Conclusions

The condition known as diverticulitis includes two separate syndromes: spasticity of the sigmoid colon and perforated diverticulitis. In the first, management should be conservative in the first place (Reid, 1951); the syndrome takes the form of an acute episode, often without past history, that settles in the great majority of cases.

Perforated diverticulitis is a highly lethal condition, particularly when it affects the elderly and chronic sick. In those who are severely ill and in poor medical condition, simple colostomy and drainage should be attempted where possible, with subsequent closure after an adequate healing period (McCollum, 1959). Those patients who will stand a major operation are best treated by resection and anastomosis; it is important to resect the whole sigmoid colon which shows tubular change and spasm. Occasionally a perforated sigmoid loop can be exteriorized in the Paul-Mikulicz manner.

I thank all my surgical colleagues at Dudley Road Hospital for allowing me to use their cases. My grateful thanks are also due to Dr. J. L. Cole and the radiological department for help with the radiological studies; and to Dr. A. E. Chaplin and the pathological department for help with the pathological studies. Fig. 7 was provided for me by Dr. C. I. Griffiths from a case of Mr. F. R. Hurford. I thank Mr. J. G. Williamson for producing the figures and Mrs. M. K. Mason for help with the manuscript.

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"The Domiciliary Midwifery Service of the University College Hospital of the West Indies was established in 1956 with the aid of a grant from the Rockefeller Foundation. The reasons for its development were: (1) To provide practical experience for medical students in the home care of obstetrical patients and to give them some knowledge of the social circumstances of these women and their families. (2) To aid research on the social and economic circumstances of Jamaican patients, by provision of a social research worker. (3) To increase the hospital's service to the community and to provide necessary experience for pupil midwives. The domiciliary team is made up of a sister-in-charge and two or three staff midwives. They have the use of two vehicles and a staff of four drivers on shift duty throughout the day and night. The patients for home delivery are selected at the antenatal 'booking clinics' which are conducted by the sister in charge of the domiciliary service. About 100 women attend each week hoping to obtain bookings for hospital confinement. Some patients are selected for hospital delivery on medical grounds. Others who seem suitable for home delivery and are willing to accept this service are booked provisionally for this and home visits are arranged. A patient is not finally booked until her home has been assessed and found to be suitable. About one-third of homes are found to be unsuitable. Medical students under supervision conduct about 30% of the home deliveries, and since March, 1958, pupil midwives also worked with the service. Students and pupil midwives assist with the assessment of patients' homes and attend antenatal and puerperal home visits whenever possible." (*West Indian med. J.*, March, 1960.)

POLIOMYELITIS IMMUNIZATION IN INFANTS IN THE PRESENCE OF MATERNALLY TRANSMITTED ANTIBODY

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It has been shown in previous studies (Perkins, Yetts, and Gaisford, 1958, 1959b) that the usual primary immunization schedule of two doses of poliomyelitis vaccine given at an interval of four weeks produced an unsatisfactory antibody response in newborn infants. The majority of the infants tested showed no rise in type 1 antibody level, and, although at the time it was not clear whether the high levels of placentally transmitted antibody present in most infants were inhibiting or simply masking the primary response, it was later shown (Perkins *et al.*, 1959a), on giving a third dose, that sensitization had not been achieved by the primary course in those infants having high levels of antibody initially.

In further studies (Perkins *et al.*, 1959b, 1959c) a number of infants aged 4, 6, and 9 months were immunized with three doses of vaccine at monthly intervals and their antibody responses tested after the second and third injections. It was found that three doses of vaccine gave much higher antibody responses than two doses, and it therefore seemed logical to try to overcome the interfering effect of maternal antibody in the newborn by providing an increased antigenic stimulus. Accordingly, a group of infants were given three doses of vaccine at 1, 5, and 9 weeks of age, each dose being 2 ml., divided between two inoculation sites. The results showed that infants with low maternal antibody responded better to this schedule than to the two-dose schedule previously used; but again in most of those infants with high levels of maternal antibody it was not possible to decide whether their responses were being masked or inhibited.

The present paper provides details of the responses to a booster dose given 12 to 16 months after primary immunization with three doses of poliomyelitis vaccine in three groups of infants who were (a) 1 week, (b) 4 months, (c) 6 or 9 months of age at the beginning of the primary course.

Procedures

Immunization of Infants.—Blood samples were taken from the infants at the time of giving the booster dose and 10 to 14 days later. All infants were given a booster dose of 1 ml. of the same batch of Pfizer poliomyelitis vaccine prepared from the Brunenders (type 1), MEF-1 (type 2), and Saukett (type 3) strains.

Titration of Sera.—Poliomyelitis antibody levels to each of the three virus types were determined by the method previously described (Biological Standards

Control Laboratory, 1957; Perkins, Sousa, and Tobin, 1958). The post-primary immunization serum samples were titrated in parallel with the pre- and post-booster serum samples in order that a valid comparison of antibody levels could be made. All titres are given as the dilution of serum in the serum-virus mixtures before the addition to cell cultures.

Response of Infants to a Booster Dose of Poliomyelitis Vaccine

A. Infants Given Primary Immunization at Age of 1 Week

Of the 45 infants who were given their primary course starting at 1 week (Perkins *et al.*, 1959b), 30 remained in the study. It was clear from the high antibody levels of the pre-booster sera that in five of these infants intercurrent infection had occurred—two to type 1, two to type 2, and one to type 3. The responses of these five infants to the booster dose were high, especially to the infecting type, and they were therefore excluded from the study, together with three others from whom insufficient serum was obtained. There remained 22 infants, whose responses to the three virus types after receiving the booster dose are shown in Fig. 1.

FIG. 1.—Booster responses of infants who were 1 week old at time of giving the first dose of vaccine.

The pre-booster antibody levels were lowest for type 1, no infant having a titre of more than 32, and many having no detectable antibody at all. Clearly the primary response must have been poor for the antibody to have fallen to such low levels during the intervening period of 15 months. For type 2 there was a distinct separation between 13 infants with undetectable antibody levels and nine with titres from 32 to as high as 4,096. It is interesting that six of the nine infants with high antibody levels were born with low levels of maternal antibodies and all had shown excellent responses to primary immunization, whereas of the 13 with low antibody levels 11 were born with high maternal antibodies and showed no apparent response to the primary course. This was also true for type 3, for five of the six infants with titres of 32 or more showed a primary response, whereas 9 of the 16 with low antibody levels had shown no apparent primary response.

In spite of the low levels of antibody in many of the infants before the booster dose was given, the majority of them produced a good booster response to all three virus types. Titres of 32 or more were shown by all except four for type 1, all for type 2, and all except three for type 3.

B. Infants Given Primary Immunization at Age of 4 Months

Of the 55 infants given three doses of vaccine during primary immunization starting at 4 months of age, 40 remained in the study. In 17 of these infants the

antibody level in the pre-booster serum sample was greater than that in the post-primary immunization sample to at least one type—three to type 1, nine to type 2, and five to type 3. These infants were thus excluded from the study together with one additional infant from whom insufficient serum was obtained. There remained 22 infants, whose responses to the three virus types after receiving a booster dose are shown in Fig. 2.

Because of their age at the time of primary immunization, many more than in the previous group had non-inhibitory maternal antibody levels when the primary doses were given. It is of particular interest that the infants with pre-booster antibody titres of 32 or more had non-inhibitory maternal antibody levels at the time of primary immunization, and all had given a primary response. On the other hand, all those with pre-booster antibody titres of less than 32 had, at the time of primary immunization, shown either no apparent response above the maternal antibody level or only a low response.

All except one infant gave booster responses to all three virus types, and even this one exception, who did not respond to type 1, already had an antibody level of 128. Although response to type 1 was not so good as that to types 2 and 3, the majority of infants nevertheless gave good antibody levels. The responses to type 2 were excellent, all infants having titres of 1,024 or more, and that to type 3 was almost as good, all infants having titres of 256 or more.

C. Infants Given Primary Immunization at Age of 6 or 9 Months

Of the 29 infants given three doses of vaccine in their primary immunization course starting at 6 or 9 months of age, 24 remained in the study. The antibody level to one of the virus types in the pre-booster serum was greater than that in the post-primary immunization sample in three infants—one to each type. These three infants, together with two others from whom the full

FIG. 2.—Booster responses of infants who were 4 months old at time of giving the first dose of vaccine.

FIG. 3.—Booster responses of infants who were 6 or 9 months old at time of giving the first dose of vaccine.

series of serum samples was not obtained, were excluded, as were three infants who were also excluded from the original study because they had an inapparent infection before primary immunization. This left 16 infants in the study—seven were 6 months old and nine were 9 months—and their antibody levels for all three virus types before and after a booster dose are shown in Fig. 3.

At the time of primary immunization of these infants the maternal antibody had fallen to non-inhibitory levels and all had responded to the three-dose vaccine schedule. There were, therefore, only a few infants with undetectable antibody at the time the booster dose was given—four to type 1, none to type 2, and two to type 3.

The booster responses to all three types were excellent except in the case of two infants who responded poorly to type 1. Apart from these two, all showed titres of 256 or more, and the majority titres of 4,000 or more. There is an indication, especially from the type 1 and 3 results, that the 6-months-old infants responded somewhat better than the 9-months-old. A similar finding was obtained at the time of primary immunization, and it is probably due to the fact that the 6- and 9-months-old infants received different batches of vaccine for the primary course and that the batch given to the 6-months-old group was antigenically the more potent.

Discussion

In all these studies our ultimate objective has been to immunize infants at the earliest possible age. On theoretical grounds the newborn period is the most appropriate time to start, but, until we can show that with suitable antigens it is possible for satisfactory responses to follow at this early age, it cannot be advocated for general use. Our studies began after a Medical Research Council (1956) report had shown that the incidence of provoked paralysis was increased by combined prophylactics, and we hoped that by immunizing against poliomyelitis in the first three months of life the combined antigens might safely be given thereafter. Unfortunately, the inhibitory effect of maternally transmitted antibody has been until now a considerable deterrent to starting poliomyelitis immunization in the newborn period. However, in this present series the results with the infants who were given three doses of vaccine starting at 1 week of age and a booster dose a year later are so encouraging that primary immunization in the newborn period must be considered a practical possibility. There is still some evidence that high levels of maternal antibody inhibit response, for, although many more infants responded to the three doses in the primary course than was apparent at the time, the poorer responses to the booster dose were almost always in those infants born with high maternal antibody.

The importance of giving to the newborn three and not two doses of vaccine as the primary course cannot be overemphasized. In our earlier study, in which 1-week-old infants were given two doses, only 5 out of 22 infants responded to type 1 after the booster dose, the highest titre being 32. In the present study, however, in which 1-week-old infants were given three doses in the primary course, 18 out of 22 gave type 1 titres of 32 or more after the booster dose, and almost all gave satisfactory titres to types 2 and 3.

It is interesting to note that, in those infants who responded to primary immunization and who retained some of their antibody for 12 to 16 months, the response

to the booster dose was much greater than that given by infants whose antibody had fallen to undetectable levels. This raises the question of the optimal time at which to give the booster dose, and consideration should be given to the effect of decreasing the interval between primary immunization and the booster dose.

As was to be expected, the booster responses in the groups of infants who received their primary immunization at 4 months or older were decidedly better than in the 1-week-old group. It is debatable, however, in view of the promising results with the 1-week-old group, whether there would be any advantage in delaying the start of immunization until after 1 week. It is more important that immunization should start as early in infancy as possible, and, since the increased antigenic stimulus as a result of giving three doses has undoubtedly been responsible for overcoming much of the inhibitory effect on maternal antibody, it is highly probable that more potent vaccines, especially in the type 1 component, will have an even greater effect in breaking down maternal antibody inhibition. With this in view, studies have already been started, using purified vaccines of higher antigenic potency (Hilleman *et al.*, 1960) than those which we have used so far.

Summary

Infants given a primary course of three doses of poliomyelitis vaccine at 1, 5, and 9 weeks of age responded better to a booster dose 12 to 16 months later than those who received only two doses as a primary course.

This finding shows that inhibition of the response to vaccine by maternal antibody can be overcome by increasing the antigenic stimulus, and it is therefore probable that the use of concentrated vaccines to increase it still further will result in an even more successful breakdown of maternal antibody inhibition.

Our thanks are due to Dr. G. V. Feldman, Dr. R. F. Jennison, and the nursing and laboratory staff at St. Mary's Maternity Hospital, Manchester, for their assistance, and to Miss P. Tumber and Mrs. B. Mitchell for their help in titrating sera. We also thank the Ministry of Health for the supply of poliomyelitis vaccine. This work was supported in part by a grant from the National Fund for Poliomyelitis Research to the Department of Child Health, Manchester University, for which we are most grateful.

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Copies of the *French Bibliographical Digest: Pediatrics*, by Maurice Lamy, have been distributed to universities and libraries in this country. The *Digest* confines itself to French publications issued before 1955, and includes the names of French paediatric periodicals and paediatric societies. The bibliography is arranged in 15 sections and there is an index of authors. The *Digest* is edited and published by the Cultural Center of the French Embassy, 972 Fifth Avenue, New York 21, N.Y., U.S.A.