POST-VACCINAL ENCEPHALITIS.

REPORT OF THE LEAGUE OF NATIONS COMMISSION.

An important session of the Health Organisation of the League of Nations was held at Geneva from August 22nd to 25th. The report of the proceedings has recently been issued by Prof. Leonardo da Lungo, Head of the General of Public Health Services, Lisbon, president, and those present were:

Members of the Health Committee: Sir George Buchanan, Senior Medical Officer, Ministry of Health, London; Dr. H. Camus, Director of the Federal Health Service, Berne; Dr. N. M. Josephus Jitta, President of the Health Council of the Netherlands, The Hague; Dr. György, Professor of Hygiene, University of Budapest; Dr. W. R. Ropers, Director of the State Serological Institute, Utrecht; Dr. F. R. Blaxall, Government Lymph Establishment, London; Prof. M. Camus, Director of the Superior Institute of Vaccine, Academy of Medicine, Paris; Prof. Dr. H. A. Gins, Robert Koch Institute, Berlin; Dr. H. Mervyn Gordon, St. Bartholomew's Hospital and Medical Research Council, London; A. Groth, Landesimpfanstalt, Munich; Prof. G. Sobernheim, Director of the Health Institute of the University, Berne.

The questions considered by the Commission were post-vaccinal encephalitis, and the preservation and preparation of vaccine lymphe. The third subject on the agenda was the relationship between the different types of small-pox virus and those of certain human and animal pathogenic viruses, but it was decided to postpone discussion until the problem had been further examined.

A preliminary discussion on post-vaccinal encephalitis by a subcommittee led to the framing of a report which was adopted by the Commission and is summarised below.

Terminology.—The term “post-vaccinal encephalitis” is used in the report for convenience, without necessarily implying that “post-vaccinal” is considered the equivalent of “propter-vaccinal.” Some observers, however, have defined post-vaccinal encephalitis morbillinum, and other workers have considered it as a complication of small-pox itself. The disease has no connexion with vaccination, but it may well be supposed that occasionally persons who have been recently vaccinated might be attacked by it, as a matter of chance, like any others. The same consideration applies to the coincidence between vaccination and attacks of epidemic poliomyelitis. Such rare coincidences, however, do not constitute “post-vaccinal encephalitis” now under consideration. Encephalitis may occur as a complication of numerous infections, such as measles, or various forms of toxaemia, and it occurs, though rarely, as a complication of small-pox itself. It would be permissible clinically, and perhaps also pathologically, to group all such encephalitis under a single term, encephalitis post-infectionem. Vaccination is an infection, and it is not implied that post-vaccinal encephalitis is not capable of being missed and, attributed to, the same ultimate causes as “encephalitis post-infectionem,” although there are practical reasons for considering it separately and by a separate name at the present time.

Cases in the Netherlands and in England and Wales.

The post-vaccinal encephalitis with which the report deals has become a problem of itself mainly in consequence of the reports of the last few years in the Netherlands and England and Wales. In each of these countries the cases which have occurred have been sufficiently numerous and similar to require them to be dealt with collectively. Their occurrence has led to the realisation that a new, or at least a previously unsuspected or unrecognised, risk attaches to the practice of vaccination. This risk, when taken at its maximum value, is minute in proportion to the vast numbers of normal vaccinations to which the cases of post-vaccinal encephalitis correspond, and it is easy to exaggerate its importance. Nevertheless, it is one whose existence, in these two countries at any rate, requires to be considered. In fact, it has in the Netherlands been considered of sufficient gravity to cause the temporary suspension of the administrative measures by which the vaccination of children is secured, while in England the subject has already received the attention of two expert committees appointed by the Ministry of Health, the second of which (the Rolleston Committee) has now presented a comprehensive report, examining the reformatory measures recommended by the first or Andrews Committee, whose work was described to the Health Commission of the League of Nations in 1926.

In the Netherlands, 139 cases of disease of the central nervous system following vaccination were described during 1923 to 1927, of which 41 died. In England and Wales, taking the arbitrary periods dealt with respectively by the Andrews and Rolleston Committees, 92 cases with 36 deaths occurred between Nov. 14th, 1922, and Nov. 1st, 1923, while a further group of 40 cases occurred between Jan. 1st, 1924, and Sept. 30th, 1925. Of these 40 cases 15 were excluded by the Rolleston Committee on account of their doubtful nature, leaving for consideration 25 cases, of which 12 died. Between the first and second groups on this basis, the same, total of 47 cases occurred, 12 of which were fatal, for England and Wales during the two periods under investigation by these Committees.

The clinical characteristics of post-vaccinal encephalitis, as met with in both countries, are quoted from the Rolleston Committee report. Pathologically, the fatal cases have shown diffuse encephalomyelitis, the inflammation being mainly perivascular in type and often accompanied by oedema. The pathological changes in some instances resemble those found in acute disseminated sclerosis, and differ in essential respects from those met with in fatal epidemic encephalitis. The presence of the vaccinia virus in the brain tissue of certain of the fatal cases has also been definitely established. This fact, however, must be considered in the light of modern knowledge regarding the dissemination of this virus after vaccination. The brains were examined at a period after vaccination when it would be anticipated that the brains of many normal vaccinated persons, could they be tested, would equally yield the vaccinia virus.

Incubation period.—The period which usually elapses between vaccination and the onset of symptoms of encephalitis (the “incubation period”) is from 9 to 13 days. The Rolleston Committee found that, out of 125 cases collected from the British and Continental sources, the onset was between the tenth and fourteenth day after vaccination in 91, and the most favoured day was the eleventh.

Age-incidence.—In both countries post-vaccinal encephalitis has occurred more rarely in infants under the age of two years than in older children and adults.

During the four years 1924 to 1927 in the Netherlands 4 cases occurred among 120,124 vaccinations under the age of two years, as against 130 cases among 192,212 vaccinations between the ages of 3 and 12; in other words, 1 case to every 3,153 vaccinations at ages 0 to 2, and 1 case to every 3,555 vaccinations at ages 3 to 12. The vaccination law is based on the supposition that the vaccinia virus does not spread on the actual vaccinations performed; they are, therefore, an over rather than an under-estimation.

In England and Wales the proportion of the disease for older children has been equally notable, though figures comparable to the Dutch of vaccinations at ages are not obtainable. The vaccinations done by school vaccination are all under the age of ten, and the vaccination law of the country are normally limited to the vaccination of infants under two years. But in the English series of 87 cases of post-vaccinal encephalitis referred to above, those under two years of age were only 19, which is not in keeping with the fact that owing to the prevalence of small-pox, an exceptionally large number of school-children have been vaccinated who had escaped vaccination in infancy, and the


majority of the English post-vaccinal encephalitis cases have occurred among these school-children. Moreover, no occurrence of any case of the post-vaccinal encephalitis cases in both countries have occurred in children whose vaccination, to judge from all ordinary signs and cutaneous reactions, has run a normal course. No single method of vaccinating has yet, with any considerable success, been as effective as the practice of using minimal quantities of vaccine lymph has, up to the present, been so little followed, however, in the Netherlands or in England that it is not possible to accord this explanation to any case of encephalitis that has followed the use of this method.

Many different vaccine lymphs have been used to vaccinate the cases which developed encephalitis, and no one source of lymph has been proved to be more specially affected than any other. In these countries, the great majority of the population was vaccinated in infancy. But, on the other hand, there are certain countries in which, like the Netherlands and England and Wales, there are large populous areas in which vaccination has carried on a large scale for periods of all ages during the past four or five years without the occurrence of any post-vaccinal encephalitis. On the other hand, in certain rural districts, sometimes in quite small villages or rural communities, local vaccination has been attended by a relatively excessive proportion of encephalitis cases. Striking illustrations of this circumstance have been supplied in the Dutch reports.

Originally in the Netherlands the local distribution of post-vaccinal encephalitis showed a notable degree of correspondence with the local distribution of known cases of vaccinic encephalitis (encephalitis lethargica), but this correspondence has not been maintained in the later series of Dutch cases, and has never been established in any of the English series.

In no country other than the two under discussion has the appearance of post-vaccinal encephalitis been on any considerable scale, but cases of the same sort have been reported in 1922 from Portugal (1); in 1924 from Prague (8), from Switzerland (2), and Germany (3); in 1925 from Poland (2), and the United States (4); and in 1928 from British Guiana (1).

Research has so far failed to give any sufficient or generally accepted explanation of the cause or causes of post-vaccinal encephalitis. The questions whether the appearance of post-vaccinal encephalitis is to be explained by the habitual use of smaller doses of vaccine, or by the adoption of different methods of vaccination, are being studied in the countries specially affected. It is hoped, however, that the proposals, in the second part of this report, are in any case of extreme rarity, the Commission draws attention to the advantage which may result from practising primary vaccination at school age for the first time on account of the appearance of smallpox. It is in such instances that the establishment of the negative, after full inquiry and observation, would be of the greatest value as a control to the English and Dutch experience.

It is of the greatest importance that the facts of occurrence of cases to be brought to the notice of the Central Health Authority merely through the ordinary channels of infectious disease notification. This circumstance can be expected to introduce bias or accidental omissions on the part of the practitioner to connect the subsequent illness with previous vaccination, or to the fact that the doctor in attendance on the case during the nervous illness cannot have performed the vaccination. A further complication in the inquiry is the occurrence of transient cases, or cases with indefinite symptoms, which are readily considered by the practitioner to be due only to vaccination, but in which cardinal symptoms of the disease (temperature, vomiting, headache, and drowsiness) may each or all occur in course of normal vaccination in a young child.

The possible fallacies of a negative return from either a country or districts in a country are therefore very great, and a statement that cases of post-vaccinal encephalitis do not occur in a given locality can only be of value if made after most careful inquiry on the spot by a competent investigator, who has access to doctors, hospitals, schools, and all other sources of information in the area. Inquiries are to be made with a view to indicating a limited number of countries or regions which would be appropriate for such investigations.

Conclusions.

The facts and considerations which have been before the Small-pox and Vaccination Commission at its present session seem to permit the following conclusions :- (a) The foremost of these is the rarity of cases of post-vaccinal encephalitis in countries other than the Netherlands and England and Wales, tends to show that children between 3 and 13 years of age are particularly susceptible, whilst infancy and adult ages are almost wholly exempt. All observations point to the conclusion that the appearance of encephalitis is not connected either with particular strains of lymph or with particular accidents of lymph preparation. (d) Passing to the aetiologically special cases, the present view is that the virus of vaccinia of itself cannot be considered responsible for the supervision of encephalitis. Rather it has to be supposed that some unknown factor exists—possibly bacterial or a fellow-virus—which, by means of a reciprocal reaction, determines the occurrence of the accidents in question.

None of the facts considered in this report lead the Commission to the conclusion that there is reason for discontinuing the use of vaccination, which remains the most powerful weapon against small-pox that we possess.

In view of the circumstances associated with the occurrence of these accidents in countries other than the Netherlands and England and Wales, there is reason to suppose that the virus of vaccinia is not one in which mere coincidence between vaccination and encephalitis can be invoked; in other words, we are not dealing with a merely fortuitous occurrence. (c) In our present state of knowledge we must conclude that post-vaccinal encephalitis is a different disease from encephalitis lethargica. The conditions under which post-vaccinal encephalitis has manifested itself in the Netherlands and in England and Wales tend to show that children between 3 and 13 years of age are particularly susceptible, whilst infancy and adult ages are almost wholly exempt. All observations point to the conclusion that the appearance of encephalitis is not connected either with particular strains of lymph or with particular accidents of lymph preparation. (d) Passing to the aetiologically special cases, the present view is that the virus of vaccinia of itself cannot be considered responsible for the supervision of encephalitis. Rather it has to be supposed that some unknown factor exists—possibly bacterial or a fellow-virus—which, by means of a reciprocal reaction, determines the occurrence of the accidents in question.

None of the facts considered in this report lead the Commission to the conclusion that there is reason for discontinuing the use of vaccination, which remains the most powerful weapon against small-pox that we possess.