monary metastases (Fig. 3). Treatment was immediately started with testosterone-propyl-propionate (100 mg. twice a week). In November a single attack of petit mal was reported. Early in December she became semiconscious and uncooperative, and was admitted on December 11. Examination revealed an incomplete left hemiplegia, a left upper neurone seventh-nerve paresis, a left eleventh-nerve weakness, and a left twelfth-nerve paresis. The diagnosis of a cerebral metastasis was in no doubt.

On December 13 bilateral oophorectomy and left adrenalectomy was done. No intraperitoneal or hepatic metastases were detected. She rapidly became worse, and the hemiplegia and the coma became complete. On December 20 right adrenalectomy was carried out. After the second stage the patient was desperately ill for two days with pulmonary oedema, but she recovered well. Her neurological state recovered remarkably rapidly and had returned to normal by January 4, 1956. A chest *x*-ray film (Fig. 4) on January 3 (fourteen days after the second stage of the operation) showed that the pulmonary metastases had almost resolved. She has remained very well up to the time of writing (September, 1956), nine months after operation.

Discussion

Bilateral gonadectomy and adrenalectomy has been done in over 300 patients with metastatic breast cancer in the five series mentioned above. Among all these only five have had involvement of the brain, of which three (including our two cases) have shown a worth-while response. While it would be foolish to draw hard-and-fast conclusions from so small a number, it appears that cerebral metastases may respond to hormone deprivation and will probably do so with the same order of frequency as metastases elsewhere. The special problem of cerebral metastasis is that the condition often becomes urgent. It is a morbid swelling within the rigid skull, and this fact should lead us to submit the patients to early surgery. Often a one-stage operation is to be preferred, as the patient will not improve until the intracranial mass begins to regress in size. We would regard this particular complication of breast cancer as a contraindication to androgen therapy, except perhaps for a short period pre-operatively.

Hypophysectomy or destruction of the hypophysis by radioactive methods, whatever its place may be in the treatment of the other manifestations of metastatic breast cancer, has no place in the palliation of cerebral metastases. R. Luft (1956, personal communication) states that Professor Olivecrona, of Stockholm, does not perform hypophysectomy if intracranial metastases are present.

Conclusions

The operation of bilateral gonadectomy and adrenalectomy is at present the only possible treatment of value for patients with intracranial metastases from cancer of the breast. It should be attempted when possible, because these patients are otherwise doomed. Two successful cases are reported above.

We thank Dr. C. Allan Birch for referring the second patient; and Dr. Stanley Rowbotham and Dr. Christine Ramsay for administering the anaesthetics. We are grateful to Mr. W. P. Greening for advice on the use of androgens and cortisone in Case 1. The photographic department of the Royal Marsden Hospital supplied prints of the *x*-ray films, which were taken by the diagnostic *x*-ray department of that hospital.

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POLIOMYELITIS IN SUBURBAN SURREY

CLINICAL AND EPIDEMIOLOGICAL OBSERVATIONS IN THE LIGHT OF VIRUS ISOLATION FROM FAECES

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In recent years the application of tissue-culture techniques on an ever-increasing scale has led to significant advances in our knowledge of virus infections generally, and especially poliomyelitis. The urgent need for more adequate facilities in this country for applying these methods to the clinical and epidemiological problems of poliomyelitis became the subject of much correspondence in the medical press during 1955. Between September 1 and December 31, 1955, virological study of a limited outbreak became possible in part of suburban Surrey. To a clinician and a medical officer of health previously without such assistance the information obtained has been of the greatest value, and it appears opportune to describe the findings.

The comparatively few studies which have been reported in this country relate to an attempt to estimate the value of quarantine in a small outbreak of poliomyelitis in East Anglia (Goffe and Parfitt, 1955), the general distribution of poliomyelitis virus types (Goffe, 1955), and the investigation of atypical disease resembling poliomyelitis (Acheson, 1954; Ramsay and O'Sullivan, 1956; Sumner, 1956).

The most extensive observations, however, have come from the United States and Canada. The value of virus isolation and antibody studies as an aid to clinical diagnosis was shown by workers from the Yale University School of Medicine (Godenne and Riordan, 1955). Detailed epidemiological and virological reports of a small winter outbreak in New York (Melnick *et al.*, 1956) and of a spring outbreak in Toronto (Beale *et al.*, 1956) have appeared. The extent of infection among contacts has been shown (Bodian and Paffenbarger, 1954; Horstmann *et al.*, 1955), and the general status of tissue-culture techniques in the isolation of poliomyelitis and other viruses has been summarized by Melnick (1955), Rhodes *et al.* (1955), and Enders (1955).

The investigation described here was conducted from the Tolworth Paediatric and Communicable Disease Unit of the Kingston Hospital Group, serving mainly the North-Central Division of the Surrey County Council, and virological investigations were carried out in the Virus Research Laboratory of Glaxo Laboratories Ltd., at Sefton Park. The North-Central Division of Surrey is a suburban and residential area with a population of about 200,000, with many of the inhabitants falling into the Registrar-General's social classes I, II, and III. There is a large daily movement of population

to and from central London. During the period of study the weather was noticeably dry and mild.

The original object of the investigation was to gain information about the characteristics of virus strains responsible for non-paralytic disease in the area, but the preliminary results were interesting enough to justify a more intensive study of paralytic disease as well. It was possible to investigate only virus isolation from the faeces of suspected cases of poliomyelitis and some of their contacts. The need for economy in tissue-culture facilities made it necessary to confine ourselves, in most instances, to the examination of a single specimen of faeces from each patient.

The incidence of notified poliomyelitis in the district was high compared with that of previous years, but in 1955 most cases occurred after September 1 (Fig. 1).

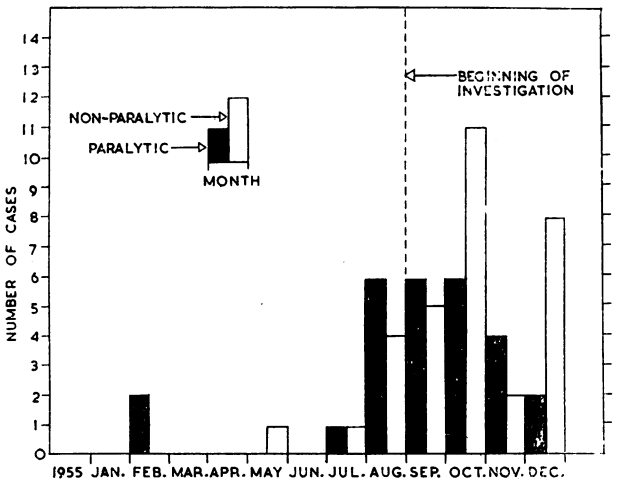

FIG. 1.—Seasonal incidence of poliomyelitis in the north central divisions of the Surrey County Council.

Poliomyelitis in Hospital

Clinical Aspects

During the period of investigation 84 patients suspected of having poliomyelitis were admitted to hospital. Faecal specimens from 66 were examined for poliomyelitis virus.

Non-paralytic poliomyelitis was diagnosed in the presence of a febrile illness, often diphasic, characterized by headache, sore throat, vomiting, painful stiffness of the neck and back, muscle pain, and a cellular reaction in the cerebrospinal fluid. Eighteen patients fell into this category. Twelve (66%) excreted poliomyelitis virus in the faeces (nine type 1 and three type 3), whereas three excreted a strain of "orphan" virus. From the other three patients no virus was isolated.

Paralytic poliomyelitis was diagnosed in the presence of an asymmetrical lower motor neurone weakness of acute onset, usually preceded by some of the features of non-paralytic disease. Twenty-seven patients were found to have paralytic disease. Poliomyelitis virus was isolated from the faeces of 85% (23: 15 type 1 and 8 type 3). No virus was isolated from the other four patients.

Poliomyelitis was excluded if there was no paralysis and no cellular reaction in the cerebrospinal fluid, or if, after observation, an alternative diagnosis could be made. In 21 patients the clinical diagnosis of poliomyelitis was not made. From four of these patients poliomyelitis virus was isolated (three type 1 and one type 3). Two other patients were found to be excreting strains of "orphan" virus. No virus was isolated from the remaining 15 patients.

The clinical and pathological features of the patients virologically investigated are recorded in the Table. Eleven patients were children of pre-school age, 47 were school-children, and 8 were over 16 years old.

Clinical Features of Value in Diagnosis

Diphasic Illness.—This occurred in 26 of the 39 patients from whom poliomyelitis virus was isolated, and in 6 of 27 patients from whom poliomyelitis virus was not isolated. The usual manifestation was one or two days of fever, vomiting, or sore throat, with an interval of from three to seven days before the onset of the major illness.

Painful Stiffness of Neck and Back.—These were the commonest physical signs. An objective observation of limited flexion was much more common than a subjective complaint of pain. Stiffness of the spine was an especially useful sign. It was found in 22 of 23 paralytic patients from whom poliomyelitis virus was recovered, but in only 2 of 15 patients who showed neither paralysis nor virus excretion. Stiffness of the neck was as common as spinal stiffness in patients exhibiting paralysis or poliomyelitis virus excretion, but it was also found in many patients in whom the clinical diagnosis of poliomyelitis was not made.

State of Consciousness.—Drowsiness was a common early symptom, but the state of anxious alertness characteristic of poliomyelitis was seen more often, usually associated with stiffness of the neck and spine.

Ocular Signs.—Nystagmus or diplopia was observed in 16 patients. Poliomyelitis virus was isolated from the stools of 14. Although 11 of these patients had paralytic disease, the ocular signs were usually noted before paralysis developed.

Other Cranial Nerve Signs.—Paresis or paralysis of the fifth, seventh, tenth, eleventh, and twelfth cranial nerves were seen in eight paralytic patients. Poliomyelitis virus was isolated from all of them. Two were rapidly fatal and two others required specialized attention for pharyngeal weakness.

Bladder Disturbance.—Retention of urine was found in 10 patients, five paralytic and five non-paralytic. All excreted poliomyelitis virus.

Tremor.—This was observed in eight patients, all of whom excreted poliomyelitis virus. Usually occurring before paralysis, it varied from transient incoordination to frank intention tremor.

Muscle Pain.—Pain in the muscles of the limbs or limb girdles occurred in virtually every patient with paralysis. It was recorded in 23 of the 27 paralytic patients from 22 of whom poliomyelitis virus was recovered. The site of pain usually bore a close relationship to the eventual site of paralysis.

Muscle Weakness.—Statutory regulations about notification require that cases showing minimal or transient weakness should be notified as paralytic. In the Table the figures for the paralytic group include many patients in whom the initial diagnostic picture was that of non-paralytic disease, paralysis being observed later.

Paralytic patients could be further classified as follows:

Bulbar Poliomyelitis With Encephalitis.—Two cases were rapidly fatal from polioencephalitis with multiple cranial-nerve paralyses, in spite of tracheotomy and assisted respiration. Type 1 virus was isolated from the spinal cord and faeces of each.

Severe Paralysis.—This was seen in eight patients, the presence of extensive weakness making the diagnosis obvious. Prompt isolation of a strain of poliomyelitis virus occurred in every patient.

Mild Paralysis.—Eight cases showed mild paralytic lesions, the diagnosis being established by the demonstration of weakness in one or more muscle groups. In five cases poliomyelitis virus was isolated from the stools.

Non-paralytic Reassessed as Paralytic.—In nine patients originally notified as non-paralytic some degree of paralysis was observed from one to six weeks after the onset of the illness. Eight patients from this group were found to be excreting poliomyelitis virus. In five instances muscle weakness was observed before the result of virus isolation was known; two small children had severe shoulder-girdle weakness.

Clinical and Laboratory Data on 66 Hospital Patients Admitted as "Suspect Poliomyelitis"

Hospital Classification (On Basis of Clinical Picture and Cerebrospinal Fluid Examination)	Results of Testing One Specimen of Faeces from Each Patient for Presence of Poliomyelitis Virus	Type of Poliomyelitis Virus Isolated		No. of Patients Exhibiting the Following Clinical Features:																								Cerebrospinal Fluid			
		1	3	Diphasic Illness	Fever	Headache	Drowsiness	Alert Apprehension	Ocular Signs	Cranial Nerve Signs	Pain in Neck	Stiff Neck	Pain in Back	Stiff Back	Pain in Trunk	Weakness in Trunk	Pain in Arms	Weakness of Arms	Pain in Legs	Weakness of Legs	Bladder Disturbance	Paraesthesia	Tremor	Dyspnoea	Coryza	Sore Throat	Vomiting	Constipation	Predominantly Polymorphonuclear Response	Predominantly Lymphocytic Response	Normal	Not Examined
Non-paralytic poliomyelitis	Poliomyelitis virus isolated (12)	9	3	10	12	12	7	8	3	—	3	10	4	10	—	—	2	—	3	—	5	3	2	—	3	—	2	5	9	1	—	2
	"Orphan" virus isolated (3)			1	3	3	—	—	1	—	1	2	—	—	—	—	—	—	—	—	—	—	—	—	1	1	3	—	—	3	—	—
	No virus isolated (3)			—	2	2	—	2	—	—	1	2	—	—	—	—	—	—	—	—	—	—	—	—	1	1	1	—	—	3	—	—
	Total (18)	9	3	11	17	17	7	10	4	—	5	14	4	10	—	—	2	—	3	—	5	3	2	—	5	2	6	5	9	7	—	2
Paralytic poliomyelitis	Poliomyelitis virus isolated (23)	15	8	13	22	17	3	11	10	7	11	22	7	22	5	10	8	10	14	10	5	2	5	3	5	6	12	6	7	8	—	8
	No virus isolated (4)	—	—	1	2	3	—	—	1	1	1	2	1	3	—	—	2	1	3	3	—	—	—	—	—	—	2	2	1	1	1	1
	Total (27)	15	8	14	24	20	3	11	11	8	12	24	8	25	5	10	10	11	17	13	5	2	5	3	5	6	14	8	8	9	1	9
Poliomyelitis excluded	Poliomyelitis virus isolated (4)	3	1	3	4	3	—	2	1	—	3	2	1	1	1	—	1	—	—	—	—	—	1	—	1	1	1	1	1	1	—	2
	"Orphan" virus isolated (2)	—	—	1	1	1	1	—	—	—	—	1	1	1	—	—	1	—	1	1	—	—	—	—	—	—	—	—	—	—	1	1
	No virus isolated (15)	—	—	3	12	14	1	1	—	—	6	5	3	2	2	—	3	1	6	3	—	1	—	—	3	3	7	1	—	—	10	5
	Total (21)	3	1	7	17	18	2	3	1	—	9	8	5	4	3	—	5	1	7	4	—	1	1	—	4	4	8	2	1	1	11	8

Diagnosis

Although several clinical features often occurred, it was on the composite picture of fever, headache, anxious alertness, stiff neck and back, and muscle pain that the diagnosis of poliomyelitis was usually made. In association with these features, ocular signs, tremor, or bladder disturbance were virtually pathognomonic. Nearly all patients in whom several of the signs occurred together were found to have poliomyelitis virus in the faeces.

Some common symptoms and signs were of little value in differential diagnosis. As might be expected in a series of patients suspected of poliomyelitis, headache and fever were almost universal. Although of no diagnostic value, coryza, sore throat, furred tongue, vomiting, and constipation were all common features. Diminution or loss of tendon reflexes was found in many patients, but always in association with muscular weakness. Paraesthesiae were described by five patients who excreted poliomyelitis virus. It may be of interest that tonsillar exudate, cervical adenitis, diarrhoea, and limb pain without back stiffness were rarely noted in patients in whom the diagnosis of poliomyelitis was made or from whom poliomyelitis virus was isolated.

Cerebrospinal Fluid Examination

The cerebrospinal fluid was examined in 47 of the 66 patients. In nine patients with obvious paralysis, and in two non-paralytic children whose siblings were affected, it was considered unnecessary. For eight patients with relatively minor illnesses not clinically diagnosed as poliomyelitis lumbar puncture was not thought to be justified. Two of them were found to be excreting poliomyelitis virus; examination of their cerebrospinal fluid would have been of interest, but could hardly have benefited the patients.

One patient with paralysis, an isolated facial palsy, had a normal cerebrospinal fluid. No virus was recovered from the faeces. All others in whom the diagnosis of poliomyelitis was made and on whom lumbar puncture was performed showed abnormalities of the cerebrospinal fluid.

Among the patients in whom the diagnosis of poliomyelitis was improbable on clinical grounds were 13 who were submitted to lumbar puncture. An abnormal cerebrospinal fluid was found in two patients, and poliomyelitis virus was recovered from the faeces of both.

Abnormalities of the cerebrospinal fluid were found in 28 patients from whom poliomyelitis virus was isolated. The changes observed consisted of a cellular response, either polymorphonuclear or lymphocytic, and a rise in protein. Sugar values were consistently normal or high. A cellular response, primarily lymphocytic, was also found in three patients excreting strains of "orphan" virus and in three other patients with non-paralytic disease from whom no virus was isolated.

Poliomyelitis virus was not isolated from the faeces of any patient found to have a normal cerebrospinal fluid.

Correlation Between Clinical and Virological Observations

Poliomyelitis virus was isolated from 35 of the 45 patients in whom the diagnosis of poliomyelitis was made, and was not isolated from 17 of the 21 patients in whom the diagnosis was not made.

The apparent discrepancies between clinical and virological observations fall into three groups:

1. *Paralytic Poliomyelitis Without Virus Isolation.*—This occurred in four patients: in each the paralysis was mild. In two cases examination of the faeces was performed relatively late in the disease. One other patient, a girl of 12, was found to have an isolated facial palsy and a normal cerebrospinal fluid. Had she not been observed during an outbreak of poliomyelitis she would probably have been regarded as a case of "Bell's palsy."

2. *"Non-paralytic Poliomyelitis" Without Poliomyelitis Virus Isolation.*—Of the six patients in this group, three were found to be excreting strains of "orphan" virus. From the other three no virus was isolated. All had a predominantly lymphocytic reaction in the cerebrospinal fluid, but stiffness of the back, muscle pain, tremor, and bladder disturbance were not seen.

3. *Poliomyelitis Virus Isolation in Cases not Clinically Classified as Poliomyelitis.*—These four patients seem to us of considerable interest:

A boy of 7 developed gross nystagmus and severe cerebellar ataxia. He had minimal stiffness of the neck and a temperature of 101° F. (38.3° C.). His cerebrospinal fluid contained 60 polymorphs per c.mm.; protein 80 mg./100 ml. Complete recovery occurred in a week. The diagnosis of encephalitis was made, but the isolation of a type 1 poliomyelitis virus from the faeces revealed a previously unsuspected aetiology.

A woman of 30 with slight spinal stiffness and severe chest pain was thought to have Bornholm disease until the isolation of a type 3 poliomyelitis virus confirmed her practitioner's original diagnosis.

These two patients both showed a cellular reaction in the cerebrospinal fluid, the only patients among the group not initially diagnosed as poliomyelitis to do so.

A girl of 5 was thought to have influenza. A strain of influenza A virus was isolated from throat washings, and a type 1 poliomyelitis virus was isolated from the faeces.

A boy of 6 was admitted to hospital for social reasons and was a contact of many cases of poliomyelitis. Neither in the history nor in three weeks' clinical observation was there any evidence of illness. A type 1 poliomyelitis virus was isolated from the faeces, however.

Infectivity and Isolation

Although it was as an aid to diagnosis that virus isolation was of the most value to the clinician, it was also of great administrative assistance. The high incidence of infection among close contacts, described below, and the demonstration of two distinct types of virus, emphasized the need for isolation of patients during the acute stage. As pressure upon accommodation increased, siblings and children excreting the same type of virus were put together.

Hospital infection may have occurred in one instance. A child of 18 months with asthmatic bronchitis was originally admitted to a 20-bed open children's ward in another hospital. Nineteen days after admission she developed paralytic poliomyelitis. No other case is known to have occurred among the ward contacts, but contact with an undiagnosed febrile illness took place six days after she was admitted. A type 3 poliomyelitis virus was isolated from the faeces after transfer to the Communicable Disease Unit.

So far as possible patients were retained in hospital for six weeks. From 12 cases faecal specimens were re-examined at this stage. Only one patient was still found to be excreting poliomyelitis virus.

Poliomyelitis Outside Hospital

The range of clinical conditions admitted to hospital as possible cases of poliomyelitis suggested that the criteria for diagnosis and for admission to hospital varied widely. Faecal specimens were examined from 33 patients treated at home who were, in the opinion of their family practitioners, doubtful cases of poliomyelitis. Poliomyelitis virus was isolated from eight patients (five Type 1 and three Type 3). Three of these eight patients were siblings of hospital in-patients.

Family Contact Infection

This was found to be common. Seven samples of multiple infection of children in a family were revealed by virological investigation, and five pairs of siblings were admitted to hospital. A history of minor illness among family contacts was often elicited, and wider investigation would undoubtedly have revealed a higher incidence of infection.

Infection Based on Neighbourhoods

Special interest in the epidemiological aspects was aroused when it became apparent that both type 1 and type 3 viruses were present in the district. A striking feature during September and October was the appearance of a number of small localized outbreaks. Two examples occurred of infection with type 1 virus in children living next door to one another, at Esher and East Molesey. In addition, three cases in one street occurred twice; a type 1 virus was incriminated in New Malden, type 3 in North Kingston. Seventeen cases of type 1 infection formed four groups, localized in time and place, in Esher, East Molesey, Kingston, and New Malden. Eight type 1 cases could be directly connected with at least one other case, and seven more could be connected indirectly through one intermediate contact.

The type 3 cases did not form such well-defined groups, but six of them occurred in or were connected with one locality in Kingston. In general, the grouping of cases at first appeared to be based primarily on neighbourhoods rather than on schools.

Infection Based on Schools

Esher School.—Three children attending Esher School developed clinical poliomyelitis—one paralytic and two non-paralytic. The younger brother of one of these patients and another pre-school child living next door developed non-paralytic and paralytic disease respectively. At this time, out of the 357 children attending the school, there were 65 absent with sore throats or febrile illnesses, an unusually high absentee rate for September. Of these children, 34 became ill again after returning to school. One section of this school is isolated from the rest except at meal-times; there were no absentees from this section. Virological investigation of the absent children would have been of great value, but facilities were not then available.

Malden School.—At the end of November, three type 1 cases (one fatal, one paralytic, and one non-paralytic) occurred together in class 4 in the Saint James's Hall section of Malden Infants' School (Fig. 2). This was a class of 41 children, aged 5 and 6, separated by an incomplete screen from a class of 16 educationally backward children, aged 7 to 9. These two classes were in a church hall some 100 yards from the main school of about 400 children. The children in these two classes shared the same meals and lavatory accommodation, but had no other close social contact. Both classes were in contact with children of their own age groups in the main school. Both classes were closed, and home and garden quarantine was imposed upon the children. Two cases of mild paralytic disease then

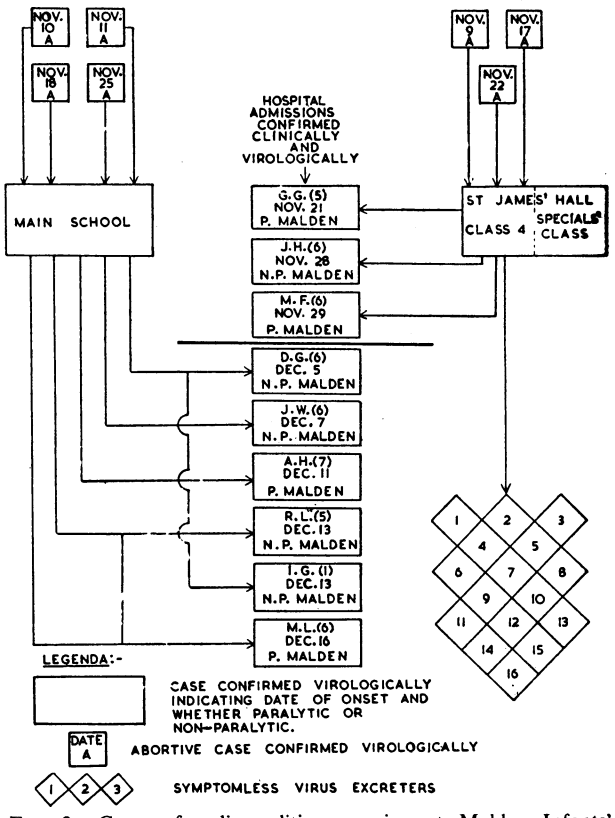

FIG. 2.—Cases of poliomyelitis occurring at Malden Infants' School.

occurred in the main school, which was also closed, and similar quarantine measures were applied to it. After the school had been closed four more mild cases of poliomyelitis among the pupils were admitted to hospital.

Complete virological study of all the children in the school was impossible. Observations on hospital in-patients and at Esher School had indicated that a diphasic febrile illness might be a guide to abortive cases. Specimens of faeces were therefore cultured for poliomyelitis virus from all the 41 children in class 4, including the three hospital patients and four who had had diphasic febrile illnesses; from the 16 educationally backward children in the adjoining room; and from 15 children in the main school who had diphasic febrile illnesses during November.

The following results were obtained: In class 4, type 1 poliomyelitis virus was isolated (*a*) from the three cases of clinical poliomyelitis admitted to hospital; (*b*) from three out of four children who had diphasic febrile illnesses; and (*c*) from 16 children who had no symptoms or signs of infection. In all, therefore, type 1 poliomyelitis virus was recovered from 22 of the 41 children in the class.

From the class of educationally backward children, however, not one instance of poliomyelitis virus excretion was found among the 16 children.

In the main school, type 1 poliomyelitis virus was isolated from five of the six children admitted to hospital as cases of poliomyelitis and from 4 of the 15 children who had had diphasic febrile illnesses during the preceding four weeks.

The first known case in this school outbreak was admitted to hospital on November 29, the last on December 25. Three pre-school siblings of children attending the school were also admitted to hospital with poliomyelitis during this period, and type 1 virus was isolated from each.

Discussion

Most cases of poliomyelitis admitted to hospital in this outbreak were fairly typical examples of the disease. Poliomyelitis virus was isolated from most of the patients in whom the diagnosis was made. Before the onset of paralysis we found little clinical difference between paralytic and non-paralytic disease, apart from the high incidence of muscle pain in those cases subsequently showing muscular weakness.

The clinical manifestations of stiffness of the neck and back, ocular signs, and tremor often occurred together before the development of paralysis. In this connexion we may recall the views of Bodian (1947). He suggested that these signs may be evidence of virus activity in brain-stem centres influencing muscle tone and movement, with particular reference to the reticular formation, vestibular nuclei, and roof nuclei of the cerebellum. Experimental evidence (Bodian, 1946) suggests that these effects of virus multiplication occur before and during invasion of the spinal cord. The clinical recognition of this stage, leading to the establishment of rest during virus activity in the vulnerable anterior horn cells, may be the most valuable prophylactic measure hitherto available (Russell, 1949; Horstmann, 1950). Similar considerations apply when muscle pain, spasm, or minimal paralysis occurs, as these signs are definite evidence of invasion of the spinal cord. The features of most value in clinical diagnosis are those giving positive evidence of disordered function in regions of the brain stem and spinal cord most susceptible to invasion by the virus.

In the absence of obvious paralysis, the difficulty of making a firm diagnosis of poliomyelitis needs no emphasis. In the past, lumbar puncture has been the most useful laboratory investigation, and its relation to virus isolation is worth consideration. In suspected poliomyelitis, abnormal findings in the cerebrospinal fluid are of great practical importance, particularly when doubt exists about the differential diagnosis, or in mild cases with an evanescent clinical picture. The demonstration of a normal cerebrospinal fluid is also valuable, suggesting that poliomyelitis is an improbable cause of the clinical picture observed, but by no means excluding the possibility. Abnormal findings in the cerebrospinal fluid give confirmation of a lesion of the nervous system, but are in no way specific for poliomyelitis. Other neurotropic viruses, such as mumps, lymphocytic choriomeningitis virus, Coxsackie virus, and herpes simplex, and bacterial infections such as leptospirosis and early tuberculous meningitis, may all produce changes similar to those found in poliomyelitis. Cerebrospinal fluid examination gives general information about the location of the disease process, but none about aetiology. Virus isolation from the faeces gives accurate information about aetiology, but by itself is no indication of invasion of the nervous system. The investigations are complementary; both may be important in any single case. Examination of the cerebrospinal fluid provides valuable information in a few minutes, whereas unequivocal isolation of poliomyelitis virus necessarily takes a few days.

The diagnosis of non-paralytic poliomyelitis was made in six patients from whom poliomyelitis virus was not isolated. These cases presented with headache, fever, vomiting, stiff neck, and a lymphocytic reaction in the cerebrospinal fluid, the features of the syndrome sometimes referred to as "aseptic meningitis." Stiffness of the back, muscle pain, bladder disturbance, and tremor, signs frequently found in patients with poliomyelitis virus excretion, were noticeably absent. However, it was impossible, on clinical grounds alone, to differentiate these six patients from two others with "aseptic meningitis" from whose faeces poliomyelitis virus was recovered. Serological investigation of the six patients gave negative results for mumps, lymphocytic choriomeningitis, and leptospirosis. Whether these were in fact cases of non-paralytic poliomyelitis remains in some doubt, but for administrative purposes the diagnosis was allowed to stand. The isolation of strains of "orphan" virus from three of these six cases was of interest. There is no conclusive evidence to show that these "orphan" viruses were causally related to the clinical syndromes in whose presence they were isolated, but similar agents have been recovered in epidemics in the U.S.A. and Canada studied by Melnick (1954) and Duncan *et al.* (1955). The clinical aspects of the cases of "aseptic meningitis" were similar to those described in the Willesden outbreak, where their incidence appeared to be unusually high (Leff, 1956).

Poliomyelitis virus of the same type was demonstrated in the faeces and spinal cord of both fatal cases, a finding that confirms the assumption that isolation of virus from the faeces is indicative of its presence in the nervous system. In fact, the high isolation rate (85%) from paralytic patients suggests that the assumption is empirically valid in most clinical cases. However, to establish a conclusive relationship between virus isolation and the concurrent clinical syndrome would require the demonstration of a rise in neutralizing antibody in paired sera taken during the acute and convalescent stages in each patient. This was not possible in the investigation described here.

Poliomyelitis virus was not isolated from 17 out of 21 patients who were not considered to have poliomyelitis. This group was variously diagnosed as "upper respiratory infection" (7), sinusitis (3), "febrile myalgia" (2), osteomyelitis (1), cerebral thrombophlebitis (1), glandular fever (1), anaphylactoid purpura (1), and migraine (1). Consistent failure to recover poliomyelitis virus from the faeces of these cases increased our confidence in virus isolation as a confirmatory diagnostic measure of precision.

Nevertheless, some caution is necessary in the interpretation of virological findings. The high incidence of inapparent infection in the Malden School outbreak suggests that poliomyelitis virus excretion concomitant with other infections might occur during heavy epidemic periods. Isolation of the virus from the faeces is only evidence of the common and often symptomless infection of the alimentary tract. In any individual patient the results of clinical examination, virus isolation, and cerebrospinal fluid examination, if necessary, should be considered on their merits. Our experience in this study leads us to believe that the isolation

of poliomyelitis virus from faeces can be regarded as reliable confirmation of the diagnosis in the great majority of clinical cases. This conclusion appears the more reasonable when it is recalled that we were compelled to limit ourselves to the examination of a single specimen of faeces from most of our patients.

In this series, type 1 virus was found to be twice as common as type 3. The excess of type 1 infection may be attributed largely to the school outbreaks described. No example of infection with type 2 virus was encountered. A rather larger proportion of patients from whom type 3 virus was isolated had severe lesions, but both fatalities and a number of severely paralysed patients resulted from type 1 infection. There is nothing in this small series of cases to suggest any clinical variation of the disease related to the type of virus.

Virological laboratory facilities were of the greatest possible value in their illumination of the epidemiological problems. In a previous survey (Morwood, 1952) epidemiological investigation of paralytic cases was sometimes significant in that close contacts often gave a history of suspicious symptoms, but in the absence of laboratory confirmation it was impossible to know whether or not they were in fact abortive cases. As a rough guide to epidemiological investigation, the diphasic fever appears to have had some value in this study.

The occurrence in September and October of small groups of cases was to some extent consistent with the hypothesis of several narrow streams of infection. One of these localized outbreaks was in Esher, where the large number of school absentees at the same time suggests that the stream of infection was, in fact, quite broad.

The use of the virus laboratory in the Malden School outbreak showed that many of these cases of minor illness, and an even larger number of symptomless contaets, were harbouring poliomyelitis virus. These observations are in accord with those made in Connecticut in 1954 (Nolan *et al.*, 1955) and in New York (Melnick *et al.*, 1956) during outbreaks based upon nursery schools.

The effect of school closure and quarantine is difficult to assess, as the outbreak occurred in November and December, when poliomyelitis outbreaks may be expected to end spontaneously. It is worth recording that all the cases admitted to hospital from this sharp outbreak occurred between November 29 and December 25. In Esher, where school closure was not applied and quarantine was imposed only on the siblings of patients with proved poliomyelitis, cases occurred over a period of two months.

The high incidence of virus isolation (50%) in class 4 at Malden School, combined with complete sparing of the adjacent class who shared the same toilet facilities and meals, strongly suggests that close personal contact was the main factor in the spread of infection. It is also to be noted that the three children admitted to hospital from this class sat close together.

Possibly the volume of the infecting dose or doses of poliomyelitis virus is important in determining whether the infection in susceptible subjects is inapparent, abortive, non-paralytic, or paralytic. If this is so, school closure and home and garden quarantine may be of some value even in the presence of widespread infection. Among children who may be already infected the reduction in physical activity, which should be emphasized in conjunction with home and garden quarantine, may be important in determining the extent of the attack. Many such problems await virological evaluation; in this respect the needs of public health authority and family practitioner are no less pressing than those of hospital clinician.

Summary

The results of a clinical, epidemiological, and virological study of an outbreak of poliomyelitis in the north-central area of Surrey during the latter months of 1955 are reported.

Single specimens of faeces from 66 hospital in-patients were examined for the presence of poliomyelitis virus by tissue-culture methods. Of 27 cases of paralytic poliomyelitis, virus was isolated from 23 (85%) (15 type 1 and 8 type 3). Eighteen cases were diagnosed as non-paralytic poliomyelitis, and of these 12 (66%) excreted poliomyelitis (nine type 1 and three type 3). Three of the remaining six patients excreted a strain of "orphan" virus. Of 21 patients in whom the clinical diagnosis of poliomyelitis was not made, four were found to be excreting poliomyelitis virus (three type 1 and one type 3).

In this study a notable clinical feature was the diphasic febrile illness. This occurred in 26 of 39 patients (67%) from whom poliomyelitis virus was isolated, compared with 6 of 27 patients (22%) from whom virus was not isolated. Other features of value for early diagnosis were spinal stiffness, ocular signs, disturbance of bladder function, and tremor.

The correlation between clinical and virological findings confirmed virus isolation as a test of great value in diagnosis. In addition there was close correlation between a cellular response in the cerebrospinal fluid and virus isolation. In this hospital series, poliomyelitis virus was not isolated from any patient with a normal cerebrospinal fluid.

Epidemiologically, the simultaneous existence of both type 1 and type 3 outbreaks was noteworthy. Direct or indirect contact could often be established between localized groups of cases infected with type 1 virus, but those infected with type 3 virus did not appear to form well-defined groups. The determination of the virus type responsible for infection was of administrative assistance in hospital, as cases excreting virus of the same type were accommodated together.

An outbreak of poliomyelitis in a school class of 41 children aged 5 to 6 was investigated. Type 1 poliomyelitis virus was isolated from three clinical cases and from three of four children with transient febrile illnesses. Type 1 virus was also isolated from 16 (47%) of the remaining 34 clinically normal children in the class, illustrating wide dissemination of virus among close contacts.

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