Memorandum on encephalitis lethargica.

Memo. 45 / Med.

MINISTRY OF HEALTH.

Memorandum on Encephalitis Lethargica.

LONDON:
PUBLISHED BY HIS MAJESTY'S STATIONERY OFFICE.

To be purchased through any Bookseller or directly from
H.M. STATIONERY OFFICE at the following addresses:
IMPERIAL HOUSE, KINGSWAY, LONDON, W.C. 2, and 28, ABINGDON STREET, LONDON, S.W. 1;
37, PETER STREET, MANCHESTER; 1, ST. ANDREW'S CRESCENT, CARDIFF;
23, FORTH STREET, EDINBURGH;
or from E. PONSONBY, LTD., 116, GRAFTON STREET, DUBLIN.

1921.
Price 1*d. Net.*

MINISTRY OF HEALTH.

MEMORANDUM ON ENCEPHALITIS LETHARGICA.

Definition.

Encephalitis lethargica, which may be classed under the head of general infectious diseases, is characterised by certain manifestations originating in the central nervous system of which the most frequent and characteristic are progressive lethargy or stupor, and a lesion in or about the nuclei of the third pair of cranial nerves.

Past Appearances of Encephalitis Lethargica.

Although the disease has only been recently recognised as a clinical entity and received the name of encephalitis lethargica, certain outbreaks have occurred in the past which possibly were of the same nature—notably the "strange fever" arising in 1685 described by Willis, the epidemics of somnolence with associated nervous symptoms recorded by Camerarius (1712), Lepecq de la Clôture (1768) and those noted by Ozanann as present in Germany in 1745, in Lyons in 1800 and in Milan in 1802. Last century, also, in the "nineties," a mysterious malady of this type termed "nona" appeared in Northern Italy and extended to Hungary, Germany, France and Southern Italy.

Encephalitis Lethargica since 1917.

The first definite record of the disease was given by von Economo and von Wiesner in a clinical and pathological study of thirteen cases which occurred at Vienna in 1917.

During March and April, 1918, a large number of cases of an obscure disease were reported in England. The disease was first regarded as "Botulism," and then as the cerebral form of acute poliomyelitis, but the detailed clinical, epidemiological and pathological investigation undertaken by Medical Officers of this Department* and of the Medical Research Council,

* Local Government Board, Public Health Reports, New Series, No. 121, 1918. H.M. Stationery Office. Price 2*s.* 6*d.* These joint inquiries have been continued, and further results obtained are recorded in the last Annual Report of the Medical Department of the Local Government Board (1918-19) and in the First Report of the Chief Medical Officer of the Ministry of Health (1919-20).

(B5403) Wt. 34161—753. 800. 2/21. **Gp 32.**

resulted not only in its identification with the clinical forms previously described in Vienna, but also in the elucidation of encephalitis lethargica as a distinct disease, its independent character being confirmed from each aspect of the investigation.

The disease is now generally recognised and during the last two years its occurrence has been world-wide. Most of the countries of Europe, Asia, America, and Australasia have been affected by it in greater or less degree.

In England and Wales the following cases have been notified in each quarter :—

		1919.	1920.	1921.
Quarter	First ...	283	268	402*
	Second ...	70	233	—
	Third ...	64	168	—
	Fourth ...	121	245	

In each of these years the winter months have shown the highest prevalence, the maximum monthly number of notifications being received in January. A similar marked seasonal distribution has obtained on the Continent. In 1919, 286, and in 1920, 318, deaths in England and Wales have been attributed to encephalitis lethargica.

Experimental Transmission and Pathology.

In 1919, Professor McIntosh, using a filtered emulsion of cerebral tissue obtained from a fatal case of encephalitis lethargica occurring in an institutional outbreak of the disease at Derby, succeeded in transmitting the disease to a monkey ; he has since been able to transmit encephalitis lethargica from this monkey, in series, to monkeys and rabbits, thus completing the experimental proof necessary to show that the disease is caused by a living virus. The virus appears to be filtrable. It enters presumably through the naso-pharynx and attacks the nervous system causing inflammation therein. The site of election is the region of the nuclei of the third nerve, but other portions of the central nervous system may be attacked. Netter has found a characteristic lesion also in the salivary glands. At post-mortem examination no conspicuous macroscopic lesions are found, and microscopically the meninges appear only slightly affected.

The lesion in the nerve centres is a definitely inflammatory one and the changes consist of a cellular infiltration of the peri-vascular lymphatic sheaths and of certain areas of grey matter. In the brain substance the changes are most conspicuous in the upper part of the pons and in the basal nuclei. In the spinal cord the lesions are slight or absent. The infiltration may be so dense as to form actual foci ; such foci resemble those seen in the grey matter of the cord in polio-

* January only.

myelitis but in contradistinction there is no special involvement of the ganglion cells which as a rule are well-defined with the presence of Nissl granules.

In acute fatal cases of brief duration great difficulty or even failure may be experienced in demonstrating the lesion in the cerebral tissue, although most careful histological methods are employed.

So far no characteristic changes have been observed in the cerebro-spinal fluid.

Clinical Types.

The disease attacks all ages, with a preference for the middle period of life, and both sexes nearly equally.

From the clinical point of view three types are distinguished :—

(1) general disturbance of the functions of the central nervous system but without localisation ;

(2) various localisations in the central nervous system ;

(3) mild or so-called abortive cases.

After a period of incubation the duration of which cannot at present be specified, a prodromal period ensues ; this includes the first seven days but may extend to two or three weeks, during which lethargic somnolence, headache, double vision, general lassitude and occasionally vomiting and diarrhœa may occur. Soreness or dryness of the throat may also be present. The acute symptoms which follow include a febrile temperature (101° to 102° F. = 38·3° to 38·8° C.) marked asthenia, stupor (alternating often with nocturnal delirium) difficulties in speech and spasmodic twitchings of the face and limbs. Skin eruptions are occasionally noted. There is no characteristic rash ; an erythema is most often seen but the eruption may be petechial, papular, morbilliform or scarlatiniform. The rashes when present appear early in the disease and during the pyrexial period. They are transient, fading in 24 hours as a rule. In the type of the disease with localisations in the central nervous system, paralysis of accommodation with diplopia is very frequent and occurs early. There may be opthalmoplegia, external or internal, with ptosis. The muscles innervated by the facial nerve may also be paralysed and likewise those of the tongue and pharynx, etc., rarely those of the limbs. The paralysis is progressive in character. Sensory troubles are the exception. There is often urinary or fæcal incontinence and sometimes retention of urine. Death appears due to paralysis of the respiratory nervous centres. It is preceded by an increase in delirium and stupor merging into coma.

The severest cases lie in bed like a log or resemble a waxen image in the lack of expression and of mobility. The immo-

bility may be accompanied by catalepsy. Various degrees of stupor have been noted. The condition may be one of deep coma with open eyes, total lack of facial expression and inability to be roused. More commonly the condition is not so grave, but the patients are in a profound sleep from which they can be aroused to answer questions or to partake of food. When undisturbed they quickly lapse again into stupor. Certain patients resent being roused and display intense irritability or utter moaning cries when touched. The duration of the stupor is very variable. It may last for only two or three days or more often may persist for two to five or even eight weeks.

Periods of remission may occur in the course of the malady. The outset of coma, although grave, does not always imply a fatal issue. Many patients display extreme emotion and are "childish" in demeanour.

Case Mortality.

Considered generally, and taking foreign experience into account, the case mortality of encephalitis lethargica since 1917 may be given as between 20 and 50 per cent. Recent inquiries regarding 500 cases notified in 1919 show that exactly half proved fatal. The true case mortality can, however, only be satisfactorily assessed when the mild or abortive cases referred to below are more fully recognised and reported.

Sequelæ.

Recovery is generally gradual and tedious chiefly on account of the great prostration and muscular weakness that are so common. The chief sequelæ hitherto observed are :—

(1) An alteration in the mental condition.
(2) The persistence of cranial nerve palsies.
(3) Myoclonus:—sudden, shock-like muscular spasms of limbs, sometimes also of diaphragm and larynx.
(4) The subsequent appearance of paralysis, apparently of spinal cord origin.
(5) Athetosis:—slow and irregular twisting movements, usually of fingers and wrist.
(6) Symptomatic paralysis agitans.

Some of these after effects, such as loss of memory, defects of speech, and changed mental disposition have been found to persist for 12 months or more after the attack.

Differential Diagnosis.

It is desirable to keep the following diseases in mind when diagnosing encephalitis lethargica:—Acute poliomyelitis, polio-encephalitis (Strümpell's type), tuberculous meningitis, cerebro-spinal meningitis, cerebral syphilis, typhoid fever, diphtheritic paralysis, renal disease (uræmia), botulism, functional disorder,

hysteria, cerebral irritation, cerebral tumour, cerebral hæmorrhage, septic meningitis, cerebral thrombosis and acute dementia. Distinguishing points are dealt with in detail in the Local Government Board Public Health Report, No. 121, already referred to.

Treatment.

No specific treatment is available. The patient as soon as the disease is recognised should be confined to bed and his case duly notified. He should be isolated from other members of the household, or if in hospital should be nursed in a separate ward or on a "barrier" system. The services of a trained nurse are almost essential, and if this cannot be provided, removal to hospital should be strongly urged. In severe cases day and night attendance are required. In violent intervals of delirium the patient has to be nursed on a mattress on the floor.

In many instances transient or permanent relief, with diminution of stupor, follows on the withdrawal of cerebro-spinal fluid by lumbar puncture. When this improvement results, lumbar puncture may be repeated with due precautions at intervals, according to the condition of the patient. Reference is made below to the examination of the cerebro-spinal fluid, which may be important for the elimination of tuberculosis or cerebro-spinal fever.

No hypnotics and no morphia or other preparation of opium should be administered; urotropin, if prescribed, should be administered in small doses with caution and the urine should be tested daily for blood and albumen.

Infectivity.

Generally, the degree of infectivity from person to person is of a low order, and cases of the disease usually appear to be isolated or sporadic. Thus the 913 cases reported in 1920 occurred in as many as 307 separate sanitary districts all over the country, and a like wide dissemination of apparently unconnected cases has been noted abroad.

Multiple cases of the disease in the same household as well as multiple cases in institutions were, however, observed in the original inquiries made in this country and their existence was subsequently established in France, and elsewhere.

Encephalitis lethargica appears to belong to that group of maladies (including also cerebro-spinal fever and acute poliomyelitis) in which the pathological agent is much more frequently present in the human organism than the clinical symptoms indicate. An attack of the disease may be regarded as the result, either of the breakdown of the immunity to the effects of the virus which the individual who harboured it had

up to that time enjoyed, or of a non-immune person having become freshly infected with a strain of the virus which has attained a degree of pathogenicity that can be considered as "specific."

No direct relation between encephalitis lethargica and influenza has been established. It has been suggested that the recent appearance of outbreaks of "epidemic hiccup" are to be connected with the infection of encephalitis lethargica. Although hiccup has been noted as a symptom in the latter disease, the inquiries made by the Medical Officers of the Ministry have not, except in one doubtful instance, so far shown any close relation between the occurrence of "epidemic hiccup" and the local prevalence of encephalitis lethargica.

Abortive, Mild or "Transient" Cases of Encephalitis lethargica.

The non-recognition of the mild infective cases may often account for the apparent sporadicity of the disease, and in the investigation of any outbreak of encephalitis lethargica it is very important to search for them. Few such cases were observed during the 1918 prevalence, but subsequently their occurrence has been more frequently and definitely established.

The symptoms presented by the mild cases are various. Usually the persons affected have been in contact with a declared case of encephalitis lethargica, and certain of them whose symptoms are restricted to soreness or dryness of the throat, naso-pharyngeal catarrh, headache, vomiting, or diarrhœa can only be recognised by this association. Other patients display mild manifestations of the symptoms seen in the prodromal period of the disease—slight lethargy or stupor (which may or may not be present) mental apathy, headache, lack of facial expression. A short febrile interval may occur or there may be transient loss of vision, the pupils being dilated but insensitive to light, transient diplopia, transient facial paralysis or transient ptosis. No after-effects have been noticed.

ACTION BY THE MEDICAL OFFICER OF HEALTH.

Encephalitis lethargica was made compulsorily notifiable throughout England and Wales from 1st January, 1919. In present knowledge the action which Medical Officers of Health are able to take on receipt of notifications or on learning of suspected cases is necessarily limited. It is, however, important that it should proceed on the following lines :—

(*a*) Full determination of the associated conditions and any facts which may throw light on the epidemiology of the disease.

(*b*) Aiding in any practicable pathological investigation and in obtaining material for the purpose.
(*c*) Aiding in securing the treatment of the case in hospital or otherwise.
(*d*) Enjoining the precautions required in the case of a disease apparently capable of transmission from person to person, especially through mild or abortive cases capable of carrying infection

Enquiry into Reported Cases.

Enquiry into associated conditions and facts will be facilitated by the use of the forms which are sent from the Ministry to Medical Officers of Health in all districts from which the disease has been notified. These enquiries should be made as far as possible in consultation with the medical practitioner who has reported the case or seen it at the patient's home. The enquiry form should be completed and returned to the Ministry as soon as possible as comparison of the report with others may reveal unsuspected connection between cases in different districts and suggest other lines on which the Central Health Department may be able to render assistance.

The Ministry is prepared for the present to examine specimens of cerebrospinal fluid (see above) from cases or suspected cases of encephalitis lethargica. The fluid should be withdrawn under strictly aseptic conditions, placed in a thoroughly sterilised bottle free from disinfectants, and forwarded in accordance with the regulations of the Post Office to the Medical Officer (Med.1), Ministry of Health, with particulars or reference to reports already sent.

Medical Officers of Health are invited to take any action which they consider useful and practicable to secure post mortem and pathological examinations by skilled workers who are investigating the disease.

Hospital and Nursing Facilities.

In view of the severity of the disease and the importance of good nursing, it is important to secure hospital treatment as far as possible. The isolation hospitals of local authorities should be available for this purpose.

Any public nursing arrangements possessed by or arranged with the Authority should be made available for cases treated at home.

Precautions against Infection.

The other occupants of a house in which a case of encephalitis has occurred or is being treated, may be assured that the disease is one of low infectivity, and that very slight risk is run by association with the patient. At the same time it

is desirable that such association should be limited to what is necessary for proper care and nursing, and the patient should be well isolated in a separate room.

School children in the affected household may be kept from school, as a precautionary measure, for three weeks after the isolation of the patient. There is no necessity to place restriction on the movements of other occupants provided they are frequently examined and remain well. Those in contact with the case, however, should be advised to use antiseptic nasal sprays or douches, and to gargle the throat with solutions such as those advised for influenza.

For example, any of the following :—

(1) One per cent. solution of peroxide of hydrogen.
(2) A solution of permanganate of potash, 1 in 5,000, in 0·8 per cent. solution of chloride of sodium (common salt).
(3) Liquor sodæ chlorinatæ, 0·5 per cent.

These solutions can be used as ordinary throat gargles or snuffed up the nostrils, or applied by an efficient spray.

Any persons in the infected household who suffer from sore throat or other symptoms suggesting an abortive attack should be treated from this point of view and isolated as far as possible until they have recovered.

The sick room should be thoroughly cleansed and disinfected at the end of the illness.

MINISTRY OF HEALTH,
WHITEHALL, S.W. 1.
February, 1921.

Printed under the authority of His Majesty's Stationery Office
By Sir Joseph Causton & Sons, Limited, 9, Eastcheap, London, E.C. 3.