POLIOMYELITIS IN AN "IMMUNIZED" FAMILY

BY

SYDNEY SELWYN,* M.B., Ch.B., B.Sc.

Department of Bacteriology, University of Edinburgh
Medical School, Teviot Place, Edinburgh

During the late summer and autumn of 1961 poliovirus isolations in the bacteriology department of Edinburgh University (which provides a virology service for the south-east region of Scotland) numbered 34 and were, with one exception, limited to poliovirus type 3. This was in marked contrast to the experience in most other parts of Britain and notably in the North of England—for example, Jamieson (1961). Northern Ireland was the only other region in which type 3 poliovirus appeared prevalent during 1961 (Virus Reference Laboratory, 1962).

The single isolation of poliovirus type 1 was from the faeces of a girl aged 3 years admitted to Cameron Infectious Diseases Hospital, Fife, suffering from a severe acute paralytic illness.

Clinical Note (Dr. E. Wilson, Cameron Hospital).—The child had complained of difficulty in moving her left leg two days before admission (October 11, 1961), and on the next day her right arm also was found to be paralysed. At the time of admission to hospital there were marked signs of meningeal irritation and extensive paralysis of both arms and legs, also of the neck and trunk muscles. Slight generalized weakness of the respiratory muscles was also present. The child was first nursed in a respirator but was rapidly weaned from this. The acute phase soon settled, leaving behind it extensive paralysis, particularly in the left arm and both legs.

Summary of Virological Investigations

Inoculation of a suspension of faeces (prepared in the routine manner) into monkey-kidney roller-tube cultures produced almost complete cell destruction of the poliovirus type within 18 hours. When the early cytopathic effect was evident, a tentative neutralization test on the original faecal suspension was performed at tenfold dilutions against polio type 1, type 2, and type 3 antisera. In this way a provisional virological diagnosis of poliovirus type 1 infection was obtained within 48 hours of receipt of the specimen and in the absence of epidemiological indicators of virus identity. Confirmation by specific neutralization tests on tissue-culture-passage fluid was obtained two days later.

A sister of the patient, aged 12 years, was admitted to hospital at the same time with mild signs of meningism. About three weeks before both the children were admitted to hospital a brother—contact No. 1, aged 8 years—had apparently complained of transient weakness and stiffness of the left leg.

Faecal specimens from these children and from other members of the family were examined but no virus was isolated. Epidemiological inquiries could not elucidate the source of infection in this family.

The results of serological investigations on the paralytic and non-paralytic patients are shown in Table I. In the paralytic case a diagnostic rise of anti-

body titre against poliovirus type 1 is evident, with an apparent heterotypic rise against poliovirus type 3 (cf. Lennette and Schmidt, 1957). An elevation of the titre against poliovirus type 1 is also seen in the non-paralytic case.

Single specimens of serum were obtained from the other two children in the family (equivalent to "convalescent" specimens) (Table II).

TABLE I.—Reciprocal Titres in Tissue-culture Neutralization Tests

	Polio Type 1	Type 2	Type 3
Paralytic case:			
"Acute" specimen ..	8	<8	8
Serum after 3 weeks ..	128	8	16
" " " 9 " ..	512	8	32
Non-paralytic case:			
"Acute" specimen ..	256	64	128
Serum after 3 weeks ..	>1,024	128	128

TABLE II.—Reciprocal Antibody Titres in Neutralization Tests

	Age	Polio Type 1	Type 2	Type 3
Contact 1 (abortive poliomyelitis?)	8	>512	128	128
Contact 2 ..	9	>512	>512	256

Immunization History

The request form accompanying the first specimen of faeces obtained from the paralytic case stated that the child had been "fully immunized against poliomyelitis." Details of the family record of immunization against poliomyelitis were subsequently obtained from Dr. H. W. Woolner (Fife Public Health Department), and were as follows:

	Date of Birth	Date of Injection of Salk-type British Vaccine			
		1st	2nd	3rd	4th
Paralytic case ..	1/1/57	20/3/58	15/5/58	4/8/59	
Non-paralytic case ..	31/5/49	14/8/57	11/9/57	10/2/59	
Contact 1 ..	21/9/53	7/8/57	4/9/57	4/3/59	
" 2 ..	14/4/52	14/8/57	11/9/57	10/2/59	20/6/61

Discussion

It was disturbing to find initially low levels of antibody against all three polioviruses in the paralytic case despite a history of a course of three injections of Salk-type vaccine. Although the good antibody response to natural type 1 infection would rule out true hypogammaglobulinaemia, the serum of the paralytic case was investigated biochemically (Dr. F. J. Scandrett, Royal Infirmary, Edinburgh). The serum protein levels in the convalescent specimen at nine weeks after the onset of illness are shown in Table III. These values were

TABLE III

Fraction	g./100 ml.	Percentage
Total ..	6.5	31
Globulin α_1 ..	0.2	
" α_2 ..	0.8	
" β ..	0.7	
" γ ..	0.6	

confirmed in a further specimen, although it had been kept for some time in the refrigerator before testing.

The interpretation of serum protein levels in young children is made difficult by the paucity of normal data. The patient's levels, however, appear to be within normal limits. It is of interest that an increase in the total gamma-globulin level of the serum does not seem to

*Lately Research Fellow of the National Fund for Research into Poliomyelitis and Other Crippling Diseases.

occur as a result of poliomyelitis even when a high level of specific antibody has been produced (Janeway and Gitlin, 1957).

The neutralizing antibody levels in both boys' sera seem adequate. In the absence of early "acute" sera, however, it is impossible to assess how much antibody is due to immunization or past infection and how much is a consequence of recent infection. Moreover, the high antibody levels against poliovirus types 2 and 3 may be, at least partially, the result of a heterotypic response (more clearly seen in the paralytic case). The titration of complement-fixing (C.F.) antibody in the sera might have helped to resolve some of these difficulties. Unlike neutralizing antibody, C.F. antibody rises slowly after antigenic stimulation, generally declines to undetectable levels within a year, and heterotypic responses are unimportant (Lennette and Schmidt, 1957). It is unfortunate that C.F. tests in relation to poliovirus are still not widely performed because of technical difficulties.

It may be concluded, then, that an apparently normal child contracted severe paralytic poliomyelitis despite a course of three injections of Salk-type British vaccine. A sister developed "non-paralytic" poliomyelitis and a brother experienced a suspicious illness in spite of similar courses of immunization.

It should be noted that the third injection was given 15 months after the second in the paralytic case, and about 18 months after the second in the case of the other children. The recommended interval is 7 to 12 months (Ministry of Health Memorandum, 1961).

If the antibody response to the first two doses is rather poor and the third dose is given more than a year after the primary course, there may be little booster effect. This may explain the low antibody titre in the blood of the paralytic case reported here; it also gives some support to the view that antibody titre is related to susceptibility to infection.

It is relevant to recall also that the antigenic potency of the type 1 component of the inactivated vaccine used in the United Kingdom has been shown to be less satisfactory than that of the type 2 and type 3 components (M.R.C., 1959).

Summary

An isolated family outbreak of type 1 poliovirus infection is reported. Although three of the four children in the family had had three and one had had four injections of Salk-type vaccine, one of them contracted severe paralytic poliomyelitis, and two of the others developed non-paralytic illness.

Attention is drawn to the recommended interval between the second and third injections of Salk-type vaccine, and also to the variability in antigenic potency of the type 1 component in vaccines hitherto available.

(The paralytic case is to be included in the M.R.C. Inquiry concerning poliomyelitis in the immunized. Ref. No. HCA/13/9/11/Part A.)

REFERENCES

- Jamieson, S. R. (1961). *Med. Offr.* **106**, 368.
 Janeway, C. A., and Gitlin, D. (1957). *Advanc. Pediat.*, **9**, 65.
 Lennette, E. H., and Schmidt, N. J. (1957). *Amer. J. Hyg.*, **65**, 210.
 Medical Research Council (1959). *Brit. med. J.*, **1**, 609.
 Ministry of Health (1961). Memorandum HM(61)(96) ECN379.
 Department of Health for Scotland Memorandum E.C.S. (M) 26A/1961.
 Virus Reference Laboratory, Queen's University, Belfast (1962). Annual Report for 1961. *Ulster med. J.* In press.

INEFFICIENCY OF PURIFIED DIPHTHERIA FORMOL TOXOID IN PRIMARY IMMUNIZATION AGAINST DIPHTHERIA

A REPORT TO THE MEDICAL RESEARCH
COUNCIL BY ITS COMMITTEE ON DIPHTHERIA
TOXOID*

It is difficult to assess the immunizing efficiency of the diphtheria plain formol toxoid (F.T.) used in the early days of immunization against diphtheria. There were considerable variations in the procedures used, such as the size and number of doses, the interval between doses, and the time and method of measuring the degree of immunity induced. Another complicating factor was that when the earlier investigations were made there was a high incidence of the disease in the child population, contributing no doubt to the stimulation of immunity. Nevertheless, plain F.T. was extensively used with clinical success, and the account by Fitz-Gerald (1928), of Canada, gives a clear example of this, although there is little precise information available about its performance in the child population of Britain during this period.

During 1931 to 1934 alum-precipitated diphtheria toxoid (A.P.T.) was introduced by Glenney and Barr (1931), and this rapidly replaced F.T. in Britain because of its greatly superior immunizing activity. In the early 1950s interest arose in the relationship between poliomyelitis and inoculations, resulting in a Report to the Medical Research Council (1956) which showed that inoculation with certain of the prophylactics against diphtheria and pertussis involved some risk of provoking paralysis due to poliomyelitis. The risk was shown to be minimal when alum-free diphtheria toxoid or plain pertussis vaccine was used singly. These findings, some of which were challenged by Holt (1959), led to the recommendations by the Ministry of Health (1957) that non-alum-precipitated antigens should be used in immunizing against diphtheria and that in general they should be given singly and not combined with other antigens. Accordingly supplies of plain F.T. were made available which contained 60 flocculating units of toxoid per ml. (60 Lf/ml.), and it was recommended that primary immunization with this material should consist of two injections each of 1 ml. at an interval of not less than four weeks.

These recommendations were not unreasonable in view of the findings of Bousfield and Holt (1954) that purified plain F.T., when given to children in two spaced doses each containing 30 Lf, was able to produce a Schick conversion rate of 96.6% when measured four weeks after the second dose. Nevertheless, it was

*Members of the Committee.—Professor D. G. Evans (chairman), Miss Mollie Barr, Dr. W. C. Cockburn, Dr. L. B. Holt, Dr. D. A. Long, Dr. A. Shaw, and Dr. J. Ungar.

Preparation of toxoid.—The diphtheria formol toxoid was prepared by Dr. L. B. Holt at the Wright-Fleming Institute of Microbiology.

Laboratory tests for antigenic potency.—The toxoid was tested for potency by Miss M. Barr, Professor D. G. Evans, Dr. L. B. Holt, and Dr. J. Ungar.

Titration of Sera.—The children's sera were titrated for anti-toxin by Miss M. Barr at the Wellcome Research Laboratories.
 Trials in children.—The scheme for the immunization and follow-up of the children was prepared by Dr. W. C. Cockburn and carried out by Professor D. B. Bradshaw, Dr. A. Shaw, and Mrs. D. Holliday, of the Public Health Department, Leeds.

Professor D. G. Evans and Dr. L. B. Holt prepared the report.