting blood sugar value at or near normal, he should repeat the test after adequate dietary preparation. The objection that such a procedure entails greater effort and time does not justify errors in diagnosis due to lack of such procedure.

"Diabetics who have taken the standard preparatory diet for three to five days have not been harmed in any way, the temporary increase in glycosuria disappears shortly after the test diet is discontinued.

"In most cases, however, a glucose tolerance test is not necessary in order to make the diagnosis of diabetes. It is in the mild cases or in ruling out non-diabetic glycosurias that the glucose tolerance test becomes of major diagnostic importance. These are just the cases in which an erroneous diagnosis of diabetes may be made if, previous to the test, the intake of food has been limited."

"The same preparatory precautions must be applied in any condition in which the glucose tolerance curve is to be used as a help in diagnosis. In hyperinsulinism, for example the glucose tolerance curve often shows a precipitous fall to hypoglycemic levels when done after the standard preparatory diet. Restriction of dietary carbohydrate for several days before the test results in a much less marked drop of the blood sugar. Hence, under these conditions, the glucose tolerance test loses its value as a diagnostic aid."

"Thus it appears evident that in order that glucose tolerance tests be in any way comparable and worthy of interpretation, they must be preceded for several days by the ingestion of an adequate diet."

Intravenous Anaesthesia—ADAMS, R. CHARLES. (*J. Iowa State Med. Soc.*, April 1940). "The ultra short-acting barbiturates, evipan soluble and pentothal sodium, are best agents available at the present time for the use in intravenous anaesthesia. Pentothal sodium, owing to its increased potency over evipan soluble, produces a more satisfactory anaesthesia. Concentrations of pentothal sodium in triple distilled water ranging from 2.5 to 10.0 per cent have been employed, but a 2.5 per cent solution has proved to be the least irritating to the intima of the veins or to the tissues, if extravascular injection should occur.

"The technique of administration employed is the fractional

method, and the average dose required for induction of anaesthesia will range between 2 and 6 c.c. of a 2.5 per cent solution in the average case, depending on the tolerance of the patient for the barbiturate. Subsequent doses for maintenance of anaesthesia range roughly between 2 and 4 c.c. Preliminary medication with morphine, atropine and nembutal is indicated in all but the shortest of surgical procedures. The average maximal dose of pentothal sodium ranges between 1 and 2 Gm. but when large amounts of the drug are required to maintain anaesthesia, it is advisable to discontinue the administration or supplement the anaesthesia. The maintenance of a free airway and the avoidance of doses producing excessive respiratory depression are of the greatest importance. In this manner, a wide margin of safety will be maintained. A 'butterfly' placed over the mouth and nose of the patient forms the most reliable guide to the clearness of the airway and amplitude of the respiratory movements.

"Intravenous anaesthesia is particularly applicable for the shorter and less extensive operative procedures, but when indicated, it may be employed for certain intra-abdominal operations in conjunction with local anaesthesia, as are many minor gynecologic operations. Among other types, one might mention certain operations on or about the eye, operations and manipulations involving the bladder and prostate gland, and operations on the thorax and thoracic wall, provided secretions

from the bronchial tree are not sufficiently excessive to cause respiratory obstruction.

"Intravenous anaesthesia should be administered only by those experienced in its use. A thorough knowledge of the contra-indications and the dangers is essential to the safety of the method of anaesthesia for children under the age of 10 years, and although elderly and debilitated patients, in the main, tolerate the intravenous anaesthesia well, a more cautious administration is required. Intravenous anaesthesia should not be employed in the presence of intestinal obstruction since vomitus may be aspirated into the trachea. The majority of operations involving the nasal and oral passages and the pharynx and larynx are performed with greater safety under local or intratracheal anaesthesia, since obstruction to the airway, either by blood, mucus or mechanical factors, is always a potential danger. Because pentothal sodium is a sulphur-containing barbiturate, it is inadvisable to administer it to patients who have been receiving another sulphur containing preparation such as sulfanilamide, unless the administration of the latter agent has been discontinued 48 hours prior to the operation. The use of the pentothal sodium anaesthesia in the doctor's office or in the home of the patient, where adequate anaesthetic equipment is not available, is not safe, but for transient anaesthesia for operations not exceeding five minutes, it may be employed. Wherever intravenous anaesthesia is employed,

facilities for the administration of oxygen and carbon dioxide should be available.

"By observance of these contra-indications and precautions, intravenous anaesthesia becomes a method with a wide margin of safety. Its usefulness has been increasing steadily and for many operations it is the method of choice. Used in conjunction with local or regional anaesthesia, it is often the safest method of anaesthesia for the 'poor risk' patient."

Some observations on Gastric and Duodenal Ulceration: MACLEAN HUGH. (*Practitioner* 144: 222, March 1940). "All cases of fairly prolonged gastric disturbance should be dealt with on the same lines as an ulcer.....It is most important to recognise that the development of an ulcer is often only a phase in the history of dyspepsia; sooner or later a person with digestive trouble is liable to show definite ulceration, though it must be admitted that some cases of chronic indigestion never seem to pass into the actual stage of ulceration." For many years the writer has made it a practice to treat all cases of bad dyspepsia as if an ulcer were present, and the results have been most satisfactory.

"It is now generally acknowledged that medical treatment is sufficient to remove the symptoms of gastroduodenal ulceration and, when carefully carried out, a definite cure should follow in the great majority of cases. Operation is quite unnecessary in the ordinary case of gastric ulceration,

for far better results can be obtained by medical means."

"There is, however, one condition in which operation is always indicated provided the lesion is not too extensive. This condition is a malignant ulcer.....Every one.....who deals with large numbers of gastric ulcers has occasionally had a patient who in all respects appeared to be suffering from a simple uncomplicated ulcer of short duration but who, later on, developed definite cancer. In these cases who are dealing with a malignant ulcer from the beginning. At first the condition may differ in no obvious respect from an ordinary simple ulcer, but as time goes on we become suspicious. Usually the patient's response to treatment is more or less unsatisfactory and any relief obtained is only temporary, whilst the symptoms tend to recur continually. This should always arouse suspicion of the possibility of a primary malignant ulcer. It is often impossible to diagnose this type of ulcer at an early stage, even when all the modern methods of investigation, such as gastroscopy, are utilized. X-rays show just an ordinary ulcer. However, an ulcer persisting for 18 months to two years without showing evidence of malignancy is not likely to be malignant... When any ulcer shows a history of two years or more... the condition is almost certainly one of simple ulceration. Fortunately, these cases of primary malignant ulceration are generally speaking,

of rare occurrence, but they turn up from time to time and should always be borne in mind, especially when an apparently simple ulcer in an elderly patient does not respond to treatment in the usual way. In the present state of knowledge, these patients give rise to a tremendous amount of worry. Any gastric ulcer which is of short duration and which shows an unsatisfactory response to treatment should be regarded with some suspicion. The condition should be investigated as fully as possible, by all means available, and if a real suspicion of malignancy persists, the ulcer should be removed by the usual surgical procedure."

"What is the best medical treatment for gastric and duodenal ulcer? An answer to this question can be given with assurance. It is put to the patient under conditions which give the stomach physical and physiological rest. Physical rest is obtained by keeping the patient in bed for some weeks. Physiological rest is provided by giving frequent doses of alkaline medicine, in order to inhibit digestion in the stomach entirely for a certain period."

The detailed procedure is as follows: "To begin with, the patient is put to bed and kept there for two to three weeks or more, according to the severity of the symptoms and the progress made. Small feeds of citrated milk are given at short intervals,

followed immediately by an alkaline powder." The powder the writer uses to begin with has the following composition :

R,

Sodium bicarbonate	180 Grains.
Heavy magnesium carbonate	360 Grains.
Calcium carbonate	1 Ounce.
Kaolin	
Bismuth carbonate aa	180 Grains.

"The length of the intervals between feeds depends on the condition of the stomach contents withdrawn between the feeds. Generally one-hourly intervals for the first two days or so, followed by two-hourly intervals for 10 days, or a little more, are sufficient in cases of ordinary severity. If diarrhoea follows, this can be corrected by small doses of bismuth carbonate; if there is a tendency to constipation, a sufficient amount of magnesia cream should be given. It is better to have the bowels not too free to begin with in order to ensure as much rest as possible: sometimes an enema may be necessary after a few days. If the patient goes on all right the same powder may be used throughout, but if there is the slightest suspicion of symptoms of alkalosis" the writer gives a similar powder but containing no sodium bicarbonate. "If, however, any definite symptoms indicating the possibility of alkalosis become evident, it is best to change the powder altogether and use in its place some such preparation as magisorbent or alcohol. None of these substances give anything like such good results as the alkaline powder but they are useful in some circumstances."

"During the first fortnight or more the patient should live entirely on liquid food, such as milk, Benger's food, Ovaltine, or Bournvita. Some patients dislike milk but it is, on the whole, the simplest and best food to give."

"After 10 days to a fortnight or more of twenty-hourly feeds followed by the powder, the patient goes gradually on to more substantial meals. Details of these meals cannot be given here: weak tea, bread and butter, lightly boiled eggs, followed by such articles as mashed potatoes with butter, and rice puddings, are sufficient for the next week. Gradually the patient goes on to ordinary food. After three weeks the powder should be taken about four times a day after the chief meals. At this stage it is important that the powder should not be given immediately after meals but about 1 to 1½ hours after the meal is finished. A large dose of powder should also be given at bedtimes during the whole period of the treatment and for at least six months afterwards. It is understood that a dose should be taken if at any time there is any gastric discomfort. Whilst further details of diet at later stages of treatment must be left to the

judgment of the medical man in charge of the case, there is one point which must be insisted on. The patient must be made to understand that he must masticate his food thoroughly. This is perhaps the most important point in the after treatment of all these cases. Other directions, such as the length of time during which the powder must be taken, must depend on various circumstances, such as the progress obtained and the intensity of the various symptoms.

"In the majority of cases observance of the above principles will give excellent results."

In addition to the above, various other drugs have from time to time been employed. Frequently the writer has used small doses of insulin to increase the weight and act as a general tonic when circumstances indicate its use. As far as he can judge, injections of substances such as larostidin are of no value. Formerly, he used to employ such drugs as belladonna and olive oil, but he practically never uses them now.

The after treatment is as follows: "In cases of severe ulceration, more specially those attended by hæmorrhage, it is found that recurrences are much less likely to occur if the patient undergoes a mild course of treatment every three months for the first year and every six months for the succeeding year." This prophylactic treatment is carried out by the patient himself. The following is a copy of the instructions given to the writer's patients after earlier treatment is finished.

"Prophylactic treatment—Take two days off each week, during which rest in bed or on a coach; this is best carried out at a week end. During these two days live entirely on milk and take from 2 to 3 pints each day, divided into feeds of 7 to 8 ounces each. To each feed of milk add 5 grains of sodium citrate (any chemist will supply this). Take a small teaspoonful of the powder after each feed of milk.

"After two days do not add any more sodium citrate to the milk.

"On the third day increase the diet by taking in addition to some milk the following articles: bread and butter, weak tea, rice puddings, eggs, mashed potatoes with butter. Take a dose of the powder four times a day after the chief meals. It is understood that a powder is always to be taken at bedtime.

"After another three days gradually increase the diet by the addition of white fish, breakfast cereals, chicken, and puddings with eggs. Keep on with this for four more days and take a powder four times a day as before.

"After this go back to the diet you were having immediately before you had this special treatment."

The writer's experience of the above described alkaline treatment has been so favourable that he is now confident that it will cure any ordinary case of simple gastric ulcer when carried out according to the general principles described.

British Equivalents and Alternatives for Foreign Proprietary Products.

The Association of British Chemical Manufacturers have done a real service to the physician who is at a loss as to what might be prescribed for the many useful preparations which he had been accustomed to prescribe prior to the war which are either not available or are too costly. The following table is an extract made from a useful brochure on such Pharmaceutical Specialities which are still available to the prescribing physician.—[*Ed., M. M. J.*]

Continental Product.	British Product.	British Makers.
Acecoline	Acetylcholine Chloride	B. D. H. B. W. Evans M. and B.
Adalin	Carbromal B. P.	Boots B. D. H. M. and B., etc.
Anæsthesin	Benzocaine B. P.	do.
Argysol	Mild Silver Proteinat B. P.	do.
Atebrin	Mepacrine hydrochloride	M. and B. I. C. I. M. and B.
Atebrin musonate	Quinacrine Mepacrine methane Sulphonate	do. do.
Atophan	Quinacrine sol. Cinchophen	Boots A. and H. B. W. B. D. H., etc.
Avertin	Bromethol	Boots B. C. B. D. H. B. W.
Betaxin	Vitamin B ₁	A. and B. B. D. H., etc.
Campolon	Berin Thianin Benerva Hepol Hepastat Neo-Hepatex Examen Perhepar	Glaxo Richter } Made in Roche } England A. and H. Boots Evans Glaxo Richter

British Equivalents for Proprietary Products

131

Continental Product.	British Product.	British Makers.
Cantan	Ascorbic acid	A. and H. Boots D. H. Glaxo, etc. Glaxo M. and B.
Cardiazol	Celin Flanavit C Leptazol Phrenazol	Boots Boots Boots
Compral	Tab. Barbitone and Amidopyrine B. P. C.	B. D. H. B. W. M. and B.
Dermatol	Bismuth Subgallate B. P. C.	A. and H. Boots B. D. H. B. W. M. and B., etc.
Devegan	Acetarsol Vaginal compound	Evans M. and B.
Doryl	Carbachol	A. and H. B. W.
Eldoform	Albumin Tannate	B. D. H. Evans M. and B.
Ephetonin	Ephedrine hydrochlor	A. and B. Boots and all chemists
Eumydrine	Atropine methyl nitrate	B. D. H. Whiffers T. and H. Smith
Euphyllin	Aminophyllin Cardophyllin Theophylline ethylene diamine Hexobarbitone	A. and H. Whiffers do. All chemists
Evipan	Soluble Hexobarbitone	do.
Evipan Sodium	Hexamastab sodium Cyclonol sodium Stibophen	Boots M. and B. B. W. Glaxo B. D. H.
Fouadin	Suramin	
Germanin	Formamol B. P. C.	A. and H. B. D. H. Evans, etc. Boots
Helmitol		
Icoral	Leptazol	A. and H.
Lipiodol	Iodised oil B. P.	Boots B. D. H.

Continental Product.	British Product.	British Makers.
Luminal	Phenobarbitone	All chemists
Novurit	Gardenal	M. and B.
	Inj. Mersalyli	A. and B.
		Boots
Pentnucleotide	Pentide	B. D. H.
Plasmoquin	Pamaquin	A. and H.
Progynon	Ovostab	I. C. I.
Prolan	Oestroform	M. and B.
	Physostab	Boots
	Antostab	B. D. H.
	Gonan	
Proluton	Luteostab	Boots
	Progestin B. D. H.	B. D. H.
Prominal	Phenitone	I. C. I.
Prontosil album	Sulphanilamide	All chemists
Sanocrysin	Crisalbine	M. and B.
	Aurobin	Richter
Unden	Oestroform	B. D. H.
	Ovostab	Boots
Uroselectan B.	Iodoxyl	Glaxo
	Pyelectan	M. and B.
	Uropac	Glaxo
		M. and B.
Vigantol	Viosterol	A. and H.
		B. D. H.
Yatren	Chiniofon B. P.	Evans
	Quinoxyl	B. W.
	Quiniosulphan	M. and B.

Extracts from the Report of the Chemical Examiner to the Government of Madras for 1939.

Human Poisoning Cases.

A few cases are selected as of interest:—

Mercury.—(1) A *Sadhu* (religious mendicant) had been in the habit of sucking alum to quench his thirst probably to impress spectators. One day he took by mistake from his bag a crystal of perchloride of mercury and sucked it thinking it to be alum. He was removed to a hospital in a collapsed condition and died there. We detected about one and four-fifths grain of corrosive sublimate in his viscera.

(2) A woman who was living alone cooked food in the evening. She then left home and returned late that night. She tasted a morsel of the food and found it to be of a peculiar taste, her tongue feeling dry and stiff. She recovered after a number of motions. The food was sent to us and we detected about nineteen grains of corrosive sublimate in it, far more than enough to have killed her if she had consumed the whole of the food.

(3) A young man had never married as he thought he could not afford to marry but this did not prevent his association with women. He first seduced a niece of an old man and then he seduced another niece of the same

man. As the young man was a bully and difficult to tackle, the old man decided to lower the young man's vitality and cure him of his misplaced lust. In the opinion of the old man, who happened to be a quack, corrosive sublimate does not kill but only depresses. So one evening, the old man borrowed some money from the young man and bought toddy with the borrowed money. He mixed some corrosive sublimate in the toddy and offered the toddy to the young man to drink. After the young man drank the toddy, the old man dashed the pot to pieces on the ground. The young man was taken extremely ill but recovered after treatment in a hospital. The pieces of broken mud pot were sent to us and we detected minute quantities of mercury in them.

The old man was arrested and tried. The Judge observed that it was only a matter of academic importance whether the accused was charged for attempted murder or for causing hurt, and sentenced the old man to five years' rigorous imprisonment for attempted murder.

Turpentine.—A young man committed suicide with poison. The post-mortem signs revealed rigor mortis passed away except in the lower limbs, discharge of

mucous and partly digested rice from left nostril and nails bluish. The lungs showed intense congestion and the large vessels and the heart contained dark fluid blood. The liver and kidneys were intensely congested. The stomach showed congestion of the mucous membrane with deeply injected patches. The intestines were congested. The bladder contained one ounce of turbid urine. The brain was œdematous with the membranes injected. About three ounces of turpentine were recovered by distillation from the viscera.

Denatured spirit.—A woman went to the bazaar and asked for "omam water" (caraway water) a popular carminative for children. The bazaar man by mistake handed to her denatured spirit instead. The mother not knowing the difference between the two administered the liquid to the child. The child developed tremors and became unconscious. The child was removed to a hospital and died twelve hours later. The stomach washings and the viscera were sent to us and we detected pyridine in the stomach washings and in the viscera, though we did not detect alcohol in them. Pyridine is a denaturant added to spirit here to make it unsuitable for drinking.

Holarrena antidysenterica Wall.—This plant commonly known as "kurchi" or "conessi" is a small deciduous tree with white flowers growing throughout the forests of India. Recent clinical experiences with the

plant have led to its adoption as a valuable antidysenteric. The alkaloids from this plant are known to be poisonous.

Two children were administered the bark of this plant as a purgative with fatal results to both the children. The post mortem examination of each revealed cardiac failure, the heart being distended with dark fluid blood, the other viscera being normal. A specimen of the plant was sent us along with the viscera of the two children. We identified the plant to be *holarrena antidysenterica* and we obtained from the plant an alkaloidal extract which killed frogs with paralysis and which gave (1) with sulphomolybdic acid a dark green colour, (2) with sulpho-vanadic acid a greenish brown colour turning to purple at the edges and (3) with formaldehyde sulphuric acid (Marquis Reagent) a reddish brown colour turning blue at the edges. An alkaloidal extract giving the above chemical tests was also obtained from the viscera of each of the children.

Madar juice.—A widow who had become illicitly pregnant was found dead in her house. The post mortem examination revealed pregnancy of four months duration and the vagina was found plugged with a cotton rag. The viscera and the rag were sent to us. We did not detect poison in the viscera but we detected madar juice in the rag.

Datura.—(1) A woman suffering from leprosy committed

suicide by poison. We detected a mydriatic alkaloid in the viscera and in the urine. Microscopic examination of the contents of the stomach revealed particles of *datura* leaf.

(2) A boy was admitted into a hospital with symptoms which were then diagnosed as due to hydrophobia. He however recovered the next day and his urine which was sent to us disclosed a mydriatic alkaloid.

(3) While a young husband and wife were travelling through a forest a *Sadhu* met them and gave them some paste to eat stating that it would help them to travel without fatigue. The husband ate a large portion and the wife a small portion. The husband lost consciousness and regained consciousness only the next morning when he found some bamboo cutters standing by him. He narrated his story to them and they discovered at some distance the corpse of the wife with signs of throttling. The viscera were sent to us and we detected a mydriatic alkaloid in them. Microscopic examination of the contents of the stomach revealed particles of *datura* seed. The remnants of the paste administered to the victims were sent to us and we detected a mydriatic alkaloid in them. Microscopic examination of the paste revealed particles of *datura* seed.

(4) A man who had six previous convictions to his credit was arrested on suspicion and a packet of powder which was

found in his pocket was sent to us by the police. We found the powder to consist of partly crushed *datura* seed.

Oleander.—A young man accepted a bet from his friends who stated that he would die if he ate yellow oleander kernels. He ate the kernels from three fruits. Vomiting fortunately came to his rescue and he was admitted to a hospital in a collapsed condition. There his stomach was washed out and he recovered. We detected oleander in the stomach wash. The young man thus apparently won his bet—though by a very narrow margin.

No poison.—(1) The body of a girl aged ten years was found hanging in a village. As suicide by hanging is rare at such a tender age, the viscera were sent to us for examination for poison. We did not detect poison in the viscera.

(2) Hysteria is often mistaken by the ignorant in this country as possession by the devil. A hysterical young girl of twenty was diagnosed to be suffering from possession by the devil and her brother who was a magician offered to drive the devil out. She was given a bath and then taken before an idol. She was beaten black and blue over her head and back with the incantation "Go away, Devil." She collapsed under the beating and gave up the ghost. The viscera were sent to us to see if there was poisoning but we did not detect any poison in the viscera.

Analytical Notes.

Mercury.—The following analytical methods are being investigated in this laboratory:—

(1) *The determination of mercuric sulphide by iodimetry.*—Mercuric sulphide dissolves easily in solutions containing sodium sulphide and excess of caustic soda or potash. Mercuric sulphide from such solutions easily dissolves in strongly acid solutions containing potassium iodide liberating an equivalent quantity of hydrogen sulphide which may be determined iodimetrically.

The filtered and washed mercuric sulphide free from hydrogen sulphide and sulphur is treated along with the filter paper in a beaker with a solution of sodium hydroxide or potassium hydroxide and a known volume of diluted sodium sulphide solution sufficient to give a clear solution. Dried specimens of mercuric sulphide may require a little rubbing with the tip of a glass rod for solution to occur. Five millilitres of a ten per cent solution of potassium iodide are now added and the contents of the beaker and its washings are transferred to a flask containing in excess a known volume of standard iodine solution previously acidified with sufficient hydrochloric acid to leave the solution strongly acid at the end. The excess of iodine left is then titrated with standard thiosulphate solution. A blank is done using the same quantities of sodium sulphide, alkali, potassium iodide and iodine with acid. The difference between the two

The Madras Medical Journal

titrations gives the quantity of mercuric sulphide present.

(2) *The extraction of mercury from aqueous solutions.*—Mercuric chloride, mercuric bromide and mercuric iodide in potassium iodide in neutral solutions give precipitates with pyridine which are sparingly soluble in water but freely soluble in ether. The mercuric bromide complex is most suitable for extracting mercury from such solutions. We have found that copper, lead, and iron are not extracted by ether under these circumstances. Mercury may therefore be separated from these metals taking advantage of this property. The neutral or neutralized solution containing the mercuric salt is treated with a few drops of a solution of sodium bromide and a few drops of pyridine and extracted with ether. About three extractions, each time with a volume of ether equal to that of the solution, are usually sufficient to completely remove mercury from the aqueous solution. The mercury in the ether solution may be precipitated as sulphide by addition of alcohol and passing hydrogen sulphide or may be extracted with dilute hydrochloric acid in two or three extractions and precipitated as mercuric sulphide from the aqueous solution. The mercuric sulphide after filtration and washing may be determined iodimetrically as shown above.

(3) *The determination of mercury in viscera.*—Mercuric sulphide dissolves in an aqueous solution containing sodium

sulphide and caustic soda or caustic potash but is insoluble when sodium bicarbonate is substituted for the caustic alkali and the solution is saturated with hydrogen sulphide. The property is utilized in the following method for the determination of mercury in viscera.

A weighed quantity of the viscus is treated with sufficient twenty per cent potassium hydroxide solution to dissolve the viscus (about 10 ml. for every 30 gm. of viscus) and sufficient sodium sulphide solution to keep the mercuric sulphide dissolved. The mixture is heated over a boiling water-bath till a clear solution is obtained. The solution is cooled, just acidified with hydrochloric acid, treated with sodium bicarbonate solution till alkaline and saturated with hydrogen sulphide. The precipitate is filtered and washed and the filter paper with the precipitate is transferred back to the beaker and treated with hydrochloric acid saturated with hydrogen sulphide. The contents of the beaker are now filtered and washed and the precipitate treated with dromine water. After the mercuric sulphide has completely dissolved, the solution is filtered, the filtrate and the washings are treated with about half a gram of potassium chlorde and the bromine boiled off from the solution. The solution is now treated with hydrochloric acid, saturated with hydrogen sulphide and filtered. The mercuric sulphide on the filter paper after boiling off free from hydrogen sulphide is determined iodimetrically as described

above. Traces of iron normally present in viscera do not interfere in the above determination. If large quantities of iron, copper or lead are present, the above solution after boiling off the bromine and neutralization is extracted with pyridine and ether as described above and the mercury in the ether solution determined as above.

Nitrites.—Both potassium nitrite and sodium nitrite are extensively used by weavers in dyeing of cloths in villages and these substances are easily available for sale without restrictions. Cases of nitrite poisoning have become increasingly frequent in recent years and as no information was available about the toxicity of nitrites, some experiments were conducted on dogs and frogs to find the toxicity of the nitrites to these animals and indirectly to calculate the toxicity to man. The toxicity to frogs works out to a fatal dose of about one milligram of nitrite-ion per ten grams of frog, when injected under the skin. The fatal dose to dogs also works out to the same extent, there being practically no difference whether the drug is injected under the skin or administered by the mouth. Calculating according to Meeh's Formula (vide *Extra Pharmacopæia, Martindale*, 21st edition, Volume I, page xxxii) the fatal dose to human beings would probably be about twenty grains of nitrite-ion for a ten stone man. This indicates that about thirty grains of sodium nitrite or forty grains of potassium nitrite would probably prove fatal to the average adult man.

A regular feature of cases of the above experimental animals killed by nitrites examined so far was the presence of methæmoglobin in the blood taken from the heart after death. A common symptom observed in the experimental dogs was respiratory distress with Cheyne-Stokes breathing, probably the result of methæmoglobinæmia. Death was rapid, occurring in about half an hour after the administration. The experiments also revealed that when the poison is administered by the mouth very little of it is left in the viscera, most of it having been rapidly absorbed or otherwise destroyed.

In one instance a dog weighing six pounds was given six grains of sodium nitrite dissolved in about a quarter of an ounce of distilled water by the mouth. We found about half a grain of sodium nitrite in the vomit of the dog and only about one-fortieth of a grain of sodium nitrite in the viscera after death, the remainder having been absorbed and otherwise destroyed.

A second dog weighing four pounds and a quarter was given four and one-fourth grains of sodium nitrite dissolved in about one drachm of distilled water. There was no vomiting in this case and the viscera after death revealed about two-fifths of a grain of sodium nitrite, the remainder having been absorbed and otherwise destroyed.

These observations appear to be in accord with our experience that in many of the cases of

human poisoning from nitrites only small quantities of nitrite are detected in the viscera, unless extremely large doses have been swallowed.

The following original articles were contributed by this department to the 1940 session of the Indian Science Congress:—

- (1) Semi-micro combustion for Carbon and hydrogen,
- (2) Colorimetric determination, of Phenols in viscera,
- (3) Determination of Arsenic in viscera, and
- (4) Toxicology of Oleanders.

Stain Cases.

The following blood cases are selected as of interest:—

- (1) A man murdered his brother-in-law against whom he had old enmity by getting the victim drunk and throwing a large stone over his head, while unconscious. The suspected stone was sent to us. We detected blood on the stone and we also found pieces of dark and grey hair sticking to the stone. We found those pieces of hair to be human hair possessing the characteristics of scalp hair and showing evidence of crushing at one end of each of the pieces. The blood on the stone was found to be human blood by the Imperial Serologist, Calcutta. The accused at first confessed to the commission of the crime as stated above but later retracted his confession. It was however elicited that the above stone had been

concealed by the accused at a particular spot and was traced by the police as a result of the original confession. The accused was convicted of murder and sentenced to transportation for life.

- (2) In the course of a quarrel in a field a man hit a young man and his mother on the head with stones. The dead bodies were recovered by the Police the next day. The injuries on the body of the young man were—

(i) one lacerated wound 5 inches long and 3 inches broad over the right temporal and occipital bones. There was an oval depressed fracture of the skull 5 inches long and 3 inches broad comprising the upper part of right temporal lower and back portion of the right parietal and upper and right part of occipital bones causing compression of the brain and the portion of the brain under the fracture was flattened and there was a hæmorrhage into its substance;

(ii) one contusion 1 inch long, $\frac{1}{2}$ inch broad, over the upper part of the right side of neck 1 inch below the right ear;

(iii) one contusion 1 inch long, $\frac{1}{2}$ inch broad, over the back part of right wrist; and

(iv) a lacerated wound $\frac{3}{4}$ inch long, $\frac{1}{2}$ inch broad, and $\frac{1}{4}$ inch deep over the middle and medial part of left thigh.

The medical officer was of opinion that death was due to coma on account of compression

of the brain and that these injuries could have been caused by stones.

The injuries on the body of the young man's mother were—

(i) a lacerated wound 2 inches by 1 inch over the upper part of frontal bone and there was an oval depressed fracture of the frontal bone 2 inches by 1 inch causing compression of the brain and the portion of brain beneath the seat of the fracture was flattened; and

(ii) a lacerated wound 2 inches by 1 inch over the lower and back part of the left parietal bone. There was an oval depressed fracture causing compression of the brain and the portion of brain under the fracture was flattened with hæmorrhage into the substance of the brain.

The medical officer stated that death was due to coma as a result of compression of the brain and he also stated that these injuries could have been caused by stones.

The stones suspected to have been used in the commission of the offence and the earth from the scene of the offence were sent to us and we detected blood on each of these two items. The blood on the stones was found to be of human origin by the Imperial Serologist who reported that the blood on the earth was disintegrated and its origin could not be determined. The defence stated that the deaths were due to lightning, though there was no

evidence of any stroke of lightning that day and the injuries on the bodies did not conform to those caused by lightning. The Judge stated that "on account of the infliction of the injuries by the stones the deceased were incapacitated to move about and while so, they might have been attacked by any wild animal" and sentenced the accused to three years' rigorous imprisonment for causing grievous hurt under each count, the sentences to run concurrently.

Miscellaneous Medico-Legal Cases.

Tatto marks.—In a murder case the accused was alleged to have cut the body of the deceased into several pieces and buried them in different places in a river bed. Some of these portions were recovered by the police and on one of these pieces there were letters which appeared like tattoo marks corresponding to the name of the deceased. The portion of the skin with the suspected tattoo marks was sent to us to decide whether these were tattoo marks or merely writing in ink. The writing was not affected by water, acetic acid, oxalic acid, ammonia, bleaching powder or potassium cyanide. A cross section of the skin showed dense fibrous tissue with superficial intracellular dark brown amorphous pigment. We therefore concluded that the letters on the skin were tattoo marks and not surface writing.

2. A village officer was ordered to hold elections for a panchayat board. It was suspected

The Madras Medical Journal

that he had not held the elections but reported falsely that he had done so on 28th September 1938 (Wednesday). This officer had issued a notice to the public that the election would be held on a particular date and day of the week and this notice was alleged to have been tampered with subsequently by altering the date and day of the week. It was suspected that the date as originally written was 5th November 1938 and that this had been altered to 28th September 1938 by overwriting. Similarly the day of the week which was supposed to have been written as "சனிக்கிழமை" (Saturday) was alleged to have been altered to "புதன்கிழமை" (Wednesday) by overwriting. The document containing the writing was sent to us with the portions suspected to have been over-written marked in two places. On examination of the document the two marked portions were in deeper shade of ink than the remainder of the paper. This was shown not only in ordinary light but also under ultra-violet light. Microscopic examination revealed the date 28th September 1938 overlapping the original 5th November 1938, 8 overlapping 5, 9 overlapping 11 and 38 being written on again. The figure 2 was over-written over a dash of the original writing. The letters "புதன்கிழமை" overlapped the letters "சனிக்கிழமை," "பு" having been prefixed, "த" being written on "ச" "ன்" on "னி" and the remaining letters having been over-written again. It is also obvious that "க" finds no place in "புதன்கிழமை" whereas it occurs in

Extracts from the Chemical Examiner

"சனிக்கிழமை" as ordinarily written. There was therefore no doubt that the date 5th November 1938 had been altered to 28th September 1938 and that the word "சனிக்கிழமை" had been altered to "புதன்கிழமை" with resulting inaccuracy in spelling.

3. **Re-used stamps.**—We often receive partially erased and re-used postage stamps for identification of the erased postal impressions. We have found that cellophane

paper is very useful in finding out whether the erased impression is that of a suspected postal impression. The postal impression is imprinted on bits of cellophane paper and these can be superimposed on the suspected stamps. A complete coincidence of the circles and of the letters and other marks that are left unerased with those on the cellophane paper or otherwise is a very useful aid in drawing conclusions.

Notice

The XVII All-India Medical Conference, Vizagapatam, 1940. (SCIENTIFIC SECTION)

Chairman:—

P. KUTUMBIAH,
B.A., M.D., M.R.C.P.

Members:—

E. ACHYUTA MENON,
F.R.C.S., M.C.O.G.

CAPT. M. G. KINI,
M.C., M.B., MCh., F.R.C.S.

G. V. S. MURTHY, M.D.

VIZAGAPATAM,
Maharanipeta P.O.

Dated 29-9-1940.

Dear Doctor,

In connection with the Scientific Section of the forthcoming 17th All-India Medical Conference at Vizagapatam during the last week of December 1940, it is proposed to have symposiums in the following subjects in addition to the reading of papers.

1. *Surgery*:—Surgical complications of Filariasis.
2. *Medicine*:—High Blood Pressure, its etiology pathogenesis and treatment.
3. *Obstetrics*:—Maternal Injuries of Child Birth.
4. *Venereal Diseases*:—Modern treatment of Gonorrhoea.

The names of the openers of discussion on the above subjects will be announced in due course. All those who propose to attend the Conference are requested to take part in the discussion and make the symposiums a complete success.

Yours faithfully,
P. KUTUMBIAH,
Chairman, Scientific Section.

Copy to:—

1. The Secretaries of Medical Associations requesting them to announce the above to their members.
2. The Editors of Medical Journals with a request to publish the above in their valuable journals at an early date.

OBITUARY



It is with the deepest regret that we record the untimely death of an esteemed colleague of ours, Captain M. Subba Rao, M.B.B.S., at Calicut on Sunday the 27th October 1940. He passed away suddenly of heart failure leaving his wife and two daughters to bemoan his loss. We are sure that we voice the sentiments of the whole service when we offer our sincere and heartfelt condolences to the bereaved family.

Captain M. Subba Rao was born on 4th September 1894 and was therefore in the prime of life at the time of his death. He filled many a post in our service with outstanding ability and brilliance. He was a genial companion and a true friend. His personality will not be easily forgotten by those who came into personal contact with him.

(Ed., M. M. J.)