THE ANTISEPTIC

1937

JANUARY 34-1

FEBRUARY 34-2

Printed at the 'ANTISEPTIC' PRESS and Published by the Proprietor U. KRISHNA RAU, Madras.

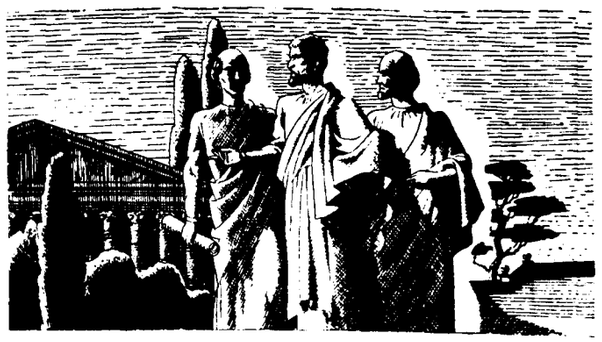
When writing to advertisers, please mention the "Antiseptic."

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

When writing to advertisers, please mention the "Antiseptic"

When writing to advertisers, please mention the 'Antiseptic'

PAUL OF ÆGINA ON PURGATIVE



'Purgative medicines being generally bad for the stomach, aloes alone are stomachic . . . Purgative medicines are to be given only to those whose powers are firm and their understandings strong.'

On Simple Purgatives, Book 7, Sect. IV.
Paulus Aegineta (625-690 A.D.)

Paul of Ægina (625-690 A.D.) was a foremost surgeon and author of the late Greek period, and appreciated the danger of the indiscriminate use of purgatives.

'PETROLAGAR' provides a soft, easily moved fæcal mass, which can be evacuated by normal peristalsis. It is a valuable adjunct in the training of the bowel to act in a regular daily manner.

For the convenience of doctors and to meet the requirements and indications of any special treatment, 'Petrolagar' is prepared in four varieties

● PLAIN
● WITH PHENOLPHTHALEIN
● ALKALINE
● WITH CASCARA

Samples on request

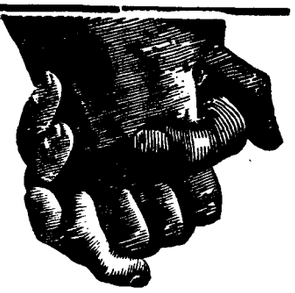
'Petrolagar'
BRAND PARAFFIN EMULSION Regd. Trade Mark

Distributing Representatives for India:
H. J. FOSTER & CO., LTD., P. O. Box 202, Bombay.

PETROLAGAR LABORATORIES LTD.
OLDHILL STREET LONDON, N.16

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

Persistent Antisepsis for normal skins.



Recently investigations have shown that the thin film left on the hands after rubbing them with undiluted 'Dettol' renders them in susceptible to reinfection by Haemolytic Streptococci for at least two hours after treatment. (*vide 'British Medical Journal,' 21st Oct 1933, p. 723*).

'Dettol' can be employed at high concentration on normal skins. The Rideal-Walker test proves it three times more potent than phenol. A two per cent solution very rapidly kills Haemolytic Streptococci and B. Coli even in the presence of pus.

Non-poisonous Non-Staining Low toxicity Pleasant aroma

'DETTOL'
Trade Mark.

THE MODERN ANTISEPTIC

DISTRIBUTING AGENTS

GRAHAM'S TRADING COMPANY (India) LIMITED,

Dept. V. 6. Post Box 90. BOMBAY.	Dept. V. 6. Post Box 30 KARACHI	Dept. V.6. Post Box 150 RANGOON

PARRY & CO., LTD., Dept. V. 6, P. O. Box 12, Madras.
E.B. CREASY & CO., LTD., Dept. V. 6, P. O. Box 37, Colombo.

Send postcard for free clinical sample to: ATLANTIS [EAST] LTD. Pharmaceutical Dept. V 6, 20/1 Chetla Road, Calcutta.
Marketing agents for Reckitt & Sons Limited, Hull and London, England.

Cheltine

STARCH-REDUCED AND OTHER FOODS.

SOLE AGENTS FOR INDIA:

Smith, Stanistreet & Co., Ltd.,

Stanistreet House, 18, Convent Road, Entally, Calcutta.

Cheltine Diabetic Foods (in three grades).
Cheltine Diabetic White and Brown Flour (plain and self-raising),
Cheltine Diabetic Biscuits (brown, white, almond, cocoa nut and assorted).
Cheltine Diabetic Brown and White Rusks.
Milk Cocoa. Casein. Marmalade. Jams from various fruits.
"CHELAX" DIGESTIVE BISCUITS (made with the famous Cheltenham Spa Water).
Special foods prepared for cases of Anæmia and Dyspepsia.
'CHELTOVA'—a Tonic Food-beverage for the family: sustains strength & stamina.

Sole Manufacturers: ***THE CHELTINE FOODS CO., Cheltenham Spa, England.***

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

The Antiseptic

ESTD. 1904.

A Monthly Journal of Medicine and Surgery.

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

Editorial and Publishing Offices:—323, Thambu Chetty St., Madras.

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

Vol. 34. | JANUARY 1937 | No. 1.

ORIGINAL ARTICLES.

Infantile Eczema*

BY

DR. S. THAMBIAH, M.R.C.P., D.T.M. & H., F.D.S.,

Dermatologist, Government General Hospital, Madras.

Definition.—This is a catarrhal inflammation of the skin with a variable duration and subject to remissions and acute exacerbations. This catarrh may be latent when retained intercellularly, or patent when it appears as exudation or weeping. It is non-contagious and also non-microbic. The aetiology of the disease is not well-understood, though a certain measure of sensitiveness to proteins derived from foods can be established.

Vernacular synonyms.—In Tamil it is called சப்பான் or கஜகான். When it reaches the eczema rubrum stage, it is called சொப்பாலை and ரசகஜகான். In Malayalam it is known as "*Thoda*" "தோட".

Signs and Symptoms.—The earliest manifestation of the disease shows itself as a reddening or roughening of the prominences of the cheeks very much akin to wind-burn or simple shaping. On close inspection it will be readily evident that the reddened area is not dry, but moist; clear serum is seen to ooze from the irregularly fissured and thickened skin. This serous discharge later dries into crusts of variable thickness. The borders

* A paper read at the Maternity and Child Welfare Conference, Madras, 1936 and sent to the 'Antiseptic' for publication.

of the lesion are indistinct and shade off into the normal skin. In a few fortunate cases the process stays more or less at this stage and then clears up under soothing protective applications. The disease may from the start be acute with a fiery red appearance, gradually making a peripheral extension of the original lesion and also fresh lesions of a minute vesicular or vesiculo-papillar character may appear. The latter types on evolution weep and crust in the same way as the original reddened type. A noteworthy point is the ever present *itching*, and to secure relief, the child resorts to scratching with the finger nails, and rubbing against the dress and bed clothes. Thus the disease spreads slowly or rapidly to other parts of the body as the forehead, the chin and the ears and neck. In much neglected cases, the wrists, the knees and the flexor and extensor surfaces of the extremities may become involved. On the face, the circum-oral, circum-nasal and circum-orbital areas remain free throughout the disease, while the cheeks, chin, forehead and ears are badly affected. So the distribution of the lesions on the face may have the characteristic mask-like spread. It may also be noted that the palms and soles also escape.

The intense itching and scratching keeps the child as well as the members of the household awake for the greater part of the night with the consequent deterioration of their general health. It is also worthy of note that the child maintains a good general condition during the earlier months of the affection.

Aetiology.—No other disease has had such numerous theories as to aetiology and hence to the methods of treatment. Babies between the ages of 6 months to two years are often affected; at the end of the two years, most of the children become free even without treatment. Teething, vaccination, food irregularities —events of importance present at this period, have been blamed without much foundation. A good many dermatologists of eminence in England are inclined towards an external irritation as the main factor in its causation. A strong hereditary tendency can be demonstrated. Patient inquiry will reveal the presence of eczema, asthma, urticaria, angio-neurotic oedema, migraine etc, in other members of the family. Children with infantile eczema on reaching adolescence, very often suffer from eczema or asthma.

Professor White in England made a study of the stools in obstinate cases of infantile eczema and showed the presence of excessive fat in 60% of cases and excessive starch in 40%; preponderance of sugar in 20 % and 10 % of proteins. He also concluded that excessive starch was associated with a dry type of

eczema and excessive fat with a moist type—points of practical clinical importance.

From the dietetic point of view, different items as the fat, starch, sugar and of late, protein have been indicted and eliminated from the menu with varying effects, on the progress of the disease. Excessive starchy food causes fermentation: the stools are mushy or loose, green and acidic with a sharp penetrating odour.

A more or less similar effect is produced by sugars. The combined action of fats and protein produces an intense sensitization and aggravation of the pre-existing eczema. The fatty acid split off from the neutral fat consumed irritates the intestinal mucous membrane making it more permeable to the protein and other substances, which, when absorbed, may cause the eczematous process. "There is evidence to show that proteins particularly may be absorbed and digested through the intestinal mucous membrane and may give rise to sensitization." This form of sensitization to products of protein is termed "allergy". Its presence in various substances can be demonstrated by intracutaneous, percutaneous and patch tests, employing a large range of allergens. But unfortunately, protein sensitization does not solve the problem of all cases of infantile eczema; yet there appears an intimate relationship between infantile eczema and protein sensitization: the exact nature of this is not determined.

There is also a certain amount of racial peculiarity in this disease; children of coloured races are less affected by this malady. In South India, I have not seen so many children with infantile eczema at the out-patient clinic of the General Hospital, as I have seen at Leicester Square. Perhaps overfeeding is not seen among the hospital class of children.

Pathology.—The pathology of infantile eczema, eczema in adults and dermatitis (due to known external irritants) is fundamentally the same. The main brunt falls on the epidermal structure. The prickle cell layer is oedematous and increased in depth owing to intercellular and intra-cellular retention of exudation and proliferation of the rete-cells. Fluid collects in small crypts, more so below the stratum corneum layer, and when sufficiently large appears as vesicles and blebs. The roof of the vesicles and blebs gives way and exudation becomes prominent. Owing to the oedema of the prickle cell layers (rete), the orderly cornification of the stratum corneum is interfered with, Keratin is not formed and the individual corneal cells retain their neuclei in addition to their coherence to one another. Normally the cells have no nuceli, they separate off cell by cell and are shed off cell by cell.

In long standing cases scaling is prominent—an indication of altered cornification (para-keratosis).

Corial changes are not so prominent. Blood and lymph vessels are dilated. Old cases show cell infiltration as well. Perhaps the process started as a change in the papillary and sub-papillary region which later affected the epidermal structures more.

Treatment.—Mild cases may be treated at home; severe ones require hospitalization and efficient nursing. To prevent scratching and rubbing, restraining devices have to be used. The Edinburgh device or the method proposed by White of Boston may be adopted. Soap and water aggravate the lesions. Saturated solution of boric acid may be used for cleansing purposes. Starch bath is comforting to the patient. Crusts may be efficiently removed by means of olive oil, soaps or cold cream.

From the dietetic point of view, and the assumption that the protein of milk caused the eczema or aggravated it, L. W. Hill of Boston proposed a protein-free diet and introduced a preparation under the name of "Sobee" (Mead Johnson & Co.). It is made up of Soya Bean flour (67.5 %), barley flour (9.5) Olive oil (19.0), sodium chloride (1.3) and calcium carbonate (2.7). Olive oil supplies the fat and the last two items, the mineral deficiency of Soya Bean (Calcium, Sodium and Chlorine). Sobee is not sweetened and sugar may be added according to the tolerance of the patient. Cod Liver Oil and orange juice may supplement the vitamin deficiency in older children. A level tablespoon of sobee added to an ounce of water will provide the full strength mixture giving a caloric value of 17. For weaker children a dilution less than indicated above may be used. This diet has yielded much satisfaction in very severe cases. In less severe cases evaporated milk and milk heated, varying from 6 to 8 hours, have been advocated and used with good results. The protein of the milk is altered or denaturized in such a way that no injurious effect can arise to a sensitized child.

Local Treatment.—Any external application which is soothing and protective will answer the purpose quite well. If weeping is predominant, an ordinary calamine solution or ½% aluminum acetate in water is all that is necessary. When drying becomes marked, cold creams may be substituted. An efficient cold cream can be prepared by adding 3 to 4 drams of zinc oxide to an ounce of well prepared carron oil. It is better to incorporate a dram or two of lanoline or laceranum to keep the cream in a homogeneous mass, and this also will be of help if any acid preparations have to be added. Among the proprietary preparations, I have found Crooks Collosal Lacto-Calamine and ordinary calamine solution to answer the purpose. The former can be diluted with an equal quantity of warm water without lessening its efficacy. Lassar's paste without salicylic acid is a better protective in that the paste when applied will stick better and cannot be easily dislodged. If scaling is predominant, 2 % calomel in Ung. Aqua Rosae or 20 minims of Liq. Carb. Diterg in an ounce of Laceranum is all that will be required. Steam distillate of tar under the trade name of 'tara-alba' may be used in refractory cases.

In spite of the above figuring and planning as regards treatment, a few cases remain without being benefitted in the least by treatment. In these cases, it is wise and proper to improve the general health of the child, so that growth may not be interfered with. The physician should remember that this is a self-limited disease and when treatment of the eruption is not yielding to external applications, it is better to treat the individual without imposing much dietetic restrictions.

The Pituitary Gland*

BY

S. SHANKARA RAMAN, M.B., B.S.,

Cuddalore.

No apology is needed for the subject of to-day's lecture when we consider the multiplicity of the functions of the Pituitary gland, which has been aptly described by Langdon Brown as the band master of the Endocrine Orchestra. More surprises have been encountered in the study of the Pituitary body than of any other organ of internal secretion. Already many active principles have been separated from the pituitary and some of them have been offered to the clinician for treatment.

This gland, first noticed by Vesalius in 1543, was not credited with any such function. It was in 1895 that the true endocrine nature of the pituitary was mentioned by Oliver and Schafer, and from then on, many functions have been attributed to the gland from day to day.

It would interest you to know that till as late as 1903, Neurologists believed that the pituitary gland was not a secreting structure. Though Howell demonstrated that injections of

* A paper read before the S. Arcot Dt. Medical Association and sent to the Antiseptic for publication.

anterior lobe extracts produced no effect and that posterior lobe extract's injections caused rise of blood pressure, it was believed that the effects corresponded with those of adrenal extract.

A view that posterior lobe was a general nerve centre and that it acted through its nervous connections with the adrenals was prevalent. Before proceeding further, let us have an idea of the anatomy of that part of the brain to enable us to appreciate the latest theories regarding the nature and functions of the secretions of the gland. The hypo-thalamus consists of the sub-thalamic tegmental region and the structures forming the floor of the third ventricle (*i.e.*) the posterior perforated substance, the Corpora Mamillaria, Tuber cinerum, infundibulum, hypophysis, and optic chiasma. The sub-thalamic tegmental region consists of the forward continuation of the tegmentum beneath the posterior part of the thalamus. The nucleus rubra, and the substantia nigra can be followed into its posterior parts, where they disappear behind the corpus mamillare.

The posterior perforated substance lies on the base of the brain in the interval between the diverging cerebral peduncles.

The corpora mamillaria are two rounded white masses, each about the size of a small pea and placed side by side below the grey substance of the floor of the third ventricle in front of the posterior perforated substance. The tuber cinerum is a hollow eminence situated between the copora mamillaria behind and the optic chiasma in front. From its under surface a hollow conical process termed the infundibulum projects downwards and is attached to the posterior lobe of the hypophysis.

The hypophysis or the pituitary body is a reddish grey, somewhat ovoid body measuring about 12 mm. in its transverse, and 8 mm. in its anterio-posterior diameter. It is attached to the end of the infundibulum and is situated in the fossa hypophyseous of the sphenoidal bone, where it is retained by a circular fold of dura-mata termed the diaphragma cellae. This fold completely roofs in the fossa leaving only a small central aperture through which the infundibulum passes, and it separates the anterior part of the upper surface of the pituitary from the optic chiasma. On each side, the hypophysis is related to the cavernous sinus, which contains the internal carotid artery, the cavernous plexus, the abducent nerve, the oculomotor, trochlear, and the ophthalmic and maxillary divisions of the trigeminal nerve. Inferiorly it is separated from the floor of the fossa by a large partially loculated venous sinus, which communicates freely with the circular sinus.

The Hypophysis consists of an anterior and a posterior lobe which differ in their development and structure. The anterior lobe is the larger of the two and is kidney-shaped, the concavity being directed backwards, and embraces the posterior lobe. It is developed from a diverticulum of the ectoderm of the primitive buccal cavity and consists of an anterior and a middle part separated from each other by a narrow cleft. The anterior part is extremely vascular and consists of granular epithelial cells of varying size and shape arranged in cordlike trabecula and separated by large thin walled blood vessels. It is continuous above with the tuberal portions which surround the infundibulum and cover the tuber cinerum. The middle part or Pars-Intermedia, is a thin lamina closely applied to the posterior lobe. It contains a few blood vessels and consists of finely granular cells between which are small masses of colloid material.

The posterior lobe is developed as a down growth from the floor of the embryonic brain and during early foetal life contains a cavity continuous with that of the third ventricle. Although of nervous origin the posterior lobe contains no nerve cells or fibres. It consists of neuroglia cells and fibres and is invaded by cell columns which grow into it from the Pars-Intermedia. Imbedded in it, are scattered masses of a colloid substance histologically similar to that found in the Thyroid gland. It draws a limited blood supply from the internal Carotid arteries.

The Integration of the Endocrine System

It was Langley who stated that the effect of adrenalin on any part was the same as stimulation of the sympathetic nerves to that part. Dale showed that acetylcholine is liberated by stimulation of the parasympathetic. These demonstrations led to the chemical nature of the Hormones to be recognised, and hormones came to be regarded as highly specialised instances of chemical messengers, which are either under direct nervous control, or under an indirect control through the Anterior Pituitary. Dodd classifies hormones as (1) complex protein bodies formed by the Anterior Pituitary, which act on other Endocrine glands, causing them to form, (2) the secondary type of hormones, which are bodies of comparatively small molecular weights and most of which have been isolated in crystalline form and some of which have been prepared synthetically. It is to be noted that the posterior Pituitary forms secondary hormones.

Physiology.—*Functions of the Anterior lobe of the Pituitary* are best demonstrated in an Hypo-physectomised animal. If the gland is removed before puberty then normal sexual development

does not occur, and the growth of the skeleton is much retarded. If the gland is removed after puberty, in the male there is rapid atrophy of the testis, external genitals and the seminal vesicles. In the case of the female, the oestrous cycle stops and the ovaries and the uterus begin to atrophy.

The following hormones are credited to the anterior lobe:

(1) Growth stimulating hormone.
(2) Sexual development stimulation hormone.
(3) Leutin cell stimulation hormone.
(4) Stimulation of sexual development by a substance that can be given by the mouth in distinction from the former which has no effect orally.
(5) Metabolism stimulation hormone.
(6) Thyroid stimulation hormone.
(7) Lowering of gaseous metabolism hormone.
(8) Water stimulation hormone.
(9) Lactation stimulation hormone.
(10) Lowering of non-protein nitrogen in the blood hormone.
(11) Hormone initiating bleeding of menstruation.

The growth hormone.—Dr. Brailsford Robertson of the California University reported that 0.125 gm. of fresh anterior lobe tissue given daily to white mice, retarded their growth in the earlier part, but in the latter part *i.e.* from the 20th to 60th week after birth accelerated their growth markedly. Dr. H. M. Evans produced abnormally large growths of rats by intraperitoneal injections of the extract of the anterior lobe. But this hormone seems to affect only the immature animals, and has no effect on normal adults. Hence we have to conclude that the injections of the growth hormone will tend to produce an acceleration in the development of the immature animal, but lose their effect when it has reached the maximum. Kemp has shown that the injections of this hormone into a special strain of dwarf mice result in the normal growth of these animals. Acromegaly is regarded as a condition in which there is an overproduction of growth hormones in persons after the age of puberty.

The gonodotrophic hormone or the œstrous producing hormone:—The anterior lobe is well named the "Motor of the Sexual Function." Hypophysectomy is followed by the rapid degeneration of the testes, or the uterus and the ovaries. If the hypophysectomised animal is implanted with anterior pituitary grafts, these changes are prevented. Hewitt demonstrated that the

injection of the acid extract of the anterior lobe into the female, either normal or hypophysectomised, induces ovulation and maturation of the graffian follicles. If an alkaline extract is injected into the female, then Luteinisation of the follicles occur without rupture and ovulation. The former is called Prolan A., and the latter is called Prolan B.

A Gonadotrophic hormone is secreted in the urine of pregnancy and the demonstration of its presence is the principle of '*Zonde-Aschheim*' test for pregnancy. Subcutaneous injections of 0.25 c.c., of the morning urine of a woman who is said to be pregnant, are made into immature female mice 3 to 5 weeks old. If the female is really pregnant, the injection is followed by congestion, and haemorrhage of the ovaries and premature maturation of the follicles. The mice are killed after 100 hours after the 1st injection and 6 injections are given on the whole, three on the 1st day and three on the 2nd.

Langdon Brown suggests that one association exists between eosinophile cells and growth, and another between basophile cells and the gonads. He says that growth precedes sexual maturity due to the early predominance of the growth hormone, when the eosinophile cells are in excess. Once the Basophile cells assert themselves over the eosinophile cells, puberty occurs.

Zondek and Bullinger point out that the hormones of the anterior lobe of the pituitary are superordinated general sex hormones and say that without the hormones of the anterior lobe of the pituitary there would be no sex hormones.

The thyrotropic hormone.—The effect of hypophysectomy is the rapid atrophy of the thyroid gland and reduction of the basal metabolism rate. It is possible to prepare from the anterior lobe a substance, which, on injection, will stimulate the atrophied thyroid of such an hypo-physectomised animal. It is also possible, by increasing the amount of the injection, to produce a condition of hyper-thyroidism. It has been further demonstrated that if the hormone is injected into an animal, the basal metabolic rate rises, stays up for some days and then falls, and will rise no further, even if further thyrotropic hormone is administered, thus demonstrating the influence of this hormone on the thyroid.

The adreno-trophic hormone.—Removal of the pituitary leads to atrophy of the adrenal cortex and premature senility or Simmonds disease results.

Lactogenic hormone.—Prolactin is responsible for the initiation of the secretion of milk. Riddle has demonstrated that the crop glands of the pigeon can be made to enlarge by extracts of

the anterior lobe of the pituitary. It is definitely proved that the oestrogenic hormones alone are responsible for building up the structure of the mammary gland suitable for a period of lactation, while lactation itself can only be induced by the hormone *Prolactin*. During pregnancy the Prolactin is held in abeyance by the large amount of oestrogenic substance present in the blood, but after parturition the sudden drop of those substances allow the Prolactin to act.

The pancreatic and parathyrotropic hormones.—The osteoporosis and fractures which occur in Cushing's pituitary basophilism suggest that parathyroids are influenced by the pituitary hormone though there is hardly any change in the calcium metabolism.

Alterations in the carbohydrate metabolism also take place in a hypophysectomised animal.

Diabetic and ketogenic hormones.—Houssay was able to demonstrate that if a pancreatectomised dog is also hypophysectomised, the ketonuria and glycosuria produced by pancreatectomy disappear. If this hormone is injected into such an animal ketosis and glycosuria reappear.

Posterior lobe.—Blair Bell brought to the notice of the profession that extracts from the pituitary was useful in shock, uterine atony and intestinal paresis.

A combination of Thymus extract with posterior pituitary hormone produces rhythmical, broken uterine contractions more like the physiological labour pains.

The posterior pituitary extract was split into *Pitocin*, having a marked muscular tonic effect and *Pitrocin* or *Vasopressin* raising the arterial tone and thus the blood pressure.

Pathology.—*Hyperpituitarism* : Acromegaly is usually a disease of the third decade of life occurring in all parts of the world, though Jews and Swedes are more prone to it.

Pathologically the pituitary gland is found to be enlarged and on section an Eosinophile adenoma is found in the anterior lobe. The pituitary gland presses on the optic chiasma and erodes the floor or roof of the Sella Tercica, the cavernus sinus and the brain. The adrenal cortex is enlarged and multiple adenomas present. The Thyroid is enlarged and contains adenomatous colloid. The parathyroids are enlarged and adenoma may be present. The ovaries and testes are usually atrophic, the stomach is of abnormal capacity and the length of the intestines is doubled. There is enlargement of the carpal and tarsal bones, which may sometimes fuse together. Radiograph shows characteristic tufting of the

phalanges. The skull is thickened, the zygomatic arches and the malar bones and the mandible are enlarged. The clavicles are also thickened. The soft tissues like the tongue and the lips are thickened and the face presents a negroid appearance.

Signs and Symptoms.—The above changes in the bones and soft tissue are present, voice becomes deep and resonant, the heart is enlarged and hypertension occurs. The smell is impaired owing to hypertrophy of the nasal turbinal bones. Pressure on the optic chaisma leads to optic atrophy, bitemporal hemianopia and later complete blindness. Ocular palsies result from pressure on the oculo-motor trochlear and abducent nerves and involvement of the fifth nerve may produce pain and hyperasthesia over its divisions. Headache is severe, vomiting sometimes present, neuritis and ataxia are common. Speech is sluggish, cerebro-spinal fluid is under high pressure and finally mania and delusional insanity bring up the rear of the symptoms.

The sexual system is not often affected, the carbohydrate metabolisam is disturbed leading to pituitary diabetes.

Gigantism results from the presence of an excess of pituitary growth hormone in childhood before the epiphysis have united. Microscopically, the pituitary gland is enlarged and adenomas of the eosinophile cells are present.

In primary eunuchoidal type, the hypogonadism is a persistent feature The eunuchs employed by the Mahomedan monarchs of old in their harems were probably examples of this type of malady.

The ordinary giant type.—In this type, in addition to general growth one part of the body may grow to a greater extent than the rest. They show supernormal muscular power at first but after some years due to muscular atrophy and atony, asthenia follows.

CUSHING'S SYNDROME OR BASOPHILISM.—Cushing himself describes this disease as 'the disorder characterised by a rapidly acquired plethoric adiposity affecting the face, neck and the trunk, the extremities being spared. It is associated in women with amenorrhoea. There is vascular hypertension, purplish stria distensae of the abdomen and acrocyanosis with cutis mammarata of the extremities. It is often accompanied by hyperglycaemia and a peculiar softening of the skeletal bones. The average duration of life in the fatal cases has been something over five years.' The disease may also occur in young girls, sexual precocity with menstuation being followed by virilism and amenorrhoea. Men are rarely affected and if affected the testes atrophy and impotence

results. Cushing maintains that these manifestations are due to the basophile adenoma of the pituitary gland.

Pathology.—There is no macroscopic enlargement and sella turcica is not widened. Secondary hyperplasia of the adrenal cortex is present along with small atretic ovaries. The thyroid gland is enlarged and lymphatic hyperplasia and enlargement of the thymus is also present. The parathyroids are unaffected, the bones are decalcified. Cushing's syndrome has opened a wide field of investigation. What is the relation between the basophile cells and the gonads? Why should there be virilism in the female and not in the male? An attempt to explain the above has been made in recent times as follows: The initial bias in sex differentiation rests on the chromozomal constitution. In insects the chromozomal constitution is the sole cause of the sex differentiation, but in mammals their effect is slight, and has to be reinforced by the endocrine activity proper to each sex; in other words, the embryo is bi-sexual at that stage of development. Then follows a period of masculinising. In the female it shows itself by producing a medullary mass in the gonad which is really a testes and in the female actually becomes the testes. This mass lives on as a testicular rudiment in the rete of the ovary, the real ovary coming from a superficial investing cortex. Hence we see that the testes is a mono-sexual organ, while the ovary is a bi-sexual organ. Hence sex reversal can only occur in the female. This above explanation is Wollard's hypothesis explaining the virilism caused by a basophile adenoma of the pituitary or hyperplasia of the adrenal cortex.

Hypopituitarism.—FROHLICH'S SYNDROME. The face is rounded and of good colour. The fat follows a feminine distribution in the male, fat depositing over the breast and mons. In the female the breasts are very pendulous; the skin on the back and upper arms bruise very easily. In males there is undescended testes and the genitals are infantile while in the female the uterus is infantile and amenorrhoea is present. Somnolescence and Fat boy Joe appearance are common. There is polycythemia and sugar tolerance is increased. Deficiency of the hormone which transports fat to the liver where it is metabolised accounts for this syndrome.

DERCUM'S DISEASE OR ADIPOSIS DOLEROSA.— In this disease fatty tumours appear which are painful, the skin over them being reddened. Pituitary adiposity cannot be reduced by controlling the diet alone.

Dwarfism and Infantilism.—In true dwarfism the adult

proportions are correct and the absolute measurements are reduced. There are no gonadal defects.

In infantilism on the other hand the development is that of child. Smith and MacDowell have concluded after elaborate researches on rats that the defective anterior pituitary secretion leads to the absence of eosinophile cells and that, when replaced by a graft of the pituitary, normal development begins.

SIMMOND'S DISEASE.—Simmonds of Hamburg came across cases of extraordinary premature senility occurring in childhood.

Signs and symptoms are: (1) premature aging; (2) gonadal atrophy; (3) early and complete amenorrhoea. (4) Loss of pubic and axillary hair. (5) atrophy of the lower jaw: (6) loss of teeth; (7) lowering of basal metabolism. (8) shrinking of the viscera; (9) secondary anaemia; (10) achylia gastrica. (11) low temperature. (12) low blood pressure and (13) bradycardia.

Pathologically there is destruction of the eosinophile cells in the pituitary.

Lawrence Moon-Biedl Syndrome consists of mental deficiency, obesity, polytactility and retinal pigmentation.

Schuller Christian Syndrome is a lipoid granulomatosis, exophthalma and diabetes insipidus.

These syndromes are due to hypopituitarism and further researches are necessary to find out the exact hormones responsible for these syndromes.

Now we come to the controversial question whether the metabolic and endocrine changes are associated solely with the lesions of the pituitary gland or whether they are due to the associated changes in the brain. Functions controlled by the anterior pituitary have multiplied to such an extent that it is incredible to associate a separate hormone for each function.

The close association of the nuclei of the tuber cinerium and pituitary gland anatomically has led to the suggestion that secretions from the pituitary are intimately associated with hypothalamic function. The frequency with which diabetes insipidus has been found clinically in association with lesions of the hypothalamic region leaves no doubt about the nature of its etiology. But persistent polyuria may also be brought about in monkeys by lesions in the supra-optic nuclei or in the pituitary stalk. Unilateral damage to the system does not give rise to polyuria and large lesions of the other parts of the hypothalamus have no effect. Injections of extracts of the anterior lobe of the pituitary cause polyuria but complete removal of the pituitary gland does not

produce polyuria. Hence for the production of polyuria there must be lesions of the pituitary and the hypothalamus.

Again marked adiposity may occur in patients with tumours of the tuber region. Tuber damage without pituitary injury frequently leads to adiposity. Adiposity as already mentioned is a feature of basophile adenomas of the anterior lobe of the pituitary. Hence hypothalamus and pituitary lesions both cause adiposity.

The view current in the present day is that the anterior pituitary, receiving impulses from the hypothalamus, produces an activating or an inhibitory hormone of a protein character according to demand which can speed up or inhibit the secretion of other glandular hormones.

Uses of pituitary hormones.—Products available to the profession that are derivatives of the anterior lobe are (1) *Accretin*, the growth stimulating hormone available in capsules of 5 grs. each dose—3 to 4 capsules a day. (2) *Antuitrin* (P.D. & Co.) is a total extract of the anterior lobe of the pituitary available in 1 c.c. amp. (3) *Apestrin*: the oestrogenic hormone of the anterior pituitary is useful in utero-ovarian hypoplasia and sterility. 1 c.c. every alternate day is the usual dose. (4) *Prolan*-A. Zondek's anterior pituitary hormone is standardised in rat units; given as intramuscular injections in infantilism, amenorrhoea and hypo-pituitarism. Dose is 100 to 300 rat units daily.

Posterior lobe preparations:—(1) Elixir Hypophysis cerebri. Dose 1 to 2 fluid drams. Contains the whole pituitary gland. (2) *Exophysin.*—Merck, is a solution of total extract of posterior pituitary. (3) *Infundin, B. W. & Co.*, is a posterior pituitary extract extensively used in obstetrics—Dose ½ to 1 c.c. (4) *Pitocin*—*P. D. & Co.* is the oxytoccic posterior pituitary hormone usuful in uterine inertia with hypertension and in arterial spasms. (5) *Pitrossin*—*P. D. & Co.* is a vaso-pressor hormone which raises the blood pressure, used in operative shock and diabetes insipidus. (6) *Vasophysin* (Merck) is an anti-diuretic and promotes intestinal peristalsis. Used in paresis of the intestines. (7) *Pituitrin*—*P. D. & Co.* Available in two strengths—obstetrical containing 10 international units per c. c. and Surgical, containing 20 units per c. c. Useful in uterine inertia, post-operative ileus, post operative retention of urine and in operative shock. (8) *Pituthymin*, is an isotonic solution of posterior pituitary—oxytoccic principle with thymus nucleo-protein, each c. c. of which contains 10 international units of posterior pituitary—useful during labour as an ecbolic—dose ½ to 1 c. c.

The Use and Abuse of Pituitary Extracts.—The indiscriminate prescriptions of endocrines have led to their abuse often. There are occasions when the pressor effect is desirable to prevent or control operative shock and the oxytoccic effect is to be avoided as in the case of a pregnant woman requiring surgical treatment for some incidental condition. Diabetes insipidus during pregnancy can be prevented by the pressor hormones—Vasopressin or Pitrocin. We can inject these hormones safely in a pregnant woman. No longer do we fear the oxytoccic action of pituitary, but all the same we cannot give whole pituitary extracts in these cases. Many physicians in America are using pituitary-thymus solutions in labour with very satisfactory results. The spastic uterine contractions of a pituitary injection are replaced by a rhythmic broken contraction that simulates physiological labour pains. It can safely be given in the first stage of labour. The treatment of infantilism and dwarfism can now be undertaken with a fair amount of success.

Among the other uses of pituitary are (1) to stimulate and strengthen labour pains during birth: (2) to expel the after-births; to involute a sub-involuted uterus: (4) to check post-partum haemorrhage; (5) to treat feverish bleeding abortions and puberty haemorrhages (6) to relieve asthmatic spasms (7) to combat polyuri and diabetes insipidus.

Pituitary must not be used to initiate and shorten confinements. The judicious use of pituitary has a very wide field. To sum up, new theories throw much light on the integration of the endocrine system. First came the realisation of the close associatian between the pituitary and the emotional centres in the sub-thalamus; then came the realisation that polyglandular syndromes were most usually based primarily on a pituitary lesion: next the roles of Prolan A & B were noticed; finally, the conception that the anterior pituitary produces an accelerating hormone in the eosinophile cells and an inhibitory one in the basophile cells; and over all, the view that the sub-thalamic region of the brain controls to a large extent the anterior pituitary which in turn controls all other endocrine glands.

References:

1. *Gray's Anatomy.*
2. *Medical Annual 1935 and 1936.*
3. *Sajon's Internal Secretion.*
4. *Harrower: Organs of Internal Secretions and Endocrine Disorders.*
5. *Cushing: Pituitary Body and Hypothalamus*
6. *B. M. J.—1936*

The Ophthalmoplegias and their Diagnosis*

With a Special Reference to External Ophthalmoplegia

BY

N. P. VENKATESWARA IYER, M.B., B.S.,

Triponithura.

Definition.—The term external ophthalmoplegia is generally used to mean the paralysis of all the external muscles of the eye-ball—the four Rectii and the two Obliques. Of these the Superior Oblique is supplied by the 4th nerve, the External Rectus by the 6th and the rest by the 3rd nerve. The last also supplies the Sphincter Iridis, the ciliary muscle, and the Levator Palpebrarum Superioris. The term Partial External Ophthalmoplegia denotes the condition where several, but not all, of the extrinsic muscles of the eye-ball are found paralysed. The term Internal ophthalmoplegia is used to mean the paralysis of the intrinsic muscles of the eye-ball.—the Sphincter Iridis and the ciliary muscle. When all the intrinsic as well as the extrinsic muscles are paralysed, the condition is called Total Ophthalmoplegia. Weakness of the Orbicularis Palpebrarum (supplied by the Facial) may be associated with it.

Clinical Picture.—External Ophthalmoplegia is easily recognisable at a glance. The patient's gaze is fixed and the eye-balls are motionless and since partial ptosis is generally present at the same time the patient has a characteristic sleepy expression. Slight protrusion of the eye-balls may be present from the relaxed condition of the paralysed muscles. The condition is always bilateral. The light reflex is present if the optic nerve is in tact.

General Aetiology. — Ocular paralysis may result from organic disease or functional disorder. Organic disease comprises affections of the nervous system and the muscles of the eye-ball together with inflammation or growth in the orbital cavity.

The nervous lesions in organic disease may be as follows:—

I. Supra nuclear.	(1) in the cortex. (2) anywhere between the cortex and the nuclei.
II. Nuclear.	(1) Fascicular — between the nuclei and the point of emergence of the nerve trunks from the brain.
III. Infra Nuclear.	(2) Basal—between 1 and 3. (3) In the cranial foramina. (4) In the terminal branches.

* Specially contributed to the 'Antiseptic'

Pathology of Supra-nuclear Lesions.—The upper neurone system may be affected by vascular lesions such as haemorrhage, thrombosis or embolism, pressure of tumours, inflammatory and degenerative disorders such as Disseminated sclerosis and General Paralysis.

Supra-Nuclear Paralysis.—Ocular paralyses from supra-nuclear lesions are generally characterised by (1) their being associated with other symptoms which aid us in localising *e. g.*, hemiplegia, (2) their being always conjugate in type. This means that the paralysis is in terms of motion lateralwards to the right or left or vertically up or down. When there is paralysis of motion to one side, the eyes may be turned to the other side by the action of the antagonistic muscles and this when present is called conjugate deviation. The power of convergence of the optic axis is retained in cases of conjugate lateral paralysis.

Conjugate lateral paralysis can be produced by affections in more than one part of the brain. Experimental and clinical evidence go to show that there is a cortical centre in the 2nd frontal convolution which is concerned with the voluntary lateral movements of the eyes and from which fibres descend to the midbrain nuclei. Another centre has been found in the occipital lobe stimulation of which produces conjugate deviation of the eyes to the opposite side. A supranuclear centre controlling lateral movements is also supposed to exist near the 6th nucleus in the pons. Conjugate deviation in lesions of the pons is the reverse of what happens in cortical lesions.

As regards conjugate vertical paralysis, Gordon Homes says, "From clinical and post-mortem studies we are justified in saying that in the upper end of the mid-brain in the neighbourhood of the anterior quadrigeminal bodies are association centres which control the conjugate vertical movement of the eyes."

(3) Absence of diplopia and strabismus.

The above considerations go to show that lesions in the upper motor neuron system, unless it be bilateral, cannot produce external ophthalmoplegia.

Anatomy and Physiology of the Ocular Nuclei.—Before dealing with the relationship of nuclear lesions to external ophthalmoplegia, it is well to bear in mind some anatomical facts about the ocular nuclei. To quote Samson Wright, "Though we speak of the nuclei of the 3rd, 4th and 6th nerves as if they were isolated structures, it is important to realise that they simply constitute one long column of grey matter controlling the movements of the eyes. This column extends from the upper part of the mid-brain surrounding the ventral and lateral part of the aqueductus sylvii (iii, iv) down to the upper part of the Pons in the floor of the 4th ventricle (iv)". The following physiological point must be emphasized.

> The oculo-motor column of each side controls the synergic eye-muscles on both sides. A lesion of the column results, not in paralysis of an individual muscle, but in loss of movement in both eyes. Enumerating from before backwards the movements of the eye-balls are controlled by the column thus: (1) Pupil reactions. (2) accommodation. (3) upward movements. (4) downward movements. (5) lateral movement of *both* eyes."

Their Relationship to Ophthalmoplegias.—The data contained in the quotation makes it easy to explain the occurrences of the three types of ophthalmoplegia—external, internal and total. In the first two types, the nuclear lesion is an incomplete one involving only either the anterior or the posterior parts, probably on account of different blood supply to these parts as suggested by Fuchs.

Pathology of Nuclear Lesions.—Nuclear lesions may arise from injury, vascular lesions, inflammation, atrophic degeneration, pressure by growths, and poisonings and they may be acute or chronic.

Acute Nuclear Affections.—Acute affections of the nuclei are described resulting from inflammation and haemorrhage.

1. *From inflammation.*—The inflammatory cases are said to have a sudden onset with fever, headache, vomiting, and convulsions which may subside after a few days leaving only the ophthalmoplegia behind. Other features of the condition are an initial transient paralysis of conjugate movements at the commencement of the attack, absence of involvement of the intra-ocular and Levator palpebrarum muscles in many of the cases

and the accompanying involvement of the facial nerve in some cases.

2. *From haemorrhage.*—In the haemorrhagic cases the onset is said to be sudden without cerebral disturbances. Some cases are rapidly fatal. In those that survive the ophthalmoplegia may be permanent or undergo slow cure.

3. *From trauma in concussion of the brain.*—Instances of nuclear ophthalmoplegia resulting from concussion of the brain are not mentioned in text-books. The situation of the ocular nuclei exposes them to mechanical injury from the violent impact of a wave of forcibly displaced cerebro-spinal fluid from the lateral ventricles into the third ventricles which is generally supposed to take place in concussion of the brain. This is the most probable explanation for cases of ophthalmoplegia with a history of onset following concussion of the brain resulting from a fall on the head.

Nuclear affections in General Diseases.—Other causes of nuclear ophthalmoplegia are:—

(A) DISEASES OF THE CENTRAL NERVOUS SYSTEM.

(1) *Nervous Syphilis*—Tabes and General Paralysis may be complicated by an external ophthalmoplegia.

(2) *Encephalitis Lethargica*—Internal and external ophthalmoplegia may occur. The conditions may be rapidly transient or permanent.

(3) *Syringomyelia and Disseminated Sclerosis.*

(4) *Myasthenia Gravis.*—A nuclear lesion it is stated, may also occur in this disease. Probably this is secondary to a primary affection in the motor end organ. The resulting paralysis is either temporary or permanent. The former begins with diplopia and ptosis. The latter is always preceded by variable paralysis. The final picture may be a persistent external ophthalmoplegia.

(5) *Tumours of the mid-brain, pons, and pineal body.*—Here there will be concomitant symptoms of increased intracranial pressure.

(B) TOXINS OF INFECTIOUS DISEASES.

Influenza, Pneumonia, Diphtheria, Measles, Small-pox, Scarlet fever are some of the diseases which may be complicated by a nuclear lesion. The resulting condition varies from defects

in accommodation to incomplete paralysis of the external muscles *i.e.*, a partial external ophthalmoplegia.

(C) POISONS.

(1) *Alcohol* is stated to give rise to an external ophthalmoplegia. According to Wernicke this depends upon a polioencephalitis Superior hæmorrhagica *i.e.*, upon an inflammation of the grey matter in the walls of the 3rd and 4th ventricles as well as in the aqueductus Sylirus. The paralysis is not infrequently associated with bulbar symptoms and then ends fatally.

(2) *Lead* is cited to sometimes give rise to ophthalmoplegia externa. This is more probably due to lesions of the nerve endings in the eye muscles rather than nuclear, according to modern knowledge of the pathology of Lead poisoning.

(3) *Botulism*—External ophthalmoplegia and ptosis may occur.

(4) *Veronal.*—Here the pupils are stated to be exempt from paralytic involvement. A paralytic conjugate deviation upwards is observed by some as lending a clue to the condition in cases of coma from veronal poisoning.

(5) *Snake poison, santonin, and carbon monoxide.*

(D) A miscellaneous group, comprising Ex-ophthalmic goitre, diabetes, and cold.

The evidence for nuclear lesions in cases of ocular palsies in this group is not strongly supportable. Against the view expressed by some authors that paralysis of the orbital muscles in cases of Exophthalmic Goitre may be nuclear, is the following observation from Foster Moore: "It seems probable that when deficient movements of the eyes occur in Grave's disease it is due to impairment of functions of the muscles as a result of their infiltration by fat or by oedema or perhaps by both, and that marked exophthalmos when present, will introduce a mechanical factor which will contribute towards the same effect".

Chronic Nuclear affection.—Chronic nuclear paralysis depends upon a degenerative atrophy of the nerve nuclei similar to that in the case of progressive muscular atrophy. Beginning in early life, the paralysis gradually and successively involves the muscles of the eye culminating in bilateral affection of all the

extrinsic muscles of both eyes and moderate ptosis without involvement of the intrinsic musculature. It is unassociated with any other morbid condition of the nervous system and does not shorten life.

Infra nuclear Paralysis.—Infra nuclear lesions may occur anywhere in one of the 4 situations given below:—

(1) *Fascicular Lesion*—Fascicular paralysis is mainly distinguished by the presence of other symptoms due to involvement of the neighbouring structures. Thus a fascicular lesion may be conceived when the paralysis of one oculo-motor or adducent nerve is combined with paralysis of the extremities of the other side. According to Bernheimier it may be difficult to clinically differentiate between fascicular and nuclear paralysis.

(2) *Basal Lesions*—Basal lesions provide the commoner instances of paralysis of the orbital muscles. The causes are meningitis often Syphilitic, gumma, an Intracranial Tumour, diphtheria, alcohol, diabetes, nicotine, sepsis, rheumatism, injury from fracture of the skull base, cavernous sinus thrombosis, aneurysm, middle ear suppuration, atheroma of the external carotid artery, and subarachnoid hæmorrhage. Basal lesions are especially to be thought of when the ocular nerves are successively involved. The presence of atrophy of one or both optic nerves or a bitemporal hemianopia would furnish conclusive evidence of the basal origin of the paralytic trouble.

(3) *Fissural Lesion*—In the Sphenoidal fissure acute periostitis may cause infranuclear paralysis similar to that in the case of the facial nerve. Pain in the eye with partial or total ophthalmic and maxillary divisions of the 5th nerve may also be involved giving rise to cutaneous anæsthesia in their area of distribution. Bone tumours may cause pressure paralysis.

(4) *Orbital Lesion.*—Orbital lesions such as cellulitis, new growths etc., may produce loss of motion of the eyeballs from involvement of the terminal portions of the oculo-motor nerves, pain, or mechanical obstruction. The diagnosis will be easy on account of characteristic associated symptoms.

Differential Diagnosis.—In the case of individual muscle paralysis of the abducens or superior oblique it may be really difficult to differentiate between single nuclear and infranuclear lesions, because each of these muscles has its own nerve supply. Indications of nuclear lesions of the 6th nerve are involvement of the 7th nerve, and loss of conjugate deviation towards the site of the lesion with preservation of convergence movement. Isolated paralysis of the 4th nerve is more commonly infranuclear and cannot be distinguished from single nuclear lesion. Single muscle paralysis among those supplied by the 3rd nerve is rare. However traumatic injuries can produce the condition and a reference is made in text-books of isolated paralysis of the inferior oblique in some rare cases of syphilis. Ptosis is a common condition. But it occurs also from cerebral lesions. Paralysis of muscle groups is more usual and may occur from a lesion of the nucleus, trunk, or terminal branches of the nerve. Nuclear lesions of the 3rd nerve affect all or most of the muscles supplied by the nerve with or without involvement of the ciliary muscle and sphincter iridis. In trunk lesions all the muscles supplied by the 3rd nerve are affected—the superior, internal and inferior rectii, the inferior oblique, and the two intrinsic muscles. Branch lesions are the least common and they spare the intrinsic muscles. Thus involvement of parts only of the 3rd nerve with or without involvement of the intrinsic muscles is most distinctly a sign of nuclear lesion. An associated involvement of the orbicularis, frontalis, and corrugator supercili indicates that the lesion is nuclear in site, for these facial muscles are innervated from a group of cells which is in anatomical continuity with the 3rd nucleus. As stated before, conjugate vertical paralysis is a sign of supranuclear lesion. But when associated with ptosis points to a nuclear lesion of the 3rd nerve. It cannot be said that involvement of both eyes points more to a nuclear lesion as lesions in the interpeduncular space can produce the same owing to the close proximity of the two 3rd nerve trunks there. An external ophthalmoplegia is produced either by a lesion of all the terminal branches of the nerves supplying the extrinsic muscles such as occurs in multiple polyneuritis or by an incomplete lesion of the 3rd, 4th and 6th nuclei. Absence of involvement of the intrinsic muscles of the eye precludes involvement of the trunk of the 3rd nerve.

Hysterical Paralysis.—Ocular paralysis of Functional origin :—

"Hysteria must never be used as a mere limbo in which to place ill-understood maladies, or those that evade diagnosis, and

which do not present its characteristic features". It is well to bear this quotation in mind before a diagnosis of hysterical nervous disorder is finally made. Clinical observations such as the tone of the muscles, correspondence or disagreement in the distribution of the group of paralysed muscles to that in the case of organic lesions in the nervous system, existence of abnormal reflexes characteristic of organic affections of the nervous system, and characteristic reactions encountered in subjecting the paralysed limb to passive movement, can be made in the case of motor disorders of the limbs and utilised to make a differential diagnosis of organic from functional affection of the nervous system. These clinical observations cannot be made in the case of the external eye muscles. Osler, in quoting Bristowe's opinion, says that occasionally external ophthalmoplegia may be functional. The chief evidences to be sought for in these occasional instances are the presence of globus hystericus, characteristic sensory loss, and the hysterical temperament—the so-called stigmate of hysteria. R. D. Greeves in the introductory portion of his article on Prognosis of ocular Palsy however states that "ocular palsy is due without exception to an organic lesion of nerve or muscle".

References :—

1. *Text Book of Medicine by Price—4th Edition, 1934.*
2. *Medicine—Beaumont. 2nd Edition, 1934.*
3. *Diseases of the Eye—Swanzey and Werner, 10th Edition, 1912.*
4. *Diseases of the Eye—May and Worth, 6th Edition, 1930.*
5. *Medical Ophthalmology—Foster Moore, 2nd Edition, 1925.*
6. *Prognosis—Vol. I., The Lancet, 1935.*
7. *Applied Physiology—Samson Wright, 2nd Edition, 1934.*
8. *Practice of Medicine—Osler, 9th Edition, 1920.*
9. *Dif. Diagnosis—H. French, 5th Edition, 1936.*
10. *Ophthalmology—Fuchs, 1933.*
11. *Text Book of Pathology—Boyd, 1935.*

The Treatment of Fibro Adenoma Prostate*

BY

I. B. MALIK, M.B., B.S.,

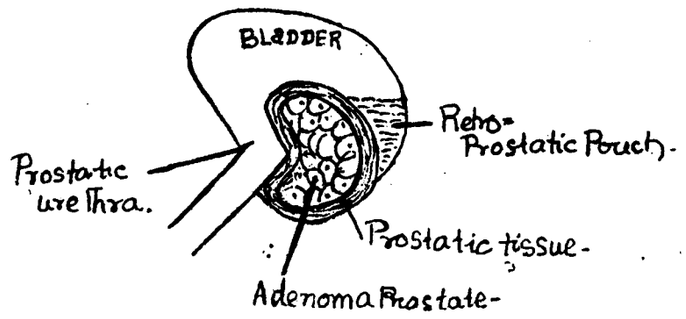
Hon. Surgeon, Bhadoti Hospital, Benares State.

ON arrival at the correct diagnosis of Adenoma-prostate, to speak the truth, enucleation of the new growth is one and the only one treatment which can give relief to the patient.

But before deciding the operation, a surgeon should think, whether, the enucleation is indicated or not, and if indicated, whether, it should be done in one or in two stages.

The following tests are conducted to decide the line of treatment to be followed :

1. **The examination of the residual urine.**—The adenoma grows in the middle of the gland, as a result, the median sulcus of



the prostate is obliterated. This new growth as it enlarges pushes the posterior wall of the bladder upwards and thus a retro-prostatic pouch is formed as shown in the figure. When the patient is asked to evacuate his bladder he will do so, but a certain amount of urine will remain in the retro-prostatic pouch which voluntarily he cannot pass out.

This amount of urine is known as residual urine and is to be measured thus :—

> After the patient has evacuated his bladder, a metal prostatic or a bi-cude gum elastic catheter is passed into the bladder and remaining urine is drawn out and the quantity measured.

* Specially contributed to the Antiseptic.

2. **The Renal Efficieny tests :—**

(1) *Urine urea.*—15 grms. of urea in 100 c. c. of water is given to the patient first thing in the morning. Then the urine is collected after the 1st, 2nd and 3rd hour in a sterile flask for estimation of quantity of urea in the specimens.

If the normal percentage of 2.5—3 be estimated in the 2nd hour specimen, the urine of the 3rd hour need not be examined.

(2) *Blood urea* :—The amount of urea in blood varies between .02 —.03 % in a normal individual. To know, whether there is any increased retention of urea in blood, this test must always be performed.

(3) *Urography* :—To know the condition of the upper urinary tract, 15 grms. of 20 % uroselectan B is injected intravenously and after an hour, X-ray photograph is taken and the radiographic plate is scrutinized for any defect in the tract.

(4) *Dye Excretion test* :—This test indicates whether, the secretory power of the Renes is normal or not.

10 c. c. of .4 % Indigo-carmine is injected intravenously. In normal person the urine of the bladder is coloured blue within 7 minutes, which is observed by means of a cystoscope.

3. **Examination of Blood and the Blood Pressure :—**

(1) Blood pressure of the patient should be found out by auscultatory method which indicates whether secondary complications have intervened or not.

(2) Total W. B. C. count is conducted to know the general condition of the blood and for any secondary septic focus.

(3) Haemoglobin percentage of blood is conducted and sometimes opsonic index is calculated.

(4) The last but not the least, the most deceiving disease of chronic-uraemia should be diagnosed from clinical and pathological examinations.

Thirst, headache, drowsiness, furred tongue and enlarged heart with 2nd aortic sound accentuated, in short, are the clinical manifestations of this disease.

Full examination of urine should also be conducted specially.

Examination for albumen, sugar and renal casts indicating uraemia, diabetes and nephritis are done to allay the grave complication after operation.

Indications for one stage operation :—

1. The Residual urine is not more than 2-3 oz.
2. The urine urea is between 2.5 % and 3 % in 2nd or 3rd hours specimen.
3. The blood urea is between .02 % and .03 % *i.e.*, 20-30 mgm. per 100 c.c. of blood.
4. When urography shows no defect in the urinary system.
5. When the secretory function of the kidneys is normal as found by indigo-carmine or other such tests.
6. When blood examination showing good percentage of Haemoglobin and the lyucocytes not more than 8,000—9,000 per c.c. m. m.
7. When no sign of chronic uraemia is detected.

Indications for operation in two stages :—

1. Residual urine is more than 3 oz. but less than 8 oz.
2. When urine urea is between 1.5 %—2 %.
3. When blood urea is between 40-50 mgm. per 100 c.c.
4. When signs of uraemia are present.

In such a case, the drainage by supra pubic cystotomy is done. When clear urine comes out by 7-10 days' time, the above tests are performed and in a favourable case the next operation of enucleation of prostate is conducted.

Contra-indications for operative treatment :—

1. Residual urine more than 8 oz.
2. Urine urea is 1 % or below.
3. Blood urea is above 50 mgm. per 100 c.c.
4. When the patient is suffering from the general diseases such as enlarged heart, diabetes, chronic nephritis etc.
5. When the patient is very old and weak.

In such a case, "catheter life" and urinary antiseptics are only to be prescribed.

Pre-operative management.—According to the condition of the patient when admitted in a hospital :

A. If a patient comes with acute retention of urine and symptoms of chronic uraemia :—

Local treatment (for retention).—(1) Put the patient to bed.

(2) Draw at once by means of bicude gum elastic or metallic prostatic catheter 15 oz. of urine only.

If the bladder is evacuated fully, at this stage there is every chance of the patient's collapse due to sudden lowering of pressure.

3. Later evacuate the bladder 4 hourly by rubber catheters, if possible.

General treatment (for uraemia).—1. Give the patient plenty of water by mouth, intravenously or sub-cutaneously with 2.5 % glucose.

2. Saline purgatives should be given freely.

3. When diuresis has begun diuretics should be freely given.

4. To promote sweating, give hot packs to the skin, hot air bath and keep the patient covered up in blanket.

N. B. If the bladder has been completely evacuated by any body previously and collapse is threatening, fill the bladder at once to allay this collapse.

B. When the patient comes to that stage, when he can evacuate some part of his bladder by himself but the upper limit of his bladder has reached the level of the umbilicus :—

Evacuate his bladder at such a rate by artificial means, so that the bladder may fall 1" below the umbilicus every day.

C. When the patient possesses no retention but residual urine is present and the patient is suffering from general diseases which contraindicate operation.

1. Advise "Catheter life"—

Indwelling Rubber catheter is put within the bladder—and to hold the urine outside a suitable receptacle is used. This rubber catheter is removed, bladder wash is given and again put within the bladder.

2. Give urinary antiseptic, and the following prescription does good.

℞

Hexamine	...	gr. x.
Amm. Chloride	...	gr. xv.
Spt. Chloroform	...	♏ xv.
Inf. Buchu	...	℥ī. T. D. S.

3. Treat for the general diseases, if the condition becomes favourable.

Do supra pubic cystotomy under local anæsthesia and let there be drainage of the bladder from 7-10 days. When the condition is improving, do the enucleation operation.

4. In many cases the condition does not improve and the patient is very miserable. In such cases a new operation of removal of part of the tumour is resorted to.

It is done by Prostatic-Resectoscope. The instrument is passed through the urethra. When it reaches the prostatic urethra a portion of the gland which obstructs the passage of urine is removed under direct vision.

The effect of this operation is temporary and it remains for a year or so; later, the tumour again grows and again Resectoscopy is performed.

The Operation.—There are two methods by which prostatic growth is enucleated.

1. *Perineal route Method.*—This is an old operation and it has got many disadvantages; so it has been abandoned now-a-days.

2. *Supra-pubic-prostatectomy.*—This is the operation of choice; in this, first cystotomy is performed and then the knife is entered through this route upto the prostatic urethra where its wall is cut through and the adenoma is enucleated by means of finger with its capsule.

The cavity is irrigated with hot douche to stop bleeding; if bleeding is profuse, packing is also required. Then a large drainage tube is put within the bladder and the external wound is closed. The tube is kept for 7—10 days.

N. B.—To avoid Epidydimitis, it is a good practice to ligature the Vas Deference at the external inguinal ring.

After-Treatment—Give the patient copious drink, diuretics and urinary antiseptics; if, after 10 days, urination is not performed per urethra, catheterization is performed to promote urination.

Spirochaetal infections of Vincent*

(Fusospirillosis of Vincent, Spirochaetal Treponema Vincent infections).

BY

C. A. HENRY, L.M.P., (MAD.)

Medical Officer, King Edward Memorial Dispensary Bandarchua, Jashpur State E. S. A.

Definition.—Vincent's Fuso spirillosis is a specific infectious disease, characterised by a local ulceration and pseudo membranous exudates usually upon a mucous membrane and by constitutional symptoms due to toxins produced at the site of the lesions. Further, lesions can be produced locally on the external surfaces of the body. When it generally occurs in the throat, it is then known as Vincent's angina, Plant Vincent angina, and Ulcer membranous angina. Various lesions from these organisms have been isolated. Among them may be mentioned Oropharynx, Vaginitis, middle ear and mastoid disease. The organisms also attack glans penis, and prepuce and are found in pulmonary abscess, Bronchiectasis, wounds particularly those made by the teeth of human beings, also infections occurred in endometrium, peritoneum and in the meninges of the Brain. Therefore, the designation Fusospirillosis is applicable.

Besides plant, vincent spirochaete associated with Fusiform bacillus, other organisms are usually found in the lesions.

Vincents angina of the throat is very often mistaken on the one hand with various kinds of septic sore throat, Tonsillar and Peritonsillar inflammations and on the other hand with Diphtheria and other specific infections of the throat. The tonsils may show the eruptions of Varicella Variola and Herpes and all the seats of inflammation in Scarlet Fever, Diphtheria, Measles, Influenza and also the seats of secondary manifestations of syphilis, both condylomatas and serpigenous ulceration being observed.

A Brief History and Etiology.—Vincent's original contribution appeared in 1896, on this subject.

Fusospirillosis was noticed in the Gangrenous wounds during the Crimean War and it was known among the Doctors in the war theatre as Hospital Gangrene. It was also common amongst the Expeditionary forces in the late Great European war, most

* Specially contributed to 'the Antiseptic'.

common among the British soldiers in trenches and was recognised as trench mouth, ulcerative, gingivitis, and stomatitis.

There is difference of opinion regarding the relationship between the spirochaete and the Fusiform bacillus but other organisms are also found in the lesions, and many surgeons believe that a symbiosis is responsible for the diseased state. Symbiosis has been extensively studied by Zoologists and Botanists but attention has been received from the medical science. Fusospirillosis is generally seen in the mouth and throat. This disease sometimes becomes epidemic. The organisms may be transmitted from one individual to the other by contact and by infected clothing and over-crowding is also responsible. It is common in India and it was endemic in Europe and in America. Young adults are susceptible to this disease and occasionally it becomes epidemic in children. Heltgem in 1910 reported that he believed it to be the first case of gangrenous Perionychia due to Symbiosis of the fusiform bacillus and the spirochaeta denticola. The term symbiosis signifies the living together of two different species either of plants or animals.

Again in 1929, Flic has reported a case of Gangrenous infection of hand and forearm following laterly the thumb in a human being, which ended fatally. In fact there was an extensive destruction of the tissues of the hand and forearm. Odour was very offensive. This was due to complication of spirochaetal pulmonary Gangrene. The patient refused amputation and died after a month as the result of the injury. Clinically wounds infeced with the spirochaete and fusiform bacillus are characterised by foul smelling. Gagrenous affections must be carefully studied for in the case of spirochaete and fusiform bacillus, the organisms are anarobic and cannot be cultivated by ordinary methods but they can be found in the examination of the thin smears of pus obtained from the depth of the wound. Wounds made by human bite should be potentially infected and so treated.

Gangrene following a human bite.—This type of infection is almost certainly a disease due to a mixture or symbiosis of organisms. A foul Gangrene following human bite with serious infections resulting from an injury is certainly a disease due to a mixture or symbiosis of organisms. Dr. Flick has said in one of his cases that other organisms besides spirochaete were always present, practically all cases of streptococci are present along with the fusiform Bacilli and spirochaetes.

Amoebic infections are probably symbiotic amoeba and will not grow in artificial culture. Why gangrene or distruction of tissue develops when certain organisms are growing together is still

in dispute and is unsettled. This is probably true in a destructive lesion in which one or more species of organisms are present. These cases suggest more frequent consideration of the possibility of symbiotic or synergetic infections in all regions of the body, where numbers of different species of organisms are likely to be present, such as the alimentary tract from the mouth to the anus.

The severe infections following lesions in the oesophagus, Peritonitis following lesions of the Gut, lesions of the respiratory tract from the common cold to the lung abscess and gangrene of the lung are examples.

Let us now consider fully Vincent's Angina.—This is one of the spirochaetal infections of Vincent. Vincent's angina has been considered a disease of symbiotic organisms, a fusibacterium. In this form there is stomatitis or pharyngitis due to the presence of bacilli fusiformis and a certain type of spirochaete. There is also ulcerative inflammation of tonsils and surrounding structures generally one side, and the above mentioned organisms are found in the lesions. It is a sort of association of two organisms causing the disease known as symbiosis. The causative organisms are present in the healthy month and are awakened into activity by local irritation or by the general resistance being lowered owing to debility. Certain bacteria have a synergistic function in the production of certain type of disease or symptoms of disease. The synergestic action should always be kept in mind in studying disease process involving tissue organism or symptoms in which mixtures of organisms are frequently associated or the main symptoms are occasionally found. There is pyrexia, the temperature rising to 101° F. to 105° F. Frontal headache is common. It is characterised by the development of ulcers on the Gnons facial pillars, tonsils or posterior wall of the pharynx; the ulcers may appear almost clean or they may be covered by a sticky fibrous yellow pseudo membrane which is adherent and on their removal causes bleeding; pains are always present: there is difficulty in swallowing. The secretion is of mucous albuminous secretion and large number of micro-organisms are found in the secretion; constipation is the rule; the urine is diminished in quantity loaded with urates. Suppuration sometimes occurs, an abscess being formed in the substance of the tonsil. The abscess sometimes ruptures spontaneously into the month and rarely leads to Haemorrhage. Abscess in the glands of the neck may sometimes occur. Albuminuria is said to occur sometimes in this affection but certainly not if it occurs when Diphtheria or

scarlet fever may be suspected. The pseudo membranous exudation which may resemble that of diphtheria is softer and more friable. The glands in the neck are enlarged but they are enlarged on the affected side. The ulcer is sometimes superficial and sometimes deep. This in turn begins to heal within a week and convalescence is rapid.

Diagnosis.—This condition has to be differentiated from diphtheria tonsillitis or syphilitic ulcerations. In order to verify the diagnosis a swab should always be taken direct, and smear examined under a microscope for the presence of specific organisms. The chronic type may resemble the mucous patch or tertiary ulcerations of syphilis. In cases of difficulty, Wassermann should be employed. Otitis media occur in connection with syphilitic sore throat. In cases of diphtheria and syphilis there is rarely present fusiform bacilli and spirilla together and the peculiar offensive smell. Please note the ulceration is one sided in Vincent's angina. In diphtheria a membrane forms ashy grey in colour which cannot be separated from the tonsils without provoking bleeding. In diphtheria both tonsils may be affected but only a single patch of membrane on each side. Diphtheritic membrane is not limited to the tonsil for long but soon spreads up to the faucial pillars and to the uvula.

Prognosis.—There is no danger except when vincent's angnia supervenes in scarlet fever, Diphtheria or some other acute fever.

Treatment.—Open the bowels by compound liquorice powder. Rest in bed. The slough should be removed gently. The patient should be removed from insanitary surroundings to a healthy place. Give him plenty of nourishing food. The ulceration reacts well to the local antiseptics of which painting the ulcers with Tr. Iodine thrice daily is the most satisfactory; a solution of neosalvarsan or emetine may be painted over the ulcers. The mouth must be kept as clean as possible by mouth washes and gargles; a mouth wash 1 in 2500 pot. permanganate solution is the best. Infected teeth and tonsils should be removed. Intravenous injections of arsenic (salvarsan) may be given but the treatment of salvarsan is contra-indicated in gangrene of hand or fore arm.

Another method of treatment.—Mill's medicinal treatment is to gargle with cheap clarat wine to obtain the benefit of tannic acid therein every 3 hours or very often. If there be high fever, pulse full and bounding, face flushed, eyes red, and evidence of

intense congestion of the throat, a 1 % solution of Belladonna is the best remedy.

℞	Liqr. Ferrisubsulphatis	...	f. ʒj.
	Glycerine	...	f. ʒj.
	Spirit frumenti—	...	f. ʒj.
	Aqua distillatae s. ad.	...	f. ʒiv.

Misce Sig. a half tea-spoonful every 2 or 3 hours according to the severity of cases can be used advantageously in the form of spray in the ulceration of throat, irrespective of diphtheria.

℞	Pot. Chloras	...	grs. 30
	Acid hydrochloric dil.	...	dr. 2
	Tr. Ferri Perchlor	...	dr. 3
	Glycerine	...	ʒi.
	Syrup Tolu Q. S.	...	ʒiii

Misce Sig. one teaspoonful in water every 2 hours before the administration of the above mixture. Give an opening medicine.

Paint the throat with saturated alcoholic solution of resorcin every other day.

Use the following as throat paint :—

(*a*)	℞	Acid carbolic	...	grs. x
		Tr. Iodine	...	♏. xv
		Glycerine	...	ʒi
		Inf. Rose ad.	...	ʒi

The throat should be painted every 2 hours.

(*b*)	℞	Tr. Iodine gutt.	...	iiss
		Sodii chloride	...	gr. v
		Aqua	...	f. ʒj

Misce as a gargle to be repeated several times during the day.

Treatment.—For Infection following human bite we will have to be satisfied with the modern antiseptic surgery as prophylactic and active treatment. X-rays are advised.

References:

1. *Text Book of Medicines by J. J. Conybeare, M.C., M.D., F.R.C.P., 1929. Edition.*
2. *The Principles and Practice of Medicine by Osler, Revised by Thomas Mccrae M. D. Edition 1930.*
3. *The Science and Practice of Surgery by W. H. C. Romanis and Philip H. Mitchiner, 4th Edition, 1932. Vol. 2.*
4. *Annals of Surgery, Edited by Lewis Stephen Pilchar, M.D. LL.D. of New York, July, 1932.*

CASES AND COMMENTS

Utero-Abdominal Fistula

By

DR. S. C. DAS GUPTA, L.M.S., M.A.C. Pr., (U.S.A.),

Surgeon-Superintendent, Town Hospitals, Katmandu, Nepal.

ABOUT six months ago, Harkha Kumari, a female, aged 38, multipara, was brought to Bir Hospital for treatment for a perforating ulcer of the abdomen. She gave a most interesting history. About three years ago she was in full term of pregnancy but the child died before delivery and after many weeks the macerated bones came out one by one for many weeks but the head was locked up within the uterus. Nearly a year ago, she noticed a small diffused swelling on the abdomen just below the umbilicus, which gradually grew and got inflamed Then there was probably adhesion between uterus and abdominal parietes Later on, it suppurated and burst out. Some of the small pieces of skull bones came out gradually from the cavity one by one and when she came to me, I saw pieces of bones projecting through the abdominal wall and on passing the forceps its end hit against the broken skull of the foetus.

Before Operation.

She was put under chloroform. The opening of the cervix admitted the tip of the little finger. The cervix was dilated, bones were crushed by means of bone forceps and delivered, and the uterus was then irrigated with Acriflavine lotion thoroughly by means of a blunt flushing curette.

The edges of the abdominal wound was scraped, and then narrowed as far as possible by means of cross-stitches of strong catgut. The irrigation was continued for a few days. The size of the uterus came down to normal condition in about two weeks and the abdominal wound also healed up a week later, and she was discharged.

A Case of Habitual Abortion

BY

HARIDAS DE, L.M.F.,

Late Senior House Physician, Campbell Hospital, Raiganj, P. O., Dinajpur.

MRS. K. S. came into my observation in the month of October, 1936. The patient, a Hindu lady, aged about 21 years, 4th para. Her husband told me that her previous three pregnancies, inspite of all efforts by *ojha* and treatment by local illiterate Dais, were terminated into miscarriages, two in the 8th month and the 3rd one in the beginning of the 9th month. With the biased idea that Allopathic medicines would do harm both to the fœtus and the pregnant mother, her husband and relations as well, did not consult any medical man during the previous three pregnancies. This time, however, in despair, he brought the patient to me for observation and treatment.

I saw the patient in the beginning of the 8th month of her pregnancy. The patient was healthy, complaining of slight occasional pain in the lower abdomen, a premonitory sign of miscarriage experienced by the patient in all her previous pregnancies. I examined the patient thoroughly and tried my best to elicit the aetiology of such kind of habitual miscarriages but to my utter disappointment, I could find no definite cause. Her husband denied any previous history of syphilis. No toxaemias of pregnancy were present. I could not examine P. V. to find the position and healthy condition of the uterus during this advanced stage. No untoward complaints were made by the patient save and except slight pain over the lower abdomen at occasional intervals.

However, I assured the patient and her husband that this time a normal healthy child would be delivered at full term. I advised the patient absolute rest both physical and mental and to keep herself in bed for one month. I advised her husband to

live separately at night. I prescribed her the following mixture to be taken thrice daily.

℞

Pot. Bromide	...	gr. x.
Liq. Sedans (P. D. & Co)	...	♏ xx.
Ext. Cascara liquid (P. D. & Co.)		3p.
Sodi Bicarb	...	gr. x.
Aqua Chloroform ad.	...	℥ i.

Rice diet was given to her in the day time and milk and bread at night time. Fruit juice, glucose D (Glaxo) were advised to be taken in abundant quantity. Calcinol tablet, one tablet in the morning and one in the evening was given to her.

After one week I went to see her and asked her whether she noticed any bleeding. She told me that with the mixtures thrice daily and the calcinol tablets twice daily, her pain in the lower abdomen had much abated; she now seldom felt any pain that was experienced in her previous pregnancies before my treatment. Her bowel was moving regularly and no complaints were felt by her. Same mixture was continued for one week more but this time the dose of liq. sedans was decreased to xv min. only. Calcinol tablet was taken by the patient regularly. This time also I assured the patient well about her normal delivery at full term and kept her in my observation for another fortnight. In the 1st week of 9th month, one night she suddenly started labour pain when I was sent for. I hastened to the spot and after examination could detect that actual labour pain had started. I assured the patient for the 3rd time, passed the whole night there doing nothing except giving assurance to the patient. Thank God, to the full satisfaction of the patient, her husband, and relations, she gave birth to a male child at about 1 p. m. the next day. Placenta was naturally expelled within half an hour. The condition of the mother and the new-born child was good. I left the place giving her ergot mixture to be taken thrice daily for a few days. The patient is quite alright with her boy and the couple are happy now. The point of interest is that Pot. Bromide and liq. sedan mixture together with calcinol tablet and Psycho-Therapy helped the lady and saved her from her habitual miscarriage.

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

The Antiseptic

ESTD. 1904.

A Monthly Journal of Medicine and Surgery.

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

Editorial and Publishing Offices:—323, Thambu Chetty St., Madras.

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

Vol. 34. | JANUARY 1937 | No. 1.

EDITORIAL

1937

With the advent of the New Year, "The Antiseptic" enters on its thirty-fourth year of existence. The year just ended marked a most deplorable and unprecedented event in the history of the British Empire *viz*,, the abdication of His Majesty King Edward VIII, for whom we offer our heartfelt sympathy. But, at the same time, it is rejoicing to find the accession to the throne, of his brother, His Majesty King George VI. We offer our humble and loyal homage to His Majesty King George VI and Her Majesty Queen Elizabeth.

One of the outstanding events of the past year in the medical world was the re-establishment of good-will and cordiality between the General Medical Council of Great Britain and the Indian Universities, which remained estranged for over five years, by the recognition, by the General Medical Council, of the medical degrees of the Universities of Bombay, Lucknow, and Madras with retrospective effect from 25th February 1930 and of the Patna University degree, from 11th May 1935.

Our Editor Dr. U. Rama Rau, who was the President of the Indian Medical Association during last year, had prepared a Draft Bill for the establishment of a College of Physicians and Surgeons in Madras, and had it circulated to all the medical organizations and prominent medical men in India for their opinion. A large volume of opinion has been collected, which will be

utilized in good time for legislative enactment in the new legislatures to be constituted in April 1937.

The Antiseptic continued as before to publish the Madras University Extension Lectures as a special number and to throw open its columns to progressive scientific thought and to the advancement of medical men whether in service or independent practice in India. In this, our humble endeavour, we had the willing co-operation and useful guidance of the members of the medical profession and the producers and distributors of medical products—not only in India but all the world over. To all of them, we offer our hearty felicitations and wish them all a happy and prosperous NEW YEAR.

The World's Food Problem

We have before us for review four volumes, entitled "The Problem of Nutrition"* prepared by the League of Nations, Geneva. They are very valuable and interesting documents and there is no gainsaying the fact that a considerable amount of time, trouble and expert knowledge have been expended in producing these volumes. For well-nigh ten years the Health Organization of the League has been engaged in the study of nutrition in relation to Public Health and at a meeting of the Assembly in September 1935, the following resolution was adopted:—

> "This Assembly, having considered the subject of nutrition in relation to public health and of the effects of improved nutrition on the consumption of agricultural products urges Governments to examine the practical means of securing better nutrition and requests the Council:—
>
> (1) To invite the Health Organization of the League of Nations to continue and extend its work on nutrition in relation to public health;
>
> (2) To instruct the technical organizations of the League of Nations in consultation with the International Labour Office and the International Institute of Agriculture to collect, summarise and publish information on the measures taken in all countries for securing improved nutrition; and

* Published by The League of Nations.
Vol. I. 98 pages—2 shillings—$ 0.50.
Vol. II. 27 pages—6 *d.*—$ 0.15.
Vol. III. 271 pages price 5 sh. 6 d.—$. 1.40.
Vol. IV. 110 pages Statistics.

> (3) To appoint a Committee including agricultural, economic and health experts instructed to submit a general report on the whole question, in its health and economic aspects, to the next Assembly, after taking into consideration *inter alia* the progress of the work carried out in accordance with paragraphs 1 and 2 above."

The Nineteenth Session of the International Labour Conference held in June 1935, also passed a resolution on lines similar to the above. To give effect to paragraph (3) of the above resolution, a Mixed Committee was set up, which included experts in the fields of public health, agriculture, economic policy and social assistance, by the Assembly of the League of Nations. Their report in four volumes has now been published.

Volume I which is the 'Interim Report' of the Mixed Committe on the problem of nutrition constitutes the Report proper. From the mass of evidence collected from various Governments and information obtained by the Committee members, it has been conclusively proved that inadequacy of diet is widespread. Malnutrition is manifest in the prevalence of rickets, scurvy, poor musculature, teeth of poor structure, anaemia, chronic fatigue, poor condition of the skin and sub-normal growth and weight, to mention the more easily observable symptoms. For these reasons special emphasis is laid by modern teaching on the great importance of certain 'protective foods'—this is, foods rich in the elements necessary to prevent the incidence of the specific maladies referred to. Now, what are these protective foods? 'They consist mainly of products of dairy farming and of the market garden and include meat, milk, eggs, cheese, vegetables, fruit and potatoes'. Though the report excludes from its purview, Asiatic countries and confines itself to the peoples of Europe and other countries of Western Civilization, the following observation of the Committee with regard to dietary conditions of Asiatic countries, is particularly significant:—

> "Again, the populations of the hot countries of Asia which know no cereals other than rice, are able to subsist on their diet by adding certain food-stuffs, such as cabbage or bamboo shoots, a few figs, eggs and pork, thereby making up for the deficiency of calcium, vitamin A and protein which characterises the cereals. Such a dietary is however, far from ideal. In these countries, the physical resources of the women are severely taxed by child-birth; mother's milk

is of poor quality and infant mortality exceedingly high. Furthermore, such races have been observed to age rapidly and have a comparatively short average length of life".

Of all the protective foods, milk is regarded as of outstanding importance, since it is food containing most or all of the materials necessary for growth and for the maintenance of life and provides these in a form ready for immediate utilization by the body. The use of milk in the diet of the human race is as old as the history of mankind. 'A land flowing with milk' was the ideal of pastoral lives in ancient times and will still remain the ideal, if the correct nutrition and health of the people recieve due considerations. 'The fine physique and stamina of the Arabs, is attributed to the nutritive value of the limited diet which they take, which consists of sour milk, supplying nearly 90 % of the energy requirements, a small quantity of barley, a few dates and the like". The contrast in health, strength and stamina is proverbial between the Hill tribes of India who partake largely of milk and those dwelling in the plains where the diet is more exclusively vegetarian, and consists largely of cereals. Next in importance come fruits. The special nutritive value of fruit depends on high vitamin C (ascorbic acid) content. "Different fruits" the Committee observes, "vary greatly in their Vitamin C content, the richest being citrous fruits (*e.g.* oranges and lemons). Tomatoes are also valuable, grapes are relatively poor." "Vitamin C is readily destroyed by heat, so that fruit jams and preserves usually contain none. It is probable that preserved fruits, however, may possess a dietary value due to their mineral content. Oranges again are rich in calcium salts, while grapes are rich in iron, and fruits generally may have a special value in supplying mineral constituents to those on otherwise restricted diets. Fruits having a yellow colour, *e.g.*—oranges and tomatoes—are often useful sources of vitamin A, owing to their carotene content".

With regard to energy producing foods, the Committee fixed a basic figure for an adult man performing an average but indeterminate output of work and this represents the requirement for maintenance to which supplements are to be added for work, growth, pregnancy and lactation. This figure is stated to be 2400 calories net (*i.e.* after deducting waste in cooking and at table) per day. Most authorities have agreed upon this figure for the type of adult under consideration, and it so happens that the figure is convenient for calculation on a basis of 100 calories per hour. Conditions and age being equal, no difference is made between the sexes.

Among the 'Energy-bearing foods' cereals form a most convenient and acceptable form of food and for centuries they have been the staple food of the great Asiatic and Mediterranean civilizations. In Europe, of late, the consumption of cereals has considerably decreased on account of the availability in larger quantities of protective food-stuffs, except under conditions of heavy manual labour or because of limitations of income. At the same time, these cereals are consumed more and more in a highly milled form. The Committee suggests that bread should be made more protective by restoring to the flour, as far as possible, the special nutritive principles contained in the husk and germ of the grain, particularly the vitamin B group. This finding is all the more important for India, because the bulk of the population eat only milled rice and protective food-stuffs are a rarity. Special attention is called to the value of potato as a food rich in calories and in starch and is particularly suited to substitute sugar and cereals in the modern European diet. The introduction of sugar and white flour to populations in remote districts has been followed by the occurrence of dental disease previously unknown. A large proportion of potatoes in the diet encourages no such predisposition to dental disease as is the case with cereals. "Potatoes are also a valuable source of iron and vitamin C and one of particular value because they retain a high proportion of their vitamin C content after cooking". India has fully understood the virtue of potato, which has penetrated into the hearths and homes of the rich and the middle classes. The poor, however, have failed, on economic grounds, to avail themselves of it, as in the case of every other food-stuff of nutritive value.

With regard to sugar, the Committee says: "Less importance may be attached to the use of sugar, which contains no vitamins or mineral salts, while indeed its excessive consumption diminishes the appetite for more important protective foods".

The need for vitamins and minerals in diet has also been sufficiently stressed.

The Committee has also dealt with such problems as the health of the pregnant mother and that of the child. Some of its findings and recommendations in this regard are very instructive and may be quoted here:—

(1) "Pregnant women, nursing mothers, infants and young children must be considered from a nutritional stand-point as the most vulnerable portion of the population in the sense that damage inflicted in childhood by bad food cannot be sufficiently repaired".

(2) "An abundant supply of milk is therefore an essential item in the diet of children in order to secure a sound physique and good health, but very few countries, if any, have as yet attained the standard which secures to the child population as a whole this essential basis for sound nurture".

(3) "Remedial treatment for the older age-groups, who must often be regarded as "damaged goods" must also have its place in the planning of nutritional campaign; but it is the preventive rather than the curative aspect of the problem which should be given the first place. From a national stand-point the cost of the investment so made in the health of the children will be more than compensated by the improved vigour and physique of the adult population."

(4) "Medical inspection of Schools revealed then (during the World War) and still reveals a large number of sickly children below the normal standard of development for their age. The considerable decline in infant mortality in some countries only renders more impressive the persistence of high infant mortality in others. Certain epidemics display a destructive power that seems due, not solely to the virulence of the infective agent, but also to a lack of resistance in the population attacked".

(5) "There is good reason to believe that a large amount of sickness and disability associated with child-bearing and the high-mortality rates of pregnant women could be substantially reduced by improved feeding of these women".

(6) "One of the commonest defects in modern civilized diets is a faulty mineral supply leading to disordered calcium metabolism, so that the mother has to sacrifice the calcium salts of her own bones for the developing off-spring.....Another defect which is likely to be deficient in the diet of pregnant women, is iron, of which the natural organism has to supply a relatively large quantity to the foetus.....It is well known also, that a deficiency of iodine in the diet of pregnant women may be of great significance. There is evidence that vitamins are commonly deficient in the diet

of pregnant women. The commonest deficiency is probably that of vitamin D, vitamins A and C are also injested in deficient amounts in many instances".

(7) "Although it is true that our knowledge of feeding in pregnancy and lactation is elementary, it can be said with some assurance, that in regard to the health of both mother and off-spring, an increase in the protective food-stuffs, would have a large effect in eliminating many of the ills of pregnancy".

(8) "Complete breast-feeding of infants is of very great importance. It is cheaper, simpler and cleaner than artificial feeding and in the case of a properly-fed mother, the benefits brought to the infant are great".

(9) "Where breast-feeeding was general, the 'nutritional peril' was usually small; when artificial feeding predominated, it was great. But although the superiority of breast-feeding over artificial feeding with cow's milk has been demonstrated, breast-fed infants may yet be improperly nourished, if, in addition to their mother's milk, they are given other untimely or unwholesome food or do not receive the necessary vitamins in the form of supplementary foods".

(10) "There is a common practice now-a-days of including cereal and cereal products in the diet of young infants. The enquiry made by the League of Nations into the causes of infant mortality made it clear that the pernicious combination of poverty and ignorance was largely responsible for the malnutrition of infancy, as indeed, for that seen in other stages of human life".

The whole problem of Nutrition, thus, hinges on ignorance and poverty. "Ignorance of the principles and main features of the modern science of Nutrition is prevalent, not only among the poor classes of the population where it aggravates the ill consequences of lack of resources: investigations made in the wealthiest countries have revealed the fact that defective, in-adequate or ill-considered nutrition exists and that even among the wealthier classes there is ill-considered nutrition due to inadequate knowledge". In the Committee's opinion, effective teaching and propaganda are likely to produce important and rapid results. The work of spreading knowledge may be conducted through many and widely different agencies and by widely different means

(Universities, elementary schools, secondary schools, schools of domestic science, demonstrations in various forms, publications, wireless, cinema &c). The means adopted in any country will have therefore, to be carefully co-ordinated if satisfactory results are to be obtained. The education of the general public should begin in the primary school, with elementary instruction in physiology in a very simple form. The child should be taught the nutritive value of the principal food-stuffs (milk, bread, green vegetables, fruit), school meals will teach him dietary habits based on reasons of health. This instruction and these habits will quickly spread from the school to the family.

The Committee considers that the subject of nutrition should find a place in the curriculum of the basic sciences and clinical medicine. "In Clinical medicine, the student learnt little more than the diagnosis and treatment of the most characteristic diseases of the digestive organs and the principal diseases of nutrition such as diabetes and gout. Clinical instruction may include not merely characteristic nutritional diseases but also pre-morbid conditions and the general effects of mal-nutrition—in short the nutritional aspect of preventive medicine. The student can be initiated into the technique of dietary surveys, family budgets and the adjustment of family incomes to nutritional requirements. In nutrition, as in the other branches of curative and preventive medicine, medical practitioners must be sufficiently well-trained to be effective agents of progress in the family and in the comunity at large".

If poverty is the main cause of nutrition, schemes of public assistance must take this into consideration. "When public assistance is afforded and can act by means of price privileges, it is of the greatest importance that it should be guided by sound nutritional precepts and that those food-stuffs should be selected of which the lack is most serious. The case of milk deserves special attention in this connection".

The economic aspects of the nutrition problems are also briefly discussed. The 'Protective Foods of which a generous supply must be ensured in the interests of a good dietary, are relatively costly. "It is thus clear that the improvement of nutrition is associated with the maintenance and improvement of the general level of income, but a first step may be taken without effecting any far-reaching changes by better organization of supplies and by widespread education with regard to the value of commonly available foodstuffs. Further, the level of food prices must depend primarily on the operation of agricultural and

trade policies. The public authorities may, however, bring the supply of essential food-products within the reach of the low income and impoverished sections of the community by various forms of direct action. Moreover, there is a vast field for activity in the attempt to promote better market organisation and to bring producer and consumer in close contact".

The report contains a chapter on malnutrition among agricultural populations and considers the question whether agricultural practice can be adapted to meet the new requirements of better nutrition so that those engaged in agriculture may themselves enjoy a good dietary.

The Committee has made recommendations to Governments on the above lines and have also invited the Assembly to recommend to Governments concerned to give their full support to the Health Organization in its enquiries into the widespread malnutrition which exists in the Tropics and certain Far Eastern countries. We trust the Indian Government will accede to this request.

Vol. II. "Report on the Physiological Bases of Nutrition" contains a report drawn up by the Technical Commission of the Heatlh Committee.

Vol. III. "Nutrition in Various Countries" gives the substance of the actual data received by the Committee, including the essential portion of the information contained in the replies of certain Governments to the Secretary General's circular letter of Nov. 30, 1935.

Vol. IV. "Statistics of Food Production, Consumption and Prices" is a document prepared by the International Institute of Agriculture and contains valuable material assembled by that Institute at the request of the Mixed Committee, reviewing the available statistics of food production, consumption and prices.

We have dwelt at some length in reviewing these Volumes, because they contain precious materials collected at great pains, with the stamp of authority impressed on them and also because conditions in India are not dis-similar to those obtaining in Western Countries and a careful study of these Volumes will amply repay perusal. No praise, we think, is too high and no reward is too great for the services which the League of Nations has rendered and is still rendering to humanity at large, in endeavouring to make life worth living in this world of sickness and sorrow, poverty and misery.

———.

GLEANINGS FROM MEDICAL PRESS

Surgery

Treatment of Angioma of the Face. Frederic A. Figi.—Arch. Otolaryng. 24:271 (Sept.) 1936. The most effective agents and procedures for the treatment of hemangioma of the face are, in the order of their usefulness, radium, electrocoagulation, excision and injection of sclerosing substances. Ligation of the afferent vessels and various plastic procedures are frequently used to supplement these measures. Other procedures have a much more limited field of usefulness. While the results obtainable with these forms of treatment vary greatly, choice of therapy is usually determined largely by the experience of the clinician with any one or group of them.

Although adults not infrequently have this type of tumor, the great majority of patients with angioma are children. Both hemangioma and lymphangioma occur about the face, but the former is more common and accordingly is of greater clinical importance. Hemangioma is most commonly classified as (1) capillary or (2) cavernous. Fraser's classification includes a third type, which he designated compact hemangiomas. Cases in which a capillary or a cavernous hemangioma spontaneously disappeared have been reported in the literature. At present radium is generally considered the most effective agent for dealing with hemangioma, especially of the face. Prior to the introduction of radium in the treatment of this type of vascular growth, surgical excision was the therapeutic method of choice, and it is still so considered by a number of able general and plastic surgeons. It appears that the results of irradiation observed by surgeons favoring the excision of angioma must have been unusually bad, and one cannot help wondering if the treatment was given by an experienced radiologist. Radium may be administered in several forms: (1) in a surface pack, using distance and screening, (2) in a plaque or in tubes applied directly to the surface of the lesion, and (3) in needles or as radon seeds implanted into the tumor. At the Mayo Clinic, patients in early childhood who have a cavernous angioma on the face measuring several centimeters or more in diameter usually receive treatment with radium packs. When a radium plaque is used it contains from 5 to 25 mg. of radium element. The plaque is most effective in the treatment of capillary angioma. Electrocoagulation has greatly improved the results of treating cavernous angioma in adults. Frequently it is of

decided advantage to precede electrocoagulation by ligation of the afferent and efferent vessels supplying the tumor. While surgical excision has been supplanted to a great extent by radium therapy and electrocoagulation in the treatment of angioma of the face, in certain cases hemangioma can be dealt with more satisfactorily by means of surgical excision. Epithelioma has frequently been observed which has developed in the dense scar left by the treatment with radium of a capillary angioma or of a mixed capillary and cavernous angioma. The injection of a sclerosing substance in the treatment of angioma is generally considered a comparatively recent development. It is said to be more effective in dealing with cavernous angioma, but it has also been used in the treatment of capillary angioma. One of the outstanding advantages cited for injection treatment is the fact that the patient is ambulatory. In the course of time this method will probably supplant some of the older methods of therapy.—*The Eye, Ear, Nose and Throat Monthly.*

Periarthritis of the Humerus.—H. Buch *Hospitalstidende*, August 11th, 1936, p. 815) gives an account of sixty-eight cases of periarthritis of the humerus treated in a Danish Red Cross Hospital in the period 1932-5. The average duration of the disease was fourteen months, and thirty-nine of the patients had already been treated elsewhere. Their ages ranged from 23 to 73 years. and about two thirds of them were between the ages of 46 and 60. Women at the climacteric seemed to be particularly prone to this disease, and as many as forty of the sixty-eight were women. Only in two cases could a disordered metabolism (diabetes and hyperthyroidism) possibly account for the disease, which in seventeen cases was traced to trauma, in twenty-four to "rheumatism", and in eight to immobilization, prolonged sojourn in bed, etc. In as many as seventeen cases the cause of the periarthritis was unknown. The clinical picture was dominated by pain and a defective range of movement, and in forty cases the tenderness on palpation about the joint did not extend to the axilla. The muscles were often atrophied, the deltoid alone in most cases. Only in four cases was there no limitation of movement. Abduction and rotation were the movements most involved, and in nineteen cases crepitation, fine or coarse, was demonstrable over the upper part of the head of the humerus. The skiagrams taken of forty-three patients showed perfectly normal conditions in as many as thirty-nine. Calcium atrophy of the head of the humerus was observed in two cases, what was probably

a haematoma in one case, and an osteophyte-like prominence in one case. The rate of sedimentation, taken in sixty cases, was normal in forty-four, raised in sixteen. The Wassermann reaction, tested in forty-eight cases, was invariably negative. Twelve patients were treated by "brisement force" under ethyl chloride and local novocain-adrenaline anaesthesia. In eleven of these cases the patients were much better on discharge, whereas the twelfth was discharged unimproved. The treatment the other patients received included diathermy, massage, etc.—*B. M. J.*

Non-specific Urethritis.—N. D. Shaw and W. M. Brunet (*New England Journ. Med.*, September 24th, 1936, p. 572) point out that non-specific or primary inflammation of the urethra is not uncommon, as urethritis is found in 5 to 10 per cent of male patients suffering from urological diseases. The genito-urinary history is a valuable aid to diagnosis and treatment and should include details of the present illness, past history, and sexual history. When gonorrhoea is excluded but discharge is present the prostate should first be examined and prostatic fluid obtained by massage. This must be examined for the amount of pus, clumping of white blood cells, number of red blood cells, amount of lecithin, and sperms. Prostatitis may be accompanied by vesiculitis, and many cases of recovery after stripping the vesicles are seen. Hot rectal douches and sexual rest are useful adjuncts in the treatment of vesiculitis. Discharge may be caused by stricture, small meatus, or some pathological condition of the bladder neck. If a discharging urethra with stricture is present this should be treated if there is a considerable relative disproportion between the size of the stricture and the calibre of the urethra. A small meatus is similar to stricture and must be treated if it will not take a No. 20 sound; if the urethra is much larger than the meatus a meatotomy may be imperative. The posterior meatus of the fossa navicularis must often be cut. Examination of the urine by the two-glass test for purposes of diagnosis is valuable. Changes in the appearance of the first urine are usually due to washings from the urethra, while abnormalities in the second glass are due to pathological conditions above the level of the prostate. Chronic posterior urethritis show little in the second urine; generally a dirty first urine with a clear second points to anterior urethritis only. If the second urine is not clear higher urinary tract study is indicated.—*B. M. J.*

Virus of Lymphogranuloma Inguinale.—The discovery by Hellerstroin and Wassen in 1930 that lymphogranuloma inguinale

is due to a filtrable virus has been followed by a large output of papers on the continent of Europe, in America, and in this country. As a result it has been demonstrated that the disease long known in the tropics as climatic bubo is identical with the lymphogranuloma inguinale of more temperate climes, while the main features of the infection have been clearly defined. The worldwide distribution of the disease is further emphasised by the series of eight reports recently published by Prof. Y. Miyagawa and his colleagues of the Government Institute for Infectious Diseases in Tokyo. So far as the pathological changes and the list of susceptible animals are concerned the results of the Japanese workers are mainly confirmatory of those obtained elsewhere. They found, however, that in addition to monkeys, mice, and guinea-pigs an Asiatic squirrel, *Eutamias asiaticus orientalis*, was highly susceptible to the virus by intracerebral, intratesticular, and intradermal inoculation. The possible aetiological significance of small granular corpuscles, readily stained by Giemsa's method, was especially emphasised, while the size of the virus was estimated by differential filtration to be between 0.125μ and 0.175μ a result also obtained by Broom and Findly. While the virus was successfully cultivated on the chorio-allantoic membrane of the chick embryo, and in actual tissue cultures of testicle, brain, and spleen of normal adult mice, difficulties were encountered in growing the virus by the Maitland technique. Actively growing cells appeared to be essential for the propagation of the virus. These growing cells also contained minute granules. Though absolutely conclusive experiments are lacking there is thus a strong probability that these granules represent the actual virus particles. —*Lancet.*

Extragenital Lesions of Lymphogranuloma Inguinale.—Vernon C. David and Mark Loring, Chicago (*Journal A. M. A.*, May 30, 1936), report four cases of inguinal lymphogranuloma (one of the mouth in a man and three of the rectum in women). They believe that the cases, strongly indicate that the ulcerating lesions of the disease take their origin by contact infection and that the lymphatics are secondarily involved, as they are in any other infection. This is in keeping with their feeling that the rectal lesions of the disease are contact infections occurring in women with vaginal infection, which because of uncleanliness directly contaminates the rectum, and occurring in perverted men practising sodomy. The importance of contact infection in inguinal lymphogranuloma has not been sufficiently emphasized. Rectal strictures

from inguinal lymphogranuloma develop without inguinal gland suppuration in most instances. Inguinal lymphogranuloma may cause serious ulcerating lesions in the colon or in the mouth, and it is suggested that the Frei test be more frequently used in granulomatous lesions of unknown origin. The relation of inguinal lymphogranuloma to meningo-encephalitis of unknown origin should also be suspected. Colostomy offers the best method of treatment of marked rectal stricture from inguinal lymphogranuloma; inactivity but never cure of the lesion results. Treatment of inguinal lymphogranuloma has not been satisfactorily developed, but the use of 1 per cent antimony and potassium tartrate or fuadin intramuscularly offers some prospect of amelioration of the disease.—*Northwest Medicine.*

Medicine and Therapeutics

Some Historic Personages as Endocrine types.—A long article on "Some Endocrine Types," by "J. B. M.," which appears in "St. George's Hospital Gazette," closes with the following interesting study of some historical persons:

The pituitary types have provided history with the most striking individuals. Caesar, judging from the appearance of his face and his life serves as a very good example. He was small, pale, emaciated, and subject to severe headaches and epileptic attacks, possibly of pituitary origin. Sexually, he was precocious and extremely active. He was engaged to be married at 17 and was divorced three times, after which he devoted himself to liaisons, one with Cleopatra. So great was his sexual prowess that his soldiers used to sing celebrations of his exploits. This active sexuality seems to be a characteristic of the hyperpituitary individual and is displayed by the other great pituitary types, Napoleon and Casanova. Caesar was a soldier, statesman, politician, jurist, and historian of the highest order. His short career included more than 300 personal triumphs. So acute was his mind that he was able to dictate to three secretaries at once.

Napoleon was so closely watched before and after his death that authentic information about him can be obtained. He was 5 ft. 6 in. in height. This, together with his sharply outlined features, powerful lower jaw, small plump hands, long straight black hair and dark complexion, all point to the pituitary with secondary suprarenal effect. His sexual libido was explosive, his impulses arising suddenly, sometimes inconveniently, and subsiding

equally rapidly if not immediately satisfied, or if his attention were suddenly taken. This explosive periodicity of sexual life, as well as constitutional difficulties with micturition, from which he suffered, have been definitely connected with the pituitary. His intellect, capability, prodigious memory and capability of prolonged strain are pituitary characteristics. His pugnacity, brutality, and genius for practical affairs indicate an active suprarenal. When his pituitary began to fail him he descended physically and mentally. He became fat, especially in the hips and thighs, and his invasion of Russia was evidence of his failing judgment. At post mortem his body showed feminization in its deposit of fat, scanty, silky hair, and atrophic genital system. The rise and fall of Napolean coincided with the rise and fall of his pituitary.

A recent biographer has described Casanova as a man of "Heculean build, very tall, unusually strong and capable of athletic feats as well as of gargantaun meals. He had a high forehead, and a long aggressive nose, edged with an inquisitive nostril." The description continues that it was in the whole man rather than in the face that the power lay: he seemed to radiate energy, to be imbued with magnetic attraction. These are characteristics of the hyperpituitary. His amorous adventures have become proverbial, his initiative made his mode of life successful, and his acrid tongue caused his imprisonment. At 38 he begins to fail, and soon became decrepit, toothless and weak at the knees, coincident with the failure of his pituitary.

Lytton Strachey gives us a typical pituitary history of Florence Nightingale in his "Eminent Victorians." Instead of the popular picture of her as the "Saint with the Lamp," we find her as an extremely aggressive woman, working Sydney Herbert to death, bullying Lord Panmure, or the Bison as she called him, and beating him and almost succeeding in revolutionizing the War Office. The capability of prolonged effort of the pituitary-centred is very well demonstrated by the energy she displayed at Scutari and again on her return home, so that in spite of being in bed with a weak heart she revolutionized the whole hospital and nursing system. As she gets older, however, we find that her pituitary begins to fail, and she becomes the fat old lady, placid and smiling, so different from the demon woman who frightened generals and statesmen.

As an example of the suprarenal type we may take that highly successful American gangster, Al Capone. The round head, dark hair, low hairline, dark complexion, and animal lower features and short, thick-set figure stamp him. His extreme

brutality and capacity for organization are also characteristics of very active suprarenals.

We have said that disease of the suprarenals may produce true or pseudo-hermaphroditism. It would seem likely that Joan of Arc was really a pseudo-hermaphrodite, since she was masculine in her nature and never menstruated. The fact that she was a remarkably good soldier and general indicates that her suprarenal activity persisted after birth.

Oscar Wilde, the archpriest of homosexuality, was thymocentric. In his fullest development he exhibited all the earmarks of the thymus pattern. He was tall and fat, with a high complexion and an almost beardless face. When his voice was under control, it was a beautiful tenor, but when angry or emotional, as during his trial, it was harsh and strident, the result of an ill-developed larynx. Pituitary compensation accounted for his high intellectual ability. In addition to the above conditions, Oscar Wilde was unfortunate in his upbringing. His mother was presumably unconsciously homosexual, and in order to compensate for her disappointment at the arrival of a son and not a daughter, she brought up Oscar as a girl, dressing him in girl's clothes and decorating him with massive jewellery at an age at which normally he should have been a violent destroyer of clothing. This upbringing plus the endocrine constitution produced Oscar Wilde.

In writing this paper I must, among others, pay tribute to Berman, whose attractive theories have been so helpfuld in the correlation between psyche and soma.—*The General Practitioner.*

Acute nephritis.—H. Best (*Zentralbl. f. innere Med.*, September 19th, 1936, p. 777, and September 26th p. 810) describes ninety-eight cases of acute diffuse glomerulonephritis treated by Volhard's methods at Volhard's clinic; cure was attained in all but two, of which one was possibly a chronic case and in the other the ensuing hypertonia, detected at the age of 50, was possibly primary. The treatment consists in a three to six days' "hunger and thirst" diet (the purpose of which is to diminish vascular tension) followed at two to six days' intervals by "water shocks." In one of these a litre of tea is given, possibly supplemented by 0.25 gram of theocin and preceded by diathermy of the kidneys. The blood pressure falls gradually—in most cases to a considerable extent during the starvation period, and later to normal or (more often) below normal: the diminution of albuminuria and oedema and the establishment of diuresis are roughly parallel with the course of fall in blood pressure, and morbid

changes in the fundus oculi (present in 18 per cent.) are only to be detected in the initial hypertonic stage. The classification of these cases as acute rather than subacute or chronic was founded on the history and clinical examination; nearly all followed infective illnesses, of which the great majority were tonsillitis or scarlet fever. The cure was proved in fifteen cases by absence of any morbid findings at discharge from hospital; of the remaining eighty-three, who left hospital with slight albuminuria and blood pressure which was not always normal or low, eighty were subsequently traced and examined. Volhard and Best maintain that the treatment described is always effective when given to the patient within six weeks after the pre-infecting tonsillitis, scarlatina, etc. The nephritis becomes cured if reduction of the blood pressure is attained within six weeks, otherwise a vicious circle is set up (the functional glomerular angiospastic ischæmia inducing a general vascular hypertension which becomes chronic if interference with renal blood supply persists) and chronic nephritis follows. After the blood pressure has fallen and diuresis has set in the dietary should be for some time poor in salt, protein, and fluid, and diathermic applications to the kidney once or twice daily are useful. Tonsillectomy plays an important part in treatment of a case which does not quickly respond to Volhard's therapy.—*B. M. J.*

Obstetrics and Gynaecology

Anaemia in Pregnancy.—P. L. ADAIR, W. J. DIECKMANN, and K. GRANT (*Amer. Journ. Obstet. and Gynecol*, October, 1936, p. 560) discuss anæmia in pregnancy. After summarizing previous studies, which result in considerably differing figures with regard to (1) physiological anæmia, they refer to (2) a type of microcytic anæmia as the commonest type of anæmia of pregnancy associated with hypochlorhydria and supervening on pre-pregnancy anæmia; also to (3) a rare macrocytic type, not unlike pernicious anæmia, not responding to liver treatment, and sometimes apparently toxæmic; and (4) a type often reported from India, not limited to pregnancy, traceable to deficiency in diet and curable in non-pregnant cases by yeast, but calling for therapeutic abortion before the third month because of its maternal mortality of 40 per cent. They then report investigation of hæmoglobin content, cell volume, and erythrocytes in 7,835 pregnant women, as compared with about 2,300 non-pregnant patients. Their figures indicate that in pregnancy the hæmoglobin concentration averages 11.56 grams

per 100 c.cm. of blood and the red cell count is 3,770,000, with a cell volume of 37.31 per cent.; compared with average for non-pregnant women 63.2 per cent have to be classed as anæmic, but a true physiological anæmia does occur. The minimum allowable is hæmoglobin 10.16, red blood cells 3,360,000, cell volume 33.11. Fluctuations in hæmoglobin during pregnancy are normal, rapid, and irregular, so that the effect of specific medication is difficult to estimate. The writers believe that even when the mother has an anæmia the hæmoglobin concentration in blood from the cord may be normal, but they have often found it subnormal. Blood transfusion proved highly efficacious, but prevention of anæmia by adequate diet and hygiene is much more effective than attempts to cure it by even large doses of iron.—*B. M. J.*

PROCEEDINGS OF CONFERENCES ASSOCIATIONS, SOCIETIES, ETC.

The XIII All India Medical Conference, 1936 Karachi.

WELCOME ADDRESS

The following are extracts from the Welcome Address delivered by Dr. A. Said, I.M.D. (Retd), Chairman of the Reception Committee :—

Teaching in Medical Institutions.—"The teaching in medical schools and colleges, as it is done for nearly two generations, has brought out certain defects which ought to be strictly avoided by those entrusted with medical education in future. A successful physician and surgeon is not necessarily a very good teacher. There should therefore be a teaching corps created for our medical institutions. Vested interests should not monopolise the key-posts and service interests should not dominate the teaching profession. It is an unfortunate experience that several of these professors have no heart for the teaching line and have not even the time to teach, as they have an eye on their private practice. At times some of these lack uptodate information of their subjects. Medicine and Surgery and allied arts are so rapidly developing that all teaching must be uptodate. Defects of medical education could only be removed if a medical corps is constituted which should consist of paid and honorary members. I doubt very much whether in this country we are making proper use of our research scholars for imparting the valuable knowledge that they have themselves garnered. I am afraid their talent is running waste for want of adequate encouragement. There is an old saying "steepers, scholars and women cannot grow without support". Research scholarship must find its way into medical colleges by proper support.

Uniform Education.—With regard to medical teaching, it should be of a uniform nature, without higher or lower grade, each student being allowed, after the course of general training, to take up the line he would like to pursue. By this method we would ensure a thorough grounding in medical knowledge with some sort of specialisation as a goal. Let every medical practitioner have the pleasure of writing the mystic letters M. D. after his name. By curtailing pre-medical education by one year, it can with great advantage be utilised for post-graduate hospital training. There is a widespread fear that, as the domain of medical knowledge is extending, and as the standard of teaching is raised, students get little time to gain practical knowledge; and the consequence is that they are more scientific and less practical. We must guard against the danger of modern medical science becoming more a scientific theory than a bedside art."

Careers for Medical Graduates.—"Let us bear in mind that India is a country of countless millions and the number of scientifically trained medical men is but a handful when the medical needs of three hundred and fifty millions of people are taken into consideration. Millions of men, women and children die in this country every year of preventable diseases only because skilful treatment does not and cannot reach them. The average expectation of life in our country is only 25 years whereas in England it is 47 years. Government by its own costly agencies can never hope directly to tackle this tremendous problem of human disease and suffering in this vast country, and ministers running government under provincial autonomy will be faced with this—the fundamental problem of all problems.

Private agencies must perforce be employed to deal with questions of rural health and sanitation and therein lies the opportunity of the private practitioner. Within the next few years communications by roads will develop rapidly on account of the road fund and medical practitioners, who are crowding into the cities and towns, can move into large villages wherefrom they can minister unto the needs of the village population provided they get a reasonable subsidy from the Government. A practitioner with a motor-cycle can cover a fairly large group of villages in a week. He can advise the villagefolks also in matters of sanitation and prevention of disease. And his close connection

with the village people will bring him added private practice. Here is a vast field for exploitation by enterprising medical practitioners of this province and country."

The Panel System.—"In the localities where the municipal dispensaries and maternity homes are abolished, the system of panel doctors may be tried, which can also be introduced all over the city in the course of time. I need not go into the question of the working of the panel system as it is well known to you, and as it was the subject of thorough investigation by our local municipality, and there is, I am sure, a large amount of support for the same. Of course, there are differences of opinion as to the practicability or utility of the scheme under Indian conditions but further thought and attention devoted to the subject at a conference with municipal and governmental authorities on one side and local private practitioners on the other side will still find a solution of the difficulties; and the Karachi Municipality will enjoy the honour of being the first in India for having adopted an economical and efficient system of medical relief."

Sick Attendance.—" It is not possible for people in poor circumstances to be attended by Nurses who charge fees which they are unable to pay. And without proper nursing in a case such as Pneumonia, Typhoid, Cholera etc. the chances of recovery are very remote. It is also impossible for all such patients to be removed to public hospitals where very often there is scarcely any room for them. Even the best skilled treatment is at times very ineffective when it is not attended by proper nursing. It is within our experience that many patients have died simply because the doctor's instructions were not carried out for want of proper nursing; and the people at home are in most cases completely ignorant as to how to nurse a patient. On the contrary they spoil many cases at home by disregarding the doctor's instructions.

I, therefore, suggest that there should be opened simple sick attendant classes, for men and women, who know how to read and write, and who can carry out the doctor's instructions. It will take about six months to give them a course of general training and they will be available for poorer families on the payment of a rupee or two during day and a little more during night. Hundreds of lives can be saved in poorer families in our towns and cities by employing such men and women nurses. The latter can be trained in the general hospitals."

The Menace of Quackery.—One of the greatest dangers besetting the system of scientific allopathic treatment in this

blue. In fresh blood the parasite will be seen actively moving. Cases from endemic areas with one or more of the following signs and symptoms should be always examined for filaria *viz.*, anaemia, periodic fever, haematuria, varices, enlarged glands, varicocele, hydrocele, funiculitis, lymphangitis, phlebitis, urticaria, eczema and erysipelas.

Preventive Treatment is every thing in this as there is no cure according to the highest authorities. The following measures are recommended:—education of the public and the creation of 'a mosquito conscience,' segregation under nets or in mosquito-proof quarters all m.f. carriers during the hours of infectivity, destruction of breeding places of filarial mosquitoes and their larvae. In Ceylon, Mansonian mosquito requires a waterplant called "Pistia Stratiotes" known to the villagers as "*Dyaparandel*" or "*Kondaipaasi*" for its propagation. Eggs are laid on the under-surface of its leaves, and the larvae and pupae live with their respiratory syphons or "trumpets" attached to the hairy roots of the plants through which they breathe, remaining under water. Hence surface oiling in order to destroy them is useless. Therefore "Pistia" must be proscribed in all anti-mosquito ordinances.

Treatment is generallay either surgical or palliative which need not be described here. Among drugs antimony and arsenic preparations are useful, and are believed to inhibit the parasite and improve the patient's general health. A case of chyluria treated with success with salvarsan is reported in the Medical Record (11, March, 1911) by Pilcher. Result of treatment will chiefly depend on whether the worm is alive or not and the infection is toxic or septic.

In my practice of over 25 years I have been freely but, of course carefully, using salvarsan in the treatment of various diseases like malaria, filaria, dracontiasis (guinea-worm infection) and rat-bite fever from 1912. I therefore give below short reports of a few cases treated successfully with salvarsan and neo-salvarsan.

Case 1.—In 1912 I was called one night to see a Sinhalese young man aged 25, suffering from haematuria, sudden and profuse. I called, in consultation, the senior surgeon of the General Hospital, who diagnosed the case as one of vesical papilloma. Next morning the urine under the microscope contained m.f. I gave at once salvarsan .6 gm. intravenously with the result that the urine was clear by evening and both the urine and the blood were free from m.f. when examined on the following day. For over three years afterwards, he was apparently all right. But in 1915 he was suffering from what appeared to be giant urticaria,

The Journal of the Indian Medical Association.—"Closely associated with the cause of the Association is the matter of the mouth-piece of our Association, namely its Journal. We are all glad to see the improvement it has made in the last few years both scientifically and financially yet it has to be so improved in both these directions with the co-operation of members that it may compare favourably with similar organs of similar Bodies in foreign countries, such as the British Medical Journal. Remember that the other countries will judge us by the standard of our official organ. Instead of fritterring away our energies in the production and up-keep of various little journals of indifferent merit, we might concentrate on improving our Journal to such an extent that it may prove worthy of the country and the Association."

Indian Medical Service.—"It is difficult to speak with restraint on this un-called-for infliction of a Military service on a civil population. With a large number of Indian medical men with the highest qualifications available for any appointment, the best appointment in the Provinces are reserved for officers of this Service with, in a good number of cases, very ordinary qualifications. The racial distinction has been carried so far that the Indian members of their own service have been relegated to smaller and unimportant stations in the Province. With the medical administration perpetually in their own hands, no wonder, their own interests every time come first.

The position of Indian entrants to the service has been brought down to a level that it is only due to the increase in unemployment, that they are able to find candidates for the service. The better qualified Indian neither desires nor is encouraged to enter the I. M. S. The Indian entrants will in future have the Viceroy's Commission. Their pay has been proposed to be reduced, and they are distinctly told that they will have no prospects on the civil side. I do not think that I have drawn an overcoloured picture. The New Reforms may or may not bring autonomy to India, but it has certainly rendered the future prospect of the Indian Medical profession gloomy. It has tightened the grip of the Indian Medical Service on the Medical administration of the Provinces, particularly of the European element thereof for a long time to come. We should bring to bear all the resources at our command, in the presently to be established Autonomous Government. We should try to convince the public, the Legislatures and the Government, that though we have no ill-will against our European colleagues, yet we as a people do not desire anybody but Doctors of our own race, to treat us just as Europeans

themselves like to be treated by no body except by doctors of their own race. Protesting and passing of resolutions have only resulted in tightening of their grip."

Provincial Services.—"Provincial services have been the back-bone of urban medical relief, just as much as the Subordinate Provincial Services have been the back-bone of the medical relief of rural areas. Inspite of all the disadvantages in which these services have been placed, they have rendered splendid service in all the provinces; yet we must recognise that times are rapidly changing and we should have, as a profession, a larger outlook and consider the welfare of not this or that service, but the future of the profession as a whole. We must admit even these services have outlived their use in their present forms. Yet Government must have a service to look after their medical obligations. If therefore a Civil Medical Service on provincial basis is constituted, to replace the present Provincial Services, and recruited by open competition from the profession in general, it should supply the need of the Government. It would have a limited cadre, each District having one District officer who would be the medical superintendent of the principal district hospital, an inspecting officer for the rural dispensaries and the principal medico-legal officer of the district. In large hospitals he would have a resident medical officer from amongst the freshly qualified young medical men from colleges and schools, as the case may be, on a temporary basis for a year or two. The main indoor and outdoor work should be distributed among the private medical practitioners with requisite qualifications on an honorary basis. Some similar arrangements would obtain in outlying rural dispensaries. Future administrative officers could be selected from amongst the most competent members of the new Provincial Medical Service. Of course, I am envisaging that the Indian Medical Service will gradually be eliminated. The proposed scheme will result in greater efficiency as each branch of medicine namely, medicine, surgery, ophthalmology, and, if necessary, gynaecology will be in charge of specially qualified men. There is no dearth of such specially qualified men amongst private practitioners. A scheme of the nature suggested would cost much less than the present medical administration, and spare sufficient money for equipment of hospitals and dispensaries".

The Public Health Services.—"I hope that our new Legislatures would devote more time to medical relief and public health. The Public Health Services are starved for want of funds and

their personnel is very inadequate. The public has paid very little attention to public health and its problems.

If we are to live amongst comity of nations on equal terms we must raise our public health standard upto that of modern civilised countries. This would need a considerable expansion of Public Health Services and sufficient funds to carry through schemes of improvement of public health. We as members of the medical profession should do all we can to focus public opinion on these matters and endeavour to bring public health questions to be given that importance which they deserve."

Unemployment.—"Closely connected with the matter of medical services is the question of unemployment among the ranks of the medical profession. If we succeed in persuading the Government through pressure of public opinion, to adopt some of the measures suggested for the improvement of medical relief and public health, the question of unemployment to a certain extent will be automatically solved. If the work of the Government, municipal and district board hospitals and dispensaries is carried out through the honorary agency in place of highly salaried and therefore limited staff of district and other hospitals, it will absorb a large number of young medical men, living so far on a slender private practice. Having the advantage of a hospital to work in, they would get additional experience and better status, they would be in a position to develop the private practice better than they have been able to do so far. The same observations would apply more or less to the outlying dispensaries. The expansion of public health services and development of public health schemes would need a large number of products of our schools and colleges. But all these suggestions, if you agree with me that they are improvements on the existing state of things, depend on the understanding and good will of others outside the profession. The question therefore that we have seriously to consider is, whether we ourselves can do something in this direction. One thing is very clear. If all the medical men, qualifying, roughly about a thousand a year from colleges and perhaps double that number from schools, concentrate on practising in the large towns as more or less they are doing at present, the overcrowding and congestion in the profession which is already existing will intensify, leading to deterioration, further unemployment and misery. The present number of qualified medical men in scientific system of medicine is estimated to be 25,000 throughout India. When we compare this number to the total population even after taking into consideration the number of practitioners of various

other so-called systems, it is a mere drop in the ocean. What then is the reason for unemployment? The reason to my mind is apparent. The majority attempt to establish themselves in large cities producing congestion and consequent unemployment. The Services can only absorb a fraction of the men qualified each year. It follows that the majority of qualified men will have to depend upon private practice for their means of subsistence. The newly qualified young medical practitioner is disinclined to move away from the city and desires to follow in the footsteps of the doctors of the past generation. It is this tendency which has led to congestion and unemployment. They have to realise, whether they like it or not, that the future of the majority of coming generation of medical men lies not in the urban but in the rural areas. The vast number of Indian population with hardly any or no medical aid is waiting for them. We as a profession have so far always thought in the urban sense, the future members of the profession will have to develop a rural sense from sheer necessity if not from a patriotic point of view.

The plan suggested to help our young medical practitioners to settle down in the rural areas is somewhat as follows:—

That a general survey of the district be made, and those areas which have no outlying dispensaries be divided into units of a certain number of villages with a small town in the centre where the practitioner is persuaded to settle and subsidised by the authorities concerned to the extent of a house, minimum equipment and a small allowance and left to develop his practice in the surrounding areas. It would necessarily mean a simpler life and perhaps an entirely new outlook in life. But he will, I am sure, in course of time be able to make a decent living, if he continues to observe the honourable traditions of the profession. He would more or less occupy the same position as a country doctor does in the United Kingdom. I am fully aware that the young practitioner, accustomed to the traditions of the town practitioners of the present day, jibs at the idea of rural life. Whether he likes it or not, the future of the majority of the practitioners lies in the rural rather than in urban areas, if ever-increasing products of our colleges and schools have to be provided for.

Another direction in which there is a considerable scope of employment for young members of the profession is, the development of industries for the manufacture of simple chemicals needed for medical purposes. These industries are developing at a more rapid rate than is generally realised. Simple chemicals like Hydrogen Peroxide, Potassium Permanganate are now imported

in enormous quantity from foreign countries, which could with a little enterprise be manufactured in this country, and our young medical men with business tendencies can find considerable scope with great benefit to themselves and the country. There is yet another field for the younger generation of medical men—to help to utilise the products of research in indigenous drugs. Researches in this direction have found, and will continue to find a number of preparations derived from indigenous drugs which have been in use in the country for centuries. This will not only give employment to a large number of young medical men with a tendency in that direction, but will cheapen the cost of treatment which is at present prohibitive for the poorer classes. These when ready in suitable number will form the basis of Indian Pharmacopœia. Col. Chopra's pioneer work in this direction has given great impetus for the future development of this important work. When we talk of unemployment in the profession we mean that a number of our younger generation of medical practitioners are sitting with folded hands in large towns, waiting for practice to come to them. This I am afraid is due to the utter lack of enterprise. Unless enterprise and determination are forthcoming, they will have to continue to wait without success for practice which is unlikely to come to them.

While there is so much talk about unemployment, ever-increasing numbers are seeking admission to the medical colleges and schools, so much so all the colleges and schools have put a limit to the number of admissions and competition for seeking admission is increasing. I wish the system of admission to the medical colleges by open pre-medical competition, which obtains in the Lucknow University will find favour with other medical educational institutions in India. Through such a competitive examination, you not only get the best material available but save a lot of favouritism and heartburning."

Medical Education.—" The advent of the Medical Council of India and the inspection of the colleges, have revealed the fact that the different universities had more or less different standards, which have now through strict inspections been brought more or less to uniformity. Some of them are lacking in equipment and personnel which when brought to the notice of the government and authorities were quickly attended to. So far as I know the medical schools have not only varying standards, but lack in sufficient equipment and efficient teaching personnel. They need considerable improvement both as regards equipment and teaching staff. Each Provincial Government treats these medical

institutions according to their sweet will. The desire of the All-India Licentiates' Association to bring all the medical schools, within the purview of the Medical Council of India is legitimate and justifiable. There is no other way of bringing uniformity of standard. But as these schools are under governing bodies called the State Medical Faculties in each province, outside interference is likely to be resented. I could suggest a number of ways to improve these institutions. But I do not want them mended but I want to see them ended. I want to bring all the schools and where there are too many to be combined in one and raise them to the standard laid down by the All India Medical Council as the minimum standard for recognition. I hope you will agree with me that there should be one standard for all the medical education in India. The system of turning out medical men with a lower standard of medical education is pernicious and obsolete.

I suggest that we tell the Government that the profession in India no longer wants a different standard of medical education in this country, and that the various schools be either brought up to the standard recognisable by the Indian Medical Council or abolished. I believe that strong and influential body of the All India Licentiates' Association agrees with us in this view. The education imparted in our medical colleges is second to none in any country. Among other things, it is shown by the fact, that our students are able to acquire the highest post-graduate qualifications of the United Kingdom and other countries without the least difficulty. They can hold their own in any open competitive examination. This is perhaps one of the reasons that the open competitive examination for the Indian Medical Services has been abolished ".

Medical Research.—"If sufficient number of medical graduates do not engage in research, it is not want of capacity but lack of facilities.

The Indian Research Fund Association inspite of inclusion of three representatives from the Indian Universities is still predominently controlled by the heirarchy of the Indian Medical Services. Indian Medical men with a flare for research do not get the encouragement which they deserve. Our graduates flock to Europe in large numbers to get post-graduate qualification at great expense and trouble. I believe time has arrived for the expansion of advanced post-graduate training in various branches of medicine in our own universities. We might formulate a scheme for such a training, and submit it for consideration

by the various universities. I have one strong grievance against the recruitment of teaching staff for our medical colleges. Some important clinical teaching appointments in majority of the universities, are still reserved for the members of the Indian Medical Services. With a large number of highly qualified Indian Medical men to draw upon, such a reservation has no longer any justification. Our protest against this unjust and un-called-for reservation should be strong and emphatic".

Indian Medical Council.—"For maintaining the uniformity of standards in medical education in our universities, a central agency with sufficient authority to enforce it is essential. This now exists in the shape of Medical Council of India. The tremendous agitation which preceded its establishment is now more or less at rest. The Indian Medical Act is by no means perfect and needs to be considerably amended before it will satisfy the Indian medical profession. Unless it satisfies the aspirations of our licentiate colleagues, it will continue to give cause for dissatisfaction. How this can be brought about, I have already suggested. The unity of action and solidarity of view and patience, shown by the medical profession against the high-handedness of the General Medical Council six years ago, have triumphed at last. They have given recognition to our universities with retrospective effect. Most of us feel satisfied with the restoration of friendly relations on an equal basis with that body. Control of ethical standards and disciplinary powers are vested in our provincial medical councils. These are functioning more or less satisfactorily. The Provincial Medical Council Acts need considerable modification, before they can be called satisfactory. The U. P. Medical Council have lately submitted a proposal to government for modification of the act. I suggest that the different provincial Medical Councils may take similar action, if not already taken."

Need for a Spurious Drugs Act.—"I have referred above to the necessity of research in indigenous drugs with a view to find out as many drugs as possible of equal potency as that of British pharmacopoeia with a view to establish an Indian pharmacopoeia, suggested by Chopra Committee. While we are attempting to bring this about, the country is flooded with drugs and preparations of doubtful and even harmful properties. A large number of agencies of foreign countries like England, America, Germany France and Italy have been established throughout India. They flood the practitioner with volumes of high sounding but worthless literature. Their agents tour the country distributing free samples and beguiling the practitioners in persuasive language to use their very doubtful wares. The practitioner is led to confuse genuine products with spurious preparations and drugs, and thus acquires a tendency of empirical ways of treatment. No law exists to prevent the flooding of the country with spurious and dangerous preparations. Such a thing would not be tolerated in any other country. We must influence the public opinion against allowing this country to be made a dumping ground for useless and harmful products from all over the world. Immediate legislation prohibiting the importation of doubtful and harmful products is called for. A clearly worded resolution expressing our views on the subject should be framed and sent to the Government of India and various provincial governments".

Medical Men and Insurance Companies.—"You are doubtless aware that a large number of Insurance companies are daily springing up all over India. I am not competent to give an opinion on the economic soundness of this development but, safeguarded with proper and well considered legislation, I believe, it is a development in the right direction. I am only concerned with the position of the Medical profession *vis-a-vis* the development of Insurance business. Examination for Insurance is a great responsibility on the medical man. He has to be adequately remunerated for undertaking this responsibility. The young practitioner with scanty practice is persuaded to do this work without adequate remuneration. This must be prevented. If the profession is united, the companies must conform to a uniform standard in this matter. I suggest that we should appoint a sub-committee of men of experience in this line to formulate proposals and advise the members of the profession to confine to them".

Indigenous Systems of Medicine.—"This brings me to the mention of the ancient and indigenous systems of medicine which have been flourishing in the country for centuries. A man belonging to our profession has to treat the subject with caution in dealing with it as we are accused of prejudice when expressing any view in this respect. However, I have not the slightest hesitation in saying that I have the highest respect for the systems and their genuine followers. My reverence for the systems is more or less of the same nature as that for Indian archaeology. Both Ayurvedic and Unani systems and their ethical code are suited to the temperament, the spiritual leaning and simple life of the people of the country. But so are many other customs and traditions. Due to our contact with the material civilisation of the west, our customs and traditions are changing rapidly. How can then the

ancient systems which have no doubt done splendid services to humanity in the past can continue to exist as they are? Acute observation, and correct deduction, urbanity of manner, sympathy, touch of spirituality and freedom from greed, for which Vaids and Hakims were famous, are now things of the past. Still the system so suited to the popular temperament must exist. It can only do so if an attempt is made to bring it into modern shape. I suggest the continuance of the ancient system on a modern basis in the following form. The preliminary educational qualification *i.e*, Intermediate in Science with Organic Chemistry and Biology, should be made the minimum requisite for any and all systems which the candidate desires to adopt finally. He should also be made to undergo a training in what are known as basic subjects, Anatomy, Physiology, Hygiene, Pharmacology and Pathology. The final two years should be reserved for clinical training in whatever system he wishes to qualify. The whole period of training should be five years as with us. This rule should not apply to Ayurvedic and Unani systems only but also to those who wish to qualify in Homeopathy. Some such similar regulations obtain in the United States of America. Training on these lines to a certain extent already exists in the Ayurvedic Faculty of Benares Hindu University and Delhi and Lucknow Tibbya Colleges. But the training in the preliminary science and basic subjects is inadequate and perfunctory. Until some such plan is adopted, there is little likelihood of all recognised systems of medicine flourishing side by side with the scientific medicine and the poor and the rich alike are not likly to receive the best medical relief. We, as a profession have neglected to study the subject of Ayurvedic therapeutics. It may not be rational but is full of valuable suggestions. There is much in it which we can learn with profit. Therapeutic value of gold and copper used by them for centuries has now been scientifically recognised by us. I have already referred to the necessity of research in indigenous drugs which have been used for hundreds of years. Such research will not only be profitable to the profession and the country but is likely to enrich the medical science".

EXHIBITION COMMITTEE CHAIRMAN'S ADDRESS.

The following are extracts from the speech delivered by Dr. J. M. Talati, Chairman, Exhibition Committee, at the opening ceremony of the Medical Exhibition, held at Karachi in December 1936:—

"Of all the sciences, Medical Science is perhaps the most rapidly advancing, so much so often what is learnt during one's student days has soon to be unlearnt even during one's practising days. If a medical man does not keep himself in touch with the current advances in medicine, he often becomes as valueless as a quack. A medical Conference gives such an

opportunity to learn, unlearn and exchange views with the medical brethren of the different parts of India and thereby educate and keep oneself up-to-date in our professional ability".

"Thus while we educate ourselves through the scientific sections of the Conference, we must keep ourselves up-to-date in the science of Drugs as you may call it, and hence the importance we attach to the Exhibition and its invariable accompaniment with the Conference. No medical Conference can afford to neglect the consideration of this side of the science viz. the supply and import of drugs, the manufacture and sale of drugs in India, the method of controlling them, the need of an Indian Pharmacopoeia, the supply of properly trained Pharmacists and Compounders, the establishment of laboratories, Research centres etc. These are matters which vitally interest our profession because we would be helpless in the treatment of diseases unless provided with efficient pharmacists and reliable drugs".

"Besides this educative value, the medical Exhibition has its economic value, as it is of great importance from the point of view of showing, inducing and stimulating our local Indian industry. A greater proportion of ill-health renders the demand for drugs and instruments proportionally greater and the national poverty means that they should be cheap and easily available. Yet perhaps the one thing that is lacking most is the encouragement to the manufacturers of drugs, instruments and accessories. India abounds in natural products but to our misfortune it is the foreigners who are taking full advantage of the munificence and beneficence of nature in our land, while we, the children of the soil, are merely looking at this exploitation, waiting and wishing for a turn of fortune! India still depends on foreign countries for her supply of drugs It is calculated that about 2 crores worth of drugs alone (exclusive of chemicals and narcotics) are annually imported into India and out of these a great many are of doubtful value, and not an insignificant number, quite useless".

"It is only within the last few days that we have read that "in view of increasing gravity of the problem and the interest it has evoked from the representative commercial and medical organisations, as well as from the public, that a definite step towards standardisation of drugs in India with the possibilities of tightening the control over the manufacture of spurious drugs is being taken, in the establishment of a Biochemical Standardisation Laboratory to be located at the All India Institute of Hygiene and Public Health, Calcutta under the direction of Lt. Col. Chopra, Director of the School of Tropical Medicine, Calcutta. The function of this Laboratory will be the preparation and maintenance of suitable standards of strength, purity and quality for drugs and standardisation of the methods of analysis and test with regard to climatic and other conditions prevailing in different parts of India. The Laboratory will also act as expert referee in respect of

disputed analysis of samples sent by local Governments, guide, co-ordinate and co-relate the work of provincial laboratories, assay and test chemicals and drugs and biological products such as serum and vaccine and organometallic compounds at the request of the Central or Local Governments, periodically issue bulletins about its progress in various branches of its activities and supply information to manufacturers and Provincial laboratories as the need may be."

"While we thank the Government even to make such belated beginning, we cannot but help remarking that the Laboratory of the Central Government is not meant to be nor will it be sufficient if it is, for dealing with the vast amount of adulteration which exists both in the imported and locally prepared drugs all over India, and therefore we suggest that all the new provincial autonomous Governments will take their cue from the example and suggestion of the Central Government and establish at least one up-to-date, fully equipped and properly manned laboratory in their provinces".

"Besides establishing laboratories in each province, the Central Government must introduce an All-India Foods and Drugs Adulteration Act or a Pharmacy and Drugs Act. Although we have received the news of establishing the Central Laboratory, we have yet to wait to hear whether the Central Government has even thought of taking up this legislation and at the rate the Government tortoise moves, we may not hear about it for a number of years to come, unless some misfortune overtakes India and hurries them up. In the meantime, I suggest that all self-governing bodies, all bigger municipalities and District Local Boards etc., should get special regulations passed, or their own Acts so modified as to give them the control over at least frankly adulterated stuff in their own areas".

"The control of proprietary preparations is another factor which is of as great an importance as or rather of greater importance to India than any other country".

"If there is any country in the world which required the the control over proprietary and other preparations, more than anybody else, it is India, and yet, it is India which awaits any such legislation".

"India abounds in the necessary raw material, even though regular systematic farming of drug plants has not yet been undertaken. In fact the foreigners who are importing the ready made drugs are depending to a large extent on our raw materials.

There is no dearth of talent in our country. We find the machineries rolling out Masters of Science and Graduates of Medicines in hundreds every year, thrown out in this wide world to pick up their ways of livelihood as best as they could. Many of these may be highly talented but in the absence of any encouragement, they are simply lost to this country. Many of these may suitably find employment in and should take active part in developing medical industries. The establishment of these industries will further give employment to Indian labour, the comparative cheapness of which, is another advantage to the Indian industry".

The XIII All-India Medical Conference, 1936, Karachi.

Resolutions Passed at the Conference

1. This Conference places on record its deep sense of loss at the untimely demise of Dr. M. A. Ansari, Col. Bholanath, Sir Kedar Nath Das, Dr. N. N. Basu, Dr. K. M. Nandkarni, and conveys its heartfelt sympathy and condolence to the members of the bereaved families. *Proposed* from the chair. *Carried.*

2. While reiterating the previous resolutions of the Conference held in 1934, regarding the amendment of the Indian Medical Council Act, this Conference resolves that a Sub-committee be formed to consider the Indian Medical Council Act in all its aspects and draw up a draft bill to be submitted to the Central Council of Indian Medical Association.

The following shall form members of the Sub-committee —(1) Drs. Narayan Rao, U. B. (2) Rochiram A. Amesur, (3) A. D. Mukerjee, (4) Jivraj N. Mehta, (5) K. S. Ray, (convener), (5) B. N. Vyas, (7) Tarachand J. Lalvani, (8) B. C. Ray. *Proposed by* Dr. Narayan Rao, U. B., *Seconded by* Dr. Primlani, C. H. *Supported by* Major C. P. Bhat, Dr. H. J. Wania. *Carried.*

3. This Conference regrets the action of the Punjab Government in not withdrawing the ban on the Government Service men to join the Indian Medical Association, and requests the Punjab Branch to arrange a deputation to bring the facts to the notice of the Punjab Government. *Proposed by* Dr. S N. Kaul. *Seconded by* Dr. Parmanand Ahuja. *Carried.*

4. This Conference resolves that the Provincial Governments be requested to so amend the local Medical Acts as to give adequate representation to the Licentiates in the Provincial Medical Councils. *Proposed by* Dr. Balbir Singh. *Seconded by* Dr. Bhupal Singh. *Carried.*

5. This Conference is of opinion that there is an urgent and vital need of passing legislation in the shape of a *Pure Drug Act and Pharmacy Act* for British India, on the lines of that of United States of America for the purpose of controlling the sale of drugs, as well as laying down the qualifications of the dispensers of drugs. *Proposed* from the Chair. *Carried.*

6. (*a*) This Conference calls the attention of the Medical Profession, the Government and Municipalities to the urgent need of Research in the causes of malnutrition of the poor people of India, and for the standardisation of "Balanced Diets" in different provinces, in accordance with the local dietetic customs of the people and the foods available during different seasons of the year.

(*b*) This Conference desires to draw the attention of the Government and the leaders of India to the fact that deficiency anaemias and diseases, tuberculosis, rickets, dental caries, infectious diseases, etc. spring from malnutrition.

That the problem of prevention of diseases is partly a problem of the provision of sufficient and nutritious food for the people. *Proposed by* Dr. H. J. Wania, *Seconded by* Dr. Parmanand Ahuja. *Carried.*

7. Whereas Tuberculosis or White Plague is insidiously making rapid inroads into populous cities in India and is responsible for high mortality incidence as shown by the vital statistics of the prominent municipal bodies in the country,

And whereas the disease is more or less endemic among the poorer section of the community and particularly among the children of school-going age whose parents and guardians can ill-afford to supply them with adequate amount of nourishing food like milk, fruits and eggs,

And whereas these children grow up poor in vitality with low resisting power which makes them more susceptible to tuberculous infection at this tender age.

This Conference strongly urges upon various local bodies, District Local Boards, Educational Institutions, Government and Private, to carefully collect the statistics of the disease in their respective jurisdiction especially amongst children of school-going age and inaugurate schemes of free milk supply to deserving children of poor parentage in humbler quarters of the cities to provide them with adequate nutrition to fortify their constitution against the fell disease. The Conference confidently hopes that such schemes if earnestly pushed forward and assiduously carried out will succeed in their object of building up healthy generation of manhood and womanhood. *Proposed by* Dr. Parmanand Ahuja, *Seconded by* Dr. J. M. Talati. *Carried.*

8. Resolved that this Conference reiterates its former resolution of 1935 that in Clause 1 of Section 5 of the Lunacy Act (IV of 1912) the words "one of which certificates shall be from a Medical Officer" be deleted and replaced by the words "from two Registered Medical Practitioners". *Proposed by* Dr. B. N. Bose, *Seconded by* Dr. D. D. Pandya. *Carried.*

9. This Conference resolves that in view of the exhibition of obscene and indecent advertisement by means of newspapers, bills and posters regarding medicines which are a nuisance and detrimental to the health of the public particularly the young inexperienced girls and boys, the Central and Local Governments and the Local Bodies be requested to take strong action to stop it. *Proposed by* Dr. Balbir Singh, *Seconded by* Dr. Parmanand Ahuja. *Carried.*

10. Resolved that the Government be requested to make the scheme for periodic health examination of school children compulsory and steps be taken for the preparation of suitable scheme for the training of medical men for the purpose. *Proposed* from the Chair. *Carried.*

11. This Conference registers its emphatic protest against the policy of the Secretary of State for India regarding nomination of candidates for the Indian Medical Service and demands that recruitment to that Service should take place through open competitive examination to be held in India. *Proposed* from the Chair. *Carried.*

12. This Conference requests the Government of India:

(*a*) to amend the Indian Medical Degrees Act of 1916 in such a way to make it unlawful for the unqualified persons to write any letters or words, with their names which may denote in a direct or indirect way the resemblance of these letters or words to be genuine or bonafide medical degrees. and

(*b*) to declare it an unlawful practice for such unqualified persons to place or write the designation of 'doctor' before their names. *Proposed by* Dr. A. K. Bose. *Seconded by* Dr. J. N. Mehta. *Carried.*

13. This Conference views with great concern the recent influx of a large number of doctors from foreign countries with which there does not exist any reciprocity and requests the Government to take necessary measures to prevent such influx. *Proposed by* Dr. J. N. Mehta, *Seconded by* Dr. A. N. Bose. *Carried.*

14. Resolved that in the opinion of this Conference, Registered Medical Practitioners should not have any connection with unaffiliated institutions for the teaching of the Western Scientific system of medicine.

Resolved that this Conference requests the Government to initiate legislation to prevent any individual or corporate body to start or run any institution for the teaching of the Western Scientific System of Medicine, until such an individual or body satisfies some preliminary minimum requirements to be prescribed by the Provincial Medical Councils. *Proposed by* Dr. A. D. Mukerji, *Seconded by* Dr. J. P. Mody. *Carried.*

15. Resolved that this Conference views with alarm the rapid increase of "Open Chemists' Shops" owned and managed or attended by the Registered Medical Practitioners where consultation may be obtained free by all classes of people irrespective of their income or position in society.

Resolved further that this Conference is of opinion that it should be declared unethical for Registered Medical Practitioners to have any connection with an open shop where prescriptions other than his own or of other Registered Medical Practitioners, are served. *Proposed by* Dr. A. D. Mukerji, *Seconded by* Dr. T. N. Ghosh.

Amendment "or of other Registered Medical Practitioners" in the last line, between the words "own" and "are served", was moved by Dr. J. N. Mehta, seconded by Dr. H. J. Wania. Resolution as amended was carried.

16. Resolved that this Conference views with concern the growing tendency of the well-to-do and middle class public of utilising free hospital facilities and thereby shutting out from the hospitals some of the poorer section of the public for whom such facilities are primarily intended and depriving the general practitioners of their legitimate income and experience.

Resolved that the Indian Medical Association be requested to take active and early steps to remedy the above state of affairs. *Proposed by* Dr. H. J. Wania, *Seconded by* Dr. T. N. Ghosh. *Carried.*

17. Resolved that this Conference notes with regret the policy of some of the teaching institutions (official and non-official) in permitting their staff incharge of beds to hold positions in more than one teaching institution, leading to a state of affairs which is detrimental to the efficiency of the institutions. *Proposed by* Dr. H. J. Wania. *Seconded by* Dr. T. N. Ghosh. *Carried.*

18. (*a*) This Conference views with great concern and strongly disapproves of the retrograde policy of the Government of India and His Majesty's Government in perpetuating the I. M. S. and making it more dominant in the future Medical Administration of the autonomous provinces. Under such anamolous state of things the Minister-in-charge will have no effective control in formulating medical and public health policy for the good of the people.

(*b*) This Conference emphatically protests against the recent notification of the Secretary of State (*Lancet* Feb. 29th, 1936) reserving some high administrative and important chemical appointments and research posts for the I. M. S. inspite of continued protest from the profession and the public. *Proposed by* Dr. Parmanand Ahuja, *Seconded by* Dr. Valiram Lakhani, *Carried.*

19. While welcoming H. E. The Viceroy's proposal as envisaged in his address in September last to the two Houses of the Indian Legislature to start a regular Central Health Board, this Conference is firmly of opinion that such a Board can serve useful purpose and achieve its object only if persons with first hand knowledge and experience in problems of health and nutrition are put at the helm of the affairs and sufficient funds placed at their disposal to administer their beneficent policy and programme. *Proposed by* Dr. Parmanand Ahuja, *Seconded by* Dr. J. P. Chowdhary. *Carried.*

20. Resolution :—(*a*) Rural medical relief and sanitation being intimately connected with any scheme of village reconstruction as fundamentally affecting the economic prosperity of a predominantly agricultural country like India, this Conference is strongly of opinion that the Government of India and the

Provincial Governments in the coming autonomous provinces should revise their Public Health policy in its essential aspects and give proper attention to it in their annual budgets.

(*b*) In provinces like Sind and the Punjab and others, where irrigation projects of immense importance and great magnitude have been launched and vast areas of land are under water for greater part of the year, this Conference notes with regret that no adequate sanitary or drainage arrangements have been provided pari-passu with the irrigation schemes. This deplorable state of affairs have resulted in unprecedented water-logging of such areas with consequent high malarial morbidity and mortality which has undermined the health of the countryside with considerable loss of man-power and economic ruination.

(*c*) While recording its sense of appreciation of the recognition, none too early, by the Government of the paramount importance of rural reconstruction and the provision of the funds however inadequate in the central budget for the purpose, this Conference is emphatically of opinion that such half-hearted measures will not touch even the fringe of the problem. It urges the Governments, Central as well as Provincial to make Public Health in the village reorganisation as the first charge on the state revenue; set up sufficient rural dispensaries under qualified hands; organise health and sanitation committees; Child and Maternity Welfare Centres; providing training facilities for dais; undertaking drainage and sanitary schemes in water-logged areas, pushing antimalarial measures with all the vigour and liberalising quinine policy. *Proposed by* Dr. Paramanand Ahuja, *Seconded by* Miss T. Kelavker, *Carried*.

21. This Conference strongly disapproves the custom of demanding counter signature of the Civil Surgeon on certificates granted by the Registered Medical Practitioners, as it casts a great slur on members of the profession. *Proposed by* Dr. H. J. Wania, *Seconded by* Dr. Rochiram A. Amesur, *Carried*.

22. This Conferencc is of opinion that the Medical Schools of the present day have outlived their usefulness and should either be brought in conformity with the minimum requirements laid down by the Indian Medical Council or be closed down without any further delay. *Proposed by* Dr. J. N. Mehta, *Seconded by* Dr. R. N. Bose, *Carried*.

CORRESPONDENCE

Madras Medical Council

WARNING NOTICE

We have been asked by the Registrar, Madras Medical Council, to announce the following, in his letter dated 16-1-'37:—

The attention of Medical Practitioners registered under the Madras Medical Registration Act (IV of 1914) is hereby invited to the Warning Notice and the Code of Medical Ethics published by the Madras Medical Council. They are informed that ignorance of Medical Ethics will not be taken as an excuse in future for any infringement of the provisions of the same.

(By order of the Madras Medical Council.)

INDEX TO ADVERTISERS.

1398

...AL NUMBER ON TROPICAL DISEASES—PART I.

REGD: No. 9 M. 429. FEBRUARY, 1937. Vol. XXXIV No. 2.

The Antiseptic

A Monthly Medical Journal

Edited by

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

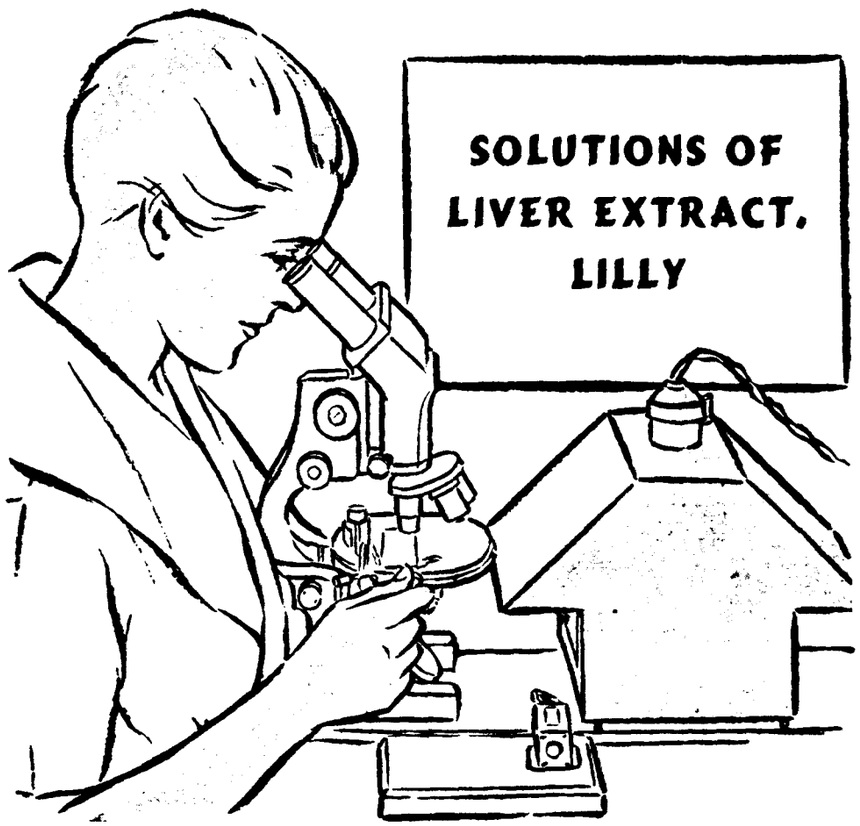
CONTENTS.

Editorial & Publishing Offices: 323, Thambu Chetty St., G. T., Madras.

London Office: 8 & 9 Ludgate Square, E. C. 4.

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

Index to Advertisements. see page 56.



SOLUTIONS of Liver Extract, Lilly, are now prepared by improved methods which conserve the antianemic materials in liver as never before. By the intramuscular use of these ampoules in cases of pernicious anemia at least thirty times the equivalent of the oral dose of liver extract can be given as a single injection.

Solution Liver Extract Concentrated, Lilly, is available in 10-cc. rubber-stoppered vials and in packages of four 3-cc. rubber-stoppered ampoules.

Solution Liver Extract No. 343, Lilly, is supplied in 10-cc. rubber-stoppered ampoules.

Distributor:
KEMP & CO., LTD.
BOMBAY, CALCUTTA, DELHI, NEW DELHI

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

Rx LACTOPEPTINE

IN ALL CASES OF DYSPEPSIA and FLATULENCE

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

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

LACTOPEPTINE
DIGESTS LIKE NATURE DIGESTS

FREE SAMPLE together with further details may be obtained from:
Messrs. Muller & Phipps (India) Ltd., P.O. Box 773, BOMBAY.

IN 3 FORMS

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

IN HEPATIC INSUFFICIENCY

— either functional or associated—

PRESCRIBE

HEPILEX

It is a combination of Fresh Liver Extract with Hypophosphites of Iron, Quinine, Strychnine combined with Potassium, Calcium and Manganese.

Indicated in all forms of Anæmia and all sorts of Debilities and Loss of Vigour.

Please send for free samples
Four Annas Stamps as Postage

For Physicians' free samples & literature, write to:—

Sole Agents: **LAXMIDAS DAHYABHAI & Co.**
CHEMISTS & DRUGGISTS 6, PRINCESS STREET, BOMBAY

Doctors! This is to your interest; : : :

Do you know the best hæmorrhoidal remedy??

All over the world in all Dispensaries & Stores.

CANNULA STOPPED
(German Patent)

Some of the many trustworthy Medical Opinions.

On the strength of the experience I have of 11 hæmorrhoidal preparations I wish to inform you, without having been requested to do so, that with HADENSA I have achieved the best and promptest results!

Yours faithfully,
Dr. med. Herbert BERGER
Dusseldorf, October 25, 1936
Grafenberger Allee 140.

HADENSA

Buy from any Chemists' Stores.
For Physicians' free samples & literature write to:—
Sole Agents: **V. M. JANI,**
P. O. Box No. 2168, BOMBAY.

With your Hadensa, I have seen the best results against hæmorrhoids. I really know no other remedy with such a relatively sure effect.
Dr. H. ROSENBUSCH, Special Physician for Internal Diseases at Munich, Innstr. 4.

BRONCHOVYDRIN. A sure remedy in cases of asthma spasmodic and irritant coughs.
Available forms: Bottles containing 12, 5 gm.

WEIL ASTHMA OUTFIT packed in small imitation leather case. This inhaler renders maximum use of Bronchovydrin possible, as it is standardized for the vaporization of this solution.

BRONCHOVYDRIN TABLETS should be used for supplementing Bronchovydrin inhalations.
Available forms: Tubes of 20 tablets.

BROMOSTRONTIURAN has proved itself for many years to be the leading curative agent in itching dermatosis of every description.
Indications: Acute and chronic eczema, neurodermatitis, urticaria, intoxication dermatitis, and pruritus.
Available forms: 25 tablets in a tube; ampoules of 5 c.c. and 10 c.c.

DROSERIN-SYRUP. A specific in whooping cough and also oridinary cough associated with cold.
Available forms: 4-oz. bottles.

Prepared by:
Drs. R. & O. WEIL, Chemical Works, Frankfurt a Main, Germany.
Obtainable from all leading Chemists & Druggists,
Sole Representatives for India & Burma,
Messrs. PARNELL & CO., LTD., 17, Mangoe Lane, CALCUTTA.

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

When writing to advertisers, please mention the "Antiseptic"

When writing to advertisers, please mention the 'Antiseptic'

When writing to advertisers, please mention the 'Antiseptic'

Special Number on Tropical Diseases.

The Antiseptic

ESTD. 1904.

A Monthly Journal of Medicine and Surgery.

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

Editorial and Publishing Offices:—323, Thambu Chetty St., Madras.

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

Vol. 34. | FEBRUARY 1937 | No. 2.

Historical Aspects of Tropical Diseases

BY

D. V. S. REDDY, M.B., B.S.

Medical Registrar, Medical College, Vizagapatam.

THE writer of this article accepted the invitation of the Editor of the Antiseptic with the hope of presenting a short historical note on some of the tropical diseases with one or two early classical descriptions of each disease on the same lines as the two recent excellent publications—"A Short History of Common Diseases" and "Classic Descriptions of Disease". As the references and quotations collected, increased beyond all expectations, that scheme had to be abandoned in favour of a less ambitious and very short summary, clearing the way for a later attempt.

A comprehensive history of tropical medicine has not yet been attempted so far. The authors of text books on tropical medicine, generally begin their contribution on each disease with a sketchy historical preface. Castellani and Chalmers, in their Manual on Tropical Medicine, have gone a step further and in addition to the historical notes under each disease, have provided, in the first part of their book, a history of tropical medicine. They begin with the primitive medicine, refer to the characteristics of ancient Egyptian, Hebrew and Indian medicine and finally describe the Grecian, Alexandrian, Roman and Arabic medical literature, thought and practice. Their remarks, based on a study of Charaka, Susruta, Vagbhatta, Madhava and Bhavamisra,

indicate how much scope there is for further investigation. " There is no doubt that the Indian Doctors were well versed not merely in medicine and surgery but the prevention of disease and in operative midwifery They apparently knew diabetes mellitus, dysentery, phthisis and diseases due to worms ". Another observation of these writers is an additional argument for the study of the history of tropical medicine. " Native peoples have very good knowledge of medical and poisonous plants growing in their vicinity and it is well for the medical man, living in the tropics, to remember that cinchona bark was originally the native Ecuador remedy and that it is not advisable to entirely dispense the popular drugs."

The beginnings of Tropical Medicine.—The beginnings of tropical medicine were the observations and clinical data in the Vedas, Bible, Talmud and the Egyptian Papyrii. Eber's papyrus (1500 B. C.) is said to contain a prescription against worms and directions to get rid of fleas and lice, while the Berlin papyrus (1400 B. C.) has recipes for the treatment of leprosy. Bible contains references to many interesting tropical diseases. The fiery serpents in the Book of Numbers may possibly refer to a description of the guinea worm. Paul of Aegina (end of 7th century) devoted considerable space to malarial fevers, gave a description of Cholera, Dysentery, Leprosy, Round-worms, Snakes, Scorpions etc. The Arabian writers like Rhazes and Avicenna converted parts of their books into veritable manuals on Tropical Diseases. Hindu and Mohammadan Physicians of the 15th and 16th centuries have given excellent descriptions of the common diseases of the Tropics. Among the early European travellers, and settlers in India, Garcia da Orta, Francis Bernier, John Fryer, and Nicholas Manucci were successful medical men with good powers of observation and a wide range of experience, of diseases and men. Their writings form excellent sources for the history of Tropical Diseases. Garrison has the following passage on tropical medicine: " Tropical medicine vaguely rooted in antiquity came into being largely through the exploration of the globe by navigators and the settlements made in tropical and torrid regions by Spain, England, Holland and France. It owes its scientific status to the development of bacteriology, parasitology, protozoology, medical entomology and medical mycology. It had its authentic start with the organisation of Indian Medical Service in 1764 and some of the best works done in early period clusters round the names of Lind, Wade, Russel, Fayrer, Macnamara, Malcomson, Waring, Vandyke Carter, Ronald Ross and Leonard Rogers ".

Early tropical medicine consists of the records of ship-surgeons and other keen observers, who made notes of their experiences during their voyages or during their stay at factories. A compact note by Castellani and Chalmers may be quoted in this connection :—" Clinical researches into the diseases affecting Europeans and natives in the tropics began with the earliest modern travellers, non-medical as well as medical and the earliest references to tropical diseases are to be found in these early works on travel. Thus, as Singer has pointed out, De Oviedo in 1526 gives a reference to a disease bubas, which we now know to include Framboesia tropica, a form of Leishmaniasis, and probably a form of Blastomycosis. In 1558 Thevet described the jigger as a little worm called ' Tom ' which entered into the feet, and wrote descriptions of Framboesia tropica under the term ' Pians '. In 1598 G. W. wrote an account of Calenture (heat-stroke), and Tabardillo, which is derived from the Spanish word Tabardo, a cloak, and was applied to the typhus fever epidemic in 1557 and therefore G. W. may have meant typhus by this term, though it is possible that he also included yellow fever under the same name. He also describes Espinals, possibly due to the bite or sting of some venomous animal : Cemeas de Sangre, or dysentery; erysipelas, which probably included filariasis; and Tinoso, or scurvy. In 1642 Bontious wrote his work, ' de Medicina Indorum '. Chalmers and Archibald have drawn attention to the description of dracontiasis, dermatophilias, epidemic gangrenous rectitis in South America; simple continuous fever, malarial fevers, dysenteries, smallpox, climatic bubo in India, malaria, endemic yellow fever, dengue, smallpox, filariasis diarrhoeas, dysentery, and yaws in West Africa, as indicated by D. L. F. in 1726 and by Aulsey in 1729."

As the European settlements increased in number and size, more medical men settled down and recorded their observations in a number of works which formed the earliest literature on tropical medicine. Chalmers and Castellani call these early medical men. " Pioneer founders of modern tropical medicine". Their works are scattered and difficult to obtain but deserve to be stocked in every medical college library. The evolution and perfection of the compound microscope gave a great impetus to the development of modern tropical medicine by enabling Leveran to discover the malarial parasite, and Manson to establish the periodicity of micro-filariae nocturna. Ross's discovery of the spread of malaria by mosquito bites aroused world wide interest in tropical diseases. Castellani and Chalmers believe that modern tropical

medicine began with these great discoveries which opened up the possibility of finding the cause, the method of spread, the treatment and the prevention of periodical diseases, the history of some of which is briefly sketched in the next few pages.

Malaria.—The name 'Malaria' was given to the disease by an Italian writer in 1753. "The word 'malaria' is derived", write Rogers and Megaw, "from two Italian words 'Mal' (Bad) 'aria' (air). This name was applied because of the old belief that the disease was due to the inhalation of poisonous emanation which rises from the ground especially in marshy places.

"The disease in some of its most recognisable forms was known thousands of years ago. Periodical attacks of fever coming on with chills and passing with sweat were naturally regarded as indicating the presence of a special disease" (Rogers and Megaw). All text books of tropical medicine usually begin the history of this disease with the description by Hippocrates of quotodian, tertian and quartan fevers. He noted their occurrence in autumn and near stagnant water. Celsus is next given credit for differentiating "two types of tertian fever, one, benign similar to quartan fever, the other far more dangerous with fever occupying 36 out of the 48 hours." Galen also described tertian and quartan fevers. In 116 B C., Varro suggested relationship between marshes and malaria. Castellani and Chalmers however admit that it is possible, that directly or indirectly, Hippocrates owed much to India and Egypt and trace the history of the disease with the following remark: "It is suggested that the reference in the Charaka Samhita to fevers spread by mosquito refers to malaria and that this fever was recognised at the time of Homer." Susruta refers to quotodian (anyedyuska), tertian (tritiyaka), quartan (chathurdhaka) fevers. Chakravarthy (1923) points out that Susruta indicates a vague relationship of malaria with mosquito bites, swampy localities where mosquitoes were developed and that a particular kind of mosquito was incriminated. "There are five types of mosquitoes (masaka) namely, (1) Samudra or coastal mosquitoes (2) Parimandala (3) Hasthimasaka (4) Krishna (5) Parvatheeya or mountainous mosquito. The bite of the mountainous mosquito (anophele) produces an effect like that of deadly insects" (Susiuta V. 8-18). "Charaka mentions a bitter (Tikta) juice of leaves or bark or concoctions of dry bark in the treatment of malarial fevers" (Chakravarty). Can it be the bark of local varieties of Rubiacea, to which family cinchona tree belongs?

Malaria had played a villainous part in wiping out ancient civilisations. McCulloch (1872) traced its influence in causing

race degeneration in various parts of the world. W. H. S. Jones in his book (1909) on "Malaria and Greek History" concluded that the disease played a large part in bringing about the decadence of Greece. Some one else has added a book conjecturing that the downfall of the great Holy Roman Empire was due to Malaria. Some of the epidemics in Bengal and South India in the mediaeval times were undoubtedly malaria. The disease also finds a place in "belle letters". The plays of Shakespeare, the diaries of Pepsy, and Evelyn refer to it. Some of the outstanding events connected with the modern development of our knowledge of malaria are given by Rogers and Megaw and also by Stitt.

"In 1638, La Contessa del Chinchon, wife of a Spanish Viceroy of Peru, is said to have been cured of an intermittent fever by the bark of an indigenous tree of Peru. The bark was introduced to Europe shortly after this occurrence and the name Cinchona was given to it in honour of the Countess. Critical historians have thrown grave doubts on the accuracy of this story but it will keep its place in the history of malaria just as the tale of King Alfred on the cakes will always retain its hold on the imagination of the schoolboy. Anyhow it was about the year 1640 that cinchona bark or Peruvian bark was first introduced to Europe". Morton and Sydenham in 1666 noted the specific action of cinchona on certain fevers. It was Torti, however, who in 1712 differentiated clinically those fevers which are cured by cinchona and those which failed to yield to this specifiic, laying the foundations of our knowledge of therapeutics of cinchona. He gave the drug in large doses for the first three days, then in smaller doses for a week and later in still smaller doses for two or three weeks. Quinine was isolated from cinchona bark in 1820 by two French Chemists, Pellivier and Caventow and soon came into general use. As Rogers and Megaw observe: "It is interesting that our knowledge of satisfactory treatment was acquired long before the cause of the disease was discovered."

The early European traders in India and their families, seem to have suffered from ague during the 16th century. The Board of Revenue in Madras referred to the ravages of this 'putrid fever' as far back as 1797. In 1869—70, elaborate enquiries were made in South India as to the prevalence and cause of this disease. The conclusions of Sanitary Commissioner for Madras on the report of Assistant Surgeon Dr. Wright, written in 1869—70 in connection with the prevalence of malaria in Godavary Agency are interesting. "My conviction is that the periodical accessions of fever in Godavary distriet are due to the geographical

position of that district in respect to malarial wind to the north and west and that the fever is due to the northern winds of the north-east monsoon sweeping over malarial jungles of the hill tracts of Northern Circars before they reach Godavary district." (Godavary District, descriptive and historical account, London, 1878). But, Quinine was in fashion already in 1876—78, as recorded by W. G. King, Civil Surgeon, Trichy. "Quinine is largely used by Native Vaidyans and indeed is one of the two English preparations in which they possess implicit faith—the other being chlorodyne."

The narrative of the discovery of the parasite is in itself an epic or a romance. On November 6,1880 Laveran at Constantine first saw the parasite of malaria while carrying on investigations as to the origin of the pigmented bodies and malaniferous leucocytes observed by Kelsch in 1875. He not only noted these pigmented bodies but also crescents and flagellates of the male gaemete. On 23rd November the same year, Laveran, made the epoch making announcement of the discovery of the malarial parasite in the blood of malarial patients describing amoeboid, crescentic and flagellate forms of the parasite. The reception of the news is described by Rogers and Megaw as follows : "The announcement was received with almost universal scepticism. Even Laveran's associates did not at first believe in the discovery while the Italians who had accepted 'bacillus of malaria' of Klebs and Crudelli, held that the bodies seen by Laveran were mere cell degenerations." It was still several years later that the full significance of the discovery was realised. In 1883 Marchiafava employed dried films stained with methylene blue and noted ring forms which later increased in size up to the sporulating stage. Golgi in 1885 traced the stages of the growth of the quartan parasite in blood corpuscles, asserted the difference between the rosettes of tertian and quartan forms, and pointed out that the malarial paroxysm coincides with the period when sporulating forms reach maturity.

About 1883, King adduced a number of good reasons in justification of the belief, popularly held in several parts of the world, that mosquitoes were responsible for malaria. In 1894, Manson formulated the hypothesis that mosquitoes might be the causative factors of Malaria. His idea was that the flagellating bodies which were set free in the stomachs of the mosquitoes might find their way into drinking water and convey the disease to persons who drink the water in which the infected mosquitoes had been drowned. Several others including Lvaeran, Koch,

Pfeiffeur, Bignami, Grassi also believed that mosquitoes were connected with the conveyance of Malaria. It must be pointed out at this stage that the conveyance of the parasite by the bite of the mosquito was not part of the hypothesis suggested by Manson, who however must be given large share of the credit for the great discovery of Ross, who was his pupil.

Ronald Ross, who was in England on leave, heard this suggestion from Manson, was impressed with the possibilities and started his brilliant work on returning to India in 1884, keeping in constant touch with Manson at every stage of his investigation. Bad luck for long months baffled Ross's research, as he was investigating the wrong mosquito. It was also Manson's suggestion that Ross should work out the life history of corresponding parasites in birds. Ross established in 1896 that the malarial parasite from the blood of sparrows are abstracted by blood sucking fly.

The great discovery in medicine, the only one in India rewarded by a Nobel Prize in medicine cannot better be described than in the words of Rogers and Megaw :

> "In 1897 (August 20) Surgeon Major Ronald Ross of the Indian Medical Service found pigmented bodies (now known as oocysts) in the stomach wall of two 'dapple-winged' (now known as anopheles) mosquitoes which he had bred from larvae and caused to feed on persons suffering from malaria ".
>
> "In 1898 Ross working in Calcutta failed to obtain suitable cases of human malaria and decided to use a parasite (a proteosoma). He found that this parasite underwent remarkable development in the stomach wall of culex mosquitoes which he fed on infected sparrows. The first change observed in the parasite was its development into the same kind of pigmented bodies as he had seen in 1897; in a few days, these became greatly enlarged and finally burst discharging shred-like bodies (now known as sporozoites) into the body cavity of the mosquito; these bodies then penetrated the salivary glands of the mosquito.
>
> "He next demonstrated that the proteosoma infection was conveyed from infected to non-infected sparrows by the bites of mosquitoes and also that control sparrows remained free from disease if protected from mosquitoes. These observations combined with his significant discovery of the previous year, fully justified him in announcing that human malaria

was conveyed in a similar way by the bite of infected mosquitoes; he also advocated the organisation of measures for the control of mosquitoes".

Ross was prevented from carrying out the final stages of his experiment demonstrating the conveyance of human malaria by his ill-health. In 1898-99, Bignami and Grassi and Bastianelli who had been kept well informed of the discoveries of Ross succeeded in demonstrating that the same cycle of events take place in anophele mosquitoes which had been fed on human beings with infected malaria and worked out the mosquito phase of the parasite. The connection between infected mosquitoes and malaria had yet to be demonstrated. "Experimental proof of the truth of this carriage was afforded by Manson producing typical attacks of malaria, with parasites in the blood in persons who had never left England by the bite of anophelene mosquitoes infected with parasites in Italy. Sambon and Low lived in the most malarial months of 1900 in one of the most malarious sections of the Roman Campagna with no other protection than good anti-mosquito measures but they did not contract malaria. That is how malaria came to be conquered.

Black Water Fever.—"The disease appears to have been overlooked in many places where it must have existed for a long time," state Rogers and Megaw. "Probably it was included in bilious remittent fevers, and the dark colour of the urine was regarded as being due to bile pigment". Stitt also thinks that the late recognition of this disease was due to the confusion between bilious remittent fever and yellow fever. It is generally acknowledged that the first description available for us is the information given by the French Naval surgeons Lebeau, Daulle and Le Roy de Mericourt in 1850-53 who drew attention to the disease in Madagascar. Stitt believes "black water fever must have been the condition referred in medical literature of the period 1850-1870 in the names "Fievre bilieuse hematurique", "haemorrhagic malarial fever" and "febrio remittens haemorrhagica". Castellani and Chalmers give a brief historical summary of the important discoveries and descriptions of this disease subsequent to its recognition in 1850.

The name black water fever, now universally adopted, was first used by Easmon. The interesting question for us Indians seems to be whether it had existed in India prior, from ancient or mediaeval times. Manson comments that it is strange that it should not have been recognised in India if the disease had existed here

for centuries. Chakravarthy in his book, "Interpretation of Ancient Hindu medicine", names or translates Pitta fever described by Susruta as bilious remittent fever or black water fever. A close study of the text of Susruta with the necessary commentaries may help to elucidate the point and confirm or controvert the above assertion. I have sent questionairre to the Agency tracts of the Vizagapatam district to gather information from the natives of those areas where black water fever has been reported, with a view to enquiring whether there is any popular tradition or local records or common treatments handed down by hereditary physicians in connection with this disease. The matter deserves close study.

Cholera.—The name cholera is of Greek origin derived from the word *cholera* meaning spout, thus describing the violent purging in this disease. Castellani and Chalmers state that cholera appears to have been known in India from the most ancient times, for Charaka and Susruta describe symptoms which most probably refer to this disease. "If in Cholera Asiatica (visuchika) and tympanites (alasaka), the teeth (the gum), lips and nails become cyanotic, there is a comatose state, active vomiting, orbits of the eyes are sunk in the sockets, the voice becomes weak and the joints become relaxed, then the prognosis is very unfavourable". (Susruta VI. 56-8) (Chakravarti 238). Rogers and Megaw add that cholera was probably endemic in China for thousands of years. Others consider that cholera was carried to China in 1669 from India. Hippocrates did not seem to be acquainted with this disease. It is interesting that Koch doubted the antiquity of Cholera. During the middle ages the earliest record of the disease is found in 1438 in Ahmed Shah's army, said to have been decimated by this disease.

At the beginning of the European intercourse with India, the disease seems to have been common. It was mentioned by Vasco De Gama in 1490. It broke out in Goa in 1543. The wars in the Deccan,during the 17th and 18th centuries, when the English and French were carrying on their conquests, naturally spread the disease all over India.

The following note from the District Gazetteer of Madura (pp. 168) is interesting :—

"Cholera is an ancient enemy of the country. A letter from the Jesuit missionary Robert de' Nobili, dated as far back as April 1609, speaks of the ravages of a virulent epidemic

disease which he calls 'mordechin' and Father Martin, writing in 1701, gives an account of this, which makes it clear that it was none other than cholera. Yule and Burnell say 'mordechin' is a fanciful French corruption of 'modachi', the Konkani and Marathi name of the disease. The remedy favoured by the Jesuit Fathers for the cure of choleric attacks was the application of a red hot spike to the soles of the patients' feet. If he did not move when this was applied, they naively observe, his case was hopeless."

There was an epidemic in Pondicherry in 1768 and in Madras in 1782 and in the West Coast in 1792-94. According to Macnamara, no less than 66 separate observers mentioned the disease between the years 1438 and 1817.

The first extensive epidemic recorded outside India began about 1817 and lasted till 1823. The first Pandemic commenced in 1826, spread throughout India, passed by 2 routes to Russia, thence to Germany, Sweeden and England. The whole of Europe was infected by 1833 and the epidemic spread to, The United States, Mexico and Australia. By a third route from India, the disease spread to Turkey and Egypt and to North Africa by 1834. Rogers and Megaw point out that this disease took 5 years to travel from Bengal to Europe and in the absence of rapid means of communication by rail and sea. John Snow of New York, first stated in an essay in 1849 that cholera is a water borne disease taken into the system by mouth. The 2nd edition of his work 'Cholera' printed in 1852, contains remarkable statements of the germ theory. It was he, who also predicted successfully in 1854 that the severe London epidemic would cease if the hands of the Broad Street pump were removed. Up-to the year 1900 seven extensive epidemics have been recorded and are described by Castellani and Chalmers. It was during the fifth epidemic which began in 1879 that Koch at the head of the Cholera Commission, visted Egypt and India and discovered the cholera vibrio in Egypt in 1883. A serious outbreak of cholera, originating in 1881, in pilgrims in the Delta of the Ganges and reaching Europe in 1882, gave opportunity for the careful studies as to the transmission of the disease by a study of the outbreak at Hamburg and in the neighbourhood of the Broad Street well in London in 1892. The story of the two well known incidents has been told and retold. It was also during the Hamburg epidemic that Dunbar noted the transmission of the disease by healthy carriers. Ferran in 1885 and Haffkine in 1893 used vaccines in prophylaxis.

Kala-Azar.—The name Kala-Azar was in use in Bengal and Assam before the nature of the disease was known. Ross points out that the correct name is Kala-Jwar or mortal sickness. It is possible that the natives named it Kala-azar on account of the black appearance of the victims. Rogers and Megaw are of opinion that the disease had existed in India for centuries. Chakravarthi translates Satata fever described by Susruta as "double quotodian" and calls it as Kala-azar. It was only in the last century that the disease came to be recognised as a separate entity. "In 1869, when the district of Garo hills in Assam was first occupied by the British,a disease believed to be a very severe form of malarial cachexia was found to be endemic". In 1875, it spread and the epidemic was characterised by high death rate. In 1882 the first account of the disease was published by Clarke from notes of 120 cases compiled by McNaught. It was regarded as a chronic malarial fever. It was soon found spreading along the main line of human inter-communications. Giles, as a result of a year's investigation, came to the conclusion that "Kala-azar is ankylostomiasis" as he found hook-worm ova in the stools of the majority of cases. In 1894, Stephens reported that the disease was distinct from malaria, while Rogers in 1896 and Ross in 1898 regarded the disease as of malarial origin. On the other hand, Bently in 1902, misled by the similarity of temperature charts and agglutination tests of the serum, claimed that Kala-azar was a malignant form of Malta fever. And yet a third hypothesis was put forward by Manson in 1903 that the disease might be caused by a trypanasome. In 1903 the mystery of the disease was solved. Sir William Leishman had found, in 1900, the peculiar bodies in a film taken postmortem from the spleen of a soldier who died in Netley, from fever contracted at Dumdum. He was at a loss to explain their significance and did not publish this discovery till 1903. In the same year, Col. Donovan of the Madras Medical College observed the same parasite in blood obtained by splenic puncture performed during life on patients suffering from "malarial cachexia". This proved that these bodies were the living parasites of the particular disease. There was much discussion as to the nature of these bodies whether they were piroplasms or trypanasomes. Rogers in 1904 cultivated the parasites and noted flagellate forms. In 1919, Gasper Vianna introduced the intravenous injections of Tartar Emetic for the treatment of the American Leishmaniasis. Castellani in Ceylon and Rogers in India experimented with the antimony treatment for Kala-azar and published extensive reports popularising the only available defence

against kala-azar. Sir U. N. Brahmachari of Calcutta, later synthesized his "Urea Stibamine."

Dysentery.—Stitt states: "Although Hippocrates was the first to accurately describe the disease which is now known as dysentery, yet there is good ground for believing that the disease existed in Egypt and in India for centuries before Christ."

The disease is mentioned in the Ebers Papyrus (1600 B. C.). Herodotus (5th century B. C.) refers to an epidemic of dysentery in the Persian army. The disease has been known in India since remote times. Castellani and Chalmers observe: "the occurrence of a bowel disease, in which blood appeared in the motions was well known to the ancients, for, descriptions of such a condition can be found in the works of the old authors, Charaka and Susruta, in which, dysentery was called 'Atissar' and acute dysentery 'Amapaka' while the chronic variety was called "Pakitsar" The term dysentery is derived from a Greek word signifying a bowel trouble and was first used by Hippocrates, who differentiated between frequent motions and motions containing blood. At first the term dysentery meant discharge of blood per anus: later, Aretaens, Celsus and Galen differentiated the disease by insisting on the presence of mucus as well as blood in the motion. The disease was believed to be due to an ulcerated condition of the bowels. The contagious nature of the disease was also recognised very early.

In the early days of the East India Company, dysentery was a troublesome and common disease. William Finch says he was himself ill (in 1608) of a 'bloody fluxie', whereof Master Dorchester died. In 1612 all the English at Surat suffered from 'Fluxie.' Coryat died of it in 1617. It was only in 1859 that Lambel noted the presence of Amoebae, in the stools of a child, affected with diarrhœa. The real advance came in 1875 when Rosch in Russia described for the first time the parasite which he found in the intestinal ulcerations as well as in the stools of the patient with dysentery and produced dysenteric ulcerations in the dog by injecting amœbae containing stools into the dog's rectum. The opinion current in India in 1876 is expressed by Surgeon Major King, writing on bowel diseases thus: "The greater part of the mortality is due to diarrhoea and dysentery, more common at the outset of cold season probably as a result of undue exposure, but, in ordinary times, these diseases are also due to inferior food and impure water".

Grassi in 1879 noted the encysted forms of amoebae, but denied their pathogenic importance.

Koch in 1883 considered that amœba was pathogenic. Two pupils of Osler, Councilman and Lafleur, described in 1891 the lesions in the bowels and called the disease amœbic dysentery, and indicated two species of amoebae, one harmless and the other pathogenic. In 1902, Rogers recognised that Ipecac was effective against amoebic dysentery. In 1903 Schauddinn reported the existence of two species of amoebae, one harmless (entamoeba coli) and the other pathogenic, named E, histolytica.

It was not until 1888 that Shiga the famous Japanese worker, isolated the causative organism of bacillary dysentery and opened up the possibilities of treatment by anti-dysenteric serum.

Filariasis (Elephantiasis):—Asia is the endemic home of filariasis. Castellani and Chalmers make the following comment on the descriptions given by ancient Indian writers:—

> "The appearance of the huge leg of elephantiasis is so striking that it was early noticed by ancient Indian writers, who give descriptions of diseases which clearly refer to elephantiasis of the leg and of the scrotum, and also less clearly to lymph scrotum. Further, they appear to have known that elephantiasis could affect the hands and other parts of the body."
>
> "The word 'elephantiasis' was first popularised by Celsus who described leprosy under this term and in this he was followed by most writers until Galen, who included true elephantiasis under the same term, an error which became firmly established as time passed. In the 9th and 10th centuries, Rhazes and Avicenna, and other Arabian physicians described true elephantiasis of the leg under the term 'da-fil' or 'danool-fil' or elephantine disease, which however only served to make the confusion between the two diseases more complete."

Bhaskara Menon, in his Curzon lectures for 1935 on filariasis, refers to the mention or description of the disease by the older ancient Hindu medical writers, Charaka, Susruta and Madhava. I was surprised to find no reference made to descriptions of the disease by the early European travellers, some of whom must have been struck with the ugly manifestations of the disease. Marco Polo, in his travels in South India at the end of the 13th century, seems to have heard the legend that the murderers of St. Thomas suffered from one leg of immense size. In the latter half of the 16th century, Ralph Finch commented on

the bad water of Quilon, "which caused many people to be like lepers. Many of them have their legs swollen as big as man in the waist and many of them scant able to go".

In the 17th century Leonicenis and Veramdaes pointed out the distinction between the diseases, leprosy and true elephantiasis. Clarke in 1709 described elephantiasis on the Malabar coast under the term Cochin leg. Hillary in 1750 gave an accurate account of the progress of elephantiasis connected with elephantoid fever and lymphangitis which gradually became permanent, producing the well known condition. Handy in 1799 gave the first account of the elephantiasis of the scrotum. Allard in 1809, Chapoten, Salase and others reported on the various aspects of the disease particularly haemotochyluria. Of particular interest to Indian medical men is probably the first contribution by an Indian in 1854 when Jamshedji described lymph scrotum. From 1712 when Kempfer described a large swelling of the leg, the disease now known as "Madura foot" began to be confused with elephantiasis. Van-dyke Carter ended this confusion in 1868 by his 'treatises on mycetoma and on elephantiasis'

Demarquay, in Paris, discovered in 1863 a microfilaria in the fluid from a hydrocele from a person in Havana. Lewis, in Calcutta, carried out a series of investigations in which he found filarial embryos in the urine of patients with chyluria and in blood and urine of persons suffering from elephantiasis of the leg. It was Lewis who called the parasite "filaria sanguinis hominis". In 1876, Bancroft in Australia discoversd filarial worm in lympha tic abscess. Hence the name 'filaria bancrofti' given by Cobbald. Meanwhile in 1872 Lewis had published his classics containing the results of all his work. In 1878, Manson in China demonstrated the mosquito transmission of the disease but thought that the fully developed embryos escape from mosquito at its death into water, which, when drunk, produced the disease. The real historical significance of this discovery is that it led to the great discovery of Ross. Some of the physicians of Madras General Hospital, published reports and books on the disease, particularly Sibthorpe and Maitland in the last quarter of the last century. The final stage in the elucidation of the method of transmission was reached only after 1900, when Low, Fulleborn and Bhar supplied the information that the filarial embryos escape from the mosquito through the proboscis and enter man during the act of biting.

Laboratory Methods

—Historical and Diagnostic—of some commonly prevalent Tropical Diseases

BY

K. VENKAT RAO, M.B., B.S.,

Medical Practitioner, Madras.

For over a century the fight against disease microbes in general and tropical diseases in particular has gone on relentlessly and now the laboratory methods in the diagnosis of most of these diseases have become standardised to a great extent, within the last twenty five years. From the time when the Dutch draper Antony Van Leeuwenhock put two lenses together to obtain a better magnification to see various objects—like the drop of water from a rain water pot, scales of a fish, muscle of a whale, sections of wood, material from the mouth scrapings etc., to the modern method of visualising the microscopic foes—magnified a 1000 times or more by modern microscopes and still more, with the help of the camera and microscope in conjunction as in the study of ultra microscopic viruses, Research in Bacteriology has advanced as the development of the cave dwelling to the modern sky scraper. The story of scientific research reads like romance. It is one of realistic and magnificent adventure, a tale of supreme human achievement. The illustrious names in this adventure, the martyrs who have fallen on this road to fresh discovery, are ever fresh in the minds of and deeply cherished by men who work at the microscopes—or inject the guinea pigs.

Antony Van Leeuwenhock, born in 1632, a draper by profession at Delft in Holland, could not afford to buy his lenses, so, took to grinding lenses and polishing them so fine, to see all objects he could wish to magnify. But what was the magnification obtained with a single lens to that obtained by a combination of lenses? It was this magnificent and ingenious idea that won for him the title of Father of Bacteriology, for his was the first eye that saw the little "wild wee wretched beasties cavorting in a drop of rain water." What he saw that day in about 1650 starts this history. *Paul De Kruif, a popular author, writes of* this discovery:

> "He, A. V. L., was a maniac observer and who but such a strange man would have thought to turn his lenses, on clear, pure water, just come down from the sky? What could

there be in water—fresh water? You can imagine his daughter Maria, she was 19 and she took such care of her slightly insane father!—watching him take a little tube of glass—but what in the world was he up to now, with that hairfine glass pipe?

"You can see her watch the absent-minded, wide-eyed man go out into the garden to bend over an earthen pot, kept there to measure the fall of the rain. He bends over the pot. He dips in the little glass pipe, goes back to his study and sticks the pipe on to the needle of his microscope.

"What can that dear silly father be up to? He squints through his lens. He mutters guttural words under his breath.

"Then suddenly the excited voice of Leeuwenhock, Come here, hurry! there are little animals in this rain water! —They swim! They play around! They are a thousand times smaller than any creatures we can see with our eyes above—Look! see what I have discovered!' His day of days had come. Alexander had gone to India and discovered large elephants that no Greek had ever seen before, but those elephants were as common-place to Hindus as horses were to Alexander. Caesar had gone to England and come upon savages that opened his eyes with wonder—but these Britons were as ordinary to each other as Roman centurians were to Caesar. Balboa? what were his proud feelings as he looked for the first time at the Pacific? Just the same, that ocean was as ordinary to a central American Indian as the Mediterranean was to Balboa. But Leeuwenhock? This shopkeeper of Delt had stolen upon and peeped into a fantastic sub-visible world of little things, creatures that lived, had bred, had battled, had died, completely hidden from and unknown to all men from the beginning of time. Beasts there were of a kind that ravaged and annihilated whole races of men, ten million times larger than they were themselves. Beings there were, more terrible than fire-spitting dragons or hydra-headed monsters. They were silent assassins that murdered babies in warm cradles and kings in sheltered places. It was this invisible, insignificant but implacable—and sometimes friendly world that Leeuwenhock had looked into for the first time of all men of all countries. This was Leeuwenhock's day of days....."

From Antony Van Leeuwenhock to Noguchi of the Rockfeller Institute is a far cry. Interest in these animalcules was

lost till an Italian scientist—ordained as a Roman Catholic priest, Abbe Lazaro Spallanzani—made professor at the University of Reggio—revived it by perfecting methods of growing these microbes in strange brews made of meat, seed soup and all strange animal and vegetable brews. He set himself the task of solving the question—"can living things arise spontaneously or does everything have to have a parent?" The theory that living things were generated spontaneously held sway for years to be disproved partly by this clergyman His experiments proved that life only comes from life, till, finally, Pasteur and Hoffman once for all solved this mystery of spontaneous generation.

Where Spallanzani's work proved that microbes must have parents, Pasteur showed that these microbes are a menace and cause disease. 25 years after Spallanzani, on 27th December, 1822, Louis Pasteur was born in a tannery of Marnoz in France. "If any one man can be looked upon as the founder of Bacteriology, that one man is Louis Pasteur", says Jordan. The list of Pasteur's contributions is too long. Outstanding among these, are his discovery of Anthrax in 1877., Chicken cholera and swine fever studies and later still, hydro-phobia research followed. His master mind has dominated bacteriology even to this day. Through his researches on silk worm disease he pointed out that a specific microbe causes a specific disease of the moths which logically led to the reasoning that human disease likewise was caused by microbes, each specific to a particular disease.

As a boy of 9 years, Pasteur was frightened away from a village blacksmith's shop where he saw the flesh of a farmer bitten by a mad dog, being burnt by red hot irons. "What makes a wolf mad, father, and why do people die of these bites?"—asked Louis running home. From this early question, to the later task of the discovery of the cause and cure of hydrophobia, is a tale of the gigantic achievement of a mastermind.

While Pasteur was saving wine and curing silk worms, Koch was just learning medicine at the University of Gottingen. Fate gave him over to scientific research. He dreamed of adventures on the high seas, in far off tropical climes, and wanted to go off as a ship's surgeon. While at his first post as an interne in a not very interesting insane Asylum in Hamburg, he met and married Emmy Fraatz who consented to share life with him, if he gave up this nonsense about an adventurous life in far off lands and settled down as a country practitioner.

Frau Koch bought him on his 28th birthday, a microscope to keep his mind off the worries of what he called his "stupid

practice". This started him on more weird adventures than are met with in any Tropical forests and led to the discovery of more virulent enemies than the wildest denizens of those forests.

Koch advanced the science of Bacteriology by his discovery of methods of isolating and growing individual kinds of germs by using solid media. Staining of these microbes was another step to their identification. Though Weigert in 1871 was the first to stain bacteria in tissues, Koch perfected other and better methods with certain aniline dyes.

Then followed a period of prolific bacteriological research resulting in the discovery of specific microbes of Typhoid, Tuberculosis, Tetanus, Diphtheria, Pneumonia, Syphilis and many more infectious diseases. In about 25 years of this period the greatest advances in this 250 years-old science of Bacteriology are grouped together. Research in plant disease, fungi, moulds, protozoan diseases went apace.

> "In 1881 when Sedillet coined the word 'microbe' to describe the tiny forms which Pasteur detected, the sceptics used to laugh and call Pasteur microbe-mad. But the whole of modern medical research is based on the work of Louis Pasteur. He taught the fighter of disease that in the germs we have alike the cause of illness and its cure."

Malaria, yellow fever, kala-azar, sleeping sickness, cholera, plague are some of the death traps set up by these invisible foes to fight man in the tropics; that the deadliness of the tropics is due to insects and fighting the winged hosts of the air relentlessly will render the tropics safe was a discovery of the father of Tropical Medicine—Sir Patrick Manson. Fate, again, as in Koch's case, gave Manson to medicine. He began life as an Engineer in his uncle's iron works. His zeal outran his strength and owing to very heavy manual labour in the yards, he developed spinal troubles resulting in his doctor's ordering him to bed for a long period. During the two hours a day he was allowed to get up, he studied Botany and Zoology and Natural History. Later, these studies led him to study medicine and go to China from where on, his contributions to popular diseases are classic. From the Chinese hospital in Formosa at 22 years of age, elephantiasis, malaria, leprosy and such other tropical diseases came under his observation. The nocturnal periodicity of filariasis and the discovery of mosquito as its intermediary host, he pointed out in 1878. Those who gained their inspiration from his lips—Ross, Samban, Low and others like Donovan, Rogers, Haffkine, Zamb Liston, Yersin Shiga, etc., have built up our knowledge of tropical diseases.

Blood infections chiefly of protozoal, bacterial and spirochaetal origin, *e.g.*, malaria, kala-azar, plague, and relapsing fevers, bowel diseases like cholera, dysentery and hookworm and sprue; infective granulomata *e.g.*, leprosy, yaws and mycetoma; tropical skin infections of bacterial and fungoid origin, tropical venereal diseases *e.g.*, the climatic bubo and infective granuloma, constitute the chief and commonly prevalent of the scourges of the tropics.

Malaria.—The best known of the protozoan diseases is malaria. Laveran in 1880 described its nature. Ross and Grassi take the credit for finding the insect host—the mosquito—as the transmitter of the disease.

It is believed that the civilizations of Greece, Ceylon and such other ancient countries have been destroyed by malaria which is still responsible for millions of deaths every year and much more of debility and lowered resistance to other diseases like Pneumonia and Dysentery.

This disease is produced by the protozoan parasite belonging to the class sporozoa. There are 3 kinds of parasites, the Benign, Quartan and Malignant Tertian which are peculiar to man who constitutes their intermediary host. Though this fever with its periodicity was known to Hippocrates and the bark of the cinchona tree was used for its cure about 1670 in Europe, the name 'malaria' meaning 'bad air' was given to it by an Italian writer in 1753. Laveran in 1880 made the epoch-making discovery of the parasites in the blood at Constantine in fresh blood preparations. Manson was the first to formally suggest the mosquito as the transmitter of malaria. Ross in 1897 found the pigmented bodies, Oocysts, in the stomach wall of two "dapple winged" mosquitoes. He worked out the mosquito cycle in bird malaria for want of suitable cases of malaria at the place where he was stationed. Grassi worked out the mosquito cycle of human malaria. Finally Manson's famous experiment once for all set at rest, any objections to the mosquito transmission theory of malaria.

Under Manson's direction in 1900 for 3 of the most malarious months, Drs. Samban, Low and Terzi lived in the most malarious parts of the Roman Campagna in Italy, in a hut from which all mosquitoes were excluded by a simple arrangement of wire gauze, while their neighbours, the Italian peasants were one and all attacked with malaria, these three and their servants, who entered the hut in the evening and stayed there till morning, escaped the fever. About the same time mosquitoes, fed on malaria patients in Rome, were sent to Manson in London and were made to bite his son and another George Warren. Both these shortly afterwards

developed characteristic attacks of malaria, the blood smears showing typical forms of the parasites.

The certain diagnostic method in malaria is the finding of the various forms of the parasite in blood. Thin or thick smears of blood are made and dried in the air. Usually the thin smear is stained by Leishman's stain—5 drops of the stain are dropped on the film and left for one minute, care being taken to see that the stain does not dry up, then 10 drops of Co_2 free distilled water are rapidly added to the stain and mixed by tilting the slide gently. The diluted stain is left on for 5 minutes. The stain is then washed off by a stream of distilled water, a few drops of which are kept on the slide for about 30 seconds and then poured off. The slide is dried in the air and examined with an oil immersion lens. Unless the smear is well made and properly stained, it is waste of time to search for these parasites. The staining of the leucocytes serves as a control. If the protoplasm and nuclei especially of the lymphocytes are well stained, the parasite also will be well stained. If not, the delicate ring forms are likely to be missed. During the first one or two attacks or if the blood is taken at the height of the fever, the parasites especially the ring in M. T. cases are likely to be missed. *A film usually taken a second time 6 hours later, will show the parasites in these cases.*

In Malignant Tertian cases small rings or rings and crescent bodies or only crescents may be formed. The rings are smaller than the Benign Tertian rings with the chromatin dot placed to one side of the ring, sometimes two or more rings are found in 1 corpuscle, some rings show 2 chromatin dots.

In Benign Tertain infection, all stages of development of the parasites, from rings to the mature and segmenting forms, can be seen while the sexual form with the single mass of chromatin and pigment scattered through the body of the parasite is also seen in some cases. The R. B. C. is enlarged in this variety of parasite and Schuffner's dots are seen.

In the Quartan, the young ring forms, very similar to those of Benign, are seen; the half-grown forms are more definite in outline and oval and bandshaped forms with coarse pigment granules are seen. The R. B. C. is not enlarged and no Schuffner's dots are seen. The segmenting forms are smaller and have 8 to 12 segments as against the 12 to 24 segments of the Benign. The sexual forms are much the same as the benign but are smaller in size.

The thick drop method usually offers a greater and more certain chance of finding the parasites when scanty in peripheral blood. Quinine should never be administered before taking the blood films as all forms of the parasites except the crescents disapper from the peripheral blood under the action of this drug.

The general blood picture is one of a rapidly progressive anaemia of the chlorotic type, the R. B. C. in extreme cases falling to 50% or less and Haemoglobin to, so low a figure as 25%. Recovery in the number of corpuscles is much quicker than in the percentage of haemoglobin.

Leucocytes also present a remarkable picture. Just before the attack, leucopenia can be noticed, which, at the height of the attack, changes to a moderate leucocytosis in the early stages. Later on, leucopenia is noticeable with a relative increase of mononuclears up to as much as 20%. In the mononuclear and polymorphos, granules of haemozoin can be found often persisting even after the parasite has disappeared, and when found, the characteristic blackish or brownish pigment granules are definite evidence of malaria.

No satisfactory serological test has been devised. Some provocative methods such as injecting adrenalin or pituitrin or subjecting the suspect to severe exercise or extremes of temperature and fatigue conditions are said to bring the parasites into the general circulation. But these are seldom made use of in ordinary subjects.

Kala-Azar.—The next common protozoal fever is kala-azar described for the first time in 1882, by Clarke in Assam, who traced it as far back as 1869 by its native name of Kala-azar or black fever. Many theories regarding its true nature were upheld chiefly that of its being a malarial cachexia, even by great tropical disease workers like Leonard Rogers, and Gibs thought it was ankylostomiasis as he found the ova of this worm in the fæces of a majority of these cases, till the parasite was accidentally discovered by Donovan and Leishman in 1903 from the splenic pulp of cases of this fever.

To Rogers, we owe an account of the clinical signs and blood picture—patient and prolonged research has recently very nearly established the sandfly as the insect vector of this disease, though experimental transmission to the human being has not yet proved successful.

In 1904 Rogers cultivated the parasite and saw the flagellate forms.

The early methods of diagnosis were chiefly by finding the parasites in smears made from the pulp obtained by spleen and later by liver puncture. In children tibial bone marrow has been reported to harbour the parasites in large numbers.

Patient search in the peripheral blood smears—in thin or preferably thick smears up to as many as six slides in some cases —very often reveals the parasites in the leucocytes or large mononuclears. The blood here again presents an outstanding picture of marked leucopenia, with a marked reduction in the polymorphonuclears. The normal ratio of about 625 R. B. C. to 1 W.B.C. changes to so low a figure as of 1 W. B. C. to as many as 1500 or more of R. B. C.; in extreme cases to as many as 1 to 4000. This proportion of 1 W. B. C. to 1500 or more R. B. C. when found, is practically diagnostic, as it is not present in any other disease except kala-azar. The differential leucocyte count also shows a great reduction of polymorphos—a relative increase of mononuclears. Very often the eosinophiles are so few that none can be seen in a count of 500 leucocytes. The R. B. C. fall to between 2.5 to 4 millions but not so rapidly nor to such a great extent in proportion to the duration of the disease, as in malaria.

In addition to this blood picture, we have two very important tests to aid us in the diagnosis of this at one time obscure disease. These are the earlier aldehyde test of Napier and more recent Chopra's antimony test.

Napier's serum formalin test—'gel' test or aldehyde test—is positive in the majority of cases of over 3 months' standing. 1 c. c. of clear serum obtained from 5 to 4 c. c. of blood drawn from a vein is placed in a test tube 3 x ½" and a drop of commercial formalin added to it. In routine cases, the serum turns milky and sets in a firm hard mass under 3 minutes. In some cases between 2 to 3 months in duration, the serum has been found to turn into an opalescent whitish jelly in about ½ an hour. The chief diagnostic point is the milky white opalescent change in the serum. In case the serum is coloured with haemoglobin, it is found to turn a muddy chocolate brown after a few hours.

Chopra's serum antimony test—A heavy flocculent precipitate—was observed on mixing sera of K. A. cases with a 4% solution of an antimony preparation like stiburea. In practice a few drops of clear pure serum are placed in a small test tube 3" x ¼" and the 4% solution of Urea stibamine is allowed to run down the sides with a capillary pipette. In definite cases of K. A., a thick flocculent whitish preciptate at the junction of the two fluids is at once formed. The quicker the appearance the more certain is the diagnosis. In some early cases the precipitate appears in about 10 minutes. The character of the precipitate—its heavy flocculent nature, so flocculent that it cannot be easily shaken up—is the

main point to be observed. In doubtful cases a 1 in 10 dilution of serum is made with distilled water and the test is repeated and result confirmed.

The coagulability as well as alkalinity of the blood are greatly reduced in these cases. The plasma globulin increases and serum albumin diminishes. The normal euglobulin to serum albumin ratio of 2 : 4 is reversed very often—but with recovery the normal ratio gets re-established again.

The final test of a cure is the disappearance of the aldehyde test, normal globulin albumin ratio and still more conclusive is a negative splenic pulp culture.

In Dermal Leishmanoids and oriental sore or Delhi boil, similar parasites are seen in the smears from the skin lesions in the former case and ulcer edges in the latter. In the latter disease, the edge of the ulcer is cleaned and clear serum is obtained free from blood and bacteria by pushing in the tip of a sterile sharp capillary pipette. This is stained as for blood or cultured in the usual N. N. N. medium at a temperature of 20—22 C. The aldehyde test in these two diseases is however negative.

Much research still remains to be done in this disease though progress in treatment has advanced so much as to render the old time practically hopeless prognosis into a bright one, as the disease can now be cured by a few injections at a small cost with very little of suffering. If the sandfly is definitely proved to be the insect host and experimental transmission is successful, measures directed against the extermination of the insect host may in a short time convert a most common disease into a rare one.

Relapsing fever.—The next group of fevers are those caused by Spirochætes—chief of which are Relapsing fever, Louse fever or Tick fever, Leptospirosis and Rat-bite fever.

Lice and ticks are the intermediary hosts for the transmission of the parasite—the Spirochaeta Recurrentis, which was first discovered in blood of patients by Obermier in 1868 at Berlin. In 1877 Vandyke Carter found it in Indian patients in Bombay. Mackie in India in 1907 showed that the body louse was the important vector. Tick-relapsing and louse-relapsing fevers have certain points of difference clinically and geographically.

But in both the demonstrations of the parasites in peripheral blood smears taken at the height of the fever are diagnostic. The spirochaetes are well stained by the ordinary Leishman's stain and present a spiral shape with long 3 to 6 bends. It totally disappears from the blood in the apyrexial intervals. In children they are reported to be present during the apyrexial period also. The dark

ground illumination method of examining the fresh blood films is the best. Thick films dehaemoglobinised also serve where the parasites are likely to be few in number.

Rat-Bite fever.—Rat-bite fever is caused by the spirillum minus or morsus muris inoculated into man by the bite of infected rats. In 1915 this organism was demonstrated in the lymphatic glands draining the bitten site from the 10th to 13th days of illness and later in the blood stream by Takaki and Taniguchi. Laboratory diagnosis can be made in some cases by searching for this parasite in the serous fluid of the papular rash or from the exudate obtained from the site of bite by dark ground illumination.

Infective Jaundice.—Among Leptospira infections, chief is the infective jaundice caused by Leptospira icterohaemorrhagica. This parasite is present in the blood and urine of patients and has to be searched for in the blood and urine of inoculated guinea pigs at the height of fever. Blood of patients 2 to 5 c. c. citrated if necessary but not kept over 12 to 24 hours, taken before the 7th day of fever, and after that, urine centrifugalised aseptically—is used for guinea pig inoculation and the parasite looked for by dark ground method in the blood of the animal at the height of the fever.

Plague.—is another of the bacillary infection in the Tropics which, from time immemorial, has devastated continents. Caused by the plague bacillus—B. Pestis, it is primarily a rat disease and is conveyed to man by the bites of fleas infected by feeding on plague rats.

Great pandemics known as black death have spread all over the world wiping out 10 to 20 % of the population of the globe. All over Europe, in the middle ages, several pandemics took place, chief among them being the 1348 one, which is reported to have carried off over ¼ of the population of Europe. The 1665 attack killed over 70,000 people, about 1/7 of the inhabitants of London.

Imported from Hongkong, it appeared in 1894 for the first time in Bombay and spread as an epidemic to several other parts of India. From 1894 to 1907 over 10 millions of persons have been killed in India alone. The 1907 epidemic alone is responsible for a million and a half deaths. Since then, there has been a decline in the death rate, though there are several endemic areas where every year it increases in virulence and spreads locally in the earlier monsoon months or later towards the cold season.

From the earliest known records, the ancients seem to have

known the rats to be in some way associated with this disease. But the exact relationship has been discovered but recently. In 1894 when the pandemic started in Hongkong, over 20 to 30 were dying daily. Yersin working patiently with the dead and the dying around, discovered for the first time this organism. The role of the ratflea in transmitting plague was worked out with great ingenuity by the Indian Plague Commission, by experiments carried out in Bombay in rat proof compartments, where all fleas were removed by chloroforming the rats by combing out all their fleas. These plague infected rats could not infect healthy rats in the absence of fleas on both, though living in the most intimate contact. So also healthy rats were protected in cages of wire gauze flea proof and kept in close proximity to plague infected rats but never got the plague The rat fleas Xynopsylla cheopis and Xastia are mostly responsible as vectors of this disease. The B. pestis multiplies upto 45 days in the gastro-intestinal tract of these fleas and in some block the œsophagus in such large numbers that when the flea bites and sucks blood, the organisms are regurgitated and spread the infection. As the atmospheric temperature rises over 85° F. and the humidity of air is lowered, the rat fleas, especially the infected ones, die and the epidemic comes to a close.

The researches of Liston, Lamb and Haffkin of the Bombay Plague Laboratories,have given to the world the protective prophylactic vaccine which is giving immunity to and saving the lives of millions of people all the world over.

How Haffkine gave his vaccine to the plague stricken areas is described dramatically by David Master :—

> " While the natives of India were dying in their thousands, one man was striving to find a means of saving them. This was W. M. F. Haffkine who strove to produce a vaccine that would give an inoculated person protection against the plague."
>
> " Working without thought of self, Haffkine pursued his quest for a vaccine, grew his germs, took the deadly cultures of virulent bacilli and treated them. The bacilli were killed, but their poisons were unaltered. Haffkine knew this, realized that his culture was dangerous, that a small injection of it would perhaps slay as surely as a bullet from a gun; yet, before he could proceed with his vaccine, it was essential to test his vaccine on himself as he could not dare do it on others. For aught he knew, death might end

his experiments, but if success crowned his efforts, he knew that the lives of thousands would be saved."

"On January 10th, 1897, he prepared himself for the ordeal. But two men knew of his intention. Dr. Surveyor, was to make the injections, and the Principal of the Grant Medical College was to witness them. The brave scientist bared his left flank, the hypodermic needle penetrated his flesh and the deadly injection was made, the needle was withdrawn, the right flank bared, and another injection made. Then the hero dressed and awaited his fate with clear courage beyond all praise."

In all the forms of the plague—Bubonic, Septicaemic, Pneumonic and Pestitis minor, the finding of the B. Pestis is diagnostic of the disease. For diagnosis, smears and cultures from material, drawn from a bubo preferably before softening has begun, as the chances of finding the bacilli are few after softening has taken place, are used. In Pneumonic plague, the sputum smears showed the parasites. Blood smears and blood cultures are of use in septicaemic plague. Acocco-bacillus of typical morphology with characteristic bipolar staining is seen in smears. Culture of blood on ordinary agar, salt agar and inoculation of white mice at the root of the tail, are diagnostic methods, infected sputum is rubbed over a shaven area of skin or applied to the nasal mucosa of the animals.

The blood changes are: increase of R.B.C. to over. 5 millions or so in the early stages with a moderate leucocytosis, which in septicaemic cases rises, upto over 60,000 from the usual 20,000. Even 1,00,000 leucocytes per c.m. m. have been recorded. During the first three days of the disease, a marked increase in the lymphocytes is seen.

Cholera.—Cholera is another of the dreaded diseases of the tropics which prevails in seasonal epidemics. From the Gangetic basin several pandemics have originated. In the ancient days when it travelled along the trade routes being carried on by pilgrims and traders, it took about 5 years for the 1826 epidemic to travel from Bengal to Europe. In 1892, however, a similar pandemic originating at the Hardwar pilgrimage spread from India to south east Europe in 5 months due to better communications by train and ships. In this epidemic, over 4,00,000 deaths took place in Europe alone, mostly in Germany. Hamburg got the worst of it and out of 16,956 persons stricken, 8605 were dead by the time the epidemic burnt itself out. The death

roll in India was appalling. In 1883 the cholera pandemic had reached Alexandria in Egypt and a strange race started between Pasteur and Koch to investigate this disease. Koch and Gaffky from Germany, with all the necessary armamentaria of microscopes and animals, left Berlin and Pasteur, as he could not go himself, sent Emille Roux and Thuillier, the then youngest of these microbe hunters, to Egypt.

As these four scientists struggled hard and "toiled in dreadful rooms cutting up the bodies of Egyptians dead of cholera; in their muggy laboratory, sweat dropping off the ends of their noses on to the lenses of their microscopes, they shot stuff from the tragic bodies of just dead Alexandrians into apes, and dogs and hens and mice and cats. But while these rival teams of searchers hunted frantically, the epidemic began to fade away as mysteriously as it came." Just as they were about to depart home, cholera laid hold of Dr. Thuillier of the French Commission and he fell a martyr. Koch was one of those who carried the body of Thuillier to its last home and laying wreaths on the coffin said "They are very simple, but they are of laurel such as are given to the brave." Koch had in the meantime secured certain specimens in mysterious boxes, which he took back to Berlin and on further investigation and careful experimenting, gave out his discovery of the comma bacillus or vibrio of cholera. He had found it in most cases of cholera.

But he wanted to prove this bacillus as the cause. So he asked the Minister of State to send him to India and coming to Calcutta once again, began in his own inimitable, patient and exhaustive ways, those experiments which conclusively proved that "no healthy man can ever be attacked by cholera unless he swallows the comma microbe, and this germ can only develop from its like—it cannot be produced from any other thing, or out of nothing and it is only in the intestines of man or in the highly polluted water that it can grow". Koch received the order of the crown with star, at the German Emperor's own hand, about this time.

For laboratory diagnosis, a fleck of mucus from the 'rice water stools' is taken and direct smears fixed and stained with 1 in 10 carbol fuchsin are examined. The typical comma shaped organisms can be identified as shoals of fish swimming in a stream. Hanging drop preparations of a drop of the motion show the scintillating rotatory movements, if vibrios are present. If present in large numbers, direct plating on alkaline agar is done. If few, an alkaline peptone water tube is inoculated with

a couple of loopfuls of the mucous flakes and incubated for 6 hours. If a pellicle is present at the end of this time, it is examined for the characteristic vibrios by hanging drop method and staining. If few, another tube of peptone solution is inoculated from the first tube, and incubated for a further period of 6 to 8 hours and then plated out on alkaline agar. From the plates the typical colonies are fished out and emulsified or if not sufficient, transferred to an agar slope and the resulting growth is emulsified and titrated with specific high titre anti-cholera serum. Agglutination of 1 in 1000 with a known anti-serum is conclusive of the organisms isolated being the cholera vibrio.

When a rapid diagnosis is needed, the first tube of alkaline peptone solution is incubated for about 16 hours and with the resulting growth a macroscopic agglutination test in capillary pipettes is done with 1 in 80, 1 in 160 and 1 in 320 dilutions of high titre sera and if the growth is agglutinated in the highest dilution, it is taken as proof of its being the cholera vibrio.

Later, the sugar reaction, cholera red reaction and haemolytic reaction are done with the growth from the alkaline agar tubes.

The patient's blood serum however, in the early days when a diagnonis is so important, does not agglutinate known strains but after a week starts agglutinating, reaching a high titre in about 3 to 4 weeks.

Dysentery.—The dysenteries form the next common group of bowel diseases. Bacterial, protozoal and helminthic in origin, very often mixed types are met with, but when present in epidemic forms, can be diagnosed by the laboratory microscopic examination of fresh specimens of stool, and by culture methods where necessary.

Epidemics of dysentery are very common. In the autumn months almost every year a large number of dysentery cases occur.

In 1898 Prof. Shiga of the Kitasoto Institute of Japan isolated the bacillus from acute cases of dysentery. In 1900 Krause also found similar bacilli in Europe. Later Dr. Flexner of the Rockefeller Institute found another organism slightly differing from the Shiga Krause bacillus in that it ferments mannite. Six different types of the Flexner group have been identified subsequently.

Acute, highly toxic forms of dysentery are most often due to the Shiga infection, while the mild forms and more chronic types are very often due to the Flexner type, though mixed infections are often seen.

For the cyto-diagnosis of the acute forms of dysentery, a

fresh specimen of the stool, as early as possible in the course of the disease, has to be examined. Preponderance of large swollen polymorphonuclear leucocytes, with clear cut ring nuclei, which constitute over 90% of the total cellular elements, presence of macrophage cells, very few or almost no micro-organisms, with an alkaline reaction, point to a certain diagnosis of Bacillary dysentery.

In the amoebic form, presence of the characteristic entamoeba histolytica, actively motile with pseudopodia in fresh specimens, some with ingested R. B. C., presence Charcot Leydan crystals; disintegrated epithelial cells, R. B. C. in large numbers but mostly clumped together, very little of cellular exudate, polymorphos very often damaged with entrusted nuclei but micro-organisms in very large numbers, with an acid reaction afford a certain means of diagnosis. In the more chronic or latent forms, a search sometimes daily for a week is sure to reveal the cysts. Only after a seven days' search has proved negative, can amoebic infection be excluded as very often some specimens do not show the amoeba or cysts. Even in the same sample of stool one part of the blood-stained mucus will reveal the entamoeba while another does not contain any. Very often by the naked eye appearance of the stool, the number of times the patient passes and the alkaline or acid reaction to litmus one can arrive at a tentative diagnosis. The bacillary dysentery patient is 'glued to the commode' with scanty stools containing bright blood red, gelatinous viscid mucus often odourless when fresh and alkaline to litmus. The amoebic motion is very offensively smelling of decomposed blood and like the liver abscess pus, resembles anchovy sauce and consists of faeces mixed with blood and mucus, most often congealed darkish blood. It is generally copious and not at so frequent intervals as in the other variety and is strongly acid in reaction when tested with litmus paper.

Isolation of the dysentery bacilli is another diagnostic procedure. For this, the stool should be as fresh as possible and collected in a dry bed pan and no urine should be passed in it. A loopful or two of freshly passed blood and mucus is picked out and cultured on suitable media. The earlier in the course of the disease this is done, the better are the chances of obtaining the growth and the fresher the stool more certain is the chance. Preferably at the bedside of the patient cultures have to be taken. If the motion has to be sent to some distance, Teague's medium—a 30% solution of glycerine in 6% saline is used for mixing with the faeces, 1 part of faeces containing the blood and mucus and two

parts of this solution will keep the bacilli alive for several hours. After isolating agglutination tests with specific high titre sera afford a conclusive test of the type of bacilli.

In chronic cases of dysentery, the serological test similar to the Widal, with the the patient's serum and known types of bacilli is employed to determine the nature of the infection. In Shiga types a 1 in 100 or more, positive reaction and in Flexner a 1 in 100 or more, positive is diagnostic enough.

Leprosy.—is the chief infective granulomatous disease of the tropics. During the middle ages it was common in Europe. Known from ancient Hindu, Chinese and Egyptian writings to exist from very early times, it is believed to have spread from Asia into Europe by the returning hordes of conquering Greeks and Romans. India is heavily infected ; some portions of Bengal and Madras presidency, Central Provinces and the coastal strip of the West Coast, more so than the rest.

Hansen in 1871 for the first time discovered the bacillus of this disease. Since then methods of strict segregation adopted succesfully have banished this disease from Great Britain and Europe completely. Much work has been done to solve the problem of transmission of this disease. But the actual mode of infection is not yet known with certainty.

The bacilli are present in the nasal secretions of almost all nodular cases and in about 30% of early skin and mixed types. Nerve cases show these very rarely if at all. Ulcerating nodules are sources of very heavy infection but not so the trophic ulcers of later stages of nerve cases as these do not contain any bacilli.

The earliest lesions are negative to bacteriological examination. In examining early cases or contacts, strip the patient as far as possible and place him in a good light The light coloured depigmented spots should be examined for loss of sensation to light touch, for cotton wool or a wisp of rolled up paper. If present, bacteriological examination is done but very often this is negative. But the surrounding red coloured areas of skin round the anaesthetic decoloured patch may often show the bacilli. The early thickened skin patch must be looked for and a piece of skin including the deeper connective tissue layers of the skin must be snipped off by a sharp pair of sterile scissors curved on the flat. The snipped portion of the skin is placed over a slide with the undersurface in contact with the glass and smeared well over the surface. This smear is stained by the usual method of staining. The smear is fixed and hot carbol fuchsin is poured on the slide and warmed till steam rises and a few bubbles form. It is set aside

to cool for about 15 minutes and the stain is then poured off and decolorisation carried out with 10% sulphuric acid for 1 minute or till all the red colour is almost washed out and a few drops of absolute alcohol are poured on and drained off. After counter-staining with aqueous methylene blue and drying, examination with oil immersion lens will reveal the characteristic bacilli in clumps, free or in large cell groups. In some, where the bacilli are few and the patch is already slightly anaesthetic, numerous red granules are seen showing that the breaking up of bacilli has started. When absent, any nodule on the lobes of the ear must be looked for and a minute linear incision with a very sharp scalpel or a big sized surgical needle is made. The opened inner surface of the wound is gently scraped and the juicy pulp taken and smeared on two slides for microscopic examination.

Clamping a juicy nodule and pricking the same and collecting the drop of 'Lepra juice' which extrudes on a slide also yields the best specimens of bacilli. In some rare cases, blood obtained by finger prick or from a vein is used for thick drop preparation and these thick dried specimens are dehæmoglobinised and stained by the usual method and show some bacilli.

Nasal smears made by rubbing a pledget of cotton wool, wound round a forceps tip, over any oedematous or red patches in the anterior nares and smearing the mucus so obtained are similarly stained and examined. Where the skin lesion is negative, it is very rare to get a positive nasal smear.

Sedimentation test has been used of late and a finding of a lower rate than normal is in favour of a positive diagnosis.

The most recent and fairly accurate test is reported to be the use of formalised sheep corpuscles with suspected patient's blood serum for the sedimentation. If the patient is suffering from Leprosy, rapid agglutination of the sheep corpuscles and sedimentation takes place very quickly. This reaction has so far never been positive in any other disease as studied by Rubino.

Filariasis.—Filariasis is another disease under which our presidency groans in common with several tropical countries. Microfilaria bancrofti was found by Demarquay as early as 1863 in hydrocele fluid. Lewis established the fact of its being a blood parasite. The adult was found by Bancroft in 1876 at Brisbane in Australia. Manson in 1878 worked out and demonstrated the development of the embryos in the intermediary host, the mosquito. The nocturnal periodicity was also described by him.

The microfilaria are present in peripheral blood in large numbers during and even long after an attack of fever especially

at night. Diurnal specimens may show in rare cases, a few of these in several specimens. But drops of blood taken at night round about 12 midnight, show large numbers of these. The patient should go to sleep or remain in the dark for at least an hour before taking the blood. The finger is pricked as usual and a big sized drop is allowed to fall on a slide and smeared with the tip of the same finger over an area of about ½ square inch. Two slides with two such dabs on each slide are dried and examined next day. The dried blood is dehaemoglobinised and stained with any of the blood stains and examined under the ordinary low power, ⅙ or even ⅓ will show the coiled up forms of the microfilaria. A fresh specimen obtained by placing a big drop of blood on a slide and covering it up with a ¾ square cover glass, the edges of which are then ringed with vaseline, will show the live and motile form of the microfilaria actively wriggling about in the blood. A thin blood smear is made at the same time as the thick drop specimen. This usually shows a leucocytosis with marked Eosinophilia which is very often diagnostic. Over 50% of Eosinophiles are seen in some cases. These embryo forms are very often absent in cases where there is elephantiasis, lymphscrotum etc., The urine in cases of filarial chyluria shows these microfilaria in the sediment on centrifugalising.

The warfare against man's microscopic foes is relentlessly going on. Many are still unknown and several though known are unseen as the filtrable viruses. Master-minds in their endeavour to lift the veil that hides these invisible foes of humanity have succumbed a prey to the very diseases they were investigating as witness the fight of Naguchi against Yellow Fever. For several decades in Mexico, Panama regions and South America this famous scientist of the RockeFeller Institute fought this dreaded disease till he came to the Gold Coast of Africa in 1928. Broken down in health, with swollen feet and puffy face, he ventured across the Atlantic and worked at his pet subject. Finally, when, as he believed he had successfully given to the world his discovery of the Leptospira of Yellow Fever, two days before he was scheduled to return home with his studies completed, he fell a prey to the very disease he had so far successfully investigated. "To trace his romantic career involves a consideration of infectious diseases throughout the world", was said in tribute to him.

To solve the various problems of many of these tropical diseases that flesh is heir to, and to unravel the workings of the human machine, many generations of scientists will have to carry

on this struggle and one is led to the conclusion with Harvey who spoke for all ages when he said that, "All we know is still infinitely less than all that still remains unknown."

References :—

1. *Manson's Tropical Diseases, 1935.*
2. *Tropical Medicine—Rogers and Megaw.*
3. *Man versus Microbes—Nickolas Kepeloff.*
4. *Practical Bacteriology—Blood Work and Parasitology—Stitt, 1927.*
5. *The Conquest of Disease—David Masten.*
6. *Microbe Hunters—Paul de Kruif.*
7. *Recent Advances in Tropical Medicine—Rogers, 1929.*
8. *Practical Bacteriology—Mackie and McCartney, 1934.*
9. *Text-Book of Bacteriology—Zinser and Bayne Zones.*

Diagnosis and Treatment of Cholera

BY

DR. P. T. PATEL, M.D., M.R.C.P. (LOND.),
D. T. M. & H. (CANTAB), F. C. P. S., (BOM.),

Medical Superintendent, City Fever Hospitals, Arthur Road, and Maratha Tuberculosis Hospital, Hon. Physician K. E. M. Hospital, Parel, Bombay.

CHOLERA has been known in India from ancient times and Charaka and Sushruta both have described graphically the symptoms which are present in the disease. It has been described also by Arab and Greek writers of pre christian era. The word "Cholera" means a spout, which name is applied to the disease because the violent purging resembles gushing out of water from the spout of a kettle. Great epidemics have been described as early as the fourteenth century and five separate cholera epidemics of appalling magnitude occurred during the nineteenth century alone.

There is no disease coming on so suddenly and assuming a grave outlook amongst infectious diseases commonly prevailing in this country as cholera. At the same time it is remarkable how valuable lives can be saved and incidence and mortality of the disease can be reduced to 10 to 15% by proper and rational

methods of diagnosis and treatment. As a vast amount of controversial and conflicting literature has appeared on the diagnosis and treatment of cholera, it is necessary to take stock and to present a precise statement of the existing facts based on the statistics and one's personal investigation and experience.

All the cases presenting acute gastro-intestinal symptoms with collapse should be suspected to be cholera and immediate steps should be taken to arrive at a correct diagnosis.

The diagnosis of cholera is partly clinical but mainly bacteriological. The main diagnostic points are as follows:—

(1) Copious vomiting.
(2) Copious diarrhœa.
(3) Rice water stools.
(4) Suppression of urine.
(5) Muscular cramps.
(6) Leucocytosis with increase of large mononuclears and relative diminution of small lymphocytes.
(7) Increased specific gravity and diminished alkalinity of blood with great loss of *NaCl* content.
(8) Symptoms of collapse:—Cold clammy skin, fall of blood pressure with weak and imperceptible pulse and whispering voice.
(9) Presence of cholera vibrios in the stools.
(10) Agglutination and Pfeiffer's reactions.

It is a common practice especially during an epidemic that cases of food-poisoning, early cases of bacillary dysentery, some cases of subtertian malaria, cases of acute metallic poisoning, cases of gastro-intestinal type of influenza and other fevers are diagnosed as cases of cholera and although in a majority of cases it is possible to clinically arrive at a fairly correct diagnosis, in a few others only careful bacteriological procedures alone, reveal the true nature of the disease.

It is especially difficult to differentiate true cholera from fulminating cases of food-poisoning; in both there may be copious vomiting, diarrhœa, typical collapse and the most agonising cramps.

According to Tomb[1] the differential features of the two diseases are as follows:—

Symptoms.	Cholera.	Food-Poisoning.
Diarrhoea.	Painless, precedes vomiting.	Associated with severe intestinal pain, generally follow vomiting.
Vomiting.	Causes no distress, watery, copious and projectile, follows diarrhoea.	Often violent and distressing, vomit consists of food and is never watery, copious or projectile. Generally precedes diarrhoea.
Nausea.	Absent.	Constant.
Retching.	Rare.	Constant, often severe.
Acute abdominal pain.	Rare.	Constant.
Tenesmus.	Absent.	Common.
Stools.	"Rice watery" and copious.	Liquid but faecal and offensive. Never colourless or copious.
Urine.	Complete suppression	Never suppressed.
Muscular cramps.	Constant. The severity depending on the amount of fluid lost from the tissues.	Present only in very severe cases. Often associated with tingling and numbness, mild and confined to the extremities.
Collapse.	Frequent. Chiefly from loss of fluid.	Never from loss of fluid. In severe cases faintness or syncope may occur from toxaemia.
Fever.	Surface temperature below normal.	Axillary temperature 99—102° F. accompanied by shivering in severe cases.
Headache.	Absent.	Frequent.

Stools in Cholera.—It is important to bear in mind that the so-called "Rice water stools" *i.e.* consisting of an opalescent colourless fluid with little odour and stools with white flocculent matter in suspension in majority of cases, is a common feature of cholera, and is the pathognomonic sign of the disease; still there are cases of cholera in which the stools are brownish containing faecal matter throughout the entire course of the disease.

In a few others they may be of a reddish colour due to haemorrhage.

Bacteriological Diagnosis.—The following is the procedure we have adopted and which has given us admirable results.

(1) All patients admitted as cholera are straightaway given a bowel wash of

Soda Bicarb	...	grs. 160
Sodi Chloride	...	„ 90
Aqua	...	pint. 1

and the washing collected for further examination. This enema serves a valuable two-fold purpose of evacuating the large intestine of its toxins and other deleterious matter and giving immediately useful material for microscopic and cultural examination. 5 to 10 c. c. of this material are placed in a sterile test tube and sent to the Laboratory.

(3) On grease-free slides these films are made from the whitish flocculli; the slides are kept slanting in order that the films may dry, and then fixed with heat by gently passing through the flame two or three times and then stained with dilute carbol fuchsin. The stain is allowed to act for about two minutes, then washed under running tap water, allowed to dry and then examined with the 1/12th objective. In typical cases, the vibrios can be easily made out, almost in a pure culture. In a few cases one may not succeed in finding the vibrios in this way even after repeated search. In some cases one may find a few vibrios but on further examination they may not be found to be agglutinable.

Treatment.—*Historical.*—Although cholera has been known in this country for centuries, there has not been any real advance in its treatment till recently. In 1833 they used to perform venesection as in all fevers and give opium and calomel—usually with disastrous results. In the middle of the last century, Dr. George Johnson during the third and fourth European Epidemics, advocated the deadly "evacuant line of treatment with castor oil or massive doses of calomel", on the false assumption that there was no relationship between the loss of fluid from the blood in cholera and the mortality, with the result which is too well-known to need further criticism.

In the New York epidemic of 1849, the so-called "Sun

Cholera mixture" was very popular especially as it considerably relieved the symptoms.

It contained. Tinct. of opium.
Tinct. of Rhubarb.
„ of capsicum.
Spt. of Camphor.
Essence of Peppermint.

All in equal parts. Dose being 15 to 30 drops in water, to be repeated in fifteen minutes if necessary.

Later workers advocated the administration of opium in combination with the purgatives or by itself. There is no single remedy which is more harmful in the treatment of cholera than opium and its derivatives. If nothing should convince its advocates, at least the brilliant experiments of Koch, who used opium in animals to quieten the intestines preceding the administration of cholera vibrios to precipitate a severe attack of the disease, ought to be an ample proof of its dangers. Opium after a preliminary relief of symptoms and a transient cessation of diarrhoea invariably leads to more extensive absorption of cholera toxins, greater injury to the renal parenchyma and generally a fatal uraemic termination with suppression of urine, progressively increasing drowsiness leading to cyanosis and coma or a maniac delirium in which the patient tries to run away from his bed and dies of heart failure.

Rogers[2,3] tried 56 alternate cases with a single hypodermic injection of morphia at two different seasons of the year, with the remarkable result that with the drug the mortality was 39.3 % against 25 % in the controls; and 25 % of the opium treated cases died of uraemia against only 3.57 % of controls.

We had also cases which had castor oil or opium given to them accidentally before admission: although they were given all the benefits of the modern treatment, they never revived.

Baird in 1893 advocated opium and sulphuric acid dil. before the collapse sets in; sulphuric acid only tends to increase the acidosis which is an invariable pathological feature of the disease.

The great depletion of the body fluids that results, due to vomiting and profuse evacuations from the bowels, led workers even from early days to the administration of simple fluids. As early as 1831-32 in Edinburgh, Latta and Mackintosh used isotonic salines with slight improvement. The mortality in their series was 84%. Wall had a death rate of over 70% in 1893. And in the

10 years preceding 1905, our Calcutta Medical College Hospital had 60% deaths in over 1,000 cases.

The treatment of the disease has been completely revolutionized and placed on a scientific basis since 1908 when Rogers' researches on the changes produced in blood by the disease, led to the adoption of hypertonic salines and later still to the use of alkaline salines in combination with the above, when Sellard [4] in 1910 in the Philippines, made the important observation that the alkalinity of the blood is also lowered in cholera. Rogers recognised that not only is there a loss of fluid by the tissues but also a marked loss of body salts mainly *NaCl* both of which should be replaced and argued that if salts were introduced in hypertonic solution, osmotic currents could be determined towards the blood from the bowel instead of away from it as induced by the toxins. Benjamin[5] Moors moreover later pointed out that the chlorides combined with the cholera toxins in the blood, rendered them innocuous and led to their being excreted by the kidneys. The recognition of the gradually increasing reduction of alkalinity of blood in cholera and the adoption of intravenous alkaline salines along with the hypertonic, led further to the reduction of mortality and especially the uraemic complications.

The discovery of cholera vibrio naturally led to the trial of several intestinal disinfectants but in spite of the varying experiences of their authors and in some cases of good results perhaps published on insufficient data, most of them have not stood the test of time.

A mixture of sulpho-carbolates of zinc 2 grs., soda 2 grs. calcium 3 grs, dissolved in peppermint had been tried. O'Gorman and Waters advise 15 minims of cresol or izal dissolved in 1 ounce of water every 2 hours. Some recommend cyanide of mercury in 1/10 gr. doses every 2 or 3 hours. Cantani advised slow intestinal injections of 3 to 4 pints of a 1% solution of tannin.

It was only when it was realised that the harmful symptoms in cholera were due to the effect of the toxins, that oxidising agent *e.g.*, pot. permanganate was introduced, which further reduced the mortality from this disease. The use of bacteriophage and serum against cholera is also reported to have reduced the mortality still further, but the data for such a belief are very meagre at present.

J. W. Tomb[6] in 1923 also found that the essential oil mixture modified by him and others, was very effective in early cases, and it also acted as a good prophylactic in a drachm dose daily.

I need not go into the history and origin of Bacteriophage here.

Since 1929 several experiments were performed with bacteriophage in the treatment of bacillary dysentery and encouraged by the goood results obtained in Brazil, Sudan and Italy in 1924 and 1925, bacteriophage was first tried in cholera by D'Herelle and Malon in various villages in the Punjab and they report 6 deaths in 70 cases treated by bacteriophage (a mortality of 8½%) against 143 deaths in 240 control cases. These workers assert that the bacteriophage are ultra microscopic living organisms which prey on or render non-virulent, the cholera vibrios, which in their absence regain their virulence in a short time in the human intestines. The presence of the cholera bacteriophage may either bring about a total destruction of the vibrios or they may live in symbiosis with phage in a less potent form, with the production of the carrier.

They classify bacteriophages as Nos. 1 to 10 in proportion to their strength and say that only Nos. 9 and 10 are sufficiently powerful and can destroy all the virulent vibrios in culture and hence useful in treatment.

In our cases during the last 2 years, we subjected no less than 20 stools from convalescent patients to the method of filtration and preparation of phage as suggested by D'Herelle[8] and subsequently tested them for the phage action against cultures of vibrios obtained from the same patients but no case could demonstrate the evidence of any phage.

J. Taylor[9] and others also arrive at the following conclusion in their cases at Rangoon. A series of 33 sporadic cases of Cholera were observed; 19 cases being used as controls and 14 treated with a phage of high activity

The respective mortalities for the two groups were 53% for controls and 57% for the treated cases. The great majority of cases recovered showed no evidence of bacteriophage in the stools active against the patient's own vibrios. Taking into consideration all these facts, the subject of bacteriophage in the treatment of cholera is still inconclusive and needs further work and trials in the different parts of the country. Although Asheshov[10] succeeded in reducing the mortality to 2.8% in 140 positive severe cases with combined saline and bacteriophage treatment, one cannot help believing that it is too early to hope to get the same results unless a phage of uniform potency is available for extensive trial throughout the county and everybody gets saline and other treatment uniformly.

A rational treatment of cholera then must naturally aim at the achievement of the following features in the disease, and will

vary in individual cases according to the clinical conditions of the patient suffering from the disease.

1st stage *Diarrhœic*	Antiseptic action by essential oil mixture, neutralization of toxins by the oral administration of oxidising agents or injections of potent antitoxic sera, or destruction of vibrios if possible by the administration of Bacteriophage.
2nd stage	Replacement of body fluids and salts by injections of hypertonic salines. Prevention and combating the acidosis by intravenous injections of alkalies and glucose.
3rd stage	Reaction, Ureamic and other types: The treatment of symptoms and complications as they arise.

Clinically it is possible to recognise roughly three well marked stages of the disease as follows:—

(1) The diarrhœic stage.

(2) The stage of collapse.

(3) The stage of reaction where-in hyperpyrexia, suppression of urine and uræmia and complications like pneumonia, enteritis, asthma andothers are the outstanding features.

1. *Diarrhœic Stage.*—The first thing is to put the patients to bed. A flannel jacket is both comfortable and prevents the loss of body heat, an important point in the disease. An alkaline saline enema referred to in the 2nd Stage is immediately given first to wash out the large bowel and then gradually about a pint of fluid is introduced for absorption with the stop-cock of the enema can well adjusted in order to ensure a gradual flow preferably by drops. A rapid flow only results in the immediate rejection of the saline enemata by the hypertonic bowel. This process is repeated every three or four hours and kept up until the normal amount of urinary flow (50 oz. per day) is restored and then it is gradually omitted.

In this stage, vomiting is an outstanding symptom and for this purpose and also for its antiseptic value, the essential oil mixture given in drachm doses diluted with half an ounce of water every hour for 6 to 8 doses is found satisfactory.

I have modified the essential oil mixture so as to increase its

antiseptic value by adding oil of cinnamon for its greater antiseptic power and camphor and atropine for their stimulating action on heart and kidneys respectively. The essential oil mixture has been put on the market by the Alembic Chemical Co. of Baroda and other companies in Bengal under the names of Cholerosol and Tesol and the modified mixture has the following composition :—

One fluid ounce respresents.

Liquor Atropine	... 2 mins.
Camphor	... 4 grs.
Tinct. Lavendula Comp.	... ½ dram.
Acid Sulphuric Aromatic	... 1 „
Spt. Aetheris	... 2 „
Oil. Juniper	... 20 mins.
„ Cajputi	... 20 „
„ Cinnamoni	... 10 „
„ Caryophilli	... 10 „

Nothing as a rule is tolerated and is given by the mouth except small pieces of ice or iced water to allay thirst. If, after 24 hours the vomiting has ceased, plain dilute coffee and glucose with grs. xv of soda bicarb added to each feed, may be given in as large quantities as possible and then rice water and these continued into the stage of reaction. Milk soups and jellies and other articles containing animal albumin, as a rule never agree in cholera and are liable to cause relapse and should be avoided for several days after the reaction. Starchy foods beginning with either arrowroot or cornflour and wheat may be given first and then, when the diarrhœa completely stops and bile appears in the stools, custard, soft rice and other light food allowed.

After the full course of essential oil mixture, the patient is given the Potass permanganate pills (enteric coated) 2 grs. each. Two of these are given every 15 minutes and continued for 12 to 24 hours till the stools become green and less copious. In the second 24 hours and in severe cases this is repeated. In the mild cases they are given 4 hourly. These pills are made with kaolin and vaseline and coated with one part of salol and five parts of Sandarach Varnish with Keratin. The most important point to remember is that the patients should be made to understand to swallow them entirely without chewing.

Atropine first suggested by Lauder Brunton in 1894,

owing to its effects on the symptoms of muscarine poisoning, which are similar to cholera, should be given hypodermically twice a day in doses of 1/100 gr. It lessens the number of saline injections to be given and somehow helps the kidneys to function normally. It is however important to bear in mind a few contra-indications to its use as a routine. It is a known fact from pharmacology that atropine does cause paralysis of the myoneural connections of the intestines and rise of temperature and it is necessary to avoid it in cases with paralytic distension of the abdomen and cases with hyperpyrexia or tendency to maintain high temperature.

2. *Stage of Collapse.*—The most important point which must be attended to is to restore the circulation by the introduction of hypertonic salines by all possible routes. As a rule in collapsed cases we omit the essential oil treatment and start with the saline and the pills. The hypertonic saline has the following composition:—

Sodium Chloride	... 120 grs.
Calci Chloride	... 4 „
Distilled Water	... 1 pint.

In an early case with the pulse of fairly good tension, it can be given subcutaneously. One can easily give 4 pints in the loose axillary tissues followed by linseed meal poultices to the region to favour rapid absorption. In severe and pulseless patients the intravenous route is the only method available and in fat subjects and especially in women, one has to cut down upon a vein and tie a cannula. In children one may succeed in giving it in the internal saphenous vein in front of the malleolus; if not, the intraperitoneal is the only available route for introducing the saline rapidly into the circulation. Many workers advise testing the specific gravity of blood in order to gauge the amout of saline to be given, but this is not feasible in a rush of cases or in private practice. With a little practice, one can fairly determine the quantity to be administered by feeling the pulse. We find here that an ideal quantity is one which gives a full bounding pulse without, in any way, producing untoward and warning symptoms such as a sense of oppression in the chest, breathlessness or hæmoptysis. The temperature of the saline should be the normal body temperature, if the patient is not cold. If the rectal temperature is not over 97° C, the saline should be warmed to 102°; if the rectal temperature exceeds 102°, the saline should be given at about 89° *i.e.* the temperature in this country.

In addition to the above, we give 1 pint of alkaline saline always intravenously.

The alkaline saline has the following composition:—

℞ Sodi Chloride	... 90 grs.
Aqua Distil (sterilized)	... 1 pint.
Pul. Soda Bicarb (sterilized by dry heat)	... 160 grs.

The above two to be mixed up just before use.

3. *Stage of Reaction.*—In this stage the restoration of the normal urinary flow and avoidance of uræmia is the prime consideration and the patients are given 1 pint of the above alkaline saline along with one pint of 5% solution of glucose intravenously once a day reinforced by rectal saline with 5% glucose, very slowly by the drop method every 4 hours until about 50 oz. of urine is passed during 24 hours, and then at longer intervals till a free flow of urine is established.

Pituitrin ½ c. c. injected once or twice a day may also help. Hot moist fomentations over the loins every 4 hours and dry cupping of kidney regions twice a day, are invaluable in starting the flow of urine and relieving the congestion of kidney if there is suppression. In addition, if pulse and the general condition of the patient permit, electric baths for 15 minutes 4 hourly may be tried.

For circulatory failure strophanthin 1/100 gr. intravenously or camphor grs. v in ether should be given 4 hourly or oftener.

For persistent diarrhoea, large doses of bismuth salicylate with kaolin and tannigen are helpful.

The following statistics from Arthur Road Hospital prove the efficacy of the modern treatment:—

BEFORE

Year.	No. of Cases Treated.	Mortality rate per cent.
1912—1920	2235	52 %.

MODERN TREATMENT.

1921—1936	600	33 In reality, 15 % after excluding moribund cases died within a few hours of admission. Hence they cannot be included in the statistics as failures in saline treatment.

Out of 109 patients treated in 1931, 83 were serious cases which were 'clinically collapsed' within an hour or so after the onset; the other 31 were mild attacks not requiring hypertonic saline treatment. Out of 31 deaths in 1931, 12 patients were in a moribund state on admission or died within a few hours after admission to the hospital, so that they cannot be included as failures from saline treatment. Thus out of 90 known bacteriologically positive cases of cholera treated in this hospital, no lees than 70 patients required saline treatment on admission. These gave a mortality of only 17%.

References:

1. *J. W. Tomb—Indian Medical Gazette. September, 1930*
2. *Rogers—Bowel Diseases in the Tropics.*
3. *Rogers—Recent Advances in Tropical Medicine.*
4. *" " "*
5. *" "*
6. *J. W. Tomb—Indian Medical Gazette. 1924 Vol. LIX 233.*
7. *D'Herelle, Malone and Lahiri—Transactions of the 7th Congress of Far Eastern Association of Tropical Medicine, Vol. 2,290.*
8. *D'Herelle, and Malone—Indian Journal of Medical Research Memoir, 14, Feb. 1930.*
9. *Taylor, Greval and Thant.—Indian Journal of Medical Research, July, 1930.*
10. *Asheshov, S. Khan and Lahiri.—Indian Medical Gazette, April, 1931.*
11. *P. T. Patel—Indian Medical Gazette, Nov. 1924, and Infectious Diseases and other Fevers in India.*

Cholera

With special reference to Cases as seen in the Cholera Ward of the Campbell Hospital, Calcutta

BY

B. C. CHATTERJEE, M.B., D.P.H., D.T.M.,

Hony. Physician in Charge, Infectious Diseases Wards, Campbell Hospital, Calcutta, and Teacher of Hygiene, Campbell Medical School, Calcutta

Definition.—An acute specific gastro-intestinal toxaemia caused by Koch's Cholera Vibrios, endemic in India and other eastern tropical countries, clinically characterised by copious watery evacuations *e.g.*, Diarrhoea and vomiting followed by collapse, cramps, suppression of urine and no pulse or very feeble pulse at the wrist.

History.—The authentic history of cholera Asiatic dates from the year 1817 when there was a virulent outbreak in Lower Bengal and the high mortality from the disease attracted the attention of the people. Previous to that date, it is believed that the disease prevailed in India and spread at intervals throughout Asia as it does now, but it is doubted whether the disease overstepped the Asiatic borders. Both, the Sanskrit writers of about 400 B. C. and Hippocrates, gave descriptions of outbreaks which might well have been cholera. Since 1817, Asiatic cholera had been studied with keen interest wherever it had prevailed and the facts regarding its prevalence in India and elsewhere had been recorded with great minuteness and care.

The story of cholera is a very simple and singularly interesting one. It presents the picture of a deadly disease prevailing perennially in certain parts of India, which have been identified as its house or field of endemic lodgement, where it waxes and wanes but never altogether disappears. A sharp shooting outbreak always takes its start initially from its endemic habitat after a recrudescence of more than usual severity and diffuses and spreads itself along the ordinary routes of commerce and pilgrimage throughout the inhabited world. The story of cholera is thus a tale of repeated invasions, presenting a remarkable similarity. It is not easy to define with accuracy the initial endemic centres from which these invasions have proceeded. Some authorities assert that there are several such centres in India, the main one being doubtlessly the delta of the Ganges and the vast creek and

river-netted alluvial plain which lies south of its confluence with the Brahmaputra. How far the endemic areas extend up the Gangetic and Assam Valleys, or whether other deltaic regions in India, as of the Godaveri and the Kaveri rivers are also endemic areas or not, it is not easy to describe. It has been asserted that the disease is endemic in Bangkok and in perhaps other parts of Siam. It is interesting to note, that even in its endemic haunts, cholera presents most of the features which characterise its epidemic peculiarities. It rises and falls, and travels onward. Every time cholera has spread beyond Indian limits, it has been always preceded by an outbreak in India of marked and unusual violence. Its westward diffusions have naturally attracted the greatest attention, but eastern diffusions have also occurred, to the Straits Settlements, Siam, China and Japan, which have not been so carefully investigated. The western diffusions have taken place by three routes namely, (1) through Afghanistan, Persia, and Central Asia, to Eastern Russia, along trade routes crossing or bordering the Caspian Sea and thence into the interior of Russia along the Volga, (2) by the Persian Gulf to Turkish Arabia and Persia, thence to Turkey in Asia and along or across the Black Sea to Constantinople and the Danube and (3) by the Indian Ocean and Red Sea to Aden and Mecca and thence to Egypt and the countries bordering the Mediterranean. The disease prefers a land route to a sea route and has sometimes travelled westward by more than one route.

History of Epidemics.—*Geography.*—The epidemic distribution of cholera is only limited by means of communication, seaports in all parts of the world being liable to outbreaks, while inaccessible countries *e.g.*, Central Africa, have so far escaped. In order to make out any adequate idea of the epidemic distribution of cholera, it is necessary to outline very briefly the six main pandemic outbreaks of the disease during the last century, as these illustrate the different routes by which the disease has spread from the endemic areas over extensive portions of the globe.

Firstly, we had the overland route from the north westerly Punjab Province of India through Afghanistan and Persia to Southern Russia, which was the route preferred by the epidemics of 1826—37, 1866—70, 1892—96. The first of these spread very slowly owing to the difficult state of communications nearly a century ago. Thus cholera was prevalent in Bengal in 1826 ; the Punjab was heavily affected from the Hardwar fair in 1827, Afghanistan in 1828, Persia in 1829, Russia in 1830, and Western Europe including Great Britain in 1831, the outbreak

thus having taken five years to spread from Bengal to Western Europe.

The second epidemic of the 19th century from 1840—1849 also travelled overland but by a very roundabout route, according to the description given by N. V. Macnamara, from Calcutta to Singapore and China, and then westward through central Asia to invade Burma from the north and the Punjab from the west and also passed on through Afghanistan and Persia to Russia, Northern Europe including Great Britain and on to North America and the West Indies.

The next widespread epidemic to catch the overland route was that of 1866—1870 which began as usual in Bengal in 1866, spread over the Punjab by the Hardwar pilgrims and also reached Afghanistan in 1867, Persia in 1868, Russia in 1869 and subsequently spread widely in Europe and North America.

In 1892, the 6th great epidemic of the 19th century travelled by the same overland route, but much more rapidly, owing to the greatly improved means of communication by Railways in India and the southern Asiatic provinces of India, Thus cholera broke out at the Hardwar fair in the United Provinces in March 1892, spread widely through the Punjab by the dispersed pilgrims in April, severely affected Kashmir, Afghanistan and Meshed in North Eastern Persia in May, North Western Persia and the ports on the Caspian Sea, Russia and Western Europe, especial. Hamburg in July, having thus travelled in five months over the same area which, the 1826—31 epidemic took 5 years to cover, a most significant fact with regard to future epidemics as evidenced by the further fact, that in 1908 the disease also spread from India to Petrograd within a few months. Kashmir was again visited in 1900 and Japan in 1901.

Secondly, the 1848-1853 epidemic was carried by sea from India to the head of the Persian Gulf, and spread to South Russia and Western Europe, although the Punjab and Afghanistan escaped. Again in 1865 cholera was carried by sea from Bombay to Arabia and Mecca and then spread widely by the returning Mecca pilgrims through Egypt and Syria to the south Europe, Mediterranean ports and to the East African coast. One branch of this outbreak also travelled by the head of the Persian Gulf and up the Euphrates Valley. Again in 1881 cholera was carried by sea from India to Arabia, Egypt and southern Europe, as a result of which sanitary measures were taken to safeguard the vast traffic through the Suez Canal.

The following table gives a clear idea of the six pandemics mentioned above. A seventh is added to bring events up to date.

Pandemic.	Duration.	Distribution.
	Years.	
1817—23.	6	Asia, Africa.
1826—37.	11	Asia, Africa, Europe, America, Australia.
1846—62.	17	Asia, Africa, Europe, America.
1864—75.	12	Asia, Africa, Europe, America.
1883—87.	4	Asia, Africa, Europe.
1892—95.	3	Asia, Africa, Europe, America.
1910—25.	15	India, China, Europe, Africa.

The epidemic of 1892 was specially severe in the previously famine-stricken districts of Russia, where it carried off 220,000 victims and in Hamburg where, of the 17,000 affected, 10,901 died. In 1914 it broke out in Austria. Cholera which reached the confines of China in the year 1817 probably by the land route, actually invaded the whole of the country by the sea route in 1820. Evidently, this diffusion was the result of the military operations of the British in Burma. The outbreak was widespread in 1821 when both Peking and Shantung provinces were affected. A second outbreak took its departure from India and reached China in 1826, a third in 1840 when the seeds of the disease seem to have been conveyed to the country by the combined European and native army despatched by the British from India. Since the year 1820, when records of cholera in China were first kept, there have been 46 invasions of greater or lesser degree.

Endemic areas of Cholera—*India*:—It has been found by Sir L. Rogers, after the careful study of 1875—77 epidemic, that there are three distinct areas from which the disease took its initial departure and in which cholera has never been absent for a single year for the three recent decades.

These areas being:—

(1) Bengal, Assam, Bihar and the five eastern divisions of the U. P.

(2) Central and South-east coast districts of the Madras Presidency.

(3) The narrow, hot and damp Konkan coast of Bombay. All India has been always blamed to be the permanent dwelling place of cholera, but it has also built its permanent endemic nests in Southern China, Dutch East Indies, Indo-China and the Phillipines.

Cholera becomes endemic in any locality where the absolute humidity runs at the critical level of 0.4 inch and never tends to fall for long below 0.4.

By absolute humidity is meant the weight of aqueous vapour in the air measured in terms of its mercury tension, so that low readings indicate both dryness and low temperature and *vice versa*. With this theory, Rogers clearly explained why some districts are infected while others escape. In consideration with other factors such as failure of rains of the previous monsoon or of the winter rains accompanied by an unusually early rise of the absolute humidity, absence of cholera in any given district for two years and the mass movement of population (pilgrims etc.), Rogers was able to forecast the probable incidence of cholera in various localities in India to a surprisingly accurate degree for 1930, 1931 and 1932.

Dr. A. J. H. Russell, studying cholera epidemics in India with the aid of mathematics defined a 6 yearly theory, as opposed to Bellow's 3 year cycle theory and found that the highest amplitude was met with at the 72nd month period in several localities. In 1926, he published another paper on the results of his studies on the influence of the monthly prevalence of rainfall, humidity, temperature and pressure on the incidence of cholera. He found a correlation between rainfall and cholera with a lag of two months in some localities. The relative humidity gave coefficients of lower value than those of the rainfall and without any lag. High temperature was also found to be closely related to a high incidence of cholera.

Seasonal incidence of cholera.—The seasonal incidence of cholera in the different provinces depends on the absolute humidity running at the critical level of 0.4" during the particular season of the year.

(1) In Assam, Bengal and south east Madras, high incidence of the disease is noticed in October, November and December.

(2) The disease tends to come down in January and February with the reduction of absolute humidity.

(3) In Bengal, it again tends to increase from the end of March onwards till it comes down with the onset of the monsoon. So, the Bengal epidemic curve has two peaks, one in October to December and again incidence of the disease becomes highest during March to

July, whereas the curve of other provinces has got only one peak.

The hot weather maximum prevalence of cholera occurs with a low and stationary ground water and it decreases to the minimum when the ground water is rising to its highest point. The mean temperature of Calcutta is never low enough to have any marked effect on the prevalence of cholera but winter lull of the malady is a well marked feature in the colder north western parts of India.

Aetiology.—The spirillum cholera discovered by Koch in Egypt in 1833 and named by him the "comma bacillus" or the cholera vibrio, is the undisputed cause of the disease. The conditions of infection as in other diseases might be complex. Not every one who takes the specific micro-organisms by the mouth necessarily gets the disease but without it there can be no cholera. Many cholera vibrios probably die in the acid juices of the stomach. There is therefore perhaps less danger in taking small amounts of infection during active digestion than upon an empty stomach. After the cholera vibrio has passed the pylorus and reaches the alkaline juices of the intestines, it may find ideal conditions for growth, or may still have a hard struggle for existence. Here symbiosis or antibiosis must be playing a dominant role.

Pettenkofer stoutly maintained that the "Comma Bacillus" was only one of the factors in the aetiology of the disease. He placed special importance upon the condition of the host and his environments and considered at least three fundamental factors in his *X*, *Y*, *Z* theory.

X—the germ.

Y—the host or soil.

Z—the environment.

Pettenkofer maintained that *X* without *Y* and *Z* would not produce cholera *i.e.* while the cholera vibrio was pathogenic in India or Hamburg where *Y* and *Z* were favourable, it would be harmless in Munich where *Y* and *Z* were unfavourable.

Bacteriology.—*Vibrios*—Motile simple curved rods with an anterior flagellum, which acts like the propeller of an aeroplane, division by transverse fission. The cholera vibrios are seen as fine curved rods, arranged as fish-in-stream manner; with recovery, the vibrios become fewer and they frequently become large and swollen in appearance; besides the vibrios, numerous

spirochaetes are found *e.g.*, S. erygyratus which are very irregular bodies.

Motility.—Very actively motile, anterior single flagellum—gram negative vibrios, can grow in strong alkaline solution, aerobes but they can also grow under anaerobic conditions.

Enrichment media.—Peptone water—consists of 1 % *NaCl* and Witte's peptone, tryptophane, Pot nitrate 0.1 % and sidi carb 0.02 %. Add 1 gm. of faeces, to 100 c.c. of peptone water in a urine glass—a vessel of large surface, incubate for six hours at 37.5 c. take a loopful from the top and examine 50 fields, if vibrios are present, then take a little of the peptone water culture and add one drop of H_2SO_4 (Conc),—Cholera red reaction. If you are not certain by this method then plate on 1/4 % bile salt agar—smooth colonies, flat edged, semitransparent.

Cholera red reaction.—Cholera vibrios when grown in peptone water, reduce the nitrates present in these media into nitrites. If a strong mineral acid is added, nitrous acid is given out from the nitrites and this forms together with the indol also produced by the vibrios nitroso indol" (Cholera red).

Interesting as this reaction is, its practical importance is limited because now-a-days more exact methods are available for cholera diagnosis as well as for other reasons. First of all, the reaction is not specific for the true type but given also by some of the cholera-like vibrios and even other micro-organisms. Further a number of other extraneous factors, *e.g.*, unsuitability of certain brands of peptone, variations in the nitrate content of the media, presence of certain nitrite destroying contaminating bacteria, may lead to erroneously negative results. It is necessary therefore to guard against these sources of error by working with pure cultures only and always making control tests with type strain known to react strongly.

Special media.—McConkey's media — not so good. Dieudonne's media—equal parts of N_1 Na OH and defibrinated, ox or sheep blood, then add 30 parts of this mixture to 70 parts of agar 3 %—the media must be dry, to see if vibrios haemolyse—green zone.

Diagnosis of vibrios.—1. Rely on cholera red reaction within 24 hours, vibrios with single anterior flagellum

2. Liquefaction on gelatine—not used in India.
3. Pathogenicity on pigeons—V. Cholera is not pathogenic.
4. Haemolysis.

Agglutination test.—to test the vibrios found in water, stools etc.

Standard high titre serum (1 in 10,000) consists mainly of somatic agglutinins derived from smooth culture, so that the vibrios found in an acute stage are agglutinated—after a few days or in water the vibrios are non-agglutinable (N. A. G.)

Two main conceptions may be said to exist at present to explain the origin of cholera epidemics. According to Koch, the disease is constantly present in the endemic areas and man is the potential reservoir; infection spreads from one individual to others either by direct contact or through contaminated inanimate objects.

Contrary to this theory, ascribing importance to the authentic vibrios only, it has been suggested that N. A. G. vibrios might become specifically A. G. and virulent, thus leading to cholera outbreaks. Even among adherents to the classical ideas, considerable divergence of opinion exists as to the importance of carriers in the spread of infection and also to the length of time, which contaminated objects, especially water, remain infective. It is necessary therefore to discuss these two subjects before dealing with the problem of the cholera-like vibrios.

Cholera carriers.—1. *Incubatory carriers who are certainly dangerous.* Morrison maintained that the infectivity of persons during the incubation period of cholera seems as high as, if not higher than, that of a patient on the first day of illness.

2. *Convalescent carriers.* Morrison, while admitting that vibrios may be present in the dejecta for some days or weeks or even months after recovery, maintains that no proof for the infectivity of such strains exists.

3. *Healthy carriers* Morrison expressing frank disbelief in their importance opines that possibly the agglutinable vibrios, carried without ill effect by the healthy individual, are inoffensive for others as well.

Greig during an epidemic at Puri found virulent organisms in the stools of 36% of patients just before discharge from Hospital.

Mackie and Freasler found that 7.2% of cholera patients remained carriers of the comma bacillus for more than 10 days after an attack of the disease. Only two out of several hundreds continued to be so up to 5 and 7 weeks respectively.

Chronic carriers are very rare and very doubtful. About 2% of healthy people after coming in contact with a cholera patient behave as carriers without actually suffering from the disease.

How to diagnose a cholera carrier who only carries. N. A. G. vibrios:

(1) Give a saline purgative.

(2) Mix 2 gms. of stool with peptone broth in a flask-incubate 6-8 hours.

(3) Then put in peptone water in a test tube, incubate 6-12 hours.

(4) Then plate—see if vibrios are on the surface; examine 3 times a day for 12 days.

The carrier problem is surely a very difficult one and represents one of the most difficult phases of laboratory work, not so much because a few vibrios may be present in solid stools, but because the discharge of vibrios in the stool may be intermittent.

It is curious to note that D'Herelle ascribes even a beneficial influence to healthy carriers because they spread bacteriophage together with non-agglutinable and avirulent vibrios

Viability of Cholera vibrios in water.—Cholera vibrio does not in general survive for any great length of time upon contaminated inanimate objects. Observers in India agree that the survival of these vibrios in water is comparatively or even absolutely short. This was found especially in connection with raw waters of the Ganges and the Jumna. Hankin (1896) ascribed it to the presence in the water of volatile antiseptic substances.

S. Khan thinks that it is mainly due to the presence of other micro-organisms competing with the V. Cholerae.

Role of N. A. G. Vibrios.—While Pasricha, de Monte and Gupta seem to contemplate that a change from N. A. G. to A. G. vibrio might occur outside the human body especially under the influence of vibriophage. Tomb and Mitra (1927) formed another theory. According to this, a widespread epidemic of cholera leaves in its wake, great numbers of chronic carriers of N. A. G. vibrios.

By some vital process, at present not understood, the N. A. G. vibrios change into the A. G. form in the intestine of some of those carriers. If the drinking water supplies of a locality are contaminated by vibrios of the latter type, cholera will become endemic, provided that the climatic conditions are suitable for the survival and multiplication of the vibrios in water.

Besides experimental evidence to support their hypothesis, Tomb and Maitra refer also to a few instances where patients with N. A. G. vibrios in their stools, led to cases of authentic cholera.

The existence of chronic carriers of N. A. G. vibrios has been doubted by other investigators.

Dunn (1929) refers to "facts tending to show that 'carriers' of such germs cease to discharge them after a comparatively short

time". Acton (1933) reported from Calcutta that N. A. G. vibrios were demonstrable in the stools of cholera patients from the 5th to the 14th day of illness but not beyond this time. They were found also in 1% of the general (cholera-free) hospital patients but only during the epidemic season and not for the rest of the year. It must be noted that Acton regards all strains reacting with dilutions lower than 1/16 of the serum titre as N. A. G. So, the authors, like Kolle and Prigge and S. Khan (1929) think that presence of N. A G. Vibrios in the stools, is always accidental in nature and importance, such vibrios being present in the drinking water and ingested with it. Others ascribe to them a role in the causation of sporadic or groups of cases with gastro-intestinal symptoms varying in intensity. The infectivity of such cases compares in no way with that of true cholera (Dunn.) and they have in fact nothing to do with the latter disease but represent a syndrome designated by some as true Paracholera (Mackie 1923).

If cholera-like vibrios do become agglutinable under natural circumstances, one would reasonably expect that such transference being most likely to take place soon after an epidemic of cholera, the disease, once pushed in a community favourable for its spread, would occur and reoccur regularly without stopping and also many outbreaks would be on record, the origin of which could not be traced, the disease having arisen, *de novo*, through transition of N. A. G. Vibrios in A. G. form. It is highly desirable to look forward with a broad mind, the result of further research, especially along the lines suggested by Pasricha, de Monte and Gupta. It should be noted however that these investigators themselves point to the incompleteness of their data, especially where the virulence of the vibrios, rendered by them agglutinable in vetro, is concerned.

The toxins of Cholera.—1. *Endo-toxin*—inside the bacterial cell, probably not so powerful.

2. *Exo-toxin.*

3. *Main toxins* are derived from the proteins in the gut, probably are amines (NH_2) in nature, soluble and extra cellular—tryptophane, aminoacids converted into indol, toxic substance NO_3, NO_2 : these two give cholera red reaction.

4. Other toxins—lysin fraction (i) kill the animal with symptoms like Cholera— fall of blood pressure, diarrhoea, petechial haemorrhages in the small intestine. (ii) the vessels of kidneys also dilate, oedema intertubular-anuria (iii) Vaso-constriction of many voluntary muscles resulting in cramps (iv) Vaso constriction of involuntary muscles, causes marked contraction of the gut wall resulting in diarrhoea and of the uterus, resulting in abortion if there is pregnancy.

Pathological findings in Cholera—P. M. appearances :—

1. The subject is well nourished.

2. The serous cavities are empty and free from fluid and the pericardium shows petechial haemorrhages.

3. In the small intestine, there is extreme congestion of the mucous coat, enlargement of the lymphatic follicles of the ileum.

4. Stomach and upper part of the large intestine congested and minute petechial haemorrhages.

5. The lungs are dry, light in weight and the blood vessels contain thick dark blood.

6. *Gall bladder* is distended with thick bile, swelling and congestion of the bile duct and duodenal mucous membrane which is the cause of obstruction of the ampoule of water, which phenomenon accounts for the colourless stools in cholera patients.

7. *Kidneys.*—intense congestion and patchy minute haemorrhages. During the collapse stage the intense congestion interferes with sufficient circulation of blood through the kidneys and so accounts adequately for the suppression of urine during the collapse stage as well as for the inevitable death from uraemia if the blood pressure does not rise to near about 100 MM during the reaction stage.

Blood changes in Cholera.—The tremendous loss of fluid from the system causes relatively a rise in the number of R. B. C's as well as white blood corpuscles.

R. B. C.—7 or 8 millions per c. m. m

W. B. C.—15,000 to 20,000 per c. m. m.

There is a definite decrease in the P. C. of lymphocytes but the P. C. of large mononuclears rises, so that the proportion of the two is commonly reversed, thus cholera can be distinguished from cases of arsenic poisoning in which leucocytosis of the ordinary polymorphonuclear variety occurs. The extraordinray deficiency of the lymphocytes in cholera is doubtless related to the great increase of the lymphoid tissue in the mucous membrane of the small intestine.

Loss of fluid from the blood in Cholera.—1. Dr. George Johnson who always advocated purgative treatment of cholera strongly maintained that there exists no relationship between the copiousness of evacuations and the death rate in cholera; therefore he thought that intravenous transfusions were useless in the treatment of cholera.

2. Wall, however, really pointed out that the effect of any given loss will mainly depend on the rapidity with which it takes place; a rapid loss of two or three pints being evidently more harmful than that of as many quarts spread over a much longer period, during which some of the loss may have been made good by absorption of fluid, given by the mouth or bowel.

It is evidently of essential importance to determine this point correctly, for it is very urgent to know how far the collapse is relatively due to loss of fluid from the body in order to decide whether steps should be taken to replenish it or not. What we do really want to know is the extent of the escape of fluid from the blood and whether there is any definite relationship between this loss and the severity of the disease. In order to find out this vital question, Sir. L. Rogers has devised means to estimate the proportions of corpuscles and serum respectively, in the blood in the acute stages of cholera, by means of an instrument called the haemocrite. The R. B. C's per c. m.m. are greatly increased in cholera. So, we may assume that the diminution in the proportion of serum is due essentially to loss of fluid from the blood and consequently also of the tissues. The blood of the Indians shows 45% of corpuscles and 55% of serum. In the mildest cases, not requiring transfusion there was a loss of 35% of fluid from the serum of the blood. In the moderately severe cases requiring transfusion but eventually recovering, there was a loss of 53%, while in the most severe and fatal cases, the loss was 64% or almost 2/3 of the blood.

This method of investigation by Rogers revealed a most marked relationship between the severity of the disease in its acute phase and the P. C. of fluid lost from the blood, while the fact that, in all but the mildest forms of cholera, from 1/2 to 2/3 of the fluid, had been lost and it can be safely presumed that a corresponding amount had been lost also from the tissues of the body, clearly indicates the urgency for and the necessity of replacing some at least of the loss, if the circulation is to be adequately maintained. This is also corroborated by the marvellous immediate results of saline infusions, which check further copious evacuations.

Mode of transmission of Cholera.—1. Water is the commonest cause. The organism lives a long time in water and the stools of cholera patients or carriers contaminate the water supplies. The tanks are invariably polluted by washing of infected clothes and by other ways. The wells are polluted by fæces either directly or indirectly by percolation through ground

from neighbouring service privy or polluted soil. Vegetables and utensils, washed in contaminated water, may convey the infection.

2. Milk, contaminated either in the cowshed, or in transit or in the house. Milk may be contaminated by the use of contaminated water in washing the cans or utensils or as an adulterant. Flies may act as transmitting agents.

3. Contact infection is a common mode of transmission of cholera. This is especially apt to be the case where a number of people live in close contact and eat and drink from a common dish or bowl, not infrequently dipping the fingers into the common food dish. Persons handling the clothing and bedding soiled with cholera discharges, are not infrequently infected.

4. Flies transmit the cholera vibrio, just as they transmit the typhoid bacillus. As the cholera vibrio does not stand drying, it is not so readily transmitted by the faeces-soiled legs and body of the fly. The cholera vibrio will live in the intestine of a fly for at least three days and the feeding habits of flies, feeding on fæcal matter and on the carbohydrates of man's food, make them especially adapted to carrying the cholera vibrio from fæces to man's food. When the flies defæcate, their stool is a rich culture of cholera vibrios. The cholera vibrio cannot withstand drying. So there is little danger of transmission through dust or an article of furniture. The vibrio may live for some days in clothing and bedding that is rolled up without any special attempt at drying.

Susceptibility.—All races, all ages and both sexes are susceptible. The disease is seen more in people of the rice-eating class.

Over-work, worry, gastro-intestinal disturbances and alcoholic excesses increase the susceptibility to infection.

N.B.—Why cholera is always prevalent in Calcutta throughout the year inspite of efficient sanitary services is attributable to:—

(1) Absolute humidity which usually does not come down below the critical level for long.

(2) Water supply.—Intermittent system, storage, handling, and habits; the people the (majority of whom have not got even the elementary ideas about personal hygiene and are devoid of sanitary consciousness) go and drink any water they can get hold of, when the filtered water is not available during the day.

(3) Distribution of filtered water in the overcrowded bustees is not sufficient.

(4) Possible leakage in the pipes and subsoil water drawn in.

(5) Unfiltered water supply for domestic purposes.

(6) Importation of cholera year after year by pilgrims, travellers and traders, especially dangerous along the river banks.

(7) Fly nuisance.

(8) Milk possibility.

Measures of control against Cholera.—1. Early diagnosis by the clinical symptoms confirmed by bacteriological examination *e.g.* isolation and identification of the cholera vibrio in pure culture. A presumptive diagnosis of cholera can be made by finding large number of comma shaped bacilli in direct microscopic examination of stained preparations or in hanging drops of mucous flakes found in cholera stools. But this is only presumptive and cannot be depended upon. The only positive diagnosis consists in the biological reactions of the micro-organism obtained in pure culture, the most reliable test being the agglutination test with a known standard serum.

2. Notification early is of prime importance so that preventive measures can be adopted early to check the further spread of the disease. Cholera is one of the notifiable diseases in Calcutta under the Calcutta Municipal Act, 1923. Either the attending physician, or the hospital people or other members of the house must inform the Health Officer about the incidence of cholera. Other notifiable diseases under the C. M. A. are small-pox, cerebro-spinal fever, diphtheria, plague, and enteric fever. The system of notification in rural areas is this : The chowkidar is ordered to report any case of cholera in the village to the local police who in their turn have to report daily to the Health Officer or Civil Surgeon during an epidemic, and the information finally would reach the Director of Public Health.

3. Isolation of the sick to a special hospital or in screened room with trained attendants.

4. Immunisation.

The question of Immunity in Cholera.—As pointed out by Harvey (1922) in an interesting discussion of this topic, man is in various ways resistant to cholera infection. When a person ingests cholera vibrios into the stomach with water or food, most of the vibrios are killed by the acid in the gastric juice. But large

masses of food and large amounts of water may protect the vibrios or dilute the gastric juice to such an extent that the vibrios are not killed in the short time they remain in the stomach before being passed on into the small intestine. If the persons have got digestive errors or worries which inhibit the secretion of Hydrochloric acid in gastric juice, and when the vibrios reach the small intestine, they find the alkaline reaction of the small intestine most suitable for their growth and multiplication. At times there are no symptoms and the patient is simply a temporary carrier of cholera vibrio. Frequently, there is a mild diarrhoea which is over in a short time; under such conditions any indiscretion in diet or any stopping of peristalsis, may lower the resistance of the intestinal epithelium and the patient may develop a sharp attack of cholera. Turning now to the question whether immunity may be acquired under natural conditions, it is certain that a manifest attack of cholera renders the patient refractory against further infection. It is probable that presence of cholera especially in its endemic form, may lead to slight attacks of illness which while remaining unnoticed, may confer immunity against infection.

Artificial Immunisation.— This has been attempted in various ways. Some of the methods used are of historical rather than of actual interest. Ferran (1885) and Haffkine (1893) first tried this with the living vibrios. Nicolle, Connor and Conseil (1912) used intravenous injections of living vibrios. Castellani (1913) used vibrios attenuated by heat. This is not surprising because among the two types of antigens existing in the V. Cholera, the heat labile one plays an insignificant part as compared to the importance of the heat stable antigen (Fairbrother 1928). Hence it seems more reasonable to employ cultures killed by heat for vaccine preparation than to run the risks arising out of the use of living vibrios. The attempts to produce passive immunity against cholera by serum have not been crowned with practical success. Moreover, achievements in this line will be more important from a therapeutical than a prophylactic view-point because passive immunity even at its best is of short duration.

Common prophylactic methods now widely used are:—

(1) *Kolle's Vaccine.* — Kolle (1896) used suspension of growth of 24 hour-old agar culture in normal saline, and killed by heat (original method) or by other process *e.g.* as in India by mere addition of 0.5% of phenol

While the efficacy of this method of inoculation and its great

practical importance, leading to its express recommendation in the last(1926) International Sanitary Convention are generally admitted, some observers look with distrust upon the statistical finding to prove the value of anti-cholera inoculation. Some of the statistics e.g. those compiled in regard to certain German armies engaged in the World War and summarised by Hetsch, seem quite reliable as well as convincing. Moreover one should perhaps stress not only sources of errors which are in favour of the method but also consider evidence which may discredit it. The experinces and observations made in this connection by Col. Stewart (1933) are well worth considering. He assayed the value of three Indian vaccines manufactured by private concerns along with the product prepared by the Bengal Public Health Service. By testing the agglutinogenic power from the various samples, he found that only one of the commercial products came near to the standard of the Government Vaccine, one gave a serum with half as good an agglutinating titre, while the third was apparently devoid of antigenic powers. It is evident that vaccines prepared with unsuitable strains are apt to discredit the method. Col. Stewart advises therefore that it is imperative to employ smooth colonies of recent origin exclusively for vaccine preparation. Wherever possible, strains of local origin are to be preferred. While the usefulness of anticholera vaccination may thus be taken for granted, the limitations and drawbacks of the method should be clearly realised.

The fear is often expressed in certain quarters that vaccination during an outbreak might be dangerous on account of its being immediately followed by a negative phase and precipitating an acute attack in a few cases. There is however no proof whatsoever for the practical importance of such a phase with increased susceptibility to infection, especially when it can be pointed out that healthy carriers do not contract infection when inoculated.

It is true however, that in this as in other methods of active immunisation, immunity developes not immediately but gradually.

Kolle demonstrated bacteriolysms in the blood serum of the vaccinated four days after inoculation and the titre reached a maximum on the 10th day.

Before inoculation the bactericidal titre was at an average 0.2; 10 days after inoculation 0.003 c.c. of the serum was sufficient to protect a guinea pig against intraperitoneal infection with 1 loop of virulent cholera culture. The serum of the convalescents did not invariably show such high protective powers. Agglutination being positive with the serum of normal persons at the

dilution of 1 in 10 only, it reaches with two dose vaccination a maximum of 1 in 150 in about three weeks. (Batteano and Lupu 1914).

The reaction following anticholera vaccination is in the majority of cases insignificant, certainly much milder than in the case of anti-typhoid vaccination. Maitra and Ahuja (1931) carried on an interesting investigation in this connection.

Noting that practitioners usually administered a single dose of 1. c. c. instead of an initial dose of ½ c. c. followed after 10 days by another injection of 1 c. c., they established that unpleasant and severe reactions had evidently nothing to do with such increased dosage. In fact subcutaneous injection with vaccine, eight times stronger than that used for man, was well tolerated by guinea pigs. Nor did variations in the phenol content seem to be at fault, double the normal strength being well tolerated by volunteers. Any marked reaction whenever noticed seems to be due to the admixture to the vaccine of foreign proteins derived from the nutrient media used in the process. As pointed out by Buerger (1916), the reaction after the second inoculation (which is sometimes stronger than that of the first), may be mitigated by injecting both times into one and the same area.

Mild as the reactions of the anti-cholera vaccination of normal persons usually are (children well tolerate doses corresponding to their age and body weight), one should be careful not to administer the inoculation to enfeebled persons and especially those with cardiac or renal insufficiency. The full efficacy of anti-cholera inoculations is evidenced by a community or herd immunity; individual protection cannot be guaranteed. Manifold experiences have shown, however that cholera, appearing in recently vaccinated persons, usually tend to run a milder course, even when prophylactic inoculation has been given during the incubation period. The duration of immunity after inoculation is generally from 6 months to a little over one year. The method does not afford absolute protection so that inoculated subjects should not consider themselves entitled to taking risks but should continue to observe reasonable precautions against possible infection.

There are really two drawbacks in this method :—

(1) It does not render carriers free from their vibrios, while the bacteriophage treatment and oral vaccination are said to be efficient in this line.

(2) In order to reach an optimum of protection two, or better still, three inoculations should be administered,

practically often difficult to fulfil. It should be noted, however, that even one inoculation confers a fair degree of protection especially if an increased dose *e. g.* 1 c. c. instead of ½ c. c. is given (Russell 1927 Raju and Sarkar 1931, Nguyen Van-Khai 1932).

Sensitised vaccine.—Shiga and collaborators (1918) recommended the use of a vaccine in which the vibrios have been treated with anti-serum and this method is now widely used in Japan. Reaction by this treatment is mild and immunity developes rapidly though it lasts a shorter time than in the case of the ordinary vaccine. Harvey, Satake (1926) concluded, however from a small series of observations, that immunity after such inoculations lasts eight months. Be this as it may, due account should be taken of the increased difficulties and the cost of preparing such vaccine, which perhaps counter-balance the advantages it may possess.

Protective inoculation as a prophylactic measure against cholera will never be popular or necessary in communities, with sufficient sanitation. It is however of great value in camps, armies on the march, physicians, nurses, ward assistants, travellers and others especially exposed.

Results of prophylactic inoculations :—

According to Rogers, six trials were done on a total of about one and a half million persons ; there were reductions in the incidence of the disease in the inoculated from 92 to 99%. In Tokio, 300,000 persons were inoculated with a sensitised vaccine during an epidemic and no case occurred in any of the persons who were given two doses of the vaccine and only three contracted the disease from amongst the series of cases who were given only one dose. Equally uniform good results were obtained in Batavia where 100,000 inoculations were done.

Besredka has recorded examples of success of inoculations during the Great War under controlled conditions which were almost equivalent to a laboratory test, for instance, there was the case of a regiment in which there were 200 Jews, who were inoculated on their own demand. 450 cholera cases subsequently occurred in that regiment but not a single case occurred amongst the inoculated Jews. The value of inoculation in the control of cholera is also shown by several instances of the abrupt cessation of an outbreak just after the second dose of vaccine.

Bili vaccine.—It is claimed that the vaccine, if taken by mouth, confers immunity against cholera, lasting for about a

year but A. J. Russell in Madras found that three oral doses were slightly inferior to the usual anticholera inoculation while the bile pills sometimes produce acute diarrhoea.

One pill of vegetable bile to be taken in empty stomach to be followed 15 minutes later by one vaccine tablet; repeat for 3 days. Each vaccine tablet contains 50 mgm of killed or desiccated cholera vibrio equivalent to 60 to 70 billions of microbes. Its value has been highly spoken of and it is worth a trial where inoculation is not possible.

Dr. J. W. Tomb's anticholera Mixture :—

Oil of Cloves Oil of Cajput Oil of Juniper	}	āā ♏ v.
Acid sulph aromat	...	♏ xv
Spt. ætheris	...	♏ xxx

One drachm dose in ½ oz. of water, once or twice daily has been advocated as a prophylactic. In the absence of properly controlled trials, it is at present impossible to say if it can ever prevent the development of cholera or not, but it may prove of use in mild suspected cases during outbreaks of diarrhœa: 6 to 8 doses should not be exceeded in any case because of the risk of damage to the kidneys due to the essential oils. Unexpected suppression of urine has also been recorded after the use of these oils ; so, caution is necessary before administering this mixture in cholera.

Other prophylactic measures against cholera. — During a cholera outbreak :

1. Avoid unboiled water or milk, uncooked foods and salads.
2. Guard against exposure to chill which is believed to be a predisposing cause. Flannel binder for abdomen is still used as a "cholera belt."
3. Fasting is prohibited as shown by the frequency of the disease among Mahomedans during the period of the great Mahomedan fast.
4. *Quarantine is justified for the prevention of this disease.*—All contacts or persons who have been exposed to infection should be quarantined for 5 days from the date of last exposure.
5. *Concurrent disinfection* :—(i) Prompt and thorough disinfection of stools and vomited matter by formaline 10% or carbolic acid 10% or milk of lime 1 in 8 or chlorinated lime 3% (ii) All articles used by and in connection with the patients must be disinfected before removal from the room. Remnants of foods left by the patient must be burnt.

6. *Terminal disinfection* :—The bodies of those dying from cholera should be cremated if practicable or otherwise wrapped in a sheet wet with a disinfectant solution. The room in which the sick person was isolated should be thoroughly cleansed by washing the surfaces with bichlorides.

7. *General measures* :—(i) Rigid personal prophylaxis of attendants by scrupulous cleanliness, disinfection of hands each time after handling the patient or touching articles contaminated by dejecta. First, hands should be washed with soap and hot water, then dipped in Mercury Biniodide solution 1.1000. (ii) Avoidance of eating and drinking anything in the room of the patient and the prohibition of those attendants on the sick patient from entering the kitchen.

8. Bacteriological examination of the stools of all contacts to determine carriers and isolation of carriers.

9. Water should be boiled if used for drinking or toilette purposes or if used for washing dishes or food containers.

10. Careful supervision of food and drink where cholera is prevalent; only cooked food should be used. Food and drink after cooking or boiling should be protected against further contamination by flies or human handling.

11 Disinfection of water supplies by the method of chlorination and permanganation of wells. Bleeching powder of average strength (25%) 1 oz. for every running ten feet of a tank or 30 grains per 100 gallons are sufficient for proper disinfection of a village tank. Pot. Permanganate usually 1 drachm is required for a well 2 ft. in diameter and containing about 8 ft. of water.

12. *Epidemic measures* :—Inspection service with laboratory for early detection and isolation of cases. Examination of persons exposed in infected places for detection of carriers, disinfection of rooms occupied by the sick, detention in suitable camps and barracks for 5 days of those desirous of leaving for another locality; those so detained should be examined for detection of any carriers amongst them.

13. *Bacteriophage* :—De' Herelle maintains that cholera cases cannot recover unless the patients develop bacteriophage in their own intestines. Distribution of bacteriophage during convalescence was the cause of decline of the epidemic. So according to his theory, it is quite wrong to disinfect water supplies during an epidemic.

Inoculation of tanks and wells with bacteriophage has been tried as a prophylactic measure in Assam and Bihar, but results are not yet known.

Clinical History.—*Incubation period of cholera* :—1—5 days usually 3 days, may extend to 10 days. In MacNamara's experiment 19 persons partook of water contaminated with a fresh rice water cholera stool and 5 of them developed cholera between 24 and 72 hours afterwards.

Clinical types :—[As grouped in the Campbell Hospital, Calcutta: (*a*) Mild—cases in which only one injection (intravenous) or no intravenous injection is required. (*b*) Severe—3 or 4 intravenous injections are required. (*c*) Very severe—about 6—10 injections are required. (*d*) Fatal—terminating fatally, inspite of repeated saline injections].

1. *Ambulatory cases* :—Such cases are characterised by diarrhœa, malaise and slight fever merely. The stools never lose their bilious colour, there is never complete suppression of urine and the disease is not accompanied by cramps. The attack gradually subsides without developing a subsequent reaction.

2. *Mild cases* :—Onset is sudden, diarrhœa is not so acute and the stools may retain the bilious colour for hours before the typical colourless rice watery ones appear; under this category may be classed those cases with hard stools streaked with mucus from which V. cholera can sometimes be cultivated.

3. The severe cases start in either of the two ways. (*a*) Like an ordinary case of diarrhœa. (*b*) With sudden onset without any prodromal symptoms.

Abdominal pain may or may not be present. The patient sometimes feels as if he is relieved each time a stool is passed. Frequent copious evacuations soon change the colour of the stools from a yellow semi-solid to a colourless fluid containing flakes of mucus, epithelial cells, spirochætes and vibrios, resembling rice water in appearance. Sometimes hæmorrhagic stools are seen.

The second important and constant symptom is vomiting, first of food, then, watery fluid, bile and even blood. The quantity of fluid lost is great, several quarts being often passed within a few hours. As purging and vomiting continue, the urine diminishes gradually till it ceases altogether. Due to dehydration of the tissues, the facial expression alters, the nose becomes sharp, the cheek bones look prominent, eyes are sunken and the skin of the fingers get shrivelled; while this is taking place, the circulation is profoundly affected and the blood pressure falls. The pulse gets weaker and weaker until it disappears from the wrist. The lips, face, nails and extremities are cyanosed. The voice becomes hoarse and husky and there may be hiccough. The respirations become hurried. Painful cramps are felt first in the muscles of the arms

and legs, ultimately affecting the abdominal muscles. The reflexes are diminished. The mind is clear but apathetic. Restlessness may be extreme. Extremities become very cold and the axillary temperature is found to be subnormal while the rectal temperature may be higher than normal.

From this, the patient may pass in 3—48 hours, (usually 4—8 hours), into the algid or collapse stage, very aptly described as living death, 5—8 times diarrhoea and 2—4 times vomiting will bring about the algid stage. The circulation fails. The pulse disappears, the heart is weak and irregular, respiration is laboured, skin is cold, clammy and cyanosed, the veins contain black tarry blood, urine is suppressed. The first heart sound is accompanied by haemic systolic murmurs. The second sound is faint. Friction sounds may be heard in the pericardium and pleura. The patient may die from auto-intoxication and heart failure or may pass on to a comatose death 12—36 hours after onset, or the patient may recover. The collapse may last for a few hours or for two or more days but if the patient survives, the stage of reaction sets in and recovery may be rapid or slow; usually the diarrhoea gradually ceases and the stools regain the bile colour. The pulse begins to increase in volume, all signs of collapse begin to fade away. The axillary temperature rises and may go up to 103° F. or more. The pyrexia is due to renewed absorption of toxins from the bowels with the recovery of the circulation and may sometimes lead to delirium and death. Typhoid state may supervene and toxic rashes in the form of erythema, papules and haemorrhages may occur. The stools are like those in typhoid or may be blood-stained. The urine may be scanty with high specific gravity, albumin and casts, or remain suppressed due to the effect of the toxins on kidneys. Acidosis induced by the limitation of diet and severe vomiting is mainly responsible for the causation of anuria. The reduction of alkalinity of blood and the presence of acetone in the urine are indicative of acidosis. If unrelieved, uraemia will set in with serious threat to life. Thus it may be seen that the reaction stage is a dangerous period for the patient and some of them are saved from the earlier stage of collapse only to die later on. In other cases, recovery is possible after a long convalescence. The patient may be declared free from infection if after three examinations, no vibrios are found in the stools. The period of communicability in cholera infection is usually 7—14 days, occasionally longer.

4. There is a rare and very severe form in which the patient collapses and dies without passing any cholera stool. In such

cases the infection is overwhelming and the fluid is poured into the intestines so rapidly that the patient dies before the bowels empty themselves. This dangerous type of cholera is popularly named as cholera sicca.

Signs and symptoms of Cholera.—At the onset, first two or three stools contain faecal matter even bile stained, but, quickly the stools change to rice water character which is colourless, watery and contain little solid matter except flakes of desquamated epithelium from the small intestines. If collected in a glass, the flakes will settle down to the bottom on standing leaving a quite clear fluid at the top. MacNamara reported a case where a person actually drank that clear fluid mistaking it for drinking water with disastrous results.

The initial stage of premonitory diarrhoea leads to the stage of copious evacuations. The evacuations are very copious, a quart or more is often passed at a time and several gallons may be evacuated in a few hours. The diarrhoea is usually painless, patient does not know that he will pass a stool but the stool actually pours from the anus of the patient, quite unconscious to the patient. This is known as effortless diarrhoea. Simultaneously with the frequent purging, watery effortless vomiting occurs even when fluids have not been taken recently, sometimes bilious vomiting takes place. The vomited matter may amount to one or two pints at a time. The combined effects of these copious evacuations bring on the characteristic picture of the malady and directly lead to a great concentration of the blood which is responsible for the collapse and disappearance of the pulse at the wrist. Next *stage is the stage of collapse* which has been described already.

Stage of reaction.—(1) Pulse returns at the wrist.

(2) Cessation of the copious evacuations.

(3) Return of the warmth at the extremities.

If the evacuation stage has not lasted for more than a few hours, the urinary secretion will recommence and convalescence may soon be established but in the more severe cases where the cold stage has persisted for more than 12 to 24 hours or more, the reaction stage is even more dangerous than the former stage of collapse, owing to the frequent occurrence of grave toxaemia. This is due to renewed absorption of the toxins from the small bowel when the circulation is restored; it is also common for the kidneys to fail to resume their function, so that fatal uraemia results.

Febrile reaction.—Rise of temperature with rigor. This serious complication is most common in those patients whose rectal temperature is above normal during collapse and it enables the danger to be seen and to a large extent prevented by administering the salines required for the collapse at a subnormal temperature in such cases. Recording of rectal temperature at frequent intervals is imperative. If hyperpyrexia is accompanied by complete loss of consciousness and delirium, the prognosis becomes exceedingly grave; for, although the temperature may be reduced, return of consciousness and recovery from this condition is rare. In addition to the hyperpyrexial form of reaction, a less common typhoid like force occurs known as cholera-typhoid. These cases are very fatal and difficult to deal with, especially if accompanied by symptoms of uraemia, as is often the case.

Post-choleric uraemia.—Continued suppression of urine after reaction from collapse, unless of strictly limited duration and if accompanied by low blood pressure below 100 m. m., always leads to uraemia later.

A rise of blood pressure to 80 m. m. (as noted in the patients of my ward) or thereabout nearing 100 m. m. may be enough to cause a return of a fairly good pulse but may not be enough to restore the secretion of urine. The result of a persistent low blood pressure will bring out a fatal uraemia in no time, because, the system fails to overcome the stasis which seems to occur in the highly congested kidneys. This sort of cases is most common in feeble Indian subjects of 50 years of age and upwards, in whom cholera is a most serious disease even at the present day. A very slight degree of granular kidney, requiring an abnormally high blood pressure to produce efficient renal secretion in a healthy subject is another not very rare cause of a fatal post-choleric uraemia. Another cause of deficient urinary secretion is the persistence of a high specific gravity of blood, 1060—1062 which leads to insufficient renal secretion, although not sufficient to induce collapse.

The urine should therefore be carefully measured and recorded regularly and if, after restoration of the pulse with the cessation of the algid stage, less than 40 ounces are being passed in 24 hours, the measures described under treatment should at once be resorted to and continued until that amount is obtained. The urine should also have a fair specific gravity indicating the presence of urea and salts and should contain little or no albumin. Low urea excretion and high albumin are bad signs.

Early signs of threatened uræmia are:—(as seen in our hospital).

(1) Eyes become congested, peculiar apathetic look of the patient.

(2) Mental cloudiness, headache, usually frontal.

(3) Tongue coated and dry.

(4) Sometimes dimness of vision and epigastric pain are complained of.

(5) Loss of sleep, burning sensation of the skin and peculiar feeling of general uneasiness which cannot be explained by the patient.

(6) Hurried breathing.

(7) Diminution of the quantity of urine all on a sudden.

(8) Greenish colour and offensiveness of stools.

(9) The pulse remains above normal rate and tends to increase instead of falling; quickening and deepening of the respirations develop, though there are no definite signs in the lungs.

(10) Vomiting and diarrhœa may again be troublesome, hiccough and rise of temperature.

If the action of the kidneys cannot be sufficiently restored, the breathing becomes more and more laboured, restlessness appears and after a struggle for breath, sometimes lasting for several days, gradual cloudiness of intellect and deepening of headache develop leading to coma or cardiac failure. About 5% of the admissions of cholera cases develop post-choleric uræmia in our hospital. These patients generally come to the hospital late after 24 hours or even after 3 or 4 days. Otherwise, early diagnosis and quick treatment and administration of alkali by the venus route may tend to lessen the incidence of this fatal post-choleric complication.

Complications and sequelae in Cholera —

(1) Hyperpyrexia.

(2) Suppression of urine.

(3) Tympanitis.

(4) Parotitis with or without suppuration.

(5) Uræmia.

(6) Heart failure, pneumonia and œdema of the lung.

(7) Abortion.

(8) Malaria.

(9) Corneal ulcer, gangrene of different parts of the body.

(10) Renal inflammation and persistent diarrhœa.

Differential Diagnosis of cholera.—1. *Mild or ambulatory cases.*—Chiefly seen during the end of an epidemic. Any doubtful diarrhœa which is seen at that time should be watched with suspicion unless it is found to be otherwise. Usually, there occur more than one case in the same house at the same time. If bacteriological examination is practicable, it should be always done to clear out any doubt.

2. *Food poisoning.* Can be as acute as in cholera with purging, vomiting and collapse. It is very difficult to diagnose this during the time cholera is prevalent in any locality. Inspection of stools and a bacteriological examination will exclude cholera. History will help a lot—a group of people partake of a common dinner and become acutely ill, simultaneously within a few hours. Whereas in cases of cholera, there is a longer interval between the onset of cases. As a rule the pulse remains fairly good and suppression of urine does not occur.

3. *Algid malaria.*—Due to malignant tertian infection, large number of the parasites are trapped in the capillary vessels of the intestinal mucous membrane. A fall instead of a rise in the specific gravity of the blood will be noticed, because malignant tertian infection produces a profound anæmia. Finding of malarial parasites in the blood-slide and an increase in the differential count of the large mononuclears without increase of the total leucocytes will settle the diagnosis in favour of malaria.

4. *Fulminant bacillary dysentery.*—Inspection of stools, mucus and blood, tenemus etc., will differentiate.

5. *Arsenic poisoning.*—Gastric symptoms, abdominal pain and blood changes.

Moribund patients of all descriptions are liable to be admitted as cases of cholera during the prevalence of cholera but a normal specific gravity of the blood will usually direct attention to the existence of some other cause for the patient's condition.

Prognosis and Mortality in Cholera

Mortality in the Cholera Ward of the Campbell Hospital, Calcutta.

Year.	Admissions.	Deaths.	Mortality.
1926	1559	369	23.73 per cent.
1927	2156	522	24.15 ,,
1928	1916	515	26.88 ,,
1929	2083	439	21.07 ,,
1930	1646	298	18.11 ,,
1931	1564	309	19.75 ,,
1932	1279	262	20.48 ,,
1933	1233	212	17.19 ,,
1934	1312	227	17.30 ,,
1935	2105	322	15.29 ,,
1936 upto Nov.	2127	300	14.10 ,,

Under the old methods of treatment, mortality was:—

60—65 % — in Bombay
59—63 % — in Indian Hospital } in Calcutta.
81—86 % — in European Hospital }

In the decade ending 1908 :

it was 54.2% among Indian troops.
62.3% in Jails.
78.3% in British Army.

In several thousands of cases treated by the old method in the villages in Bombay, the mortality in an epidemic of 1912 was recorded at from 51—60% but probably some of the mild cases are not returned as cholera.

The mortality in the eleven years 1895–1906 inclusive of 1243 cases treated by the old method in the cholera ward of the Calcutta Medical College Hospital, was 59% but among 1249 treated by the fully developed new method from 1905—1919 the death rate was only 20.8% or approximately 1/3 of the former rate. In the Calcutta European Hospital the latest information available gives 26 cases with only one death against a former mortality of 81.6% in the twelve years 1895—1906.

In the Calcutta Hospital cholera wards, not more than 10% recovered under the old method of treatment, but under new treatment 68% of recoveries were obtained in collapsed cases treated with hypertonic salines and permanganates and no less than 55% in patients admitted with no pulse at the wrist; whereas patients in this state scarcely ever recovered under former methods. These data show how great is the improvement in the prognosis when the modern treatment is efficiently carried out. The prognosis in individual cases is now favourable under proper treatment except in feeble Indian subjects of over 50 years of age with collapse and in acute cases in children under 5 years who have little resisting power. Bad features are collapse which has lasted for many hours before coming under treatment, with complete suppression of urine, rectal temperature below normal, or very high, blood pressure remaining below 100 m.m. in the reaction state and uræmia with a blood alkalinity under N/80. Occasional outbreaks still occur in which the virulence of the disease is so great that a high mortality results even though the modern treatment is carried out.

TABLE A.

Cholera in the Campbell Hospital. Calcutta
Seasonal incidence and Deaths.

Month.	Total Number of admissions.	Total Number of Deaths.	Percentage of Mortality.
January 1935 ...	100	18	18.00
February ,, ...	170	39	22.94
March ,, ...	216	45	20.83
April ,, ...	167	41	24.37
May ,, ...	141	21	14.89
June ,, ...	179	22	12.29
July ,, ...	178	33	18.53
August ,, ...	79	6	7.59
September ,, ...	49	2	4.08
October ,, ...	27	1	3.70
November ,, ...	64	10	15.62
December ,, ...	65	18	27.69
Total ...	1435	256	17.83

TABLE B.

Cholera in the Campbell Hospital. Calcutta
Caste and Sex incidence, by Months.

Month.	Hindu		Mahommedan		Other Castes		Total
	Male	Female	Male	Female	Male	Female	
January 1935 ...	59	20	16	3	0	2	100
February ,, ...	93	50	21	5	0	1	170
March ,, ...	123	65	21	7	0	0	216
April ,, ...	93	38	22	13	0	1	167
May ,, ...	73	22	35	9	0	2	141
June ,, ...	87	42	36	11	0	3	179
July ,, ...	91	56	22	7	2	0	178
August ,, ...	51	18	9	1	0	0	79
September ,, ...	33	8	8	0	0	0	49
October ,, ...	14	6	5	2	0	0	27
November ,, ...	41	15	4	2	0	2	64
December ,, ...	44	12	8	0	0	1	65
Total ...	802	352	207	60	2	12	1435

TABLE C.

Cholera in the Campbell Hospital, Calcutta
Age incidence and Mortality.

Age Group.	Total admissions.		Deaths.		Cured	Percentage of Mortality.
	Number	Percentage	Number	Percentage		
1 to 4 years ...	53	3.83	23	8.98	30	43.39
5 to 9 ,, ...	70	4.80	21	8.20	49	30.00
10 to 14 ,, ...	54	3.76	12	4.68	42	22.22
15 to 24 ,, ...	342	23.83	38	14.84	304	11.11
25 to 34 ,, ...	475	33.10	59	23.04	416	12.42
35 to 44 ,, ...	249	17.35	40	15.19	209	16.06
45 to 54 ,, ...	137	9.54	41	16.01	96	29.92
55 years and over	55	0.03	22	8.59	33	40.00
Total ...	1435		256		1179	17.83

TABLE D.

Cholera in the Campbell Hospital, Calcutta
Mortality Month by Month.

Month.	Number of Cases.	Patients recovered.	Patients died.	Percentage of Mortality.
January 1935 ...	100	82	18	18.00
February ,, ...	170	131	39	22.94
Maroh ,, ...	216	171	45	20.83
April ,, ...	167	126	41	24.37
May ,, ...	141	120	21	14.89
June ,, ...	179	157	22	12.29
July ,, ...	178	145	33	18.53
August ,, ...	79	73	6	7.59
September ,, ...	49	47	2	4.08
October ,, ...	27	26	1	3.70
November ,, ...	64	54	10	15.62
December ,, ...	65	47	18	27.69
Total ...	1435	1179	256	17.83

Treatment of Cholera

Let us discuss what has happened to the patient in cholera before we deal with the treatment of the disease.

(1) Enormous loss of fluid from the system dealt with before.

(2) Loss of chlorides with the evacuations.

(3) Specific gravity of the blood has been greatly raised due to dehydration.

(4) Power of absorption of the intestinal mucosa has been lost.

(5) Function of the kidneys greatly impaired.

(6) Reduction of the alkali content of the blood has occurred.

The specific gravity of blood is a guide to transfusion in cholera :—

The haemocrite observations, already described require a laboratory for carrying them out but equally useful record

can be much more easily done at the bed-side by noting the specific gravity of the blood and this method is accurate enough as a guide to treatment. In the cholera ward of the Campbell Hospital, we prepare stock solutions of glycerine and water of accurate specific gravities by a hydrometer, ranging from 1054—1064.

Six small round phials labelled, 1054, '56, '58, '60, '64, are kept in a small wooden box, and there is also another extra phial which contains normal saline. The instrument for actually taking the blood consists of a capillary pipette with a small rubber tube fitted at one end and the other opening of the rubber tube tied by a string. The finger is pricked by the needle by a sharp plunge and the escaping blood is drawn up in the capillary tube without pressing the finger. A drop of blood is introduced in the solutions of known sp. gravity in the different phials one by one. The phial in which the drop of blood just floats for a second or two indicates the actual specific gravity. Care should be taken that the capillary pipette is absolutely dry and the reading should be taken immediately, otherwise the drop of blood would absorb moisture, become heavy and sink down in every phial if the reading is not taken at once.

A rise to 1063 indicates approximately 3 pints of fluid loss from the blood, 1064—4 pints.

In the acute stage of the disease, the specific gravity nearly always varies between 1060—1066 in our hospital, the normal specific gravity in health is about 1054. This figure of 1054 is an average figure which has been calculated from several thousands of normal healthy people.

The common point in the majority of cases is about 1062—1064, which means a loss of about half the fluid from the blood and is always accompanied by general symptoms indicating the necessity for transfusion. If the specific gravity is over 1060, it is wise to give an intravenous injection, even when the general condition of the patient does not appear to demand it, as any further loss of fluid is liable to induce a sudden and dangerous collapse.

The method of taking the specific gravity of the blood, just described, is so simple and rapid, that it can be repeated towards the end of the transfusion, to ascertain whether the blood has been diluted upto or beyond the normal point, being thus of great help in deciding how much fluid to run in. If the blood has reached normal concentration, but the pulse has not improved as much as desired, the rate of flow should be greatly reduced to allow time for the additional fluid to pass into the tissues.

Should collapse recur, the degree of concentration of the blood can again be estimated in the same way and the amount of fluid necessary for an additional transfusion calculated. After reaction has taken place, if the renal secretion is still deficient, the specific gravity will directly show if the blood is still concentrated and requires additional fluid in the circulation to help the kidneys to resume their function.

The estimation of specific gravity of the blood at this stage is very helpful for the intravenous or even the subcutaneous injection of fluid may easily induce dangerous oedema of the lungs, if the blood be overdiluted.

The loss of salts from the blood and its significance :—

The percentage of salts in the blood diminishes greatly along with the loss of fluid. Edmund Parkes in 1849 showed, that the rice water cholera stools contained from ½ to 1% of salts, but very little albumin. Rogers confirmed Parkes' observation, for some estimations he made gave an average of 0.53%of chlorides in rice water cholera stools,although there was only a very small amount in the watery evacuations of the stomach. This would mean a loss of half an ounce of chlorides with every 100 ounces of stools. Rogers found in the most severe fatal cases, in whom two thirds of the fluid of the blood has been lost on the average, the chlorides in the serum were highly lower than the normal, instead of being three times as great as would have been the case if no salts had disappeared from the circulation. In some of the worst cases the percentage of chlorides was actually below normal as little as 0.6%· having been met with, while the serum showed distinct hæmolysis, which however disappeared immediately, on the chlorides being raised to a little over the normal point by a hypertonic saline injection.

In the recovering cases the percentage of chlorides was slightly above the normal, although owing to the great loss of fluid, the total amounts of salts in the circulation must have been greatly reduced. Another very significant fact is, that when the chlorides in the serum have been raised to 1% or over, death rarely took place in the collapse stage, but in the fatal cases this percentage was seldom reached, so that a comparatively high salt content of the blood is of good prognostic significance. All these points very clearly indicate the necessity for replacing the lost salts as well as the lost fluid and furnish a complete scientific basis for the use of hypertonic saline transfusions in cholera.

Intravenous injections of normal saline solutions in cholera have been always a failure, because they commonly contained only 60 grains of sodium chloride to the pint or 0.65,% although we now know that the healthy blood contains 0.85%. By running in 0.65% saline solution, the percentage of salts in the blood would actually be lowered and the immediate reappearance of the copious evacuations would follow leading to rapid recurrence of the collapse. In the worst types with very low saline content and commencing haemolysis, normal salines would do nothing to relieve this dangerous condition. The use of hypertonic solutions immediately raises the saline content of the blood to a considerable degree, with the result that the osmotic currents will tend to carry more fluids into the blood rather than allow it to escape from it and the diarrhoea is checked instead of being encouraged as by normal saline solution.

There is however a very definite limit beyond which it is not advisable to go in this direction because too high a salt content of the blood might possibly give rise to reabsorption of fluid which may contain a large amount of toxins. The marked fever reactions following hypertonic solutions may in part be due to this factor but with proper care, excessive reaction can almost always be avoided and if the blood pressure be fully restored rapid excretion of the toxins by the kidneys takes place.

Reduction of Alkalinity of Blood.—This is an important and dangerous change in the blood in all severe cases of cholera from an early period of the evacuation stage.

SELLARDS (1910) in the Philippines maintained that we could give the patient any amount of alkalies per mouth, but they could never render the urine alkaline due to the pre-existing acidosis and therefore alkalies by intravenous injection were needed as a prophylaxis against post choleric uraemia. Sellard's conception was scrutinised by A. J. Shorten and L. Rogers and were found to be correct. They went through 100 cases and found actually that there occurs a material reduction in the alkalinity of the blood in 79% of cases including all the severe ones. They also estimated that when the reduction reached the high degree of N/100, fatal uraemia always followed. Usually the alkalinity of the blood is found to be reduced from a normal of about N/25 to N/60 or N/80. It is highly important to recognise this feature as we shall see that by injecting a solution of sodium bicarbonate into the vein at an early stage, this dreaded acidosis can be averted. Once the danger point (N/100) is reached, no amount of alkalies will prevent a fatal uraemia.

So the principles of modern treatment of cholera are based on the observations of the blood changes described.

Old methods of Treatment.—By comparing the mortality figures, it is seen that no material advance in the treatment of the disease resulted from the greatly increased knowledge of the causation and pathology during the latter half of the 19th century. The views of the authorities of older days are therefore worthy of careful consideration even at the present day.

ANNESLY (1833).—1. Performed bleeding with the idea of removing the oppression from the venous system and restoring the balance of the circulation. He remarks: "If blood flows freely till the color changes from black to red, the patient will generally recover".

2. Used 2 grains of opium with 20 grains of calomel, being repeated in an hour if the disease appears to be arrested.

3. Applied turpentine sinapisms to the extremities and body.

4. Cold drinks with dilute nitric acid.

FREDERICK CORBYN (1832).—1. 60—150 drops of tincture opium with 15—20 grains of calomel.

2. Purgatives like Jalap, aloes etc.

TWINING (1833).—1. Bleeding in the early febrile and inflammatory stages.

2. Purgatives *e.g.*, calomel, blue pill, cathartic extract and castor oil.

3. One grain of opium every half an hour during purging to afford relief. He never recommended calomel.

GEORGE JOHNSON.—1. Advocated the evacuant plan of treatment. He boldly asserted that there was no relationship between the loss of fluid through vomiting and purging and the severity of the case and therefore concluded that the collapse and circulatory difficulties could not be due to concentration and diminution of the quantity of blood but he attributed it to a tonic contraction of the small arteries of the lungs producing obstruction of the circulation through them. This arterial spasm, he considered to be an evidence of a poison circulating in the blood which must be removed by elimination through the mucous membrane of the alimentary tract by encouraging vomiting and purging—Castor oil being the best remedy for the purpose.

The results of his eliminative treatment in India have been so disastrous as to lead to its complete abandonment. Johnson's pupil Dr. C. N. MacNamara completely condemned this form of treatment.

CHARLES MOREHEAD (BOMBAY 1860).—1. One or two full doses of opium combined with astringents *e. g.* acetate of lead, in both the premonitory and evacuant stages of cholera.

2. During collapse, drugs are useless because they are not absorbed; warmth to the body, a little water with an occasional small dose of ammonia or wine, friction applied for cramps.

3. He never used saline transfusions as previous experience had been conclusive against their use.

JOHN MACPHERSON (1866).—He remarks that the average treatment since 1817 had been wonderfuly uniform with the exception that venesection had been abandoned and points out that even Sydenham after commencing with purging, fell back on opium if the desease became alarming.

EDWARD GOODEVE (1866).—1. 2 grains of opium should first be given in the evacuation stage.

2. Calomel was not good.

3. An astringent mixture of lead acetate and acetic acid was given every half an hour and one grain of opium repeated after one hour.

4. No drugs during collapse stage but only cold water or ice to suck.

5. Ether and ammonia or a little brandy.

6. A little common salt should be added to the food to compensate for the loss of saline matter from the blood.

7. Do not stop diarrhoea in the uraemic stage but give lots of water as a diuretic.

C. N. MACNAMARA (1870).—1. Opium with dilute sulphuric acid.

2. Chloroform to relieve cramps.

3. Cantharides for suppression of urine.

4. He had little experience of saline injections but thought them worthy of further trial.

A. J. WALL (1893).—1. Castor oil and calomel are highly injurious, saline purgatives are even more fatal.

2. Tinct opii m. 12 with acid sulph dil m. x repeated if necessary after two hours. If it was vomited out, he injected m. 12 of the liquid extract of opium subcutaneously. Once collapse has set in, the time for the use of these drugs is past.

3. If there is no pulse and dyspnoea is present, an immediate intravenous injection is necessary. He used 0.4% of sodium chloride and 0.2% of sodium carbonate dissolved in

sterile boiled water. In severe cases as much as five pints were given and repeated again and again if necessary. According to Wall, intravenous salines were first used by Latta and Mackintosh in Edinburg in the first English pandemic of 1831—32, the mortality in 166 operations having been 84%. Wall himself lost a little over 70% of 193 transfusions.

4. Copious tannic acid enemata if the diarrhoea persisted.

5. Opium and calomel and cantharides are dangerous.

KENETH MACLEOD (1907).—Used 60 grains of sodium chloride and 30 grains of sodium carbonate in one litre or 35 ounces of distilled water.

Wall's treatment may therefore be taken as the one that has been generally followed during the last two decades, although intravenous injections have been much less employed than advised and we have seen that the mortality has remained at about 60% for natives at Calcutta and considerably higher, 80%, for Europeans up to 1907.

Rogers' system of treatment of cholera.—*Main principles.*
1. Whenever collapse occurs, and blood pressure is below 70 m. n., replace the lost fluid and salts by a hypertonic saline intravenous injection of sufficient amount to raise the blood pressure to normal if possible, so as to ensure a rapid excretion of the toxins through the kidneys.

2. Freely administer by the mouth oxidising agents to destroy the toxins which are being formed in the gastro-intestinal tract.

3. Carefully watch and control the temperature during the reaction stage.

4. Continue to observe the blood pressure after reaction and use all available means to maintain it at a point which will ensure a free excretion of urine.

Although these indications are sufficiently obvious, yet it is only by the most minute and unremitting attention to details that the best possible results can be obtained as there is no other disease in which sudden changes for the worse so frequently occur, requiring both an accurate knowledge of the condition present and prompt application of correct measures to combat them successfully.

Treatment of cholera is an art, each patient is an individual problem; observe carefully and remember for what you are treating. Treat the life entrusted to you as your own kith and kin.

and never lose hope when there is life. Neglect means Death—Life lost, "All Labour lost."

Drug treatment in Cholera.—Oral administration of drugs in the collapse stage of cholera is useless, as the intestines have lost the power of absorption. Therefore, over-drugging a patient at this stage is positively dangerous because, during the reaction stage, all of the drugs might be absorbed all at once, giving sometimes symptoms of poisoning.

1. *Calomel.*—indirect cholagogue, antiseptic and general disinfectant to the alimentary canal. Fractional doses check vomiting, least harmful to the system, and have increased recovery rate.

Calomel gr. 1/8 Sodi Bicarb Gr. 11	One powder every 1/2 an hour for 10-12 doses.

If the colour of the stools does not change after giving 8—10 powders, it should be repeated with caution and at less frequent intervals, say, every one or two hours

2. *Pot. Permanganate.—Calcium permanganate.*

Not used in the cholera ward of the Campbell Hospital now-a-days. Discontinued for its nasty taste, it produces nausea and has a depressant action on the system. Still used extensively outside for its antitoxic and antimoicrobic properties.

Pot. permanganate is given in pills made by mixing 2 grains of the powdered crystals with a little Kaolin and Vaseline. Also permanganate of Potash or Calcium (2—5 grains to the pint) is given as a drink. Two such pills are given every quarter of an hour for the first two hours, then two, every half an hour until the stools become green.

A former worker in the Campbell Hospital has given his opinion as follows about permanganates:

> $KMNO_4$ is a gastro-intestinal and renal irritant, excreted in the urine and in the intestine. Most of the patients treated by this drug run into toxaemia resulting in Uraemia and obstinate hiccough, due to absorption of the endo-toxin from the dead organisms.

Kaolin.—One part of kaolin with three parts of water, well stirred, can be drunk in tumblerfuls to an unlimited amount. It forms a soothing coating on the intestine. Walker says that Kaolin adsorbs cholera toxins but it does not destroy the bacilli

nor the infectivity of the stools. Patients can never be encouraged to swallow the big quantity of Kaolin and when forced to do so, it was simply vomited out. In cases of bloody stools, kaolin acts beautifully by stopping the blood in no time.

Tomb's anti-cholera mixture not used in the Cholera Ward of the Campbell Hospital.

Alkaline mixture.—One ounce doses given three times a day, usually it is vomited out by the patient, should be given from the beginning and continued till the urine is free.

Adrenalin.—Useful when given under the tongue. Injections only give a temporary effect and it has got the property of constricting arterioles, even of the kidneys and thereby checks to some extent the excretion of urinary solids, which is not at all desired in cholera.

Pituitrin.—The use of pituitrin is regarded futile if it is used with the expectation of temporary improvement of the pulse or with the hope of combating the serious cardiovascular depression in cholera. Pituitrin is preferred because it does not constrict the arterioles of the kidneys, though it constricts other vessels. Hence a larger amount of blood will circulate through the kidneys. Urinary solids will be increased. The use of pituitrin with eserine sulphate or physostigmine sulph is preferable as it acts well in cases with intestinal paresis and tympanitis. ½ c.c. of pituitrin may be injected intramuscularly in all cases of collapse with cyanosis immediately after saline transfusion.

Stimulants in Cholera.—In cholera, a large quantity of fluid has drained away from the system, so we would certainly be more justified in replenishing the amount of fluid, than in treating such cases by stimulants. Use of stimulants in cholera cases is more likely to cause damage, when we do know that infusion of salines is the only salvation in genuine cases of cholera. So our suggestion in the treatment of cholera would be with saline infusions at once, with a minimum amount of stimulants as far as practicable.

Atropine Sulph.—A cardio-vascular and respiratory tonic. It can be used morning and evening in 1/100 grain doses in cases with repeated collapse or where there is any apprehension of oedema of the lungs.

Indication:—

1. Extreme collapse with cyanosis.
2. Pulmonary complications.
3. When the heart is failing.

5. Where response of pulse is not satisfactory after saline transfusions.

Contra-indications:

1. High rectal temperature.
2. Tympanitis.

Caffeine et Sodi Benzoas.—This preparation acts nicely in cholera cases. Excellent result is seen in our hospital cases with profound cardiac weakness, sometimes it acts like a charm in the early stage of Uraemia by producing a fair secretion of urine.

Caffeine (Pure) gr. 48
Sodi Benzoas „ 48 } to be sterilised by boiling

20 minims to be injected intramuscularly, once or twice daily according to the severity of the case. Freshly prepared solutions should always be used. Old preparations turn acid in reaction and if injected gives violent local inflammation, usually leading to suppuration.

Salines in Cholera (as used in the Campbell Hospital, Calcutta).

1. *Hypertonic saline*:

Sodium Chloride	...	gr. 120.
Calcium Chloride	...	„ 4.
Aqua distillata	...	pint 1.

2. *Normal saline*:

Sodium Chloride	...	gr, 90.
Aqua distillata	...	pint 1.

3. *Normal saline et sodi bicarb*:

Sodium chloride	...	gr. 90.
Sodi bicarb	...	60 „
Aqua distillata	...	1 pint.

4. *Hypotonic saline with soda.*

Sodium chloride	...	60 gr.
Sodi Bicarb	...	160 „
Aqua distillata	...	1 pint.

5. *Glucose et soda*:

Liquid glucose	...	1 oz.
Sodi bicarb	...	60. gr.
Aqua distillata	...	1 pint.

6. *Glucose saline*

Liquid glucose :	... 1	oz.
Sodi bicarb	... 90	gr.
Aqua distillata	... 1	pint.

7. *4 % Soda solution* :

Sodi bicarb	... 360	grs.
Aqua distillata	... 1	pint.

8. *50 % Glucose solution* :

Glucose	... 2	oz. } Sterilise
Aqua distillata	... 1	oz. } by heat.

9. *Hyponormal saline with soda* :

Sodium chloride	... 60	gr.
Sodi bicarb	... 90	,,
Aqua distillata	... 1	pint.

The above solutions should always be perfectly sterilised before transfusion. To prepare solutions of saline with Soda, the required amount of Sodi Bicarb should be in paper packets and sterilized in autoclave. First boil the water with sodium chloride, then when cool, add the requisite amount of Sodi Bicarb, previously autoclaved. Never boil sodium bicarbonate because there will be a precipitation of Soda Carb with milky discoloration of the solution and if such milky fluid be ever transfused, fatality is sure to follow instantaneously.

Routes of saline injections as used.—1. *Oral administration.*—not at all preferred because all are vomited out.

2. *Rectal administration*—Very small amount is absorbed, so it is really useless in collapse cases where rapid intravenous infusions are urgently required to bring back life to the patient. It may be helpful in mild or very early cases when the purging is not too frequent. Sometimes, rectal saline becomes a thing of choice in cases of infants, as it is often a difficult problem to locate a vein for transfusion, while subcutaneous saline becomes very painful.

Subcutaneous method.—Method of choice in infants along with rectal saline. In adults, it would be an ideal treatment if carried out along with intravenous transfusion. In our hospital, we always give a pint of normal saline subcutaneously every day for 3 or 4 days according to the severity of the case, in conjunction with intravenous salines. Sepsis is always avoided if strict asepsis is maintained and I have seen very few cases of

sepsis with suppuration after subcutaneous saline out of several thousands treated.

Advantages of subcutaneous saline :—

(1) Reserve quantity of fluid for slow absorption when collapse repeats frequently.
(2) In hyperpyrexia with extreme collapse.
(3) When specific gravity of blood is just raised above normal.
(4) In asthenic condition with heart and lung involvement.

Disadvantages :—

(1) The operation is very painful.
(2) Big quantity of fluid cannot be pushed in.
(3) Absorption is very slow.
(4) Sepsis and tetanus.

4. **Intravenous method.**—Method of choice, quick replenishment of the amount of fluid and salts lost and consequent adjustment of circulation.

Indications :—

(1) Profound collapse with cyanosis, restlessness and painful cramps.
(2) Feeble or no pulse at the wrist.
(3) Specific gravity of blood above 1056.
(4) Suppression of urine.

Contra-Indications :—

(1) Extreme cardiac asthenia.
(2) Bronchitis or Broncho-Pneumonia.
(3) High rectal temperature (above 100° F).
(4) Distressing tympanitis.
(5) High specific gravity of blood with fair pulse.
(6) Low specific gravity of blood with nil or very feeble pulse.

Temperature of the saline should always be at room temperature. In hyperpyrexial cases cold saline should be preferred. Use of non-conducting aluminium jackets for keeping the temperature of the saline constant was specially devised by Late Dr. A. N. Sen and my humble self. The rate of flow of the infusion

should be 4 ounces a minute—so in five minutes one pint can be safely given.

We observe the following principles before we give intravenous salines:—

(1) If duration of the disease is within 24 hours—hypertonic saline in adequate quantity should be given.

(2) If duration is over 24 hours but within 48 hours, normal saline with soda.

(3) If duration is over 48 hours.—Salines with miximum quantity of sodi bicarb *e.g.* hypotonic saline with soda.

Because in the early cases within 24 hours, the patient has lost a large amount of fluid and salts from the blood, at this stage we give fluid and maximum concentration of salt (Nacl.) *i.e.* Hypertonic saline. By giving this saline in adequate quantity, the salt content of the blood is raised to nearly 1 % and with subsequent purging and vomiting, it will again come down and stay on at the 0.85 % level. So, there is no need of putting in hypertonic saline again after 24 hours had passed. After 24 hours, the patient has lost fluid and salts no doubt but the alkalinity of blood has diminished also or in other words the patient is running into the acidosis stages. So we give normal saline with soda.

When the duration of the disease is more prolonged, the acidosis is more and more deepening or in other words the patient is nearly running on to the uraemic stage. So, the rational treatment would be to push in gradually increasing doses of alkalies with lesser quantity of salts in the intravenous transfusions. If specific gravity is running high indicating more fluid to dilute the blood, we use hypotonic or glucose soda in the later stages but if it is not high we inject 4 % soda—10 oz. intravenously required in individual cases:—

If specific gravity of the blood is 1058 with signs of collapse and no pulse, inject 1½ pints.

If 1060, 2 or 2½ pints are necessary. If 1062 and 64, 2½, and 3 pints according to the existing condition of the patient.

Each intravenous transfusion should invariably be supplemented by a pint of subcutaneous saline (Normal).

It is certainly wise to push in less quantity of saline and repeat it as often as necessary than to overload the system with the

maximum amount at one sitting. Cases treated in a deliberate way like this has been met with fatal complications like oedema of the lungs, tympanitis and cardiac failure.

Judgment is always necessary during and before administration of salines and each patient presents an individual problem. In each case, the primary cause of collapse must be investigated beforehand, because collapse may be due to loss of a large amount of fluid from the system without any asthenic condition of the heart or it may be due to primary cardiac weakness without much loss of fluids or the collapse may be due to a combination of both. Always remember these conditions clearly before you give the infusions and never be dogmatic in your treatment—if collapse is primarily due to a loss of fluid, replenish the required amount by an intravenous infusion, which will really bring back life. When collapse is due to a primary weakness of the cardiac musculature, intravenous transfusion would overload the already damaged heart; the peripheral arterioles will not be able to accommodate the forced fluid and a disastrous result will follow in no time. Cases with moderately high specific gravity of blood should be treated with the greatest caution and transfusions should be limited to small amounts. But in cases, where the specific gravity of blood is just above normal, compensation for that small amount of fluid loss can be made by giving a subcutaneous injection of normal saline with a view to gain the reaction stage by slow absorption and without producing the least amount of embarrassment of the heart. A fair number of cases with low specific gravity of the blood has been treated in this way with success and it has been found that many such cases carry on with very feeble or hardly any perceptible pulse for days together and ultimately come round nicely. In cases of collapse with low specific gravity, the patient's condition should be investigated thoroughly, for, there may be combinations of other diseases. Anaemia will never show high specific gravity, though associated with profound collapse in cholera.

The main principle in the treatment of cholera is to counteract the frequent collapses by repeated administration of intravenous salines, guided strictly by the specific gravity of blood and finally we would arrive at a point when there will be no longer any apprehension of recurrences of the collapse—that is, the so-called stage of vascular equilibrium will be reached when the patient will continue on, keeping a reasonable pulse at the wrist and will be passing urine in fair amounts. One should always be on guard, for as the case progresses from day to day, there

may again be chances of collapse setting in, which, at this stage is due more to the weakness of the heart than to the actual depletion of fluid from the system. Further transfusions in such conditions should always be strictly guided by the specific gravity of the blood, otherwise fatality is sure to follow.

As for the varieties of salines used.—Hypertonic is the ideal in the first instance. Succeeding ones should consist of salines with gradual increase of alkali (Sodi bicarb) in them. In cases of threatened uraemia with a high specific gravity of the blood, which indicates intravenous fluid to dilute it, 1—2 pints of alkaline saline (Hypo soda soln.) would work as a charm. In hopeless cases, without any urine at all or very little, 8—10 ounces of 4 % soda should be given. Uraemia is the chief cause of death (about 45 %) but it can be very much modified if soda is given intravenously in time.

A certain percentage of cases is complicated by a high rectal temperature. Intravenous infusions should never be done unless the temperature has been lowered by hydrotherapy *viz.*, iced water enema, bath and ice pack, otherwise, the reactionary fever will hasten death. If the temperature drops down to normal by hydrotherapy and keeps on at that temperature for a few hours, then and then only intravenous transfusions should be carried on, otherwise subcutaneous saline is the only resource at our hands. Sometimes, cardio-vascular depression is so profound in these cases that subcutaneous saline alone fails to keep up the patient, hence pituitrin ½ —1 c. c. should be injected subcutaneously. It should be the first and foremost duty of every physician to have a thorough examination of the lungs in all cases. In all suspicious cases treatment should be managed with subcutaneous saline as far as practicable. In very acute cases only, small amounts should be given intravenously.

During the course of treatment, if the patient developes lung complications, intravenous transfusions should be altogether withheld—the only alternative now left being subcutaneous saline to keep the patient going.

Treatment of cholera in children.—The characteristic rice-water stools and effortless vomiting etc are hardly seen in children. The stools are usually greenish white at first, gradually becoming curd like and restlessness and suppression of urine with rapid onest of uraemic symptoms and collapse are typical features of cholera in infants. Collapse and cyanosis are extreme though the specific gravity of blood is rarely higher than 1056-1058 Hence saline injections are generally needed in pulseless conditions even with

1056 or 1058 specific gravity. Never transfuse more than 4 or 5 ounces at a time, more means death in children.

Post choleric complications.—*Tympanites*: If slight, apply turpentine stupes on abdomen, insert flatus tube. In addition to this, inject pituitrin 1 c. c. with phisostigmine sulphate Gr. 1/100, if it is severe.

In spite of marked tympanites, if patient is collapsed and pulseless, never hesitate to transfuse at least a pint of fluid to keep the patient going. Wait until tympanites subsides for full amount of transfusion. If tympanites continues and collapse returns, do not transfuse more than a pint of fluid each time. Always supplement by subcutaneous saline. Never inject Atropine in such cases. Strychnine with or without stropanthine better, if pituitrin and physostigmine fail.

Lung complications.—May be due to:

(1) Uraemia.
(2) Pneumonias.
(3) Extreme loss of fluid.
(4) General asthenia.
(5) Myocardial degeneration.
(6) Hypostatic congestion.

Treatment as per cause.—*Oedema of lungs.*—Transfusion is contra-indicated—50 % glucose 15 c. c. I. V.

Praecordial distress during transfusion—slower rate—push subcutaneous and rectal saline 25 % glucose 20 c. c. I. V.

Hurried breathing during transfusion—Oedema of lungs—Stop injection.

Violent headache during transfusion—stop; slower rate—lower temperature of fluid.

Uraemia :—

(1) Alkaline mixture freely given 1 oz. every 4 hours.
(2) Glucose et soda drinks ad lib.
(3) Glucose et normal saline per rectum by the drop method.
(4) 1 oz. of castor oil—start with and repeat until bowels move freely, followed by intravenous 4 % soda 10 ozs.
(5) Dry cupping and fomentation over the loins—caffeine and atropine injections.

(6) Diuretin 7—10 grain doses twice or thrice daily.

(7) If no urine, repeat 4% soda intravenous after 24 hours.

(8) If still there is suppression 4% soda intravenous must be repeated : give 25% glucose, 15—20 c.c. I. V.

Soda bicarb has been given with success up to 1200 grains but remember risks of alkalosis, convulsions, coma and death.

Patients should not be disturbed unnecessarily ; attend to the eyes by Boric lotion wash, clean mouth with dilute E. C. and boroglycerine. Guard against bed sores. Alkaline sponging (one drachm of sodi bicarb to the pint) will relieve itching of the skin. Rectal temperature to be recorded every 4 hours because you can get subnormal temperature at the axilla while the rectal temperature is very high. Keep a record of the number of stools and urination. Feed with barley water, fruit juice and glucose solution. Examine the urine for reaction, albumin and acetone bodies. Venesection has been recommended by some in severe cases. In sudden coma and amaurosis, venesection or intravenous infusion of hypertonic saline is said to be of help.

Cases complicated with epistaxis, bleeding gums, and malæna are treated with calcium lactas gr. 15 T. D. S. or intravenous injection of calcium chloride 10%, 2—5 c.c. Headaches should be treated with bromides or chloral hydrate with bromides or both ; gastric irritation is treated by Tr. Iodine m. ii in a drachm of water or chloretone.

Hiccough—an obstinate complication ; it is usually toxic in origin causing irritation of the phrenic nerve.

Castor oil in an ounce dose acts nicely at the very outset.

Tr. Iodine m. i. in ½ oz. of water given every ½ an hour for 6–8 doses. Chloretone gr. x B. D. Atropine sulp. gr. 1/100 injected hypo. Mustard plaster on the epigastric region. Gastric lavage with 4% soda solutions.

Corneal ulcer—Normal saline wash, liquid paraffin drops, cauterisation of the ulcer with tinct of Iodine. Atropine drops and H. O. F. ointment at night.

Rash—Usually appears in the convalescent stage. Its appearance indicates that the patient is getting over the disease.

Cholera typhoid state—Very severe complication, patient get continuous typhoid-like temperature and it usually terminates in fatality.

Anticholera serum :—

(1) Dr. H. N. Ghose's serum 25 c.c. mixed with 75 c.c. of normal saline and given intraperitoneally was tried in a fair number in our hospital, but results were not so satisfactory.

(2) Bayer's Anti-cholera serum 20 c.c. intravenously is worth a trial.

Bacteriophage in the treatment of cholera.—Give gr. i sodi bicarb to the patients. Then, after a few minutes give one ampoule 2 c. c. of cholera phage and repeat these every 4 hours. This treatment is done in addition to the other usual routine treatment.

Bacteriophage was extensively tried in a pretty good number of patients by Pasricha, de Monte and O' Flynn in the Cholera Ward of the Campbell Hospital, Calcutta, and they have drawn the following conclusions :—

(1) A series of 1369 cases of cholera admitted in the Cholera Wards of the Campbell Hospital during the year ending 30th July 1935 have been investigated. Of these, 684 cases were treated with specially prepared phage and 685 were not treated with cholera phage. This selection in the two series was made by taking alternate admissions into the wards.

(2) Comparison of the results of the experiment, taking recovery or death as the sole criterion of the value of cholera phage, shows that bacteriophage has caused a real reduction in cholera mortality in cases passing vibrios and that this reduction is more marked in those cases passing agglutinable vibrios.

(3) There is no significant effect on cases passing non-agglutinable vibrios only or in cases bacteriologically nagative.

(4) There is a marked reduction in the incidence of uraemia in the phage treated series.

My own clinical experience with cholera phage.—It seems to be effective towards amelioration of symptoms *e.g.* vomiting and purging lessen quickly. The initial toxic symptoms like restlessness, hiccough and headache seem to be less marked in the cases treated with phage.

Administration of bacteriophage in the cured cases seems to be a valuable adjunct to the routine treatment of cholera in association with saline injections. The number of saline injections required for the phage line cases is less than those in the non-phage cases. Its value as a curative agent in cholera is less

convincing, as the clinical course of events looks just the same in both lines ; bacteriophage has never created any particularly more definite impression on us from a purely clinical point of view. Incidence of the cases that are called uraemia clinically, which is usually due to failure of the kidneys and paretic condition of the vasomotor system, is almost the same in both lines.

Bibliography:—

1. *Acton (1933)—Bull. Mens. off Internant D'Hyg 25, 1171.*
2. *A Sheshov, S. Khan, Lahiri and Chatterjee—Ind. Jl. Med. Res. 20, 1134.*
3. *Balteano and Lupu (1914) C. R. Soc Biol. 76, 680.*
4. *Besredka (1922) Bull. Pasteur 20, 1, 41.*
5. *Cunningham (1877) Quot by Mackie 349.*
6. *Dunn (1929) Bull. Mens. off Internant D'Hyg 25, 1445.*
7. *Gibson (1916) Brit Med. Jl. ii, 454.*
8. *Gill and Lall (1930) Ind. Jl. Med. Res. 18, 1255.*
9. *Goyle and Gupta (1932) Ind. Jl, Med. Res. 20, 35.*
10. *Greig (1929) A. System of Bacteriology, 380.*
11. *Haffkine (1893) Anticholera inoculation, Cal. 1893.*
12. *D'Herelle, Malone and Lahiri 1930 Ind. Med. Res. Memo 14.*
13. *S. Khan (1929)* (a) *Ind. Jl. Med. Res. 17, 147,* (b) *Ibid 164, Ibid 18, 361.*
14. *Kolle (1896) Zbl. Bkt, I Orig 19, 97.*
15. *Linton (1932) Ind. Jl. Med. Res, 20, 347.*
16. *Maitra and Ahuja (1931) Ind. Jl. Med. Res. 19, 159.*
17. *Lint, Shrivastava and Mitra—Ind. Jl. Med. Res. 21, 385.*
18. *Morgan (1933) Bull-Mens. off Internant D'Hyg, 25, 89.*
19. *Raju and Sarkar (1931) Ind. Med. Gaz. 66, 135.*
20. *Pasricha, De Monte and Gupta (1932)* (a) *Ind. Med. Gaz. 67, 64;* (b) *ibid 487;* (c) *Ibid 68, 448.*
21. *Morison—Bacteriophage in the Prevention and Treatment of Cholera.*
22. *Nicolle, Connor and Conseil C. R. Acad Sci, 154. 1823.*
23. *Russell (1927) Transact, 7th Congress Far East. Assoc. Trop. Med. 1,523.*
24. *Stewart (1923) Bull Mens. off Internant d'Hyg, Publ. 25, 995.*
25. *Tomb and Maitra (1927) Transact 7th Congr. Far East. Assoc. Trop. Med. 2, 208.*
26. *Stitt—Tropical Diseases.*
27. *Megaw and Rogers—Tropical Diseases.*
28. *Rogers—Cholera and its Treatment.*
29. *Guin—Cholera and its Treatment.*
30. *Parke's Text book of Hygiene.*
31. *Currie—Text book of Hygiene and Public Health.*
32. *Rosenau—Preventive Medicine and Hygiene.*
33. *Wu-Lien Teh. Cholera (National Quarantine Service China).*
34. *Tice—Text book of Medicine.*
35. *Byam and Archibald—A practice of Medicine in the Tropics.*
36. *Ind. Med. Gaz. 1930 Sept., March.*
37. *National Med. Journ., 1926, XII.*
38. *League of Nations, Health Organisation 1927, Geneva.*
39. *Ibid.*
40. *National Quarantine service reports, China 1932.*
41. *Ind. Med. Gaz. 1931 LXVI Trop. Dis. Bulletin, 1931.*
42. *Ind. Journ. Med. Research 1930, July.*
43. *Journ. R. A. M. C. 1927, XLVIII.*
44. *Pasricha, de' Monte and O'Flynn—Ind. Med. Gaz. Feb. 1936.*
45. *Shiga, Takano and Yabe (1918) Kitasato Arch. Exp. Med. 2, 1.*

Cholera and its Modern Treatment

BY

H. S. BARUA, M.B., B.S., D.T.M., D.P.H., (LONDON),

Asst. Surgeon, incharge of Civil Hospital, Palampur, (Kangrao), the Punjab,

CHOLERA is an infectious disease characterised by violent purging, vomiting, cramps, suppression of urine and collapse. Cholera has been known since ages, even Charaka and Susruta have described symptoms which probably refer to this disease. The earliest record of this disease is found in 1438 when Ahmed Shah's army is said to have been decimated by it. After this, there are several references, for it is mentioned by Vasco de Gama in 1490, in Pondicherry in 1768 and in Calcutta in 1781. In 1817 it spread in a very extensive epidemic form starting from Bengal (the endemic home of cholera) and spreading towards Arabia, Ceylon, Burma, Singapore and China. Generally Pandemics and Epidemics used to start from Bengal. In 1837 it also visited Europe, Africa and America. The disease went on appearing in one of the three-Demic forms in the world till in 1900 when it broke out in India after a severe famine; the disease with its virus is said to be continuing up to this day.

Etiology.—The specific germ is one or other variety of cholera vibrio generally known as comma bacilli. It is found in intestinal wall contents. stools, vomits, gall bladder, bile, and mesenteric glands. It is said that some vibrios are even found in the faeces of healthy people who have never shown signs of the disease, hence some predisposing causes like mental worry, underfeeding, any slight disorder of alimentary canal as diarrhœa and insanitary conditions are the precursors of the disease. In the bowels the cholera produces a powerful toxin called (cholera Amines) made from tryptophane and this toxin when absorbed is responsible for the chief features of the disease. It leads to the passage of fluid from blood to bowels producing great concentration of blood—its specific gravity going as high as 1078. The alkalinity of blood is decreased and its coagulability power is altered.

Manner of Infection.—It always comes from cholera cases or carriers and infection is usually indirect through contamination of water, milk, and raw green vegetables. The flies play a great part in carrying infection to food or water. It very rarely occurs by direct contact with the patient. When travelling from one place

to another it always adopts channels of human communications viz: ships, rivers, roads and railways.

Symptomatology.—The attack sets in suddenly with diarrhœa; motions coming in succession one after the other. These may be painless or accompanied by griping and tenesmus. Quickly the typical choleric symptoms develop. The stools become large, odourless, pale and watery like rice water. The early stools are full of Bacteria i.e. nothing but pure culture of Cholera Vibrio. Stools are alkaline and are of low specific gravity. Soon vomiting, thirst, and sometimes hiccough follow. As purging and vomiting proceed urine diminishes and even stops. Agonising cramps begin to appear in the muscles of calf, abdomen and back. Rectal temperature shoots upto 103° F. or more. Pulse quickens but mind remains clear. Due to loss of serum the patient becomes collapsed and presents a peculiar appearance :—the face is pinched and drawn, nose becomes sharp, eyes sunken and the skin of the fingers and toes wrinkled up like goose skin. Pulse is now thready and Blood Pressure falls below 80 m.m. and Specific Gravity rises to 1065, or more—(normal is 1056.) Respiration is shallow, breath cold and voice husky. The temperature falls and mind becomes cloudy. The patient may develop coma and die of Toxæmia or exhaustion, or may pass on to third stage. In favourable circumstances, after a short time the patient begins to improve. Vomiting and purging stop, urine is passed, pulse returns at the wrist, cyanosis lessens, skin warms up and mind becomes clear and cramps pass away. There may be a slight reaction fever also. In other cases due to superadded infection the fever may keep on for weeks or secondary septic infection of the bowels may occur and patient relapses into a Typhoid state and may die of Uraemia. (*Cholera Typhoid.*)

Clinical Varieties.—1. *Ambulatory type.*—i.e. cases without any signs of disease. The vibrios may be obtained from the fæces. Such are genuine carriers.

2. *Cholerine or Choleroid Type.*—They are mild cases with rice water diarrhœa; slight relapses and with quick recovery.

3. *Choleric Sicca.*—(dry form) They are cases with severe Toxaemia. The patient dies of toxæmia without any reaction.

4. *Choleric Gravis.*—The form above described.

Differential Diagnosis.—Sporadic cases may simulate Arsenic, Mercury or Copper or even Food poisoning. Acute cases of Gastro-Enteritis, or Choleric form of Pernicious Anaemia may simulate Cholera.

Diagnosis.—Easy in times of Epidemic, as clinical features are distinct. Confirm the diagnosis by finding *comma* bacilli in stools or vomits by making films from rice flakes. To the stools add 1% NaCl solution or 50% Ox Bile and after making the film stain it with diluted Ziel Carbol Fuchsin, 1/50, for 10 minutes or with Loffers Blue for 5 minutes.

3. Make cultures of it on Mackonkeys Lactose Agar plate and incubate at 35°C. Colonies of the cholera and cholera like vibrios develop as delicate small yellowish roundish dots within 12 to 18 hrs.

Prophylaxis against cholera.—1. Keep the house in perfect sanitary condition.

2. Boil well the drinking water, milk etc.

3. Take only recently cooked food while hot.

4. All foods should be covered and protected from flies.

5. Eat no raw food and take no unboiled milk.

6. Sterilize carefully all the utensils of the patient and disinfect all the discharges of the patient.

7. Protect your hands with gloves when dealing with a case. Protect the excreta of the patient from flies and screen off all foods from them.

8. All cases of diarrhœa in times of Epidemic should be carefully treated.

9. Get prophylactic inoculation done with anti-cholera vaccine (Kasauli type). Strength 8000 Million in 1 c.c. First dose is ½ c.c. and 10 days later, a second dose of 1 c.c

10. Instead of inoculation, one can even take a course of *anti cholera billi vaccine.*

11. Don't go out of the house with empty stomach. Acid drink or alcohol may be taken twice a day.

12. Essential oil mixture is also used as prophylaxis morning and evening.

13. Rest of the measures are to be taken by the Health Dept.

Treatment.—The treatment of cholera must aim at the destruction and removal of vibrio, the neutralization of the toxin, the prevention of secondary infection through the damaged intestinal mucosa, the healing of which must also be assisted, and the relief of symptoms.

General Measures.—The patient should be kept in a fly-proof room in a horizontal position in the bed. Keep him warm. His discharges and excreta should be well disinfected. Bed pans and urinals should be used. No food but sips if ice water are

allowed in the beginning, and later on plenty of water to drink in sips. Skin should be kept dry and if there is any tendency to collapse, pack him up with hot water bottles. Stimulants should also be given.

Medicinal Treatment.—1. *Calcium or Potassium permanganate solution* 4 grs. to a pint to be given to drink freely. They are also given as pills. The whole idea is to oxidise the cholera poison. $KMNO_4$ pills are given as Keratin or Salol coated pills. Two pills are to be given every 15 minutes for the first three hours and then two pills every ½ hour unless stools are greenish and less copious; it takes about 12 hours; then, stop for that day. For the next 2 days two pills every ½ hour for two hours daily. The stomach should, if necessary be washed with $KMNO_4$ solution (4 grs. to a pint). Along with the above treatment *Kaolin* suspended in water to the consistency of a porridge (5 oz. to a pound) should be given: 8 oz. at once, 2 to 3 oz. after every 15 minutes with the $KMNO_4$ pills. It adsorbs and renders the cholera toxin inert and increases the efficiency of $KMNO_4$ action. *Kaolin* itself has got no action on cholera vibrio.

2. *Essential Oil Mixture Treatment.*—It is given to contacts and person suffering from diarrhoea and vomiting. It is useless in advanced cases of the disease. In mild cases it is effective. The formula is:—

Oil of Cloves	...	♏ v
Oil of Cajuput	...	♏ v
Oil of Juniper	...	♏ v
Acid Sulph Aromatic	...	♏ xv
Spt. Aetheris	...	♏ xxx

This dose in half an ounce of water is given every ½ hour till 8 doses are given.

There is another modified Essential Oil Treatment which is effective in early cases. It is:—

Oil *Caryophylli*	...	♏ i
Oil Cajuput	...	♏ i
Oil Cinnamoni	...	♏ i
Camphorae	...	grs. 2

Misce et solve. One dose in a lump of sugar with tepid water.

Rogers' Saline Treatment.—It is the modern treatment for cholera. It reduces the mortality from 50—60% to 11%. Its *Technique* is:—

(1) Hypodermic Injection of *Atropine Sulph* gr. 1/100 to be given at once and to be repeated morning and evening throughout the treatment. The Sp. Gr. of blood, its B. P. and Temp. in mouth and rectum, should be recorded.

(2) Repeated free use of saline infusions should be carried out. They prevent collapse, dilutes the toxins, stimulates the heart and excites free action of kidneys. Three solutions are used.

Hypodermic Saline Infusion Solution:—

Sodium Chloride	...	grs. 120
Potassium Chloride	...	grs. 6
Calcium Chloride	...	grs. 4
Aqua	...	pint 1

It is given Intravenously or Subcutaneously.

(1) *Isotonic Saline Solution*:—

Sodium Chloride	...	grs. 60
Potassium Chloride	...	grs. 6
Calcium Chloride	...	grs. 4
Aqua	...	pint 1

It is given per rectum and subcutaneously.

(2) *Alkaline Hypodermic Saline Solution*:—

Sodium Chloride	...	grs. 120
Potassium Chloride	...	grs. 6
Calcium Chloride	...	grs. 4
Soda Bicarb	...	grs. 180
Aqua	...	pint 1

It is given in acidosis and when uraemia is threatened.

Value of the injection.—Begin the injections as early as possible and give as much as is necessary each time and repeat as often as is required judging from the amount given each time and the solution given and the route and also the "Specific Gravity of blood and B. P, which act as guide. Blood pressure is taken by Sphygnomanometer and Sp. Gravity by adding drops of blood to a series of dilution of glycerine and water in a set of bottles. The Sp. Gr. in various bottles vary from 1050 to 1066.

Normal B. P. is 120 to 140 m.m. and Sp. Gr. 1056. Speaking generally, the lower the B. P. and higher the Sp. Gr. the greater is the need for Hypodermic saline solution, intravenously whereas with a slight fall of B. P. or slight rise of Sp Gr. it will be enough to give Hypertonic Solution hypodermically, or Isotonic per rectum.

Amount to run in.—Enough solution should be run in to raise B. P. to 90 m.m. and lower the Sp. Gr. to 1050 Usually 4 to 6 pints are required. One can judge what to add from glycerine water dilution bottles. If drop quickly rises in 1062 bottle, then only Hypodermic or Rectal infusion is necessary. If it floats or sinks slowly in 1062 bottle then run in 4 pints Hypertonic intravenously at once and if drop sinks also in 1066 bottle, make the amount to 6 pints. The solution should be run in at body temperature generally but if Rectal temperature is above normal then solution temperature should be below body temprature In addition to the above treatment give *Isotonic* saline per rectum, ½ pint every now and then unless the collapse stage is passed. For cases who are admitted late with suppression of urine, give Hypertonic Saline intravenously. To the first pint add 180 grs. of soda bicarb and then continue ordinary Hypertonic Saline.

When to repeat.—Take B. P. and Sp. Gr. regularly morning and evening and at any time when pulse fails or patient becomes restless, repeat it. Any fall in B. P. to 70 m.m. or rise of Sp. Gr. to 1063 occurs, then repeat Hypertonic intravenously and in each repetition make the first Hypertonic Saline pint alkaline. When restlessness, cyanosis and cramps are marked, give intravenously.

Technique:—Place ligature round the *Arm* or leg to distend Veins. Disinfect the part and fill in the saline infusion apparatus with the required solution and puncture the vein with the needle in the direction of the heart. Lower the apparatus and let the blood appear in the glass window, then remove the ligature and let the fluid run in slowly not more than 4 oz a minute till the pulse returns and after that run in more slowly so that one may not overdo it. Listen to the accentuation of the secondary Pulmonary sound and see that there so no crepitations at the bases of the lungs. Run in the solution so much that B. P. is 100 m.m and Sp. Gr. 1050. When Uraemia threatens and B. P. is low besides using Vaso constrictors as Pituitrin, Adrenalin, Digitalin, Caffeine and Strychnine, give hypertonic saline intravenously. Tinc Iodine and Emetin are also worth trying.

Rest of the treatment is symptomatic :—

Suppression of urine :—(1) Catheterise and draw the urine.

(2) Apply hot fomentations and dry cupping over the loins.

(3) Irrigate the colon with 120° F. hot isotonic saline using long rectal tubes.

(4) Hypertonic saline with glucose to be given intravenously or subcutaneously.

(5) Pitutrin, H Injection ½ c.c.

Cramps:—(1) Hot mustard foot bath or even hot bath.

(2) Locally hot fomentation or mustard compresses or turpentine Stupes.

(3) Brisk rubbing.

(4) If cramps are very bad, give Chloroform or morphia injection.

Vomiting:—(1) Wash out the stomach with a weak solution of Condy lotion or hot isotonic solution.

(2) Mustard plaster over the pit of the stomach.

(3) Chopped ice to suck and withdraw all food.

(4) If need be, give morphia injection.

Collapse:—(1) Start saline infusion early. Keep the patient warm and packed up with hot bottles.

(2) Constantly wipe off the sweat with flannel.

(3) If collapse occurs, add alcohol, tea-spoonful, to saline infusions.

(4) Stimulant injections to be given.

(5) Rigor, Restlessness or Delirium in the collapsed state requires careful treatment. Rectal temperature 104° is bad. In such cases don't surround the patient; packing him up with hot bottles is contra-indicated.

General reaction:—Return to normal diet very very slowly, and if constipation occurs, open bowels with enema not with aperient.

Saline Treatment in Cholera

BY

H. N. BAKSHI. L.M.S., D.T.M.

Teacher, In-charge of Infectious Wards,
Campbell Medical School and Hospital, Calcutta.

Intravenous Saline.—The intravenous injection of saline in the treatment of cholera was probably tried, for the first time, in the history of the disease, by Latta and Mackintosh in Edinburgh during the first English Epidemic of 1831—32, which broke out in that city, among other places, in October, 1831. Among 166 patients treated by this method, the death-rate remained as high as 84 per cent.

Owing to the disappointing and unsatisfactory results, the treatment by this method had fallen into disuse for a considerable time and nothing was heard about it till, towards the latter part of the nineteenth century, it was revived again by A. J. Wall who, with his extensive knowledge and vast experience regarding the disease, not only used it himself but also advocated its extensive use in almost all cases during the collapse stage. Hence, though not the first to use this method, he may, without fear of contradiction, have the honour of being regarded as the pioneer in the field of the treatment of cholera by intravenous saline in more or less scientific line.

Unfortunately, the result obtained by Wall, though much better than that of Latta and Mackintosh, was not as satisfactory and encouraging as could be expected. It is true that the death rate was lowered to some extent among his patients but it still remained as high as 70%. This high death rate was evidently due to the low chloride-contents of the saline used by him as proved, later on, by Sir Leonard Rogers. The composition of the saline used by him (Wall) consisted of 0·4 P.C. of sodium chloride, 0·2 P.C. of sodium carbonate dissolved in sterile boiled water. He used to inject about 3½ pints of this solution to a moderately severe case and about 5 pints in a very severe one.

Whatever might be the percentage of death, there was no doubt that the injections used to bring about at least a great temporary relief to his patients. It failed, however, to produce in most cases, a sustaining and permanent beneficial effect owing to subsequent copious evacautions following shortly after the injection. Hence repeated injections, at short intervals, were required to effect a cure in most of his patients.

The treatment advocated by Wall was followed with more or less modification, according to the choice and discretion of the attending Physician, for want of a better substitute, up to 1908 when Sir Leonard Rogers introduced, as a result of his close and careful observations as well as prolonged and thorough investigations, the injection of hypertonic saline in place of the one recommended by Wall which had, as already stated, a very low content of chloride. The introduction of the hypertonic saline brought about a revolution in the treatment of the disease and a great relief to the suffering humanity by reducing the mortality to the minimum as a result of a very large p.c. of cure undreamt of before and earned for him the gratitude of mankind in general and the Medical profession in particular for all time to come.

Before the introduction of the intravenous injection of hypertonic saline, the treatment of cholera, in the Allopathic System of Medicine, was very unsatisfactory owing to a very high percentage of deaths as mentioned above. No specific drug was till then or, as a matter of fact, has as yet, been discovered to combat the ravages of the disease. Owing to its antiseptic and antitoxic properties, Rogers advocated Potassium Permanganate by mouth, inspite of all its drawbacks and disadvantages for want of a better substitute. He found that the judicious administration of this drug in suitable form along with intravenous injections of hypertonic saline brought about an enourmous inprovement in the field of treatment by reducing the death-rate in Cholera to 20 p.c. or below as against 70 p.c. or above.

Cause of Death in Cholera.—In order to appreciate thoroughly the importance of this method of treatment—its advantages and disadvantages, the Physician must have a clear idea and comprehensive knowledge regarding the causes of death in cholera.

Death must occur in this disease as a result of one or more of the following factors:—

(1) Collapse.
(2) Complications.
(3) Sequelae.

Of the causes mentioned above, collapse, the most important of the three, is described below, as this is responsible for the largest number of deaths, especially in untreated cases, which can be saved by timely injections of an adequate quantity of intravenous saline in suitable form. The other two, namely, complications and sequelae may be dealt with in a separate article.

Collapse.—The largest number of deaths occurring within a short time of the attack is mainly due to dehydration resulting in extreme collapse. Want or insufficiency of the circulating fluid as a result of profuse diarrhœa and copious vomiting and consequent death from cardiac failure may undoubtedly be averted by timely and judicious infusion of a sufficient quantity of suitable saline which, by keeping up the circulation, will invariably prevent the immediate death from this cause. The main object of the saline infusion is, therefore, to maintain the circulation and to avert thereby the catastrophe due to collapse as well as to get rid of the toxins from the blood through the excretory organs which, as a result, become usually so active as to prevent death from complications; for, the kidneys—the chief organs of excretion and elimination of toxins—remain practically inactive during the stage of collapse on account of too much concentration of blood and too low blood pressure.

But, unfortunately, however beneficial the intravenous saline may be to avert death from collapse, it has not, so far, proved itself to be an unmixed blessing from all points of view; for, although there is no doubt that it has saved and is still saving thousands of patients from rapid and otherwise inevitable death, it is at the same time equally true that it increases the liability of death due to vaso-motor paralysis and uræmia (toxæmia) owing to free and fast absorption of a large amount of poison from the alimentary canal on account of the improvement in the circulation resulting therefrom. The absorption of toxins is obviously the least during the collapsed stage owing to the very feeble circulation of blood through the intestinal capillaries. Hence death from vasomotor paralysis or uræmia is very rare among those who, under other systems of treatment, escape death from collapse.

Though the saline infusion has not yet attained the ideal stage for want of a suitable antitoxic substance which, when administered at the same time, can safely destroy or neutralize the toxins circulating in the blood, it is unquestionably up till now the best and the only scientific method of treatment discovered.

Indications for Intravenous Saline.—The intravenous saline should be given in one or more of the following conditions:—

(I) Collapse.
(II) Frequent Retching and Nausea.
(III) Uraemia (Toxæmia).

Of these conditions No. III may be dealt with under complications, No. II will be discussed later on under subcutaneous saline and No. I is described below:—

Treatment of collapse.—The indications for saline infusion in this condition are evidenced by the following signs and symptoms of dehydration:

(1) Pinched face, sunken eyes, loose skin and shrivelled fingers and toes.
(2) Pulselessness or very feeble or almost imperceptible pulse.
(3) Husky voice.
(4) High Sp. Gr. of blood.
(5) Low blood pressure.
(6) Cyanosis.
(7) Restlessness.
(8) Severe cramps.
(9) Anuria.

No one single sign or symptom mentioned above may be sufficient for absolute indication for the saline infusion. When all or at least some of these symptoms are the result of sudden and rapid loss of fluid from the body, intravenous saline may safely be given not only in cholera but in any other condition irrespective of the cause leading to this stage of dehydration, as for example in Acute Bacillary Dysentery, with great benefit and without even the least possibility of any untoward result therefrom.

Quantity of Saline to be Injected.—There cannot be any hard and fast rule or a positive indication to determine previously the exact amount of saline which a patient may require at one sitting. The amount must depend on the changes occurring in the condition of individual patients as observed by the Physician during the process of transfusion of saline. Very large amount of saline cannot possibly be injected at one sitting without the occurrence of severe headache or cardiac embarrassment. The largest amount I have given, at one sitting, is up to 6 pints to a stout and previously healthy patient in a collapsed stage without any untoward sign or symptom. It may, however, be necessary to repeat the injection several times at frequent intervals during the course of the disease on account of repeated collapse.

It has often been noticed in many cases that during the course of saline injection, the patient vomited or purged profusely,

bringing out a huge quantity of fluid, even when none was given by mouth shortly before the infusion. This fluid is evidently withdrawn from the blood as a result of very rapid excretion into the stomach or intestine or into both, as the case may be, and expelled involuntarily by the patient either as vomit or stool or both. Hence a larger amount of saline may be needed by him to replenish the amount thus lost even at the same sitting.

Specific gravity of Blood as a Factor for the determination of the quantity of Saline required :--It has been said that the amount of saline should be determined by the specific gravity of blood and there are some renowned Physicians and specialists in cholera who would consider it criminal to give intravenous saline without taking it as a routine measure. With due deference to their opinion, I thoroughly disagree with them; for, what, after all, does the specific gravity of blood indicate? If it is found to be higher than normal, it may, at the utmost, be assumed that the blood has lost a portion of its fluid constituent. But from this fact alone one cannot possibly calculate by any means the total loss of fluid from the blood—not to speak of the whole system—unless the specific gravity of it *viz.*, the blood, immediately before the attack is known. Assuming it to be known it would not, as a matter of fact, be easy to estimate the total loss of fluid even from the blood which would be continually recouping the lost fluid as far as possible, from the tissues producing the signs and symptoms of dehydration and collapse as indicated by pinched face, sunken eyes, shrivelled skin, husky voice etc. Intense and insatiable thirst is only an indication that the system is crying for fluid to replenish the amount lost. So, it is evident that the specific gravity of blood cannot give even the faintest idea of the total loss of fluid from the body.

Unnecessary and impracticable though it is, the only means by which this can approximately be ascertained is by finding out the weight of the patient at a particular time during the disease and deducting from it his weight previous to the attack provided the latter is known. The difference is evidently the total amount of fluid lost by the patient as a result of vomiting and purging at that particular moment during the disease.

But the knowledge of an approximate or actual loss of fluid from the system at any moment during the disease will not help in the least to determine the exact or perhaps even an approximate amount of saline required by the patient at that particular hour; for, it is neither possible nor safe to make good the whole loss by transfusion of saline in one sitting without endangering

the life of the patient by cardiac failure—the tissues fail to recoup the lost fluid as rapidly as the blood receives the saline during transfusion. The heart, therefore, finds it difficult to adjust itself so as to work against the increased pressure resulting from the sudden and rapid influx of a large quantity of saline which cannot, at any rate, find its way into the dehydrated tissues as quickly as it enters the circulation. Hence, cardiac embarrassment with concomitant symptom of severe headache followed by præcordial pain or cardiac distress and subsequent death from heart-failure occurs as a natural sequence.

From the above, it is quite evident that the best guide, as to the actual amount of saline required by the patient at any time during the course of the disease, is evinced by the changes in the signs and symptoms in his condition during the process of influsion and not by any one of the above mentioned indications which undoubtedly point to the necessity for intravenous saline injection.

When to stop infusion :—Although signs and symptoms already mentioned indicate that the patient requires saline infusion, yet none of them practically gives an idea as to the actual amount needed. It can only be determined by keeping a careful watch on the patient during the course of injection of the saline which may usually be continued as long as the patient can receive it with ease and comfort until the pulse becomes full and bounding. If any sign or symptom as stated below appears which contra-indicates the further continuance of saline infusion, it should be stopped at once.

Contra-indications :

(1) Severe Headache.
(2) Severe rigor.
(3) Restlessness.
(4) Præcordial pain or cardiac embarrassment.

If the patient complains of or is found to have any one of the above symptoms, the infusion of saline should be discontinued forthwith or at least the rate of flow should be slowed down, as all these except rigor indicate that either too much saline has been given or too rapid infusion has been made.

Danger of too little Saline.—It will not be out of place to mention here that too little saline is on many occasions found to be as dangerous, if not more so, as too much, though not in the same way. Insufficient saline undoubtedly saves the patient for the time being from immediate death due to collapse; but it increases, at least to some extent, the liability of death from uraemia

(toxaemia). For, although the circulation is maintained in a degree just sufficient to allow the free absorption of toxins through the mucous membrane of the gut, it is not likely to be powerful enough to get the poisons eliminated in sufficient quantity at least through the kidneys which remain almost inactive on account of the low blood pressure and feeble circulation of blood through the organs The free secretion of urine under the circumstances cannot possibly be established owing to the pressure remaining too low and the blood still too concentrated. Hence, the kidneys get more and more inflamed in their constant though unsuccessful attempts to excrete the concentrated and irritant toxins already accumulated in the blood. Thus, total suppression of urine inevitably occurs in many cases with consequent development of uraemia.

Varieties and Composition of saline.—

(1) *Hypertonic* :—

Sodium Chloride	...	gr. 120
Aqua Distillata	...	pint. 1

(2) *Compound Hypertonic or Hypertonic with Calcium Chloride* :—

Sodium chloride	...	gr. 120
Calc. chloride	...	gr. 4
Aqua Distillata	...	1 pint.

(3) *Iso-tonic* :—

Sodium chloride	...	gr. 90
Aqua Distillata	...	1 pint.

(4) *Hypo-tonic* :—

Sodium chloride	...	gr. 60.
Aqua Distillata	...	1 pint.

(5) *Alkaline Isotonic* :—

Sodium chloride	...	gr. 60
Sodium Bicarbonate	...	gr. 120
Aqua Distillata	...	1 pint.

(6) *Rectal Saline* :—

Sodium chloride	...	gr. 90
Sodium bicarbonate	...	gr. 160
Glucose sol. (5%)	...	oz. 2
Aqua ad.	...	1 pint.

'Soloid' calcium chloride comp. is available in the market,

of which 4 dissolved in one pint of water will make the hypertonic saline, and three in a pint will make iso-tonic saline. The latter will serve quite well the purpose of rectal or sub-cutaneous injections.

Indications for Hyper-tonic Saline.—Of these the second *i.e.*, the compound hyper-tonic saline, with or without the addition of * Potassium chloride gr. vi per pint, should always be injected intravenously during the collapsed stage; for, this is more likely to prevent rapid collapse by reducing the number of stools. As the alkalinity of the blood is invariably found to be more or less diminished during the course of the disease, the practice of injecting alkaline iso-tonic saline has been advocated and adopted to combat this condition. But, I found this, in my own experience, at least in some cases, very unsatisfactory especially when injected in large quantities repeatedly; for, the combined effect of both the addition of sodium bicarbonate and the reduction in the quantity of sodium chloride in the collapsed stage of the disease contributes greatly to the increased possibility of rapid collapse by not only continuing but aggravating the diarrhoea and thus bringing about repeated collapse and consequently more or less asthenia which, it is very difficult for the patient to get rid of. I have already dealt with this elsewhere while discussing about uraemia.

Indication for Iso-or Hypo.Tonic Saline.—Iso-or Hypo-tonic saline should, on no account, be given intravenously in the early or collapsed stage of the disease as they are likely to increase the diarrhoea and also to cause oedema of the lungs; but they may, if necessary, with the addition of sodium bicarbonate and 5% Glucose solution, be injected even intravenously in the stage of reaction if the urine is found to be suppressed or at least not free; for, the injection may occasionally prevent the development of uraemia by restoring the normal function of the kidneys which very often begin suddenly to secrete fairly large quantities of urine after the injection.

Temperature of the Saline.—This is very important and it should always be borne in mind by the Physician when giving intravenous saline to a cholera patient as the indiscriminate use of saline at any temperature, irrespective of the rectal temperature of the patient at the time of injection, may often lead to disastrous consequences owing to subsequent hyperpyrexia or shock. The temperature of the saline should always be regulated by the rectal temperature of the patient at the time of injection. The

* Potassium chloride has now been given up by Sir Leonard Rogers owing to its depressant action on the cardiac muscles.

suggestions of Sir Leonard Rogers may, with benefit, be more or less strictly adhered to as a guide in this respect; for, they are based on his vast experience in the treatment of cholera extending over a long period.

(1) If the rectal temperature of the patient at the time of injection be found to vary between 96° and 100° F. that of the saline should be of the normal body temperature.

(2) If it is 97° F. or below, the saline should have a temperature between 102° and 104° F.

(3) If the rectal temperature, however, is found to be above 100° F., the temperature of the saline should be much below normal.

(4) If the temperature in the rectum is, on the other hand, found to be above 102° F. the saline should be given at the temperature of the room.

Rate of Flow of Saline.—In transfusing saline it is always advisable to regulate the flow so that the first 2 or 3 pints may enter quickly, *i.e.* about 4 ounces a minute but later on, the rate of flow should be slowed down so as to allow sufficient time for the heart to adjust itself to the sudden rise of pressure and to enable the tissues to recoup, as far as possible, the amount of fluid already lost from the system as a result of previous vomiting and purging.

Technique of Intravenous Injection.—Though undoubtedly easy and simple for an expert, the intravenous injection of saline may occasionally present some difficulty to an inexperienced and untrained novice on account of the ignorance in respect of details of the operation. A brief description is, therefore, necessary and is given below for the guidance of such as may need it.

Methods of Injection.—The injection may be performed by:

(1) *Open Method*:—*i.e.* exposing the selected vein by cutting the skin and dissecting off the superficial structures around it.

(2) *Closed or Direct method*:—*viz.*, inserting a fairly big needle directly into the chosen vein without dividing the skin and subcutaneous tissues such as is done during the intravenous injections of neo-salvarsan, salts of antimony etc.

1. *Open Method*:—Being the oldest method, used almost

universally by most of the physicians, it is described first in preference to the other, *viz*, *Closed or Direct Method* which, inspite of its advantages, is taken recourse to only on rare occasions.

Instruments and Appliances required.—The following instruments and appliances should always be kept ready and well sterilized before starting the operation:—

(1) Scalpel—one.
(2) Dissecting forceps—one pair.
(3) Aneurism needle—one.
(4) Scissors—one pair (preferably a sharp pointed one).
(5) Suturing needle—one (straight or curved).
(6) Artery forceps—2 pairs (not essential but they may be kept ready for emergency).
(7) Silk ligature to tie the vein—one piece.
(8) Horse hair or silk-worm gut—one length for suturing the skin.
(9) Graduated glass-bulb or flask—one.
(10) Rubber tubing—one piece (sufficiently long and of suitable calibre to connect the bulb with the cannula preferably with an intervening glass connection).
(11) A fairly big tray—one (to hold the above)
(12) Tinct. Iodine—one ounce (for sterilizing the skin and the wound.)
(13) Carbolic soap—one cake (for washing hands before operation).

Besides the above, a few pieces of sterilized (cut) gauze, Boric or absorbent cotton wool and a bandage must also be kept in readiness beforehand.

Choice of Vein.—Any superficial vein, sufficiently big to allow the easy entrance of the cannula, may conveniently be selected for the purpose. The best ones are, however, those in front of the elbow *viz.*, median basalic and median cephalic veins as well as the vein in front of one or the other internal malleolus of the ankle on account of their more or less fixed nature. Too slippery veins such as those on the dorsum of the hands are not very suitable for obvious reasons and should, therefore, be avoided if possible. In selecting the vein, care should always be taken to see that there is no valve immediately above the point of incision as it is likely to obstruct the flow of saline during the process of

injection. It should also be ascertained that at the selected site there are neither any superficial vein or veins which are likely to be divided during the operation nor any tributary or branch joining the selected vein immediately above the point of opening; for, in either case there is the possibility of too much bleeding to interfere with the operation and subsequent manipulation.

Operative Procedure.—After selecting the suitable vein, the site of operation should be scrupulously cleaned and thoroughly disinfected. Simply rubbing off the skin with a piece of gauze or a little cotton wool soaked in tincture of iodine is ordinarily sufficient for the purpose unless there is too much dirt on the part requiring careful washing with soap and water before the application of tincture of iodine. A towel—preferably sterile—with a piece of Mackintosh or oil cloth (if available) underneath to prevent soaking and soiling the beddings is placed beneath the stretched elbow or ankle as the case may be. The selected vein, which in most cases is found to be collapsed, must always be made to stand out as prominently as possible by tying a bandage with a slip-knot a little above the site of operation on its proximal side with just sufficient force to stop the venous but not the arterial circulation. A mark about ¼" to 1" long, according to the skill and experience of the operator, is then made on the skin along the course of the vein by the point or edge of the scalpel and by retracting the skin to one or the other side of the vein with the tip of the left thumb, a bold and fairly deep incision along the mark is made so as to cut the skin and superficial fascia. This is essential as repeated incisions cause laceration of the skin and the tissues underneath as well as unnecessary pain to the patient. On account of its elasticity, the skin returns to the original position as soon as the traction on it is removed by raising the thumb fully exposing the vein under the whole length of the incision. A little manipulation with a scalpel and a pair of dissecting forceps is all that is required to free the vein from its sheath and subjacent structures. A double strand of silk ligature is then hooked round it by means of an aneurism needle and the vein is tightly ligatured at its distal end by means of the strand and a loose loop, which may at any moment be tightened, is made by the other on the upper or proximal end of the exposed vein. The slip knot on the arm previously made by the bandage is now loosened or removed altogether. The exposed vein is then raised from its bed by means of a pair of fine dissecting forceps, catching not more than half the circumference of the vein, and a v-shaped opening is made on it obliquely from below upwards and backwards by means of a

pair of—preferably fine pointed—scissors just above but as closely as possible to the distal ligature. The silver cannula, which is attached by means of a long rubber tubing to the graduated flask or bulb filled in previously with required saline, can by a little manipulation be easily inserted into the vein through the v-shaped opening already made on its wall. The loose loop at the proximal end of the vein is now tightened on to it to prevent the cannula slipping off from the vein. It must, however, be always remembered that the saline apparatus, namely, the graduated flask or bulb with rubber tubing and cannula should be made ready with saline before opening the vein for insertion of the cannula. All air-bubbles in the tubing should be carefully driven out by squeezing the tube from below upwards; for, the failure to do so may occasionally lead to disastrous consequences resulting from air embolism. Before introducing the cannula into the lumen of the vein through the v-shaped aperture mentioned above, the stop-cock should invariably be turned on for a moment to allow the expulsion of a small quantity of the saline in a jet, to ensure the proper and efficient working of the apparatus later on as well as to drive out along with it the remnant of the air, if there by any, still left inside the tube. Neglect to carry out this instruction strictly, may give endless troubles subsequently during transfusion on account of complete or partial blocking of the cannula or the tube preventing the saline to run in as quickly or as easily as desired. Obstruction to the free passage of the saline may also be due to other causes such as either the inversion of the valve higher up in the course of the vein or the passage of the cannula into the space between the vein and its sheath instead of into the lumen owing to the imperfect dissection or incomplete division of its wall. The obstruction due to the former cause may sometimes be overcome by forcible massage from below upwards along the course of the vein in the direction of the flow of the saline and that due to the latter can only be remedied by taking out the cannula and re-introducing it into the lumen of the vein after necessary manipulation such as removal of the sheath of the vein or enlargement of the opening on its wall.

Some difficulty may occasionally arise in the insertion of the cannula into the lumen of the vein through the opening on its wall even if there be no fault or defect in the operation especially when the wall of the vein is very thin and collapsible. But it can easily be obviated by pulling the vein up from its bed by the thread of the distal ligature and making a jet of saline from the cannula strike against the v-shaped cut on its wall in a suitable

direction to open up the aperture on it by everting the flap which then facilitates the introduction of the cannula through the opening into the lumen of the vein on very little but careful manipulation.

At the close of the operation, when the full amount of the required saline has already run in, the ends of the silk thread of the proximal (the upper) ligature with which the cannula has been fixed to the vein are caught hold of by the fingers—one end between the tips of the thumb and index fingers of the left and the other between those of the right hand—and exert a steady pull in opposite direction while the cannula is pushed out of the lumen of the vein by means of the tip of the ring or any one of the other suitable free fingers of either hand pressing the stop-cock backwards so that the knot is tightened automatically on the vein as soon as the cannula is out allowing very little chance for bleeding. Both ends of the silk-threads used for the upper and lower ligatures are now cut off close to the knots by a pair of scissors and the wound stitched up by means of a horse-hair or silk-worm gut and dressed aseptically after carefully cleaning the part and painting it with tincture of iodine. The operation which is a very simple and easy one should, when carefully performed, be usually a clean and almost bloodless affair causing too little pain to require any general or local anaesthetics.

If more than one injection be needed, which is very often the case, a different vein should preferably be selected on each occasion. But if a suitable vein be not available for the purpose, the injection can, however undesirable it may be on account of the greater possibility of sepsis, be given through the same opening provided the second injection is given within twelve hours of the first. In doing so, the stitches must be divided and the original wound should be opened up and cleaned antiseptically. The proximal ligature on the vein should then be cut open and any clot or clots above the knot must carefully be squeezed out by repeated forcible massage from above downwards along the course of the vein until blood begins to flow freely through the original opening on the wall of the vein. When this occurs, the cannula can easily be introduced into the lumen of the vessel through the aperture and fixed to the wall of the vein by a fresh ligature with a piece of silk-thread as on previous occasion. The subsequent steps are the same as those of the first injection.

2. *Closed or Direct method.*—This method of injecting intravenous saline is undoubtedly much simpler than the other, namely, the open method described above, for obvious reasons. From

the comparative statement, which is appended below, its advantages over the open method as well as its disadvantages will be found to be so clear and convincing that it hardly requires any explanation. But unfortunately, this method, though very clean and practically painless, cannot universally be accepted as the most suitable one in all cases, as for example, in children and fat persons especially females. In the case of the former, the veins are, as a rule, too small and in that of the latter, they are very often too deeply embedded in the adipose tissues to suit the purpose. Besides, the injection by direct puncture can only be given safely and without much difficulty in suitable cases by such trained men as are practised to give intravenous injections in a very large number of patients. It is, however, not so easy and simple, even in a suitable case, for one who had no previous training to give intravenous saline successfully by this method, especially in a cholera patient whose veins are usually in a collapsed state: for, he is almost sure to miss the vein or transfix it during the attempt or attempts to push the needle into the lumen of the vessel. Hence an untrained hand should not try this method as repeated failures may occasionally lead to troubles and difficulties even in the subsequent open operation owing to the complications resulting from the injury or injuries to the vessel as well as bleeding around the vein and its surrounding tissues.

It is also evident that the flow of saline in this method cannot be as rapid as in the open method for the calibre of the needle must, of necessity, be much smaller than that of the cannula used in the open operation; so the time to complete the injection must necessarily be much longer and therefore more tedious both to the patient and his medical attendant.

This simple method of injection by direct puncture does not, however, require any elaborate arrangement either for assistants or for instruments and appliances. What is needed is a moderately large hypodermic or serum-syringe needle attached to a graduated flask or bulb by means of a fairly long piece of India rubber tubing of suitable calibre having, if possible, an intervening connecting glass tube as close as possible to the needle in order to enable the operator to ascertain if the needle has successfully penetrated into the vein, the entrance into the lumen of which is indicated by the regurgitation of blood through the needle into the tubing as seen through the glass connection.

Operative Procedure.—The selected vein—usually either the median basalic or the median cephalic in front of the elbow—is made to stand out prominently in the same way as in the case of

open operation by a fairly tight ligature around the arm a little above the point of puncture. If this fails to make the vein as conspicuous as desired, the forearm may alternately be made to flex and extend a few times with the fist closed as tightly as possible without at the same time interfering with the ligature. The process may further be helped, if necessary, by forcible massage from below upwards, that is, towards the ligature along the course of the veins in the forearm. When, as a result of the above manipulations, the selected vein stands out prominently, the needle of the apparatus, already made ready for injection in the meantime in the same way as described under the open method of operation with the tube clipped or pinched to prevent the saline running out, is carefully pushed into the lumen of the vein which, if successfully done, is indicated by the regurgitation of blood into the tube (as seen through the glass connection in it) on account of the obstruction to the onward flow of blood by the ligature round the arm. Both the ligature round the arm and the clip of pinch on the tube are now released to allow the saline to run in freely till the full amount is passed into the system. At the close, the needle is drawn out and the puncture-wound is sealed with collodion or tinct. benzoin co. No further dressing is needed. The same vein may be used as many times as required for the purpose.

The Retractile pointed cannula invented by Sir Leonard Rogers may with advantage be used as a substitute for the hypodermic or serum-syringe needle. If a graduated flask or bulb be not available, it may very well be substituted by the barrel of an ordinary four or eight ounce glass syringe, to the nozzle of which one end of the rubber tubing may easily be attached.

Comparative Statement.—A comparative statement in tabular form of the advantages and disadvantages of the two methods are given below:—

CLOSED OR DIRECT METHOD.	OPEN METHOD.
1. The vein remains patent throughout.	The vein becomes obliterated for good.
2. Any number of injections can be given through the same vein.	Not more than two injections can be given through the same opening and that even when the second injection is given, it should be given within twelve hours of the first.

CLOSED OR DIRECT METHOD. —(*Contd.*)	OPEN METHOD. —(*Contd.*)
3. No pain during injection or after.	There is always more or less pain during and after the operation.
4. No chance or possibility of sepsis.	There is always some chance or possibility of sepsis.
5. Expert and trained hands are necessary.	Not so much training is required.
6. No scar formed.	Some scar is always formed.
7. No elaborate arrangement needed.	Elaborate arrangement for operation is unavoidable.
8. No instruments or appliances other than a needle, and a bulb or flask connected by a piece of rubber tubing, are wanted.	A large number of instruments and appliances besides the cannula bulb and rubber tubing is of unavoidable necessity.
9. Not much assistance or help is needed.	Some assistance or help is absolutely necessary.
10. Operation is a quick one.	Operation is a protracted one.
11. The time to complete the injection is longer.	Time to complete the injection is shorter.
12. The rate of flow is slower.	The rate of flow is quicker.
13. Success is doubtful unless the selected vein is a superficial and conspicuous one.	Success is almost assured under almost all circumstances.
14. Children and fat persons are not good subjects.	Any person is a good subject as long as a sufficiently big vein is available.
15. Repeated failures due to missing or transfixing the vein may present difficulty in subsequent injection through the vessel even by open operation.	No such contingency is likely to occur.

Sub-Cutaneous Saline.—The method of treatment of cholera by sub-cutaneous saline may only be taken recourse to when slow absorption of a small quantity of the solution extending over a prolonged period is desired or needed. It has no special merit or advantage over the intravenous injection although it may occasionally be used either alone or as an adjunct to the latter—viz., the intravenous saline.

Indications and contra-indications of sub-cutaneous saline with its advantages and disadvantages are more elaborately described below:

Indications:—

(1) Threatened uraemia.

(2) Persistent retching, nausea or vomiting.

(3) Unsuitable veins.

(4) Oedema of lungs.

1. *Threatened uraemia.*—If there be a fair and steady though somewhat feeble and rapid pulse as well as little or no apprehension of immediate or rapid collapse, as is the case in the early stage of a mild or the reaction stage of a more severe type of the disease, this method, *viz.*, the sub-cutaneous injection of saline, is very often adopted by many physicians to avert or prevent uraemia (toxaemia), which may occasionally result from the scanty secretion or total suppression of urine on account of the feeble circulation of the inadequate amount of too concentrated blood with low pressure during these stages. Even in such cases slow and cautious administration of a suitable quantity of intravenous saline, according to the need of individual patients, is found in my own experience to be more effective.

2. *Persistent retching, nausea or vomiting.*—It may also be given with benefit to relieve the troublesome and distressing symptoms of constant or frequent retching, nausea or vomiting which may occasionally be found in some patients during the course of the disease inspite of the apparent general improvement in all other respects, even when the urine is fairly free but not copious. This is almost always due to insufficiency of fluid in the system and a pint or so of saline, given either by sub-cutaneous or slow intravenous method according to the need of the patient, brings about a speedy and sure relief.

3. *Unsuitable veins.*—Though not always very satisfactory or successful in all cases, there may be no other alternative but to give subcutaneous saline even in the collapse stage, sometimes

repeatedly in case of babies or small children, when a sufficiently big vein for the introduction of even the smallest size of cannula for the purpose of intravenous injections cannot be found. In many such cases where apparantly it seemed impossible, I found that the saline could be successfully administered intravenously by means of an improvised capillary pippet made out of an ordinary glass tube.

4. *Oedema of lungs.*—The most suitable cases for the sub-cutaneous saline, however, are those in whom, inspite of sufficient indications, the intravenous injection is positively contra-indicated owing to the greater possibility of subsequent oedema of lungs as a result of the sudden and rapid influx of saline into the blood raising its pressure to some degree and reducing its concentration to some extent at least for the time being. The diluted blood, on the other hand, failing to get rid of the excess of fluid from the circulation through the inactive excretory organs—especially the kidneys—allows it to find its way in and is deposited into the loose tissues even of the internal organs of which the lungs, owing to the peculiarity of its structure, become the main target invariably causing more or less oedema of these organs.

Whereas in the case of sub-cutaneous saline, the slow absorption of the fluid, though undoubtedly dilutes the concentracted blood to some extent, fails at any rate to raise the pressure to such an appreciable degree as to necessitate its rapid excretion into the loose tissues of the body—not to speak of the lungs—even when the natural paths of elimination, *viz*, the excretory organs including the kidneys, on account of some reason or other, remain completely inactive during the course of the disease.

It must, however, be always borne in mind that though not likely it is not absolutely impossible even for the sub-cutaneous saline to cause oedema of lungs on rare occasions. Hence if not urgently needed, the saline injection—even by sub-cutaneous method should by all means be avoided.

Variety of Saline to be injected.—Iso—or, if need be, hypotonic saline should be injected for quick absorption though, according to Sir Leonard Rogers, the hyper-tonic saline is preferable especially when the patient is in the collapsed stage as it is supposed to be absorbed as quickly as the other varieties. Moreover the hyper-tonic saline has the double advantage of replacing the lost chloride and preventing the rapid collapse.

Danger of alkaline saline.—Without fully realizing the gravity of its consequence or perhaps quite unmindful and ignorant of the subsequent danger attending its use, some Physicians give,

as a routine measure, sub-cutaneous injections of saline made alkaline by the addition of some sodium bicarbonate to it in order to combat the acidosis or more correctly speaking, the diminished alkalinity of blood which usually occurs at least to some extent in most of the cases during the course of the disease. This, however, is a dangerous practice and is undoubtedly detrimental to the best interest of the patient as it may often lead in some cases even to ultimate death from asthenia resulting from septic absorption consequent upon the formation of abscess or abscesses as described below.

Formation of abscess.—The addition of sodium bicarbonate to the sub-cutaneous saline does greater harm than good in more ways than one; for, not only, owing to the irritation set up by it, does the alkaline saline thus made up cause intense pain and suffering to the patient but it is almost invariably responsible for the formation of a big abscess or abscesses at one or more sites of injections on account of the tissue-necrosis resulting in suppuration. The huge abscess or abscesses thus formed may not only cause prolonged illness and protracted convalescence, but these may ultimately bring about in many cases fatal termination on account of asthenia resulting from long continued septic absorption. It is very unfortunate and is also a matter of great regret that the patient, who is actually cured of the original disease, should die of an avoidable complication which occurs only as a result of the improper and injudicious treatment.

The liability to tissue-necrosis and consequent suppuration is increased to a very large extent when the bicarbonate, which is mildly irritant, is converted into a more irritant carbonate during the process of sterilization by boiling the solution The bicarbonate of soda, for this reason, ought always to be sterilized by heating in an autoclave in the form of a dry powder even when required for the intravenous saline. This dry sterile powder is to be added to the already boiled and sterilized saline immediately before use.

Quantity of saline to be injected.—Not more than one pint of saline at the temperature of blood, i.e. about 100° F, be injected at a time in any one of the sites mentioned below at one sitting. The process may, however, be repeated as often as necessary, each time selecting a different site for the purpose.

Site of injection.—The most suitable sites for the purpose of sub-cutaneous injections are either the axillary or lumbar regions where owing to the presence of loose sub-cutaneous tissues, a fairly large quantity of saline can easily be accommodated with

the least possible pain and suffering to the patient. It may, however, be safely injected in the thighs if necessary.

Aseptic and antiseptic precautions.—Whatever may be the variety of saline—hyper—iso—or hypotonic, it must always be remembered that the saline, necessary instruments and the selected site of the patient's skin, must invariably be carefully and thoroughly sterilized, or else an abscess or cellulitis may occasionally develop, to the great detriment of the patient owing to his low vitality and poor resisting power. Tincture of iodine or absolute alcohol, if well rubbed on the dry skin of the selected site, serves the purpose quite well. But the saline and necessary instruments must be thoroughly sterilized by boiling for a sufficient period before using them for the patient.

Disadvantages:—

(1) Futility in Collapsed stage.

(2) Liability to Uræmia.

1. *Futility in Collapsed stage.*—It is useless or perhaps worse than useless to inject sub-cutaneously a small quantity of saline—say about a pint or two—when the patient is in a collapsed state, with little or no pulse at the wrist, indicating feebleness of the peripheral circulation, resulting in most cases from enormous loss of fluid from the system. As death, in these cases, may occur at any moment from cardiac failure for want or insufficiency of the circulating fluid, it is imperative to push in immediately and as rapidly as possible a sufficient quantity of suitable saline directly into the circulation to prevent such a catastrophe. Owing to slow absorption, the sub-cutaneous saline cannot, in this condition, help in the least as death will probably occur before the absorption of a sufficient quantity of fluid in the system to avert or prevent it. It is a well-established fact based on repeated and careful observations that the absorption of saline is the slowest, if at all, in the collapsed stage, when the peripheral circulation is very feeble or almost at a stand-still. This, therefore, is a further proof of the unsuitability or, as a matter of fact, uselessness of the sub-cutaneous saline in this condition.

2. *Liability to uræmia.*—Another disadvantage, which I have already mentioned in connection with the intravenous saline holds equally good, if not more so, in the case of sub-cutaneous injection, *viz.*, that on account of the smaller quantity of saline and its slower absorption, although the circulation may, somehow or other, be kept on or become more or less free, the main organs of excretion, *viz.*, the kidneys fail to act or remain blocked owing

to too low pressure and too little dilution of the blood which still persists to be too thick to permit free secretion of urine. Hence the toxins which continue to be absorbed, rather more freely, as a result of improved circulation, cannot as quickly be eliminated and so become more and more concentrated in the blood. These increasingly concentrated toxins, by their action on the nervous system, may lead to the development of uraemia (toxaemia) or vasomotor paralysis.

It is evident from what has already been stated regarding the advantages and disadvantages of the sub-cutaneous saline that though it is still continued to be used on several occasions by many Medical Practitioners, it is neither essential nor unavoidable for the treatment of cholera and so can safely be discarded at least in most cases without any cause for regret or repentance.

Intra-Peritoneal saline.—This method which has unfortunately been given up now-a-days, for all intents and purposes, before sufficient and adequate trial has been given to it, especially in suitable cases under favourable circumstances, is undoubtedly much superior to sub-cutaneous saline in almost all respects though not as good or efficient as the intravenous method. It can be used as a substitute for sub-cutaneous saline in almost all cases, where the latter is indicated, probably with greater benefit and better results.

Its Advantages are :—

(1) Simplicity.
(2) Quickness.
(3) Rapid absorption.
(4) Less painful.
(5) Fairly large quantity may be injected.
(6) No previous training necessary.

A fairly large quantity of saline—2 to 3 pints—may safely be injected at a time in an adult within a short period not exceeding 10 to 15 minutes, for fairly rapid absorption with very little pain or distress to the patient by even an ordinary Medical Practitioner without previous special training as is required for the treatment of cholera by intravenous method. The injection may be repeated as many times as necessary even through the same site or opening.

Hence when a large number of new and fresh cases occur daily, during a general outbreak of the disease in a locality, not provided with a sufficiently big and well-equipped hospital to

the comparative statement, which is appended below, its advantages over the open method as well as its disadvantages will be found to be so clear and convincing that it hardly requires any explanation. But unfortunately, this method, though very clean and practically painless, cannot universally be accepted as the most suitable one in all cases, as for example, in children and fat persons especially females. In the case of the former, the veins are, as a rule, too small and in that of the latter, they are very often too deeply embedded in the adipose tissues to suit the purpose. Besides, the injection by direct puncture can only be given safely and without much difficulty in suitable cases by such trained men as are practised to give intravenous injections in a very large number of patients. It is, however, not so easy and simple, even in a suitable case, for one who had no previous training to give intravenous saline successfully by this method, especially in a cholera patient whose veins are usually in a collapsed state: for, he is almost sure to miss the vein or transfix it during the attempt or attempts to push the needle into the lumen of the vessel. Hence an untrained hand should not try this method as repeated failures may occasionally lead to troubles and difficulties even in the subsequent open operation owing to the complications resulting from the injury or injuries to the vessel as well as bleeding around the vein and its surrounding tissues.

It is also evident that the flow of saline in this method cannot be as rapid as in the open method for the calibre of the needle must, of necessity, be much smaller than that of the cannula used in the open operation; so the time to complete the injection must necessarily be much longer and therefore more tedious both to the patient and his medical attendant.

This simple method of injection by direct puncture does not, however, require any elaborate arrangement either for assistants or for instruments and appliances. What is needed is a moderately large hypodermic or serum-syringe needle attached to a graduated flask or bulb by means of a fairly long piece of India rubber tubing of suitable calibre having, if possible, an intervening connecting glass tube as close as possible to the needle in order to enable the operator to ascertain if the needle has successfully penetrated into the vein, the entrance into the lumen of which is indicated by the regurgitation of blood through the needle into the tubing as seen through the glass connection.

Operative Procedure.—The selected vein—usually either the median basalic or the median cephalic in front of the elbow—is made to stand out prominently in the same way as in the case of

open operation by a fairly tight ligature around the arm a little above the point of puncture. If this fails to make the vein as conspicuous as desired, the forearm may alternately be made to flex and extend a few times with the fist closed as tightly as possible without at the same time interfering with the ligature. The process may further be helped, if necessary, by forcible massage from below upwards, that is, towards the ligature along the course of the veins in the forearm. When, as a result of the above manipulations, the selected vein stands out prominently, the needle of the apparatus, already made ready for injection in the meantime in the same way as described under the open method of operation with the tube clipped or pinched to prevent the saline running out, is carefully pushed into the lumen of the vein which, if successfully done, is indicated by the regurgitation of blood into the tube (as seen through the glass connection in it) on account of the obstruction to the onward flow of blood by the ligature round the arm. Both the ligature round the arm and the clip of pinch on the tube are now released to allow the saline to run in freely till the full amount is passed into the system. At the close, the needle is drawn out and the puncture-wound is sealed with collodion or tinct. benzoin co. No further dressing is needed. The same vein may be used as many times as required for the purpose.

The Retractile pointed cannula invented by Sir Leonard Rogers may with advantage be used as a substitute for the hypodermic or serum-syringe needle. If a graduated flask or bulb be not available, it may very well be substituted by the barrel of an ordinary four or eight ounce glass syringe, to the nozzle of which one end of the rubber tubing may easily be attached.

Comparative Statement.—A comparative statement in tabular form of the advantages and disadvantages of the two methods are given below:—

CLOSED OR DIRECT METHOD.	OPEN METHOD.
1. The vein remains patent throughout.	The vein becomes obliterated for good.
2. Any number of injections can be given through the same vein.	Not more than two injections can be given through the same opening and that even when the second injection is given, it should be given within twelve hours of the first.

CLOSED OR DIRECT METHOD. —(*Contd.*)	OPEN METHOD. —(*Contd.*)
3. No pain during injection or after.	There is always more or less pain during and after the operation.
4. No chance or possibility of sepsis.	There is always some chance or possibility of sepsis.
5. Expert and trained hands are necessary.	Not so much training is required.
6. No scar formed.	Some scar is always formed.
7. No elaborate arrangement needed.	Elaborate arrangement for operation is unavoidable.
8. No instruments or appliances other than a needle, and a bulb or flask connected by a piece of rubber tubing, are wanted.	A large number of instruments and appliances besides the cannula bulb and rubber tubing is of unavoidable necessity.
9. Not much assistance or help is needed.	Some assistance or help is absolutely necessary.
10. Operation is a quick one.	Operation is a protracted one.
11. The time to complete the injection is longer.	Time to complete the injection is shorter.
12. The rate of flow is slower.	The rate of flow is quicker.
13. Success is doubtful unless the selected vein is a superficial and conspicuous one.	Success is almost assured under almost all circumstances.
14. Children and fat persons are not good subjects.	Any person is a good subject as long as a sufficiently big vein is available.
15. Repeated failures due to missing or transfixing the vein may present difficulty in subsequent injection through the vessel even by open operation.	No such contingency is likely to occur.

Sub-Cutaneous Saline.—The method of treatment of cholera by sub-cutaneous saline may only be taken recourse to when slow absorption of a small quantity of the solution extending over a prolonged period is desired or needed. It has no special merit or advantage over the intravenous injection although it may occasionally be used either alone or as an adjunct to the latter—viz., the intravenous saline.

Indications and contra-indications of sub-cutaneous saline with its advantages and disadvantages are more elaborately described below:

Indications:—

(1) Threatened uraemia.

(2) Persistent retching, nausea or vomiting.

(3) Unsuitable veins.

(4) Oedema of lungs.

1. *Threatened uraemia.*—If there be a fair and steady though somewhat feeble and rapid pulse as well as little or no apprehension of immediate or rapid collapse, as is the case in the early stage of a mild or the reaction stage of a more severe type of the disease, this method, *viz.*, the sub-cutaneous injection of saline, is very often adopted by many physicians to avert or prevent uraemia (toxaemia), which may occasionally result from the scanty secretion or total suppression of urine on account of the feeble circulation of the inadequate amount of too concentrated blood with low pressure during these stages. Even in such cases slow and cautious administration of a suitable quantity of intravenous saline, according to the need of individual patients, is found in my own experience to be more effective.

2. *Persistent retching, nausea or vomiting.*—It may also be given with benefit to relieve the troublesome and distressing symptoms of constant or frequent retching, nausea or vomiting which may occasionally be found in some patients during the course of the disease inspite of the apparent general improvement in all other respects, even when the urine is fairly free but not copious. This is almost always due to insufficiency of fluid in the system and a pint or so of saline, given either by sub-cutaneous or slow intravenous method according to the need of the patient, brings about a speedy and sure relief.

3. *Unsuitable veins.*—Though not always very satisfactory or successful in all cases, there may be no other alternative but to give subcutaneous saline even in the collapse stage, sometimes

repeatedly in case of babies or small children, when a sufficiently big vein for the introduction of even the smallest size of cannula for the purpose of intravenous injections cannot be found. In many such cases where apparantly it seemed impossible, I found that the saline could be successfully administered intravenously by means of an improvised capillary pippet made out of an ordinary glass tube.

4. *Oedema of lungs.*—The most suitable cases for the sub-cutaneous saline, however, are those in whom, inspite of sufficient indications, the intravenous injection is positively contra-indicated owing to the greater possibility of subsequent oedema of lungs as a result of the sudden and rapid influx of saline into the blood raising its pressure to some degree and reducing its concentration to some extent at least for the time being. The diluted blood, on the other hand, failing to get rid of the excess of fluid from the circulation through the inactive excretory organs—especially the kidneys—allows it to find its way in and is deposited into the loose tissues even of the internal organs of which the lungs, owing to the peculiarity of its structure, become the main target invariably causing more or less oedema of these organs.

Whereas in the case of sub-cutaneous saline, the slow absorption of the fluid, though undoubtedly dilutes the concentracted blood to some extent, fails at any rate to raise the pressure to such an appreciable degree as to necessitate its rapid excretion into the loose tissues of the body—not to speak of the lungs—even when the natural paths of elimination, *viz*, the excretory organs including the kidneys, on account of some reason or other, remain completely inactive during the course of the disease.

It must, however, be always borne in mind that though not likely it is not absolutely impossible even for the sub-cutaneous saline to cause oedema of lungs on rare occasions. Hence if not urgently needed, the saline injection—even by sub-cutaneous method should by all means be avoided.

Variety of Saline to be injected.—Iso—or, if need be, hypotonic saline should be injected for quick absorption though, according to Sir Leonard Rogers, the hyper-tonic saline is preferable especially when the patient is in the collapsed stage as it is supposed to be absorbed as quickly as the other varieties. Moreover the hyper-tonic saline has the double advantage of replacing the lost chloride and preventing the rapid collapse.

Danger of alkaline saline.—Without fully realizing the gravity of its consequence or perhaps quite unmindful and ignorant of the subsequent danger attending its use, some Physicians give,

as a routine measure, sub-cutaneous injections of saline made alkaline by the addition of some sodium bicarbonate to it in order to combat the acidosis or more correctly speaking, the diminished alkalinity of blood which usually occurs at least to some extent in most of the cases during the course of the disease. This, however, is a dangerous practice and is undoubtedly detrimental to the best interest of the patient as it may often lead in some cases even to ultimate death from asthenia resulting from septic absorption consequent upon the formation of abscess or abscesses as described below.

Formation of abscess.—The addition of sodium bicarbonate to the sub-cutaneous saline does greater harm than good in more ways than one; for, not only, owing to the irritation set up by it, does the alkaline saline thus made up cause intense pain and suffering to the patient but it is almost invariably responsible for the formation of a big abscess or abscesses at one or more sites of injections on account of the tissue-necrosis resulting in suppuration. The huge abscess or abscesses thus formed may not only cause prolonged illness and protracted convalescence, but these may ultimately bring about in many cases fatal termination on account of asthenia resulting from long continued septic absorption. It is very unfortunate and is also a matter of great regret that the patient, who is actually cured of the original disease, should die of an avoidable complication which occurs only as a result of the improper and injudicious treatment.

The liability to tissue-necrosis and consequent suppuration is increased to a very large extent when the bicarbonate, which is mildly irritant, is converted into a more irritant carbonate during the process of sterilization by boiling the solution The bicarbonate of soda, for this reason, ought always to be sterilized by heating in an autoclave in the form of a dry powder even when required for the intravenous saline. This dry sterile powder is to be added to the already boiled and sterilized saline immediately before use.

Quantity of saline to be injected.—Not more than one pint of saline at the temperature of blood, i.e. about 100° F, be injected at a time in any one of the sites mentioned below at one sitting. The process may, however, be repeated as often as necessary, each time selecting a different site for the purpose.

Site of injection.—The most suitable sites for the purpose of sub-cutaneous injections are either the axillary or lumbar regions where owing to the presence of loose sub-cutaneous tissues, a fairly large quantity of saline can easily be accommodated with

the least possible pain and suffering to the patient. It may, however, be safely injected in the thighs if necessary.

Aseptic and antiseptic precautions.—Whatever may be the variety of saline—hyper—iso—or hypotonic, it must always be remembered that the saline, necessary instruments and the selected site of the patient's skin, must invariably be carefully and thoroughly sterilized, or else an abscess or cellulitis may occasionally develop, to the great detriment of the patient owing to his low vitality and poor resisting power. Tincture of iodine or absolute alcohol, if well rubbed on the dry skin of the selected site, serves the purpose quite well. But the saline and necessary instruments must be thoroughly sterilized by boiling for a sufficient period before using them for the patient.

Disadvantages:—

(1) Futility in Collapsed stage.

(2) Liability to Uræmia.

1. *Futility in Collapsed stage.*—It is useless or perhaps worse than useless to inject sub-cutaneously a small quantity of saline—say about a pint or two—when the patient is in a collapsed state, with little or no pulse at the wrist, indicating feebleness of the peripheral circulation, resulting in most cases from enormous loss of fluid from the system. As death, in these cases, may occur at any moment from cardiac failure for want or insufficiency of the circulating fluid, it is imperative to push in immediately and as rapidly as possible a sufficient quantity of suitable saline directly into the circulation to prevent such a catastrophe. Owing to slow absorption, the sub-cutaneous saline cannot, in this condition, help in the least as death will probably occur before the absorption of a sufficient quantity of fluid in the system to avert or prevent it. It is a well-established fact based on repeated and careful observations that the absorption of saline is the slowest, if at all, in the collapsed stage, when the peripheral circulation is very feeble or almost at a stand-still. This, therefore, is a further proof of the unsuitability or, as a matter of fact, uselessness of the sub-cutaneous saline in this condition.

2. *Liability to uraemia.*—Another disadvantage, which I have already mentioned in connection with the intravenous saline holds equally good, if not more so, in the case of sub-cutaneous injection, *viz.*, that on account of the smaller quantity of saline and its slower absorption, although the circulation may, somehow or other, be kept on or become more or less free, the main organs of excretion, *viz.*, the kidneys fail to act or remain blocked owing

to too low pressure and too little dilution of the blood which still persists to be too thick to permit free secretion of urine. Hence the toxins which continue to be absorbed, rather more freely, as a result of improved circulation, cannot as quickly be eliminated and so become more and more concentrated in the blood. These increasingly concentrated toxins, by their action on the nervous system, may lead to the development of uraemia (toxaemia) or vasomotor paralysis.

It is evident from what has already been stated regarding the advantages and disadvantages of the sub-cutaneous saline that though it is still continued to be used on several occasions by many Medical Practitioners, it is neither essential nor unavoidable for the treatment of cholera and so can safely be discarded at least in most cases without any cause for regret or repentance.

Intra-Peritoneal saline.—This method which has unfortunately been given up now-a-days, for all intents and purposes, before sufficient and adequate trial has been given to it, especially in suitable cases under favourable circumstances, is undoubtedly much superior to sub-cutaneous saline in almost all respects though not as good or efficient as the intravenous method. It can be used as a substitute for sub-cutaneous saline in almost all cases, where the latter is indicated, probably with greater benefit and better results.

Its Advantages are :—

(1) Simplicity.
(2) Quickness.
(3) Rapid absorption.
(4) Less painful.
(5) Fairly large quantity may be injected.
(6) No previous training necessary.

A fairly large quantity of saline—2 to 3 pints—may safely be injected at a time in an adult within a short period not exceeding 10 to 15 minutes, for fairly rapid absorption with very little pain or distress to the patient by even an ordinary Medical Practitioner without previous special training as is required for the treatment of cholera by intravenous method. The injection may be repeated as many times as necessary even through the same site or opening.

Hence when a large number of new and fresh cases occur daily, during a general outbreak of the disease in a locality, not provided with a sufficiently big and well-equipped hospital to

accommodate, if necessary, such patients and where adequate number of trained and experienced Medical officers and qualified nurses or attendants are not available for the proper treatment, nursing and after-care of these patients, the intravenous method of saline treatment is not only difficult and inconvenient but practically impossible to carry out efficiently in order to cope with the unfortunate outbreak and to bring it under control.

Thus during a general outbreak of cholera among coolies, working in tea-gardens, workshops, factories, mills and mines, who usually live in huts or hovels, huddled together, very often in most disgraceful and filthy conditions, as well as among the pilgrims, who gather in very large numbers from all parts of the country, during a religious fair or festival in a place which is quite inadequate to provide suitable and sufficient accommodation to such a sudden rush of people and who have got to make their own arrangements for accommodation and food in the most insanitary conditions, as for example in Puri, at the time of the Car festival, the treatment by intrevenous method of all cases, becomes practically impossible. The intraperitoneal method, for the advantages already mentioned, should be the method of choice in the circumstances as this is probably the only feasible means by which a small number of inadequately equipped, untrained, inexperienced and very often temporarily recruited Medical Officers, can render medical aid to these poor, unfortunate and helpless sufferers in their dire distress during the illness. As these Medical Officers who have got to carry out their onerous duty in the most inconvenient and trying circumstances, find it usually very difficult and often impossible to use intravenous injections to cope with or combat the ravages of the disease which break out suddenly in very large number, the intraperitoneal saline may be tried with fairly satisfactory results, at any rate, in suitable cases and may save a large number of lives which would otherwise be lost.

Another advantage of this method is that it can be carried out more quickly than even the intravenous method by a lesser number of Medical men who have no previous experience or training for the treatment of cholera as stated above. Besides, there is hardly any danger of subsequent rigor and hyperpyrexia after intraperitoneal saline. A rigorous after-care is, therefore, not essential in these cases and so a large number of patients can be dealt with within a short time.

But it must also be remembered that it is not always safe to depend on this method, especially when, in the collapse stage, the

patient is in danger of imminent death from heart failure due to excessive loss of fluid which is required to be replenished at once or, at least as quickly as possible, to prevent the calamity; for absorption of saline, in this condition is very little, if any, even from the peritoneal cavity to be of any use to the patient. The intravenous saline is, therefore, the only means by which the patient's life may be saved under the circumstances.

The absorption, no doubt, is much quicker from the peritoneal cavity than from the sub-cutaneous tissues as long as there is a perceptible pulse at the wrist indicating a fair though feeble peripheral circulation. But neither of these can save the patient once he is allowed to drift into the state of extreme prostration, collapse and pulselessness.

From what has been said above, it is quite evident that though the intraperitoneal saline cannot, by any means, replace the intravenous in the treatment of cholera, it may be tried as an adjunct, when necessary, perhaps with better result than with the subcutaneous saline even when there is indication for the latter.

Technique of Injection:—A suitable cannula with trocar or even an aspirating needle which can be attached to the bulb containing the saline by means of a piece of rubber tubing, may be pushed into the peritoneal cavity while an assistant holds the abdominal wall up to prevent any injury to the viscera inside and the required amount of saline allowed to run in. But if the patient shows signs or symptoms of distress during the process of injection, it should be stopped at once. The abdomen must on no account be allowed to be overdistended by saline as it may cause very great distress to the patient on account of cardiac embarrassment resulting from the pressure on the heart.

The cannula invented by Sir Leonard Rogers is very suitable for the purpose and may safely be used without the least danger of injury to the internal organs.

The best site for injection, according to Sir Leonard, is just below the unbilicus. A small but fairly deep incision, not opening the peritoneum, should be made in the middle line and the cannula which has its distal end sharpened like that of corkborer is inserted into the peritoneal cavity by boring movement and then the saline is allowed to run in. The wound should be stitched up and sealed either with Tinct. Benzoin Co. or Collodian after the injection is finished.

It is needless to say that saline instrument and the site of injection should be carefully and thoroughly sterilized before the operation to prevent local sepsis or subsequent peritonitis.

Hypertonic saline when injected at about the temperature of blood or a little higher, say, between 100° to 104° F, is said to give the best and the most satisfactory result.

Though, personally, I never tried this method, I was told by the Medical Officers who did use this method of treatment among the coolies during the construction of the Hardinge Bridge at Paksey, under the instruction and guidance of Dr. Bishop, the Chief Medical Officer, that they found this method fairly successful when carefully carried out.

In conclusion, I would like to say that my remark regarding the use of subcutaneous saline in the treatment of cholera holds equally good in respect of intraperitoneal injections. If there is no insurmountable difficulty or inconvenience for its use, the intravenous method of treatment should, under all circumstances, be chosen to the exclusion of all other methods, as it will always give the best and the most satisfactory result, in most cases, in the hand of a trained and experienced medical practitioner.

---

* Though Dr. Bishop recommended the hypertonic saline for the purpose, my friends and colleagues, Dr. Bonbehari Mukherjee M. B. and Dr. Bibhuti Bhusan Mukherjee, who had personal and practical experience of the intraperitoneal method of saline treatment in cholera, while working at Paksey under Dr. Bishop during the construction of the Hardinge Bridge, are of opinion that isotonic saline is always preferable to hypertonic for intraperitoneal injections as the latter *viz.*, hypertonic saline is absorbed very slowly and causes much distress and discomfort to the patients owing to great distention of the abdomen causing pressure on the heart

Amœbiasis Problem

BY

AKHIL RANJAN MAJUMDAR, M.B.

Teacher of Medicine and First Physician, Campbell Medical School and Hospital, Calcutta.

THOUGH the obvious manifestations of Entamoeba Histolytica infection are often subacute or chronic dysentery, a disease essentially limited to the Tropics—yet, from investigations that are going on and more facts that are brought to light, it is being more and more realised that its clinical manifestations are more than dysentery and it has a wide-spread territorial distribution. So, the proper expression for the disease should be " Amoebiasis ", in its comprehensive sense rather than its one manifestation only viz. dysentery.

In considering, therefore, Amoebiasis as a disease-entity, its various manifestations, especially where dysentery is not a prominent symptom, should be kept in mind. Further, though the more acute symptoms of the infection are easily controlled, complete sterilization with permanent cure is not quite so easy. The reasons are many. Consequently, the problems of relapses, chronic invalidism, carrier state and prevention of the spread of the infection are to be considered.

Clinical Manifestations of Amoebiasis.[1]—The primary seat of the disease is the alimentary canal where the pathological changes are most marked in the caecum and to a less extent in other flexures. The parasites penetrate through the mucous membrane being favoured by a comparative stasis of the intestinal effluent in these places and probably also by some pre-existing damage to the epithelium by haemolytic streptococci.

Even if the process is mild, the parasites do not remain idle in resting state at any time. They live by histolysis, make room for themselves and multiply. Ulcerative processes in the intestines go on side by side, with repair, may be for many months or years without any symptoms or occasional attacks of mild diarrhoea or colitis. Such cases are usually said to be in the 'carrier state.'

In reality, the carriers are also suffering from an infection of pathogenic E. histolytica. Such persons are not only dangerous to others being a source of infection through cysts, they are passing, but they themselves are also in constant danger at any time on account of the lowering of the defence; the process of repair may fall short of destruction and grosser manifestations of

the disease may appear. The difficulty is that such cases in the quiescent state are not often diagnosed and efficiently treated.

So, people suffering from a milder type of infection are, from the public health point of view, a serious problem to the society.

There are many manifestations of amoebiasis in which dysentery is not a prominent symptom. These require careful consideration.

I. *Gastro-intestinal Manifestations*:—

1. Sometimes, the condition is one of recurrent attacks of indigestion following a comparatively slight attack of cold or irregularity of diet: or loss of appetite, flatulence, acidity, epigastric pain or chronic morning diarrhoea with passing of 3 or 4 liquid stools with peri-umbilical pain. If this is allowed to continue, progressive weakness, anæmia and muscular wasting follow. A slight intermittent temperature is also present in some cases and the condition may be mistaken for early pulmonary tuberculosis.

2. The first manifestation of the infection may be sudden profuse melæna in an apparently healthy person in active work. More often, such cases have a previous history of or follow an attack of subacute dysentery.

In other cases, acidity, epigastric pain coming two or three hours after food and periodic attacks of melæna are the main symptoms and may consequently be mistaken for duodenal ulcer. Amœbic ulcers in the cæcum and also probably of the appendix cause a 'delayed pyloric reflex' responsible for the symptoms resembling duodenal ulcer.

But if carefully examined, it is found that (*a*) the time of onset and the intensity of pain are variable; (*b*) there is no marked tenderness in the epigastrium, rather it is in the caecum; (*c*) the liver is often found slightly enlarged and tender; (*d*) constipation is not so constantly present, rather, periodic attacks of diarrhoea occur; (*e*) the examination of the stool may show vegetative or cystic E. histolytica; (*f*) X-ray examination with barium meal often shows a big sagging caecum with erosion of the mucous membrane.

3. Others again are dyspeptic with poor appetite and lowered digestive functions or are fairly healthy but suffer from periodic attacks of alternating diarrhoea and constipation. The patient feels best, one or two days after an attack of diarrhoea. But, for the next 3 or 4 days, he has a sensation of increasing fulness of the abdomen, flatulence and even slight pain which terminate, may

be after a heavy meal, into severe colic and is relieved by evacuations.

Here the main condition is one of intestinal paresis resulting from chronic ulceration and cicatrisation. This causes stasis, decomposition of faecal matter and liberation of irritating substances responsible for periodic colic and diarrhoea.

4. Some cases are of acute or sub-acute appendicitis threatening suppuration. The condition is one of spread of the the ulcerative process to the appendicular orifice. The history of a previous attack of dysentery may not be present and the stool may not show entamoebae and so the diagnosis is not quite easy.

In four of my cases of acute appendicitis, emetine injections brought in rapid improvements. So, in all cases of appendicitis, before surgical operation, possibility of amoebic infection should be thought of.

5. In rare cases, an apparently healthy person doing fairly active work, following a short period of mild colitis may have sudden perforation with localised peritonitis, retrocaecal abscess or more generalised infection and death.

E. histolytica cause deep ulceration and also marked softening of the intestinal wall which even with a comparatively slight degree of pressure may perforate.[2] So, the popular impression that amoebiasis is an ambulatory disease requires revision.

II. *Amoebic Embolism* :—

The first place where the parasites are transported to is the liver. Amoebic abscess is luckily getting rare on account of the popularity of Emetine. But acute amoebic hepatitis is fairly common.

The milder cases, however, cause greater difficulty and history of previous attack of dysentery may not be present. The symptoms are often of a feeling of weight or even slight pain in the right hypochondrium. Appetite is poor and mouth has bitter taste, the complexion is sallow and the bowels act fitfully. This is more common in males of active habit and is popularly called " sluggish liver." The liver is slightly enlarged and tender. The caecum is lumpy, gurgling and tender.

Emetine has gained a great reputation in the treatment of sluggish liver. Undoubtedly so, not because it has any specific action on the liver but because many such cases are amoebic in origin and emetine acts as a specific amoebicide.

Unless properly treated in time and chronic inflammation is

not allowed to continue, progressive destruction of the liver parenchyma follows ending in cirrhosis.

Other embolic phenomena are so uncommon that they are more or less pathological curiosities. These are pulmonary, splenic and cerebral abscess ; also pyelitis, cystitis and epidydimitis.

Even more rarely, E. histolytica have been demonstrated in the bone marrow, glands of Hodgkin's disease and in bones of osteoarthritis.[3] A careful investigator should keep all these in mind.

III. *Some secondary effects are seen in long-standing cases* :—

The healthy intestinal mucous membrane not only helps digestion and absorbs various nutritive principles, but it is also a great protection against the invasion of the general circulation by bacteria and toxins.

In a case of long-standing chronic amoebiasis, on account of extensive ulceration and scarring, a large part of the absorbing surface of the colon is lost. Such a state consequently interferes with general nutrition.

On account of intestinal stasis in chronic cases, the bacteria grow abundantly. So, these along with various toxins present in the colon, run into the general circulation through the ulcerated mucous membrane.

The effects are many :—

(1) Many of the chronic sufferers complain of progressive weakness and inability to do much mental and physical work. Low intermittent fever, muscular wasting and marked anaemia are also present. In more advanced cases, the ankles become oedematous and ascites developes.

Anaemia is due to several factors : continued loss of blood from the ulcerated mucous membrane, infection by haemolytic streptococci and deficiency of the blood-forming materials in the nourishment absorbed.

Anaemia is commonly microcytic hypochromic but in advanced cases, the gastro-hepatic hormone necessary for the maturation of the red cell is deficient and hyperchromic anaemia developes.

(2) Bacterial leak especially of S. viridans is sometimes associated with chronic amoebiasis and causes subacute arthritis, synovitis, myositis and perineuritis.

(3) Allergic phenomena are also sometimes seen, causing asthma and relapsing articaria.

(4) Pigmentary disturbances are sometimes seen. Sallow or muddy complexion is common in hepatic amoebiasis. Cloasmic spots sometimes appear on the face and forehead and are often persistent. Leucoderma is also sometimes associated.

(5) In some cases, the symptoms are of nervous prostration which may pass on to chronic invalidism. The power of prolonged muscular or mental exertion is lost. He becomes introspective, irritable and neurotic.

(6) Finally, prolonged bacterial leak may sometimes lead to gastroduodenal ulcer and form the nuclei of hepatic or renal calculi.[4]

Treatment of Amoebiasis [5]—This also presents many complicated problems. They are :—

(1) E. histolytica deeply embedded in the tissues are best attacked by a drug reaching them through the circulation especially so when the parasites are in the liver and other places outside the alimentary canal.

(2) Usually emetime hydrochloride ½ to 1 gr. is given daily hypodermically, intramuscularly even intravenously, the total quantity not to exceed 10 grs. in one course. Several short courses of 3 or 4 injections are often required with intervals of a week or 10 days. Intervals are essential because emetine is cumulative and toxic to the circulatory and the nervous systems.

(3) Consequently, this is a limitation to reach and maintain an effective concentration of it in the blood sufficient for rapid sterilization. Further, in long continued cases, so much scarring of the mucous membrane of the colon may take place that circulation in that place becomes feeble and emetine does not reach there sufficiently. E. histolytica consequently live in the fortified nests so formed, well protected from any drug that may reach there through the circulation.

(4) The presence of other infective organisms especially dysentery bacilli and acid forming organisms of the intestine, tends to impair the activity of emetine and so these are also required to be found out and treated at the same time.

(5) No other drug has been found to be suitable for administration by injection. Kurchi alkaloids are so readily excreted by the kidneys when injected that they do not concentrate sufficiently on the colon.[6]

(6) Consequently, for the treatment of chronic cases, drugs reaching the site of disease directly have to be sought for. These are emetine bismuth iodide, emetine periodide, kurchi alkaloids, carbarsone, treparsol, stovarsol and yatren. All these are given orally, and carbarsone (200 c.c. of 1% solution with 2% solution of sodium bicarbonate) and yatren 105 (200 c.c. of 2.5 to 5% solution) per rectum also. The results in chronic cases and in the carrier state have not been uniformly successful.

(7) The policy to be followed in the treatment of amoebiasis should be to choose a cheap and non-toxic drug capable of oral administration which the patient can himself take fairly long with safety and effect complete cure. The nearest approach to such an ideal is kurchi alkaloids. But these are not as efficient as emetine. These may however be given orally along with emetine by injection and continued during the interval period also. As kurchi alkaloids are not emetic, only a soluble preparation should be prescribed.[7]

Summary :—1. E. histolytica infection should be called 'Amoebiasis' in preference to Amoebic Dysentery, the latter being only one manifestation of the infective process.

2. Though essentially a disease of the Tropics, it has an extensive world-wide distribution and is an important therapeutic and public health problem.

3. The infection should be diagnosed early enough before the graver complications appear and much destruction with scarring of the intestinal mucous membrane has taken place.

4. In acute cases, emetine hypodermically and kurchi alkaloids by the mouth and during the intervals of emetine injection, carbarsone should be added.

5. In chronic cases, hypodermic, oral and rectal medications should be combined.

6. The expression "healthy carrier" is a misnomer because E. histolytica are always cytolytic in them as in others, the only difference being the intensity of the process and so they also must be given intensive curative treatment.

7. The problem of amoebiasis is still waiting solution in several of its items.

References :—

1. *Majumdar, A. R. Medical College Magazine, Dec. 1935.*
2. *Acton and Knowles, Dysenteries in India (1928).*
3. *Kapoid, Boyers and Swezy, Proc, Internat. Conf. on Health Problems, (1924).*
4. *Manson—Bahr, Tropical Diseases, (1935).*
5. *Majumdar, A. R. Difficulties in the Treatment of Amoebiasis, Jour. Ind. Med. Asso. Sept. 1936.*
6. ———, *Modern Pharmacology, (1930).*
7. ———*Ind. Med. Gazette, (1930)*

A few Hints on the Diagnosis and Treatment of Amœbic Dysentery

BY

CAPT. P. GANGULI B. A., D. T. M.,

(P. G. ZEU, UNIVERSITY OF VIENNA)

Physician, Medical College, Calcutta,

IT is a well-known fact that although the immediate chemotherapeutic action of amoebicidal drugs is revealed by amelioration of symptoms and disappearance of vegetative active amoebæ in the stools, yet such action represents only part of the healing process and is not in itself sufficient to bring about a complete cure of the infection. For this immunising processes are essential. The curative effect of the drugs is brought about by the parasites taking up substances which lead to the death of their cells by hydrolysis, oxidation or other chemical processes. The surviving parasites are finally destroyed by the immune forces of the body.

This immunity requires a certain time which varies from person to person, for its development. Treatment does not interfere with the development of immunity, which is determined by the body's power of resistance and is the same, no matter whether the treatment is prompt and energetic or delayed and deficient. Yet, prompt and energetic treatment is essential to make the infected persons carry on the ordinary avocations of their lives.

The immediate therapeutic action of some of the drugs is an indirect one and is quite different from chemotherapeutic action on the parasite itself. They may combine with the tissue cells and make them either resistant to the Entamoeba Histolytica or unfit for ingestion by the latter so that the parasites are starved out. The Ent. Histolytica live on tissue cells and when they find that no food material is available within a host, they prepare to leave it and seek fresh hosts where they can thrive. Some of them now assume the resistant or cystic forms and are expelled with faeces. When cysts are thus found in the stools, it does not mean that all the amoebae have been thus transformed but there are still certain vegetative forms multiplying by binary fission within the tissues from which these cysts are derived. Usually the numbers of these vegetative forms are so small that no active symptoms are manifested. Yet if the stools are repeatedly examined, it will be seen that, though many samples of the stools are free from cysts from day to day for prolonged periods, still at times the cysts come out in showers. The chronic symptoms are produced by the vegetative forms lurking within the tissues. It is extremely difficult to eradicate Ent. Histolytica, when once they have established themselves in a host. Numerous "carriers" persue their ordinary avocations, but they are far from normal and below par in the economy of national life. Besides, they are dangerous to the health of their associates.

Diagnosis.—A doctor without a microscope is worse than an astronomer without a telescope. The routine examination of stools affords much more valuable information than the routine exa ination of the blood in tropical countries. But, although the diagnosis of acute amoebic dysentery, with stools abounding in numerous vegetative Ent. Histolytica is easy by the aid of microscope, yet it may require several careful examinations to detect cysts in the stools. Again, several varieties of Entamoebae may be found in the stools and it is always easy to differentiate Ent. coli or Ent. Nana and their cysts from Ent. Histolytica. There is one variety however which cannot be thus differentiated and requires the aid of kitten for diagnosis. Ent. Dispar. looks exactly like Ent. Histolytica and can be only differentiated by the injection of stool into the rectum of kitten.

Although the vegetative Ent. Hystolytica usually remain within the tissue cells of the large gut, yet they can thrive well within the lumen of the large intestines and live by feeding on the numerous bacteria which are normally present in the gut. These are latent infections and no chemotherapeutic drugs can have

ordinarily any access to them if given by injections, unless they are excreted in the large intestines.

Sigmoidoscopic examinations are essential for diagnosis of chronic recurrent types of dysentery and swabs from ulcers will reveal numerous amoebae, even when these ulcers are painless and are not attended with any dysenteric symptoms.

When repeated microscopic examinations of stools fail to discover any amoeba, it is a good plan to culture the stools on a special media composed of serum obtained from man or cat, glucose, chlorides made alkaline with bicarbonate of sodium. The complement fixation tests are too delicate for ordinary diagnosis of chronic amoebic dysentery.

The differential diagnosis from other varieties of flagellate dysentery rests entirely on the microscope and unless they are diagnosed properly, the treatment is ineffective (and the physician comes into disrepute).

Treatment of amoebic dysentery.—*Kurchi*: From time immemorial, Ayurvedic physicians used decoctions and powders of barks of kurchi plant which abounds in *terrais* or the fertile areas at the foot of the Himalayas and the Western Ghats. The plant belongs to the natural order of Apocyanaceae and its medicinal value as anti-dysenteric and tonic was highly praised by ancient physicians practising Ayurvedic system of medicine. In his epic work of compendium of indigenous medicines, Dr. Kanailal De, highly extolled its properties, which have been fully corroborated by subsequent writers. In fact, according to certain authorities, the active principle of kurchi, which is known as *connessine* was regarded as equally effective as *emetine*, if not more, without the drawback of being a protoplasmic poison and highly depressant to the cardiac muscle. Although Keidel studied its pharmacological properties in 1878, it was H. C. Brown who was perhaps the first person to mention its amoebicidal properties in *B. M. J.* 1922, Vol. 1, Page 993. Manson Bahr corroborated these findings in 1925. Subsequently R. N. Chopra carried out pharmacological researches on this drug and its compound, bismuth kurchi iodide. A. R. Mazumdar also carried out systematic research on numerous patients in the Campbell Medical School at Calcutta. The value of this drug was also substantiated by the writer in the Medical College Hospitals and various pharmaceutical firms of Calcutta put up numerous preparations like *kurchicine*, *kutayen*, *kurchisol* and such others in the market and these preparations are now extensively used in Bengal.

Emetine.—This perhaps is the most popular drug in the

treatment of amoebiasis and its complications. It is one of the active principles of Ipecacuanha, the powdered root of which was used for many centuries for treatment of dysenteries. Other crystalline alkaloids can be obtained from the roots which are known as Cephaeline and Psychotrine and are reputed to have amoebicidal properties as well. The alcresta ipecac tablets, containing total alkaloids of Ipecacuanha are largely prescribed by doctors in chronic cases. Veddar of Vienna found that *emetine* possessed highly amoebicidal properties even in dilution of 1 in 100,000. Dobelle and Laidlaw corroborated the findings of Veddar in 1926 and found that it is effective even in a dilution of 1 in 5,000,000. Rogers first introduced injections of emetine in Calcutta and was struck with the remarkable results in curing the symptoms of the disease. The hope of eradication of amoeba from the injected person, however, was not realised and the investigations initiated by the British Medical Research Association showed that a large percentage of relapses occurred even after 12 grains of emetine were injected in 12 days. It was found to be powerless against the cystic forms of amoeba. It was however found that if this treatment be followed with a course of *Bismuth emetine iodide*, 3 grains per day in empty stomach for 15 days, most of the cases would be completely cured. The latter drug was however horribly nauseating and in some cases produced abdominal pain and purging and hence other substitutes were put in the market. Martindale's *emetine priodide*, was found to be less nauseating and could be administered after meals, in doses of 2 grains, thrice daily. It was found out that several courses of 120 grains in 20 days with intervals of ten days were not effective in preventing relapses. It was however observed that if it was given in combination with 5 gr. capsules of oxbile, it was more efficacious than emetine bismuth iodide.

Another substitute in the shape of *auremetine* was introduced by Martindale. It is a combination of *auramine and emetine priodide*. This preparation is insoluble in water and is not dissolved in the stomach. It has no nauseating effect like emetine bismuth iodide. It has been found to be ineffective in preventing relapses and hence it was advised to give it alternately with *interversal*. The same firm introduced rectal administration of emetine base dissolved in olive oil. The combination is known as *emetol* and this preparation has to be further diluted with 4 times its volume of olive oil and twice its volume of ether. Emetine has been administered orally as a treatment for destroying cysts in the form of *paremetol* which is composed of 1 % suspension of emetine in

liquid paraffin. Jepps recommended 3 grs. of bismuth emetine iodide in suspension *in 2 drams* in 2 drams of olive oil. *Gavano* is another preparation of emetine, which has been prepared by Bayer, but it failed in eradicating cysts out of injected person.

It has been found that none of the emetine preparations can cure amoebic dysentery, but it has remarkable power of ameliorating the acute symptoms of the disease. It has no destructive action against cysts. But the almost magic action of emetine injections in changing the whole aspect of the patients suffering from amoebic dysentery induced physicians to overstep the limits of caution and to employ heroic doses of emetine in their attempt to cure the disease. Gradually, deleterious effects were noticed and reports appeared in medical journals about toxic effects of emetine rather in quick succession during and after the Great War. The effect of these reports tended to reduce the total quantity of emetine used in amoebiasis. Formerly, even 21 grains were used in 21 days. Now the total quantity has been reduced to 7 grains in 7 days. Even then, as other drugs are available which have the same or even better therapeutic effects, there is no reason why this dangerous drug should be used as a routine measure in preference to other drugs. A certain number of references are given below with the idea of dissuading physicians from its routine use in amoebic dysentery. It has now been definitely realised that 7 grains of emetine have no curative effect and that subsequent treatment with bismuth emetine iodide, yatren or other arsenical preparations must be used for preventing relapses. Col. Chopra has shown by the aid of electrocardiographic tracings that even therapeutic doses of emetine produce myocardosis. Lastly it is a dangerous drug and may produce not only damaged heart but show in some cases many manifestations of "vagus effects" as will be detailed hereafter. In some cases, death has been so sudden that no remedy was of any avail.

Some reports on toxic manifestations of emetine.—Johnson and Murphy records the effect of emetine (Tropical Dis. Bulletine 1917, IX) as follows:—

Case No. 1.—After a total of 25 grains given over a period of 21 days from August 10 to Oct. 3rd, pulse became rapid; there was motor weakness and nervousness. Next day marked dysphagia, motor weakness manifested by falling forward of the head, irregularity of the pulse and later extreme acceleration and evidence of congestion of the base of the lungs. He died on October 5th. Autopsy showed acute atypical lobar pneumonia in lower lobes of both tee lungs and septic bronchitis.

Case No. 2.—A case of recurrent amoebic dysentery was treated with emetine. First course consisted of ½ gr. twice daily for 12½ days, the second course, ½ gr. daily for 14 days, increased by ½ grain daily owing to a positive amoeba stool. A total of 23½ grains was given till Oct. 12th. He complained of exhaustion and weakness, unable to hold head upright, difficulty of swallowing food, regurgitation and muscular tremor. On Oct. 17th there appeared congestion of lower and middle right lobes, dyspnoea and extreme cardiac distress. Death occurred on the 18th October. Autopsy showed dilatation and fatty degneration of the right heart, atypical lobar pneumonia and septic bronchitis.

Both these cases showed "Vagus effects of dysphagia, hepatisation of the lungs and rapid uncontrolled effects on the heart as seen in experimental animals after section of the vagus nerve.

In the same issue of Tropical Disease Bulletin, mention is made of another case reported by R. Dalmier:—

> "An amoebic dysentery case received 1.44 grains in 18 days. There followed flaccid paresis of all the muscles and especially of the neck, with failure to hold up the head; there were troubles with deglutition, mastication, speech, oedema of the face, marked diminution of the cutaneous and tendonous reflexes and rapid and feeble heart's action. The urea and chlorides in the urine diminished".

In England, Dale sounded a note of warning in 1915 in the *B. M. J.* of Dec. 18, in his article "A preliminary Note on Chronic Poisoning with Emetine." Again in China, Kelkore mentioned dizziness and diarrhoea as bye-effects of moderate doses of emetine (*China Medical Journal* 1917, xxxi, p. 212). He laid great emphasis on peripheral neuritis in which the symptoms were general muscular pain and weakness, usually more pronounced in the legs, sometimes going on to paresis. The neuritic symptoms often developed after the cessation of emetine injection and went on progressively worse for some time. In 1915, Syons describing some ill effects of emetine in *Am. J. M. Sc.* (cl. 97-109) mentions a case of a physician under his care who took 1⅓ grs. of emetine daily for 16 days. During the last few days of the injection, his legs became weak and he suffered with pains especially in the calves. There were also some general muscular weakness. Eshleman reports a case that developed a general eruption, purpuric in character, associated with severe perepheral neuritis and also flaccid paresis of the muscles with diminished tendon reflexes. Another note of warning was sounded by Levy and Rowntree in

Arch. Int. Med. (March 1916, p. 420) who mentioned a case ending fatally after receiving 29 grains of emetine, given in 20 days. From the 16th day onwards signs of grave kidney disease developed. There were marked acidosis and acute renal insufficiency with blood in the urine. Broncho pneumonia supervened and after a period of dyspnoea, the patient collapsed and died ten days after the last injection. Another patient developed intense diarrhoea, with pain and tenesmus after receiving ½ grain daily for 4 days. They concluded with the following remarks which are worth quoting. "In using emetine, one must be on the lookout for such danger signals as intense diarrhoea, albuminuria, and peripheral neuritis. In 1918, Zapata (*Trop. Dis. Bulletin* xii, 289) reported another fatal case after taking 10 centigrams of emetine and 3 grs. of ipecacuanha in 15 days. The toxic symptoms were trachycardia, fall of blood pressure, paralysis of muscles of the neck and of respiration and difficulty of swallowing.

The effect of emetine on the heart was studied by the writer in 1931 in the laboratory of Prof. Rothberger of Vienna with the help of electrocardiograph on experimental days by the injection of emetine hydrochlor solution into the jugular veins. It was found that it produced profound depression on the heart muscles, and the duration of O. R. S. gradually lengthened like those obtained with poisonous doses of quinine till the dog died. Arrillaga and Guglielmette observed that emetine was a cardiac poison in his experiments on frogs and dogs (Trop. Dis. Bulletin 1923, xx, 63). In most cases, death was accompanied by auricular fibrillation. Blair reported a fatal case of a Javanese woman (Tr. Dis. Bulletin 1923, xx, 63), the total quantity of the drug being only 1080 mgm. divided into 3 series of six injections, each of 60 mgm. in six weeks. The clinical symptoms, muscular weakness and acceleration of the pulse, became manifest two days after the last injection was given. Post mortem examination revealed a serious parenchymatous degeneration of the heart muscle. In 1924, Louis and Traband reported two cases (Trop. Dis. Bulletin, 1924, xxi, 413) in which sciatica was a prominent symptom. They think that emetine does not affect all nerve fibres without discrimination; these are affected by preference which conduct sensibility to pain, suggesting that the toxic action is mainly on the posterior roof.

Connessine, the alkaloid from kurchi bark is not so dangerous and the advantages of connessine over emetine are as follows :—

(1) It is not a gastro-intestinal irritant like emetine and does not produce vomiting.

(2) It has much less depressant action on the heart, and unless given in toxic doses, does not slow the rate of heart beat nor has it any effect on the force of contraction of the heart muscle. It can therefore be used even in cases suffering from heart diseases.

(3) Emetine injections are very painful and they produce tissue necrosis and haemorrhages. Connessine is not half so painful as emetine. It has no such deleterious effect on tissues. It can however produce some oedema in the parts injected.

(4) It has no abortifacient effect and can be used with safety in pregnant women.

Connessine brings about a cessation of the acute clinical symptoms as rapidly as emetine and also acts on the metastatic foci in the liver.

In practice, however, the writer never uses emetine as a routine treatment of amoebic dysentery since the discovery of the alkaloid of kurchi. He has only used it in some presuppurative hepatitis cases, but extreme care was taken over the doses on account of its great toxicity and this drug was alternated with connessine. The disadvantages of both the drugs however are that they have no action on cysts. It is essential that a follow-up treatment with some other drugs should be undertaken so as to prevent the development of chronic dysentery or of relapses. The efficacy in this respect of *Bismuth emetine iodide* has already been mentioned. The preparation, *kurchi bismuth iodide*, was found by Acton and Chopra to be superior to Bismuth emetine iodide in the treatment of amoebic cysts in many respects. The former has no emetic properties and much larger therapeutically effective doses (viz. 10 grains) can be used against 3 grains daily of the latter. Ten days' administration of the former compound is required for getting rid of the cysts against 15 days' administration of the latter.

It has been already mentioned that some of these drugs can altogether eradicate the system of amoeba and the final destruction of the parasite depends upon the development of immunity in the body; for this, some tonic should usually be given and the writer usually prescribes *spirocid* or some other arsenic preparation with the main object of improving the constitution of the patient in addition to the specific action of the latter which will be described hereafter.

Another follow-up treatment of amoebic dysentery in sub-

acute or chronic stages can be done with *yatren*, which has been highly recommended by Manson Bahr in his "Hand book on tropical diseases". This drug has got high antiseptic value and contains 26.5 per cent of iodine. The chemical composition is 7—iodo—8—hydroxy-quinoline—5—sulphuric acid plus, sodi bicarb (25 %) to render it water-soluble.

The disadvantage of this drug is that some susceptible persons showed undesirable symptoms of irritation. Even one pill produced violent purgation. But this factor should not be taken seriously as tolerance is soon established and gradually increasing doses can be given which can be well tolerated by the patient and the consistency of the stools quickly becomes normal and healthy-looking. Very frequently, however, one pill (4 grains) thrice daily is well tolerated on the first day. For the next four days, two pills containing 8 grs of yatren are given thrice daily and if this is well tolerated, the dose is increased to 3 pills thrice daily for the 6th and 7th day. Then after an interval of 4 days, the last dose is repeated for 3 consecutive days, then again rest for 4 days. This treatment is continued till the cysts disappear from the stools. Usually three weeks' follow up treatment is necessary for eradicating the cysts. Afterwards *spirocid* should be given for increasing immunity and preventing relapses. In intractable cases, better results are obtained if an enema of 0.5 per cent solution of yatren is given and very good reports have been obtained if this solution is retained in the intestine for 7 to 8 hours. Another compound of emetine and yatren such as *Emetron* has not been favourably reported.

Preparations of arsenic.—The revolution of treatment of amoebic dysentery was effected by the discovery of Merchonx who first used organic arsenic preparation in amoebic dysentery cases. Various preparations were recommended. *Stovarsol* was tried but it was found to be not very satisfactory. Another combination of emetine and novarsenobillon, known as *E. N. V.* was put into the market but this failed to give satisfaction.

One of the best remedial preparations is *carbarsone*, which was prepared by Ehrlich and put into the market by Eli Lilly & Co., in the form of 0.25 gram tablets. Its therapeutic activity is eight times stronger than stovarsol and is much less toxic. It has been found that about 80 per cent of amoebic dysentery cases are clinically cured by exhibition of two tablets daily for ten days. The cases which are not cured by one course may require a further course of 20 tablets in ten days.

Uptill now *carbarsone* appears to be the best drug for

treatment of amoebic dysentery. A new preparation containing bismuth and salvarsan was prepared by Bayer and has been found by the writer to be the most effective of all arsenic preparations in eighteen cases treated so far. This preparation, Bayers 5547 has not been yet put into the market as trial has not been given to sufficient number of cases.

Dysentery

BY

CAPT. J. M. GHOSH, M.B., (CAL.) D.T.M. & H., (CANTAB), D.P.H., (LOND.),

Calcutta.

Dysentery.—A clinical condition characterised by the passage of a good number of mucoid stools (with or without fæcal matter), with varying amounts of blood, accompanied by more or less fever, griping or tenesmus.

Causes:—When we have seen such a case, the usual question we are required to answer now-a-days, by the knowing public, is, whether we are going to inject Serum or Emetine. The proper and honest reply, of course, will be that it is not possible to answer the question till the examination report of the stool is available, because Dysentery Bacilli or Entamoeba histolytica are not the only factors to be dealt with.

The causes may be put under the following heads:—

(1) *Protozoal.*—Entamoebae histolytica, giardia intestinalis malarial, Leishman Donovon, Balantidium coli infestations.

(2) *Helminthic.*—Schistosomiasis (Bilharzial), ankylostomiasis, ascaris lumbricoides, oesophagostomum apiostomum infestations.

(3) *Bacterial.*—Various strains of Shiga or Flexner, Salmonelia coliform, Typhoid group, Koch's Bacilli or spirochaetal.

Of course, more than one factor may be working at the same time.

How to differentiate?—*Amoebic cases*:—A fair number of stools, 8 or 10 times a day, with griping, specially at the time of passing stools, near about the umbilicus, with hardly any temperature; even when the number of stools are many more, these cases

are not proportionately ill. Appetite and thirst are not affected and nothing particular about the tongue.

The stools—These are soft to thick fluid in consistency with a fair quantity of faecal matter with blood tinged mucus (the mucus is not sticky). The stools are acid in reaction and rather offensive in smell. Microscopical examinations show Red Blood Cells (mostly in clumps), Pus cells (much damaged), Charcot-leyden crystals, a few Epithelial cells, a good number of Bacteria and vegetative or pre-cystic or cystic forms of Entamoeba histolytica.

Giardia intestinalis:—These cases resemble the amoebic ones. I have found them more often in children than in the adults.

Stools show the vegetative and cystic forms in large numbers.

Malarial :—In subtertian infestations of the abdominal type, one sometimes comes across these cases. The temperature may be high, or even subnormal with marked collapse.

Stools show a good deal of blood, may be haemorrhagic. Examination of the blood shows the parasites.

Leishmaniasis :—Kala azar cases in the terminal stages may show dysenteric symptoms.

Stools look like those of colitis. History of the case diagnosed by Aldehyde or Chopra's test for the detection of the L. D. bodies, by Spleen or Liver puncture smears or culture. Post mortem examination shows L. D. bodies in the intestinal ulcers.

Balantidium coli :—Not found here. Pigs and apes harbour these parasites and human beings get infested by association. Stools show the parasites.

Schistosomiasis :—These are imported cases found since the war. The characteristic eggs give the diagnosis away.

Ankylostomiasis :—These cases resemble the amoebic ones rather closely, so far as the character of the stools is concerned. Anaemia is a marked sign. The ova are easily detected in the stools.

Ascaris lumbricoides :—The symptoms are less marked than the amoebic ones, unless the infestation is very heavy. Stools resemble the amoebic cases and the finding of the ova makes the diagnosis easy.

Oesophagostomum apiostomum :—Not seen in this country. Association with gorillas etc. brings it on. Eggs characteristic.

Shiga and Flexner cases :—These cases are really ill. Symptoms are urgent. Temperature fairly high. Stools numerous. Restlessness and thirst marked. Tongue dry and sore. Abdomen tender. Toxaemic.

Stools :—A few drops of sticky bloody mucus, alkaline in reaction, not offensive in smell, without any faecal matter.

Microscopical examinations show an extremely large number of Pus cells (not much damaged and with clear-cut nucleus), Red blood cells (mostly discrete), epithelial cells in fair numbers together with a good number of macrophage cells, no Charcot-leyden crystals and very few Bacilli.

Cultural examinations will bring out non-lactose fermentors and can be identified by non-motility, appropriate sugar fermentation and serological tests.

Salmonella, coliform etc.—These cases resemble the Bacillary Dysentery ones. The mucus is not sticky; pus cells do not show the clear cut nuclei of the Bacillary variety. The Bacteria are more numerous.

Salmonella etc, are identified by culture and serological tests—Koch's Bacilli, by straining, history of the case and animal inoculation. Spirochaetal cases are not so acute, and resemble the amoebic cases and can be found out by straining the stool.

Cases of an anomalous nature are now and again met with. As for instance, there was a case passing about 30 stools a day, starting on the 3rd day of delivery, with a temperature of 99.2°. Patient fairly ill and restless, stools looked of a doubtful variety—blood-stained liquid mucus, with a little faecal matter, acid in reaction, not very foul. Microscopical examination showed a few macrophage cells, no Charcot-Leyden crystals, cells did not show the characteristic nuclei, red blood cells mostly discrete and a fair number of vegetative form of Entamoeba Histolytica together with a large number of Bacilli. Culture showed only B. coli communius, no non-lactose fermentor.

Naturally Emetine was injected and the number of stools came down to 10 on the 3rd day, but no further improvement followed emetine injections and then 2 injections of the B. coli vaccine brought forth prompt result.

A second case.—The patient came with the history of continued temperature of a fortnight's duration 99°—100° in range, passing 6 or 7 stools a day. She had had already 7 injections of emetine given her. Apparently the stools had not been examined, Widal test was now found positive against typhoid which was verified by the stool culture.

A third case.—A lad came with the history of several previous attacks of Dysentery. The stools looked almost haemorrhagic, there was no faecal matter, the mucus was not sticky, the quantity was not scanty and the boy did not look very ill. Emetine which

had cured the condition before, failed this time, although vegetative forms of E. histolytica were still present. B. coli found on culture. Kurchibine Tab. twice a day proved effective for the time being but a relapse followed when further adminstration of the drug was found useless. Carbarsone capsules repeated twice, each time for 10 days, with a weeks' interval in between finally brought the condition under control.

In passing, I may mention a case, unique for the opportunity it afforded. A sample of stool which to all intents and purposes, looked like a Bacillary dysentery one, except that there were many small clots of blood in it, showed a few Microfilaria Bancrofti on examination. On enquiry it was found that it had started with high temperature, and that although the fever left in a couple of days, the dysentery continued. On the 3rd day of the attack when I saw him, inspite of the stools he did not look very ill. I took a smear of the peripheral blood *when the patient was wide awake at 1 a. m., chatting with friends* and found some microfilariae in it. So far as my information goes Microfilaria has never been found in stools before. I need hardly affirm that those were Microfilariae Bancrofti.

A Fourth case.—In one house, one after the other, 2 cases died of cholera (?). A similar case occurred in another part of the same house but this case had a temperature of 104° and M. T. rings were found in the blood and the patient came round under quinine. The next day, a 3rd case in the first house came under supervision; the stools were greenish, blood-streaked mucous, the patient in extreme collapse with subnormal temperature. Blood examination showed M. T. rings and the patient came round.

A Fifth case.—A convict from the Andamans showed progressive loss of weight and slight evening temperature. He had no cough and could produce no sputum for examination, although physical examination was rather suspicious. X-ray was not possible. All of a sudden he developed an acute attack of Dysentery which ordinarily would have been taken for a Shiga infection. Acid-fast Bacilli were found in the stools. P. M. examination showed ulceration of the intestines (large) and involvement of both the lungs.

A Sixth case.—An old man got an attack of Dysentery (?) after a feast the night before. The stools were blood stained mucous, in very large numbers. Griping was very severe. In about 5 hours cramps came on, collapse extreme. Comma vibrio found in stools and the culture clinched the diagnosis.

A Seventh case.—A typical bile-less rice water stool with flakes of mucus, alkaline in reaction, in a child, showed B. Flexner in culture.

Treatment.—*In Amoebic cases*: usually starts with a little castor oil emulsion adding a little opium if the gripings are severe. Bismuth salicylas is given after the primary cleansing of the bowels. Injections of emetine, I generally keep reserved for the very acute cases or when the liver seems affected. It should be borne in mind that emetine has a depressing effect on the heart, and destructive effect on the liver cells. When I give it, I generally give it consecutively for the first 3 days and then on alternate days or on every third day, for a course of 7 injections; another course of 7 injections given every third day follows after a week's interval.

If the symptoms are less acute one often gives Emetine Bismuth Iodide or Kurchibine or Carbarsone.

One sometimes comes across cases which may be termed emetine-fast. Carbarsone appears to prevent relapses better.

In Ankylostoma and Ascaris cases.—Santonin and Ol. Chenopodium given in empty stomach followed by a saline purge has proved very effective. A second dose is given after a week.

In Giardia infestations.—Bismuth combined with castor oil and continued for some time is the treatment of choice.

Stovarsol is also advocated.

In Balantidium coli cases.—Preparations of silver are reported to be useful.

In Schistosomiasis.—Antimony preparations are the drugs of choice.

In Bacillary or coliform dysenteries.—Sulphates hold the ground. In bad cases one injects the antiserums in the former variety, in addition. B. Coli Vaccines in small doses have given distinctly good results in the coliform cases. Treatment with 'Phage' has not been fruitful in my limited observations. In very bad cases recourse may be had to saline injections, subcutaneously or intravenously.

Sulphates *i. e.*, Mag. Sulp. and Sod. Sulp. 2 to 4 dr. of each per dose are given and if that does not produce too many stools a second dose is given after 3 hours, and if it does, no further dose is given, on the first day. On the second day, the same procedure is followed and as the case improves, the quantities are cut down. Sometimes with the sulphates a patient may appear dull, when they are stopped for the time being and calcium injected intravenously or given orally.

Opium preparations and acid sulphuric dil are conveniently added to the sulphates.

Diet:—One need not be over strict in the amoebic cases. Except in the very severe ones soft rice with vegetable soup or dahi or meat broth or chura (Perched rice) washed with boiled water and soaked in the same afterwards may be substituted for rice. Fruit juices, glucose (specially when emetine is being given), rice pudding etc. may be safely given. In bad cases only liquid foods are allowed.

In Bacillary dysenteries, milk preparations had better be withheld and only meat soup or vegetable soup or fish soup, fruit juice, glucose etc. given.

Preventive measures.—In Bacterial cases, the infection takes place through food or drink, or by careless handling of infected materials (as when attending a case). Flies may convey the infection from place to place, by taking the germs in their legs, or by contaminating articles of diet by their vomit or faeces. A "carrier" may play the same role. Infected dust may be blown into articles of food or drink. I had a case where the master of the house was repeatedly having attacks of colitis; the source of infection was subsequently traced to one of the cooks being a "carrier" of an organism of the Salmonella type. Sensitized vaccine seems a good method to eradicate the evil. Billi-vaccine is now widely practised as a prophylactic measure against Bacillary dysentery.

Bad conservancy is primarily responsible for the amoebic and helminthic cases.

Conclusion.—1. Dysentery is fairly common in this country.

2. Provention means a thorough grinding into the public mind of efficient measures for both personal and public hygiene, and seeing to their observance.

3. Correct diagnosis involves painstaking laboratory methods.

4. Treatment begins with the actual cases and ends in rounding up the "carriers" and rendering them "free".

Reference:—

Manson—Bahr's Tropical Medicine.

Abscess of the Liver

BY

LT. COL. B. G. MALLYA, M.D., F.R.C.S.E. L.R.C.P., I.M.S.,

Civil Surgeon, Howrah.

Abscess of the Liver may be broadly classified into :—

1. Tropical or Amoebic.
2. Septicaemic.

1. The Tropical or Amoebic abscess of the Liver is the commoner variety and is amenable to treatment whereas very little can be done for the Septicaemic Abscesses.

The tropical abscess of the Liver is met with in areas where amoebic dysentery is prevalent and a history of an attack of dysentery is always forthcoming. The Amoebae gain access to the liver through the portal vein and set up a condition which has been described as amoebic hepatitis and this condition passes on to the stage of abscess formation in cases where the hepatitis is not treated thoroughly with emetine injections.

The pus is of a dark brown colour and is sterile in culture. Amoebae may be found in the pus.

Signs and Symptoms :—These may be divided into general and local. The *General symptoms* are :—

(*a*) Remittent type of fever.
(*b*) Profuse sweats.
(*c*) Exhaustion.

Local :—

(*a*) Enlargement of the Liver which is tender on palpation.
(*b*) Pain on pressure on the right lower chest and pain referred to the right shoulder.
(*c*) A fluctuating swelling may be present below the ribs.
(*d*) Signs of congestion of the base of the right lung may be found.

Examination of the blood shows a total leucocyte count which is high but without an increase of polymorphoneuclears.

Diagnosis is easy where the classical signs of liver abscess are present. Blood and stool examination should be carried out in

all cases. "X"Ray examination does help as the position of the diaphragm and the variation in the density of the liver shadow may give an idea about the location of the abscess.

In cases where there is no access to a laboratory nor facilities for "X"Ray examination, the therapeutic test should be applied by giving a course of emetine injections.

Treatment:—To what extent the teaching, "Where there is pus let it out", is applicable to the treatment of liver abscess, is a debatable point. There are two schools here with views diametrically opposed to each other. One school advocates treatment by emetine injections alone without any form of surgical interference, while, the other advocates emetine injections and aspiration. Each case should be dealt with on its own merits. Emetine injections should be given before any aspiration is done. The improvement in the general condition of the patient after two or three injections of one grain of emetine per diem is dramatic. In case the swelling does not diminish in size, aspiration should be carried out by inserting a large bore needle through an intercostal space which is most tender on pressure. An injection of a few minims of novocaine solution makes the procedure simple, painless and devoid of shock. The needle should not be pushed into the liver substance beyond 3½ inches as there is danger of injuring the large vessels. In cases where the swelling reappears aspiration should be repeated. A full course of 12 to 15 grains of emetine injections should be given to the patient who should not be allowed to get out of bed too soon.

The use of ipecacuanha in dysentery was originally empirical but now it is put on a scientific basis. Insufficient treatment with emetine mostly due to the negligence of the sufferers who do not undergo thorough treatment results in the appearance even now of cases of large abscesses of the liver and our records at the Howrah General Hospital show a mortality of fifty per cent and this however is not due to want of skilled treatment but solely due to the conversion of the entire liver tissue into a large abscess as ascertained by post-mortem examination in every case and the absolutely helpless condition in which the doctors find themselves in dealing with such hopeless cases.

The open operation and drainage of liver abscess which was the treatment in the olden days has been replaced by emetine injections and aspiration with highly satisfactory results except in the very advanced cases where all treatment fails. It used to be taught that after aspiration, some solution should be injected into the cavity. Quinine and emetine solutions have been used but

there is no necessity to introduce any solution as long as the pus is removed.

Is open operation necessary at all? This question should be answered in the negative though some surgeons would not agree. It is not the question whether the liver abscess can be approached with the aid of the surgeon's knife or not but what the result would be. Even in the most advanced cases which are pointing, aspiration is quite sufficient and this may be repeated. Nature provides the safety valve which the surgeon's drainage tube cannot and as such there should be no justification to drain a liver abscess unless it is pointing and is about to burst in which case the hole made by the introduction of the aspirating needle suffices to provide drainage.

Complications such as bursting of the abscess into the lung, stomach, peritoneal cavity and hepatic flexure of the colon are met with. Whenever the abscess bursts, the temperature falls and the general condition of the patient improves and the prognosis is good provided emetine injections are given. In a case that was operated in the Howrah General Hospital for a cystic swelling in the epigastrium, an encysted abscess was found which was an amoebic abscess of the liver which had burst into the peritoneal cavity. This case left Hospital perfectly fit after a course of emetine injections. Rupture of the abscess into the lung is the commonest termination in untreated cases and large quantities of dark brown pus is expectorated and with emetine injections the patient makes a complete recovery.

2. Septicaemic Abscesses of the liver are mostly met with as terminal infections and are fatal. They may be classified into:—

(*a*) Portal Pyaemic.

(*b*) Cholangitic.

(*c*) Bacillus Coli.

(*d*) Staphylococcal.

Portal pyaemic abscesses are caused by an ascending infection from the intestine through the venous channel. Surgical treatment is of no avail in these fatal cases.

(*a*) I came across a case of portal pyaemia in a patient who was operated on for haemorrhoids. The patient was highly toxic and the liver was enlarged and tender. This patient died within 48 hours of the onset of the signs of portal pyaemia.

(*b*) Cholangitic infections are rarely met with.

(c) Bacillus Coli :—A patient was getting repeated rigors with enlargement of the liver. Blood culture was positive to Bacillus Coli. An abscess of the liver was drained through an incision in the 8th intercostal space. This patient died of toxaemia.

(*d*) Staphylococcal abscess of the liver is described and may be dealt with surgically if diagnosed and accessible.

Tropical Liver Abscess

BY

DR. HARI DASS, M.B., F.R.C.S.,

Ranbir Hospital, Jind.

IT may be defined as a suppurative condition of the liver caused by Entamoeba histolytica in tropical countries or in other words it is suppurative Amoebic Hepatitis.

Aetiology.—Causal factor is Entamœba Histolytica. The infection comes to the liver from the intestines via portal circulation, so invariably history of dysentery is traceable. In 98% of fatal cases, Rogers either obtained a history of dysentery or found amoebic ulcers or scar of ulcers in the large bowels. The patient has had dysentery in the past or is still suffering from it in about 75% of cases, there is history of diarrhoea which is probably a mild form of amoebic dysentery and in the remaining 10% cases, amoebic ulcer has probably been present in caecum or ascending colon, where they do not necessarily give rise to any symptoms. The abscess may occur at any stage of the disease and may be quite an acute manifestation coming on during the first ten days; on the other hand it may appear months or years after all dysenteric symptoms have disappeared when hepatitis developes an attack of dysentery, the latter becomes less severe as the inflammation in the liver progresses. Alcoholism is an important factor but not an essential one as many cases occur in India who have not even tasted alcohol. Abscess occurs generally in those cases which have not been treated or those in which emetine has not been continued for a sufficient period. It is rare before the age of 20 and is most common between the ages of 20 and 40 years. It is more common in men than in women, more common in European inhabitants than among the natives of the country.

Entamoeba histolytica is not always and alone both the predisposing and exciting cause. If this were so, then the natives and the females would suffer as frequently as the European residents and males there. Some additional factor is necessary. Possibly intemperate habits and exposure lead to special liability to hyperaemia and congestion in the liver in man and this causes diminished resistance to pathological influences, so, really the causes of liver abscess are first the predisposing—hyperaemia and degenerative condition of the liver from free living and exposure and secondly the exciting—Entamoeba histolytica or in other words dysentery combined with chill, dietetic excesses or traumatism (Manson). Geographical distribution of the disease is identical with that of Amoebic Dysentery, but as it may develop chronic cases and long after the onset of dysentery, it may be seen in any place to which such patient has gone, and so it is not rare for such cases to occur in Europe.

Pathology:—The amoebae which collect in the thrombosed veins at the base of dysenteric ulcers pass on to the liver via portal veins. Infection appears to be widespread and uniform throughout the liver. An abscess forms if a local accumulation of amoebae gives rise to thrombosis in a portal radicle. The circulation is obstructed and necrosis of surrounding tissue occurs; at the same time pus is secreted as a result of the irritant action of the amoebae on the liver tissue. The wall of the abscess is at first formed by necrotic liver tissue, but the cavity gradually becomes limited by fibrous capsule produced by the inflammatory reaction. The pus in the cavity is usually yellow pus in the very early stages, which becomes chocolate coloured from admixture with blood and necrotic liver tissue and looks like Anchovies Sauce. It is very viscid and not offensive. The pus itself is usually sterile, but may contain amoebae, which are practically always found in the scraping from the wall.

In 70% of cases, a single abscess is present, in 15%, two abscesses, in 7% three and in the remainder four or more. A single abscess is found five times as often in the right lobe as in the left lobe of the liver (Hurst). The posterior and upper part of the right lobe is the favourable site or the seat of election. When a liver abscess reaches surface, adhesions form between the liver and the adjoining structures so that the contents of the abscess may burst into the pleural cavity, lung, pericordial cavity and heart, peritoneal cavity, stomach, bowel or open externally without infecting any serous cavity. Rarely the abscess shrivels up and its contents become inspissated.

Symptoms.—The symptoms vary and necessarily depend on situation, size, and duration of the abscess.

Fulminating Abscesses of the liver.—About 10% of the cases are of this type in India. There is always definite history of dysentery which may still be present. The liver rapidly increases in size, is very painful, and extremely tender. Jaundice may be present. Temperature is high and shows rapid remissions. Rise occurs in the evening and is accompanied by rigors, and fall by sweating which is usually profuse. Leucocytosis is marked. Death occurs between the 6th and 18th day.

Subacute type is the one most commonly seen. Usual and common history is that sometime back the patient had an attack of dysentery from which he appeared to have recovered and resumed work. After several weeks or months, he got chill or was indiscreet in his diet and began to feel out of sorts, developed headache, foul tongue, want of appetite, irregularity in bowels, disturbed sleep, unusual langour, depressed spirits and irritability of temper. About the same time he began to feel discomfort and sense of weight and fulness in the right hypochondrium. Later, he became feverish especially towards the evening, the onset of fever being preceded by a sense of chilliness. He feels uneasy if he lies on his left side. The pain may become so severe that he is hardly able to move. Pain of dull or acute or burning type may shoot back to the intrascapular region or be referred to the right shoulder and occasionally to the right arm, especially when the upper part of the liver is involved and the diaphragm gets adhered. This is due to the fact that the nerve supply of the shoulder and diaphragm comes from the same nerve—fourth cervical. Pain from pressure with the finger tip in the intercostal space and over a limited area is a common and localizing sign. Pain is stabbing, stick-like in character and is increased by deep inspiration or coughing or sudden jarring movement. Cough is dry and hacking and of reflex character. There is often a tendency to stoop to the right side and to coughing on deep inspiration. Respiration is entirely thoracic and shallow. Diaphragm is almost motionless. Decubitus is dorsal or right dorsal, right leg may be slightly drawn up. The appetite first impaired is lost now, and the patient becomes weak and emaciated. Wasting is marked.

The liver is definitely enlarged, palpable and tender but the rigidity of the abdominal muscles may be so great as to prevent one from feeling the edge. Area of hepatic percussion dullness is usually increased upwards and downwards. The lower ribs bulge and the intercostal space becomes wider. The temperature is

generally remittent varying between 101° in the morning and 103° or 104° F. in the evening. This evening rise in temperature is rather characteristic and may be accompanied by rigors. In severe cases temperature remains high with small remissions, but in more chronic cases, especially when the abscess bulges through the capsule of the liver and the tension consequently falls, the fever gets less marked and may even disappear. The remission is usually accompanied by sweating which is usually profuse and is mostly nocturnal. Complexion is yellow and earthy, cachectic and may be slightly letric. Pulse rate relatively slow, may be 80 to 100 per minute.

Leucocytosis is usually present, the proportion of polymorphonuclear cells being increased considerably. If their percentage is less than 70, then it is a case of simple hepatitis and pus has not formed yet.

X-Rays show right side of diaphragm abnormally high, movements diminished or lost. If the abscess has perforated into the pleural cavity, signs of Empyaema are visible. There is increased density in liver shadow.

If the abscess ruptures into the lung, large quantities of thick reddish pus—chocolate brown in colour, viscid and jelly like in consistence and occasionally streaked with blood are coughed out. In such cases rapid recovery is likely, if emetine treatment is given.

An abscess in the anterior or lower part of the right lobe causes a tender swelling in the right side of the pit of stomach area, the lower ribs often become bulged and lower border is found displaced downwards. When such an abscess reaches surface, it forms adhesions with the anterior abdominal wall and in advanced cases the skin becomes oedematous and deep fluctuation may be elicited and the abscess may burst externally. Less frequently the abscess reaches the under surface of the liver, when it may open into the duodenum or hepatic flexure of colon, and the pus is evacuated out from the rectum ; this causes immediate improvement in the general position of the patient, temperature falls, pain disappears and spontaneous recovery may result.

An abscess in left lobe generally gives rise to a tender swelling in the epigastrium. If it becomes adherent to the anterior abdominal wall, skin would become œdematous and deep fluctuation obtained. Finally it would burst externally. In other situations an abscess is hard to make out. An abscess in the lower part of left lobe may rupture into the stomach and the pus may be vomited out, one in the upper part may rupture into the pericardial or left pleural cavities or left lung.

Duration.—Liver abscess may run its course in three weeks. Usually it is an affair of several months. In very rare cases, the liver abscess may become encysted and give rise to further symptoms.

Diagnosis.—In an obscure abdominal case, hepatic abscess is always to be thought of especially if there be history of dysentery, if the patient is addicted to alcohol, progressive failing in health with more or less pyrexia of remittent type and accompanied by chills and sweats, pain in the liver area, which is tender to touch and shows increase upwards. The most characteristic local symptoms are progressive enlargement of the liver, pain in the right hypochondrium and in the right shoulder and tenderness over the liver. Lævulose test would show some impairment of the liver function. White cell count shows leucocytosis with relative increase in the polymorphonulcear cells. If still there be doubt, one should not hesitate to have early recourse to aspirator after giving a few injections of emetine. A point to note in exploring is that when the aspirator needle enters the liver, an up and down pendulum like movement will be communicated to the outer end of the needle as the organ rises and falls with the respiratory movements. If this movement is not visible, then the point may be in the abscess cavity as shown by pus coming out, but this abscess is not in the liver.

It is mostly confused with malaria in which the liver is never enlarged so much as in the abscess, but spleen is much enlarged. Blood picture is different, malarial parasite may be seen in the film, but in tropical countries two diseases are apt to occur in the same patient and cause further confusion. In such a case, quinine or more modern anti-malarial medicines should be employed as therapeutic tests.

It may be difficult to distinguish it from suppurating hydatid cyst, syphilitic gumma, sub-phrenic abscess, pylephlebitis, cholœcystitis, pleurisy, encysted empyæma and some general conditions like pernicious anaemia, but blood examination and X-Ray pictures would help in clearing the diagnosis.

Lastly, amoebic hepatitis is very confusing. Such a condition is the first stage of localised abscess formation and clears up with emetine treatment alone and exploring needle in different directions does not reveal any pus.

Mortality.—It used to be considered from 50 to 80%, but the present improved technique of treatment has brought it down considerably—10% according to Turner.

Prognosis.—Prognosis, with early modern treatment on

single abscess cases, is fairly good, provided there be no complications. In multiple abscesses or in single abscess if there be active dysentery or other serious complications, the prognosis is bad. If there be more than two abscesses, it is helpless.

Treatment.—The medicinal treatment is at once started. The patient is advised absolute rest and is put on a low diet. Pain is relieved by local application of heat *e.g.* antiphlogistin, wet or dry cupping over the liver area. Ammonium Chloride, grains 20 three times a day and intra-muscular injections of emetine hydrochloride gr. 1 in 1 c.c. of sterile distilled water daily are prescribed. After two or three injections, aspiration is tried and a full course of 8 or 10 injections is completed. After this one powder containing Pulv. Ipecac and Tannic acid at bed time, three hours after a light meal is advised.

For aspiration, select a suitable Potain's aspirator and test it beforehand to see if it is in proper working order. It is hardly necessary to say that strict aseptic precautions must be observed in the way of cleaning the patient's skin and surgeon's hands and everything that is used must be surgically clean and sterile. A medium or full sized aspirator needle is to be selected as owing to the nature of pus, it may not flow through a cannula of small bore.

Site.—If there be localizing signs such as tender spot, a fixed painful spot, localized œdema, localized pneumonic crepitus, pleuritic or peritoneal friction, these should be taken as indicating the seat of pointing of abscess and most suitable for puncture.

If no localizing signs are present and abscess appears to be in its most common place in the upper part of the right lobe, then the needle in the first place should be inserted in the anterior axillary line in the 8th or 9th intercostal space about $1\frac{1}{2}$" above the costal margin. The needle is pushed in a direction inwards slightly upwards and backwards. While the needle is being introduced, the patient is given a dose of spirit ammonia aromatic to divert his attention. This is not very painful, especially when his attention has been diverted, so, as a rule no local anæsthesia is required in ordinary cases. The needle may be pushed in from 3 to $3\frac{1}{2}$ inches. If still pus be not struck, the needle may slowly be withdrawn, a good vacuum being maintained all the while, so that if the abscess has been transfixed and the point of the needle has entered the sound tissue beyond, slow withdrawal of the needle would bring the point into the abscess cavity and the pus would appear in the bottle and show that the needle now is in the proper place. The pus is now allowed to flow into the bottle. When

the flow stops, fresh vacuum is made and the pus would start coming again. In this way several pints of pus can be evacuated. After the pus has completely been evacuated, an emetine solution of gr. 1 in one ounce of sterile distilled water may be injected into the cavity. The needle is then withdrawn and the puncture sealed with Collodium flexile. A pad of cotton wool is applied and fixed in place with a bandage. The shock to the patient is almost nil and relief is immediate. It is possible that pus may re-accumulate, it can essily be evacuated again. More than two or three aspirations are never needed.

If the first puncture has failed, the surgeon must try another spot. It has been advised that at least six punctures should be made before the attempt to locate pus is given up. The author does not recommend more than three punctures at one sitting especially when no anæsthesia has been given. The surgeon is advised to make early use of aspiration by the fact that its employment even when no pus is discovered is not infrequently followed by rapid improvement in all symptoms. The Harley's phlebotomy of removal of a few ounces of blood from the liver is a measure of decided value in hepatitis. There is very little risk of hæmorrhage if proper precautions are taken.

Puncture can be made anywhere below the line of nipple and angle of scapula or wherever the physical signs point.

Such a line of treatment has obviated the necessity for open operation which is full of risk and so has to be avoided if possible. Open operation is advised only in very rare cases *e.g.*, when the situation cannot be determined and the bacteriological examination of pus obtained by aspiration shows that the pus contains already the pyogenic bacteria.

When the abscess has ruptured into the lung, stomach, or bowel, emetine treatment is to be pushed in and nothing more may be needed especially when the temperature comes down to normal and continues to be so; pus passed out decreases gradually, and the body weight increases or at least is maintained. In such cases recovery gradually takes place without any aspiration or operation.

If temperature persists, amount of pus continues the same or increases or if the patient continues to lose weight, an attempt should be made at all risks to reach and drain the abscess cavity from outside. If the abscess has ruptured into a serous cavity, the particular serous cavity involved must be opened at once and treated on general principles.

Ocular Findings in Dysentery

BY

CAPT. M. AZAVEDO, M.B., B.S.,

Nova-Goa (Portugese, India.)

OCULAR complications in connection with different types of dysentery have been reported during the last sixty years. The reports may be first summarized as follows :—

Conjunctivitis; Corneal ulcerations; Bilateral inflammation of lacrimal gland; Iritis; Iridocyclitis; Optic atrophy; Paralysis of accommodation; Amblyopia.

It is reasonable to assume that the production of these ocular complications, if they are really caused by dysentery, is more or less dependant on the morphological and biological peculiarities of the different dysentery organisms, of which there are 2 main groups, *bacillary* and *amoebic*. It would be well, therefore, to discuss the above-listed ocular complications according to the different types of dysentery organisms held responsible for their production.

In the case of bacillary dysentery we will use, for the purpose of discussion, the classification found in Hiss' book (Text-Book of Bacteriology, 5th Ed. 1922, p. 706), which seems very rational. According to that book, the main types into which the organisms of bacillary dysentery may be divided, on the basis of sugar fermentation, are (1) Shiga type; (2) Flexner type; (3) "Y" (Hiss and Park) type; (4) "Strong" type.

Bacillary Dysentery.—1. *Shiga type*: Zlocisti reported in detail 2 cases of *acute conjunctivitis* in dysentery caused by bacilli of Shiga type, and he shared Bartel's view that the dysentery had some connection with these cases. The conjunctivitis was followed by arthritis.

Zoeller and Manousakis, working with guinea-pigs and rabbits claimed to have produced conjunctivitis by the use of Shiga bacilli which they introduced locally into the eye. 48 hours after the instillation there appeared in 50 per cent of the guinea-pigs and in all the rabbits an oedema of the conjunctiva, purulent secretion, and cloudiness of the cornea with partial ulceration. The kerato-conjunctivitis cleared up in 10 days. Dysentery serum diminished the inflammatory symptoms, but did not affect the corneal ulceration. None of these animals showed any dysenteric symptoms, and they developed no agglutinating substances against

the dysentery bacilli. In the guinea-pigs, after recovery, there developed a recurrence of the eye condition. In rabbits which had been previously inoculated with killed bacilli, it was not possible to produce any kerato-conjunctivitis by the instillation of an emulsion of living dysentery bacilli. Subconjunctival injections in guinea-pigs produced subconjunctival abscesses and kerato-conjunctivitis. These animals showed no dysenteric symptoms but formed agglutinating substances against the bacilli. Exceptions from this were shown by 2 rabbits, in which subconjunctival injection caused death from acute dysentery without ocular symptoms.

Maxwell and Kiep together reported 6 cases of *iridocyclitis* in the course of dysentery caused by Shiga organisms. No other causes were present to account for the eye symptoms. In one case in which an iridectomy was performed there were in the iris tissue gram positive cocci, and the aqueous agglutinated Shiga organisms in dilutions of 1-80 to 1-160. The ocular symptoms usually appeared one month after the onset of dysentery, and in 4 cases they were associated with arthritis. The course resembled that in gonorrhoea.

Bey reported a case of optic neuritis following bacillary dysentery. There was bilateral neuroretinitis with vitreous opacities and very marked reduction of vision. Bacilli resembling the Shiga type were isolated from the stool and autovaccine was given with improvement of the eye condition. When dysentery recurred the neuritis came back, which disappeared again with the improvement of the dysentery.

2. *Flexner type*:—No reports found in the literature.

3. "*Y*" (*Hiss*) *type*:—Worms and his co-workers reported articulo-ocular affection in many patients suffering from dysentery due to B. Hiss. He observed conjunctivitis frequently associated with arthritis. The same author reported severe ulceration of cornea associated with iritis in a case of dysentery due to the same bacillus. No mention was made as to whether any organisms were present in the eye or not.

4. "*Strong*" *type*:—No reports found in the literature.

5. *Dysentery organisms the type of which was not determined or not mentioned*:—As early as 1871 Krauter mentioned acute conjunctivitis in dysentery (type ?) associated with effusion into the joints. Markwald and Vossius in 1904 observed bilateral conjunctivitis associated with urethritis of non-gonorrhoeal origin 3 weeks after the onset of dysentery (type ?). In the secretion some bacilli were found which resembled B. Coli. The conjunctivitis was followed by iridocyclitis. Garrod in 1917, mentioned a case in which conjunctivitis occurred during an attack of dysentery (type ?) and the discharge contained B. Coli. Fiessinger and Leroy observed in a series of cases of bacillary dysentery (type ?) in France in which they found the syndrome of conjunctivitis urethritis-synovitis appearing between the 10th and 12th day of the disease. The eye complication was usually unilateral and lasted for about 48 hours. No micro-organisms were found in the eye or the urethra. Coses and Delord (1917) described 8 cases of conjunctivitis in an epidemic of bacillary dysentery (type?) in France. The cases were classified into two groups. In the first group, the dysentery was severe, the conjunctivitis developing about 15 days after the onset of the disease, and lasting 8-10 days. At the same time there were symptoms in the joints. In the second group of cases the dysentery was mild, no affection was present in the joints, and the conjunctivitis was limited to the lower palpebral conjunctiva, appearing 5 to 12 days after the onset of dysentery and lasting about a week. Bartels (1917) reported in detail four cases of acute conjunctivitis associated with dysentery (type ?) and with effusion into the joints. The suspicion was strong that the dysentery had some connection with the conjunctivitis, although no organisms were found. He saw several similar cases. The sequence of events was usually as follows:—First dysentery, then acute conjunctivitis, and a short time afterwards, an effusion into different joints. The inflammation was not particularly violent and produced little secretion. He had the impression that the conjunctivitis was of endogenous origin partly because of the fact that no organisms were found. It was not possible to say if the conjunctivitis was of infectious nature, because the blood culture was also negative. It is possible that the toxin of the disease circulated in the blood and lymph and thereby caused the conjunctivitis as well as the arthritis. The author was not sure in these cases whether or not there was a direct transference of any organisms into the conjunctiva. Further observation of more cases may clear up the question. According to Kubik the conjunctivitis may be due to metastatic transference of dead bacilli in the circulation.

Maxwell reported 6 cases of bacillary dysentery (type ?) showing conjunctivitis, in which 4 had arthritis, and 3 in addition had uveitis.

Hemorrhagic conjunctivitis.—Was observed by Aubik. It always cleared up. It may be associated with arthritis.

In contradistinction, to other authors, Morax saw only one

case of eye complication out of 250 cases of dysentery (type?) probably of bacterial origin. The man developed acute conjunctivitis 2 weeks after the onset of dysentery. Three weeks later, he developed iritis in the right eye. He also had arthritic symptoms.

Bilateral dacryo-adenitis.—Was reported by Marcisiewicz in connection with dysentery type.

In Vossius case the dysenteric conjunctivits finally ended in a severe iridocyclitis with vitreous opacities. The conjunctivitis was at first thought by the author to be due to mechanical transference of the organism by the patient's hands from the urethra to the eye (the patient also had urethritis presumably caused by the same organism), but when iridocyclitis developed in both the eyes he was inclined to attribute both to a metastatic process? The iridocyclitis was so severe that within 4 days of its onset, it reduced the vision to light perception. However, the case ended finally in complete recovery and no further relapses were observed. It was assumed by another author in this case that the infection was not produced by the dysentery organism, but by B. Coli which had entered the circulation through a defect in the intestinal wall.

Iridocyclitis in dysentery (type?) has been further observed by Houdart Schidowsky and Browing?

Jackson reported optic atrophy following dysentery (type?) He summarized this case as follows: "The patient, then aged 35 years had been attacked with dysentery while at Honolulu with the United States forces in September, 1898. There was some sharp pain through the head, but not very marked signs of meningitis. There was no history of malaria or the use of large doses of quinine, or other causes for a toxic amblyopia. A few days after the attack of dysentery the sight began to fail and had gradually grown worse, until in the last few months it seemed almost stationary. In the right eye vision was reduced to 10/200, the field greatly contracted, and colour vision lost. The left eye had no light perception. Both eyes showed paper white discs devoid of small vessels, with sharp outlines and doubtful disturbance of the retinal pigment layer. The retinal vessels were slightly narrowed.

Paralysis of accommodation was claimed to occur in dysentry by Lawnson.

Comment.—If the organism of bacillary dysentery has ever produced any eye complication the reason is perhaps not far to seek. Hiss states, "Of all the various types which have been described the strongest, poisons have been produced with bacilli of Shiga-Kruse variety, less regularly active ones with bacilli of flexner and

of the "Y" type. In fact, investigations carried out with Shiga bacilli have tended to show that the disease itself is probarbly a toxæmia, its symptoms being referrable entirely to the absorption of the poisonous products of the bacilli from the intestine." If there is really such a severe toxæmia in dysentery then the production of ocular symptoms may perhaps be explained accordingly.

Amoeba.—Luna reported a case of acute iritis with posterior synechiæ which he attributed to amæbic dysentery. Under emetine treatment the eye condition improved simultaneously with the disappearance of amœba from the stool.

Mills reported 4 cases of plastic iritis due presumably to non-dysenteric amaebic infection. One of the cases was considered typical and was summarized by him as follows: "The patient is a middle-aged woman, who suffered from intractable, plastic iritis in the eye for 10 tears (!!!). This finally led to occlusion of the pupil, secondary glaucoma and blindness the intolerable pain finally forcing an enucleation. An identical iritis started in the remainning eye 3 weeks after the enucleation of the first. The outstanding general symptoms have been marked constipation, pallor, pains in the joints, and intense weakness and lassitude. The noteworthy physical findings were a well-marked secondary anaemia, decided tenderness over the colon, and the presence of large numbers of Endamœba dysenterae in the stools. A simultaneous cure of the iritis, of the abdominal symptoms and signs, and of the general extreme depression resulted from 2 intensive courses of treatment with Ipecac and emetine, and coincided with the disappearance of the amoebæ from the stools. Inasmuch as no change in the treatment was made other than that of the specific anti-amoebic measures, it seems reasonable to assume that this is a case of bilateral iritis arising from non-dysenteric amœbiasis, and, believe, the first case of the sort ever recognised. The four cases observed all gave the characteristic histories, of non-dysenteric amœbic infection of the intestine, and all showed Endameba dysenterae in the constipated stools. In each case the fact that there was no dysentery threw the various physicians who had cared for these patients during many years completely off the diagnostic track.

The same author made another enthusiastic report comprising 88 cases of chronic ocular conditions, chiefly uveitis, occurring in connection with intestinal parasitism, principally in non-dysenteric amœbiasis. Presumubly a thorough examination was made in almost all these cases to exclude other cases. He remarks: "It

is not clear why the sceptic should consider the eye inviolable in such cases (*i.e.* cases of intestinal parasitism) when amœbic invasion of the intestinal wall, the liver, lungs, pleura, lymphatic glands, brain, blood, kidneys and even of the skin, testis, and bone has repeatedly been proved. The investigation which this paper records has confirmed and extended the opinions expressed in the original paper that protozoa notably Entamœba dysenterae were fundamentally the cause of a certain proportion of cases of chronic recurring and intractable inflammations of the eyes. Whether the ocular lesions result from direct protozoan invasion, from secondary bacterial invasion by way of the damaged intestinal wall, or from other foci of infection, it is certain, however that the arrest or cure of chronic irridocyclitis, choroditis, retinitis, episcleritis, keratitis, and conjunctivitis has followed the faithful use of ipecac and its derivatives when the recognition of the protozoan background has ended repeated vain searches for a bacterial etiology. Not seldom a remarkable improvement in the chronic conjunctivitis, with in fact the symptomatic relief which is often present, results from the first injection of emetine. In fact, the symptomatic relief which follows the use of emetine in some cases of amœbic iritis is enough to raise the question as to its possible value in iritis and scleritis of other origins. Reversely, the exacerbation of colonic and hepatic discomfort and tenderness which is now believed to represent encystment of the amœbae and renewed activity of the basic infection, often is heralded by functional discomfort of the eye, mild photophobia, tearing, conjunctival inflammation and a flare of iritis in that sequence. The relation between the periodicity of the abdonimal discomfort and other ocular inflammation has been noted many times. Relief, arrest or cure has resulted in nearly every patient who was able and willing to undergo the required medical and surgical treatment. A single course of treatment sufficed in a few cases, but the majority required 2 or more courses before the ocular condition could be considered as arrested. It is my opinion that the ocular lesions often clear up before the intestinal condition is wholly mastered

Ferguson in 1924 reported a case of amblyopia due to amœbic dysentery which ended with complete recovery of vision. The patient aged 53 was in a very poor condition, and in January 1923 had disturbance of vision. He had been in Sudan and contracted dysentery and malaria (since when?) He had emetine treatment. O. U. 6/60 was not improved by glasses. Stools showed cysts of Amoeba. Emetine was given hypodermically in addition to the

introduction of saline into the intestinal tract. Thus the living amœbae were killed by emetine and the cysts were evacuated by diarrhœa. On October 10th 1923, the patient came back with 6/5 vision in both eyes. General condition was also much improved.

Comment.—Although the opinion expressed by these authors appear to be incompatible with our present knowledge of the etiology of ocular disease, we are not in a position to accept or to refute them, and therefore we cannot here do more than to record their statements in order to show the conflicting observations and interpretations of different authors and the necessity of undertaking further investigations to throw more light on the question, which the reports thus far reviewed do not make any way clearer. Mill's papers, on careful analysis do not give the impression that sufficiently thorough investigation has been made to exclude even such common etiological factors as syphilis and tuberculosis, not to mention other diseases.

Distribution of Filarial Infection in India

BY

S. SUNDAR RAO

Calcutta School of Tropical Medicine.

ALTHOUGH *Microfilaria Bancrofti* was discovered by Wucherer in Brazil in chylous urine in 1866 and by Lewis (1872) in Calcutta in the blood and the adult parasite (*Wuchereria Bancrofti*) by Bancroft in South Queensland in 1876, their significance and relation to filarial diseases have been clearly understood only in recent years. Our present knowledge of the subject is mainly due to the classical researches of Manson on the transmission and pathology of the disease.

Filarial infection is extremely prevalent in several parts of this country and causes considerable suffering, deformity and disablity, in some cases even death by acute inflammatory attacks. The fatal attacks are generally the result of a virulent streptococcal infection. Notwithstanding the importance of this infection, our knowledge of its distribution in India has hitherto been somewhat meagre. As the knowledge of distribution of filarial infection in India is likely to be of help to the medical practitioner, it is proposed to give in this paper the results of survey carried out by the writer during the last fifteen years.

The difficulties in making a filarial survey are many. Many of them such as the vastness of the country with its varying geographical and climatic conditions, large population and the illiteracy among them, differences in the customs and manners among the people in different areas are common to surveys of this nature. Besides these, there are a few difficulties which are peculiar to a filarial survey, the chief of them lies in the fact that the microfilariae appear in the peripheral circulation only at night. Blood samples have therefore to be taken generally at midnight. This restricts to a large extent the number of specimens that can be obtained for examination. In addition to this it should be pointed out that the parasite in the blood is seen only in the early stages of the infection and is generally absent in cases of filarial diseases owing to lymphatic obstruction. Again several other diseases such as dermatolysis, hypopituitarism, giant urticaria are often mistaken for filarial diseases.

Prior to 1927, a few studies in filarial distribution have been made in isolated endemic areas in India. Mention may be made of the work of Cruickshank and Wright in Cochin (1914), Roy

and Basu in Puri (1922) and Korke in some areas in Bihar and Orissa (1927). The first systematic attempt to study the distribution of filarial infection in India was made by Megaw and Gupta in 1927. These authors published a map* showing the distribution of the disease based on data collected from medical officers stationed at various parts of India. In the publication of this map the number of blood samples examined was meagre, and consequently the map was incomplete. Systematic work based on examination of a large number of blood samples from persons in endemic and non-endemic areas have been made by the author for a number of years. A number of visits have been made to various endemic areas and thick smears were taken at night from persons in these areas. A careful examination has also been made of the records about the incidence of filarial disease in these regions. In many cases the co-operation of jail authorities has been requisitioned and blood films from the convicts taken at midnight were obtained for examination. It is thus now possible to have a fairly accurate idea of the distribution of filarial infection in this country.

The distribution of the infection in the various provinces has been dealt with in the following pages :—

Bengal.—The province of Bengal extends from the Himalayas on the north to the Bay of Bengal on the south. It comprises of two distinct regions, the non-deltaic and the deltaic. This appears to be the most heavily infected province in India as the climatic conditions are very favourable for the transmission of the infection. The province has a heavy rainfall, the eastern districts having a much higher rainfall than the western. The results of filarial survey show that the districts of Midnapore, Howrah, Bankura, Burdwan, Birbhum and Murshidabad (West Bengal) have the highest microfilaria rate, ranging between 12 to 15 per cent. In the central districts of Dinajpore, Rangpur, Rajshahi, Malda and Bogra, the microfilaria rates were found to be between 6 and 10 per cent, whereas in the districts of East Bengal *viz.*, Dacca, Mymensingh, Pabna, Nadia, Jessore, Faridpur, Khulna, Barisal and Noakhali, the rates of infection were the lowest *i.e.* below 5 per cent. Hill districts of Darjeeling and Jalapaiguri in the north and Chittagong Hill tracts in the east are free from the infection. These figures show how in the hilly and submontane districts there is no filarial infection, while as we go towards the sea the infection increases. The incidence of filarial infection is less in

* A modification of Megaw and Gupta's map was published by Acton and Rao (1931.)

East Bengal than in the districts in West Bengal. This is explained as being due to the large system of rivers in East Bengal which drain the country and thus prevent water-logging.

Calcutta.—Filarial infection in this city is more or less constant *i.e.* below 10 percent. Wards lying on the eastern border of the city show heavier infection than the others, owing to the higher incidence of mosquitoes in them. It may be pointed out that the microfilaria rate is comparatively low (8 to 9 per cent) in this city. This figure would probably be still lower if it were not for the fact that a number of imported cases come to Calcutta for treatment and are included in our statistics. This low incidence in the city is due to the satisfactory drainage system and the good sanitary conditions which reduce the number of breeding places for mosquitoes. During the rainy season there are a few permanent breeding places in the city and with the onset of winter there is a large increase in *Culex fatigans*. As the temperature and humidity conditions during the winter months are not very favourable for the transmission of the infection, the microfilaria rate is kept low. On the other hand, owing to a large influx of filarial patients from different endemic areas in the neighbourhood the filarial disease rate for Calcutta is very much higher (6 per cent) than what may be expected from its low microfilaria-rate.

Assam.—In Assam, as in Bengal, the infection is present in most of the districts but its intensity is less than that in Bengal; while most of the districts in the hilly and submontane region are free, districts lying on the banks of the Brahmaputra show a fair amount of infection. It was thought at one time that the Brahmaputra valley was free from filarial infection but the present survey disproves that idea. Low-lying areas such as Sylhet, Tezpur and Jorhat on the banks of the Brahmaputra show heavier infection than the other districts in Assam. Towns like Dhubri and Srimangal did not show any infection. One case of filarial infection was noticed in Shillong. This was evidently an imported case as Shillong is 6000 feet high and may consequently be expected to be free from filarial infection.

Bihar and Orissa.—The endemic areas in Bihar and Orissa lie along the coastal districts of Orissa which are among the most heavily infected regions in India. In certain wards of Cuttack the infection rate reaches as high a figure as 25 to 34 per cent of the population. Puri also shows a similar high incidence. This abnormally high incidence of infection in these two towns is primarily due to the defective drainage system and the presence of numerous stagnant sullage pits. These combined with the high

temperature and humidity during most of the months in the year offer the most favourable conditions for the breeding of the mosquitoes and the transmission of the infection. In 1921, the writer carried out an intensive survey of the town of Cuttack and an interesting fact relating to the distribution of the infection in this town was revealed during the course of this work. The infection was very heavy in the most crowded parts of the town, whereas in the outskirts, with a scattered population, the corresponding figures were much less. This is in contrast to what we find generally in the infected cities or villages. This is explained by the fact that the incidence of mosquitoes is much heavier in the more thickly populated areas of the town than in the outskirts. In the cities or villages the mosquitoe incidence is generally heavier in the outlying areas than in the central parts.

This province may be divided into three regions *viz.* (1) the northern area comprising the districts of Bihar (2) Orissa and coastal tracts and (3) Santal Parganas.

Of these, Orissa and the coastal districts comprising Puri, Cuttack and Balasore form the heaviest endemic areas. Sambalpur which is situated inland about 300 miles from the sea shows comparatively low infection (2 per cent). The northern area (districts of Bihar) is comparatively less heavily infected than Orissa. The distribution of filarial infection in the district towns of Bihar is more or less uniform. The last region (Santal Parganas) comprises the hilly tracts of Ranchi, Hazaribagh, Manbhum and Chaibassa. Of these Ranchi and Chaibassa are free from the infection whereas Purulia (Manbhum District) shows a microfilaria rate of 7.3 per cent and Hazaribagh of 3 per cent. According to Korke (1930) filarial infection in Bihar and Orissa is highest in the sea-coast belt, high in the Gangetic plain (level 0-0250 ft) and lowest in the submontane arable areas. He is of opinion that areas rich in rice cultivation are the endemic centres (Korke 1930 a).

United Provinces.—Filarial infection is moderately heavy in the United Provinces especially the low-lying districts on the banks of the Ganges. The Himalayan and sub-Himalayan districts and the Western districts of the province are free from the infection. The infection tends to diminish as one proceeds from east towards Lucknow. The infection rate for the whole province is low. This is due to the fact that the humidity conditions are not favourable for the breeding of *Culex fatigans* and also to the fact that the period of transmission is confined to less than two months in the year owing to extremes of climatic conditions

Among the towns in this province, Allahabad shows the heaviest infection (7 per cent), next comes Gorakpur with a microfilaria rate of 4 per cent. Benares which has a large floating population shows only slight infection (less than 1 per cent). A number of towns such as Bareilly, Saharanpur, Derah Dun and Shajahanpur do not show any infection at all. According to Forman (1928) the districts most heavily infected in this province are :—Fyzabad, Gonda, Baraich, Basti, Gorakpur, Azamparh, Balia, Ghazipur, Benares and Mirzapur—all of which lie to the north and east of Allahabad.

The Punjab and Sindh.—This area is singularly free from filarial infection. Preliminary investigation carried out with material obtained from jail population in the Punjab and Sindh areas had revealed that infection was absent there. Even the districts lying on the banks of the Indus do not show any infection. In order to investigate the reasons for this absence, the districts of Muzaffargarh, Mianwali, Sargoda, Lahore and Karachi were visited in 1931 and samples of blood were obtained from jails, hospitals and the public. Statistics were collected from hospitals and examination of hospital, school and college papulations was carried out. Special study was given to climatic conditions, mosquito breeding and prevalence and population distribution. These investigations have shown that filarial infection is entirely absent in these areas in spite of the fact that the carrier mosquito—*Culex fatigans* is prevalent throughout. The absence of infection must therefore be attributed mainly to extremes of climatic conditions, scarcity of rain, and sparsity of population.

Tracts adjoining these provinces such as the North-West Frontier province, Kashmir and the states of Rajaputana, all form part of the non-endemic region. Indeed it may be said that all districts lying to the north and north-west of an imaginary line drawn from Karachi to Delhi are non-endemic.

Central Provinces.—This province is situated in the centre of the Peninsula and here the infection is very low. A number of towns have been surveyed here, and Nagpur shows the heaviest infection (5 per cent). We have on record a few patients, belonging to Raipur and Bilaspur which lie on the main lines of communication and adjoining Orissa, seeking advice for treatment of filarial infection. The rest of the districts in this province are free from the infection. A low rainfall, (average 35 inches annually) and consequently a low humidity is not favourable for mosquito breeding and transmission and hence the low rate of infection. Amraoti, Jubbulpore and Betul showed very slight infection (less than 1 per cent). Akola, Hoshangabad and Yeotmal showed no infection. The flat land around Nagpur forming part of the Godavary valley probably accounts for the larger infection in this place. Most of the non-endemic districts are on an elevated region with several ranges of hills running along them.

Bombay.—There are only a few isolated endemic areas in this presidency *e.g.* Thana, Surat and Ahmedabad : otherwise the province may be said to be free from filarial infection. Gujrat is a lowland region and is affected with filarial infection. Surat which lies in Southern Gujarat and is the wettest part is the most heavily infected, showing a microfilaria rate of 8 per cent. Central Gujrat which is drier shows practically no infection. Kathiawar and Cutch show moderate infection. In Baroda no case of microfilaria infection was found.

A survey of Goa, Daman and Diu showed that these areas are practically free from infection.

South India.—Filarial infection is comparatively heavy. The area may be divided into the following groups according to the incidence of infection in them. (1) The most heavily infected areas which comprise the native states of Travancore and Cochin and the districts of Malabar and South Canara. Here the rainfall is very heavy (above 100 inches). Temperature and humidity are very high practically throughout the year. The conditions are therefore most favourable for the transmission of infection. These are also the most heavily populated regions. A thorough survey of Travancore has recently been made by M. O. T. Iyengar (1932 and 1933). Although infection is very heavy in this State, certain areas, especially the Hill tracts, are practically free from infection.

The infection is particularly heavy in Trivandrum, the infection rate being 10 to 20 per cent. An interesting point, which may be observed in this connection, is the presence of two distinct species of filarial parasites in this State. In Trivandrum, the prevailing species is *Wuchereria bancrofti* whereas in North Travancore *Microfilaria malayi* (Brug) is found. It may be observed in this connection that the prevalence of the latter species in India has so far been recorded by Korke (1929) in Balasore area and by the writer (1936) in Patnagarh.

Cochin.—has been known to be very heavily infected from very early times. The place has the distinction of having given the name 'Cochin leg' which is mentioned by early writers as synonymous with elephantiasis of the leg. The first systematic

survey was carried out by Cruickshank and Wright in 1910. The present author has also surveyed this region subsequently and records a similar high rate (21 per cent). The low flat land about the town surrounded by large backwaters combined with the high rainfall, optimum temperature and high humidity constitute ideal conditions for the maintenance and spread of the infection. The incidence of filarial infection decreases as one goes towards the mainland. Thus, in Trichur, which is only 40 miles inland, no case of filarial infection could be found. That better drainage conditions conduce to effective checking of the infection is illustrated by the fact that in Ernakulam which is separated from Cochin by only the backwater, the infection rate falls to about 6 per cent.

All the big towns in the districts of Malabar and South Canara such as Calicut, Cannanore, and Mangalore show high infection.

Of the moderately infected areas which comprise the districts of Tanjore, Godavari, Krishna and Vizagapatam on the East Coast, Tanjore district is the most heavily infected. Nagapatam, Kumbakonam and Tanjore show an infection rate of over 10 precent. A house to house survey has been made by King, Pandit, Menon and Iyer (1929) in Saidapet. Infection rate was found to be 16 percent and all types of lesions are observed, elephantiasis, however, being the most common. In Vizagapatam, the infection is moderately heavy. But Waltair, which is adjoining Vizagapatam, is free from the infection as the place is situated on an elevated region.

Non-endemic areas or areas with low infection comprise the districts of Tinnevelly, Madura, Ramnad, Bellary and the Ceded districts. Even here large towns which lie along the lines of communication show some infection.

Burma.—Filarial infection is confined to regions lying along the Irrawady and the sea-coast in Burma. The climate of these regions is wet on account of heavy rainfall. Basein, Tharrawady, Prome, Meiktiala and Mandalay, which lie on the banks of the river Irrawady, show a microfilaria-rate of 2 per cent. The northern and eastern districts showed no infection, these are hilly areas and in spite of heavy rainfall no infection was found in them. Central Burma where the rainfall is low and the climate is very dry does not show any infection.

It is thus seen that filarial infection is more or less confined to the coastal regions and along the banks of important rivers. Bengal, Orissa, Travancore, Cochin and Malabar are the most heavily infected areas. All these areas are low flat countries, have

high rainfall and are water-logged for over a long period in the year. The temperature and humidity are both high for over six months in the year. Conditions are, therefore, very favourable for the breeding of mosquitoes and for the transmission of the infection. Among the important towns in these provinces the most heavily infected are Cuttack, Puri, Trivandrum, Cochin and Calicut. The moderately infected regions comprise the whole of the East Coast from Ganjam to Tinnevelly, United Provinces, Behar and certain areas in the Bombay Presidency such as Surat, Ahmedabad and Thana. Among the towns in these areas, Vizagapatam, Saidapet, Nagapatam, Tanjore, Allahabad, Gorakhpur, Bhagalpur, Darbhanga, Monghyr and Surat are heavily infected. Slightly endemic areas comprise the whole of the Deccan platean, Central Provinces, Assam, Bombay Presidency and certain districts such as Basein, Tharrawady in Burma. Non-endemic areas comprise Central Burma, Sindh, the Punjab, North-West Frontier Province, Kashmir, Central India and Rajaputana. All the areas lying north and north-west of an imaginary line drawn from Karachi to Delhi and all hilly tracts and places in elevated regions are free from the infection.

In this connection it should be remembered that the intensity of infection is not uniform even in the same endemic area. For instance, in Cuttack the microfilaria rate varied from zero in the European ward to 26 to 34 per cent in the crowded wards. Similarly in Calcutta, wards lying on the eastern boundary of the city Show heavier infection rate (15 to 20 per cent) than the central and southern wards. The factors which are responsible for such differences in the infection rate appear to be (1) optimum climatic conditions (2) number of breeding places for culex mosquitoes and (3) density of infected population. The influence of these factors in the variation of the infection rate has been discussed in detail by Acton and Rao (1930).

Laboratory experiments have shown that the optimum conditions of temperature and humidity for the development of the embryo in the mosquito are a range of temperature between 80° to 90° F and a humidity of over 60 per cent. Under the optimum conditions, the embryo developes in the mosquito in 6 to 7 days; when the conditions are not so favourable the embryos take a longer period to mature, in some cases the period extending over 3 weeks. Apart from the longer time taken for the metamorphosis, the number of the embryos which develop in the intermediary host also becomes correspondingly less when the conditions of temperature and humidity are not favourable. One may therefore

expect that the infection will be heavy in regions where the climatic conditions approximate the optimum laboratory conditions of temperature and humidity required for the metamorphosis of the embryo. Thus in Cuttack, for instance, where the temperature ranges from 80° to 90° F. and the humidity ranges from 70 to 20 per cent for over 7 months in the year, the infection rate is over 20 per cent.

References :—

1. *Wucherer, (1866) -Cit Fantham, Stephens and Theobold 'The Animal Parasites of Man' London, p. 390.*
2. *Lewis, T. (1872)—'On a Haematozoan in the Human Blood' Report of the Sanitary Commissioner to the Government of India.*
3. *Bancroft, J. (1876)—Lancet, 1878, Vol. 1, p. 464.*
4. *Cruickshank, J. A. and Wright, R. E. (1914)—Ind. Jl. Med. Res. 1, p. 741.*
5. *Roy, S. K. and Bose. S. C., (1922)—Ind. Med. Gaz. 57, p. 281.*
6. *Korke. V. T., (1927)—Ind. Jl. Med. Res. 16, p. 1023.*
7. *Megaw, J. W. D. and Gupta, J. C., (1927)—Ind. Med Gaz. 62, p. 299.*
8. *Acton, H. W. and Rao S. S,. (1931)—Ind. Med. Gaz. 66, p. 39.*
9. *Korke, V. T., (1930 a) (1930 b)—Ind. Jl. Med. Res. 18, pp. 3 and 13.*
10. *Forman, D. N., (1928)—Antiseptic 25, p. 649.*
11. *Iyengar. M. O. T., (1932 and 1933)—Ind. Jl. Med. Res. 20, pp. 671 and 921.*
12. *Korke, V. T., (1929)—Ibid 16, p. 1023.*
13. *Rao, S. S.. (1936)—Ibid 23, p. 871.*
14. *King. H. H.. Pandit. C. G., Menon, K. P. and Iyer, P. V. S., (1929)—Ibid 17. p. 406.*
15. *Acton, H. W., and Rao, S. S., (1930)—Ind. Med. Gaz. 65, p. 355.*

Filariasis

BY

CAPT. N. SESHADRINATHAN, M.B., B.S., D.T.M.,

Madras.

THE purpose of this paper is to set forth the salient recent advances in the knowledge of filarial disease due to infection by Filaria Bancrofti only. This disease is widespread in our country and its ravages are insidious and persistent. It results in unsightly swellings and frequent attacks of fever, which causes economic loss by disabling labour.

Filarial disease is more widespread than perhaps we are aware of. Complete survey in India has not yet been done. In the world at large the endemic areas are extensive in the sub-tropical and tropical regions. In India, the whole of West Coast from Konkan downwards, in the East Coast, the deltaic areas of the Cauvery, Negapatam, Cuddalore, Madras upwards to Orissa and Bihar. The lower stretches of rich cultivable areas along the navigable portions of the Ganges and the Brahmaputra are also filarially infected. In the areas along the Coast and in the Cauvery delta, a careful investigation is likely to show almost 90% of the population being affected in varying degrees of intensity.

Epidemiologically, the conditions favouring the abundant breeding of the mosquito, Culex fatigans, are found to be also favourable for the spread of filarial disease. From 500 feet to 1000 feet above the sea-level, low sub-soil water giving high humidity, high atmospheric temperature (85 to 90° F.), wells and ponds and open drains, all these facilitate the breeding and harbouring of Culex fatigans, and consequently the spread of filarial disease. In such areas it has been found that Culex fatigans and human beings both show a high degree of infection with Filaria Bancrofti.

Apparent localization of the disease in certain areas with relative freedom in the immediate neighbourhood has been noted. The explanation in such cases can be traced to the absence of certain conditions favouring mosquito breeding such as good protected water supply and good drainage. Such instances are Madras and Saidapet, Cochin and Ernakulam. In Madras the better water supply and sanitation is responsible for the low filarial rate. In Saidapet, the wells, the open drains and cesspools breed and harbour the mosquitoes and filarial infection is maintained and spread by them. In Cochin, the sanitation is poor,

the streets are very narrow, the houses are naturally ill-ventilated. and the water supply is un-protected consisting of wells and ponds; At Ernakulam there is better sanitation and water supply. No filarial survey can be complete without blood examination of the population for microfilaria. If this were done, a high rate of filarial infection can be discovered even in such apparently free areas.

It is generally observed that the poorer classes of people suffer most from this disease, as they do from other infectious diseases. Over-crowding, and dirty clothes give rise to better chances of biting for the mosquitoes.

The theory is still current that the infection may be water-borne. For this, the support is found in the prevalence of the disease among the washermen of Saidapet and the coir manufacturers of Travancore, whose occupation entails their legs being constantly wet. It is also supported by the fact that certain habits of the people make them use dirty water for ablutions. This habit is supposed to explain the high incidence of filarial disease of the external genitals. The idea is that the infective filaria escaping from dead mosquitoes into the water penetrate the moist skin and the perianal and scrotal regions during wading and ablutions. Those who uphold this theory are not perhaps aware that the disease is prevalent among a population using only purified tap water. It has not also been proved that the infective filaria are present in the well water or pond water used by the people for ablution. The washermen of Saidapet also suffer from leprosy to a larger extent than the rest of the population. Washermen have to keep large bundles of dirty clothing from various sources in their houses and have to handle them. Dirty clothing easily attracts mosquitoes. Thus the higher incidence of filarial disease and leprosy among these people can be explained. Experimental and statistical evidence has advanced far enough to concentrate our attention to the discovery of the missing links in the chain of the mosquito bite transmission theory. The transmission has been effected by mosquito bite in the case of dog filariasis.

Nothing new has been discovered with regard to adult Filaria Bancrofti within the last few years. Another variety of microfilaria has been discovered, *viz.*, mf. bancrofti (Brug 1927). Since then other workers have confirmed the discovery and the distinguishing points have been thoroughly described. The adult worm corresponding to this microfilaria has not yet been discovered. The claim put forward by some writers that mf. malayi is associated with the genital type of filariasis has not been substantiated.

The most common mosquito carrier of filariasis is culex fatigans. Of the other varieties of mosquitoes described as being responsible for filariasis, no new varieties have been recently added. The present list comprises, Aedes Variegatus, Aedes Togoi, Mansonoides and Anopheles rossi, A. Costalis and A. Algiers.

The course of development of the microfilaria in the mosquito as noted by recent research is a little different from what has been described before. The exhausted larvae have been described as leaving the stomach of the mosquito by piercing its walls. The present idea is that some larvae may escape by this route, but most larvae have been found to progress forward to the anterior part of the gut some hours after a feed and pierce the walls of the midgut to gain entrance to the midgut some hours after a feed. From thence the developed infective forms are found invariably going to the base of the proboscis after development in the thoracic muscles.

The habitat of the adult worms have been definitely proved to be the lymphatic channels and the lymphatic glands. Recently radiographic pictures and post-mortem findings have shown the presence of these worms in the superficial lymph channels and glands of the lower and upper limbs and the external genitalia and also some parts of the internal genital organs of the male *viz.*, the Spermatic cord and Tunica Albuginea. The female internal genital organs have, however, been found to be free. The only way possible for this invasion of the internal genital organs of the male only is probably the proximity of the internal genital organs to the external genitals.

In Fiji and several other places it has been found that the epitrochlear and subinguinal group of glands are the earliest to be affected by filariasis. This is as it should be, considering that the limbs are the most exposed to mosquito bite.

The causative factors that bring about the elephantoid condition are not quite clear yet. The general trend of evidence is towards a more or less mechanical obstruction theory. By the expression "more or less", it is meant here that the condition is not entirely due to mechanical obstruction by the worm, but a toxic factor initiates the lymph channels. That a toxin is excreted by the worms is evident from the fact that the intradermal inoculation of an extract of the dog filiarial worm is followed by a local allergic reaction in the filarial subject. It is also evident from the fact that around these worms a definite eosinophilic infiltration is noted. That eosinophilia is associated with helminthic toxin and allergic conditions is well known.

By experiments in dogs it has been found possible to produce artificial elephantiasis by the injection of sclerosing solution into the main lymphatic trunks—a strong support for the obstruction theory. Attacks of lymphangitis occur along the lymphatics in which the adult worms are present. As a result of repeated attacks of lymphangitis, irregular inflammatory masses of tissue project into the lumen of the lymphatic vessels. As a result of such projections, obstruction to the flow of lymph takes place, the degree of such obstruction depending upon the number of attacks of lymphangitis in and around the vessels. "Around dead and disintegrating worms the inflammatory reaction extends along the length of the worm so that the whole parasite is enclosed in a case or core of inflammatory tissue inside the affected lymphatic vessel". The dead worms gradually get calcified.

The role of bacteria in the causation of such lymphangitis is still a disputed question, the main findings tend to prove a non-bacterial early inflammation, though in the later stages pyogenic cocci have been definitely found to be responsible for abscess formation and chronic fibrotic changes. In the early stages of lymphangitis repeated attempts to obtain bacteria from inflammatory tissue have been unsuccessful, the nature of the inflammatory cells (*viz.*, eosinophilic and lymphoid) is against bacterial origin of the inflammation. The polynuclear phase observed during the early acute inflammatory stage is very transient.

Simple blockage of the lymphatic channel high up in its course results in dilation and true hypertrophy. In the case of the intra-abdominal lymph channels when rupture takes place chylous ascites and chyluria may result according to the site of rupture.

The changes in the tissues that bring about the elephantoid condition are as follows. In the early stages lymphatic stasis with escape of lymph into the tissue spaces takes place. Subsequent attacks result in greater number of dilated collateral lymph channels and escape and stasis of more lymph into the tissues. A lymphoid hyperplasis takes place in and around lymph channels. The exuded lymph becomes collagen. The rest of the changes are mainly confined to the skin over the affected area and is a later phenomenon. The skin becomes progressively thickened on account of soddening and chronic irritation due to lymph stasis, and supervening bacterial invasion of low virulence enough to produce mild erysipelatous inflammation without actual pus formation. The result is keratinization and hypertrophy of the papillae.

Clinical manifestations of filariasis usually begin in lymphatic glands of the arms and the legs, the epitrochlear and the subinguinal glands. This initial enlargement is due to the infective larvae getting lodged in these glands after entering through the skin of the arm and the leg. After entry the infective larvae develop into adult forms in the lymph channels and begin to discharge microfilaria into the circulation. How the microfilaria get into the blood from the lymph channels has not been thoroughly studied. The adult filaria have been found in such remote places like the lymphatic plexus round the spermatic cord and in the tunica albuginea of the testes where they cause funiculitis and hydrocele.

The subsequent stage in the filarial disease is a lymphangitis of the superficial lymphatics of the thigh and the leg and the upper arm. This may or may not be accompanied by fever. Sometimes severe fever sets in with hyper-pyrexia (104 or even 105° F.) preceding the attacks of lymphangitis. Repeated attacks of lymphangitis are followed by permanent unyielding swelling of the limbs. The causation of the fever still remains obscure. Elephantiasis is very common in the external genitals in the male and in rare cases of the female. Ten years and beyond is the age period in which filarial disease becomes manifest.

The final touches are given to the elephantoid disease, when owing to chronic neglect of skin hygiene and secondary invasion by bacteria a verrucose condition of skin results. The process takes years to progress. The disease may limit itself at any stage from mere enlargement of glands to the chronic verrucose skin depending upon the immunity response, dosage of infection initial and repeated, and the intensity of mosquito infestation. Secondary invasion with virulent pyogenic cocci may result in abscess formation around a dead or degenerating worm.

A much discussed problem in filariasis is the periodicity of the microfilaria in the blood and the explanations given for this phenomenon, still continue to be speculative in nature. Clayton Lane put forward the theory that the periodicity is due to a daily parturition of microfilaria by the adult females, followed by a daily destruction of the same number of microfilaria. Several experiments have been carried out in dogs and man to find out the fate of the microfilaria. Several observations have been made. Another theory also holds the field *viz.*, that the microfilaria migrate into the lung capillaries and other internal organs during the day and come out into the peripheral capillaries during the night owing to the reduced resistance in these during the sleeping hours. When the sleep is soundest at about midnight the

microfilaria are found in largest numbers in the peripheral capillaries. There is plenty of experimental and other evidence to support this theory. Reversal of sleeping habits has been followed by reversal of periodicity. The inoculation of blood containing microfilaria into the circulation of an uninfected individual showed the same periodicity as in naturally infected individuals. Yet another theory has been in existence, viz., that the microfilarial periodicity is coincident in time with the biting habits of the mosquito vector, an adjustment to enable the microfilaria to complete its life cycle in the mosquito. Certain observations support this theory. This theory is consistent with the absence of nocturnal periodicity in certain areas where the prevalent mosquito bites during the day.

The second theory has the greatest support at present, the third has a number of adherents. Clayton Lane proposes to hold on to his theory as long as the other theories have not been substantiated, even though there is very little experimental or observational evidence to support it No definite proof has been obtained for the daily parturition of such a large number of microfilaria, and there has been absolutely no evidence to prove the daily destruction of such a large number of microfilaria in the tissues of the host. It is computed that as many as four and a half million microfilaria are seen in the peripheral circulation at a time. Such a large number of microfilaria when destroyed everyday ought to cause an enormous phagocytosis to take place and also varying degrees of protein shock and consequent systemic reactions. There is no evidence for the existence of such phagocytosis or reaction. When microfilaria from an infected dog are introduced into the circulation of an uninfected dog they are found to migrate out of the blood into the lymphatics and various tissue spaces including the cerebrospinal fluid.

The diagnosis of filarial disease in an endemic area is not difficult. In the very early stage of lymphadenitis and lymphangitis the night blood in most cases will reveal microfilaria. It is cleaner to use a thick blood film, allow it to dry and stain as for malaria after washing out the haemoglobin. In the later stages, the characteristic fever with vigour is diagnostic. Here again a blood film will help by showing an eosinophilic increase. The fever is invariably followed by tenderness and enlargement of the superficial lymphatic glands of the limbs with mild or marked inflammation of the lymphatics which drain the glands. In the case of chronic swellings the previous history of repeated attacks of lymphangitis is enough to clinch a diagnosis.

For the differential diagnosis, it is better to remember the following conditions: phlegmasia alba dolens in parturient women, elephantiasis after operative removal of lymphatic glands for cancerous infiltration or otherwise, after traumatic injury to the main lymph channels, and a few other varieties including those after local cicatrisations due to chronic ulcerations.

An intradermal test has been devised with an extract of dog-filaria as antigen. A complement fixation test has been described with a similar antigen. These are at present of more academic interest. Adhesion phenomenon similar to the one for leptospira has been demonstrated.

The prognosis as regards life is very favourable, but the disease progresses insiduously, incapacitates the individual, and interferes with the general efficiency of labour in plantations and factories on account of repeated absence due to the periodical fevers and physical deformity.

The treatment of this disease is very unsatisfactory. The only remedy lies in prophylactic measures undertaken by authorities to reduce the breeding of mosquitoes by efficient water-supply and drainage. Many drugs have been tried without success. Fouadin 2 to 5 c.c. injected intravenously every day for 5 to 14 days is said to have produced a reduction of microfilaria in the dog, Sulfarsenol injected locally under the tissues at the site of a 'local spot' in the limb where the adult worm is said to be lodged, has been described as successful. Arsenical preparations like Neosalvarsan and sulfarsenol have continued to be in use in this country with apparent success in reducing the periodicity of the febrile attacks. Recently injection of animal charcoal has been reported favourably from Indo-China as aborting the filarial fever. The Rontgen Ray treatment for chyluria and filarial lymphangitis has been favourably reported. For details, the reader is referred to the Transactions of the Royal Society of Tropical Medicine and Hygiene, 1934, January 31, Vol. 27—No. 4. pp. 385—398.

An attempt has been made in this paper to bring out without bias, the trend of opinion regarding the various problems connected with filarial disease due to filaria bancrofti. The sources of inspiration have been the excellent reviews in the Tropical Diseases Bulletin of the Bureau of Hygiene and Tropical Diseases, London, The Transactions of the Royal Society of Tropical Disease, London, and the recently published 'The Maharaja of

Travancore, Curzon's Lectures', University of Madras—' Problems of Filariasis ' by Dr. Bhaskara Menon, with a foreword by Major General Sir Frank Powell Connor, KT. D.S.O., K.H.S., F.R.C.S., I.M.S., 1935. (Printed by Messrs. Thompson & Co. Ltd., Madras. Cost Re. 1/-).

Filariasis

BY

V. VENKATASUBRAMANIAN, L.M. & S.,

Villupuram.

"THE health of the people is really the foundation upon which all their happiness and all their powers as a state depend " is a trite saying attributed to Disraeli. Filariasis is one of those fell diseases whose ravages are not properly assessed and it is strange to note the step-motherly attitude of the health authorities in combating this very common affection. Active measures must be taken to prevent this disease and promote the general health of the people. The need for taking well considered steps in these directions is very great in India, but the pace of progress unfortunately remains that of a snail.

" Filariasis may be compared to an evil genius, whose stakes are human lives and whose dice are heavily loaded. Surely, we must do something to destroy this genius, or at least to unload the dice. The incidence of filarial disease is at present incalculable. Its ravages have been traced throughout vast areas of the tropical and sub-tropical world, parts of southern Europe, India, China, the Pacific Islands, Australia, the West Indies, and many other tropical lands are known to be infected. Clinically one soon discovers that it is broader and longer than its allotted span, or, to change the metaphor, that it often calls in accomplices, more malevolent than itself, to work its wicked will. " The Streptococcus is one of the worst of these ", thus wrote Sir Frank Connor, sometime Surgeon General with the Government of Madras, while he was the Professor of Surgery at the Calcutta Medical College. And so the civic consciousness of the public must be awakened and the public must be educated to prevent the huge economic waste caused by this disease. In recent years Cancer, Tuberculosis, Malaria, Venereal Diseases, Leprosy, Maternity and Child Welfare etc. have all received a good deal of

attention not merely from the health authorities, but also from the lay public and this fell disease remains uncared-for.

Dr. Tirumurthy, in his address to the Graduates of the Andhra University, deplored the lack of proper methods of propaganda for awakening the health consciousness among the masses. Some people are of opinion that ancient Hindu customs stand as a stumbling block to sanitary progress in India, and once Col. Megaw wrote that progress in preventive medicine was very slow in India on account of "the new wine of scientific sanitation having been poured into old bottles of antiquated customs." But it is not so and we can do a great deal to alleviate the ravages of this tropical disease by organised mass education regarding the mode of transmission of this disease, improvement of general sanitation, anti-mosquito measures, isolation of infected persons and attention to general health. These will greatly reduce the incidence of filariasis, if not eradicate it altogether.

Filaria Bancrofti, most pathogenic of man, is commonly found in India. Its life cycle is completed in two sets of hosts—man and certain species of mosquitoes, chiefly Culex Fatigans. Manson has conclusively proved that Culex spreads the disease from man to man. The mosquito sucks embryos out of infected human blood at night, and these embryos pass on to the thoracic muscle of the mosquito and there undergo metamorphosis ; as immature filaria, they travel through the prothorax and reach the proboscis, from whence they are inoculated into the blood stream of man. From blood, these pass on to the superficial lymphatics and through the deep lymphatics, they ultimately reach the abdominal lymphatics. Here they attain maturity and the female worm after impregnation begins to lay plenty of eggs. These eggs get into the general circulation. These worms live only in lymph plasma, and in no other body fluid can they propagate their species. The immature filaria are able to get into the abdominal lymhatics only when they are not obstructed in their passage through various lymph channels. When there is no obstruction to the passage of filaria, and when there is no secondary focus of infection in the body, there are usually no symptoms of filarial fever or of any kind of surgical filarial affection.

Filaria Bancrofti are slender catgut-like cylindrical worms measuring about 4 inches in length with one end rounded off and the other end tapering. The tail of the male is sharply incurvated. The female is longer and larger than the male. Practically, the whole body of the female worm is occupied by two uterine tubes filled with ova in various stages of development. Sometimes, both

male and female worms are coiled together and found like balls in cyst-like dilatations of lymphatics. They are rarely found loosely in the Thoracic Duct and some large lymphatics. The female worm gives birth to a large number of embryos, and many of them disappear in some unknown way, or else the blood will contain them in very large numbers. These embryos are not pathogenic, but the finding of these in the peripheral blood is of very great importance in arriving at a correct diagnosis of the malady. The breadth of an embryo is the same as that of a R.B.C., and the embryo is enclosed in a loose sheath formed by the stretched out egg capsule. During day time these embryos get into the blood vessels of the thorax, mainly vessels of the lungs. After dusk, specially between 8 p. m. and 2 a. m., these get into the peripheral blood stream. Should a victim of the parasite alter his usual habits and begins to sleep during the day, the filarial periodicity is reversed and the embryos appear in the peripheral blood stream during the day time. In fresh specimens of peripheral blood, the microfilaria will be seen moving very actively among the blood cells.

Serious pathological conditions result on account of obstruction caused in the lymphatics by both adult worms and embryos. Secondary infection by staphylo or streptococcus worsens the condition. The symptoms vary according to the obstruction being complete or partial. the site of obstruction, the formation of collateral circulation, and the superimposition of secondary infection. Thus, hydrocele results from obstruction near Juxta-aortic glands; when the iliac and the inguinal groups of glands are involved elephantiasis of the scrotum and elephantoid œdema of the legs occur. Most of these resultant affections must be dealt with only by the surgeon's knife and the cure is rarely satisfactory.

Blood examination of an affected individual reveals eosinophilia. This, in addition to the occurrence of temperature clearly indicates that some sort of toxin is circulating in the system. Probably toxin is produced at the time of the laying of the embryos. Acton and Sunder Rao have tried to prove it by analogy and indirect evidence. The toxin produces chronic irritation which ultimately results in hypertrophy of the reticuloendothelial tissue of the lymph glands where an adult or an immature worm may be arrested in its progress. Here the worm eventually dies and is converted into fibrous tissue. The extent of chronic irritation and the severity of the granulation and hypertrophy of the gland, is directly proportional to the amount of toxin, to the

continuity of infection, and the duration of exposure to such an infection. Acton and Sunder Rao, who have published learned articles on "Kataphylaxia" and the importance of secondary infection in the causation of filarial lymphangitis, are of opinion that the eradication of secondary sepsis will lead to success in treatment. For a general practitioner, specially in a mofussil centre, it is well nigh impossible to find out the site of election of the septic focus and then make a bacteriological examination for the secondary organism ; the septic focus may be from septic tonsils, P.A., intestinal infection etc., Clinical manifestations are of a varied nature and depend on the site of infection and the species of coccus involved. When the lymph channels of the extremities which are already devitalised by filarial toxins are invaded by the staphylo or streptococcus, acute lymphangitis results. A number of attacks occurring one after another completely block the drainage of lymph from the extremities and the typical elephantoid skin results. There is a periodicity in filarial fever and no one has found out definitely the cause for the same.

In medicine, we have diagnosis which is a matter of faith; prognosis which is a question of hope ; and treatment which is only too often an affair of charity. By the use of our innate intelligence we can easily diagnose this disease. Generally there is a history of the patient having stayed in an endemic or hyper-endemic area, with a previous history of bouts of fever attended by adenitis of inguinal glands, or a history of recurrent lymphangitis. An examination of peripheral blood taken during the early part of the night aids the diagnosis. Very rarely a case is mistaken for malaria. Here, prognosis is really a question of hope. Though this is not a fatal disease, complete cure is very rare and we must hope for the best with robust optimism. Treatment is an affair of charity in this malady. In some cases, even doctors resort to quackery and magic charms to get a complete cure from this fell disease.

There is no drug which can reach and kill the adult filariae in the deep lymphatics of the abdomen; hence we have no specific for this. Attendance to the general health, eradication of secondary sepsis and sometimes change of climate help the recovery of some patients. Avoidance of intestinal stasis adds to the comfort of the patient. Triple sulphate mixture is commonly given during the periodical attacks of fever. This has great resemblance to the treatment of old, advocated in Ayurvedic text books, *viz.*, giving of purgatives and bitter principles. At present, knife is indicated in many an affection caused by filariasis and as the cure is neither

permanent nor satisfactory, there is an attitude of despair and despondency. We must have a more optimistic outlook and hope to find a specific for this fell disease at no distant date. At present, the drugs tried and acclaimed as the specific are many. Various preparations of arsenic and antimony have been tried and none has given a satisfactory result. Nonspecific protein shock therapy and varieties of mixed vaccines are also being tried by eminent doctors and so far no remedy has given a uniformly encouraging result. We must hope and pray for the speedy discovery of a specific. In the meanwhile civic and sanitary consciousness of the public must be thoroughly awakened.

Filariasis

BY

DR. I. DAVID, B.A., L.R.C.P., L.R.C.S., (EDIN.), L.M., (DUB.),

Colombo.

FILARIA is the chief extra-intestinal somatic parasite in man. It is widely distributed in the tropics and sub-tropics. There are several varieties of filaria of which F. Bancrofti and F. Malayi are the ones found in Ceylon. About 25 years ago, Bahr made a survey of a few villages in Ceylon and found that 26% of the villagers examined were infected. My own experience is that a larger number of the people of Ceylon are infected although many of them are not aware of it.

In 1863 Lewis in Calcutta and Damarquay in Brazil discovered the embryos in the blood of man. In 1876 Bancroft discovered the adult worm in the lymphatics. In 1876 Manson proved that Culex fatigans was the transmitter. Since then many other species of mosquitoes both culicines and anophelines have been found to act as intermediate hosts. The adult *filaria nocturna* (Manson) is found in the lymphatics as thin as hair, white or brown in colour, male measuring 30—40 mm. and the female 70—80 mm. It has been shown by Low and James that the embryo reaches the base of the proboscis and escapes by the rupture of the Dutten's membrane which is the thinnest portion of the proboscis. This has been proved experimentally by Stitt, Lichtenstein, de Langden, and Bahr. After escape the larva crawls and enters the skin in the same way as a hook worm larva enters the skin. But some are still of opinion that there must be more than one mode of entry into the host. Infected mosquitoes die in water used for drinking and bathing purposes and the parasites escape into the water and are believed to be conveyed into the human stomach through drinking water in the same way as D. medinensis (guinea-worm) enters the stomach.

Others think that it enters the skin of a person in the act of bathing and for this reason, cases of elephantiasis, varices and glands are more common in areas where there are tanks and back-waters and that with the introduction of pipe water, the disease gradually disappears. Manson's original idea was also similar to this. The facts that cases of elephantiasis of legs and scrotum were more common in Madras and other South Indian towns before the introduction of pipe water and that varices and chyluria were the chief manifestations in certain other areas like Allahabad suggest different routes of entry for the embryo. Another theory that the parasite is injected or inoculated as in malaria cannot hold water because the filarial embryo lies at the base of the proboscis at the level of the Dutten's membrane and is never found in the salivary glands. In malaria the sporozoites are lodged in the salivary glands. In whatever way the embryo enters the host the adults are found in the lymphatics where they are found rolled up together. When fertilised the female produces eggs which develop into embryos which again enter the blood probably through the thoracic duct and appear in the peripheral blood at night; or during day if the patient is a day-sleeper. In Filaria Loa they are present by day only. I remember a fellow passenger travelling with me in whose anterior chamber there was a tiny worm playing about, probably a Loa as the passenger was from Africa. In F. perstans there is no periodicity. In a case infected with F. nocturna, Manson found the embryos lodged in the lungs and thoracic vessels, post mortem. Periodicity is said to be due to the habits of both the mosquito and man, *viz.*, the time the mosquito bites and the time the host sleeps. The life history of micro-filaria in the body of the mosquito is interesting. The embryo moving freely within its sheath while the sheath itself is but little displaced enters the stomach and then quits its sheath, becomes actively motile, reaches the thoracic muscles of the mosquito and there undergoes its metamorphosis. It attains its full development in about two weeks. From there it migrates to the proboscis wherefrom it is transferred to the lymphatics of man as already described.

Pathology.—M. F. are considered harmless as they are too small to cause any obstruction and the host in the majority of cases is not aware of their presence in his blood. Elephantiasis,

chyluria, and other lesions are said to be the result of blockage leading to back pressure caused by the adult worm. But I am certain that the embryos too by their presence as parasites and foreign bodies circulating in the host's blood give rise to symptoms which are generally overlooked or misread—symptoms such as headache, muscular and joint pains, urticaria, palpitation, dyspnoea, fever, anaphylaxis etc., which I deal with later. Many such cases are generally mistaken for malaria, rheumatism, asthma, erysipelas and skin diseases.

The lesions which are met with in filariasis are of two kinds:—

(1) Those which are due to the parasite or its toxins; and

(2) Those which are due to secondary infection. In most cases both are at work at the same time. Inflammatory reactions, obstruction, and back pressure, periodic fever, mechanical and toxic irritation,'kataphylaxia' resulting in a break down in local resistance may be caused by both. These lesions may be classified under two heads, (1) Varices, (2) Elephantiasis. In varices, lymphatics in the kidneys, bladder, tunica vaginalis and other places are dilated and filled with chyle which sometimes rupture and precipitate an attack of chyluria, chylocele, and chylous effusions into the pleura or peritoneum. When the thoracic duct is blocked its contents return to blood by a reverse current causing dilatation of the lymphatic vessels of the abdominal wall, pelvis, groin, and scrotum.

In elephantiasis blockage leads to solid oedema. But it may not always lead to it owing to collateral circulation. As I have already pointed out not only blockage but other disturbing factors are at work—a combination of causes associated with foreign body, irritation, release of toxins, sepsis and inflammatory processes, and a number of other conditions not well understood.

Diagnosis.—Is simple in a straightforward case. But in addition to the familiar symptoms, history of residence in tropics and subtropics particularly endemic to this disease, presence of m.f. in the blood, aided by dermal or complement fixation tests will clinch the diagnosis. In order to examine m.f. under microscope a thick long film prepared from blood taken, in the case of f. nocturna, after sunset, and in the case of f. diurna, during the day, is necessary. After drying the film it is stained with Loffler's methylene blue 1 in 29 of water when the filaria will be stained

blue. In fresh blood the parasite will be seen actively moving. Cases from endemic areas with one or more of the following signs and symptoms should be always examined for filaria *viz.*, anaemia, periodic fever, haematuria, varices, enlarged glands, varicocele, hydrocele, funiculitis, lymphangitis, phlebitis, urticaria, eczema and erysipelas.

Preventive Treatment is every thing in this as there is no cure according to the highest authorities. The following measures are recommended:—education of the public and the creation of 'a mosquito conscience,' segregation under nets or in mosquito-proof quarters all m.f. carriers during the hours of infectivity, destruction of breeding places of filarial mosquitoes and their larvae. In Ceylon, Mansonian mosquito requires a waterplant called "Pistia Stratiotes" known to the villagers as "*Dyaparandel*" or "*Kondaipaasi*" for its propagation. Eggs are laid on the under-surface of its leaves, and the larvae and pupae live with their respiratory syphons or "trumpets" attached to the hairy roots of the plants through which they breathe, remaining under water. Hence surface oiling in order to destroy them is useless. Therefore "Pistia" must be proscribed in all anti-mosquito ordinances.

Treatment is generallay either surgical or palliative which need not be described here. Among drugs antimony and arsenic preparations are useful, and are believed to inhibit the parasite and improve the patient's general health. A case of chyluria treated with success with salvarsan is reported in the Medical Record (11, March, 1911) by Pilcher. Result of treatment will chiefly depend on whether the worm is alive or not and the infection is toxic or septic.

In my practice of over 25 years I have been freely but, of course carefully, using salvarsan in the treatment of various diseases like malaria, filaria, dracontiasis (guinea-worm infection) and rat-bite fever from 1912. I therefore give below short reports of a few cases treated successfully with salvarsan and neo-salvarsan.

Case 1.—In 1912 I was called one night to see a Sinhalese young man aged 25, suffering from haematuria, sudden and profuse. I called, in consultation, the senior surgeon of the General Hospital, who diagnosed the case as one of vesical papilloma. Next morning the urine under the microscope contained m.f. I gave at once salvarsan .6 gm. intravenously with the result that the urine was clear by evening and both the urine and the blood were free from m.f. when examined on the following day. For over three years afterwards, he was apparently all right. But in 1915 he was suffering from what appeared to be giant urticaria,

For over a fortnight he was under the care of a skin specialist without benefit. When he came to me I remembered his previous history. On examining his blood and urine, his blood and not his urine, contained m.f. As before, I injected him with N. S. .9 gm. Finding no improvement and as the patient was suffering much, I repeated the injections every ten days, reducing the dosage when indicated. He had in all seven doses. Since then he has been enjoying good health.

Case 2.—Younger brother of case No. 1, aged 23. In 1913, he consulted me for attacks of fever supposed to be malaria. As there was no M. P. in his blood his night blood was examined and found to contain M. F. His inguinal glands, cord and testicles were enlarged, inflamed and painful. He was given two injections and when his fever and other manifestations disappeared he stopped treatment. In 1930 he consulted me again for what he thought was an attack of gonorrhoea which on careful examination proved to be really an attack of chyluria. This time I treated him with injections of antimony preparations and found it did not do any good. I then gave him N. S. .9 gm. once only, when, the urine was clear in about two days. When, after a month, he got another attack of chyluria he started taking Ayurvedic treatment. When I met him two years ago he said he was not better and that he wished to put himself again under my treatment, but has not come so far. In this case attacks of fever, lymphadenitis, orchitis etc., never returned after the injections although chyluria did.

Case 3.—A Dutch Burgher, male, aged 35, consulted me for fever in 1923 and the treatment was for 'malaria!' He again came to me with an attack of chyluria in 1933. I put him on injections of N. S. at ten days' interval. Although his general health improved, chyluria continued for nearly 3 months when after the ninth injection urine became clear and is continuing to be so. M.F. which was present in urine at the commencement is now absent. No relapse so far. In this connection, I may mention the fact that the patient had also a goitre about the size of an orange which I treated, as I have been treating for some years with success, with injections of acid carbolic in 15 minim doses weekly or fortnightly well into the substance of the gland but not all in one place. The goitre is now not bigger than a small marble. Some of the cases of goitre were early cases of ophthalmic goitre. I do hope that some of your great surgeons will condescend to give this treatment a fair trial and report the results in your journal.

Case 4.—Also a Dutch Burgher, male, aged 30, was for some years, suffering from sudden attacks of pain in the lower abdomen. During one of these attacks he enterered the General Hospital for an operation. While under observation, his pain disappeared and the surgeon discharged him. One night on 12–8–36 I was sent for to see him. As I found M. F. in his blood I gave him N. S injections three in all. He has not had a relapse so far.

Case 5.—A young Indian, aged 30, consulted me in 1930 for an attack of funiculitis. During the past five years according to his statement he had several attacks. As his father was under my treatment for elephantoid legs, I examined this boy's blood and found microfilaria in it. He was given N. S. injections three in number; since then he has not had any attack.

Case 6.—An Indian lady aged 38, married, mother of five children, was suffering, for some months since June '36, from attacks of paroxysmal pain and constriction in her chest coming on suddenly at night. Examination during one of these attacks revealed nothing abnormal except that she was weak, anaemic and dyspeptic. Blood examination showed haemoglobin, colour index, and red cells just below normal and eosinophilia 25% micro-filaria found after repeated examinations.

She was residing in Galle which is endemic for 'galle leg' (elephantiasis). Gave her N. S. .6 gm. 6 gm. with immediate benefit on 28–10–36. Refused more injections. She has been free from attacks so far. Cases of asthma occasionally improve under arsenical treatment, but this was neither a case of asthma nor of hysteria. This line of treatment of mine may not give the same good results in the hands of other medical men for various reasons. Despite this fact, I feel it my duty to draw the attention of the profession to a new avenue to be explored: I admit that the number of cases reported is small indeed.

References:—

1. *Tropical Diseases by Manson-Bahr.*
2. " *Stitt.*
3. " *Lichtenstein and de Langden.*
4. " *Chopra.*
5. " *Castellani and Chalmers.*

Epidemic Dropsy

BY

BREVET—COLONEL R. N. CHOPRA, C.I.E., K.H.P., M.A., M.D., (CANTAB)., M.R.C.P. (LOND) I.M.S.,
Director, School of Tropical Medicine, Calcutta,

AND

DR. R. N. CHAUDHURI, M.B.,
Assistant Professor of Tropical Medicine, School of Tropical Medicine, Calcutta.

CHEVERS, as long ago as 1826, drew attention to a form of disease associated with malnutrition and anasarca occurring in epidemic form among the Hindus whose diet was very poor. In 1876—'77 there was a great famine in Southern India during which, a disease, at that time called 'beri-beri' made its appearance. Since then, several outbreaks of dropsy in epidemic forms, have appeared particularly in Bengal, Assam, Bihar, Orissa and the adjoining portions of the United Provinces. Formerly it was generally confined to the urban areas but in recent years many villages have been ravaged by epidemic dropsy as much as the towns. It may occur in epidemic, endemic and sporadic forms in a locality. While our knowledge of the disease has considerably increased, the exact causation, still lies in obscurity.

Various theories have been propounded from time to time. The following are the important ones :—

(1) That it is nothing more than beri-beri. This view is no longer held. Experimental production of beri-beri by feeding men with polished rice proves that it is caused by avitaminosis, while the same cannot be said about epidemic dropsy nor can it be cured by the administration of food, rich in vitamin B, and rice polishings. The seat of lesion in epidemic dropsy lies principally in the vascular system without any degenerative changes in the nerves which characterise the other condition. Cutaneous manifestations, abortions and glaucoma are not met with in beri-beri. Epidemic dropsy is hardly ever seen in children while infantile beri-beri is common. These considerations should not lead to any further confusion in distinguishing the two fundamentally different diseases.

(2) That it is due to consumption of infected rice. Rice

stored under unhygienic conditions is liable to be infected with gram-positive spore-forming bacilli giving rise to degeneration of starch cells and liberation of a water soluble base with histamine fraction. These organisms can multiply in the intestines; hence there is a remarkable excess of gram positive bacilli in films made from the culture of stools of epidemic dropsy cases. Infected rice can be recognised by the presence of variable number of grains showing central opacity which is more easily recognised if seen through water. Such grains often become fragile and may at times be crushed with fingers.

Objections have been raised against rice being the sole cause of the disease. In rural areas people using unpolished rice, which has not been stored, have been known to be affected. Rice is taken generally after throwing away the rice water. Most of water-soluble toxin is liable to be discarded along with the rice water. Instances have been noted showing that individuals not using rice, have contracted the disease. Attempts to reproduce the disease with suspected rice has hitherto failed.

(3) That it is due to the use of adulterated mustard oil. Mustard oil has been incriminated chiefly because the Europeans and the Marwaris who do not use it are not affected. Adulterants used for the oil might be in the form of seeds with fungs growth or mixture with cheaper oils or mixture with synthetic substances added to give a pungent smell and taste preferred by the consumer. In Fiji (1927) Indians and Fijians consumed the same rice but only the former who used mustard oil got the disease. On the other hand, an outbreak in a Burma Jail was reported where no mustard oil was used. Adulteration goes on unchecked throughout the year, but epidemic dropsy usually breaks out periodically with seasonal variations. Persons avoiding mustard oil as a precautionary measure have been known to contract the disease. Volunteers and animals fed with mustard oil (cooked and uncooked) have not shown any evidence of it.

These facts show that vitamine deficiency has got nothing to do in the causation of this disease. Epidemic dropsy breaks out

as a rule in the races who use rice as the staple diet and mustard oil for cooking. It has been found that very poor people who husk their rice in small quantities for daily consumption and cannot afford to buy mustard oil for cooking commonly escape the disease. This shows intimate relation of the disease with these two articles. It is however not clear how it is caused.

Thus it is a disease that seems to lend itself to theorizing on inadequate grounds. The medical literature in this country contains innumerable papers in which one or two cases are quoted proving or disproving in the author's opinions, some particular theory. Single instances can neither prove nor upset any theory. For example, the rice toxin theory is not upset by the fact that all members of one family that have not taken rice for some time suffer from clinical symptoms indistinguishable from those of epidemic dropsy. Rice may be the best pabulum for the production of the specific toxin, and yet there may still be other foodstuffs in which it can occur. On the other hand it cannot be assumed just because all the victims of an outbreak are rice eaters that rice is the cause of the disease.

The concensus of opinion, at present is in favour of infection theory. The infecting organisms may be the sporeformers as commonly found in the infected rice and the stools of majority of epidemic dropsy cases. Or it is quite possible that the disease is due to a specific organism yet unknown to us. Researches in this line are being carried on in the school of Tropical Medicine. Every case in the hospital is investigated from clinical, bacteriological and biological points of view. Embryonic tissues are being cultured in the plasma of epidemic dropsy patients with a view to find out whether it is of the nature of virus infection.

An epidemic generally breaks out after the rainy season. The monthly admission rate in the Carmichael Hospital for Tropical Diseases for a period of 12 years, shows a sharp rise from June to a maximum in August (the period of rainy season); then there is a rapid fall up to October and more gradually through the winter months to almost none in April.

Epidemic dropsy usually occurs in the prime of life, extremes of age being rarely affected. Both sexes are equally affected. The disease is peculiarly prevalent among the Bengalis and the persons on a Bengal diet (rice and mustard oil). An analysis of 131 cases treated in the Carmichael Hospital showed that 94 were Bengalis, 21 Anglo-Indians domiciled in Bengal and 16 from other provinces. The upper and middle classes of people are the common victims while the poor labouring classes often escape.

Pathology.—Essential pathological changes consist of widespread dilatation of capillaries in different parts of the body. For instance, in the skin capillaries are dilated particularly in the subcutaneous fatty tissue. They are engorged, walls are stretched, their permeability is increased; and fluid is exuded giving rise to oedema. When the very superficial vessels are affected, an erythematous rash results. The phenomenon may be associated with perivascular infiltration with endothelial cells giving rise to formation of new capillaries which may grow as angiomatous nodules, called sarcoids. In the heart, the capillaries between the muscle fibres are similarly dilated giving rise to cardiac inefficiency. Vascular engorgement likewise takes place in other tissues, *viz.*, lungs, liver, intestines, uterus etc. The eyes show normal corneoscleral junction, the ciliary processes show enormously dilated capillaries. The capillaries between the sclera and choroid are dilated and engorged, but there is no evidence of any inflammatory process. The increase of vascularity and functional activity of the ciliary processes results in an over-production of the aqueous humour which cannot be drained away sufficiently rapidly thus producing increased intra-ocular tension and glaucoma.

Symptoms.—Incubation period is not definitely known, possibly a few days only. The onset may be sudden or insidious. The causative agent (bacteria or toxin) frequently gives rise to initial gastro-intestinal irritation. There may be sudden attack of diarrhoea with or without nausea or vomiting. The patient usually attributes it to some fault in diet, but is surprised to find within a short time swelling of the leg when the condition is actually diagnosed. The severity of diarrhoea is variable; it may be mild or so severe as to simulate cholera. The stools may contain mucus or blood or both resembling dysentery.

Oedema is usually observed first over the skin bone. In the majority of cases it is confined to below the knees, but the thigh, lower part of back and hands may be affected; the trunk, neck and face are rarely involved. Oedema increases towards the evening. There may be collection of fluid in the serous cavities.

Cutaneous manifestations are remarkable features of epidemic dropsy. An erythematous rash over the legs and thighs commonly occurs but it may be generalised all over the body. Sometimes it occurs in small patches only and a peculiar mottling of the skin on the inner aspects of the thighs is often seen.

Hyper-pigmentation of the skin of certain parts of the body namely the face, hands and feet may occur. Two types of pigmentation have been observed; a generalised form in which the

face, the neck and the limbs turn uniformly dark, and a patchy form, the pigmentation being most marked on the forehead and the cheek bones, simulating kala-azar pigmentation.

Sarcoids appear in certain cases of epidemic dropsy : their number is variable and distribution on the body is most irregular. They are not confined to the skin, but may appear on mucous surface such as that of gums, cheeks, tongue and nose. The size of these growths varies from a pinhead to a walnut. A sarcoid begins as a tiny red papule which gradually increases in size and after a variable period begins to disappear. Scales are often formed on the surface during this process and if the scales are rubbed off the bright red sarcoid becomes visible again. This process goes on till the whole sarcoid is dried up leaving a pigmented area. Large sarcoids are prone to become pedunculated and infected with secondary organisms.

Many patients suffer from fever of a mild remittent or intermittent type, especially in the acute stage. Rarely the temperature may be high, but it is never associated with rigors or sweating. In a series of 131 patients treated in the Carmichael Hospital of Tropical Diseases, 94 had fever during the course of the disease, while 37 were absolutely afebrile Anorexia, deep-seated pains, itching and burning sensations, are often present.

Cardiac involvement is the rule in epidemic dropsy but severity varies. Palpitation and breathlessness on exertion are very common symptoms. Clinically, the heart may be enlarged and systolic bruits heard. Tachycardia out of proportion to the degree of pyrexia is a constant feature. Cardiac affection, is usually of three forms :—

(1) Acute cardiac failure is present from the very beginning and rapidly progresses so that death may occur in a few days. The clinical picture is that of an acute heart failure.

(2) Subacute or chronic. Thess cases present usually right heart failure with slight cyanosis, jugular distension and general venous congestion.

(3) *Forms frustes.*—In these the heart escapes or is only very slightly affected.

Electrocardiographic changes—Trachycardia of sinus origin is the commonest feature in epidemic dropsy and is usually associated with shortening of T. P. interval. An interesting finding not infrequently seen is an abnormally short P.R. interval (0.1 second only). This abnormally short P. R. interval is not dependent on

the rate of the heart as it has been found associated with heart rate of 70 as well as of 140. Nor there is any evidence of nodal rhythm in which P. R. is shortened. The rhythm has been found to be regular in the majority of cases. Extrasystoles, sometimes occur indicating increased excitability of parts of the heart, other than the sino-auricular node. Auricular activity has been found normal in most cases. Ventricular activity, as judged from the height and contour of Q. R. S., has been found to be increased in 30 per cent of cases pointing to an increased physiological hyper-activity. In a series of 50 cases, one showed auricular fibrillation and two coronary T. waves. Abnormal T. waves were noticed in a number of cases. These facts indicate that organic changes, possibly of the nature of myocardial degeneration, may be produced in the heart by epidemic dropsy.

The blood pressure is variable : sometimes, it is unusually raised especially in those cases who are constipated. The liver is frequently enlarged and tender and spleen is not enlarged. In severe cases, there may be collection of fluid in the peritoneal cavity. Cough, dyspnoea and orthopnoea, observed in some cases are evidently due to cardiac condition or œdema of the lungs and effusion into the pleural cavities. Haemoptysis may occur due to pulmonary congestion. The rectal congestion may give rise to painful piles.

Knee jerks remain normal, sometimes slightly exaggerated, but seldom lost. General asthenia, loss of appetite, weakness and insomnia are common complaints. There is no impairment of sensation or motor power. Glaucoma of a primary non-inflammatory type is a common eye complication. Haloes are seen around the lights followed by progressive dimness of vision. Tension rises high and field of vision is gradually contracted leading to complete blindness.

Abortions are very common in pregnant women suffering from epidemic dropsy. No special features are noted in these cases, the labour pains start prematurely and the dead foetus is expelled sometimes accompanied with excessive haemorrhage in a few hours.

The Blood.—The blood picture shows a marked diminution of the red cells, the percentage of haemoglobin is diminished and the anaemia is usually of a microcytic hypochromic type. The leucocytes are normal or slightly increased in number. Coagulation time of blood is within normal limits, calcium, cholesterol and phosphorous contents are normal ; uric acid is commonly increased

in the blood. The urine shows no albumin or casts; the culture is as a rule sterile.

Sequelaes.—The patient is incapacitated for regular work for a long time; palpitation, periodical pain and breathlessness follow on exertion and general weakness and debility persist for a long time. The patient may lose his sight if the symptoms of glaucoma are overlooked.

Acute cases, if not fully cured, may pass into subacute or chronic condition. The clinical picture in such cases is rather obscure. Two types are generally observed:—

(1) The cardiac type, in which the symptoms of cardiac distress viz. breathlessness, palpitation, fatigue and praecordial pain on exertion, are complained of. Objective signs such as increased pulse rate, dilatation of the heart or dropsy may also gradually appear and eventually constitute the picture of congestion cardiac failure.

(2) The asthenic type, in which general debility and nervous prostration may be very marked and persistent, rendering the individual incapacitated for work. A chronic sufferer frequently notices oedema of the legs. This is manifest especially after an exertion or on restoration of rice in the diet.

Treatment.—All acute cases should be treated as bed cases until convalescence is well established. Bowels should be kept regularly open to help elimination of the offending organisms and their toxins. Astringents are better aids to check diarrhoea. If it is very severe kaolin may be prescribed in big doses. Intestinal antiseptics such as salol have been advocated by some, but are not very helpful.

Patients should be put on rice-free high-protein diet with adequate vitamins. Liquid diet such as lime whey, butter-milk, fruit juice and glucose are given in cases with marked gastro-intestinal symptoms. Other articles are gradually added as the condition improves. Ephedrine is prescribed to combat the capillary dilatation. The tincture preparation is usually used in half a drachm doses three times a day. It has also got direct stimulant action in the myocardium. It is advantageous to combine it with calcium lactate—10 grains per dose, which acts as a cardiac tonic and also decreases the permeability of the capillary walls. Diuretics like diuretin, extract punarnava liquidum and salyrgan may be used if the Oedema does not subside readily. Congestion cardiac failure if present, should be treated by venesection or administration of leeches and digitalis in suitable cases. Glucose and diffusible stimulants like cardiozal, camphor etc., are beneficial. Injection of atropine is used if there is pulmonary Oedema. Soothing ointments are given for painful piles. Sarcoids, when septic or bleed are treated surgically. Eyes are to be carefully watched for glaucoma in every case. Operation is recommended when it is associated with diminution of visual field.

General tonics such as iron and strychnine are prescribed for convalescent cases. Rice or its preparations are to be restored into the dietary, gradually.

Average duration of the disease is about six weeks. Mortality is 2 to 8 per cent.

Prophylaxis.—Rice, stored in a dry and well-ventilated place and pure mustard oil, preferably the jail oil, should be used. During an epidemic, it would be advisable to avoid them as far as possible. Hygienic precautions against the contamination of foodstuff with the excreta of patients suffering from epidemic dropsy are recommended.

Selected References:—

1. *Acton, H. W.. (1922)—The Causation of Epidemic Dropsy. "Indian Med. Gaz.", Vol. LVII, p. 331.*
2. *Idem, (1932),—The Classification and Grading of Different Qualities of Indian Rices in connection with Epidemic Dropsy. Ibid., Vol. LXVII, p. 640.*
3. *Acton, H. W. and Chopra, R. N., (1925)—The Problem of Epidemic Dropsy and Beriberi. "Indian Med. Gaz.", Vol, 60 p. 1.*
4. *Idem, (1927)—Further Investigations into the Etiology of Epidemic Dropsy. Ibid, Vol. LXII, p. 359.*
5. *Chopra, R. N. and Basu, U. P., (1930),—Cardiovascular Manifestations of Epidemic Dropsy and their Treatment. Ibid, Vol. LXV, p. 546.*
6. *Chopra, R. N. and Bhattacharjee, S. N., (1935)—Observations on Epidemic Dropsy Cases admitted into the Tropical Diseases Hospitals from 1922—1933. Ibid, Vol. LXX, p. 498.*
7. *Chopra, R. N. and Bose, S. C., (1933)—Cardiovascular and other Manifestations of Epidemic Dropsy. Ibid, Vol. LXVIII, p. 605.*
8. *Chopra, R. N. and Chaudhuri, R. N., (1935)—A Preliminary Report on an Epidemic Dropsy Outbreak in Purulia. Ibid, Vol. 70, p. 481.*
9. *Chopra, R. N. and Chaudhuri, R. N., (1935)—Cutaneous Manifestations of Epidemic Dropsy. Part I. A Clinical Study. Ibid, Vol. LXX, p. 493.*

10. *Chopra, R. N. Chaudhuri, R. N., and Panja, D., (1935)—A Histopathological Study, Part II. Ibid, Vol. LXX, p. 496.*

11. *Chopra, R. N., Mukherjee, R. N. and Gupta, J. C., (1935)—Studies on the Protein Fractions of Blood Sera, Part IV. Epidemic Dropsy. "Indian Journ. Med. Res.", Vol. XXIII, No. 2, p. 353.*

12. *De. M. N. (1933), Discussion on Pathological Aspect of Epidemic Dropsy. Calcutta Med. Journ. Vol. XXVII, p. 229.*

13. *Kirwan, E. W. O'G. (1932)—Epidemic Dropsy in Glaucoma. Ibid, Vol. LXVII, p. 636.*

14. *Megaw, J. W. D., (1910)—Note on Cases of the Epidemic Dropsy Type of Beriberi at the Presidency General Hospital, Calcutta. "Indian Med. Gaz., Vol. XLV., p. 121.*

15. *Megaw, J. W. D., (1923)—The Beriberi and Epidemic Dropsy Problem. Ibid, Vol. LVIII, Part 1, p. 145. Part II, p. 193.*

16. *Megaw, J. W. D., (1927)—Epidemic Dropsy and its Bearing on the Beriberi Problem. "Trans. 7th Congress". Vol. III.*

17. *Megaw, J. W. D. and Banerjee, R. N., (1923)—Two Family Outbreaks of the Epidemic Dropsy Type of Beriberi. "Indian Med. Gaz.". Vol. LVIII. p. 49.*

18. *Megaw, J. W. D. and Bhattacharjee, S. P., (1924)—An Outbreak of the Epidemic Dropsy form of Beri-beri in Calcutta. Ibid, Vol. 59, p. 169.*

19. *Pasricha, C. L., de Monte, A. J. H., Banerjee, K. and Lal, S., (1936)—Bacteriological Studies in Epidemic Dropsy "Indian Med. Gaz.", Vol. LXXI, p. 189.*

20. *Shanks, G., and De. M. N., (1931)—The Pathology of Epidemic Dropsy. "Indian Jour. Med. Res., Vol. 19, p. 469.*

Rickets in Tropics

BY

B.N. PRASAD, Ph.D., (EDIN.), M.Sc., M.B., D.T.M., (CAL.),

From the Department of Pharmacology and Therapeutics, P. W. Medical College, Patna.

FULLY developed rickets with all its clinical mainfestations and confirmed by radiographic and biochemical changes, is a very rare condition of the tropics. While mild rickets, the identity of which is still very controversial and which is identified mainly clinically, is not infrequently met with, in this part of the country. Condition manifesting clinically mild rickets and confirmed by therapeutic diagnosis *i. e.* cases cured clinically by regulation of diet and administration of calciferol, is the subject of discussion of this paper.

Aetiology.—Rickets of the North Temperate Zone is a disease found among the poorer class in large towns generally and is associated with deficiency of fat soluble vitamin D. Its incidence and severity reach their height in early spring due to the diminished availability and intensity of the antirachitically effective rays of the sun during winter months [1] & [2]. In this country, there is no seasonal relationship with the disease and perhaps it is due to the fact that antirachitically effective rays of the sun are never wanting. A recent publication by Ghosh *et al* [3] also shows that ultraviolet rays are to a certain extent screened off by dust and smoke in bigger towns of India and the intensity of activity varies during different months and also during different parts of the day but still they have found that, though in lower intensity, they are present all over the year. This condition is generally met with in low middle class people who can with great difficulty manage to have two healthy square meals a day. Among them the nourishing articles of diet are rather a thing of luxury than necessity : milk or meat is a rarity and is enjoyed occasionally and cereals form the bulk of their menu. There is another class of people, who can afford well-balanced diet but are very conservative and attach orthodox and religious importance to the dietetics and thus lack in providing nourishing food. Women of these classes live in purdah and so cannot develop proper amount of vitamin D, an internal secretion of the skin and therefore supply of this vitamin is an indispensable food factor for them.[4] Children of such mothers, brought up under these unfavourable conditions, are found to suffer from rickets between six and eighteen months. The histories of these

cases generally point that the maternal diet during the period of excessive demands of pregnancy and lactation as well as the food of the infant are totally unbalanced. The child is weaned very late, milk is very scanty in the mother's breasts and so the child gets heavy compensatory supply of cereal diet from very early part of its infancy.

Symptomatology.—The child is brought to the physician for muscular hypotonicity, weakness and "pot-belly" appearance associated with diarrhoea or bronchitis or both. These signs and symptoms are similar to those found in other conditions where the bones are not affected. The interpretation of these manifestations, in the absence of radiographic and biochemical findings, is a matter of individual opinion. In temperate countries, rickets in its severe form, has of recent years been much less common; it is open to question whether minor grades of the disease do not still occur as commonly as they ever have been (²). The question becomes still more controversial when similar cases are to be labelled as 'mild rickets' in this country. These cases generally present the following signs and symptoms:—

(1) *The Head.*—There is delay in closure of the anterior fontanelle. Cranial bossing with typical square, large head is rather the only bony manifestation. There is also delayed dentition.

(2) *The Trunk.*—Inability to sit and "pot-belly" appearance are well marked features.

(3) *The Limbs.*—There are marked evidences of muscular hypotonicity and weakness.

(4) *Gastro-intestinal.*—Disturbance in digestion associated with the resulting symptoms of dyspepsia, flatulence and diarrhoea is the trouble for which a physician is consulted.

(5) *Respiratory.*—These children are very prone to naso-pharyngeal and bronchial infections.

(6) *Nervous.*—The nervous irritability and fretfulness are very common features.

(7) *The Skin.*—There is unnatural softness and pallor.

Therapy.—In this land of perpetual sun-shine, it is always possible for the inhabitants of this country to build their own supply of vitamin D. Whether these invalid children suffer from

vitamin deficiency or not is rather very difficult to assess. With their mother living in purdah, these children are generally kept confined indoors, which is not a very healthy surrounding. This environmental factor gives a good ground to think that these children are not developing the proper requirement of calciferol under their skin. They are very susceptible to gartro-intestinal and respiratory complications and other infections which suggest that they are also getting inadequate supply of anti-infective vitamin in their diet. Ganerally, these fat soluble vitamins A and D are distributed together in daily food supply. It is quite natural that when these rickety children have lived upon a diet,deficient in all animal fats, they suffer from a deficiency of both vitamins A and D. Therefore, it is advisable to administer both of these vitamins. They can be supplied in cod-liver oil or halibut oil. One should always bear in mind that probably these children are suffering from partial deficiency and therefore they do not require full curative dose of these vitamins. Rickety children often suffer from digestive disturbances and cod-liver oil is apt to produce diarrhoea. A very good preparation for such cases is Haliversol (P. D. & Co.) in 3 to 5 drops doses twice daily on some fruit. The author has found it very effective in such cases. Another advantage of this drug is that it becomes obligatory to give some fruit to the child with it. This measure is required only for sometime till the child has become fit to develop its own calciferol fully.

As the trouble is due to unbalanced diet rich in cereals and poor in milk and animal fat, measures should be adopted to correct this error. Cutting down the cereal to its minimum and increasing the quantity of milk to its maximum have always proved effective. A normal adult requires about 0.5 G. of calcium and this can be had from a pint of good milk. Growing children require more of calcium for their bony development and consequently, if this requirement of calcium is to be obtained from milk only, they are to get more of milk. Where the supply of calcium is not possible from milk alone, it should be supplemented with some calcium preparation. Sodium calcium lactate or Kalzana is a good preparation for this purpose. Some cases improve quite satisfactorily only under this regime. Probably increased supply of milk, derived from cows fed on fresh vegetables, contains rich amount of anti-rachitic vitamin and thus vitamin deficiency is derived from this milk supply.

Discussion.—A great disagreement exists between the clinical diagnoses of the various observers as well as between the clinical and Roentgenographic diagnoses of the same observers. Literature

on this subject shows that clinical diagnosis without roentgenograms is unreliable (5), (6), (7). Again these signs and symptoms (described above) are similar to those found in other conditions where the bones are not affected (2). There is evidence that even when the calcium phosphate ratio in the food is correct, lack of vitamin D results in defective bone formation, and on the other hand, a free supply of vitamin D can correct an improper calcium phosphate ratio. Between these two extremes, however, there is a considerable range over which the result obtained from partial vitamin D deficiency is modified by the calcium phosphate ratio (4). The essentials for the production of ricket thus appear to be an inadequacy of vitamin D accompanied by a relative deficiency of calcium or phosphorus or an absolute deficiency of either or both (7). High cereal diet which is lacking in calcium and fat soluble vitamins are adopted, at the cost of food derived from animal sources, under hard economic conditions of the parents. Mothers of these children are under adverse conditions and so the nutrition of the child suffers since its prenatal life. Post-natal life is passed indoors mostly in purdah with the mother. Considering these facts, along with the improvement in the child under antirachitic regime, one feels bold enough to hazard his opinion and to label these cases as " mild rickets ".

Conclusion.—(1) Cases clinically recognised as mild rickets are met with in this part of the country.

(2) Its aetiology and diagnosis have been discussed.

References:—

1. *Price—A Text-Book of the Practice of Medicine, (1934).*
2. *Pearson and Wyllie—Recent Advances in Diseases of Children.*
3. *Ghosh. P. N., Ukil, A. C., and Sen, M. K. (1936)—J. Ind. Med. Ass. VI, 53.*
4. *Clark—Applied Pharmacology (1934).*
5. *Eliot, Martha M. (1925)—J. A. M. A. 85 : 656.*
6. *Eliot. Martha M. & Jackson, Edith. B.,—(1935). Am. J. Dis. Child, 46, 1937.*
7. *Jeans, Philip C. (1936). J. A. M. A. 106, 2066.*

The Application of Cobra Venom in Modern Medicine

BY

CAPT. J. SINGH, CHOWHAN, M.B., B.S., A.I.R.O.,

From the Department of Pharmacology, School of Tropical Medicine, Calcutta.

THE importance of snakes and the uses of the snake venoms has long been known. The snakes have become an emblem of the art of healing, magic and authority in Greek mythology. The emblematic figures of 'Asklepios' as an old man reclining on a staff with snakes coiling around it and his sister Hygeia as a woman holding a snake in one hand and a bowl in the other, are well known.

The God Asklepois (Aesculapius), son of Apollo and Coronis, was worshipped as an earth power, as a reliever of disease, giver of health, and a great boon to mortals. The snake, coming out of the ground, was early related to Mother Earth and her power. It was believed to possess the magic of prophecies, dreams and healing. Then it became the symbol of the underworld powers and an aid to physicians who, it was thought, used the serpent tongue as a therapeutic agent. Thus the serpent, mysterious product of the earth, became a ritualistic symbol.

While working on the pharmacological action of Indian poisonous snakes with my co-workers in the school, it was found that cobra venom had a depressant action on the central nervous system, particularly on the respiratory centre and on the nerve terminal in the muscles. Chopra and Ishwariah (1931) have shown that venom produces a transitory rise of blood pressure, probably due to its action on the peripheral blood vessels, followed later on by a marked and maintained fall. In the case of Indian Dabioa (Russell's viper) venom, the main action was more or less restricted to the circulatory system and on the capillaries and this action was almost similar to that of histamine shock. The selective action of snake venoms was demonstrated in a remarkable manner on the protozoa. Though both these venoms are highly fatal to man, their actions differed markedly on paramacia. Chopra and Chowhan (1931 and 1932) showed that while cobra venom killed these protozoa in as high a dilution as 1/30,000 to 50,000, the Russell's venom had practically no action on them even in as high a

concentration as 1/500 to 1/1000. This difference in actions was due to the fact that cobra venom was toxic to these protozoa since it acted on the rudimentary nervous system of paramacia. Russell venom on the other hand showed no action on them since this venom acts on circulatory system only and these protozoa have no formed representation of the vascular system, hence remained immune to this venom. Later, Chopra and Chowhan (1934) showed that Russell venom in high concentration retards the coagulation time of blood. Macfarlane and Barnett (1934) showed that in high dilution it acts as a coagulant. Owing to this strong coagulant property, the Russell venom is now used successfully locally in stopping the severe bleeding of hæmophilia, local oozing of blood in after-operation and as a good coagulating plug in cases of severe bleeding wounds and after-extraction of teeth. Messers Burrough's Wellcome and Co., have put in the market, dried and finely powdered Russell viper venom in glass ampoules under the name of "stypven" for local application to be used in the form of a solution of 1/10,000 concentration in cases of extensive bleeding from the wounds.

Chopra and Chowhan (1935) reported that snakes and their venoms have been regarded as of great medicinal value in India. Snake venom is called 'sarap visha' in Hindi and 'garala' in Sanskrit. The use of snake venom in Hindu medicine is of comparatively recent origin, as references to it are only met with in such modern works as Ratnavali, Sarkaumudi, etc., Ainslie (1826) wrote that the flesh as well as the skin of certain snakes was believed to possess medicinal properties in some of the Eastern countries. In *Ulfez Udwiyeah*, the flesh of snakes is described as possessing 'hot' and 'dry' effects. The dried and powdered flesh of 'Tamool' (an inoffensive hill snake), and the Malay 'Paumboo' has been known as a remedy against leprosy. The slough of snakes powdered and mixed with the oil of *Dalbergia* arborea, when applied externally, is considered of value in epilepsy. The blood has also been used in Mohammedan medicine in the treatment of leucoderma. A preparation of arsenic and dead cobra is applied externally to leucoderma patches and syphilitic rashes in Northern India. It is mixed with arsenic, opium and musk and is used as a tonic, aphrodisiac and a prophylactic against many diseases. It has been used as a hepatic stimulant in ascites, cholera, collapse, etc.

Of recent years, a good deal of literature regarding the different uses of snake venom has been published by various workers in

different parts of the world. The action of Cobra venom on different systems of human body may be summarised as follows:—

Action of Cobra venom on Tissues.—Chopra, Das, and Mukherji (1936) have shown that when introduced into a tissue culture of chicks embryo, in concentration of 1/20,000, Cobra venom inhibits the further growth of the culture; on the other hand, in higher dilutions such as 1/50,000 to 1-80,000, it stimulated the growth of the tissue cells. That cobra venom has a destructive action on the granulation tissue was shown by White (1931) by his experiments on rats. Rousseau (1935) reported that this local action of cobra venom can be enhanced if it is heated to 70 C for about 30 minutes. Such activated venom causes a rapid disintergration of the cells of adenocarcinoma, if injected to the tumour itself.

From the above observations it may be concluded that in high concentrations and after certain modifications, cobra venom, if injected into the growth, has the power of destroying the neoplastic cells of tumour or at least of inhibiting their metastatic progress. In very high dilutions it may be able to stimulate the reconstruction of the degenerated nerve and help in normal tissue growth.

Action of Cobra venom in Cardio Vascular System.—Beeren and Cuypers (1935) reported that injections of cobra venom into the marginal ear vein of rabbits produced a transient fall of blood pressure which at times is preceded by a rise due to sympathetic stimulation. The fall occurs even after vagal section, consequently it is held to be due to a reflex via the nerves of Hering. Meurling (1935) showed that the action of adrenaline on frog heart is inhibited by such low concentrations of cobra venom as 1/100,000,000. With concentration of 1/100,000 of cobra venom the action of pilocarpine is diminished but with weaker solutions this action is enhanced. It also inhibits the action of parasympathetic nerves on the isolated intestines of mammals. The venom of *Naja tripudians* has been shown to have no blood coagulating principle. This venom in fact destroys the thrombo kinase of the blood. Venoms of other snakes which have similar action are *Naja flava*, and Sepedon hæmochetes. Vellard and Vinna (1935) reported that repeated small injections of 0.1 to 1 mg. of the Lechesis atrox venom in man produce intense lysis of the red blood corpuscles and lucocytes, a decrease of fibrinogen and complement and increase the coagulating power of the serum. Hepatic and the renal cells may be damaged. Chopra, Mukerji, and Chowhan (1937) have studied the physical changes produced

in the blood after giving intramuscular injections of therapeutic doses of cobra venom in anthropoids. In doses, which are similar to therapeutic doses for man it produced a lowering of the surface tension, increase of viscosity of the plasma, slight alteration in the ph value and a diminution of the buffer action of the blood particularly after bigger doses. Laignal, Lavastine, Warmser and Koressios (1934) showed a hypotensic effect on intravenous injection of 1/100 to 1/50 mg. of cobra venom. It persisted after double vagotomy and even after an injection of atropine. After injection of the venom the hypertensive action of adrenaline is definitely decreased.

Action and uses of Cobra Venom in Nervous Diseases.—The venom of the Indian cobra, *Nia tripudians* has a strong depressant action on the vasomotor and the respiratory centres, as well as in the neighbouring ganglia of the 9th, 10th, 11th, and 12th cranial nerves also a curara like action on the motor end plates. It has been said to be useful in delirium, hallucination, aphasia, and melancholia, and some improvement has even been claimed in apoplexy, meningitis, hysteria, and chorea. On account of its depressing effects on the sensory nerve endings it has been given intra-tumourly to stop the severe pains of inoperable carcinoma and intravenously in neuritis and neuralgias. Macht (1935) reports that the analgesic effect of cobra venom was demonstrated in man and guinea-pigs after its injections, sub-cutaneously or intramuscularly. The sensibility to pain produced by electric currents was greatly diminished and this effect lasted for several hours. Dye and Manaelesser noticed a complete disappearance of pain in severe neuralgia and malignant tumours, further in sciatica, neuralgia, tabes dorsalis etc. In most cases they succeeded in relieving the pain completely but the results with regard to the growth of tumours were not clear. An important factor in these observations is the liberation of patients of morphium preparation so that often an increase in appetite, body weight and in body and mental resistance could be observed. In 17 cases of sciatica, intercostal, cervical, occipital and trigeminal neuralgia, absolute painlessness was reached within a very small number of days.

Action and uses of Cobra venom in Cancer and other Growths.—Laignal, Levastine and Korossios (1933) experimented and studied the efficacy of cobra venom in pain produced by malignant tumours. They reported that doses of 0.001 mg. relieved the pain in patients who otherwise needed large doses of morphia for relief. The injections of Cobra venom only needed to be repeated every 8th or 10th day. Prof. Gossset, (1938) for Academy of Medicine (Paris) at Salpetrior, reported its usefulness in inoperable neoplasms. Macht (1936) treated 105 cases of carcinoma of breast, uterus, rectum, jaw, ovary, tongue, and bladder. He started with 2 to 3 m.u. and then gave a full dose of 5 m.u. Injections were given intramuscularly and repeated daily till a relief of pain was obtained. At first an initial small dose was given to see if there was any idiosyncrasy to snake venom and later the dose was increased. He concluded that in 38 per cent. of cases, a marked relief of pain was obtained; in 28.6 per cent. definite amelioration; in 21.9 per cent. slight relief; in 7 per cent, doubtful and only 9 per cent of cases showed no beneficial effect. It was observed that the relief of pain was due to the action of the venom on the higher centres resembling that of morphine action, but the treatment did not lead to addiction or any dangerous after-effect.

Action of Cobra venom in Diseases of Muscles and Joints.—Persons suffering from rheumatism noticed a great relief or even disappearance of the symptoms after they had been stung by bees. David Epstein in a private communication (1935), reports that encouraged by the above fact, Pollack (1928) employed a preparation of bee venom (apicosan) with great success in all forms of articular rheumatism, myalgia and finally in case of rheumatic iritis which was persistent to ordinary treatment. The use of cobra venom has been reported to have given relief in the pains of sciatica and severe neuralgia and tabes dorsalis. In specific non-rheumatoid arthritis, so-called rheumatoids, there was a strong decrease in the swellings of the joints particularly in the gonorrheal and tubercular processes and together with relief of pain. Special observation deserved 4 cases of spondylitis in which the improvements exceeded the results of the bee toxin treatment, particularly with regard to the relieving of pain and the increase in movability. In the thankless and therapeutically obstinate class of the degenerative arthrosis the results obtained were remarkable. Altogether 15 cases of arthrosis in particular of the knee, shoulder-joints and spinal column were treated. The analgesic effect was very considerable. After the freedom of the pains there was also a considerable functional improvement in the affected parts.

Report on the cases treated with Cobra Venom.—About forty different types of cases were treated with Cobra venom in the Carmichael Hospital for Tropical Diseases and in the

out-patient Department of the School of Tropical, Medicine Calcutta.

The cases of neuritis, neuralgia, myalgia, angina pectoris and paraesthesia showed a marked improvement after treatment. The relief of pain was felt usually after the 3rd or 4th dose of the venom. In every case about 10 doses of cobra venom (1 to 10 m.u.) were given. In some cases the same course of injection was repeated a second time after an interval of 2 weeks. Regarding the case of epithelioma of tongue, the patient was well advanced in age and hence very small doses were given. The local application of carbolic acid and silver nitrate paints and radium applications produced a little relief only. At the time of treatment there was a good deal of sloughing, salivation and foul smell was coming from the mouth. The injections were started with 1/10 m.u and then given at weekly intervals and later on twice weekly. The maximum dose being 8 m.u. After the 4th dose the pain disappeared and after the 6th, the growth became clean and dry and started peeling off. The treatment had to be discontinued since after the 10th dose the surface of the growth became so much bare that it started bleeding. The patient however reported 75 per cent relief in pain and salivation. The treatment enabled him to talk and to swallow his food with much less difficulty than before. In the case of locomotor ataxia the wooliness in feet, disability in walking and girdle pain was markedly reduced after the dose of the venom. He received two courses of 10 injections each. He gave history of injury to skull bones and fracture of the three last dorsal vertebrae two years ago. The progress was however delayed due to involvement and suppuration in frontal and maxillary sinuses. But after the sinuses had been regularly drained and venom treatment continued there was no more return of symptoms. In the case of sciatica the pain was not much relieved. In chronic cases of sciatica where there is a possibility of more adhesions or organic growths pressing against the sciatic nerve, much relief of pain cannot be expected. The lathyrism case was treated with a view to see if the venom could in any way stimulate the degenerated nerve cells in the anterior cornua of the spinal. There was no improvement at all even after two courses of injections and his muscles showed no change to electrical stimuli. This was a case of 6 years' duration and a permanent damage had been done to the nerves. In cases of neuroleprosy, the venom produced a great relief in the shooting character of pain which was not otherwise relieved with the usual leprosy treatment with hydnocarpates.

Summary.—1. The action of cobra vemon on different systems of the body and its application in diseases has been discussed.

2. The cases treated by the author were of neuralgia, neuritis, sciatica, myalgia, locomotor ataxia, neuro leprosy, angina-pectoris, lathyrism and epithelioma of the tongue.

3. All these cases showed a marked relief of pain but regarding the curative effect of cobra vemon on the growth and tumours is yet too early to form an opinion.

4. The injectable cobra venom was prepared in the Pharmacological Department of the School of Tropical Medicine, Calcutta.

5. The doses of the venom used were one to ten "mouse units" injected intramuscularly twice or thrice weekly.

Bibliography:—

1. *Chopra, R. N. and Ishwariah, V.—On experimental investigation into the action of the Indian cobra (Naia naia vel tripudians). "Indian Jour. Med. Res.", Vol. 18, April.*

2. *Chopra, R. N. and Chowhan, J. S., (1931)—An experimental investigation into the action of Cobra venom of the Indian Daboia.*

3. *Chopra, R. N. and Chowhan, J. S., (1932)—Act of the venom of the Indian Daboia in certain protozoa.*

4. *Chopra, R. N. and Chowhan, J. S., (1934)—Action of the Indian Daboia (Viper Russell's venom on the muscular system). "Indian Jour. Med. Res.', Vol. 21, p. 493.*

5. *Macfarlane, R. C. and Barnett, B, (1934)—The haemostatic possibilities of snake venom. "Lancet", Vol. 12, p. 985.*

6. *Chopra, R. N. and Chowhan, J. S., (1935)—The Pharmacology and Therapeutics of snake venoms. "Ind. Med. Gaz.", Vol. 70, August, p. 249.*

7. *Ainslie, (1826)—"Materia Medica of Hindus", Vol. 11, p. 290.*

8. *Chopra, R. N. and Chowhan, J. S., (1935)—Snake venoms in Medicine. "Ind. Med. Gaz.", Vol. 67, Oct., p. 441.*

9. *White, W., 1931—Cobra venom on granulation tissue absorption. "Lancet", Vol. 1, p. 1293.*

10. *Rousseau, E., (1935-36)—Fermenting properties of phosphodiastase of cobra venom after beating it to 70° c. "compt. rend, Soc., Biol", Vol. 117, p. 565—6.*

11. *Vellard, J., and Vianna, M., (1935)—Changes in cobra venom on cardio vascular system. "Trop. Dis.", Vol. 32, p. 378.*

12. *Chopra, R. N. and Chauhan, J. S. and Mukherji, S. N., (1937)—Physical changes in blood of monkeys after therapeutic doses of cobra venom (in press).*

13. *Laignel—Levastine, Koressios, N. T., (1934)—Cobra venom therapy. "Jour. of Med., Paris", Vol. LIII, p. 652,*

14. *Macht, D. I., (1935)—Action of Cobra venom on the pain threshold. "Compt. Sen soc. Biol", Vol. 120, p. 286.*

15. *Laignel—Levastine and Koressios, N. T., (1933)—Cobra venom in the treatment of cancer. "Jour. Med, Asso.", Vol. 100, April, 25.*

16. *Gosset, (1933)—Cobra venom in cancer, "Lancet", Vol. 1, p. 826.*

17. *Beeran, J., and Guypers, H, (1936)—Action of Cobra venom on the circulation. "Trop Disease, Bult.", Vol. 33, No. 5, p. 389.*

18. *Meurling, S., (1935)—Action of Cobra venom on the frog's heart and on the mammals. Smooth muscles and Autnomic nervous system. "Compt. Rend, Soc. Biol., Vol. 120, p. 286.*

INDEX TO ADVERTISERS.

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

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

The Discovery of Bacteria

"I SAW with wonder that my material contained many tiny animals which moved about in a most amusing fashion. I had the impression that I was looking at several thousands in a given part of water mixed with a particle of the material from the teeth no larger than a grain of sand."

These were the simple words used by Anton Van Leewenhoeck in his letter to the Royal Society of London in 1683, in which the Dutch Microscopist so graphically described his famous discovery of Bacteria through his observations upon tartar scraped from the teeth.

It was not until two centuries later, however, that Professor W. D. Miller first associated mouth bacteria with tooth decay. Shortly after, Dr. N. S. Jenkins, a noted American dentist practising in Europe, began his study to develop an agent that would not only cleanse the teeth but destroy the oral bacteria. Working in cooperation with Professor Miller, Dr. Jenkins continued his experiments until 1908 when the success of his efforts was confirmed by leading medical and dental scientists in the U. S. A. and Europe.

In disclosing his formula at the meeting of The American Dental Society of Europe held in London, Dr. Jenkins said: "This preparation [Kolynos] will cleanse and polish the surfaces of the teeth without the least danger of abrasion. It will overcome the defenses of bacteria and destroy the germs. It will produce a condition of true cleanliness in the entire mouth."

The outstanding advantages of Kolynos—its germicidal and cleansing properties, have been recognized by dentists in many countries ever since the Kolynos formula was published to the dental and medical professions twenty-nine years ago.

On request our distributors will gladly send a professional package, free of charge.

Distributors:
MULLER & PHIPPS (Asia) LTD.,
P. O. Box 773, Bombay, India
THE KOLYNOS COMPANY
NEW HAVEN, CONN., U.S.A. X857