Report on the outbreak of poliomyelitis during 1961 in Kingston-upon-Hull and the East Riding of Yorkshire.

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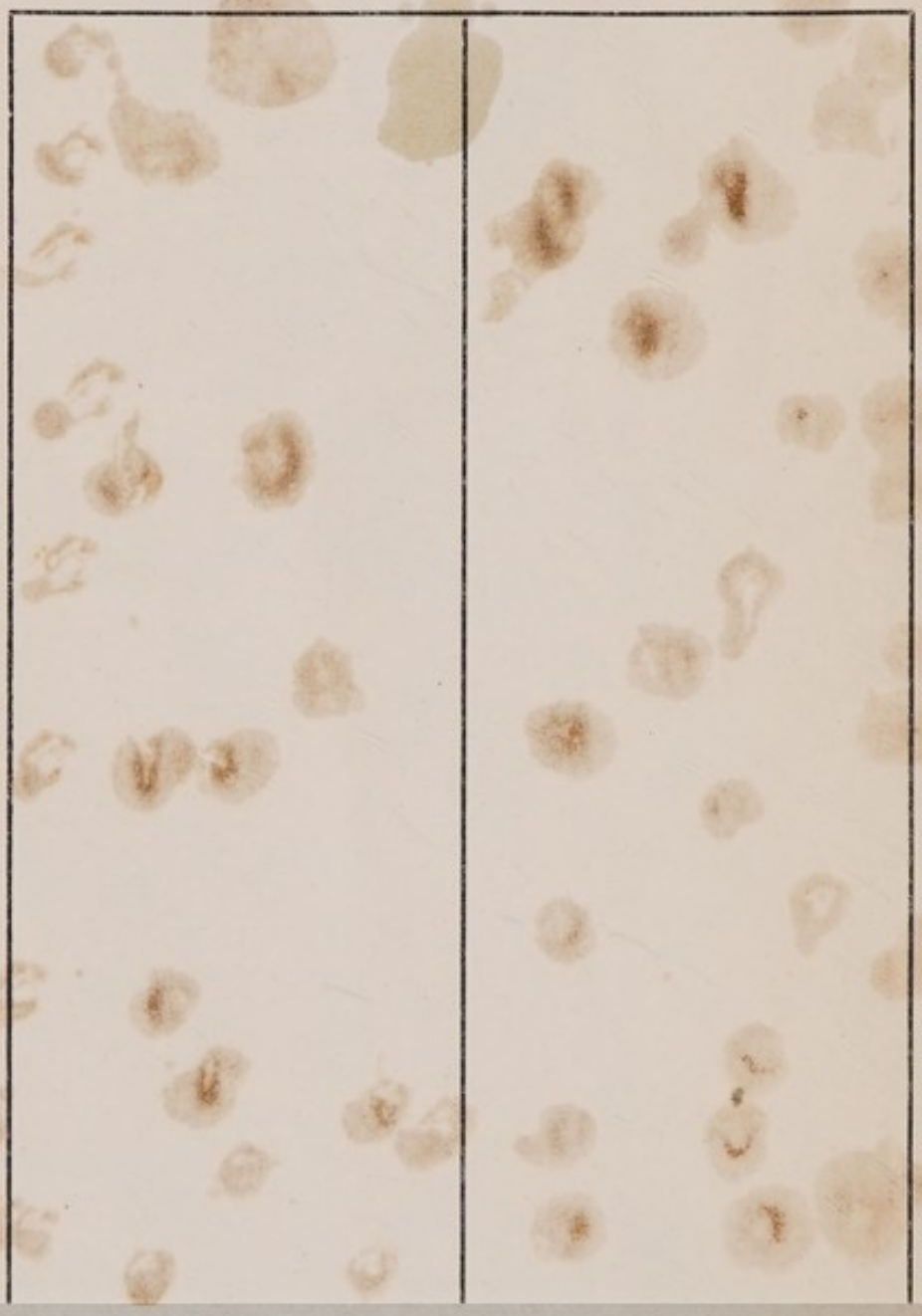

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Report on the Outbreak of Poliomyelitis during 1961 in Kingston-upon-Hull and the East Riding of Yorkshire

LONDON: HER MAJESTY'S STATIONERY OFFICE
1963

CONTRIBUTORS TO THE REPORT

J. B. Cook, M.D., M.R.C.P.
J. H. Hale, O.B.E., M.D., M.R.C.P.
A. Hutchison, O.B.E., Ph.D., M.D., D.P.H., D.P.A., F.R.F.P.S.
S. R. Jamieson, M.D., D.P.H.
Professor J. Knowelden, M.D., D.P.H.
B. P. Marmion, M.D.
J. H. McCoy, M.B., B.Ch., B.A.O., D.P.H.
F. T. Perkins, Ph.D.
A. T. Roden, M.D., D.P.H., D.C.H.
Professor C. H. Stuart-Harris, M.D., F.R.C.P.
R. Watson, M.A., M.B., B.Chir., D.P.H.

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PREFACE

by the Chief Medical Officer

The outbreak of poliomyelitis, which forms the subject of this report, was of particular interest because, for the first time in England and Wales, oral poliomyelitis vaccine was used on a large scale in an attempt to arrest the spread of the disease. Experience in other parts of the world had given encouraging results and there was every reason to believe that the new vaccine would meet with equal success in this country. Its introduction here afforded a unique opportunity to explore the administrative and technical problems associated with a mass vaccination campaign and to derive as much information as possible concerning the efficacy and safety of the vaccine. For these reasons the outbreak was studied with special care.

During the early part of 1961 the Central and Scottish Health Services Council's Joint Committee on Poliomyelitis Vaccine had given careful consideration to live poliovirus vaccines and had made detailed recommendations as regards their use in an epidemic situation. The Minister of Health accepted these recommendations and arranged for a stock of oral vaccine to be held in readiness for a possible emergency. Although the general incidence of poliomyelitis was higher that summer than in the previous year, no situation which could be described as an emergency arose until the early part of October, when it became evident that a relatively intense focus of infection due to Type 1 poliovirus had developed in Kingston-upon-Hull. In accordance with the advice given by the Joint Committee a heterotypic vaccine prepared from Sabin's strain of Type 2 poliovirus was made available for a mass vaccination campaign. The decision to use the vaccine was taken on 12th October and the campaign began on the 17th. Within three days more than 300,000 persons resident in Kingston-upon-Hull and neighbouring districts of the East Riding of Yorkshire had come forward for vaccination. By the end of the month the outbreak had ceased, the date of onset of illness of the last confirmed case being 29th October, twelve days after the start of the campaign.

The magnitude of the enterprise, and the speed with which it was mounted, called for strenuous efforts by the local Public Health Departments, assisted in the execution of their plans by numerous voluntary workers. Particular importance was attached to the problem of surveillance and detailed arrangements were made for the ascertainment and investigation of all persons thought to be suffering from poliomyelitis. The Regional Hospital Authority and the Public Health Laboratory Service co-operated fully in these arrangements. Intensive virological investigations of hospital patients were made by the Public Health Laboratory Service, which also undertook virus studies in the general community. Part of the laboratory work was done in collaboration with the Immunological Products Control Division of the National Institute for Medical Research.

This report aims to present a factual account of the outbreak and vaccination campaign, with the results of the clinical, epidemiological and virological investigations which were undertaken. It includes also a summary of the scientific and historical background to the use of oral poliomyelitis vaccines in general and a discussion of the conclusions which could be drawn from the particular experience under consideration. The wealth of material which was made available to the compilers of the report was due to the combined efforts of many organizations and individuals. A small editorial committee assembled the material and gave it its final form. I should like to pay a tribute to all who collaborated in the most completely successful immunization campaign yet organised in this country and in the recording and study of its effects. Its success can only be measured in terms of the completeness of acceptance by the residents of the area and it cannot be claimed that the epidemic was manifestly halted by the vaccine. Yet it did cease in the manner to be expected if the vaccine had brought this about and it can fairly be claimed that the results are consistent with the use of the vaccine being effective.

G. E. GODBER.

CONTENTS

I

THE USE OF ORAL POLIOVIRUS VACCINE IN ROUTINE IMMUNIZATION AND IN THE CONTROL OF OUTBREAKS

The numerous small-scale and large-scale trials of oral poliovirus vaccines in many different countries have established a solid basis for the use of these materials (Live Poliovirus Vaccines, 1959, 1960). Such vaccines prepared from viruses attenuated in the laboratory by artificial cultivation have been shown to produce an infection of the alimentary canal which is accompanied by the formation of neutralizing antibodies in the blood. This infection can be produced in those previously unimmunized and also in those who have received a full course of Salk vaccine. After oral vaccine the alimentary canal resists a second exposure to the homotypic virus infection providing that there was actual multiplication of virus on the first occasion. It is thus likely that immunity of the alimentary canal to poliovirus is not dependent solely on antibody formation, though infection with one serotype of poliovirus does not prevent a subsequent infection with a different type of virus. For this reason routine immunization with oral vaccine requires the use of all three types of poliovirus and these can either be given *seriatim* on three separate occasions or combined as a mixture of trivalent vaccine which must be given on more than one and preferably three occasions. (Report of the Public Health Laboratory Service, 1961.)

It has been established that the presence of neutralizing antibodies in the serum before the use of oral vaccine in those who have never received an inactivated poliovirus vaccine may inhibit subsequent infection by the attenuated virus present in the live vaccine. Such natural immunity may of course have originated from a subclinical infection or a frank attack of poliomyelitis. For this reason oral poliovirus vaccine achieves its highest rate of successful infection in infants over 6 months of age who have had no previous contact with poliovirus, as shown by the absence in their sera of neutralizing antibodies to any of the three types of poliovirus (triple-negative sera). In older children or adults who have been exposed to natural poliovirus infection, or who have received Salk vaccine, a less uniform response occurs when oral vaccine is given. The response in such persons has been shown to depend upon the quantity of virus present in the oral vaccine and also on the titre of neutralizing antibodies present in the serum at the time of administration (Hobson, Hoskings, Lane, Elliott, Perkins and Yetts, 1962). Nevertheless, a satisfactory boosting of antibodies occurred in the trials of monovalent Sabin vaccine (Types 1 and 2) used by these authors in schoolchildren or adults who had already received a full course of three doses of Salk vaccine. The trial conducted in 5 to 7 year-old children (Report of the Public Health Laboratory Service, 1962) using trivalent Sabin vaccine as a reinforcing infection seven to twelve months after a primary course of two doses of Salk vaccine also gave satisfactory evidence of a boosting of antibodies against all three types of poliovirus.

Routine Immunization

In the use of oral vaccine for routine immunization the aim is to produce alimentary infection and to stimulate antibody formation. For the completion of immunization at least two and preferably three doses of trivalent vaccine are required because of the competition which exists between simultaneously administered polioviruses. This competition is believed to be due to virus interference—a phenomenon which may be exhibited between viruses of the same species such as polioviruses or between the vaccine and other viruses such as the Coxsackie or ECHO viruses or even adenoviruses. Mutual interference between polioviruses perhaps depends on some quality such as the degree of infectiousness of the viruses. The different types of the three Sabin attenuated viruses differ in this property and the Sabin Type 2 virus given in a trivalent vaccine composed of equal amounts of the three viruses interferes with the successful implantation of the other two viruses in a proportion of instances (Report of the Public Health Laboratory Service, 1961 ; Hale, Lee and Gardner, 1961a). In persons who respond to the Type 2 strain but not to the Types 1 or 3 on the first occasion when trivalent vaccine is given, the second dose of oral vaccine is followed by a satisfactory formation of antibodies to Types 1 and 3 presumably because Type 2 can no longer re-infect the alimentary canal.

The occurrence of an outbreak of poliomyelitis in a population in whom a large proportion of the most susceptible persons have received inactivated poliovirus vaccine is clearly an indication of a relative failure of immunization. Intensification of routine immunization with particular effort to obtain cooperation from those who have never received vaccine is one method of dealing with the situation, but requires time. Mass immunization with oral vaccine differs from that with inactivated vaccine in that it offers the possibility of utilising the interference phenomenon as well as of achieving specific immunization. For interference to succeed in preventing further spread of the epidemic virus it is necessary rapidly to obtain colonisation of the alimentary canal in as many persons as possible. That this has in fact been achieved may be judged from the various outbreaks in which oral vaccine has already been used.

Mass use of oral vaccine during outbreaks

The first use of oral poliovirus vaccine during an outbreak of poliomyelitis was in the Belgian Congo towards the end of 1957. Courtois, Flack, Jervis, Koprowski and Ninane (1958) gave the Koprowski Chat Type 1 virus vaccine to all of the few thousand inhabitants of four villages in the Congo among whom a few cases of poliomyelitis had already occurred. No cases were observed after the vaccine was used on this limited scale. In 1958, a sharp outbreak of poliomyelitis due to Type 1 poliovirus occurred in Singapore. Large-scale administration of Sabin Type 2 vaccine was begun in the twelfth week of the outbreak and continued for twelve weeks thereafter during which 200,000 of the half-million children under 10 years of age were vaccinated. (Hale, Lee, Doraisingham, Kanagaratnam, Leong and Monteiro, 1959). The protective effect of the vaccine was assessed by Knowelden, Hale, Gardner and Lee (1961) who compared the number of cases of poliomyelitis in vaccinated and unvaccinated children week-by-week. No sparing effect on paralytic disease was found until an interval of 8 or more days had elapsed after the

oral vaccine had been given but thereafter a substantial degree of protection was manifested. This experience also demonstrated that the vaccine was not associated with cases of poliomyelitis either in those to whom it was given or in contacts, for only one case of poliomyelitis due to Type 2 poliovirus occurred during the entire outbreak even though widespread carriage of Type 2 virus was demonstrated in healthy infants who had not themselves received vaccine.

In July, 1959, there began the largest outbreak of poliomyelitis ever experienced in Tashkent City of the Usbek, U.S.S.R. Nearly 88 per cent of the cases occurred in children under 5 and the majority of strains of polioviruses recovered were serologically Type 1. At the end of the 4th week of the outbreak, 304,000 (89·4 per cent) of the 340,000 children under 15 received a single dose of trivalent oral vaccine prepared from Sabin's strains. The number of cases of poliomyelitis declined sharply during the next 4 weeks and, though a significant number still occurred in those who had received vaccine, the attack rate in the latter was reduced compared with that in unvaccinated children. No precise estimate of the degree of protection was made, though the report from the Institute of Poliomyelitis of the Academy of Medical Sciences of the U.S.S.R. (Chumakov, 1960) and local health authorities concluded that many cases of poliomyelitis had been prevented.

In the late spring of 1960 an outbreak of poliomyelitis due to Type 1 virus developed in Berlin, where the previous public acceptance of Salk vaccine had been poor. Sabin vaccine had been used in the previous winter and early spring in East Berlin and between May 11th and 20th, 290,000 residents of West Berlin received a single dose of trivalent oral poliovirus vaccine prepared from Cox-Lederle strains. It was estimated that 80 per cent of school children and 56 per cent of pre-school children received the vaccine and altogether about half of the total 306,317 children aged 6 to 18 were vaccinated. No final report has yet appeared concerning the effect of this mass immunization though it is known that a number of cases of poliomyelitis subsequently occurred both in vaccinated and unvaccinated persons. Thus of 50 cases which occurred from May 15th to December 31st, 16 were in persons who had previously received Cox vaccine within 30 days and 5 were in close contacts of vaccinated persons (Anderson, 1962). Yet the age distribution of these 21 cases was that usually experienced in recent years in West Germany. There was a further report that some of the vaccinated children experienced febrile reactions during the first week after receiving vaccine and that, during the second and third weeks, others developed encephalomyelitis (Henneberg, 1961). The origin of the illnesses in those who had been vaccinated was not discovered.

A somewhat similar problem occurred in Miami, Florida, where Cox trivalent vaccine was used early in 1960 during a sporadic incidence of poliomyelitis. A few cases of poliomyelitis occurred in adults soon after the administration of vaccine, both in those receiving vaccine and in contacts. (Erickson, Flipse, Menzin, Clayton, Markush and Hardy, 1960). This experience was one reason for the caution exhibited by the Expert Committee on Poliomyelitis of the World Health Organisation. The Third Report of this Committee (1960) urged that particular care should be taken when introducing oral poliovirus vaccine in countries where poliomyelitis occurred in adults in

a moderate to high incidence (20 per cent of paralytic cases in persons over 15). This was because of the known severity of such adult cases of poliomyelitis and of the probable existence of non-immune adults in such countries.

In the U.S.A., where much Salk vaccine has already been used, oral poliovirus vaccine was also given on a mass scale in 1960 in the cities of Rochester, New York and Cincinnati, Ohio at times when poliomyelitis was not occurring. In these cities vaccines prepared from Sabin strains were used and no illnesses resembling poliomyelitis were recorded in either city as being attributable to the vaccine. Experiences in Cincinnati were published by Sabin and others in 1961.

In the summer of 1961 cases of poliomyelitis due to Type 1 virus occurred in Syracuse and adjacent counties of New York State. A mass administration of Sabin Type 1 vaccine was begun on 29th August during the 5th week of the outbreak. Nearly 50 cases of paralytic poliomyelitis had already occurred when the administration of 400,000 doses of vaccine was begun. Thirty-two cases occurred after this date, including 20 in persons who had received oral vaccine (P.S.U. Report, No. 249, 1962). This number includes some patients with an onset of symptoms before or in the first few days after receiving vaccine. It was considered that the vaccine had interfered with the progress of the outbreak (Feldman, 1961).

In two smaller outbreaks of poliomyelitis in 1961 in Atlanta, Georgia and Newberry County, South Carolina, Type 3 poliovirus was responsible for the infection. Type 3 Sabin vaccine was used in mass oral programmes in both areas. A few cases of poliomyelitis occurred in vaccinated persons but in all the onset of illness occurred less than one week after receiving the vaccine.

Selection of the oral vaccine for use at Kingston-upon-Hull

At the time when the outbreak of poliomyelitis, due to Type 1 virus, began at Kingston-upon-Hull in the autumn of 1961 there was evidence from the previous work cited above that oral poliovirus vaccine given to a large proportion of the population would interfere with the course of an outbreak. There was also evidence of a need for careful clinical and laboratory surveillance of the population, subsequent to the use of vaccine, in order to watch for the occurrence of possible illnesses, particularly of paralytic poliomyelitis, which might be connected with vaccine administration. This need arose partly from the natural tendency to blame immunization for the occurrence of illnesses subsequent to the administration of vaccine. But the fact that those to whom oral poliovirus vaccine is given become infected and excrete polioviruses in the faeces for several days or weeks is both helpful in relation to the control of poliomyelitis and also a special characteristic of the vaccine. Thus it is known that the excreted viruses differ from the vaccine virus in several biological properties which have been studied by various genetic "markers" in the laboratory. Of particular interest in this connection is the fact that those conducting small-scale trials (Dick and Dane, 1957; Clarke *et al*, 1958; Benyesh-Melnick and Melnick, 1959; Dane *et al*, 1961) have noted that occasional viruses recovered from the faeces of vaccinated persons exhibit an enhancement of neurovirulence for the monkey. Although this neurovirulence is many times less than that of epidemic poliovirus strains, it is greater than that

of the attenuated virus used in preparing the vaccine. The lack of evidence of a progressive increase in monkey neurovirulence during the course of vaccine infection and the absence of harmful effects either in those to whom vaccine is given or in their contacts who may become infected is of great importance.

The mass use of Sabin oral vaccine in Czechoslovakia (Skovranek, 1959, 1960) and the U.S.S.R. in 1959 and 1960 (Chumakov, 1960) is the best evidence that there is no risk either for those receiving the vaccine or for the unimmunized in spite of the variation noted in the laboratory characters of the excreted viruses. When vaccine is used during outbreaks of poliomyelitis there is a particular need to exonerate it from harmful effects because of the fact that cases of poliomyelitis are likely to occur in those already incubating the infection at the time when vaccine was given or because of a failure to prevent the spread of the epidemic strain. If it can be shown that the virus recovered from cases of poliomyelitis occurring after the vaccine has been used differs from the vaccine virus in certain identifiable ways, then the vaccine virus cannot be held responsible for the illness.

Nor is it possible to use biological characters, such as the "t" marker based on the ability to multiply in tissue cultures at 40°C, to distinguish the wild polioviruses occurring naturally. Most of the viruses recovered from persons receiving attenuated viruses present in vaccines lack such characters, i.e. they will not multiply at 40°C. Occasionally, however, variant viruses may be found in the stools which may be difficult to distinguish from wild viruses. Thus, they may possess biological properties resembling those of the latter or they may be intermediate in character between the vaccine and wild viruses. For this reason studies based on biological markers alone may be inconclusive in differentiating the possible sources of viruses recovered from persons to whom vaccine has been given. But an unfailing character such as the serotype of the vaccine virus is needed to differentiate the progeny of such virus from epidemic viruses, particularly when dealing with viruses recovered from cases of paralytic poliomyelitis. There is therefore a substantial advantage from the standpoint of surveillance if the vaccine contains virus belonging to a different serotype from that causing the outbreak. The use of the Sabin Type 2 virus in Singapore exemplified this advantage and the statistical proof that it produced protection against the epidemic Type 1 virus provided a second argument in favour of using Type 2 rather than a trivalent vaccine in Hull.

The third consideration which governed the decision to use the Sabin Type 2 vaccine was that the field trial of this material in the West Riding of Yorkshire (Hobson *et al*, 1962) had shown that a quantity of vaccine containing $10^{5.8}$ 50 per cent. tissue culture infectious doses would infect 50 per cent. of adults who had previously received 3 doses of Salk vaccine. There was therefore reason to believe that the strain as prepared in Britain as a vaccine would infect a high proportion of those to whom it was given and would interfere with the spread of the epidemic Type 1 virus through the already partially immunized population. Such interference would, of course, be limited to the period of actual multiplication of virus and after a suitable interval, the immunization of those who had received no other vaccine would require completion.

II

POLIOMYELITIS IN KINGSTON-UPON-HULL AND THE EAST RIDING OF YORKSHIRE

General Background

Kingston-upon-Hull is a County Borough in north-eastern England with a population of 303,000. It lies on the north bank of the Humber Estuary some 20 miles from the sea. The city is divided roughly into an east and west part by the River Hull which flows into the estuary. There are seven miles of water front. About two-thirds of the population of the city live on the west side of the River Hull and the remainder on the east. It is to the east of the river that most of the city's new housing projects have been developed during the past 15 years.

Kingston-upon-Hull is the third largest port in the United Kingdom and the largest fishing port in the world. In addition it is an industrial city, the main industries being engineering, the manufacture of animal feeding stuffs, flour milling, the manufacture of pharmaceutical products, cod liver oil, fish meal, fertilisers, and the distribution of timber. The port acts as an outlet and inlet for many of the industries in the West Riding of Yorkshire and the North Midland region.

Parts of the administrative county of the East Riding of Yorkshire immediately adjoin Kingston-upon-Hull. These are the Urban District of Haltemprice, which runs along the whole of the western and part of the northern border of the city, the parishes of Bilton and Preston-in-Holderness Rural District on the eastern border, and the parish of Wawne in Beverley Rural District which fills in the gap remaining along the northern border.

The built-up portions of the city are, generally speaking, not continuous with any built-up areas of the county, except along the five roads leading respectively to the village of Bilton, and to the Cottingham, Willerby, Anlaby and Hessle areas of Haltemprice Urban District. Elsewhere there are undeveloped areas between the boundary of the city and the nearest residential centres. Similarly, beyond the western border of Haltemprice Urban District there is a band of open country before the next centres of population are reached. It is, therefore, only in the limited areas along these five roads that there is what might be termed " door-to-door " social contact between people who live on different sides of the County Borough boundary.

As regards school children, the city and the county are independent of each other in respect of the provision of places in infant, primary and secondary modern schools but nearly 600 children from the surrounding areas of the county travel each day into Hull to attend grammar, special and privately maintained schools which are situated in the city.

There is a large daily movement into Hull of adults resident in the East Riding, most of whom live in Haltemprice Urban District, the southern part of Beverley Rural District, the Borough of Beverley and its surrounding area, the small Borough of Hedon and those parts of Holderness Rural District

which immediately adjoin Kingston-upon-Hull. From further afield also commuters travel daily to the city from Bridlington, Hornsea and Withernsea. There is also a considerable traffic in the opposite direction. Between 1,400 and 1,500 workers, many of them women, travel from Hull each day to work in the various industries in Beverley and over 3,000 travel along the Humber Bank to work in factories in North Ferriby, Welton and Brough. The aircraft factory in Brough also draws labour from Beverley, Goole and Selby and from further afield in the West Riding. Finally, Kingston-upon-Hull acts as a business and commercial centre for most of the eastern half of the county and there is a big influx from the rural areas each Saturday.

For all practical purposes, however, the part of the county influenced by the outbreak in 1961 lay within a radius of about fifteen miles from the centre of the city. This area consists mainly of the Haltemprice and Holderness Health Divisions, with an estimated population of 115,162.

During the past fifteen years the annual incidence of poliomyelitis in Kingston-upon-Hull and the East Riding of Yorkshire has followed the national trend except on four occasions. In 1954 the number of cases was proportionately higher than in England and Wales as a whole and in 1955 and 1957 proportionately lower. In 1958 there was a relatively high incidence in the East Riding, but not in Kingston-upon-Hull.

Summary of Past Outbreaks in Kingston-upon-Hull

The worst outbreak occurred in 1947 when a high incidence was reported from many parts of the country. Altogether there were 77 cases reported in Kingston-upon-Hull that year—72 suffering from acute poliomyelitis and 5 from polio-encephalitis. The first case was notified on the 4th July and, by dates of onset, the cases occurred in the following months: June, 1; July, 18; August, 31; September, 20; October, 5; November, 2. A peak was reached in the week ended 6th September, 1947, when there were 10 cases. After this there was a sharp decline, with only one or two cases weekly, until the week ended 15th November, when the outbreak ceased.

The age distribution of the cases was as follows—under 5 years of age—32; 5 to 14 years—23; 15 to 39 years—21; 40 years and over—1. No one area of the city was affected more than another. The attack rate was 0·27 per thousand of the population and the case fatality 3·9 per cent. These figures compare with an attack rate of 0·17 per thousand of the population in England and Wales during the second half of that year and a case fatality of 8·8 per cent.

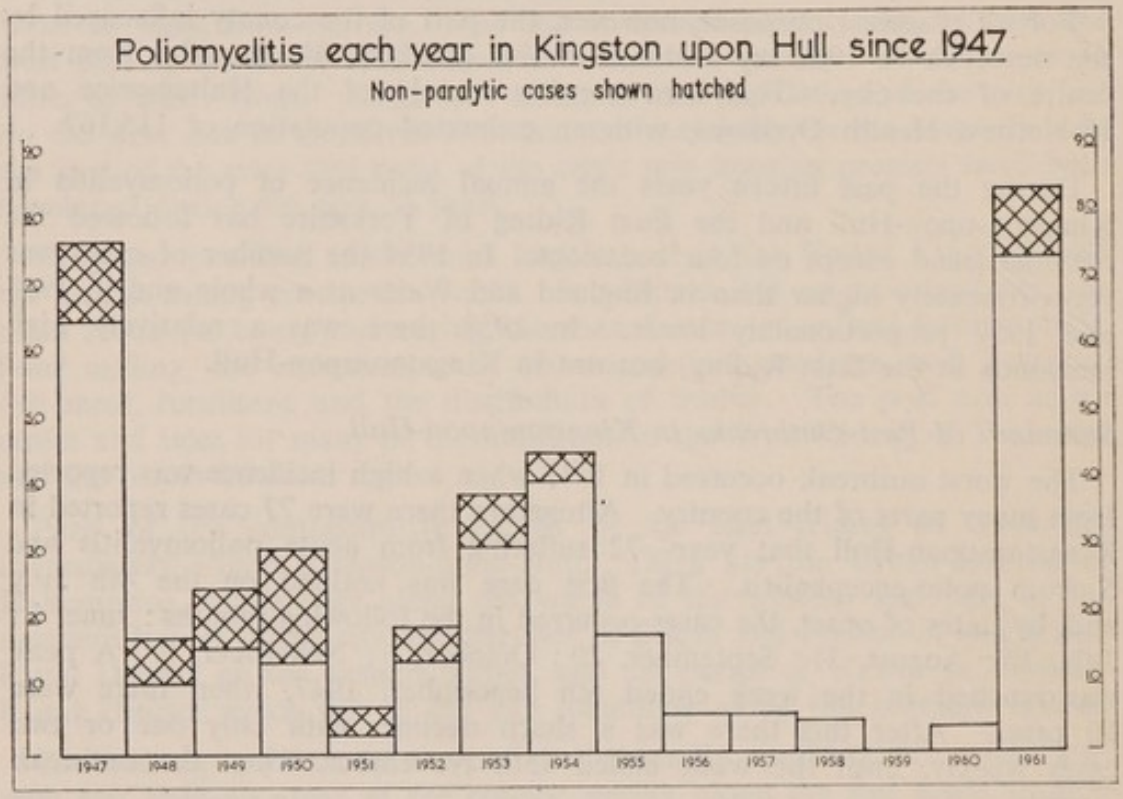
Following this outbreak the number of cases occurring in the next five years was 18 in 1948, 25 in 1949, 31 in 1950, 7 in 1951 and 19 in 1952.

In 1953 the number of cases rose to 39 and in 1954 there was a further increase to 45. In the latter year there had been a fall of over 50 per cent. in the total cases reported in England and Wales compared with 1953. There appeared to be no particular explanation for the higher incidence in Kingston-upon-Hull. The disease was not concentrated in any particular area, and cases occurred during each month of the year except December. The highest number of cases was in July when 10 were reported. There were 4 deaths.

In 1955 the number of cases in Kingston-upon-Hull fell to 18, although there was a large increase in the total for England and Wales compared with the previous year. There were six cases in 1956 and again in 1957, while in 1958 there were only five. No case was confirmed in 1959 and only four in 1960.

Fig. 1 shows corrected notifications of poliomyelitis in Kingston-upon-Hull for the years 1947 to 1961 inclusive.

Fig. 1



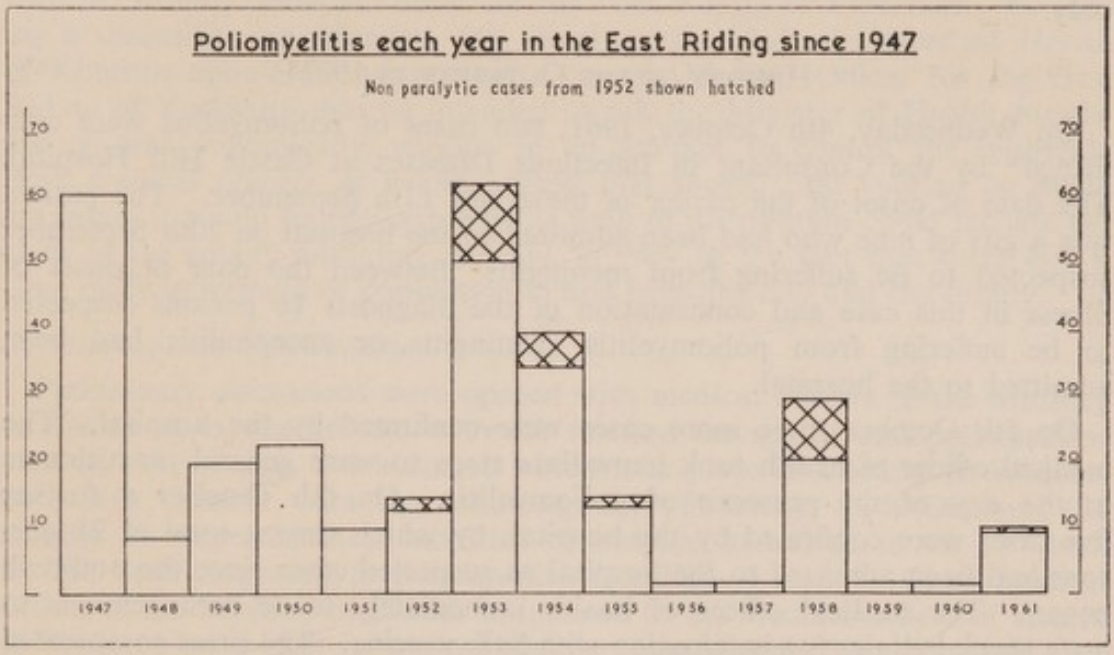
Summary of Past Outbreaks in the East Riding

The East Riding experienced no serious outbreak of poliomyelitis until 1947 when 61 cases were notified, of which 21 came from Haltemprice Urban District, 15 from Beverley Municipal Borough and Rural District and 7 from the Holderness area, i.e. 43 cases in the county within about fifteen miles of Kingston-upon-Hull. After this and until 1956 there was no year with fewer than 8 notifications. In 1953 notifications reached a total of 62, largely due to an outbreak of 32 cases in the Beverley area. During this outbreak there were 9 cases from Haltemprice Urban District and 13 from the Holderness area. In the following year, 1954, there were 39 notifications in the county, including 11 from Beverley area, 14 from the Haltemprice area and 8 from the Holderness area.

During the years 1955 to 1960 inclusive there were only 3 cases notified from Haltemprice (2 in 1956 and 1 in 1960) and 2 from the Beverley area. The last of the Beverley cases was in 1958, and was associated with a short but sharp outbreak in and around Driffield. In this outbreak there were 16 cases, most of whom were young children.

Fig. 2 shows corrected notifications of poliomyelitis in the East Riding of Yorkshire for the years 1947 to 1961 inclusive.

Fig. 2



Poliomyelitis-like illnesses in 1961 *prior to the outbreak*

From 1st January to 13th September 90 persons in whom the possibility of poliomyelitis was considered (80 from Kingston-upon-Hull, 10 from the East Riding) were admitted to Castle Hill Hospital. In none of them was there sufficient clinical or virological evidence to establish a diagnosis of poliomyelitis.

Eighteen of these cases were sent into hospital as suspected poliomyelitis. The final diagnoses were : influenza, one case ; urticaria, two cases ; gastro-enteritis, one case ; bronchitis, two cases ; arthritis, two cases ; upper respiratory infection, two cases ; meningitis, two cases ; lymphocytic menin-gitis, two cases ; serum reaction, one case ; myalgia, one case ; mumps meningo-encephalitis, one case and gingivitis, one case.

A further 67 were admitted as suspected meningitis. The final diagnoses were : pyogenic meningitis, 6 cases ; virus meningitis of various types, 16 cases ; aseptic meningitis, 26 cases ; other diseases, e.g. pneumonia, cerebral haemorrhage, 19 cases.

Of the 16 cases of virus meningitis, six were due to mumps, three to ECHO viruses (two being type 9), and three to unidentified cytopathogenic agents. One of the 26 cases of aseptic meningitis showed a rise in titre to type 1 poliovirus but the patient had received four injections of Salk vaccine and had no other evidence of poliomyelitis. In the other 25 cases of aseptic meningitis, virological examination was negative.

Three of the remaining five patients were admitted as cases of pneumonia and the other two as P.U.O. They were examined clinically and viro-logically to exclude the diagnosis of poliomyelitis. Final diagnoses of pneumococcal meningitis, meningococcal meningitis, purulent meningitis, mumps meningitis and arthritis were made.

On the 16th June, 1961, a case of non-paralytic poliomyelitis in a single woman, aged 25, was notified from the village of North Ferriby in the southern part of the Beverley Rural District. The patient was isolated and nursed at home for four weeks. The diagnosis was made on clinical findings only.

History of the Outbreak in 1961

On Wednesday, 4th October, 1961, two cases of poliomyelitis were confirmed* by the Consultant in Infectious Diseases at Castle Hill Hospital. The date of onset of the earlier of these was 11th September. The patient was a girl of nine who had been admitted to the hospital on 20th September suspected to be suffering from meningitis Between the date of onset of illness in this case and confirmation of the diagnosis 16 persons suspected to be suffering from poliomyelitis, meningitis or encephalitis had been admitted to the hospital.

On 5th October three more cases were confirmed by the hospital. The medical officer of health took immediate steps to warn general practitioners in the city of the presence of poliomyelitis. On 6th October a further five cases were confirmed by the hospital, by which time a total of 21 persons had been admitted to the hospital as suspected cases since the outbreak began. The medical officer of health immediately made arrangements to open special clinics for vaccination with Salk vaccine. The press co-operated excellently in making these arrangements known to the general public.

One unusual feature which caused some concern was the arrival of the Hull Fair. This fair, scheduled to last from 7th to 14th October, is held annually and is one of the largest in England. Showmen and their families come from many parts of the country, remain for the fair, and then disperse widely over the whole country. In addition, large numbers of visitors are attracted from outside the city. Despite many exhortations to advise that the fair be cancelled, the medical officer refused to do so, and maintained that the city life should go on as normal. The Health Department's mobile immunization van was stationed close to the main entrance to the fair and, when the fair eventually dispersed, a letter giving details of the outbreak of poliomyelitis in Kingston-upon-Hull was sent to the medical officers of health of areas to which it was known that any of the showmen were proceeding. It is interesting to note that none of the showmen or their families contracted the disease whilst in the city or after leaving it.

The occurrence of poliomyelitis in Kingston-upon-Hull during the last week of September, 1961, and the fairly rapid build-up of cases during the early days of October, had the effect of increasing the demand for poliomyelitis vaccination with Salk vaccine in the East Riding, especially in the south and south-eastern parts of the county. This demand was sufficient to justify the organisation of "open" vaccination sessions in Beverley and Withernsea, and in the Beverley and Holderness Rural Districts, and all general practitioners experienced extra requests for vaccination, especially from adults. As vaccine was generally in short supply some difficulties and delays were at first experienced but those were overcome by the middle of the month.

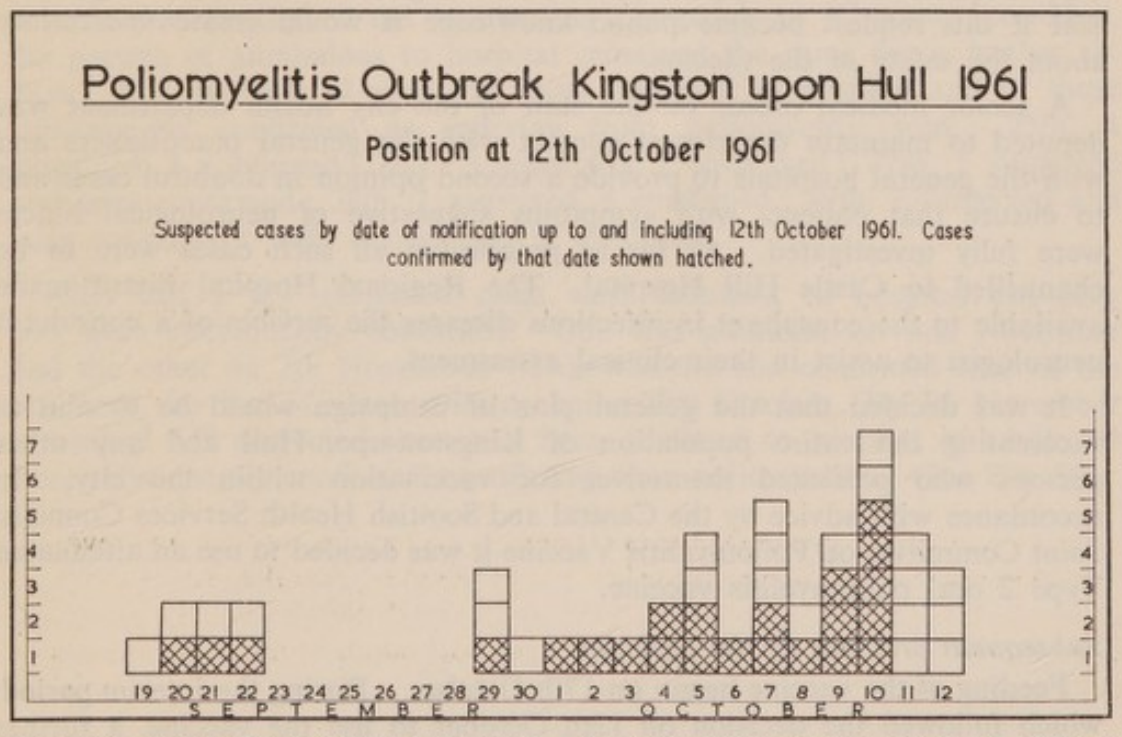
* The term "confirmed" in this context does not necessarily imply laboratory evidence of poliovirus infection.

Meanwhile further patients were admitted to the hospital on 7th and 8th October and, by 9th October, 32 suspected cases had been admitted of which 11 had been confirmed. From the onset of the outbreak the Medical Officer of Health of Kingston upon Hull had kept in the closest contact with the County Medical Officer for the East Riding of Yorkshire. Following a discussion on Monday, 9th October, the Medical Officer of Health of Kingston-upon-Hull informed the County Medical Officer for the East Riding of Yorkshire that he intended to ask the Minister of Health for the use of oral poliomyelitis vaccine in an attempt to control the outbreak. Both medical officers of health agreed that should oral vaccine be made available, it would be preferable if the area of distribution could include the parts of the county adjoining the city, in view of the fact that there was a large daily movement of population to and from the city and the county.

Decision to use oral vaccine

Preliminary discussions were opened with medical officers of the Ministry of Health as to whether the outbreak merited the use of oral poliomyelitis vaccine. A meeting was arranged which took place in London on Wednesday, 11th October. On the following day, Thursday, 12th October, the number of suspected cases admitted to hospital had risen to 46, of which 23 had been diagnosed as poliomyelitis (see Fig. 3) and the Chief Medical Officer of the Ministry of Health telephoned to the Medical Officer of Health of Kingston-upon-Hull informing him that the Minister had intimated that should the Local Health Authority apply for the use of oral poliomyelitis vaccine such application would be granted. That same morning a meeting was held in Kingston-upon-Hull between representatives of the Local Health Authority, the Local Medical Committee, and the Consultant in Infectious

Fig. 3



diseases of the Castle Hill Hospital. At this meeting the Medical Officer of Health outlined the progress of the outbreak and of his consultations

with the Ministry of Health on the previous day. There was general agreement that the use of oral poliomyelitis vaccine was justified. An emergency meeting of the City Council's Health Committee was held early in the afternoon, half an hour before the normal meeting of the City Council itself. Having heard the report of the Medical Officer of Health, the Health Committee resolved to ask the City Council in its capacity as Local Health Authority to request the Minister of Health to sanction the use of oral poliomyelitis vaccine. The Council agreed to the Health Committee's request and by mid-afternoon a formal application for the use of the vaccine had been sent by telex to the Minister of Health.

Arrangements for vaccination and for surveillance

Arrangements were immediately put in hand for the carrying out of the campaign. An informal meeting was held in Kingston-upon-Hull on Saturday, 14th October, between a senior medical officer of the Ministry of Health, the Consultant in Infectious Diseases at the Castle Hill Hospital, a representative of Leeds Regional Hospital Board, the director of the Public Health Laboratory Service in Hull, the Consultant Virologist of the Public Health Laboratory Service, Leeds, and the Medical Officer of Health for the city, at which several technical points were discussed, including (*a*) an initial survey before the first feeding of oral vaccine in order to determine as far as possible how much wild virus was circulating in the community, and (*b*) the necessity for the fullest investigation of any doubtful neurological lesions occurring either in cases seen by general practitioners or at hospitals. Past experience had shown that general medical practitioners tended to refer all cases of suspected poliomyelitis either to the Medical Officer of Health or to the Consultant in Infectious Diseases for an opinion. The Medical Officer of Health was averse to asking general practitioners specifically to report cases of neurological illness, on the grounds that if this request became public knowledge it would create uncertainty about the safety of the vaccine.

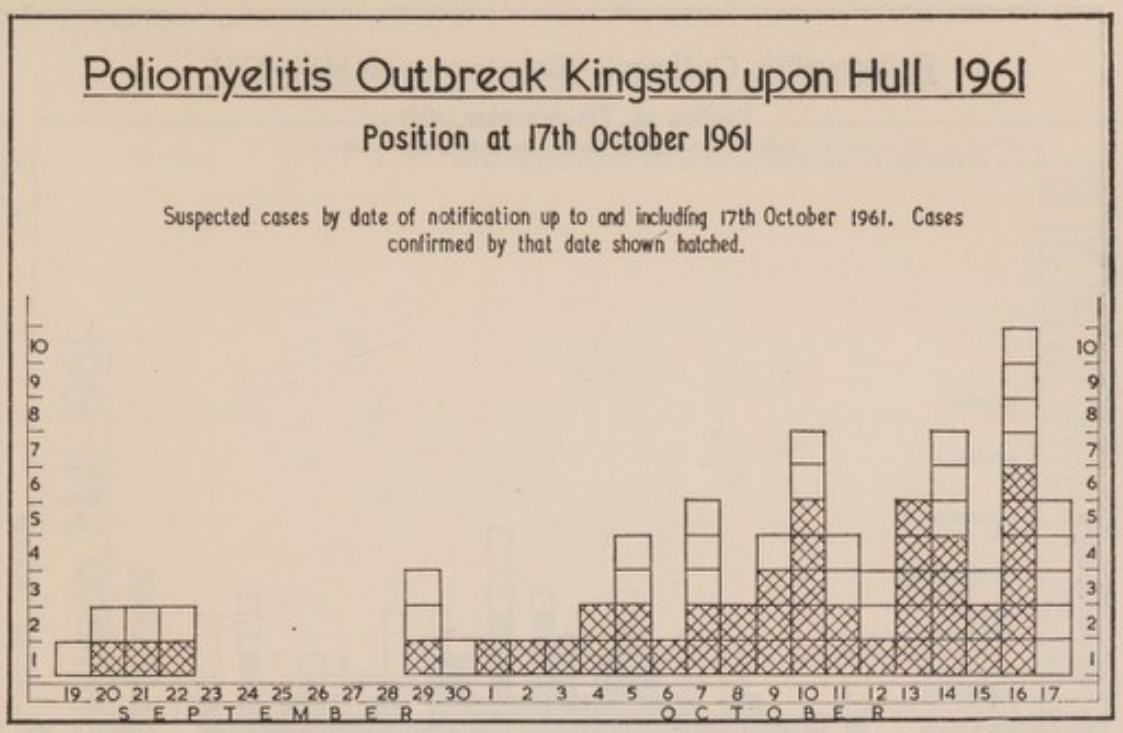
A senior medical officer on the staff of the city health department was deputed to maintain the closest contact with the general practitioners and with the general hospitals to provide a second opinion in doubtful cases and to ensure that patients with symptoms suggestive of neurological illness were fully investigated. As far as practicable all such cases were to be channelled to Castle Hill Hospital. The Regional Hospital Board made available to the consultant in infectious diseases the services of a consultant neurologist to assist in their clinical assessment.

It was decided that the general plan of campaign would be to aim at vaccinating the entire population of Kingston-upon-Hull and any other persons who presented themselves for vaccination within the city. In accordance with advice by the Central and Scottish Health Services Councils' Joint Committee on Poliomyelitis Vaccine it was decided to use an attenuated Type 2 oral poliomyelitis vaccine.

Subsequent progress of the outbreak

Feeding of the vaccine began on 17th October. During the interim period, which followed the decision on 12th October to use the vaccine, a further 30 cases were admitted to hospital and the total number of confirmed cases rose by 17th October to 44 (see Fig. 4) and subsequently to 53.

Fig. 4

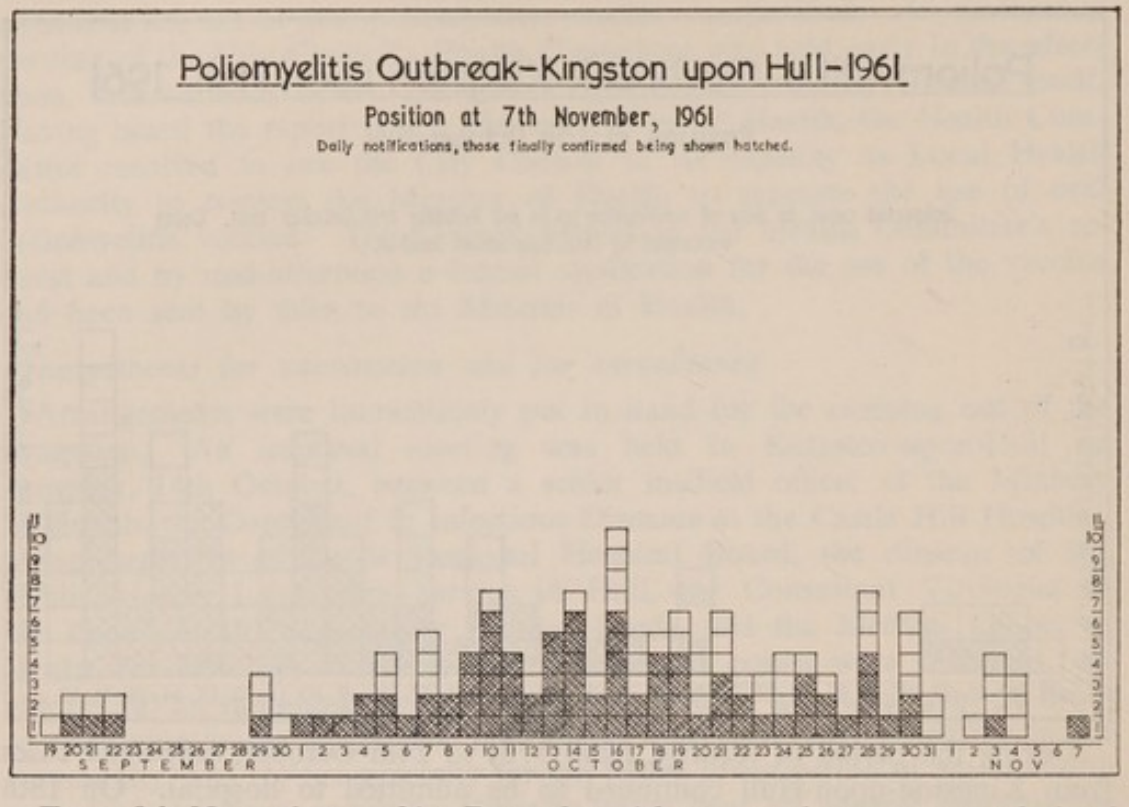


During the period of feeding, from 17th to 24th October, suspected cases from Kingston-upon-Hull continued to be admitted to hospital. On 18th October five patients were admitted, four of whom were subsequently confirmed as suffering from poliomyelitis. Six patients, four subsequently confirmed were admitted on 19th October. From 20th to 24th inclusive suspected cases were admitted daily as follows: 4, 6, 3, 3, 4 and, of these, a total of eight was subsequently confirmed.

After the closing of the vaccination campaign in Kingston-upon-Hull, the pattern of admissions to hospital remained the same for a further six days. The numbers of suspected cases admitted to hospital and of those subsequently confirmed as suffering from poliomyelitis were: 25th, 4 suspected, 3 confirmed; 26th, 3 suspected, 2 confirmed; 27th, 1 suspected and later confirmed; 28th, 7 suspected, 4 confirmed; 29th, 1 suspected and later confirmed; 30th, 6 suspected, 2 confirmed.

After this a few suspected cases were admitted to hospital but only two were subsequently confirmed. One was admitted on 3rd November and the other on 7th November. This was the last confirmed case of the outbreak, the date of onset of illness being 29th October. By 7th November a total of 140 suspected cases had been admitted to hospital of whom 84 were subsequently confirmed as suffering from poliomyelitis. (See Fig. 5.)

Fig. 5



From 8th November to 31st December, 16 suspected cases were admitted to hospital, but only 2 of these were subsequently confirmed. Their dates of onset were 24th November and 4th December, respectively, about a month after the outbreak proper had ceased.

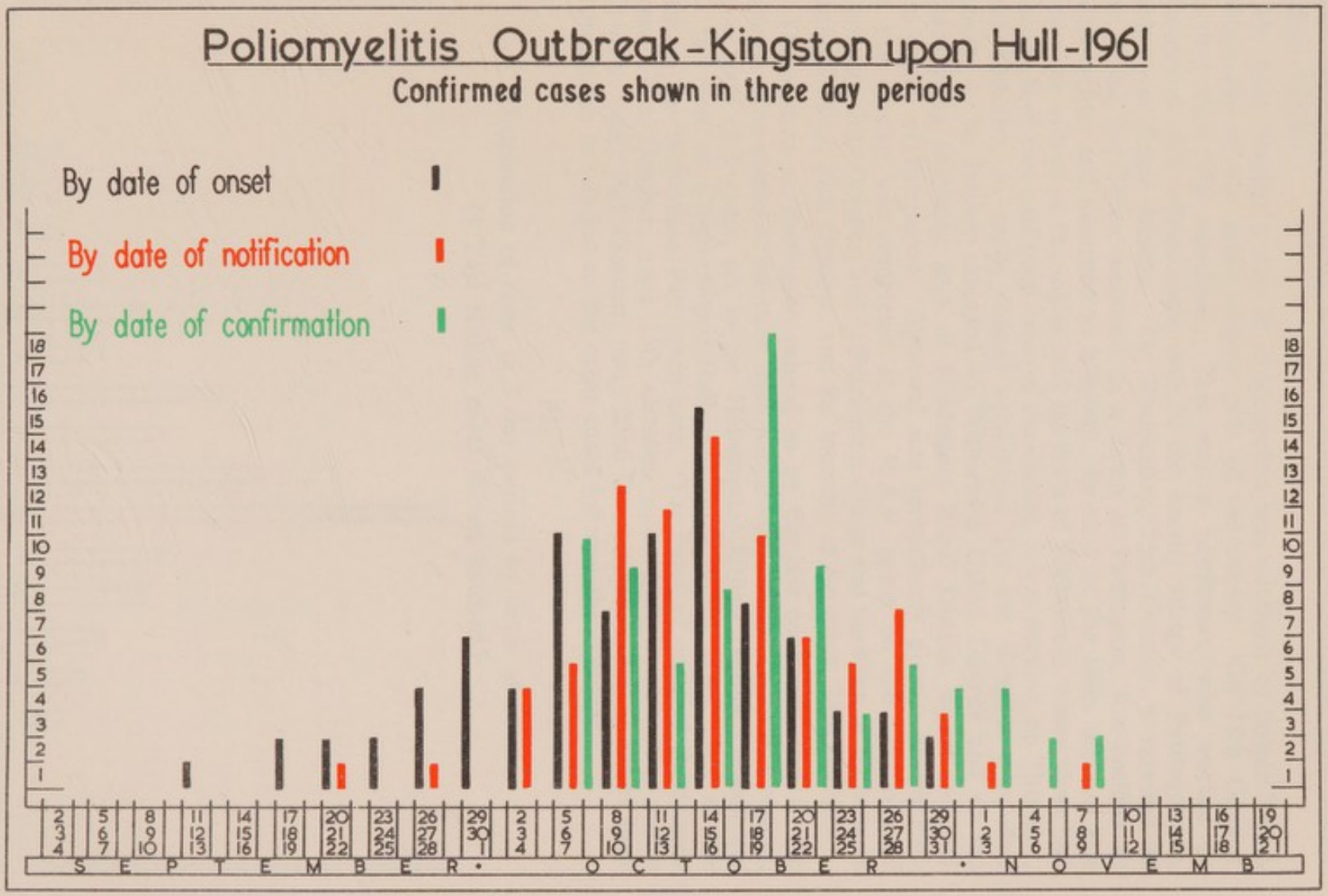
The distribution in time of the 84 cases, which were regarded as forming the outbreak, is shown in Fig. 6 by dates of onset, notification and final confirmation.

Extension to the East Riding

Soon after it had been announced that oral vaccine was to be distributed in Hull, representations were made to the county medical officer of the East Riding by Haltemprice Urban District for inclusion in the area of distribution of the vaccine. This district immediately adjoins the south-western part of Hull, where most of the cases had occurred. The request was not met at this stage of the outbreak, since no case had yet occurred in Haltemprice and it was thought desirable to concentrate available supplies of vaccine in Hull. The medical officer of health of Kingston-upon-Hull, however, arranged that persons living outside the city, who worked or had occasion to visit there, could receive oral vaccine at the city's distribution centres.

On 16th October a patient was admitted to hospital from the Hessle area of Haltemprice and on 17th October another patient was admitted from the Cottingham area. Both were subsequently confirmed as cases of paralytic poliomyelitis and, in view of this and the continuing increase in the number of cases in the adjoining western part of Kingston-upon-Hull, the question of extending vaccine distribution to Haltemprice was again considered. The clerk of the county council was authorised to submit a formal request to the Ministry of Health. This was sent on the evening of Wednesday, 18th October.

Fig. 6


Poliomyelitis Outbreak - Kingston upon Hull - 1961
Confirmed cases shown in three day periods
By date of onset
By date of notification
By date of confirmation
SEPTEMBER · OCTOBER · NOVEMB

Agreement to the extension was received by the county council on 19th October and arrangements were immediately put in hand for the Kingston-upon-Hull scheme to be extended to Haltemprice for three days from Monday to Wednesday, 23rd to 25th October. By this date four more cases of poliomyelitis had been admitted to hospital from Haltemprice Urban District.

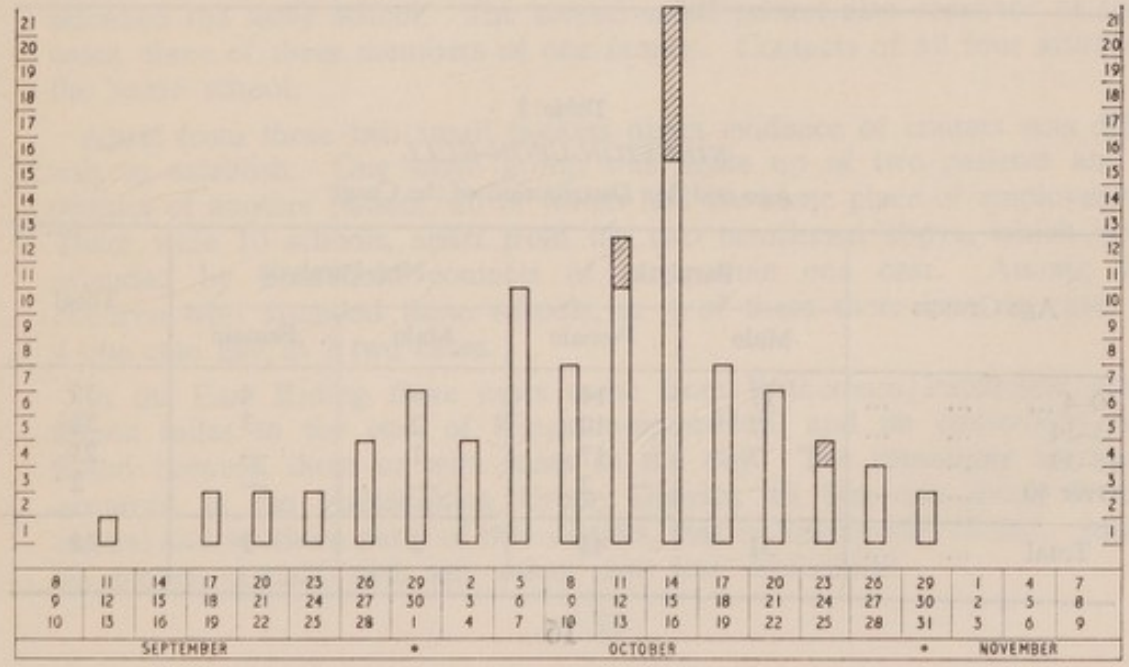
On 14th October a case of poliomyelitis was admitted to hospital from Withernsea in the south eastern part of the county. On 18th October another case was admitted. This was a hairdresser who worked in Withernsea and whose home was in the nearby village of Patrington in Holderness Rural District. On Wednesday, 25th October, a member of the Royal Air Force, stationed in a camp at Patrington, was notified as poliomyelitis and admitted to hospital. In view of the links between this camp, the village of Patrington and the town of Withernsea, where there had already been two confirmed cases of the disease, it was decided, on Thursday, 26th October, to make formal application for the Kingston-upon-Hull scheme to be further extended to Withernsea Urban District and to the immediately adjoining area of Holderness Rural District, which included the parish of Patrington. Approval was immediately given. Distribution of the vaccine was completed at the R.A.F. camp on the afternoon of Thursday, 26th October, and in Patrington village and the town of Withernsea during Friday, 27th October, and the morning of Saturday, 28th October.

The airman at Patrington proved to be the last confirmed case in the county. The spread of infection from Kingston-upon-Hull resulted, therefore, in a total of 9 cases, six in the Haltemprice Urban District immediately to the west of Kingston-upon-Hull, and three fifteen miles away to the east, in the Withernsea/Patrington area. The dates of onset of these cases were: 11th October, one; 13th October, one; 14th October, two; 15th October, two; 16th October, two; 22nd October, one. Fig. 7 shows their distribution in relation to the other cases forming the outbreak.

Fig. 7

Distribution of cases in 3 day periods by dates of onset.

(9 East Riding cases shown hatched.)



III

DISTRIBUTION OF THE CASES IN THE POPULATION

Age and Sex Distribution

Table 1 shows the estimated age and sex distribution of the population of Kingston-upon-Hull and Table 2 the age and sex distribution of the 84 confirmed cases of poliomyelitis comprised in the outbreak. It will be seen that, out of the total population of 303,000 in the city, there were 12,000 more females than males. The number of males in the 0–4 and 5–14 age groups exceeded the number of females, but in the 15–39 and over 40 age groups females predominated.

Of the confirmed cases there were more females at all ages, although in the 0–4 age group the number of females exceeded the number of males only by one. The age specific attack rates per 100,000 estimated population were : 0–4 years, 130 ; 5–14 years, 42 ; 15–39 years, 21 ; 40 years or over, 2 (see Table 10).

Table 3 shows the age and sex distribution of the 9 confirmed cases of poliomyelitis in the East Riding.

Table 1

KINGSTON-UPON-HULL

Age and Sex Distribution of the Population

Age Groups	Male	Female	Total
0–4	13,852	13,148	27,000
5–14	27,000	25,700	52,700
15–39	58,750	59,250	118,000
Over 40	46,064	59,536	105,600
Total	145,666	157,634	303,300

Table 2

KINGSTON-UPON-HULL

Age and Sex Distribution of the Cases

Age Groups	Paralytic		Non-Paralytic		Total
	Male	Female	Male	Female	
0–4	17	14	—	4	35
5–14	7	10	2	3	22
15–39	7	17	1	—	25
Over 40	—	2	—	—	2
Total	31	43	3	7	84

Table 3

EAST RIDING

Age and Sex Distribution of the Cases

Age Groups	Paralytic		Non-Paralytic		Total
	Male	Female	Male	Female	
0–4	—	—	—	—	—
5–14	1	—	—	—	1
15–39	2	5	—	—	7
Over 40	—	1	—	—	1
Total	3	6	—	—	9

Spatial Distribution

The spatial distribution of the cases through the city presented an extremely interesting picture. Fully 30 of the 84 confirmed cases lived in a densely populated area where a considerable proportion of the property is substandard. The remaining cases were scattered throughout the city, except for two small pockets of four cases each. Such a concentration of cases had not been seen in the city before. Even in the 1947 outbreak, when 77 cases occurred, all were more or less uniformly scattered. The distribution in the 1961 outbreak bore a very close relation to the standard of housing. The great bulk of the cases occurred in substandard housing accommodation and the smallest number in post-war housing estates.

Of the two small pockets referred to, one consisted of four cases living in close proximity. One of the cases and family contacts of three of them attended the same school. The second small pocket also consisted of four cases, three of them members of one family. Contacts of all four attended the same school.

Apart from these two small pockets direct evidence of contact was difficult to establish. One small group was made up of two patients and a contact of another patient, all of whom had the same place of employment. There were 10 schools, apart from the two mentioned above, which were attended by household contacts of more than one case. Among the children who attended these schools, in 4 of them there was no case, in 4 one case and in 2 two cases.

In the East Riding three cases came from Withernsea/Patrington area, fifteen miles to the east of Kingston-upon-Hull, and no connection was found between them or with cases in the city. The remaining six cases occurred in the Haltemprice Urban District, all but one living in the central and southern parts of that district, that is Anlaby and Hessle. Again no proven contact with any other case was established.

Social Class Distribution

Table 4 shows the social class distribution of the population of the city and of the 84 confirmed cases. The five social classes, in accordance with the Registrar General's classification, are :—

I. Professional, e.g. doctors, dentists, company directors, etc.

II. Intermediate occupations, e.g. estate managers, land agents.

III. Skilled occupations, e.g. mine workers, transport workers, clerical workers.

IV. Partly skilled occupations, e.g. street masons, machine minders, printing machine assistants.

V. Unskilled occupations, e.g. building and dock labourers.

The first line of the table shows the percentage of the population of Kingston-upon-Hull which falls within each of the five social classes. The second line gives the numbers that would be expected to fall within each social class out of a population of 84 if the class distribution of the cases was the same as that of the population, and on the third line the actual class distribution of the 84 cases. The last line of the table gives the percentage of the expected population falling in each social class. It will be seen that, while the number of cases in class IV was almost equal to the expected figure, the numbers in classes II and III were less and the number in class V greater. In other words, in this outbreak a disproportionately large numbers of cases occurred in the lowest social class.

Table 5 gives a more detailed analysis of the cases by age group, state of paralysis and social class.

Table 4

KINGSTON-UPON-HULL

Social Class Distribution of Population and Cases

	Social Class				
	I	II	III	IV	V
Percentage of total population	1·8	10·9	48·4	16·0	22·9
Expected cases	1·5	9·1	40·6	13·5	19·2
Actual cases (84)	—	3	32	13	36
Per cent of expected	—	33·0	79·0	96·0	187·0

Table 5

POLIOMYELITIS OUTBREAK—KINGSTON-UPON-HULL, 1961

Cases in Age Groups by Social Classification

Age Groups	Paralytic										Non-Paralytic										Paralytic					Non-Paralytic					Total					
	Male					Female					Male					Female					Male and Female					Male and Female										
	i	ii	iii	iv	v	i	ii	iii	iv	v	i	ii	iii	iv	v	i	ii	iii	iv	v	i	ii	iii	iv	v	i	ii	iii	iv	v	i	ii	iii	iv	v	
0— 4 ...	–	1	9	1	6	–	1	2	6	5	–	–	–	–	–	–	–	–	–	4	–	2	11	7	11	–	–	–	–	4	–	2	11	7	15	35
5—14 ...	–	–	2	–	5	–	–	5	1	4	–	1	–	1	–	–	–	2	–	1	–	–	7	1	9	–	1	2	1	1	–	1	9	2	10	22
15—39 ...	–	–	2	1	4	–	–	8	3	6	–	–	1	–	–	–	–	–	–	–	–	–	10	4	10	–	–	1	–	–	–	–	11	4	10	25
Over 40 ...	–	–	–	–	–	–	–	1	–	1	–	–	–	–	–	–	–	–	–	–	–	–	1	–	1	–	–	–	–	–	–	–	1	–	1	2
Total ...	–	1	13	2	15	–	1	16	10	16	–	1	1	1	–	–	–	2	–	5	–	2	29	12	31	–	1	3	1	5	–	3	32	13	36	84

Vaccinal State of the Population at 30th September

Table 6 shows the population of Kingston-upon-Hull at 30th September, 1961, and the numbers who had received Salk vaccine by age groups.

In the 0–4 years age group 50 per cent of the children had received two or more injections. No poliomyelitis injections were offered to children under the age of six months.

In the 5–14 age group 83 per cent had received two or more injections and in the 15–" 40 " age group 41 per cent had had two or more injections. Although this latter figure was not as good as could have been hoped for, closer scrutiny of this group revealed that in the 15–28 age group 59 per cent had been vaccinated, while in the 29–" 40 " age group 22 per cent had been vaccinated.

Table 6

KINGSTON-UPON-HULL

Total population (all ages)	303,000
Vaccinated with 2 or more injections	104,800
Percentage vaccinated	35
0–4 *years (incl.):*	
Population in group	27,000
Vaccinated with 2 or more injections	13,400
Percentage vaccinated	50
5–14 *years (incl.):*	
Population in group	52,700
Vaccinated with 2 or more injections	43,550
Percentage vaccinated	83
15–" 40 " *years (incl.):*	
Population in group	118,000
Vaccinated with 2 or more injections	47,850
Percentage vaccinated	41

N.B.—" 40 " years refers to those persons who were under 40 years on 1st February, 1960, the date upon which the routine vaccination scheme was extended to include all under 40 years of age.

Table 7 shows the percentage of the population of Kingston-upon-Hull who had had one, two, three, or four injections of Salk vaccine. While only 35 per cent of the total population of the city had had injections of Salk vaccine there remained a large proportion of the population (i.e. all those over " 40 " years of age) to whom the offer of the vaccine had not been made. The figures show that at the 30th September just over half of the population who had had an opportunity to be vaccinated had in fact received one or more injections of Salk vaccine.

Table 7

KINGSTON-UPON-HULL

Salk Vaccinal State of Population at 30th September, 1961

Number of Injections	Number Vaccinated	Percentage of Total Population	Percentage of Population under "40" years of age
1	1,700	0·6	0·9
2	16,800	5·5	8·5
3	66,400	21·9	33·6
4	21,600	7·1	10·9
Total ...	106,500	35·1	53·9

Table 8 shows vaccination figures for the East Riding. There was a reasonably high acceptance rate among children but that of young adults could have been better.

Table 8

EAST RIDING

Salk Vaccinal State of Population at 30th September, 1961

	Whole County	Area of County within 15 mile radius from centre of Kingston-upon-Hull
Population	223,783	115,162
Percentage of total population vaccinated—2 injections or more	32	35
Percentage of total population vaccinated—3 injections	27	29
Percentage of children born 1943–1961 vaccinated—2 injections	79	79
Percentage of young adults born 1933–1942 vaccinated—2 injections	44	45
Percentage of children aged 5–11 years vaccinated—4 injections	52	56

Table 9

POLIOMYELITIS OUTBREAK—KINGSTON-UPON-HULL, 1961

Cases in Age Groups showing Salk Vaccinal State

	Paralytic										Non-Paralytic										Paralytic					Non-paralytic Male and Female					All Cases					Total
	Male					Female					Male					Female					Male and Female															
No. of Doses Salk Vaccine	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	
Age Groups 0— 4	11	2	3	1	–	10	2	2	–	–	–	–	–	–	–	2	1	–	1	–	21	4	5	1	–	2	1	–	1	–	23	5	5	2	–	35
5—14	3	2	1	1	–	2	2	3	2	1	–	–	1	1	–	1	–	1	1	–	5	4	4	3	1	1	–	2	2	–	6	4	6	5	1	22
15—28	3	–	1	1	–	8	1	1	3	–	–	–	–	1	–	–	–	–	–	–	11	1	2	4	–	–	–	–	1	–	11	1	2	5	–	19
29—39	2	–	–	–	–	2	2	–	–	–	–	–	–	–	–	–	–	–	–	–	4	2	–	–	–	–	–	–	–	–	4	2	–	–	–	6
Over 40	–	–	–	–	–	2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2	–	–	–	–	–	–	–	–	–	2	–	–	–	–	2
Total ...	19	4	5	3	–	24	7	6	5	1	–	–	1	2	–	3	1	1	2	–	43	11	11	8	1	3	1	2	4	–	46	12	13	12	–	84

Table 10

POLIOMYELITIS OUTBREAK—KINGSTON-UPON-HULL, 1961

Age-specific attack rates by Salk vaccinal state at 30th September, 1961

Age Groups	Population	Cases	Rate per 100,000
0–4 *years:*			
2 injections or more	13,400 (50%)	7	52
Not vaccinated	13,600	28	206
Total	27,000	35	130
5–14 *years:*			
2 injections or more	43,550 (83%)	12	28
Not vaccinated	9,150	10	109
Total	52,700	22	42
15–39 *years:*			
2 injections or more	47,850 (41%)	7	15
Not vaccinated	70,150	18	26
Total	118,000	25	21
Over " 40 " *years:*			
Not vaccinated	105,600	2	2
Total	303,300	84	28

Note.—" Not Vaccinated " includes persons who (*a*) have had no injections or (*b*) have had one injection only.

Salk Vaccinal State of the Cases forming the Outbreak

Table 9 shows the 84 cases in Kingston-upon-Hull classified by age, sex and number of injections of Salk vaccine. In the two youngest age groups, 0–4 years and 5–14 years, there was a marked difference between the attack rates among the vaccinated and unvaccinated, consistent with the known protective action of the vaccine. The difference in the older age groups was less, but this was to be expected on account of the higher proportion of persons in later life who have acquired natural immunity. Table 10 shows the age specific attack rates according to Salk vaccinal state.

In the East Riding there was only one case in the two youngest age groups, a child of 12 years who had had 3 injections of Salk vaccine. Seven cases occurred among persons aged 15–39 years, of whom one had had no injection of Salk vaccine, 2 one injection and 4 three injections. The remaining case was an unvaccinated person over 40 years of age.

IV

DETAILS OF THE CASES

All cases of suspected poliomyelitis occurring in Hull and the East Riding of Yorkshire were admitted to Castle Hill Hospital, Cottingham, East Yorkshire. The patients were sent first to a cubicle ward and remained there until the diagnosis was confirmed, when they were transferred to one of the three large wards set aside exclusively for cases of poliomyelitis. Cases showing evidence of bulbar and respiratory paralysis were admitted direct to the respiratory centre which is a 20-bedded single cell cubicle block containing operating theatre, anaesthetic room, X-ray development room, along with a battery of positive pressure respirators, where a 24-hour resident medical anaesthetic service was maintained by the consultant anaesthetists and their staff.

All patients were kept in hospital for a minimum period of three weeks before being sent home, or transferred to an orthopaedic hospital. When a patient could not be transferred to an orthopaedic ward set aside solely for poliomyelitis, then the patient was kept in Castle Hill Hospital for six weeks. Paralysed cases were seen by a consultant orthopaedic surgeon who advised on orthopaedic treatment and disposal of the patient. All patients received neurological supervision by a consultant neurologist.

Diagnostic Criteria

The diagnosis in each of the cases which were regarded as forming the outbreak was established after consideration of all the available details of medical history, clinical examination and virological findings.

The clinical criteria adopted were as follows : a suggestive prodromal illness, signs of meningeal irritation, cerebrospinal fluid changes consistent with poliomyelitis with or without evidence of anterior horn cell, cranial nerve or medullary involvement.

Virological investigations were made in all cases. Specimens of faeces were obtained from each case within 24 hours of admission. Where a specimen could not be obtained naturally, a saline enema was given. Rectal swabs were only accepted when it was impossible to obtain faeces. Virology reports were obtained in three days and this was very important when the turnover of patients was at its height and the demand on cubicles was high. Acute and convalescent (paired) sera were also obtained from all suspected cases in the first and third week of the disease and in some instances a third specimen of serum was obtained for further testing.

The virological techniques used are described in detail in the Appendix to this Report. Patients were considered to have a poliovirus infection either when a poliovirus was isolated from their faeces or when they had positive complement-fixation or neutralizing antibody tests. The complement-fixation test was considered to be positive when acute and convalescent-phase sera showed a four-fold or greater rise in antibody against any of the three poliovirus antigens or when there was an unchanging antibody titre of 1/64 or more against poliovirus type I antigen alone, the titres against types 2 and 3 being $<1/4$. The neutralizing antibody test was considered to be positive when acute and convalescent-phase sera showed a four-fold

or greater rise or fall of antibody against one or more of the three poliovirus serotypes or an unchanging titre of 1/16,000 or more against poliovirus Type I.

Classification of Cases

A distinction was made between paralytic and non-paralytic cases, in accordance with the Public Health (Acute Poliomyelitis, Acute Encephalitis and Meningococcal Infection) Regulations, 1949. Paralytic cases were classified as of spinal, bulbar or bulbo-spinal type.

After the initial muscle evaluation the charting of muscles was carried out at weekly intervals. The degree of muscle power was graded according to the system adopted by the Nerve Injuries Committee of the Medical Research Council (1954).

The general assessment of the severity of paralysis adopted for cases on admission, on discharge, and follow-up at two months and three months after onset was as follows :—

Minor paralysis—where there was weak but functional extremity.

Significant paralysis—where there was flaccid paralysis of extremity.

Severe paralysis—where the patient was confined to bed or wheel chair or required extensive bracing for paralysed limbs.

Clinicat Findings

Of the 93 cases forming the outbreak, 15 showed no paralysis at the time of admission to hospital, but 5 of these developed paralysis after admission. The classification on discharge or transfer from the hospital was paralytic 83 cases, non-paralytic 10 cases. The paralytic cases comprised 68 of spinal type, 1 of bulbar type and 14 of bulbo-spinal type.

The case which was classified as of bulbar type was the first case of the outbreak, a child aged 8 years who was admitted to hospital with severe paralysis of the face, palate and pharynx. The 14 bulbo-spinal cases had involvement of limb or trunk muscles as well as of the face, palate or pharynx. In the remaining 68 paralytic cases the sites affected, while under observation in hospital, were : one limb only, 16 cases ; more than one limb without involvement of the trunk, 6 cases ; back muscles, with or without involvement of a limb, 37 cases ; thoracic or abdominal muscles, with or without involvement of a limb, 9 cases.

On admission 36 patients had minor paralysis, 19 significant paralysis and 23 severe paralysis. Five patients with pharyngeal paralysis were fed nasally, one patient needed an immediate tracheotomy and another within 48 hours of admission required tracheotomy and artificial respiration by means of a positive pressure respirator.

Twenty-eight patients who had shown varying degrees of paralysis were discharged from hospital at the end of three weeks, having made a complete recovery. Twenty-two patients still had minor paralysis, 14 significant paralysis and 20 severe paralysis. Three of the five patients with pharyngeal paralysis were discharged at the end of three weeks, but two of them were kept in hospital for a longer period owing to persistent palatal weakness with nasal speech and slight difficulty in swallowing. One of the patients

who needed tracheotomy, a boy aged 8, was still severely paralysed at the end of three weeks but eventually made a complete recovery. The other, a man aged 31, who also had extensive paralysis of the limbs, died on 6th January, 1962, eleven weeks after his admission to hospital. Forty-five of the cases were transferred to orthopaedic hospitals and the remainder discharged to their own homes.

The patients were followed up at intervals of two months and three months after transfer or discharge. At the end of three months 47 showed no evidence of paralysis, 21 had minor paralysis (including one case originally classified as non-paralytic), 7 had significant paralysis, 17 severe paralysis and one had died.

The majority of patients, who were left with residual weakness, had shown paralysis of significant or severe degree at some time during their stay in hospital. Table 11 shows the correlation between residual weakness and previous maximum severity of paralysis.

Table 11

		Maximum Severity of Paralysis in Hospital				
		Non-paralytic	Minor	Significant	Severe	Total
Residual Paralysis after 3 months	None	9	29	4	5	47
	Minor	1	9	5	6	21
	Significant ...	—	1	4	2	7
	Severe	—	1	1	16*	18
	Total ...	10	40	14	29	93

* Including one death.

Age and Sex Distribution

Table 12 shows the 93 cases classified by age, sex and presence of residual paralysis at the end of three months.

The number of females exceeded the number of males in each age group. The difference was slight among children aged 0 to 4 and 5 to 14 years and greatest in the 15 to 39 year age group. The total numbers were male 37 cases, female 56 cases.

There was a relative preponderance of cases among children aged 0 to 4 years. This group contained 35 of the total of 93 cases (37·6 per cent) and 25 of the 46 cases (54·3 per cent) who showed residual paralysis at the end of three months. Nearly three-quarters of the patients aged 0–4 years were left with residual weakness, compared with about one-third of the patients in the other age groups.

Table 12

Age (years)	Sex	Type of Case			Total Number of Cases	Number with Residual Paralysis
		Non-paralytic	Spinal	Bulbar or Bulbo-spinal		
0–4 ...	M	—	17	—	17	14
	F	4	10	4	18	11
	Total	4	27	4	35	25 (71·4%)
5–14 ...	M	2	7	1	10	2
	F	3	7	3	13	6
	Total	5	14	4	23	8 (34·8%)
15–39 ...	M	1	8	1*	10	3
	F	—	17	5	22	7
	Total	1	25	6	32	10 (31·3%)
40+ ...	M	—	—	—	—	—
	F	—	2	1	3	3
	Total	—	2	1	3	3 (100%)
All ages	M	3	32	2	37	19 (51·4%)
	F	7	36	13	56	27 (48·2%)
	Total	10	68	15	93	46 (49·5%)

* Including one death.

Among the adult female patients two were pregnant. The first of these, who was aged 21 years, was 7 months pregnant. This patient had a minor degree of paralysis of one leg and was discharged to her home, completely recovered, at the end of three weeks. She was subsequently delivered of a healthy premature infant of birth weight 5 lbs. The second patient, who was aged 23 years, was 5 months pregnant and aborted 6 days after admission to hospital. This patient had severe paralysis, which affected both of the arms, both legs, back and abdominal muscles. At the end of three months there was severe residual paralysis of both legs and back.

Salk vaccinal state

Table 13 shows the 93 cases classified according to the number of previous injections of Salk vaccine and the degree of residual paralysis after 3 months. None of the patients who had had three or more injections was left with significant or severe paralysis.

Table 13

		Number of Injections of Salk Vaccine					Total
		0	1	2	3	4	
Residual Paralysis after 3 months	None	18	7	8	14	—	47
	Minor	13	2	2	3	1	21
	Significant ...	6	1	—	—	—	7
	Severe	11	4	3	—	—	18
	Total ...	48	14	13	17	1	93

Virological Findings

The results of virological examination of the ninety-three clinically confirmed and notified cases are shown in Table 14. Poliovirus serological type 1 was isolated from the stools of 55 (59 per cent) of them—together with poliovirus 2 in one instance—and poliovirus 2 alone was isolated from one patient. Twenty (21 per cent) patients with negative stools had positive complement-fixing or neutralizing antibody tests. Thus, in total, 76 of the 93 patients—82 per cent—were shown by the Virus Laboratory to have a poliovirus infection. In addition, an unidentified cytopathic agent, not Coxsackie B1–6, Coxsackie A9, ECHOviruses 1 to 20 or adenovirus, was isolated from one patient with non-paralytic poliomyelitis and no laboratory evidence of poliovirus infection.

The bulk of the isolations of poliovirus was made from the younger patients; many of the older ones being diagnosed on serological grounds alone. This finding and other aspects of the virological investigations are considered in more detail in Section VIII of this Report.

Table 14

Results of the virological examination of the 93 notified cases of poliomyelitis by age and type of laboratory test for poliovirus infection.

Age in years	Poliovirus isolated from faeces		Poliovirus not isolated		All tests negative	Total
	Type 1	Type 2	CFT +	CFT – ve Neutr. +		
0–4	33*	0	1	1	0	35
5–14	15	0	1	4	3†	23
15–39	7	1	3	8	13	32
40 + ...	0	0	0	2	1	3
Total	55	1	5	15	17	93

* One with both viruses Types 1 and 2.
† Includes one patient with an unidentified cytopathic agent in the stool.
CFT+ = complement-fixation test positive.
Neutr.+ = neutralising antibody test positive.

Subsequent cases

Two cases were notified in 1961 after the outbreak proper had ceased. The first of these was a man aged 43 years who was taken ill on 24th November and admitted to hospital on 4th December. Within 12 hours of admission he developed respiratory paralysis needing tracheotomy and artificial respiration with a positive pressure respirator. His condition improved temporarily but soon deteriorated. He developed quadriplegia and died 8 days after admission to hospital. Examination of post-mortem material showed histological evidence of poliomyelitis and Type 1 poliovirus was isolated from the medulla.

The second of these subsequent cases was a girl aged 1½ years who was taken ill on 4th December and admitted to hospital on 8th December with paralysis of the right leg. Type 1 poliovirus was isolated from the faeces. This patient subsequently made a complete recovery.

V

THE VACCINATION CAMPAIGN

The vaccination campaign in Kingston-upon-Hull preceded that in the East Riding and the details of the administrative arrangements, which were made by the two Local Health Authorities concerned, differed considerably. They are, therefore, described separately.

KINGSTON-UPON-HULL

The planning of the vaccination campaign began immediately the Local Health Authority resolved to ask for oral vaccine, the Minister having indicated previously that a formal request for its use would be approved.

It was decided to open the campaign on Wednesday, 18th October, and to close it on the evening of Tuesday, 24th October. It was estimated that about five days (which included a Saturday and a Sunday) would be necessary to prepare for the campaign, allocating centres, printing record cards and obtaining the vaccine and other necessary supplies and equipment. Meanwhile it was necessary to maintain medical, nursing and clerical staff at the emergency clinics where Salk vaccination was in progress.

The decision to open the campaign on 18th October was in fact amended on the morning of Tuesday, 17th October. The state of the outbreak had worsened and, as it appeared that all the necessary preliminary arrangements would be completed on the afternoon of the 17th October, it was decided to open as many of the centres as possible at 5 o'clock that evening.

Owing to the short time which was available for planning it was decided to break up the work into sections and to appoint someone to be in charge of each section, e.g. medical, nursing, clerical, transport, dilution of vaccine, distribution of vaccine and other supplies. The person in charge of each section was instructed on the procedure to be followed and given authority to act as he considered necessary, making decisions on the spot. Co-ordination of the work and planning was brought about through regular meetings of these heads of sections.

In addition to his overall responsibility for the organisation and management of the campaign, the Medical Officer of Health specifically undertook responsibility for public relations. In order to persuade as many people as possible to come forward for vaccination it was essential that co-operation be sought from the press, radio and television services. In addition it was most important that general medical practitioners should be kept fully informed of the progress of the outbreak and the steps being taken by the Local Health Authority. The Consultant in Infectious Diseases agreed that all publicity and information about new admissions to hospital should be dealt with by the Medical Officer of Health so that press and other reporters were able to obtain all their news about both the outbreak and the vaccination campaign from one source.

The local press were extremely helpful in publicizing details of the campaign and conveying to the public the urgency of the need to receive the oral vaccine. The British Broadcasting Corporation, with its radio and television services, and the Independent Television Authority, with

its various programmes, gave excellent cover to the story, whilst the Rediffusion Service assisted by making regular announcements through its local station. Advertisements in the local press gave details of centres and times of opening, posters were displayed in large stores and public buildings and announcements made at football matches. The Hull Daily Mail distributed small posters to the shops of newsagents when delivering bundles of newspapers.

The reaction of the public was immediate. Large numbers telephoned the Department each day from early morning until late at night seeking advice on the action which they or their families should take. In addition many calls were received from press officers in all parts of the county. In order that essential work might proceed and, later, that contact could be maintained with the centres distributing the vaccine, five additional telephone lines were installed with privately circulated numbers.

To ensure that the vaccine was easily available to everyone, it was decided that as many fixed distribution centres as possible should be opened. Since the most widely distributed and best known public buildings were the schools, it was agreed with the Education Department that accommodation would be made available in 40 of them, situated in various parts of the City. These were supplemented in strategic positions by a further 11 centres in hospitals, clinics, church halls, and a large central store. Apart from one or two exceptions it was planned that the centres should be open from 9 a.m. to 9 p.m. each day of the campaign, including Sunday. This was amended subsequently because by Saturday, 21st October, the numbers who had already attended were so great that it was possible to reduce the number of centres to 12 and to shorten the hours of opening.

Four groups of people were given special consideration in the planning of the distribution of the vaccine. Firstly, there were the school children. It was decided that those at schools at which fixed centres were established would be given the vaccine during a slack period by the staff stationed there. Children attending schools at which there was not a fixed centre would be visited by mobile teams. Letters and consent cards were distributed through the schools to the parents.

Secondly, there were workers in large factories and large shops. Mobile teams were organised to visit a number of these establishments. Altogether a total of 15 mobile teams were operating in factories, shops and schools at the peak of the campaign.

The remaining two groups to be given special consideration were the handicapped and the homebound. The names and addresses of handicapped persons were obtained from various welfare organisations and through the press. These were all recorded in lists of convenient numbers and volunteer car drivers took them to the nearest centre. Similarly, the names and addresses of the homebound, a group in which the public showed a particular interest, were listed and, with the slackening of pressure towards the end of the campaign, these were visited by the mobile teams.

In order to mount the campaign and carry it through it was necessary to concentrate most of the staff of the Health Department on this one task. All Local Health Authority and School Health Service Clinic and other routine work was suspended from one day before the opening of the

campaign until it ended, the only exception being that ante-natal clinics continued to function. Even so it was impossible for the Health Department to provide enough staff for the headquarters, fixed centres and mobile teams. An appeal, therefore, was made in the press for nurses to volunteer to assist with the dispensing of the vaccine, whilst the Women's Voluntary Service was asked to undertake the task of organising volunteers to help with the clerical work at the centres and the Civil Defence Corps to provide staff for marshalling the public. The Women's Voluntary Service also co-ordinated the work of recruiting voluntary car drivers for the transport of handicapped people and for collecting supplies of vaccine and record cards from the centres when they closed in the evening. The number of persons who did in fact contribute to the campaign in either a paid or a voluntary capacity is not known precisely, but is estimated at around 3,000.

The printing of stationery was an urgent problem. There was no precedent and everything had to be drafted from scratch before being handed over to the printers. Such items as advertising posters were dealt with first, then letters to parents of school children, record cards, and letters to general practitioners. It was realized that it would be impossible to follow the general practice of the Health Department of sending a note to the general practitioner of each person on his list who had been vaccinated. It was decided, therefore, to give to each person presenting himself for vaccination a short letter stating that he had received oral vaccine. He was requested to insert his name and address on the letter and then to put the letter into his doctor's letterbox.

Special record cards were designed. The details required were kept as simple as possible—surname, Christian name, sex, date of birth, address, name of school attended, date of administration, batch number, and a general consent. To expedite printing and avoid confusion the same wording was used for all record cards, although the name of school attended was needed only for the school children. A colour system was introduced in order to help the subsequent sorting of the cards. The system was as follows:

Kingston-upon-Hull residents...	A grey card for all children attending school or under school age.
	A deep pink card for all persons above school age who had had one or more injections of Salk vaccine.
	A cream card for all persons above school age who had not had any injections of Salk vaccine.
For all persons resident outside the City boundary.	A pale pink card.

It was foreseen that at times there would be concentrations of cars and other vehicles at the headquarters, particularly early in the morning when the vaccine was being taken out to the centres. The Chief Constable was therefore asked to waive parking restrictions and ensure that access was always available at premises being used for the campaign. He readily agreed.

Whilst the planning of the campaign had been carried out by a relatively few senior officers, the successful execution of the scheme involved up to 300 staff plus the large number of volunteers. The permanent staff, therefore, had to be made fully aware of how the campaign was planned and what their own particular duties and responsibilities were. The briefing of the staff was carried out in two ways. Firstly, a memorandum was prepared and a copy given to each officer engaged in the campaign. Spare copies were available at each centre for the information of volunteer helpers. This memorandum gave details of the general scheme, set out the individual responsibility of the medical, nursing and clerical staff and the voluntary workers, gave details of supplies, and included instructions for obtaining further supplies of all items, the method of calling for emergency medical aid, ordering transport, completing record cards, the procedure to be followed at the centres, the hours of duty and other details. It also included a technical note on the vaccine, how to dispense it and how to use the sterilized droppers. The memorandum also contained a complete list of centres with their telephone numbers and the telephone numbers of the private lines to the headquarters and of other lines on which particular officers could be contacted at the headquarters. Secondly, on the afternoon of Tuesday, 17th October, the medical, nursing and clerical staff involved were called to a meeting at which the Medical Officer of Health outlined the scheme and answered questions of a general nature. The nurses and clerks then divided into two groups and were given more detailed instructions as to their particular duties.

At the offices of the Health Department the administrative staff were organised as follows :

The Medical Officer of Health was generally responsible for the campaign, with specific duties as regards press and public relations.

The Deputy Medical Officer of Health was responsible for medical and technical aspects of campaign, including all matters to do with the vaccine.

One senior medical officer was made responsible for seeking the co-operation of shops, factories and other establishments in publicizing the campaign and for arranging for the mobile teams to visit the large factories. A second senior medical officer undertook liaison work with the general medical practitioners and the hospitals, particularly as regards patients referred to the Medical Officer of Health for a second opinion.

The Superintendent Nursing Officer's duty was to ensure that a nurse was present at each centre at all times for dispensing the vaccine. In addition she undertook the organization of mobile teams to visit the homebound, the factories and the schools.

The chief clerk was responsible for providing adequate clerical staff for the headquarters, fixed centres and mobile teams, for all necessary supplies, routine advertising and transport arrangements.

Staffing of Centres

After considering the legal implications, the Town Clerk advised that no one holding a lesser qualification than that of a State Registered Nurse should be allowed to dispense the vaccine. This advice was accepted and consequently the staff at fixed centres was as follows :—

Senior medical officers were each responsible for supervising an area containing about one quarter of the centres. Assistant medical officers were allocated to each area. Their duty was to tour all the centres in their area so that any medical question which arose could be dealt with quickly on the spot. In practice few problems were encountered and assistant medical officers undertook dispensing duties from time to time to relieve the nursing staff.

A nurse was on duty at each centre at all times. The nurse was the senior member of the team and had the sole responsibility for dispensing the vaccine, except when she was relieved by one of the assistant medical officers.

A full-time clerical officer of the Local Authority was allocated to each centre. This officer was responsible for ensuring the completion of record cards, the maintenance of adequate supplies of vaccine, and other items, and for the orderly marshalling of all persons attending for vaccination. These duties involved communication with headquarters at fixed times to report on the position at the centre.

The Women's Voluntary Services and the Civil Defence Corps provided from two to four volunteers at all times at each centre to assist with the clerical and marshalling work.

Supplies

Each centre was issued with a supply of vaccine and droppers, lump sugar, trays and tissue paper for the sugar, one litre of syrup (B.P.), 100 disposable spoons, record cards, letters for general practitioners, rubber bands for parcelling cards, transparent adhesive tape for sealing part-used vials, ball-point pens, pencils and posters for display outside the centre.

In planning the organization of a fixed centre, it was expected that each person attending would be interviewed by a clerk who would fill in the required details on the appropriate record card which would then be signed by the applicant. The applicant would then proceed to the nurse and pick up a lump of sugar on which the nurse would put two drops of vaccine. The sugar would then be eaten in the presence of the nurse and the applicant given the letter which he was asked to complete and take to his own doctor. Very young children were to be given the vaccine in a spoonful of syrup if they were unable to eat a lump of sugar.

The enormous response on the first evening and the following days was such, however, that, in order to keep the queues moving, the clerical staff concentrated on giving the appropriate record card to each applicant, who was then asked to complete the details himself. He then handed the card to the clerk who checked the details and in return gave him the letter for his doctor. The applicant then proceeded to the nurse, obtained the vaccine and left the centre.

It was impossible for the headquarters staff to decide on the amount of vaccine to be diluted unless they were kept fully informed of the position at the centres. The responsible clerk at each centre was required, therefore, to ring headquarters at fixed times so that further supplies of vaccine could be diluted when necessary or excess supplies at one centre be sent to another centre where the demand was heavy.

Mobile Teams

The mobile teams which visited schools and factories each consisted of one nurse and one clerk, who took with them their estimated requirements of vaccine, sugar, record cards and letters to general practitioners. These teams were transported to their first operational point and thereafter supplied with further transport on request. In practice many of them were taken to their next point by staff of the factory or school at which they had been working. The record cards of the school children had been completed in advance by the parents. The teachers brought the children forward as required, and up to 600 could be fed the vaccine by one nurse in an hour. In the factories, nursing and clerical staff employed there assisted the mobile teams so that large numbers of workers received the vaccine in a very short space of time.

The Course of the Campaign

On the morning of 17 October the Consultant in Infectious Diseases at Castle Hill Hospital notified the Medical Officer of Health of 12 new cases, bringing the total number of patients admitted during the outbreak to 71 and the number of confirmed cases to 44. As the dilution of the vaccine had proceeded more quickly than had been expected it was decided to bring forward the opening time of the campaign from 9 a.m. on Wednesday, 18th October, to 5 p.m. on Tuesday, 17th. This necessitated a re-arrangement of plans within the Department and with the voluntary organisations.

Queues started to form at centres in the suburbs during the afternoon after an announcement on the 1 o'clock news and the publication of the afternoon newspapers had given details of the earlier openings of the campaign. Consequently many centres opened as soon as staff arrived and well before 5 p.m. By the official opening time urgent requests for more vaccine were being received from all these centres, so much so that it was soon realized that further supplies of vaccine and record cards would be required. Arrangements were immediately put in hand for more cards to be printed and for the vaccine which was due to arrive on Wednesday afternoon to be delivered earlier. This second delivery of vaccine finally arrived at 1.30 a.m. on Wednesday, 18th, and dilution was started immediately. A third supply was due on Thursday but, owing to the tremendous demand, contact was made with the Royal Air Force to find out whether they would be prepared to fly an emergency supply from the factory in the South of England to an airfield near Kingston-upon-Hull. They readily agreed and on Wednesday, 18th October, sent a plane to the factory from Kingston-upon-Hull which flew back by the early afternoon with the much needed vaccine.

On the first evening of the campaign some 76,000 people were vaccinated within four hours. On the following day, which was stormy and blustery, 157,000 were vaccinated and demand for vaccine was such that some of the centres had to close temporarily through shortage. Fortunately the Royal Air Force arrived with the additional supply which was diluted immediately and all the centres were operating fully by late afternoon. The next day some 69,000 persons were vaccinated and the figures for the

remaining days were : Friday—31,000 ; Saturday—12,000 ; Sunday—2,000 ; Monday—6,000 ; and Tuesday—5,000 ; a grand total of 358,000. This was 55,000 more than the entire population of the City.

During day-time operations departmental transport dealt with the problem of replenishing supplies at the centres ; volunteer transport supplemented the staff vehicles in the evenings. Each night up to 20 volunteer drivers were used to bring in cards and unused vaccine from the centres. The vaccine was stored at 0–4° C. overnight. From Wednesday to Friday the transport of mobile teams to schools and factories was carried out by four 12-seater sitting-case vehicles, each vehicle carrying a number of teams to their first location. Thereafter the teams requested transport as necessary to move to their next point, but in many cases they were taken by staff of the schools or factories where they were working.

By the end of the campaign sorting and storage of 358,000 cards had become a real problem. The demand for vaccination on Tuesday evening and on Wednesday was such that, on occasions, the colour system broke down and clerks found it necessary to use wrongly coloured cards which they then marked for identification. It was necessary, therefore, after the campaign to check every card and the opportunity was taken to introduce additional categories. By Saturday, 28th October, all 358,000 cards had been counted and sorted into the following categories :

Kingston-upon-Hull Residents—

(1) Children under 15 years of age—86,400.*

(2) Persons between 15 and 40 years of age who had had one or more injections of Salk vaccine—52,619.

(3) Persons over 40 years of age who had had one or more injections of Salk vaccine—2,125.

(4) Persons between 15 and 40 years of age who had not had any injections of Salk vaccine—46,529.

(5) Persons over 40 years of age who had not had any injections of Salk vaccine—104,366.

These figures represent 96 per cent of the population of Kingston-upon-Hull.

Others—

Residents of Haltemprice Urban District—30,442.

Residents of other areas of the East Riding County Council—26,946.

Residents of areas outside the East Riding County Council—8,847.

This task took 25 clerks plus 15 volunteers, working 13 hours a day, three days. At this stage no attempt was made to sort cards into alphabetical order.

Part played by Mobile Teams

Eight teams visited factories on Wednesday, whilst all day on Thursday and on Friday morning up to 15 teams were visiting schools at which there was no fixed centre. By Friday noon all the schools and the scheduled

* Including school children over the age of 15 and children resident in the East Riding who attended schools in Hull.

factories had been dealt with and on Friday afternoon the mobile teams were able to switch to visiting old people's homes and homebound patients. This work continued all day on Saturday and Sunday and on Monday morning. There were approximately 1,500 homebound patients. Route lists were prepared for mobile teams, each team being allocated about 20 cases per session. In addition approximately 650 aged and handicapped persons were transported by volunteer drivers to suitable centres for vaccination.

East Riding

The distribution of oral vaccine in the Haltemprice and Withernsea/Patrington areas of the East Riding was not made by separate arrangement but by extension of the Kingston-upon-Hull scheme. The number of confirmed cases of poliomyelitis (six in Haltemprice and three in Withernsea and Patrington) might not in itself have justified the emergency use of oral vaccine but the occurrence of cases in areas so near the City made it difficult to avoid, particularly in view of the wide publicity which had been given to the campaign in Hull.

Apart from the fact that the populations to be dealt with were smaller, the organization of the campaigns in the East Riding was made easier because they were planned as extensions of the Kingston-upon-Hull arrangements and because of the help offered by that Authority and its officers. It was possible to draw vaccine from the supply already sent to Kingston-upon-Hull and to take advantage of the dilution arrangements already organised in the City.

When authority was given on 19th October for the scheme to be extended to Haltemprice, the main problems to be met were the printing of record cards and posters, press advertising and planning and staffing of distribution centres. The centres were organised entirely by the Divisional Medical Officers. Nursing and clerical staff were provided by the District Council and County but most of the workers at the centres were volunteers from the Women's Voluntary Service, the St. John Ambulance Brigade, the British Red Cross Society and others. The help of the Women's Voluntary Service at short notice was invaluable.

With some variations the arrangements closely followed those made in Kingston-upon-Hull. The main difference was that information slips for the family doctors were forwarded by the Health Department instead of being delivered by those who had received the vaccine. The Chairman of the Local Medical Committee was consulted about these arrangements and a letter of explanation sent to each doctor in the area.

The distribution of vaccine was made in ten stations in Haltemprice, each being open from 9.30 a.m. until 8.30 p.m. from Monday, 23rd October to Wednesday, 25th October. Special visits to schools were arranged to deal with the school children.

When, on 26th October, it was agreed that the scheme could be further extended to Withernsea and Patrington, the preliminary work done for the Haltemprice extension made it possible for the distribution of the vaccine to the Royal Air Force camp personnel to be arranged in a few hours on the 26th October, and for one centre to be organized at Patrington from

12 noon until 7 p.m. on Friday, 27th October, and one at Withernsea from 12 noon until 7 p.m. on 27th October and from 9 a.m. until 12 noon on Saturday, 28th October. Again, a letter of explanation was sent to each doctor in the distribution area.

The number of persons who were vaccinated at these centres were: Haltemprice, 9035; Patrington R.A.F. Camp, 420; Patrington Village, 791; Withernsea, 4002; making a total of 14,248.

The Medical Officer of Health of Kingston-upon-Hull had made it clear that persons living outside could receive doses of oral vaccine at the centres in the City. It was soon evident that a large number of people from the neighbouring County areas, and even further afield, had taken advantage of this offer. Although arrangements had been made to record all out-city applicants on cards of a special colour, the pressure on staff dealing with the distribution in Kingston-upon-Hull was so heavy that accurate assessments of their numbers and areas of residence could not be made before the scheme was extended to the East Riding. In retrospect it was evident that an over-generous provision of centres and staff was made in the Haltemprice area. In the Withernsea and Patrington areas, the experience at Haltemprice enabled a more accurate assessment to be made. The provision of one vaccination centre for each area, in addition to special arrangements at the R.A.F. camp, proved to be adequate. Lack of early information made it difficult also to estimate the number of doses of vaccine that would be needed.

The combined population of Haltemprice and the Withernsea/Patrington areas was nearly 50,000. About 85 per cent of these were vaccinated, but only 14,248 persons attended the centres provided in the areas and a number of these came from other parts of the County. Including 121 doses distributed to members of hospital staffs, 71,757 East Riding residents were fed with oral vaccine and of this number 57,388 attended centres in Kingston-upon-Hull.

Table 15 below shows how this total of 71,757 was distributed in the County. The greatest numbers to be vaccinated came from the Haltemprice and Holderness Divisional Health areas which are nearly all within a 15-mile radius from the centre of Kingston-upon-Hull. Within this radius 61 per cent of the population received oral vaccine and 48 per cent travelled into Kingston-upon-Hull to obtain it without waiting for any local arrangements to be made.

Table 15

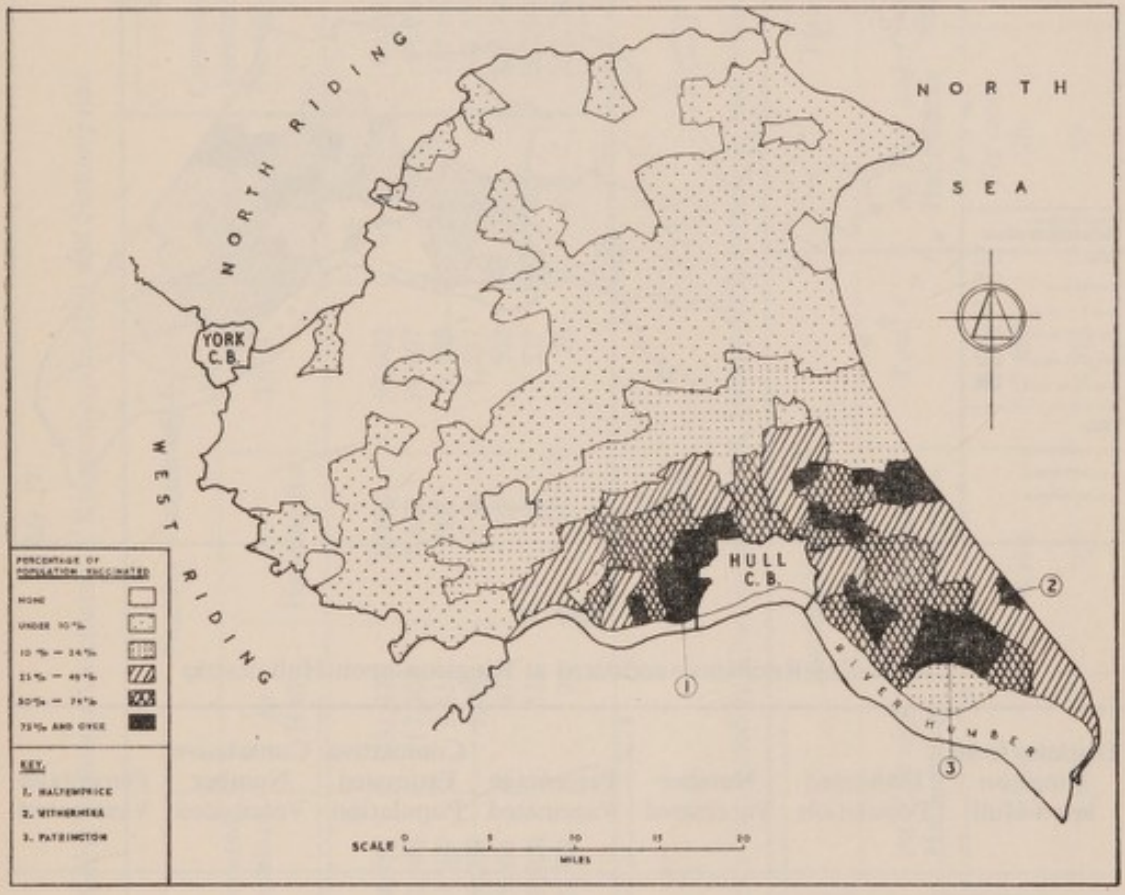
ORAL POLIOMYELITIS VACCINATION—OCTOBER 1961
EAST RIDING

	Estimated Population 1961 (Provisional)	Number of East Riding residents vaccinated					Percentage of Population Vaccinated	
		Under 5	5–14	15–19	Over 40	Total	At Hull and E.R. Sessions	At Hull sessions only
Holderness Division:								
Beverley M.B.	16,024	283	396	1,832	1,527	4,038	25	22
Hedon M.B.	2,338	139	315	743	834	2,031	87	86
Hornsea U.D.	5,949	58	57	492	577	1,184	20	19
Withernsea U.D.	4,963	340	902	1,107	1,745	4,094	83	22
Beverley R.D.	23,133	753	1,264	3,657	3,730	9,384	41	34
Holderness R.D.	20,367	803	1,771	4,400	4,192	11,166	55	44
Total	72,774	2,376	4,705	12,211	12,605	31,897	44	34
Haltemprice Division:								
Haltemprice U.D.	42,388	3,073	6,247	11,982	16,016	37,318	88	72
Buckrose Division:								
Bridlington M.B.	26,007	14	17	356	315	702	3	3
Driffield U.D.	6,890	2	14	144	101	261	4	4
Filey U.D.	4,705	—	3	10	7	20	0·4	0·4
Bridlington R.D.	8,699	7	12	60	36	115	1	1
Driffield R.D.	10,860	9	14	152	119	294	3	2
Total	57,161	32	60	722	578	1,392	2	2

	Estimated Population 1961 (Provisional)	Number of East Riding residents vaccinated					Percentage of Population Vaccinated	
		Under 5	5–14	15–19	Over 40	Total	At Hull and E.R. Sessions	At Hull sessions only
Howdenshire Division:								
Norton U.D.	4,773	—	—	1	—	1	0·02	0·02
Derwent R.D.	13,631	1	1	5	1	8	0·06	0·06
Howden R.D.	12,115	59	114	435	288	896	7	6
Norton R.D.	7,008	—	1	2	3	6	0·09	0·09
Pocklington R.D.	13,933	7	19	121	92	239	2	2
Total	51,460	67	135	564	384	1,150	2	2
East Riding:								
Total	223,785	5,548	11,147	25,479	29,583	71,757	32	26

Map A shows the *total* oral vaccination acceptance rates for the County after the distribution had taken place in Haltemprice, Withernsea and Patrington. Map B shows the acceptance rates for vaccine obtained at the distribution centres in Kingston upon Hull. Table 16 shows the extent to which those who lived at different distances from the City travelled there to obtain vaccine. Tables 17 and 18 show the effects of the distribution of vaccine, respectively, in Haltemprice and the Withernsea/Patrington area.

Map A



Map B

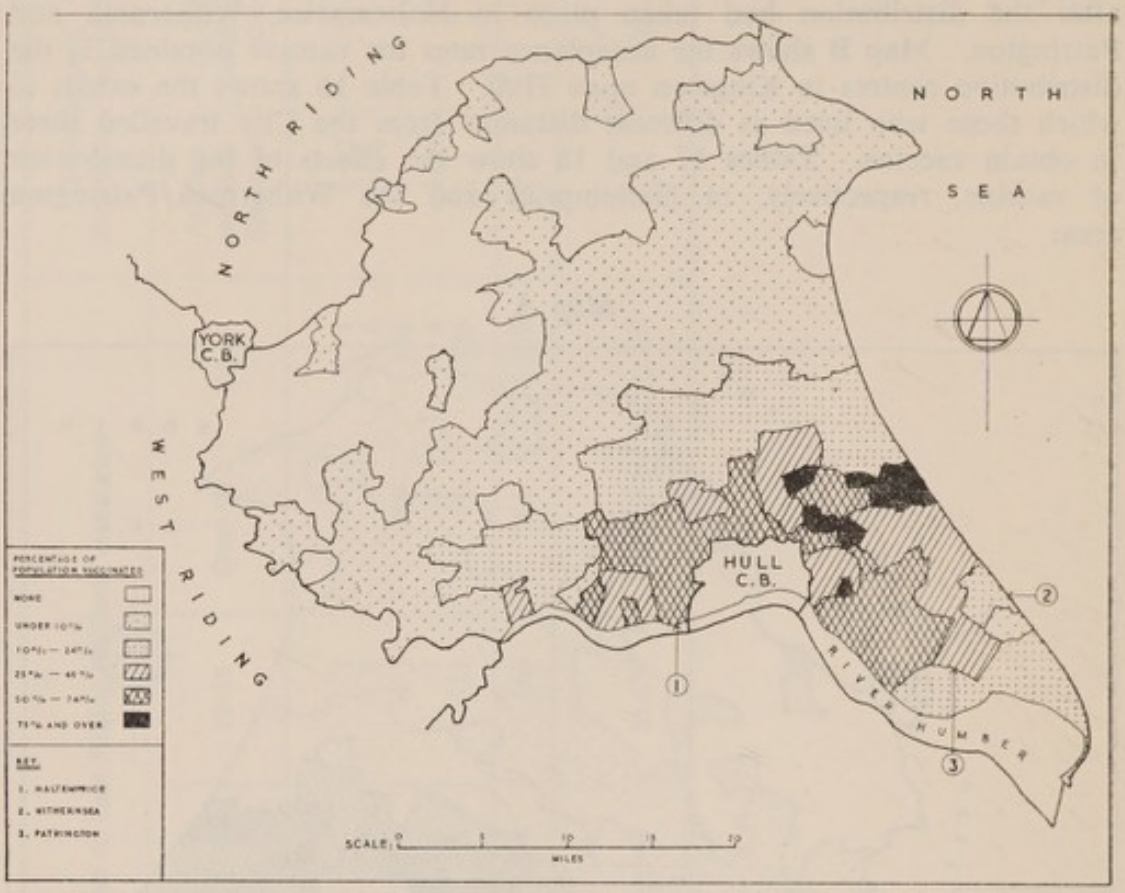


Table 16

East Riding Residents vaccinated at Kingston-upon-Hull centres

Distance from Kingston upon Hull	Estimated Population	Number Vaccinated	Percentage Vaccinated	Cumulative Estimated Population	Cumulative Number Vaccinated	Percentage Vaccinated
Under 5 miles	44,951	31,926	71	44,951	31,926	71
5–10 miles...	42,903	17,508	41	87,854	49,434	56
10–15 miles...	27,308	5,557	20	115,162	54,991	48
15–20 miles...	26,027	1,383	5	141,189	56,374	40
20–25 miles...	25,601	477	2	166,790	56,851	34
25–30 miles...	36,206	511	1	202,996	57,362	28
Over 30 miles	20,787	26	0·1	223,783	57,388	26

Table 19 summarizes the results of the campaign and shows the numbers, to the nearest hundred, to whom oral vaccine was fed in Kingston upon Hull and the East Riding.

Table 17

East Riding Residents Vaccinated at Kingston-upon-Hull and Haltemprice

Distance from Kingston upon Hull	Estimated Population	Number Vaccinated			Percentage Vaccinated	Cumulative Estimated Population	Cumulative Number Vaccinated	Percentage Vaccinated
		At Hull	At Haltemprice	Total				
					Per cent			Per cent
Under 5 miles	44,951	31,926	6,976	38,902	87	44,951	38,902	87
5—10 miles	42,903	17,508	1,659	19,167	45	87,854	58,069	66
10—15 miles	27,308	5,557	205	5,762	21	115,162	63,831	55
15—20 miles	26,027	1,383	154	1,537	6	141,189	65,368	46
20—25 miles	25,601	477	25	502	2	166,790	65,870	39
25—30 miles	36,206	511	16	527	1	202,996	66,397	33
Over 30 miles	20,787	26	—	26	0·1	223,783	66,423	29

Table 18

East Riding Residents Vaccinated at Kingston-upon-Hull, Haltemprice, Patrington and Withernsea

Distance from Patrington/ Withernsea	Estimated Population	Number Vaccinated			Percentage Vaccinated		
		At Hull and Haltemprice	At Patrington and Withernsea	Total	At Hull and Haltemprice	At Patrington and Withernsea	Total
					Per cent	Per cent	Per cent
Under 5 miles	10,638	2,784	4,914	7,698	26	46	72
5–10 miles	7,883	4,518	267	4,785	57	3	60

Table 19

ORAL POLIOMYELITIS VACCINATION CAMPAIGN

Numbers Fed 17th–28th October

(Nearest 100)

Area in which Resident	Kingston upon Hull Campaign									Extension to East Riding			Grand Totals
	17th	18th	19th	20th	21st	22nd	23rd	24th	Total	23rd–25th	26th–28th	Total	
Kingston upon Hull	70,300	131,700	56,500	21,100	5,300	700	3,600	2,900	292,100	—	—	—	292,100
East Riding County	4,900	22,800	11,700	8,600	6,300	800	1,200	1,100	57,400	9,000	5,300	14,400	71,800
Other authorities ...	500	2,800	1,300	1,300	800	300	1,100	700	8,800	—	—	—	8,800
Totals	75,700	157,300	69,500	31,000	12,400	1,800	5,900	4,700	358,300	9,000	5,300	14,400	372,700

Follow-up with trivalent vaccine

When the campaign had ended the question arose of further vaccination to complete immunization against all three types of poliovirus. Discussions were held at the Ministry of Health on 22nd November, 1961, when the following general policy was agreed:

(*a*) To offer further vaccination against poliomyelitis only to persons in the existing priority groups, i.e. all persons aged 6 months to 40 years and certain categories of people at special risk irrespective of age.

(*b*) To offer Salk vaccination to those who had begun, but had not completed, a course of three doses of Salk vaccine.

(*c*) To offer no further vaccination to those who had completed a course of three doses of Salk vaccine.

(*d*) To offer two doses of oral poliomyelitis vaccine (trivalent) to persons in the priority groups who had received oral poliomyelitis vaccine (Type 2) but had not begun a course of Salk vaccination.

(*e*) To offer these two doses, respectively, in the first half of December and the first half of January.

Oral poliomyelitis vaccine (trivalent), containing $10^{5.5}$ T.C.D. of each type of virus per 0·1 ml. dose, was sent to Kingston-upon-Hull on 27th November. Administration began on 30th November. About 30,000 persons came forward in Hull and slightly more than 2,000 in the East Riding.

VI

SUPPLY AND DISTRIBUTION OF VACCINE

According to information supplied by the manufacturers, the vaccine had to be stored at −20°C. until required for dilution and at this temperature it would maintain its potency for a period greatly in excess of six months. Once thawed the vaccine was not to be refrozen, due to the risk of disruption of virus particles and a consequent reduction in the number of virus particles per dose.

The consignments arrived in refrigerated vans in cases each containing 150 ampoules and were stored in a local cold store until required for dilution. Each case measured 25 inches by 25 inches by 21 inches (7·9 cubic feet). An average consignment of 12 cases, therefore, required a minimum of 96 cubic feet of cold storage space. Each case weighed approximately 140 lbs. and could be handled in the open by two men without difficulty. The vaccine was contained in an inner wooden box, 14 inches square and 9 inches deep, completely surrounded by "dry ice".

As an experiment, the lid was replaced on two containers opened on 18th October and the cases were left in a hallway at room temperature. "Dry ice" still remained in the cases six days later, but had evaporated completely on the seventh day. The cases when stored at room temperature in a draughty hall appeared to be capable, therefore, of maintaining the vaccine frozen for at least five days in winter. For vaccine packed as directed above, and intended to be diluted within 48 hours of arrival, storage at −20°C., though desirable, appeared not to be essential.

Vaccine removed from the cold store was kept in a domestic type refrigerator at 0°C. to 4°C. until required for dilution. Once diluted it was returned to the refrigerator until issued to the vaccination centres. The manufacturers indicated that under continuous refrigeration at 0°–4°C. the diluted vaccine would show no loss in titre for at least seven days.

The exact requirements of the vaccination centres could not be foreseen at the time of despatch of diluted vaccine from the distribution centre. Initially a proportion of the ampoules of diluted vaccine sent out in the morning were returned unused in the evening after vaccination had stopped. These ampoules were, therefore, subjected alternately, for approximately equal periods, to refrigeration and room temperature. The following morning these ampoules were re-issued and as far as was possible, ampoules of diluted vaccine were subjected to only one cycle of alternating temperatures.

No technical problems appeared to be involved in dilution. 5·5 ml. of vaccine, to deliver 5 ml., was contained in a penicillin type ampoule of 10 ml. capacity. The volume of sterile buffered saline required as diluent was 3 ml. It appeared, therefore, that dilution could be carried out by injection without opening the ampoule. The ampoule of diluted vaccine could then be returned to the refrigerator and need not be opened until required at the vaccination centre. The only equipment required for dilution appeared to be an unlimited supply of sterile buffered saline, of sterile syringes and of a volatile antiseptic for sterilizing the rubber caps of the ampoules after removal of the protective metal tear-off centre. Sterile

disposable syringes graduated to 2 ml. were in routine use in the Health Department. Experiment showed that by withdrawing the plunger to its fullest extent, the syringe would deliver 3 ml. From this point onwards the dilution appeared to present no problems other than those of organisation. Three empty ampoules were available for demonstration by 14th October and experiments were carried out to estimate the possible rate of dilution. It was concluded that two men, one filling the syringes with diluent, the other injecting, could without difficulty dilute 100 ampoules per hour.

For dilution a large room was available in the Health Department's offices close to the main storage and distribution centre for diluted vaccine. Desks covered with blankets and clean sheets were arranged in two lines with a short cross bench at one end. Two diluting teams were formed, composed in all of 22 persons, drawn from the technical staffs of the Public Health Laboratory and the City Analyst, and from the staff of the Health Department. The whole process was under the supervision of the Director of the Public Health Laboratory Service in Kingston-upon-Hull.

Cases of vaccine were opened at one end of the room and individual boxes of vaccine were unpacked at the cross bench, where ampoules remained at atmospheric temperature until thawed. After thawing, which required about two hours, the ampoules passed to the diluting teams where the following operations were carried out in succession.

Number 1 in the team removed the central tear-off metal foil exposing the rubber cap. Number 2 swabbed the cap with alcohol or acetone and placed the ampoule in position for Number 3. Meanwhile at the other end of the line Number 6 in the team opened sterile syringes and placed them in position for Numbers 4 and 5 who filled the syringes with sterile buffered saline and put them within reach of Number 3. Number 3 therefore received ampoules from one direction and the filled syringes from the other. He injected the saline into the ampoules which were taken by Number 7 standing directly opposite who replaced the diluted ampoules in one of the original cardboard containers. The use of the original containers for the diluted ampoules facilitated checking of the rate of dilution and allowed an accurate estimate of the numbers of ampoules diluted to be made at any time.

Distribution of the vaccine

For the opening of the vaccination centres at 9 a.m. on Wednesday, 18th October, it was planned to have available 100,000 doses of diluted vaccine. The dose of diluted vaccine was 0·1 ml. or two drops of vaccine from dropping pipettes supplied with the undiluted vaccine. After dilution each ampoule should contain at least 80 doses of vaccine. 1,250 ampoules therefore required dilution for the actual distribution.

The first consignment of vaccine arrived by road at 4 p.m. on Monday, 16th October, in refrigerated vans. The vaccine was contained in insulated cases lined with expanded plastic material and contained, packed in carbon dioxide snow, a foil lined inner container holding 15 cardboard boxes each holding 10 ampoules of vaccine. Each case contained, therefore, 150 ampoules of vaccine representing 12,000 nominal doses after dilution.

Two cases of vaccine were unpacked at 5 p.m. and left to thaw, a process which took two hours. Dilution then proceeded as planned without incident,

the two teams diluting 600 ampoules, or 48,000 nominal doses, in rather less than an hour. The time required for complete thawing of the ampoules had not been foreseen. For the dilution of subsequent batches of vaccine, containers were unpacked several hours in advance of the time set for dilution.

On the morning of Tuesday, 17th October, dilution began shortly after 10 a.m. and by 12.30 p.m., 1,200 ampoules had been diluted, a total of 96,000 nominal doses. 144,000 nominal doses of vaccine were then available for use. In consequence, the time and date of opening of the vaccination centres was advanced from 9 a.m. on Wednesday, 18th October, to 5 p.m. on Tuesday, 17th October.

When the centres closed on the night of Tuesday, 17th October, 76,000 persons had received vaccine. 1,690 ampoules of diluted vaccine had been issued to the centres of which 530 were returned unused. The actual number of inoculations per ampoule of diluted vaccine was thus 76,000 divided by 1,160, or just over 67 instead of the 80 doses on which calculations had been based.

The drop volume from a pipette is constant only when the pipette is held vertically and the drops are delivered at a rate not exceeding one per second. Experiments in the laboratory with the pipettes in use at the vaccination centres showed that 75–80 doses could be obtained per ampoule with the pipette held vertically but only 40 when the pipette was held horizontally. The care in dropping exercised under laboratory conditions could not reasonably be expected to be reproduced in the somewhat different conditions prevailing in the vaccination centres. It appeared that if attendances for vaccination continued at the rate experienced, more vaccine would be required for dilution and arrangements were made to hasten the delivery of vaccine due to arrive on Wednesday, 18th October.

1,200 ampoules were delivered by road at 1.30 a.m. on Wednesday, 18th October. The vaccine was unpacked at 3 a.m. to thaw and dilution began at 5 a.m., the volume of diluent being increased to 4 ml. This increase in diluent necessitated two injections of 2 ml. diluent into each ampoule and required some reorganization of the diluting teams. It was necessary to have four persons engaged in filling syringes with diluent instead of two as formerly. The rate of dilution was in consequence somewhat slower, but nevertheless by 8.30 a.m., 1,200 ampoules had each been diluted with 4 ml. sterile buffered saline. It was expected that under the actual conditions of dropping the vaccine at the centres, 75 doses would be obtained per ampoule diluted with 4 ml. saline. This batch was expected therefore to yield 90,000 doses.

By midday, as reports of numbers vaccinated came in from the centres, it became evident that a shortage of vaccine might occur towards the evening.

1,500 ampoules of vaccine arrived by air at 3 p.m., and dilution started at 5 p.m. after the usual two hours to allow thawing of the ampoules after unpacking. Owing to the unprecedented demand for vaccine, it was decided to increase the dilution to 1 in 5. This dilution required the

addition of the 5 ml. vaccine in the ampoule to 20 ml. saline in a sterile " Universal " container. The diluting teams were quickly instructed in the new procedure, which entailed opening each ampoule, and dilution proceeded. As the dropping pipettes in use were not long enough to reach the bottom of the " Universal " containers holding the diluted vaccine, each " Universal " container sent to the centres was accompanied by the empty original ampoule which was successively refilled with diluted vaccine for administration.

After 230 ampoules had been diluted 1 in 5, the dilution was reduced to 1 in 4, i.e. 5 ml. vaccine was added to 15 ml. saline and a further 330 ampoules were diluted.

When the centres closed on the evening of Wednesday, 18th October, 157,000 persons had received vaccine. On the first two days of the campaign, therefore, 233,000 persons had received vaccine.

In the remaining six days of the campaign in Kingston-upon-Hull and including the extensions to the East Riding, 139,700 persons were vaccinated. During this period the dilution of the vaccine remained at 1 in 4, and only enough vaccine was diluted daily to meet requirements.

Dosage

The undiluted vaccine contained approximately fifteen million tissue culture doses (T.C.D.) per ml. 3,000 ampoules were diluted with 3 or 4 ml. of diluent providing an actual dose of approximately one million T.C.D. 1,180 ampoules were diluted with 15 or 20 mls. diluent providing an actual dose of approximately half a million T.C.D.

Therefore, of the persons vaccinated approximately 54 per cent received a dose of approximately one million T.C.D., and the remainder, 46 per cent, received a dose of approximately half a million T.C.D.

When the volume of diluent was 3 ml. the ampoules delivered 67 doses ; when 4 ml. were added 75 doses were obtained. Comparable figures when 15 and 20 millilitres were added were 145 and 180.

Table 20 summarises these findings.

Stability of the vaccine after dilution

The titre of virus was estimated in samples (*a*) undiluted (*b*) diluted and stored overnight at refrigerator temperature (*c*) diluted, stored overnight at refrigerator temperature and then left for a further 12 hours at room temperature.

Tenfold dilutions of specimens were made in tissue culture maintenance medium and inoculated in 0·1 ml. amounts into monkey kidney tissue culture tubes, using 2–4 tubes for each dilution. The maintenance medium was Parker 199 with bovine albumin but without serum. Final readings for cytopathic effect were made 6–7 days after inoculation.

Table 21 shows the results of the virus titrations, which indicated that the vaccine did not deteriorate under the conditions in which it was diluted and stored before use.

Table 20

ORAL POLIOMYELITIS VACCINATION CAMPAIGN

NUMBERS FED AT VARIOUS DOSAGES

(Figures for Kingston-upon-Hull and the East Riding)

Nominal Dose in T.C.I.D. 50	No. of Vials	Nominal		Effective*		Estimated No. of Persons Vaccinated
		Doses/ Vial	Total doses	Doses/ Vial	Total Doses	
(1) 10^6 (5 ml. dil. to 8 ml.)	(2) 1,800	(3) 80	(4) 144,000	(5) 67 (84 per cent)	(6) 120,600	(7) 115,000
$10^{5\cdot9}$ (5 ml. dil. to 9 ml.)	1,200	90	108,000	75 (83 per cent)	90,000	86,100
$10^{5\cdot6}$ (5 ml. dil. to 20 ml.)	950	200	190,000	145 (72 per cent)	137,750	132,000
$10^{5\cdot5}$ (5 ml. dil. to 25 ml.)	230	250	57,500	180 (72 per cent)	41,400	39,600
GRAND TOTALS			499,500†	—	389,750‡	372,700§

Note

* "Effective" dose per vial rates were those found in practice at clinics.

† Total "loss" of vaccine = 499,500 − 372,700 = 126,800 doses = 25·5 per cent.

‡ Difference between grand totals of columns 6 and 7 is due to loss of vaccine resulting from spillage, breakages, small quantities thrown away as not warranting re-issue, etc., equivalent to approximately 3·4 per cent. wastage.

§ Actual number of persons vaccinated = 358,300 in Kingston upon Hull.
14,400 in the East Riding.

Total ... 372,700

Table 21

Virus titrations of Type 2 vaccine

	Dilutions for the titration					
	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}
	No. of tubes showing cytopathic effect					
Undiluted vaccine ($10^{6\cdot5}$ $TCID_{50}$ per 0·1 ml.) ...	4/4	4/4	4/4	3/4	2/4	0/4
Diluted vaccine (10^6 $TCID_{50}$ per 0·1 ml.) ... Stored at 0 to 4°C for 12 hours.	2/2	2/2	2/2	1/2	0/2	0/2
Diluted vaccine (10^6 $TCID_{50}$ per 0·1 ml.) ... Stored at 0 to 4°C for 12 hours and room temperature for 12 hours.	4/4	4/4	4/4	2/4	0/4	0/4

VII

VIRUS STUDIES IN THE COMMUNITY

Investigations were undertaken to obtain information about enteroviruses, including poliovirus, present in the community before oral vaccination was begun, and about the effects produced by administration of the vaccine. These included studies of the proportion of the population infected by the vaccine virus, its influence on the ecology of other intestinal viruses, the duration of the excretion in the vaccinated population and its spread to unvaccinated individuals. Attempts were made to ascertain any genetic changes in Type 2 virus excreted by vaccinated persons and in Type 2 virus strains, isolated from unvaccinated persons, which might have been acquired by secondary spread. A small serological survey was made two months after the campaign had ended.

Collection of Specimens

In the short time available between the decision to use oral vaccine and the opening of the campaign it was possible to collect a certain number of specimens of faeces from children in residential or day nurseries in Kingston-upon-Hull and from older children and adults resident in Hull or Haltemprice. After feeding of the Type 2 oral vaccine faecal specimens were collected on 23rd, 24th and 25th October from vaccinated persons, mainly children, living in their own homes in Kingston-upon-Hull. A further collection was made two months later, shortly before trivalent vaccine was used to complete the immunization of previously unvaccinated persons. It was not possible to sample all the same individuals at each of these three collections. In one of the residential nurseries in Kingston-upon-Hull specimens were taken before oral vaccination and, from the same children, one week later.

At regular intervals faecal specimens were obtained in various areas outside Kingston-upon-Hull from children under 5 years of age who had not received oral vaccine. These were selected as the most likely group in which to detect spread of vaccine virus.

All faecal specimens were examined for the presence of poliovirus and other enteroviruses by the techniques described by Hale, Lee and Gardner (1961a).

Specimens of blood for serological investigation were obtained 5 weeks after oral vaccination from persons, mainly children, who had not at any time received Salk vaccine.

Table 22

Faecal Survey—Before Vaccination

Age Group	Number	Poliovirus Type 1	Other Enteric Viruses
0–6 months ...	8	—	—
–2 years	24	3	—
–5 years	21	—	1
–10 years... ...	25	—	—
–15 years... ...	12	—	—
Over 15 years ...	102	—	—

Virus Isolations

Table 22 shows the number of isolations of virus from specimens obtained before the vaccination campaign began. A total of 192 specimens were tested. Poliovirus Type 1 was isolated from three children under 2 years of age and one other enteric virus (Coxsackie A9) from a slightly older child. No poliovirus Type 2 was isolated.

Table 23

Faecal Survey—After Vaccination

Age Group	Number	Poliovirus				Other Enteric Viruses
		Type 1		Type 2		
		Number	Per cent.	Number	Per cent.	
0–6 months ...	74	4	5·4	69	93·2	—
–2 years	63	4	6·3	57	90·5	—
–5 years	86	9	10·5	71	82·6	—
Total: 0–5 years ...	223	17	7·6	197	88·3	—
5–10 years	44	2	4·5	35	79·5	—
–15 years	31	3	9·7	13	41·9	—
Over 15 years ...	83	—	—	32	38·6	—

Table 23 shows the results of the faecal survey which was made at about one week after administration of the vaccine. A total of 381 specimens were tested, 22 of which yielded Type 1 poliovirus and 277 Type 2. In no instance were both types of poliovirus found to be excreted by the same individual. No other enteric virus was isolated. It is evident that Type 1 poliovirus was still present in the community after the vaccination campaign had ended. A comparison with the results shown in Table 22 might be thought to suggest that its prevalence had increased, but this conclusion is not justified since the samples were taken from different groups of the population and the number of young children in the first sample was relatively small. The proportion of persons infected by the vaccine virus declined progressively with increasing age, from a maximum of 93·2 per cent in infants under six months to a minimum of 38·6 per cent in persons over 15 years.

Table 24

Isolations of poliovirus from residential nursery children before and after vaccination

Age Group	No. of Children	Pre-vaccination specimen	Post-vaccination specimen
6 months—2 years	3	Type 1	Type 1
	4	None	Type 1
	3	None	Type 2
2—5 years	2	Type 1	Type 1
	2	None	Type 1
	13	None	Type 2

The findings at the residential nursery, which are not included in the previous tables, are shown separately in Table 24. Of the 27 children investigated five were found to be excreting Type 1 poliovirus before oral vaccination. All five continued to excrete Type 1 virus after vaccination and none became infected by the vaccine virus. Of the remaining 22 children, 6 were found to be excreting Type 1 poliovirus after vaccination and 16 (72·7 per cent) became infected by the vaccine virus.

Table 25

Faecal Survey—2 months after Type 2 and before trivalent vaccination

Age Group	No.	Poliovirus				Other Enteric
		Type 1		Type 2		
		No.	Per cent	No.	Per cent	
0—6 months ...	1	—	—	—	—	—
—2 years	38	5	13·2	3	7·9	—
—5 years	40	7	17·5	—	—	—
Total 0 to 5 years ...	79	12	15·2	3	3·8	—
5—10 years... ...	3	2	—	—	—	—
—15 years... ...	6	2	—	—	—	—
Over 15 years ...	7	1	—	—	—	—

Table 25 shows the results of the faecal survey which was made two months after administration of Type 2 vaccine and before trivalent vaccine was brought into use. By this time Type 2 poliovirus had largely disappeared; only 3 of 95 specimens were found positive. This finding was consistent with the experience described by Sabin *et al.* (1960) and Skovranek (1960). Type 1 poliovirus was isolated from 17 individuals of various ages, indicating that the epidemic strain was still present in the community, as far as could be judged in undiminished proportions.

Table 26

Faecal specimens from unvaccinated children under 5 years of age.

Distance from Hull	District	Specimens collected	No.	Cytopathogenic agents isolated		
				Polio 1	Polio 2	Other Enteric Viruses
Less than 10 miles	*Beverley*	27.10.61	11	—	—	—
		1.11.61	23	2	2	—
		10.11.61	16	—	3	—
		14.11.61	17	1	—	—
		22.11.61	16	—	—	—
		1.12.61	13	1	—	—
10–20 miles	*Market Weighton* ...	27.10.61	13	—	—	—
		3.11.61	13	—	—	—
		10.11.61	12	—	1	—
		14.11.61	11	—	—	—
		22.11.61	9	—	—	—
		1.12.61	11	—	—	—
	Driffield	31.10.61	13	—	1	—
		8.11.61	17	—	1	—
		14.11.61	14	—	1	—
		22.11.61	16	—	1	—
		1.12.61	9	—	—	—
20–30 miles	*Bridlington*	26.10.61	7	—	—	—
		2.11.61	21	—	—	—
		9.11.61	19	—	2	—
		14.11.61	18	—	3	—
		22.11.61	11	—	1	—
	Pocklington... ...	27.10.61	11	—	—	—
		3.11.61	11	—	—	—
		10.11.61	12	—	—	—
		14.11.61	12	—	—	—
		22.11.61	9	—	—	—
		1.12.61	11	—	—	—
	Howden	27.10.61	13	—	—	—
		3.11.61	10	—	—	—
		10.11.61	9	—	—	—
		14.11.61	10	—	—	—
		22.11.61	9	—	—	—
		1.12.61	9	—	—	—
	Eastrington	3.11.61	4	—	—	—
		10.11.61	5	—	1	—
		14.11.61	3	—	—	—
		22.11.61	3	—	—	—
		1.12.61	4	—	—	—

Distance from Hull	District	Specimens collected	No.	Cytopathogenic agents isolated		
				Polio 1	Polio 2	Other Enteric Viruses
	Barley (nr. Selby) ...	27.10.61	5	—	—	—
		2.11.61	8	—	—	—
		10.11.61	9	—	—	—
		14.11.61	10	—	—	—
		22.11.61	11	—	—	—
		1.12.61	10	—	—	—
More than 30 miles	*Fulford (nr. York)* ...	27.10.61	2	—	—	—
		2.11.61	9	—	—	—
		10.11.61	8	—	—	—
		14.11.61	6	—	—	—
		22.11.61	8	—	—	—
		1.12.61	7	—	—	—
	Filey	22.11.61	9	—	—	—
		1.12.61	10	—	—	—

Spread of Vaccine Virus to Unvaccinated Children

Table 26 shows the types of virus isolated from unvaccinated children under 5 years of age living at various distances from Kingston-upon-Hull. The nearest district from which specimens were tested was Beverley, where a substantial proportion of the population had received oral vaccine (see Table 15). In this district some children were found to be infected with the epidemic Type 1 strain and some with Type 2 virus. From the more distant areas no Type 1 virus was isolated, but Type 2 virus was found in several districts up to a radius of 30 miles from the centre of Hull. These were all districts in which a proportion of the population had received oral vaccine. Specimens obtained from three areas more than 30 miles from Hull were found to contain no poliovirus.

"t" marker Tests

All the Type 2 strains isolated from unvaccinated children in the districts outside Kingston-upon-Hull were examined for their ability to grow at 40°C. by a technique, suggested by Sabin (1960), which involves an assay in tubes incubated in a waterbath. Seven of these strains showed a change in this

Table 27

"t" marker tests of type 2 strains isolated from three unvaccinated children

Child	Date isolated	"t" marker	Child	Date isolated	"t" marker	Child	Date isolated	"t" marker
A	31.10.61	—	B	9.11.61	—	C	9.11.61	—
	8.11.61	—		16.11.61	+		16.11.61	±
	15.11.61	±		14.12.61	+		23.11.61	—
	21.11.61	±					14.12.61	—

respect from the character of the vaccine virus. Three gave good growth at 40°C. and were designated t+. Four showed slight growth at this temperature and were designated t±. In three instances several faecal specimens were collected at intervals from the same child. Table 27 shows the results of "t" marker tests on these specimens. Children A and B continued to excrete virus of changed character. Child C was found to be excreting a virus of changed character on one occasion only and subsequent isolations had the properties of the vaccine virus. This phenomenon has been described by Dick and Dane (1957) and by Sabin (1959).

Fourteen strains of Type 2 poliovirus isolated from vaccinated individuals in Kingston-upon-Hull were found to be unchanged from the original vaccine virus in "t" marker tests. The specimens were collected one week after vaccination.

Serological Investigations

Five weeks after the vaccination campaign specimens of blood were obtained from persons who had been given oral vaccine but had not received Salk vaccine. Time did not permit the collection of specimens before vaccination.

Table 28

Neutralizing antibody levels in Salk negative individuals 5–6 weeks after feeding type 2 vaccine

Age	No.	Titre Type 2 antibody				
		10 or less	10 to 100	100 to 500	500 to 1,000	More than 1,000
0–6months...	1	—	—	—	—	1
–2 years ...	14	—	1	3	1	9
–5 years ...	16	—	2	4	4	6
–10 years ...	20	1	—	—	2	17
–15 years ...	27	—	—	—	1	26
Over 15 years	11	—	—	1	1	9
Total ...	89	1 (1·1)	3 (3·3)	8 (9·0)	9 (10·1)	68 (76·4)

(Percentage of total in brackets.)

Table 28 shows the titres of Type 2 antibody which were found after vaccination. Titres of 10 or more were obtained in 88/89 (98·9 per cent) and of 100 or more in 85/89 (95·5 per cent). These high proportions can be interpreted as due in part to naturally acquired antibodies and in part to the effect of vaccination. It was not possible to assess the antibody responses to vaccination alone.

VIII

CLINICAL AND VIROLOGICAL INVESTIGATION OF SUSPECTED CASES OF POLIOMYELITIS

The arrangements for surveillance in the community and for the investigation of patients with symptoms suggestive of neurological illness have been described in Section II of this Report. Apart from suspected cases of poliomyelitis admitted direct to Castle Hill Hospital, doctors in general medical or hospital practice asked the Medical Officer of Health during the course of the outbreak for a second opinion on 107 patients. Thirty-one of these (23 from general medical practices and 8 from various hospital departments) were found to have clinical evidence suggestive of poliomyelitis and were admitted to Castle Hill Hospital. The remaining 76 (53 from general medical practices and 23 from hospital departments) were thought not to be suffering from poliomyelitis. The final diagnoses in these 76 cases were : coryza, 31 cases ; tonsillitis, 29 cases ; myalgia, 11 cases ; injury to the back, 2 cases ; bronchopneumonia, 1 case ; glandular fever, 1 case ; disseminated sclerosis, 1 case. Subsequent follow-up of this group failed to elicit any neurological sequelae, except in the patient who was suffering from disseminated sclerosis.

A number of persons reported various symptoms, which developed after the administration of oral vaccine. These included sore throat, diarrhoea, headache and pain in the back. Others claimed that there had been an improvement in their state of health, with alleviation of such complaints as cramp, rheumatism and arthritis. In no instance could these alleged effects be definitely attributed to vaccination. On 23rd October enquiries were made from a representative sample of schools in the city as to the number of children who were absent after the oral vaccination campaign had begun. These revealed that nothing out of the ordinary had been noticed by any of the headmasters or their staff. The total number of children in the 14 schools concerned was about 5,600 and the sample, therefore, was fairly large. Enquiries were also made at some of the large industries in the city and none reported any rise in absentee rates or anything else at all unusual.

To exclude acute polioencephalitis as a cause of sudden death, either before or after the administration of Type 2 vaccine, a full post-mortem examination was requested on all patients, both in hospital and in the general population, dying suddenly without adequate ante-mortem diagnosis. Sudden deaths in hospital were screened by the hospital pathologists. Through the courtesy of H.M. coroner, notifications were received of sudden deaths in the general population in the three weeks following mass vaccination.

Five sudden deaths occurred during the period, all in children, aged 8 days, 3 weeks, 5 weeks, 1 year, 1½ years. The causes of death established by full post-mortem examination were acute enteritis 1, acute bronchopneumonia 3, endocarditis following mumps 1. Histological and virological examination of brain and cord revealed no evidence of poliomyelitis.

Hospital admissions in relation to oral vaccination

During the first phase of the outbreak up to and including 17th October, when the vaccination campaign began, a total of 81 suspected cases of poliomyelitis (76 from Kingston-upon-Hull and 5 from the East Riding) were admitted to Castle Hill Hospital. None of these received oral vaccine. The number of cases subsequently confirmed* as suffering from poliomyelitis was 56 (53 from Kingston-upon-Hull and 3 from the East Riding).

From 18th October to 7th November, the date of admission to hospital of the last case of the outbreak, a total of 82 suspected cases (64 from Kingston-upon-Hull and 18 from the East Riding) was admitted, of whom 53 (43 from Kingston-upon-Hull and 10 from the East Riding) had received oral vaccine. The number of subsequently confirmed cases was 37 (31 from Kingston-upon-Hull and 6 from the East Riding) of whom 19 (18 from Kingston-upon-Hull and 1 from the East Riding) had received oral vaccine.

The dates of onset of illness in 6 of the confirmed cases were found, in retrospect, to have preceded oral vaccination. In the remaining 13 cases in the outbreak, who had received oral vaccine, the dates of onset ranged from 0 to 10 days after vaccination. In the two subsequent cases the intervals were 35 days and 48 days, respectively.

After the outbreak proper had ceased, from 8th November to 31st December a total of 17 suspected cases (16 from Kingston-upon-Hull and 1 from the East Riding) was admitted, of whom 11 from Kingston-upon-Hull and 1 from the East Riding) had received oral vaccine. Only two of these cases, both from Kingston-upon-Hull, were confirmed as suffering from poliomyelitis. Both had received oral vaccine.

These findings are summarised in Table 29.

Table 29

Hospital admissions in relation to oral vaccination

Dates of admission to hospital	Oral vaccination		Total
	Yes	No	
11th September–17th October	—	81 (56)	81 (56)
18th October–7th November	53 (19)	29 (18)	82 (37)
8th November–31st December	12 (2)	5 (—)	17 (2)
Total	65 (21)	115 (74)	180 (95)

Confirmed cases of poliomyelitis shown in parentheses.

Details of the confirmed cases have been given in Section IV of this Report.

* " Confirmed " in this context does not necessarily imply laboratory evidence of poliovirus infection.

Virological Investigations

Special arrangements were made to provide virological reports as rapidly as possible on the faeces of all suspected cases of poliomyelitis admitted to the Infectious Diseases Hospital. This was done primarily to detect at once any illness which might be attributable to the feeding of the oral Type 2 poliovaccine. It also facilitated, to some extent, the diagnosis and segregation of patients within the hospital. Under these special arrangements faecal samples were brought daily by road to the Virus Laboratory, Public Health Laboratory, Leeds, and were processed and inoculated into tissue culture on the same day. It was often possible to give a provisional positive result the next day and almost always within three days. Serum specimens were collected from the new admissions and held at −20°C. in the Hospital Laboratory until the convalescent-phase sample was taken about 20 days after onset of illness and the pair of sera sent to Leeds by post. These sera were tested for complement-fixing and neutralizing antibodies to poliovirus and to a range of other viruses which sometimes cause illness simulating non-paralytic poliomyelitis. Details of the technical methods for the examination of faeces are given in the Appendix. Complement-fixing and neutralizing antibody tests for poliovirus infection were considered positive (+) when there was a four-fold or greater change in antibody titres between acute and convalescent-phase sera, or, less frequently, when antibody titres against poliovirus Type 1 were exceptionally high (for details see Appendix). This follows established practice in the interpretation of serological results in virology. It must be emphasized, however, that in poliomyelitis this method of interpretation is conservative and designates as negative those cases in which CF or neutralizing antibody has already reached a peak titre at the time when the acute-phase sample of serum is collected. In such cases, as there is no change in titre between acute and convalescent-phase samples, it is not possible to make a distinction between antibody resulting from a current or past infection. There are ample examples in the literature of this particular pattern of raised but unchanging antibody titres in cases of paralytic poliomyelitis from which virus was isolated. It may also be stated that four-fold or greater *changes* in complement-fixing or neutralizing antibody titres during a 3–4 week interval covering the course of an illness are unlikely to be related to previous Salk vaccination unless the latter has been injected within 2 to 3 weeks of the start of the illness (Lennette *et al.* 1961).

Results of laboratory examinations

Specimens were received at the Virus Laboratory from 175 of the 180 suspected cases of poliomyelitis admitted to Castle Hill Hospital. Poliovirus Type 1 was isolated from a total of 57 patients—from the faeces of 56 patients (together with poliovirus Type 2 in one instance) and from the brain (medulla), but not the faeces, of a fatal case. Poliovirus Type 2 alone was isolated from the faeces of 10 patients and an unidentified cytopathic agent, not poliovirus, from the faeces of one patient. Genetic "marker" tests showed that twelve of the strains of Type 1 virus were t+ and ten of the strains of Type 2 virus were either t− or t±. Specimens from 40 patients were tested for Coxsackie viruses by inoculation into suckling mice, but no strains were isolated.

Table 30

Correlation of the results of faecal culture and complement-fixation tests on 152 patients

		Complement Fixation			
		+	±	−	Total
Faeces	Poliovirus Type 1 isolated ...	40	10	5	55
	Negative	8	23	66	97
Total		48	33	71	152

Faecal specimens and adequately spaced acute- and convalescent-phase sera (" paired sera ") were available from 152 patients. Table 30 compares the results of culture for poliovirus with the presence or development of complement-fixing antibody. In general the correlation is good. The groups faeces +/CF+ and faeces −/CF− were the largest and together included 106 (72 per cent) of the 152 sets of observations. The interpretation of the laboratory findings in the 23 patients with a negative faecal culture and a doubtful (±) complement-fixation test was uncertain.

Table 31

Correlation of the results of complement-fixation and neutralizing antibody tests

Neutralizing antibody	Complement Fixation			
	+	±	−	Total
Positive*	11 (85)	21 (70)	34 (48)	66
Unchanging titres or no antibody...	2	9	36	47
Total	13 (100)	30 (100)	70 (100)	113

( ) = per cent of total in sub-group.
* = for definition see text and appendix.

Patients whose paired sera gave doubtful or negative complement-fixing reactions were tested for changing or very high titres of neutralizing antibody indicative of current infection with poliovirus. Table 31 shows that 70 per cent of those patients with a doubtful (±) CF reaction and 48 per cent of those with a negative CF reaction had positive neutralizing antibody responses. Few neutralizing antibody estimations were done on sera reacting positively in the CF test as this group did not constitute a diagnostic problem. 85 per cent of those tested were, however, positive.

Analysis of the patterns of antibody response detected by the two tests showed that 41/52 (79 per cent) of the patients with positive complement-fixation reactions and 37/74 (50 per cent) with positive neutralizing antibody tests were recognisably infected with poliovirus Type 1 ; that is, the response was greatest against the Type 1 antigen or virus. The remaining patients showed a variety of responses either against a serotype other than Type 1 or against 2 or all 3 serotypes and no final decision as to the infecting type was possible.

Table 32

Laboratory findings in relation to diagnostic catego ries

Category	Faeces +		CF + (all cases)	Faeces − CF +	Faeces − CF − neutr. +	Faeces − CF − neutr. −	Number of Cases
	Type 1	Type 2					
Paralytic poliomyelitis ...	49†	1	42	6*	14	15	85
Non-paralytic poliomyelitis	7	0	3	0	1	2‡	10
Other illnesses	0	9	7§	3	28	40	80
All cases	56	10	52	9	43	57	175

* Type 1 virus isolated from medulla of fatal case.
† Type 1 and 2 virus isolated from one case.
‡ One patient with unidentified cytopathic agent.
§ Includes four of the cases from which Type 2 virus was isolated.

Correlation of clinical and laboratory findings

Table 32 shows the laboratory findings in relation to the main diagnostic categories. Poliovirus Type 1 was isolated from 56/95 (59 per cent) of all confirmed cases and 49/85 (58 per cent) of paralytic cases. This result was at variance with the widely held opinion that more than 80 per cent of patients with paralytic poliomyelitis yield virus. The isolation rate might have been increased if more than one stool had been examined from each patient and indirect evidence of infection might have been obtained by examining specimens from household contacts, but the available laboratory facilities did not permit of this additional work. The serological results suggested the possibility of poliovirus infection in a substantial number of patients from whom virus had not been isolated.

The interpretation of these results was explored in several different ways : firstly, by an analysis of the 85 paralytic cases, relating the laboratory findings to the severity of paralysis at the time of discharge from hospital : secondly, by an analysis of all the cases, confirmed and suspected, relating the laboratory findings to the severity of paralysis at the time of discharge from hospital : thirdly, by an analysis of all the cases, confirmed and suspected, relating the laboratory findings to the ages of the patients and their diagnostic categories ; and finally, by an independent appraisal of the cases and their classification according to clinical patterns of illness without reference to any laboratory evidence of poliovirus infection.

Table 33

Correlation of severity of paralysis and laboratory findings for 85 paralytic cases

Degree of paralysis on discharge from hospital	Type 1	Type 2	Faeces — CF +	Faeces — CF — Neutr. +	Faeces — CF — Neutr. —	Total
Severe	17	—	3*	—	—	20
Significant	13	—	—	—	1	14
Minor	12†	—	—	4	6	22
Complete recovery	7	1	3	10	8	29
	49	1	6*	14	15	85

* Type 1 virus isolated from medulla of fatal case.
† One case excreting both Type 1 and Type 2 virus.

Table 33 shows the correlation of severity of paralysis and laboratory findings. Poliovirus Type 1 was isolated from 30/34 (88 per cent) patients with severe or significant paralysis on discharge from hospital and from 19/51 (37 per cent) patients with lesser degree of muscle weakness. The proportion of patients from whom Type 1 virus was isolated was similar for those with either severe or significant paralysis, in contrast with the lower

Table 34

Faecal isolation rates of poliovirus Type 1 by diagnostic categories, age and Salk vaccination state

Category on discharge from hospital	Faecal virus isolation	Age Group				
		0–14 years		15 + years		
		Salk Injections				
		0–1	2+	0–1	2+	Total
Paralytic—Severe and significant	Type 1	21	3	6	0	30
	Total	21	4	8*	1	34
Paralytic—Minor and complete recovery	Type 1	12	6	1	0	19
	Total	13	12	17	9	51
Non-Paralytic	Type 1	4	3	0	0	7
	Total	4	5	0	1	10
Other illness	Type 1	0	0	0	0	0
	Total	15	20	26	19	80

* Type 1 virus isolated from Medulla of fatal case.

proportion among both those who showed minor paralysis and those who had made a complete recovery. This difference could be attributed in part to the fact that virus was isolated more readily from the more severe cases and in part to the age distribution of the patients. Table 34 shows the isolation rates of poliovirus Type 1 by diagnostic category, age and Salk vaccination state. Success in isolating virus from the faeces, particularly from patients with lesser degrees of muscle weakness, was seen to decline with increasing age and also appeared to be influenced by previous Salk vaccination.

Table 35

Analysis by diagnostic categories, laboratory findings and age

Category	*Age (Years)	Faeces+ Type 1	Faeces+ Type 2	Faeces− CF+	Faeces− CF− Neutr.+	Faeces− CF− Neutr.−	Total
Paralytic — Severe and significant.	0–14	24	—	1	—	—	25
	15+	6	—	2*	—	1	9
Paralytic — Minor and complete recovery.	0–14	18	—	1	5	1	25
	15+	1	1	2	9	13	26
Non-Paralytic	0–14	7	—	—	—	2	9
	15+	—	—	—	1	—	1
Other illnesses	0–14	—	7	1	10	17	35
	15+	—	2	2	18	23	45
All categories	0–14	49	7	3	15	20	94
	15+	7	3	6*	28	37	81

* Type 1 virus isolated from medulla of fatal case.

Table 35 gives an analysis of all the cases, confirmed and suspected, by diagnostic categories, laboratory findings and age. In the group of 34 patients with severe or significant paralysis on discharge from hospital evidence of poliovirus infection was found by isolation of Type 1 virus from the faeces in 30 cases and by positive complement-fixation tests in 3 of the remaining 4 cases. The corresponding figures for other paralytic cases were 19 by isolation of Type 1 virus and 3 by positive complement-fixation tests out of a total of 51 cases. Among the 85 paralytic cases there were 29 with negative faeces and complement-fixation tests. None of the 29 had received oral vaccine and 14/29 (48 per cent) had evidence of poliovirus infection by neutralizing antibody. The 14 cases with evidence of poliovirus infection by neutralizing antibody response alone were in the group with minor paralysis in which, as already noted, other means of laboratory diagnosis were unrewarding.

No strains of poliovirus Type 1 were isolated from the 80 cases in the category "other illness" but 3 patients with negative stool cultures had a positive complement-fixing antibody response and of a total of 72 cases in which sera were available 38/72 (53 per cent) had a positive neutralizing antibody response. These neutralizing antibody responses were more frequent among patients with signs or symptoms compatible with minor aspects of poliovirus infection (meningitis, muscle pain, inflammation of the throat, etc.) but without definite and lasting paralysis.

The significance of these less well-defined illnesses was explored further by using an independent appraisal of the 175 confirmed and suspected cases of poliomyelitis, from whom specimens were received, made from the clinical viewpoint without reference to virological tests. It was also necessary to compare the virological findings with those of this independent clinical review because, it will be recalled, the confirmed cases were partly defined in terms of positive virological results and would represent a selected series in any determination of the absolute efficiency of virological diagnostic procedures. The review was carried out by the Consultant Neurologist with the assistance of a Senior Registrar appointed by the Regional Hospital Board. The cases were classified into four descriptive groups.

1. Illnesses suggestive of poliomyelitis, with residual muscle weakness at approximately 3 weeks after admission.

2. Illnesses suggestive of poliomyelitis with transient muscle weakness.

3. Illnesses suggestive of poliomyelitis, without muscle weakness.

4. A composite group made up of illnesses not consistent with the general clinical pattern of groups 1, 2 and 3 together with some cases not seen by the reviewers.

Table 36

Correlation of clinical patterns of illness and laboratory findings

Descriptive Group	Age (years)	Faeces+		Complement-fixation test			Faeces − CF− or ± Neutr.+	Oral vaccine received	Total
		Type 1	Type 2	+	No sera	Total tested			
(1) Poliomyelitis-like with residual weakness.	0–14	30	0	24	0	32	1	9 (28 per cent)	32 (100)
	15+	6	0	8*	0	12	1	3 (25 per cent)	12* (100)
(2) With transient muscle weakness.	0–14	8	2	10	0	22	7	11 (50 per cent)	22† (100)
	15+	1	1	1	0	30	13	8 (26 per cent)	30 (100)
(3) With no muscle weakness.	0–14	11	1	4	1	16	3	6 (35 per cent)	17‡ (100)
	15+	0	2	4	0	12	6	8 (66 per cent)	12 (100)
(4) Other illness	0–14	0	4	1	5	18	4	9 (39 per cent)	23 (100)
	15+	0	0	0	2	25	8	9 (33 per cent)	27 (100)
Total		56	10	52	8	167	43	63 (36 per cent)	175 (100)

* Type I virus isolated from medulla of one patient.

† Unidentified cytopathic agent isolated from one patient.

‡ One adenovirus infection.

Table 36 shows the correlation of these clinical patterns of illness with the laboratory findings. The results are complementary to those given in Tables 33, 34 and 35 and show that diagnosis by isolation of Type 1 virus or complement-fixation test was most successful in the younger age groups and the patients with residual paralysis. Other analyses, not given in detail here, showed that the rate of isolation of Type 1 from the faeces was also partly influenced by previous Salk vaccination (see also Table 34). The findings again draw attention to the interesting and clinically difficult group of patients (categories 2 and 3, Table 36), particularly those over 15 years of age, with a poliomyelitis-like illness and either transient or no muscle weakness. (No analysis of category 4 of Table 36 is shown, as the reviewers had not seen all the cases in this group). A substantial proportion of these two groups had negative stool cultures and complement-fixation tests but a positive neutralizing antibody response. Patients in all groups had received oral vaccine and the possible effect of this on the serological findings has to be considered. It would be wrong to assume, however, that merely because a patient has received oral vaccine, infection with poliovirus Type 2 has occurred. In fact unassailable evidence of infection with Type 2 virus, namely by isolation of virus from the faeces was observed in only 10 patients in the whole sample of 175 and, moreover, evidence of Type 1 virus infection was obtained in at least 23 patients who had oral vaccine (see below and Table 37). In the group of 81 patients in categories 2 and 3 of Table 36 there were 50 with negative stool and complement-fixation tests and of these 29/50 (58 per cent) had a positive neutralizing antibody response. When all patients who had received oral vaccine were removed from the group of 50 there still remained 34 of whom 17 (50 per cent) had positive neutralizing antibody responses.

Tables similar to 32 and 36 were also constructed using only those cases admitted to hospital before 17th October (i.e., before the mass feeding of oral vaccine) and excluding all who had received an injection of Salk vaccine within a month of onset of illness. The proportions of patients, with negative stool cultures and complement-fixation tests and a positive neutralizing antibody response, in the categories under discussion were not significantly altered. So the conclusion that there were some patients in whom poliovirus infection was diagnosable only by a neutralizing antibody response appears to be valid.

The existence of this group of patients with a poliomyelitis-like illness with negative stool cultures is of some importance both in determining the significance of illness after vaccine feeding and also for the virological diagnosis of poliomyelitis general. These questions are considered in greater detail in the Discussion.

Virological investigation of patients admitted to hospital after the beginning of the vaccination campaign.

Among the 180 suspected cases of poliomyelitis there were 99 who were admitted to hospital on or after 18th October (see Table 29). Type 2 oral vaccine had been administered to 65 of these. The remaining 34 had not received oral vaccine.

Specimens for virological investigation were available from 63 of the 65 vaccinated persons. Poliovirus Type 1 was isolated in 18 cases—

together with Type 2 in one instance—and another 5 had complement-fixing antibody reactions suggestive of Type 1 virus infection. Poliovirus Type 2 alone was isolated in 10 cases. The remaining 30 patients were found to have neither Type 1 nor Type 2 virus in the faeces and negative or doubtful complement-fixing reactions.

Table 37

Intervals between oral vaccination and onset of illness in 65 vaccinated persons subsequently admitted to hospital as suspected cases of poliomyelitis

Laboratory Results	Onset of Illness								Total Number of Cases
	Before vaccination	After vaccination (days)							
		0—	5—	10—	15—	20—	25—	30+	
Cases with evidence of Type 1 infection.	6* (6)	7 (5)	6 (6)	1 (1)	1 (—)	0	0	2 (2)	23 (20)
Type 2 virus excreters	1 (—)	4 (1)	2 (—)	2 (—)	1 (—)	0	0	0	10 (1)
Negative or doubtful	2 (—)	9 (—)	5 (—)	6 (—)	1 (—)	1 (—)	1 (—)	5 (—)	30 (—)
Not tested	0	0	0	1 (—)	0	0	0	1 (—)	2 (—)
Total	9 (6)	20 (6)	13 (6)	10 (1)	3 (—)	1 (—)	1 (—)	8 (2)	65 (21)

Confirmed cases of poliomyelitis shown in parentheses.

* One case excreting both Type 1 and Type 2 virus.

Table 37 shows the intervals between oral vaccination and the onset of illness in each of these three groups. The observed distributions were similar and there was no tendency for the onsets of illness to aggregate in the period between 5 and 20 days after administration of the vaccine. All but one of the 21 confirmed cases of poliomyelitis (19 paralytic, 2 non-paralytic) were in the subgroup with evidence of Type 1 infection. The remaining confirmed case (paralytic) was found to be excreting Type 2 virus, but no causative association was suspected, since the muscular weakness developed within two days of administration of the vaccine (see Table 39, Case M.D.). Six of the 10 Type 2 virus excreters had an illness graded as 2 or 3 in terms of the descriptive categories of Table 36, a proportion similar to that observed in those with negative or doubtful laboratory results. Details of the clinical and laboratory findings in the

10 Type 2 virus excreters are shown in Table 39. There was every reason to conclude, therefore, both from the clinical patterns of illness and from the intervals between oral vaccination and onset, that the vaccine was not responsible for any of the observed illnesses but that the cases represented a coincidence of oral vaccination with illness due to other causes.

There remained the possibility that the vaccine virus might have spread from the recipients to unvaccinated contacts, gaining in virulence in the process. With this possibility in mind the findings in the 34 unvaccinated patients admitted to hospital on or after 18th October were examined. Specimens for virological investigation were available from 33 of the 34. Poliovirus Type 1 was isolated in 5 cases and Type 2 in none. The remaining 28 patients were found to have negative faeces and negative or

Table 38

Intervals between the start of the oral vaccination campaign and onset of illness in 34 unvaccinated persons subsequently admitted to hospital as suspected cases of poliomyelitis

Laboratory Results	Onset of illness						Total Number of Cases
	Before 18.10.61	On or after 18.10.61 (days)					
		0—	5—	10—	15—	30+	
Cases with evidence of Type 1 infection	3 (3)	2 (2)	0	0	0	0	5 (5)
Type 2 virus excreters	0	0	0	0	0	0	0
Negative or doubtful	15 (11)	4 (1)	3 (1)	2 (—)	0	4 (—)	28 (13)
Not tested	0	0	0	1 (—)	0	0	1
Total	18 (14)	6 (3)	3 (1)	3 (—)	0	4 (—)	34 18

Confirmed cases of poliomyelitis shown in parentheses.

doubtful complement-fixing reactions. Table 38 shows the intervals between the start of the oral vaccination campaign and the onset of illness in each of the groups. Of the 19 confirmed cases (18 paralytic, 1 non-paralytic) one developed on the 5th day after the start of the campaign and the remainder either before the vaccine was distributed or on the 1st or 2nd day after. Analysis in terms of descriptive clinical categories and examination of the patterns of neutralizing antibody responses of the nine patients, who became ill 5 or more days after distribution of the vaccine, did not reveal any poliomyelitis-like illness which could be attributed with certainty to Type 2 virus infection.

Table 39

Summary of clinical and laboratory information on ten patients admitted to hospital after receiving oral Type 2 vaccine and found to have poliovirus Type 2 in the faeces.

Case	Sex	Age	Vaccination state		Diagnostic Category	Descriptive Group	Date of onset of illness		Fæces Poliovirus	Serological tests *					
										CF			NA		
										Type			Type		
			Salk	Oral Type 2 (date given)			Main	Preceding	Type	1	2	3	1	2	3
J.B. ...	F	7	0	18·10	Tonsillitis ...	3	21 or 22/10	18/10	2	−/<4	<4/16	−/<4	<32/<8	128/256	<8/8
M.A.C.	F	4	3	18·10	Fract. femur ...	4	(4/11)	—	2	256/128	32/64	−/<4	4096/16,384	1024/512	512/512
M.D. ...	F	20	0	19·10	L. arm/bulbospinal poliomyelitis	2	19 or 21/10	16/10	2	−/<4	−/<4	−/<4	256/256	64/256	512/1024
J.R.F. ...	M	20	0	19·10	Pharyngitis ...	3	20/10	—	2	8/128	8/64	8/64	256/4096	<8/1024	1024/32,768
L.H. ...	F	10	4	18·10	Tonsillitis ...	2	23/10	19/10	2	−/<2	−/2	−/<2	4096/2048	512/2048	4096/4096
H.K. ...	F	4 mths.	0	19·10	Upper resp. tract infection	4	18/10	—	2	−/<4	<4/32	−/<4	16/16	<32/512	<32/8
H.L. ...	F	3	3	18·10	Tonsillitis ...	2	27/10	23/10	2	−/<4	256/256	256/128	16/8	65,536/8192	256/128
K.M. ...	F	33	1	18·10	Upper resp. tract infection	3	21 or 22/10	17/10	2	8/64	<4/16	4096/16	4096/16,384	512/4096	4096/16,384
D.R. ...	M	3	2	18·10	Myalgia ...	4	30/10	—	2	−/<4	128/64	−/<4	32/64	1024/2048	64/32
J.G.S. ...	M	2	3	21·10	Tonsillitis ...	4	1/11	—	2	<4/<4	64/32	−/<4	<128/1024	4096/8192	128/256

* Reciprocals of titres of complement-fixing (CF) and neutralizing (NA) antibodies against poliovirus 1, 2 and 3 found in acute and convalescent-phase sera. This 8/64 = a rise in antibody titre from 1/8 in acute-phase to 1/64 in the convalescent-phase serum.

IX

DISCUSSION

Oral poliomyelitis vaccine for use in the event of an emergency was made available in Great Britain at the end of April, 1961, but it was not until October that the outbreak at Kingston-upon-Hull gave rise to the first epidemic situation which appeared to warrant the application of a method of control hitherto untried on a large scale in this country. Earlier in the year poliomyelitis had been fairly widespread in Liverpool and other parts of the North-Western Region, but the infection there had moved slowly and local foci did not develop great intensity. Elsewhere there had been a few localised outbreaks, but the numbers of cases and the populations involved were considered to be insufficient to justify the introduction of a new form of vaccination.

Indications for mass vaccination

The rapid build-up of cases in Kingston-upon-Hull during early October constituted the most threatening situation that had yet appeared. By the 12th of the month, when the decision to use oral vaccine was taken, the number of confirmed cases had risen to 23 in a population of just over 300,000. This represented an incidence of more than 7 per 100,000 in a period of four weeks, with every indication that more cases could be expected. The arguments in favour of adopting exceptional control measures were : that an incidence in the range of 5 to 10 cases per 100,000 in a large population over a short period of time was unduly high ; that the momentum of the outbreak appeared to be increasing ; that the area involved could be clearly defined ; and that the local health authority was prepared to launch a mass vaccination campaign at the earliest possible opportunity.

In retrospect it is clear that the outbreak had, in fact, advanced well beyond the extent which had become evident at the time. The dates of onset of cases subsequently confirmed indicated that 32 of these had been taken ill on or before 12th October, an incidence of more than 10 per 100,000. By 17th October, when the vaccination campaign began, 65 cases subsequently confirmed from Kingston-upon-Hull were already ill and 8 cases had occurred in the East Riding. These findings showed that there had been ample justification for the decision to institute emergency control measures and raised the question of how early in the course of the outbreak such measures could have been adopted with advantage.

As a guide to the control of other outbreaks of poliomyelitis an answer to this question would have been of much practical value in the circumstances which obtained in 1961, when oral vaccine was recommended for use only in an emergency. Arrangements for mass vaccination were then of an all or none character. With the introduction in 1962 of oral vaccination as a routine immunizing procedure the need to define an epidemic situation ceased to be so critical. Once the vaccine had become generally available the occurrence of even a few cases of poliomyelitis in a district

constituted good reason for immediate intensification of routine immunization, with preparations for mass vaccination if this should be indicated by evidence of further spread of infection.

Success of the campaign

The campaign in Kingston-upon-Hull met with a remarkable degree of public acceptance. The extent of the outbreak and its rapid development caused great concern to the local inhabitants, who were more than willing to take advantage of the protection which oral vaccine was believed to confer. Newspapers and radio and television services kept the public continually informed of the progress of the outbreak and of the arrangements made by the local health authority for distribution of the vaccine. The organisation of the campaign and the ease of administration of the vaccine enabled large numbers of persons to be vaccinated in a short period of time and the response was such as to achieve the desired objective of vaccinating almost the entire population of the city and a very high proportion of residents in adjacent areas.

Effectiveness of vaccination

The outbreak ended within two weeks of the start of the campaign, a result compatible with the view that mass vaccination had arrested the spread of the disease. Oddly enough, the very success of the campaign in securing such a high rate of acceptance militated against a statistical assessment of its effectiveness. In their analysis of the Singapore outbreak Knowelden *et al.* (1961) were able to compare the incidence of poliomyelitis in vaccinated and unvaccinated groups of children. At Kingston-upon-Hull no such comparison was possible, since persons who remained unvaccinated were so few in number. An attempt was made to draw some conclusion from the day-to-day distribution of the cases but, in the absence of any known means of predicting the natural course of an outbreak of poliomyelitis, this proved to be abortive. When arranged by dates of onset a peak in the daily number of cases was seen to have been reached shortly before the campaign began, but this in itself gave no indication of how long the outbreak might have been expected to continue in the absence of oral vaccination. The fact was that the outbreak ceased quickly and the opinion of those on the spot was that oral vaccination had brought it to an end. This view was endorsed by several observers, including the Consultant in Infectious Diseases and the Medical Officer of Health for Kingston-upon-Hull, whose previous experience of local outbreaks of poliomyelitis was that none had ceased so abruptly. It must be recognised, however, that the circumstances precluded statistical analysis of the effectiveness of the vaccine and that it could well be fallacious to deduce a cause and effect relationship from the data available. If the outbreak at Hull had not subsided it could have been said that the vaccine had failed to exert the desired effect, but the converse is not necessarily true. It would appear that the value of mass vaccination will eventually be established by the consistency or otherwise of apparent changes in the course of outbreaks. The experience at Hull will take its place alongside previous observations of the use of oral vaccine and there will doubtless be other occasions in the future which will afford opportunities for further comparison.

Choice of vaccine

Certain disadvantages emerged from the selection of the heterotypic Type 2 virus for the campaign. The most important was the need to follow the vaccination of those, who had received no previous immunization, with a further course of oral vaccine containing polioviruses Types 1 and 3. The acceptance of this measure proved to be not as good as with the original Type 2 vaccine. It could therefore be argued that a more solid degree of immunity, particularly of those who had not been immunized before, would have been achieved by using trivalent vaccine in the first place. This would have complicated the problem of surveillance and might not have achieved the purpose of widespread colonisation of the gut. In future outbreaks, however, the background of primary immunization with trivalent vaccine will inevitably make the task of surveillance by virological methods more difficult. Recourse to tests with genetic-markers on the viruses found in the gut of vaccinated persons who contract poliomyelitis may or may not help to decide upon the source of the virus responsible for the illness. Clinical surveillance will need to be most stringent.

Virus studies in the community

The examination of faecal specimens collected from children and adults just before and at intervals after mass vaccination indicated a much higher percentage of excreters of the Type 2 vaccine virus among children than among adults. Epidemological studies have shown that natural poliovirus infection is spread during outbreaks largely through infants and children rather than adults. Restriction of mass vaccination to those under the age of 15 may in the future be found to interfere with the spread of an epidemic strain of poliovirus as effectively as vaccination of the entire population.

The vaccine virus showed little tendency to persist in the population. The faecal survey carried out two months after the administration of the vaccine yielded only two strains of Type 2 virus from 95 specimens. This non-persistence of vaccine virus was noted by Sabin in Toluca, Mexico and in Cincinnati, Ohio (Sabin and others, 1961). It was also observed in Hungary (Dovnok *et al.* 1962) and in Czechoslovakia (Skovranek, 1961). But whereas all these authors noted that mass vaccination at times when no outbreak of poliomyelitis was in progress appeared to reduce the circulation of wild polioviruses in the community, observations in Hull suggested that such an effect was not obtained. The carriage of the epidemic Type 1 virus was still high in Hull children under 5 years of age two months after the administration of the vaccine containing the Type 2 strain, even though a successful implantation of the vaccine had been demonstrated by the faecal survey which was made at an earlier date. Probably the existence of an outbreak at the time of mass vaccination may make it more difficult for the attenuated vaccine virus to eliminate wild polioviruses. The findings recorded in Section VI of this Report indicated clearly that the vaccine virus failed to establish itself in persons already infected with the epidemic Type 1 virus. The results also suggested that the prevalence of Type 1 virus infection, as judged by the proportion of excreters found in sample groups of children under 5 years of age, may have increased during a period of two months after the vaccination campaign had ended. If this were so, it would follow that some children were still

being infected by the epidemic virus after oral vaccination, although cases of poliomyelitis were no longer occurring. Any beneficial effect which might be claimed for the vaccine could not, therefore, be attributed wholly to interference with the spread of the epidemic virus. This raised the question of whether heterotypic immunity may not have been a factor in protecting individuals against the clinical effects of subsequent Type 1 virus infection.

Investigation of patients admitted to hospital

The results presented in Section VIII of this Report illustrate some of the difficulties in the correlation of laboratory evidence of poliovirus infection with clinical forms of illness. Isolation of virus from faeces and demonstration of a positive complement-fixing reaction using acute- and convalescent-phase sera were most successful in the groups of patients who showed severe or significant degrees of paralysis on discharge from hospital or subsequent residual muscle weakness. These tests were found to be positive much less often among patients who showed minor degrees of paralysis or no subsequent residual muscle weakness. The difference was materially influenced by age and previous Salk vaccination. These findings are in agreement with observations by American workers (Magoffin *et al.*, 1961, Lennette *et al.*, 1959) who were able to isolate poliovirus from only about two-thirds of all cases of clinical poliomyelitis and showed that the isolation rate varied directly with the severity of paralysis and inversely with the number of doses of Salk vaccine previously administered.

Neutralizing antibody tests for poliovirus antibody were positive in a number of cases with no other evidence of poliovirus infection. Some of these were diagnosed clinically as poliomyelitis and others were not. An independent appraisal failed to reveal a clinical pattern of illness common to all the patients who were found to have positive neutralizing antibody tests, though the proportion with such evidence of poliovirus infection was higher among those whose illnesses were suggestive of poliomyelitis. All laboratory tests for poliovirus infection were negative in nearly 20 per cent of cases diagnosed clinically as poliomyelitis and about 50 per cent of those diagnosed as suffering from other illnesses.

The negative laboratory findings in those patients whose illnesses were regarded clinically as poliomyelitis may be interpreted either as evidence that existing virological techniques sometimes failed to reveal poliovirus infection or as evidence that the illnesses were caused by other agents. There was little to suggest that infection by viruses, other than poliovirus, was responsible in more than a few instances. Among all the cases, confirmed and suspected, only two such infections (one with adenovirus and one with an unidentified enteric virus) were detected and the virus survey in the community had revealed no general prevalence of enteric viruses other than poliovirus. Positive neutralizing antibody tests in patients not considered to be suffering from poliomyelitis could likewise be interpreted either as evidence that the full range of pathogenic effects of poliovirus infection was not recognised clinically or as evidence of coincidental poliovirus infection of persons suffering from illness due to other causes.

The occurrence during an outbreak of poliomyelitis of illnesses, mostly mild in character, of equivocal causation was of practical importance in the

surveillance of the community for possible ill-effects arising from the administration of the oral vaccine. The vaccination campaign had embraced almost the entire population of the city and it was inevitable that some individuals would have received the vaccine during the incubation period or the early stages of an illness for which they would be subsequently admitted to hospital. A proportion of such individuals could be expected to show evidence, by laboratory investigation, of recent infection by the vaccine virus. A spurious cause and effect relationship might be deduced from coincidences of this kind. Hale *et al.* (1961b) have shown that the situation may be made even more complicated from the virological standpoint when superinfection by the vaccine virus displaces a pathogenic virus from the patient's intestine and so gives a misleading laboratory result.

Safety of mass vaccination

Virus studies were made in 63 of the 65 patients who were admitted to hospital after they had received a dose of oral vaccine. Eighteen of these patients were excreting Type 1 poliovirus and seven others had serological evidence of Type 1 infection. Poliovirus Type 2 was isolated from 10 patients and in the remaining 28 neither Type 1 nor Type 2 virus was isolated and the serological findings were equivocal. The dates of onset of illness in each of these groups showed no tendency to aggregate in the period from 5 to 20 days after oral vaccination, when illness attributable to the vaccine could be expected to occur. All the cases with severe or significant paralysis on discharge from hospital or subsequent residual muscle weakness fell in the group which gave evidence of Type 1 poliovirus infection. The positive identification of Type 1 poliovirus infection in these cases was an important finding which exonerated the vaccine as a cause of paralytic illness. The laboratory findings in the cases of equivocal causation, which were observed both before and after the vaccination campaign, did not materially assist in forming a conclusion. There was, however, no evidence to suggest that the vaccine virus was responsible for any neurological lesion and every reason to attribute the illnesses of the Type 2 virus excreters to some coincidental happening.

A further aspect of surveillance in the community was the possible role of Type 2 vaccine virus as a cause of non-neurological or minor illnesses in those who did not reach hospital. This was investigated by special enquiry concerning absenteeism either from work or at school. It was, of course, known that the usual seasonal increase of respiratory tract illnesses had begun to occur in the Hull area and in other parts of Yorkshire during October but there was no sudden change in numbers of cases in the period immediately after mass administration of vaccine. No evidence emerged suggesting that the vaccine was responsible for any illnesses with alimentary or respiratory symptoms. It was concluded that the oral vaccine had proved to be entirely safe.

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APPENDIX

Technical Methods

Examination of faecal samples for virus

Tissue culture. Suspensions of faeces, approximately 10 per cent w/v, were made in Dulbecco's phosphate-buffered saline pH 7·0 containing 200 micrograms/ml. penicillin and streptomycin and centrifuged at 4000rpm. in an angle centrifuge at 4°C. for 60 minutes. The supernatant fluids were inoculated, in 0·1 ml. amounts, into two tubes containing primary monolayer cultures of rhesus, or occasionally vervet, monkey kidney cells (MKTC) with a maintenance medium consisting of Hank's balanced salt solution, 0·25 per cent w/v lactalbumin hydrolysate, 1 per cent v/v heat-inactivated calf serum and 0·15 per cent v/v bovine albumin (Armour Laboratories). The maintenance medium was changed on the day after inoculation and the tubes inspected daily for cytopathic changes. Fluids from tubes showing such changes were typed for neutralization tests with a range of antisera to the enteroviruses obtained from the Standards Laboratory, Colindale, or the World Health Organisation.

From 17th October, when the oral Type 2 vaccine was given to the population of Hull, the technique was modified to cover the possibility that both Type 1 and Type 2 viruses might be present in the stools of patients. The faecal extracts were inoculated into three tubes of MKTC. To the first was added a drop of hyperimmune rabbit serum against poliovirus Type 1, to the second a drop of serum against Type 2 virus, but no serum to the third tube. The final concentrations of serum in the fluid phase of the culture were enough to neutralize 10,000 or more infective units ($TCID_{50}$) of the homologous serotype of virus. The tubes were held at room temperature for 3 hours or more, positioned so that the mixtures of faecal extract serum and maintenance medium were not in contact with the cell sheets. Then they were incubated at 37°C. with the cell sheets covered by the mixture.

Faecal samples shown to contain Type 2 virus by this initial test were retested for Type 1 virus by inoculating volumes of 3·0 ml. into 1 or 2-oz. bottles of MKTC with a fluid phase of Parker's medium 199 with bovine albumin but no calf serum. Before inoculation the faecal extracts were mixed with a serum from a monkey hyperimmunized against poliovirus Type 2. The final concentration of antibody in the mixture was 50 times the homologous titre and the mixtures were held at 37°C. for 3 hours. Monkey rather than hyperimmune rabbit serum was used so as to diminish the likelihood of heterotypic neutralization—i.e., the suppression by the Type 2 serum of small amounts of Type 1 virus which might be present in the faecal extracts (Hale *et al.* 1961a).

Faecal extracts from those patients with a clinical diagnosis of paralytic poliomyelitis, but without laboratory evidence of poliovirus Type 1 infection, were retested in bottles of HeLa, Hep. 2 and monkey kidney cells held for periods long enough to allow the growth of adenovirus and slow-growing enteroviruses. They were also tested by suckling mouse inoculation for Coxsackie viruses.

Suckling mice inoculation. Litters of suckling mice were inoculated within 24 hours of birth by injecting about 0·1 ml. by the subcutaneous and intracerebral routes. They were observed daily for 12–14 days before being discarded. Passage of mouse carcass to fresh litters was carried out when signs of paralysis were observed or there was a high death rate after the fourth day from inoculation.

Serological examinations

Acute and convalescent-phase sera ("paired" sera) were tested for complement-fixing (CF) antibodies to the three poliovirus, antigens and for those to mumps, influenza A, B and C, and adenovirus antigens by the technique of Stoker, Page and Marmion (1955). The CF antigens were obtained from the Standards Laboratory, Colindale. It was found to be particularly important to use strong concentrations of the poliovirus CF antigens to detect antibody. To ensure this the antigens were titrated in "chessboard" fashion with convalescent-phase sera from some of the patients from whom poliovirus had been isolated and that concentration of antigen which gave the highest serum titre and which was also free from anticomplementary activity was chosen for the test proper.

The complement-fixation test was considered to be positive (+) either when there was a four-fold or greater rise in antibody titre between acute and convalescent-phase sera against one or more of the three poliovirus antigens or when there was an unchanging titre of 1/64 or more against Type 1 antigen alone, that against Types 2 and 3 being less than 1/4. It was considered to be doubtfully positive (±) when there was a two-fold rise against any of the three antigens, or an unchanging titre less than 1/64 against Type 1 alone, or unchanging titres of 1/64 or more against any two or all three types of antigen. It was considered to be negative (−) when titres of less than 1/64 were found with more than one of the three antigens.

Neutralizing antibody tests for poliovirus antibodies were carried out by the metabolic inhibition method ("colour test") at the Medical Research Council's Division of Immunological Products Control, Hampstead (Perkins and Evans 1959). The neutralizing antibody tests were considered to be positive (+) when paired sera showed a four-fold or greater rise or fall of antibody against one or more of the three serotypes of poliovirus or when there was an unchanging titre of 1/16,000 or more to Type 1 virus.

Miscellaneous tests

Genetic "marker" tests on strains of poliovirus. The ability of certain isolates of poliovirus 1 and 2 to multiply at 40°C. (rct40° or "t" test) was also determined in the Medical Research Council's Hampstead Laboratory by the method of Sabin (1960).

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