turn is underlain by a pelitic series much injected by granite. As regards the Darjeeling district, Wager suggests that the Daling series are the equivalent of the Everest pelitic series, while he agrees with the large-scale inversion suggested by Mallet.

Before concluding this section reference must be made to a new edition of Burrard and Hayden's *A Sketch of the Geography and Geology of the Himalaya Mountains and Tibet*, first published in 1908. In the new edition, published this year, the part dealing with the geology has been brought up-to-date by Dr. A. M. Heron, and it should be in the hands of every geologist interested in Indian geology.

Cerebro-Spinal Meningitis.

By Capt. P. Ganguli,

Additional Physician, Medical College, Calcutta.

HISTORY.

IN 1805, an epidemic of cerebro-spinal meningitis occurred in Geneva and Vieusseux was the first man to describe the disease. In 1806 and 1807, the disease was prevalent in the Prussian army. From 1805 to 1830 it occurred in the United States of America and gradually spread from east to west. France was next attacked in 1837 and the disease spent its force in 1874. From 1854 to 1874, the disease occurred both in Europe and in America. From 1875 till now, the disease has spread throughout Europe and America and many places of Asia.

The present Indian epidemic started in the beginning of 1932 in Calcutta, when nearly 40 cases were admitted to the Calcutta Medical College within a month. Subsequently all the cases were admitted to the Campbell Medical School. The disease continued in its sporadic form and has now spread throughout Northern India.

EPIDEMIOLOGY.

Age.—Children are more susceptible to the disease than adults. In the Danzig epidemic, 93 per cent. were under 5 years of age. In Calcutta, however, the disease is particularly prevalent amongst adults. Majority of the cases among children were of chronic character.

Sex.—In Calcutta, more males were attacked than females. As fatigue, chill and overcrowding are predisposing factors, the adults are more liable to infection than others. The purdah system is responsible for keeping the women indoors. The incidence is therefore less among the women. In certain cases, however, where women were exposed to overcrowding, the disease attacked them as well.

Example.—A female came from a moffussil to Calcutta for the anti-rabic treatment of her son. She had to attend the crowded out-door of the Pasteur Institute in the School of Tropical Medicine and Hygiene, and ten days after, she contracted cerebro-spinal meningitis and died within three days of the attack.

The congregation of individuals in meetings, cinema houses, markets, big railway stations, third class compartments, and such like are favourable to the formation of multiple foci and spread of the disease. In well-equipped jails, barracks and schools of Calcutta, however, no cases have been reported. One case was reported from Dumdum jail amongst detenues. According to Major Malaya not a single case has been reported from the Calcutta police lines with a population of six thousand.

The lowered vitality of the population owing to depressed economical condition must be one of the factors. Bad sanitary conditions of the Northern part of Calcutta was responsible for the larger incidence of the disease in that part of the city. The disease is not, however, highly contagious and is not spread by clothing.

Season.—In the case of the European epidemics, the incidence is usually very high in winter whereas in Calcutta, in 1932, the highest incidence was recorded in the months of April and May. 20 per cent. of the cases gave history of exposure to mid-day sun.

Mode of the spread of the disease.—Weigert found presence of purulent rhinitis in many cases of cerebro-spinal meningitis. The meningococci are also found in the nose of many healthy persons, who are the carriers of the disease. The habit of many people to blow out the secretions of their nose indiscriminately in rooms and streets is responsible for the dissemination of

meningococci. During and preceding epidemics, the career rate rises from 2 to 4 per cent. normal to 20 to 30 per cent.

Route of Infection.—The route of infection is through the nasopharynx. The organism sets up rhinopharyngitis, then the meningococci infect the meninges directly from the nose. This is the view held by Nelter and Detere (1911). The other view is that it is a hæmatogenic infection. The meningococci pass into the blood stream and are thereby carried to the meninges. This view is supported by the fact that in 25 per cent. of the cases, blood culture is positive. Esler, for example, reported that he recovered meningococci from the blood of 10 cases out of 41. Moreover, the organisms can be cultured from petechial spots just as *B. typhosus* can be recovered from roseolar rashes of the enteric fever.

BACTERIOLOGY.

It was in the year of 1887 that Weichselbaum of Vienna first discovered the organism which on account of its intracellular character was named *diplococci intracellularis meningitidis*. That the organism was the cause of the disease was proved by the fact that Weichselbaum was able to cause the death of rabbits by subdural injection of the organisms into the skull and he recovered the cocci from culture of cerebro-spinal fluid of experimentally infected rabbits. Intra-pleural and intrathecal injections of the organisms caused death of guinea-pigs in 1 to 3 days. In dogs, subdural injections caused leptomeningitis with acute encephalitis and death occurred within 12 days.

In 1905, Von Lingelsham produced the disease in monkeys. In 1907, Flexner made experiments with *Macacus rhesus* which died within 18 hours to 4 days preceded by general convulsions. In post-mortem examinations, leptomeningitis, encephalitis, abscesses, hæmorrhages into pia-mater were found.

Serological Classification.—The English workers recognise four types (I, II, III, IV) as serologically determined by Gordon. The Rockefeller Institute recognises two types as determined by Dopter, *viz.*, meningococci and parameningococci. Dopter further subdivided parameningococci in α, β and γ varieties respectively. Nicolle, Debains and Jonan divided meningococci into types A, B, C and D. These types were differentiated according to the predominance of different antigenic contents, *viz.*, A, B, C and D. In type I, A predominates. Similarly, in types II, III and IV, B, C and D predominate. These antigenic contents are not equally balanced. This can be illustrated by the following scheme:—

Gordon's I and III strains correspond to Nicolle, Debain and Jonan's type A.

Gordon's II and IV strains correspond to Nicolle, Debain and Jonan's type B.

Dopter's meningococcus corresponds to Nicolle, Debain and Jonan's type A.

Dopter's parameningococcus α corresponds to Nicolle, Debain and Jonan's type B.

Dopter's parameningococcus β corresponds to Nicolle, Debain and Jonan's type B or C.

Dopter's parameningococcus γ corresponds to Nicolle, Debain and Jonan's type D.

Causes of Sporadic Occurrences.—Meningococci carriers are not uncommon. The germs inhabit the nasopharynx. They are usually non-virulent in non-epidemic times but certain strains of the cocci are sufficiently virulent to attack very young children who lack defensive forces and are susceptible. Hence we have cerebro-spinal fever occurring sporadically amongst us.

Morbid Anatomy.—The meninges are actually congested and fibro-purulent exudation collect between dura and pia mater. In acute cases, the whole cortex is covered with thick pus. The cord is also involved and covered with purulent exudate, which is distributed more in the dorsal and lumbar regions than the cervical regions.

Microscopically, the exudate is full of polymorphonuclear cells, containing meningococci. These leucocytes are closely packed in fibrinous material.

DIAGNOSIS.

Clinical Diagnosis.—Besides Kernig's and Brudzinisky's signs, the disease can be clinically diagnosed mainly by the sudden onset of fever, pain, stiffness, rigidity and retraction of the muscles of the neck, pains in the back, orthotonus, tremor and headache. In severe cases, the patient becomes delirious and unconscious. In children, clonic spasms are frequent, and in a few adults, both clonic and tonic spasms are sometimes manifested. Herpes is common due to affection of the posterior ganglion. The pupils are usually contracted and sometimes unequal. Strabismus is not uncommon.

Classification of the Disease.—(1) In the beginning of the epidemic, *foudryant* or malignant forms are common. There is sudden rise of temperature which, however,

is not very high, but malaise, lassitude, stupor, low condition, feeble pulse and such other symptoms all indicate the seriousness of the disease. There is usually the appearance of rash, petechial, purpuric and sometimes this resembles the Malaccan smallpox. The patient quickly becomes unconscious and death occurs in 5 to 24 hours.

(2) The ordinary form has already been described.

(3) In the chronic form, the fever is persistent for two to six months and is characterised by a series of ups and downs. In favourable cases the temperature gradually comes down, spasms become less and less manifest and consciousness returns. Various complications may, however, arise in this condition. They are hydrocephalus, abcess of the brain, pneumonia, pleurisy, pericarditis, parotitis, polyarthritis, persistent headache and such like.

(4) Some cases occur as abortive forms, in which the onset is like that of acute cerebro-spinal fever, but the symptoms suddenly subside and the patient recovers quickly.

Other Varieties of Cerebro-Spinal Meningitis.—Besides meningococci which invade meninges in sporadic and epidemic forms, there are other organisms which may cause cerebro-spinal meningitis. They are pneumococci, streptococci, tubercle bacilli, influenza bacilli, bacilli typhosus including (para A and B), plague bacilli, virus of mumps and such others.

The *pneumococcal meningitis* is invariably fatal. A few cases have recently been reported to have recovered after exhibition of Felton's serum. It occurs more commonly in children than in adults.

The *streptococcal meningitis* is usually an extension of septic infection from middle ear disease and perforated wounds of the skull. The streptococci are usually of hæmolytic type. The disease is usually fatal.

The *tubercular form* is usually common in children and is practically always fatal.

The *influenza bacilli* can cause meningitis. The bacilli are found in long thread-like forms in cerebro-spinal fluid. They resemble Pfeiffer's bacilli but differ in exhibiting a high pathogenicity. Intra-peritonial injection of these bacilli into guinea-pigs and rabbits is followed by purulent effusion into serous cavities. According to Bender, influenzal meningitis is fatal in 91 per cent. in children and 44 per cent. in adults.

The meningitis which occur as complication of typhoid or paratyphoid fevers is fatal in 50 per cent. of the cases. The cerebro-spinal fluid is clear or turbid but seldom purulent like that of meningococcal meningitis.

Laboratory Diagnosis.—The blood examination shows polymorphonuclear leucocytosis with increased stabkernige and younger forms. Traces of albumin are present in the urine. The most important method of laboratory diagnosis is the examination of cerebro-spinal fluid got from lumbar or cisternal puncture. The fluid is centrifuged and the sediment is spread over a slide, stained by Gram's iodine and counterstained by carbolfuchsin. The meningococci are gram-negative diplococci usually found within the polymorphonuclear cells which are abundantly increased. In cerebro-spinal meningitis, the polynuclears predominate, in tubercular meningitis the lymphocytes are most abundant. The coccal organisms are gram-positive in streptococcal and pneumococcal meningitis. These gram-positive organisms can be easily differentiated by morphological appearances and their disposition. The cerebrospinal fluid of tubercular meningitis shows reduction of both sugar and chlorides. The normal amount of sugar in cerebro-spinal fluid is 45 to 95 mg. and of chlorides is 720 to 750 mg. per 100 c.c. In tubercular meningitis, the estimation of chlorides is very important for prognostic purposes, especially in children. Ordinarily the amount of chlorides is reduced to 650 or 680 mg. but in children 580 to 500 mg. may be reached. The globulin is increased even in early stages.

For determining whether globulin is increased or not, either Ross Jone's test or Pandy's test may be done. In Ross Jone's test a distinct white ring of globulin is formed at the junction of saturated solution of ammonium sulphate and cerebro-spinal fluid in a test tube. In Pandy's test, if a drop of cerebro-spinal fluid is put in a saturated solution of carbolic acid, a smoke-like white cloud is formed instead of faint opalescence as with normal cerebro-spinal fluid.

For final diagnosis of tubercular meningitis inoculation of guinea-pigs is confirmative.

Vincent and Bellot's Precipitin Test.—Half a c.c. of antimeningococcal serum is added to 5—10 c.c. of cerebro-spinal fluid and kept in an incubator at 37°F. for 12 hours. A turbidity is developed if the patient is suffering from cerebro-spinal meningitis.

Culture.—This is the surest way of diagnosis. One c.c. of cerebro-spinal fluid is spread over two or three plates of ascitic agar or Gordon's trypagar. Colonies are formed within two days. The cocci are suspended in normal saline. A small quantity of this emulsion suspension is treated with each type serum in water bath for 4 hours at 55°C. If agglutination occurs against a particular type serum, the meningococci belongs to that group.

Agglutination Test of Blood Serum.—The test is positive only in 50 per cent. of cases. The agglutinins are not formed in markedly toxæmic cases. According to Symmeris and Wilson, the serum of cerebro-spinal meningitis occasionally agglutinated *B. typhosus* and *B. coli* even in high dilutions.

Naso-pharyngeal Culture.—The organisms live in the posterior nasopharynx. The smear should be collected with West's swab, which is a bent wire applicator with a sterile cotton tip put within a bent glass tube, so that the cotton tip can be protruded or retracted at will. This tube is introduced into the nose and when it has passed the soft palate, the cotton swab is pushed out so as to get the material from the nasopharynx and is at once smeared on ascitic or serum agar. The smear from the nasopharyngeal region can also be examined on a glass slide but it has to be differentiated from micrococcus catarrhalis. The meningococci are usually found within the polymorphonuclear cells but they may be extracellular. They may be easily differentiated after culture.

Autolysis.—Occasionally, the cerebro-spinal fluid is full of pus cells but no meningococci can be detected in them nor is the culture positive. In these cases, the meningococci have undergone autolysis. The streptococci and pneumococci do not undergo any such autolysis. Hence if the cerebro-spinal fluid contains abundance of pus cells, yet no meningococci, the case is almost surely meningococcic meningitis.

Prognosis and End Results.—During irritative stages. the pupil remains contracted and deep jerks become exaggerated. The dilatation of the pupils and disappearance of the jerks indicate impending death. Oedema of the lungs is always of bad prognosis.

Prophylaxis.—The disease is notifiable. Cases should be isolated at once. The contacts should have gargles of thymol solution or salt solution. The nasopharynx can be reached by means of intranasal sprays of chloretone inhalent, mistol, hexyl resorcinol, or they can be applied by bent camel hair brush through the opening of the mouth. It has been found, however, that all these methods of local disinfection are valueless. Even prophylactic treatment with immune serum has not got any definite value.

During an epidemic, 20 to 30 per cent. of healthy persons carry meningococci in their nasopharynx. In congregation and overcrowding, the infection may spread from carriers to healthy people. It is necessary to stop meetings, cinema and theatrical shows unless the houses are air-conditioned and adequately ventilated. In barracks and jails, systematic examination of nasopharynx should be done and carriers isolated in a separate block. The spacings between cots should be increased and strict supervision of sanitary measures should be undertaken.

Vaccination.—Vaccination is quickly followed by production of antibodies in the system and is certainly effective so far as prophylaxis is concerned. The carriers do not usually get the disease. The medical practitioners, nurses and hospital attendants seldom get the disease. The English naval statistics indicate that the disease almost always develops in those who have previously shown negative cultures from nasopharyngeal smears. This is an additional factor to support that carriers develop antibodies in their system to some extent, but they may get the disease if they are exposed to resistance reducing factors, like exposure to chill, cold, excessive fatigue and such like. These carriers are vastly more common in winter than in summer.

TREATMENT.

The patient should be kept quiet; all causes of irritation should be removed. Special attention is to be directed against bed sores. The hair should be clipped or shaved; icebag should be applied to the head. Water should be given freely.

As the patient usually suffers from constipation, 5 grains of calomel should be given in the evening followed by saline purge next morning. Later, daily enema of soap and water in which two tea spoonfuls of castor oil or an ounce of olive oil is mixed, should be given.

For severe headache, general pains and vomiting, morphia has been frequently used. It quietens the restlessness and irritability, relieves pain and vomiting and procures sleep. Dr. Koplik is, however, of

opinion that morphia is harmful. Every one is, however, agreed about the efficacy of lumbar puncture, which relieves headache by reducing the pressure on duramater. The elimination of toxins with cerebro-spinal fluid will cause subsidence of irritation of vomiting centre. If these symptoms are not relieved by lumbar puncture, chloral hydrate and bromide, ten grains each, should be tried before giving morphia.

Hydropathy.—Hot baths are very soothing, and, if possible, should be given every 3 hours. It will reduce the temperature and sometimes induces sleep.

Serum Therapy.—Jochmann first introduced this treatment. In 1907 and 1908, Flexner and Jobling prepared sera from goat, horse, rabbit and guinea-pig. Out of 1,294 patients treated with serum, 891 recovered and 400 died. The mortality was thus reduced from 74 to 30 per cent. The earlier the serum was given, the better was the result. The leucocytes which increased to about forty thousand, fell to normal within a week after serum treatment. Pus cells became fewer and the cerebro-spinal fluid became less turbid. Another striking feature was that the complications were lessened by serum therapy. The usual complications in those epidemics were iridocyclitis, panophthalmitis, deafness due to internal ear disease, pleurisy, pericarditis, endocarditis, arthropathies, insanity and others.

The mode of preparation of serum varied in different countries. There is no laboratory method by which therapeutic power may be correctly determined. Some rely on *compliment fixation* test, some on *opsonin* content, some on *protective* power. Gordon relies on *anti-endotoxic* power. Riviere and Roux proposed a *precipitin* test.

The failure of serum in many hands is due to preparation from different strains. In the year 1932, out of 43 patients admitted into the Medical College Hospitals, Calcutta, only three survived although everyone was treated with foreign brand serum. A great majority of these cases were foudryant or malignant forms; no impression was manifested by exhibition of those sera. It was understood that the failure was due to sera obtained from different strains of American and European *meningococci*. Failing to get any good result from foreign brand sera I sent some cultures and cerebro-spinal fluids of my patients to Dr. B. B. Sen of Bengal Immunity Co., requesting him to find out the type of meningococci and also to prepare the serum from the local strains isolated from my patients. He brought materials not only from me but also from the Campbell Hospital, Calcutta, where special accommodation for treating meningitis cases was subsequently created. Out of 25 samples collected by him, one contained streptococci and another pneumococci; from the rest eleven strains of meningococci were isolated. Nine were found to correspond to Gordon's type IV and two to type II. That is to say, at the beginning of the year 1932, the prevailing organism of the epidemic were of Gordon's II and IV types, which were the same as Nicol, Debaun and Jonan's β-type or Dopter's parameningococcus α-type. Next year, research workers of the Bengal Chemical Works took up the investigation. Out of 150 samples of cerebro-spinal fluid, 120 showed meningococci. It was found that in none of the samples type II or IV were detected. All of them showed either Gordon's type I or type III which were the same as Dopter's typical meningococci and Nicol's, Debaun's and Jonan's type A. It is, therefore, evident that the types may vary in different epidemics in the same place in different years.

In the latter part of the year 1932, several more cases were treated by me. In all of them locally manufactured sera were used. The result was very satisfactory, as 5 of them recovered, and 2 died, giving a mortality of 39 per cent. In the year 1933, the results were still more satisfactory. 15 cases were treated with sera manufactured in Calcutta, both intrathecally and intravenously and no less than 13 survived and the mortality was 14·3 per cent. All these patients also received Schering's urotropin, intravenously every day as a routine measure.

Dose of Serum.—The quantity of serum to be given intrathecally varies in different individuals and depends on how much cerebro-spinal fluid is withdrawn. On no account serum should be introduced in quantity larger than the amount taken up. Sometimes, the cerebro-spinal fluid comes out under great pressure and even after 100 c.c. have passed out, the rate of flow still remains over 60 drops per minute. In these cases it has been advised to draw out fluid in two or three instalments of 60 c.c. each, and give intrathecally 20 c.c. of the serum. On the other hand, Stitt recommends that the cerebro-spinal fluid should be drained out

till 4 or 5 drops come out in a minute. Personally I have not seen any untoward result by draining up large quantities of cerebrospinal fluid. In my cases when the rate of flow becomes less than 30 per minute, I raise the head and the shoulders a little, with the result that it flows out more quickly and then once the rate flow goes down below 30, it quickly comes down to 9 or 10 per minute, when no more fluid is allowed to come out. 20 to 30 c.c. of serum is then introduced slowly with the head brought down to level position. After this, the head and the shoulders are kept low, and the pelves raised. At the same time 60 to 80 c.c. of serum is given intravenously. The intravenous medication is more urgently indicated if meningococci are found in blood culture. In 1918 Herrie recommended this combined method of medication. The total amount of serum for every individual was an average 100 c.c. intrathecally and 400–600 c.c. intravenously. In Herrie's experience the mortality where serum was given intrathecally was 34 per cent. but by combined intravenous and intrathecal methods the mortality was 14·8 only My own experience was entirely corroborative of Herrie's.

Cisternal Route.—In some cases, where there was arrest of clinical improvement due to the impairment of communication between ventricular and spinal fluids, cisternal puncture was done and serum introduced by this route. Lenkowicz found that the spinal fluid became thick owing to the increase of protein contents. He found that communication of ventricular and spinal fluid was arrested when the protein contents of spinal fluid becomes more than 5 times that of ventricular fluid. In such cases, where lumber route gives a dry puncture, cisternal puncture should be done. Vast numbers of cases were treated by this route in the Campbell Medical School of Calcutta with success.

Serum Meningitis.—In two cases, patients were seen to relapse after 10 or 12 days of apparent improvement and became delirious comatose again. The temperatures, which were normal, shot up again to 101° or 102°. Both these cases complained of joint pains and itching sensations all over their bodies. This led me to suspect serum meningitis in which urticaria is generally present. But the dark complexion of these patients perhaps masked these appearances in their skin. Injection of adrenalin and calcium gluconate quickly restored the temperature to normal and the patients gradually recovered.

In cases of doubt, lumber puncture should be done. In serum meningitis, the fluid is usually clear and the poly-morphous cells do not show meningococci. There is increased albumen but glucose is not diminished as in tubercular meningitis which shows a relapse of these bad signs after apparent improvement.

Value of Vaccines.—There is no doubt that those cases which show tendency to become chronic are quickly benefited by exhibition of vaccine. The antibodies are rapidly developed. Taylor is of opinion, however, that the antibodies do not pass into the cerebrospinal fluid.

Value of Hexamin.—Osler recommends 30 to 50 grains of hexamin daily as prophylactic measure. In all my cases, urotropine was given as a routine measure, both *per os* and intravenously. Dr. P. Banerjee of Howrah got excellent results with cylotropine in five cases.

Value of Mercurochrome.—0·1 per cent. solution of mercurochrome was tried intrathecally with doubtful results.

Complications.—Respiratory disturbances may appear in some cases, which are best treated with Tr. Ephedra or adrenalin. In a few cases arthropathies develop for which serum may be injected into the joints. I would strongly recommend vaccine in these cases.

Conclusions.—(1) Besides general hygienic measures, prophylaxis by means of vaccine may be attempted.

(2) Serum should be given both intrathecally and intravenously.

(3) Local brands of serum are strongly recommended.