meningeal symptom developed paralysis which was usually very severe. (Case 22 was excluded from these tables.)

Summary

Forty-four patients convalescent from poliomyelitis, who were old enough to describe their symptoms, were questioned at length regarding their early symptoms and also the amount of physical activity during the early days of the disease.

The so-called meningitic symptoms appear in nearly all cases during the pre-paralytic stage of the disease and are of great value in diagnosis. These symptoms are often more suggestive of involvement of nerve roots than of meninges. They consist of pain in the head, neck, dorsal, lumbar, or sacral spine, scapular region, thighs, or the lower chest.

The meningitic symptoms may be slight or severe. At their onset the patient may be afebrile and may feel quite well.

The meningitic symptoms may abate and the patient feel better shortly before paralysis develops.

Physical activity of any kind during the pre-paralytic stage increases the danger of severe paralysis.

Complete physical rest in bed during the whole of the pre-paralytic stage seems to protect the patient from severe paralysis.

This study would never have been attempted but for the encouragement given by Dr. Allan McFarlan. I am particularly indebted to Dr. P. M. Daniel for helpful criticism, and to the following for access to cases under their care: Dr. H. C. Jennings, Oxford; Dr. W. H. Kelleher, London; Dr. A. Joe, Edinburgh; Dr. L. Guttman, Stoke Mandeville Hospital; and the Medical Superintendent of Monsall Hospital, Manchester.

NOTE.—Case records giving the details required for this study will be welcomed for further analysis.

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POLIOMYELITIS AND POLIO- ENCEPHALITIS

THE CASE FOR A REVIEW OF TERMINOLOGY

BY

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From studies of clinical reports on cases notified as poliomyelitis and polio-encephalitis during the present epidemic it is evident that value can be obtained from a review of the varied manifestations of this disease, and an attempt made to correlate them into a reasonable clinical classification. As a result of this review certain recommendations are put forward.

Illness of Infection.—The existence of a true illness of infection is now accepted. This usually takes the form of mild fever and headache, with or without a nasopharyngitis, lasting one to two days, or of gastro-enteritis. Its onset probably occurs one to four days after the infection. Cases have been described in which the patients suffer from this initial illness but do not subsequently develop paralysis. Such cases are recognizable only among contacts of poliomyelitis during the course of an epidemic or unusual pre-

valence. It is impossible, in the state of our present knowledge, to estimate the proportion of persons who have an illness of infection, but it may well be very large, and it is unknown as yet whether they assist in the spread of the disease as temporary carriers; such a possibility, however, must be entertained.

Incubation Period of Recognizable Poliomyelitis.—This is normally seven to 14 days, but there are outside limits of two days to 25 days, although it has been recorded that the virus was discovered in the stool of a person who developed clinical signs 19 days later. A few cases are on record of patients suffering vague signs and symptoms, persisting throughout the whole of the incubation period from the illness of infection—tingling in a muscle or muscle group, restlessness at night, listlessness, or vague signs of being off colour (Gartside, 1947).

Proposed Classification.—The subsequent progress of the disease may follow different courses. Clinically each case may be put into one of the following two categories: (1) non-paralytic poliomyelitis—(a) subclinical and (b) clinical; (2) paralytic poliomyelitis—(a) spinal, (b) bulbar, and (c) bulbo-spinal. In this classification—a clinical one—it will be noted that the term “abortive” has not been included in the types of disease. It is thought better to discontinue the use of this term, as “abortive” encourages a wrong concept of the disease. What have been called abortive cases—like the subclinical cases (see below)—are true infections with the poliomyelitis virus, and as such, particularly when it is appreciated that these two types form by far the greatest number of cases in an epidemic, have an equal if not more important role in the spread of the disease than the paralysed case, whose activities are necessarily restricted by virtue of the illness. Abortive cases should be termed “non-paralytic poliomyelitis,” as there is no difference in the initial symptoms and signs of this type and those cases which go on to paralysis.

Non-paralytic Poliomyelitis

Subclinical Poliomyelitis

In 1945 a team of workers in Chicago made a detailed study of 22 children after a known exposure to a case of poliomyelitis (Casey, 1946); 14 had a febrile illness between seven and 25 days after exposure. No comparable illness occurred in a group of 15 children, not so exposed, who lived near by. Among the 14 children who developed fever one had frank poliomyelitis; two had frank poliomyelitis without paralysis but with stiff neck, stiff back, head-drop, and increased cells and protein in the cerebrospinal fluid; four had fever and mild symptoms without stiffness in back or neck, or paralysis, but two of these gave a cerebrospinal-fluid protein above 45 mg. The other seven children (the subclinical group) had axillary temperatures between 98.8° and 99.8° F. (37.1° and 37.7° C.), but seemed to have no symptoms; four of these, on lumbar puncture, gave protein figures of 45 mg. or more. Stool examinations revealed the presence of the virus just before or at the onset of the symptoms among most of the contacts with fever.

Though the figures are small, and further investigation is necessary, it does seem to indicate that poliomyelitis, during an increased incidence of the disease, is a mild, widespread, highly communicable disease particularly of young children, leaving no paralysis. It is impossible to state just how widespread is the dispersion of the virus, but it can with confidence be said that it is very considerable.

Clinical Poliomyelitis

It is felt that undue stress has been laid on the term “prodromal stage” or prodromal signs and symptoms, with the tendency to regard those cases which do not progress

beyond this stage as abortive cases, but the production of any prodromata is dependent on the virus having already gained entry to the body and on its producing its effect, so that, strictly speaking, there is no true prodromal illness, unless one regards the illness of infection as such.

In those cases in which symptoms referable to a prodromal period are present the virus has already gained a footing, but its action is slowed down, and instead of producing a clinical paralysis as a presenting sign it causes other effects referable to the central nervous system.

To indicate the march of the virus in the central nervous system after its invasion Faber (1933) describes the clinical features of the early stages of the disease as occurring in two phases.

Phase 1.—Drowsiness or restlessness and listlessness or irritability, mild fever, inversion of sleep rhythm, possibly vomiting, anorexia, and constipation. It is suggested that these symptoms are explicable by a subcortical origin in the thalamus or hypothalamus probably due to involvement of the brain stem or basal nuclei. Many cases do not progress any further than this stage, and recover rapidly and completely.

Phase 2.—Thalamic and hypothalamic symptoms persist, but the virus spreads to the posterior columns and root ganglia, producing sensory symptoms—neck stiffness, increased reflexes, muscular ataxia and tremors, muscle spasm, and spontaneous pains in muscles when the patient is touched or even approached.

In many cases the symptoms produced by phases 1 and 2 merge gradually one into the other, but often they are separated by a distinct interval with complete abatement of symptoms ("dromedary" cases). The severity of these early signs and symptoms bears no relation to the extent or degree of the ensuing paralysis or to the subsequent course of the disease.

The disease may halt at the end of these two phases and complete recovery take place. These are the true non-paralytic cases. If the early signs and symptoms were mild such cases were usually labelled "abortive"—i.e., abortive only in reference to the non-production of paralysis—but are nevertheless overt cases of infection by the virus.

Support for this concept of the disease, postulating some degree of general infection with a progressive invasion of the central nervous system, is given by Bodian (1947), who advances the theory, supported by neuropathological evidence, that every case of poliomyelitis has demonstrable pathological lesions in the brain.

The virus has been demonstrated in mesenteric and cervical lymph nodes and in the abdominal sympathetic plexus. Should further advances in laboratory technique simplify the demonstration of the virus it is a matter for speculation whether it will be discovered regularly in the blood and parenchymatous organs generally throughout the body. Such a possibility cannot be excluded on the existing evidence.

Lumbar Puncture

In this epidemic it has been the experience of many clinicians that changes have been discovered in the cerebrospinal fluid in the early stages of the disease—in some cases when the diagnosis was doubted and the clinical signs and symptoms of central nervous system involvement were minimal or absent. Fluids taken early tend to show a moderately increased cell count. Polymorphonuclear cells may amount to 90% of the total, but most specimens show lymphocytes and mononuclear cells almost exclusively. A slight rise in the protein content may or may not be found. The pressure is not often raised, but negative findings in the cerebrospinal fluid in the early stages do not necessarily exclude a diagnosis of poliomyelitis. Paralysis not infrequently develops later, after such a report has been obtained. The findings of Casey *et al.* (1946), described

under the heading of subclinical poliomyelitis, illustrate that changes are produced in the cerebrospinal fluid in a large number of persons who have been contacts of the disease in the presence of an epidemic or increased incidence of poliomyelitis.

Lumbar puncture is a valuable diagnostic aid in subclinical and non-paralytic cases, but should be carried out only after deciding that a degree of urgency to establish the diagnosis exists, because some clinicians believe that unnecessary manipulation of a poliomyelitis patient may increase the extent of the paralysis, should it occur, and lengthen convalescence.

Polio-encephalitis

From a study of the clinical reports on cases that have occurred in this epidemic it is obvious that many of those which have shown signs and symptoms of non-paralytic poliomyelitis—i.e., in one or both of the phases described by Faber—have been notified as polio-encephalitis. Other clinicians have based the diagnosis of polio-encephalitis solely on the production of cranial-nerve palsies—on the basis that the pathological lesion is within the skull. It is obvious that no single clear clinical picture of what constitutes polio-encephalitis is universally accepted.

In 1912, under the original Notification Order, it was not thought necessary to refer specially to acute polio-encephalitis—as the generic term "poliomyelitis" was comprehensive enough to cover all cases of the illness, including those in which cerebral symptoms predominated. In 1919, when cases of the then obscure encephalitis lethargica began to appear, it was decided to supplement the Regulations of 1912 and to require the separate notification of polio-encephalitis. This was to allow a differentiation between the incidence of the two diseases.

In 1919 the ratio of polio-encephalitis notifications to poliomyelitis was 1:10 (56:539). The comparative ratio for 1947 up to the end of October was 1:12 (587:7,438). This leads to the assumption that there has been neither any great variation in the number of cases exhibiting cerebral symptoms nor of the criteria adopted by practitioners in making the diagnosis polio-encephalitis; but confusion does exist, and must continue to exist so long as symptoms referable to one stage of a disease are singled out as a requirement for a separate notification. It is more paradoxical in the light of recent literature, which tends to show that in all cases of poliomyelitis pathological lesions can be demonstrated in the brain. It is therefore illogical to require the separate notification of polio-encephalitis.

Paralytic Poliomyelitis

As suggested above, cases which develop a lower motor neurone lesion may adequately be classified as (a) spinal type, (b) bulbar type, (c) bulbo-spinal type.

In the majority of cases in which paralysis occurs the virus exerts a selective action on the anterior horn cells of the lumbar and cervical enlargements of the spinal cord (the spinal type). In many cases signs of involvement of the cranial nerves appear either alone (bulbar type) or combined with peripheral nerve lesions (bulbo-spinal type). Because the bulbo-spinal cases form a large proportion of all clinical cases it is convenient to recognize them as a clinical group. These include all cases of paralysis in limbs, diaphragm, intercostals, abdominal muscles and neck and back muscles, and of the cranial nerves—all lower motor neurone lesions.

In 1885 Strümpell (quoted from Peabody *et al.*, 1912) described cases for which he used the term "polio-encephalitis." The onset was sudden, with fever, vomiting, and convulsions; after this the child (24 cases—all under

6 years of age, and 19 below the age of 4) developed a hemiplegia. Occasionally a monoplegia, or even an ataxia without paralysis, was noted. There was no atrophy or wasting of the muscles. Athetosis and disturbances of speech and intelligence were sometimes sequelae. Other similar cases of this type with spastic paralysis have occasionally been recorded in medical literature. These cases, presuming that they were true cases of poliomyelitis, could be accurately termed of cerebral type, with the site of the lesion in the motor cortex. It is possible that a true cerebral type exhibiting an upper motor neurone lesion will eventually be a recognized clinical type occurring in poliomyelitis, although Bodian (1946) produces evidence for the cerebral origin of spasticity in poliomyelitis in monkeys without lesions in the cord. It is wiser not to include this cerebral type until it is generally accepted that upper motor neurone lesions can be produced in monkeys and that the virus can be isolated from lesions producing these symptoms in man, and to restrict the clinical types of paralytic poliomyelitis for classification to bulbo-spinal, which category will include all cases producing signs of bulbar paralysis or of spinal paralysis alone, or both combined.

Notification

Under existing regulations poliomyelitis is notifiable to the Registrar-General as poliomyelitis or polio-encephalitis. It would be an advance if the regulation making the separate notification of polio-encephalitis as distinct from poliomyelitis was superseded by one reverting once more to the generic term "poliomyelitis," which is to be used as a synonym for polio-encephalomyelitis. And if, in the future, poliomyelitis infections were to be classified as (a) poliomyelitis, non-paralytic, (b) poliomyelitis, paralytic, great assistance would be given to the medical officer of health and other epidemiologists in whose hands lies the responsibility for the control of epidemics in general and of preventing further cases of poliomyelitis in particular. The further division of non-paralytic cases into subclinical and clinical varieties has no place in an essentially administrative procedure like notification, but the information it would reveal would be invaluable in field investigations, were it easily available.

Summary

The essential importance of the subclinical case and the mild non-paralytic case in the spread of the disease is demonstrated.

The concept that the diagnosis should take into account the signs and symptoms of involvement of the central nervous system other than paralysis is stressed.

The problem of the diagnosis of polio-encephalitis is discussed, and as a result a proposal is made to supersede the regulation requiring the notification of polio-encephalitis as a separate clinical entity and to revert to the single generic term "poliomyelitis" (syn. polio-encephalomyelitis).

The use of the term "abortive" is discussed, and a suggestion made that if further differential notification is desired the classification should be non-paralytic and paralytic.

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DIFFERENTIAL DIAGNOSIS OF JAUNDICE BY FLOCCULATION TESTS

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The differentiation of jaundice due to obstruction of the larger ducts from that of hepatic origin is sometimes very difficult, particularly in patients over 40 years old. The van den Bergh test—a qualitative reaction—has proved of little value for this purpose, and many other tests of hepatic function have been tried singly and in combination. From the published reports of this work one or other of the flocculation tests would seem to be the best single diagnostic procedure, and they also have the advantage of being simple to carry out and requiring only small amounts of serum. Their chief disadvantage is that positive reactions occur in a small proportion of patients without evidence of hepatic disease.

These tests are more popular in the U.S.A., and although they have been used in this country, particularly by MacLagan (1944a, 1944b, 1947) and by Dick (1945) and Maizels (1946), it appears from comment in a leading article (*Lancet*, 1946) that their application is still not widely appreciated here. For that reason this report on the results obtained with the cephalin-cholesterol flocculation and serum-colloidal-gold tests has been drawn up.

The cephalin-cholesterol flocculation test was introduced by Hanger (1939) as an empirical procedure. Later work with electrophoresis showed that in parenchymatous disease of the liver there was an increase of the gamma fraction of the plasma globulin and a decrease of albumin. From the results of experiments *in vitro* Moore and his co-workers (1945) attributed flocculation of cephalin-cholesterol emulsion and also the precipitation of colloidal gold to these changes; Gray (1940) introduced the latter test. Positive results are reported commonly in hepatic and rarely in obstructive jaundice, and the tests are accordingly claimed to be useful in the differential diagnosis of these two conditions.

Material and Technique

Our intentions in this investigation were to determine the value of two flocculation tests in jaundice, to establish that negative results were the rule in normal subjects, and to observe the results of the tests on patients without clinical evidence of hepatic disease. Accordingly observations were made on 110 patients with diseases of the liver, of whom 74 showed jaundice, on 100 controls drawn from donors of blood, and on 281 patients who suffered from a variety of conditions but showed no clinical evidence of hepatic disease. Both tests were carried out on the same sample of serum from each of the 491 subjects tested.

Cephalin-Cholesterol Flocculation Test.—The method and the technique for the preparation of the emulsion were those of Hanger (1939). The cephalin was used immediately, without a period of storage, to make the stock emulsion. This showed no change in sensitivity when kept as long as three months in a refrigerator, as Dick (1945) has recorded. The test was read at 24 hours.

Colloidal-Gold Reaction.—The method was that of MacLagan (1944a). The gold sol was made according to the method of Mellanby and Anwyl-Davies (1923).

In order that the superannuation scheme under the National Health Service may function satisfactorily from the appointed day, the Ministry of Health has requested voluntary hospitals to supply relevant particulars of their employees. The scheme does not apply to medical schools attached to teaching hospitals.