Observations
ON
**ENCEPHALITIS, POLIOENCEPHALITIS,
AND VACCINIAL ENCEPHALITIS**
IN CHILDREN*

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Acute diseases of the brain are not rare in children. Apart from epidemics, meningitis is more frequently seen than encephalitis, and tuberculous meningitis remains much the most common—occurring in my experience in a ratio of 6 to 1 to other acute cerebral lesions. With greater attention and better methods of diagnosis much is being brought to light about encephalitis, and undoubtedly many cases which were formerly called meningitis were really encephalitis. It had been recognized for a long time that encephalitis may occur in infants from the virus of poliomyelitis, and the recognition of epidemic encephalitis (lethargica) greatly helped to focus attention on the occurrence of encephalitis as distinct from meningitis. Encephalitic diseases show a distinct epidemic tendency, even vaccinal encephalitis being seemingly more prevalent at one time than another. Encephalitis may follow vaccinia, variola, varicella,² zoster, encephalitis lethargica, and poliomyelitis, all of which are virus diseases. It may, in addition, follow pertussis, mumps, rubella, and influenza—all diseases likely to be of virus origin.

The pathology of encephalitis is that of widespread and marked degeneration of ganglion cells, with vacuolation, neurophagy, areas of hyperaemia, and small haemorrhages. The virus reaches the nerve cells via the blood or the perineural lymph vessels, and the fluids which surround and protect the nerve tissues.¹ Inflammation and hyperaemia occur, with exudate, so that some nerve cells are put out of action temporarily by pressure. These have the power of recovery if pressure is removed, but those directly destroyed by the virus are irreplaceable. Virus diseases can cause encephalitis either by direct action or by activating a neurotropic virus. Most probably they act directly, because, taking vaccinia as an example, the virus of this disease has been demonstrated in the blood of a vaccinated person from the third to the tenth day after vaccination, and the onset of vaccinal encephalitis falls usually about the tenth to the thirteenth day. The more severe the general disease the greater is the likelihood of encephalitis. The virus diseases therefore, in all probability, cause a direct encephalitis. One could better understand a virus disease operating by activation of a neurotropic virus in the case of delayed primary vaccination, or of revaccination, because the older the child the greater the likelihood of an unsuspected and dormant lesion in the brain. Revaccination does cause encephalitis,³ but probably not so often as does primary vaccination. All virus diseases show a distinct tendency to a selective action on certain areas of the brain, but it is unlikely that each virus infection causing encephalitis is selective of area, and further experience is needed before we can decide the question.

VACCINIAL ENCEPHALITIS

The occurrence of encephalitis in relation to vaccination was described a long time ago, but its recent more frequent—and even epidemic—occurrence is of great interest and importance. Quite a number of cases have

been reported, especially in Holland, England, and Germany. Rolleston⁴ shows that out of 5½ million people vaccinated there were roughly 175 cases and 91 died. This is one case in 33,000 vaccinations and one death in 60,000. In Holland there were 146 cases, and the deaths were 1 in 5,000. It is curious how groups of cases are reported from some countries and not others. The lymph is not at fault, because in Holland the vaccine was brought in from several different countries. Nor is it due to the use of rabbits in the preparation of the lymph, because rabbit lymph has been used with no untoward results in Spain. The pathological changes are those of a severe disseminated encephalomyelitis, evidently caused by a neurotropic virus. This has been found in the blood and in the tissues in vaccinated persons, but not in the cerebro-spinal fluid, unless nervous symptoms have supervened. A serum from immune persons has an effect on the virus. The inflammation is therefore probably due to the specific virus of vaccinia. Thirty to forty per cent. of cases die three to ten days after onset, with necropsy findings of a severe generalized encephalitis. Convulsions are not infrequently seen and local palsies like hemiplegia may result, but the tendency is to a general cerebral distribution of the lesion.

In one case now under my care for eclampsia, vaccination was performed at 23 days old. On the second day after vaccination a pustule developed, followed by a very severe vaccinia. The symptoms of encephalitis began three weeks after vaccination, and were those of many slight generalized convulsions, a curious "semi-suppressed" hiccup, stupor, and other brain symptoms. Eclamptic attacks and some degree of mental disability have persisted.

The symptoms, which usually begin some ten to thirteen days after vaccination, are those of severe encephalitis of acute onset, with headache, fever, vomiting, drowsiness, retention of urine, constipation, and signs varying from convulsive irritation to flaccid paralysis. Spinal puncture shows fluid under pressure, with usually moderate cell increase of lymphocytes. The age of onset is interesting, as it is usually from 3 to 13 years. This indicates that vaccination should take place in infancy and at as early an age as possible. Revaccination is not so likely to cause encephalitis, though cases have been reported.⁵ Immunity from previous vaccination may have disappeared or a neurotropic virus may be activated.

Treatment.—If a case occurs every effort should be made to inject serum from an immune person, intrathecally if possible. Horder⁶ gave 5 c.cm. in his case intrathecally with very good results. Hekman⁶ records nine cases treated by intravenous injections of serum of the parents vaccinated at the same time, with good results. Encephalitis occurred in the proportion of 1 to 25,000 in 199,000 cases vaccinated under the age of 2 years, and in 1 to 3,570 of 660,000 vaccinated between 2 and 11 years old.⁷ It is therefore obvious that vaccination is advisable at the earliest age possible, when the infant may have some advantage from maternal immunity. If vaccination has to be undertaken at a late age, the risk of encephalitis (which is really very small) can be still further limited by using a dilute lymph, say 1 in 5, by giving a dose of convalescent serum at the same time as the vaccination, and by vaccinating in only one place, so that the patient can have the disease as mildly as possible. The inner side of the upper arm has been recommended as the most protected place, and a certain amount of rest when the disease is at its height is advantageous as in other illnesses.

POLIOENCEPHALITIS

This is an inflammation of the grey matter due usually to a specific virus, which reaches the brain via the perineural lymphatics from the nose and throat, or possibly,

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from the gastro-intestinal tract. The trachea and bronchi are possible areas also, but polioencephalitis tends to occur in the dry, dusty autumn, and not as much in the winter and spring, when chest diseases are common. In a typical attack the child may have prodromal pharyngeal catarrh and fever and vomiting. Then follow symptoms of an acute brain lesion, with a moderately raised temperature, headache, retraction, and perhaps coma, or at least stupor. There is, however, much less tendency to stupor in encephalitis than in meningitis. In addition, there may be neuritic pains, the pain making the child apprehensive of movement. There is cerebral irritation in both diseases, but the irritative apprehensive state of encephalitis is to be distinguished from the irritative stuporose state of meningitis. Lumbar puncture shows increased pressure, with, as a rule, a clear cerebrospinal fluid, negative for micro-organisms and showing only moderate cell increase; albumin may be increased, but sugar and chlorides remain normal. Sometimes the cell increase is very great, and is highly suggestive of tuberculous meningitis. The virus is present in dust of rooms inhabited by infected persons, and resists drying and sunlight, so that even the dust of the roads may be infective—in fact, epidemics seem to spread along the high-roads and occur in the early autumn. Carriers are probably numerous during epidemics, in the form of those who are in the catarrhal stage of an abortive attack with no paralysis. Such an attack is mistaken for a "cold." The incubation period is most commonly five to eight days, but may vary on either side of these figures. Children who are having an attack are infectious, but not strongly so. The disease does not often spread in a ward, and attendants rarely catch it. A carrier—that is, a child or person who has the virus present (perhaps intermittently) in his nose and throat—may start an epidemic. It is my opinion that some of the children who have had infantile paralysis may become periodically infective. This would explain the steady stream of sporadic cases. A case with two recurrent attacks of poliomyelitis is reported by Peremans.⁸ Instances of infection of several members of a family are not very rare, but much rarer than one would anticipate, except perhaps in epidemics. The following case is of interest in this connexion.

H. W., aged 3 years and 8 months, was attended as a case of acute infantile paralysis recovering. He was seen in September, 1913, and had begun to be ill on July 16th. His twin brother was affected on July 17th, and died on July 20th, after a feverish illness, with mucus in the bronchi and furred tongue. Death was sudden and due to collapse. An elder brother, aged 7, began on July 15th with headache and a feverish cold, followed by paralysis with sudden collapse and death on July 17th.

Food does not appear to be so infective as does dust. Poliomyelitis occurs in hot, dry (fly) weather, and once the stable-fly (*Stomoxys calcitrans*) was under suspicion. It is a fly quite unlike the horse-fly, and like the house-fly in shape and size, but with black-and-white body stripes. Its mode of attack is by puncture and drawing blood. It may do so through a thick sock. It is not likely to be a carrier, because the virus is not transmitted by the blood stream. Domestic animals might be carriers. Bruno⁹ and Lovett and Sheppard¹⁰ reported on epidemics affecting human beings and animals. Cleland¹¹ reported the conveyance of the virus of human acute infective polio-encephalitis-myelitis occurring in Australia to monkeys, sheep, a calf, and a foal.

Treatment.—General preventive measures are suggested by the study of epidemics, and have been already indicated in the discussion on causation. They include prompt isolation of actual cases and of possible carriers, the avoidance of dust from infected rooms or neighbourhoods, care with domestic animals, and other precautions. Local preven-

tive measures, such as douching of mucous membranes, unless they have an astringent action, are to my mind ineffective, and may lead to a chronic inflammatory state. A healthy undouched nose is possibly more antagonistic to infective agents than is a healthy douched one.

We can attack the virus and prevent the spread of destruction of the nerve cells by injection intrathecally and intravenously of 20 to 50 c.cm. of convalescent serum from a person who has had the disease. Convalescent serum has been used extensively in Australia.¹² It is not very easy to obtain. The need for the Wassermann test is one difficulty, the keeping of the serum another. Again, it is usually wanted urgently and in large quantities, but only at infrequent intervals and seasons. It is, of course, best kept in the veins of the convalescent, but as such is not so readily available. One plan is to keep at a children's hospital a regular supply obtained from cases which have recovered from infantile paralysis and have been Wassermann-tested. Other active measures may include the use of 10 to 15 grains of hexamine four-hourly and symptomatic treatment. It is extremely important to protect neurones and to prevent undue spread by promoting rest. A glance at the pathology of the disease shows this. Nerve cells surrounding those destroyed, or about to be destroyed, are temporarily put out of action by pressure of exudates. Rest will perhaps save them, and haemorrhages may be prevented. I have been struck by the fact that a long journey by train or motor has preceded some of my severe cases of infantile paralysis. One, a girl who died of an acute ascending type, had made a long train journey just before. Another, a boy with severe symptoms, had ridden a long way with his father in a motor car. In both cases the infection had probably taken place some days before the ride, but the shaking of the long journey may have transformed what might have been a mild case into a severe one. Rest, immediate and prolonged, is therefore of first importance in the early stages. Medical examinations should be as few as possible, the room should be quietened and darkened, sedatives should be given as soon as the diagnosis is established, and journeys undertaken only when absolutely necessary. Nature may aid us in the worst cases by plunging the child into unconsciousness which, though often a precursor of death, may be salutary. I have known patients remain unconscious for many weeks and yet recover. In such cases the disturbance of lumbar puncture must be avoided whenever possible. Cooling applications to the head may soothe. Irritative symptoms must be controlled by bromides or luminal. Some cases need nasal feeding. Orthopaedic rest appliances, like plaster beds or splints, are to be used if necessary.

EPIDEMIC ENCEPHALITIS (LETHARGICA)

There may be coma in the severe cases, but most show the peculiar sleepy lethargy which has given the name to the disease. Headache is as a rule very persistent, and another characteristic sign, diplopia, is often not mentioned by the child unless special inquiry is made as to its presence. Persistent hiccup may be an early sign. Myoclonic and paretic cases occur, while on the other hand some cases may be so slight that they are ambulatory, with only lassitude and drowsiness. Sequelae of the disease are common, and take the form of irritability, debility, and sleeplessness at night, when the child may whistle, or sing, or be up and doing until the early hours. Some have asthmatic attacks, some become mentally unbalanced as regards morals, and some may develop Parkinsonism. These peculiarities seem to indicate that the disease is a special form of encephalitis. The disease was becoming common, but has been less frequent lately. When epidemics occur it is very infectious, and cases may arise at any age, even in early

infancy. Not many cases make a complete recovery from a severe attack. Robb¹³ gives the proportion as 8.8 per cent., but a certain percentage more had only a slight change mentally and nervously. However, a large proportion of cases which have encephalitis lethargica are permanently and severely damaged.

Pathologically there may be no naked-eye lesions. In the acute stage microscopical lesions are diffuse, and tend to be in the basal nuclei, the cerebrum, and mid-brain, especially the latter. Occasionally they are in the cortex cerebri, pons, medulla, and posterior cornua of the cord. They are not in the anterior cornua. Later the typical cuffing appearance is seen round the perivascular lymphatic spaces. There is a similarity between the distemper and epidemic encephalitis. This is discussed by Pugh¹⁴ and in articles in the *Lancet*.¹⁵ In the distemper cases there was sleepiness, hiccup, and ocular palsies, and there were similar "cuff" lesions in the brain. This is an argument in favour of the encephalitis syndrome being caused by more than one virus, and might even support the idea that encephalitis lethargica is really a variety of influenza.

Treatment consists in alleviating distress, providing rest to the nervous tissues, and aiding the elimination of toxins. Lumbar puncture may relieve pressure, and various chemical drugs can be given intravenously. Belladonna and hyoscine may be useful in the later stages, and for sequelae, but they are not so important for the acute stages. For sequelae trypan-blue is the latest drug recommended.¹⁶ Vaccines have been tried,¹⁷ and the serum of convalescents is, as with other virus diseases, perhaps the most likely method of affording some immediate action on the disease and its acute stages. Up to the present, however, this does not appear to have been tried to any extent.

EXANTHEMATAL ENCEPHALITIS

This may follow an acute infectious disease, especially measles. Encephalitis of measles is often severe in effect at first, but tends to clear up and leave no bad effects.

One patient of mine, a child of 8 years, developed encephalitis after measles. She became unconscious, had a high temperature, and a cerebro-spinal fluid under pressure, but with only a very moderate cell increase. The optic disks were normal, and there were no signs of other disease. She remained "blind" and semiconscious for some seven or eight days, and then slowly improved and made a complete recovery.

Pathologically there are perivascular zones of demyelination in the brain and cord in fatal cases, and the lesion is very like that of vaccinia encephalitis.¹⁸ Measles does not seem to produce such severe after-effects as do the neurotropic virus diseases. It may not be a true inflammatory process, but rather a toxic condition. Acute toxic encephalitis may occur in diphtheria.¹⁹

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TREATMENT OF CARCINOMA OF THE BREAST BY RADIUM EMANATION

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In writing on any form of radium treatment at the present time one is faced by the dilemma that either one's conclusions are premature or one's methods are out of date. It is, however, only by the accurate record of new technical methods and of their results that progress can be made, and even a small group of cases of the same class treated by the same methods and carefully watched is of definite value. From this point of view the small group of fifty-two cases of carcinoma of the breast here recorded is of interest, since all the cases were treated with very nearly the same technique, radon seeds, and over a period of three years up to one year ago, more recent cases having been excluded.

The technical advantages of seeds over needles are very obvious to those who have used the former. Yet in this country they have scarcely received the recognition which they deserve, while on the Continent they are almost ignored. It is asserted by those who have not used them that they cannot be introduced with accuracy, and that they act for too short a time to be effective. With proper apparatus, however, almost mathematical accuracy can be obtained, and the results here recorded are at least evidence of their effectiveness. It will, of course, be many years before sufficient evidence is accumulated to show whether irradiation or amputation gives the best results, and it is possible that both may be replaced by beam radiation with large quantities of radium or by some other form of treatment. At present, however, it would seem to be useful to place on record the results which have been obtained by a uniform and systematic technique.

The technique which I now adopt has been slightly modified from that which I described three years ago in an article on the use of radon seeds (*British Medical Journal*, August 23rd, 1930). Radon seeds are implanted into the tissues beneath the breast in such a manner that the whole of the breast and its lymphatic drainage is exposed to a uniform radiation sufficient to destroy any carcinoma cells whether in the tumour, in the breast, or in the lymphatics. The seeds are introduced by means of a special introducer described in the article mentioned, and consisting essentially of a long hollow needle and a rotating barrel, which holds the seeds. The seeds can be introduced to any depth and planted in long columns. Both the columns and the seeds in each column can be accurately spaced from one another; this is of vital importance, as otherwise some portion of the suspected tissues may escape irradiation. About 100 seeds may be introduced, each containing 0.5 to 1 millicurie, the precise amount varying with the dimensions of the breast, and the bulk of the seeds will lie in the fascia covering the pectoralis major. Through a single puncture it is quite possible, by displacing the skin, to insert four parallel rows of seeds in the fascia beneath the tumour. Through a second puncture another group can be inserted in the same situation, but in lines at right angles to the first,