

correlates in a graphical form the clinical and laboratory observations on one volunteer who showed a typical response of rather more than average severity.

Thirty-three volunteers were inoculated with Hanks's saline or medium from uninfected cultures of human-embryo-kidney cells. One of these developed a mild cold and six developed mild symptoms, mainly respiratory, at some time after their inoculation; but only two or three of these volunteers would have been regarded as experiencing mild illnesses by the criteria used in evaluating the clinical data on the volunteers receiving E.C.H.O. 20 virus.

However, the volunteers who were inoculated with virus and from whom virus was not recovered had more symptoms than the uninoculated controls and fewer than the virus-infected volunteers. This might have been due either to infection by another virus, which would not multiply in the cultures used, or to infection by E.C.H.O. 20 virus which we failed to detect. We think the latter is the most probable explanation, since most of the illnesses occurred in the experiments in which large doses of partly neutralized virus were given; while, on the other hand, no illnesses occurred in the volunteers inoculated with the mixtures of low-titre throat-washing virus and immune serum.

Discussion

The following conclusions can be provisionally drawn. When material containing E.C.H.O. 20 virus from throat swabs, nasal washings, or tissue culture was given to volunteers, illness as a rule followed and virus multiplication could generally be demonstrated in those that were ill. The illnesses were mainly undifferentiated minor febrile disease with sore throat; coryza occurred rarely.

These results support the view that the illnesses suffered by some of the children in the U.S.A. from whom the viruses were isolated (see Cramblett *et al.*, 1958) were probably due to E.C.H.O. 20 virus. The general results of these studies may be compared with those obtained using Coe virus and E.C.H.O. 11 in similar experiments. E.C.H.O. 20 produced illness rather less often than did these viruses and the clinical picture was different. In Coe virus infections general symptoms with fever were quite common, but coryza occurred in every case. In E.C.H.O. 11 virus infections coryza was not seen, but sore throat occurred and abdominal symptoms were quite common.

Summary

Forty-three human volunteers living in isolation were inoculated with E.C.H.O. 20 virus as nasal washings or tissue-culture fluids. Twenty-seven volunteers became ill. The main symptoms and signs observed were headache, malaise, aching limbs, sore throat, and fever. Two volunteers showed a syndrome resembling the common cold and eight had abdominal symptoms. Virus was readily found in the throat and faeces of most volunteers, and antibody responses fourfold or greater occurred in 20 out of 25 volunteers from whom virus was recovered.

We thank Miss J. B. Macdonald for help with the clinical observations and Miss P. K. Pearce for technical assistance. The experiments would have been impossible without the willing help of the volunteers, to whom we are grateful.

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ACUTE DIVERTICULITIS A REVIEW OF EMERGENCY ADMISSIONS

BY

P. GILROY BEVAN, Ch.M., F.R.C.S.

Consultant Surgeon, Dudley Road Hospital, Birmingham

This paper is based on 138 cases of diverticulitis admitted as emergencies to a general hospital for acute cases over a recent two-year period. The diagnosis was confirmed in every case by operation, barium enema, sigmoidoscopy, or necropsy—often by a combination of these methods. "Diverticulitis" is a general term including a range of conditions that are defined below.

Incidence

In a series of 116 consecutive necropsies in patients over the age of 40 the colon was examined specifically for diverticulitis. This gives the absolute incidence of the condition. Of the 116, 14 (12%) showed the presence of diverticulitis. This incidence compares with that of other series (Edwards, 1954; Aird, 1957), but is greater than that of Wakeley (1936). In men, 6 out of 68 necropsies showed diverticulitis in the colon (9%), and in women 8 out of 48 (17%). The absolute incidence rose with age: in the 60-69 decade 3 out of 26 showed diverticulitis (12%), in the 70-79 decade 3 out of 16 (19%), in the 80-89 decade 4 out of 16 (25%), and in the over-90's 3 out of 3 (100%).

The relative age incidence of the 138 clinical cases is shown in Fig. 1. It can be seen that the highest number of cases is in the 70-79 age-group. None occurred below the age of 40.

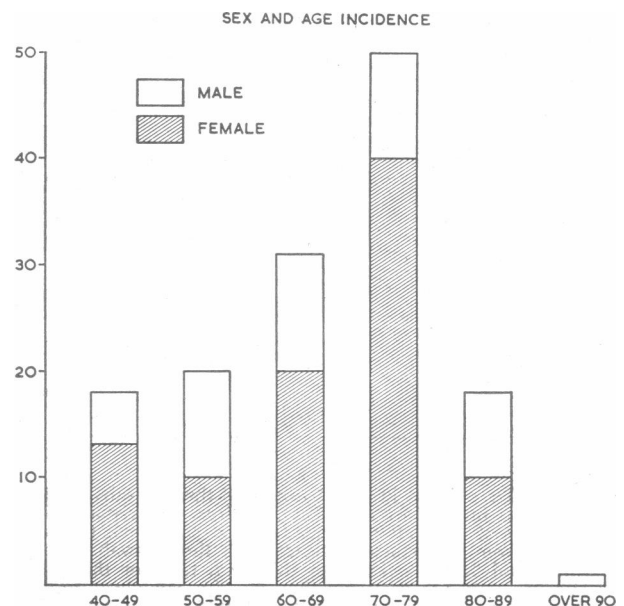


FIG. 1.—Age and sex incidence in 138 cases of acute diverticulitis.

The sex incidence is almost identical in the clinical series and in the necropsy series. Of the 138 clinical cases, 93 were female and 45 male, a preponderance of 2 to 1 in favour of women. This sex incidence appears to have changed during the last decade (Todd, 1955).

Diverticulitis is an acquired disease, and a disease of old age, especially of women.

Pathology

The site of the disease in the colon was studied in 100 consecutive cases in which barium-enema examination showed diverticulitis. The results are given in Table I. It can be seen that the sigmoid or pelvic colon

TABLE I.—Site of Disease in 100 Cases in which Barium Enema Showed Diverticulitis

Sigmoid colon	62
" and descending colon	17
" descending, and transverse colon	4
" and transverse colon	2
" " ascending	2
" transverse, and ascending colon	2
Descending colon	3
" and transverse colon	1
Ascending colon	1
" colon	1
Whole colon	5

is involved mainly or entirely in 89% of cases. It is suggested that the pathological state of the sigmoid colon is the underlying cause of the disease.

The traditional account of diverticulitis describes four successive pathological stages—the prediverticular, diverticulosis, diverticulitis, and perforation (Aird, 1957). However, this seems to be an oversimplification and does not explain all the clinical features. The prediverticular stage is of special interest and holds the secret of the beginnings of the condition, although it has received less attention than the other stages.

In order to understand the pathology more fully, the complete colon was examined and dissected at necropsy in 10 cases showing diverticulitis. The following findings are felt to be significant:

1. The typical colon bearing diverticula shows excessive fat deposited in the mesentery and the appendices, covering the bowel itself, often burying it and the diverticula. This fat may contribute to the formation of diverticula (Illingworth and Dick, 1956).

2. There is striking narrowing of the sigmoid colon, which appears tubular and stenosed (Fig. 2). The wall of this segment of the colon is considerably thickened. Histological slides were made of this thickened muscle wall, showing that its whole width consists of increased muscle tissue; the wall of the diverticulum is mucosa only, supported by a thin layer of fibrous tissue (Fig. 3).

3. The diverticula occur in characteristic arrangement. Primary diverticula occur in pairs, related to the site where the arteries pierce the muscle layers adjacent to the appendices, just on the mesenteric side of the two anti-mesenteric taeniae. This agrees closely with the conclusions of Edwards (1954). This is a constant arrangement in most cases, but in some, secondary diverticula form at intervening sites. The degree of stenosis is related to the extent of diverticulum formation; the diverticula are of the pulsion type, and as the mucosa prolapses through deficiencies in the muscle layer the wall of the bowel between adjacent taeniae is taken up and stenosis results or is made worse. This can be likened to a windlass mechanism.

4. There is an abrupt transition between the sigmoid colon which is the seat of diverticulitis and the more normal bowel proximally, although this proximal bowel may show the presence of diverticula (Fig. 4). On the mucosal aspect of the bowel the normal proximal mucosa contrasts with the oedematous and congestive mucosa of the sigmoid; on the serosal aspect the haustrations of the normal proximal

segment give way to close bands of circular spasm in the sigmoid. This zone of transition can usually be seen clearly in barium studies (Fig. 5).

5. The diverticula occur in sets of two or more opposite each other on the same circumference of the bowel, separated by bands of circular constriction. Thus pairs of primary diverticula form a "ladder" pattern when seen from the lumen, and when viewed from the serosal aspect narrow bands of circular spasm alternate with expansions bearing the diverticula.

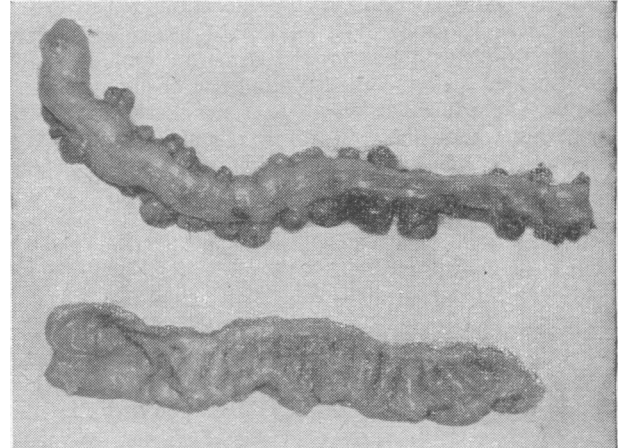


FIG. 2.—Specimen above shows typical narrowing of sigmoid colon which is the seat of diverticulitis, and is compared with a normal sigmoid colon, below. Both are fresh necropsy specimens.

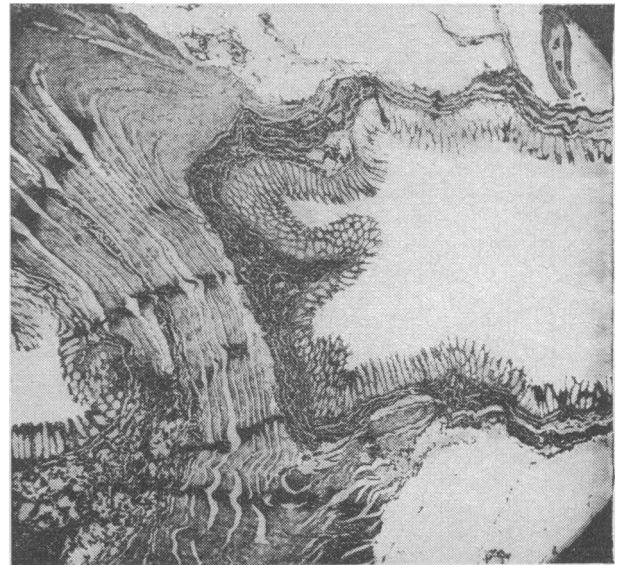


FIG. 3.—High-power view showing that thickened sigmoid wall on left is due mainly to hypertrophied muscle. Wall of diverticulum on right consists of mucosa and fibrous tissue only.

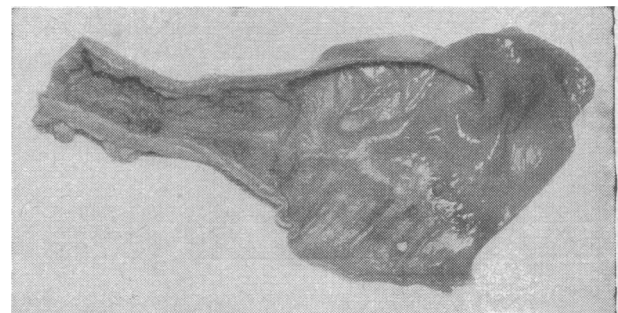


FIG. 4.—Specimen showing abrupt transition between the thickened sigmoid wall with its oedematous and congestive mucosa which is the seat of diverticulitis (left) and the normal colonic wall (right).

The theory is advanced that the clinical condition called diverticulitis is caused initially by a condition of spasm of the sigmoid colon. This spasm may be intermittent or persistent, and may be brought on by various influences—dietary indiscretion, allergy, or infection, for example. This condition of spasm is also segmental and limited to the sigmoid colon, especially the distal sigmoid and rectosigmoid region. It may be related to the function of the colon, inasmuch as this lower sigmoid segment normally forms a type of sphincter which relaxes at the time of defaecation. In diverticulitis there is probably a failure of relaxation. As a result of persisting sigmoid spasm, pulsion diverticula are formed owing to the resulting rise of pressure in the colon. These diverticula are most numerous in the sigmoid, where the persisting spasm squeezes them out. However, diverticula also occur in the proximal colon; the ileocaecal valve is most efficient, and when sigmoid spasm leads to distal obstruction the whole of the intervening colon is a closed loop, and as the pressure rises or continues high diverticula form proximally, progressing retrogradely from the sigmoid.

There are therefore two pathological stages in the disease: (1) Spasm of the sigmoid colon and rectosigmoid area. This is the so-called "prediverticular" stage, illustrated in Fig. 6. (2) Formation of diverticula.

Clinical Studies

In the disease termed diverticulitis there are two clinical syndromes, corresponding to the pathological stages.

Spastic Colon.—Sigmoid spasm leads to symptoms of altered bowel habit—constipation, diarrhoea, or both. Commonly there is persisting or recurrent pain in the left iliac fossa, with tenderness on palpation. The rigid sigmoid can often be felt in the early stages and is tender. Sigmoidoscopy and necropsy examination of the sigmoid mucosa in diverticulitis reveals oedema, congestion, and granular areas that bleed easily on touch. Rectal bleeding is a common symptom of the condition, the blood being bright red and mixed with the faeces; it may frequently be copious. In all the cases and specimens studied here, bleeding from a diverticulum or diverticular opening has been encountered on only one occasion. In this case a giant

diverticulum was found to be bleeding copiously and the haemorrhage was arrested by diverticulectomy. Apart from a rare occurrence such as this, the rectal bleeding in diverticulitis originates from the inflamed mucosa present in the spastic segment of sigmoid. The main underlying feature of diverticulitis is thus sigmoiditis (Todd, 1955). Finally, the sigmoid or rectosigmoid spasm may lead to obstruction. In most cases the episode of obstruction responds to conservative measures.

Leaking from Diverticula.—The diverticula are formed by unsupported mucosa and are very apt to leak or perforate, especially in the sigmoid colon, where the state of spasm causes persisting high pressure. Usually the perforations are small, and may be so minute that they may not be found at operation. In four cases in this series a generalized faecal peritonitis was found at operation in the presence of diverticulitis without the actual site of perforation being discovered.

Diverticular perforation may take two forms: (a) generalized faecal peritonitis, which in elderly patients is a highly lethal condition; and (b) a small leak from a diverticulum which becomes sealed off, forming a pericolic abscess: as the leak is fed by faecal material issuing from a sigmoid in spasm (the spasm made worse by the perforation), the process of suppuration progresses and tends to infiltrate along soft-tissue planes and into adjacent viscera—bladder, small intestine, and adjacent loops of colon. Internal fistulae result characteristically. Fig. 7 illustrates the manner in which leaking diverticulitis may infiltrate into adjacent tissues. Commonly, intestinal obstruction supervenes, due to paralytic ileus associated with intraperitoneal pus or to involvement of small intestine. This type of obstruction demands urgent operation.

Clinical Groups

All the 138 cases of diverticulitis studied were admitted as emergency cases. In the great majority of these patients symptoms were of recent development, a matter of days or weeks. Symptoms had been present for longer than three months in only 14 cases, and previous episodes of diverticulitis lasting more than three months had occurred in only five. Thus in 119 of the patients the disease was of recent onset.

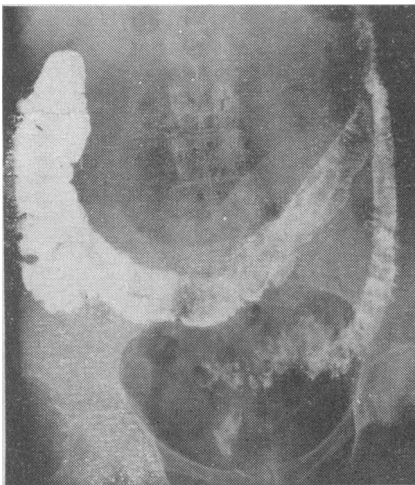


FIG. 5

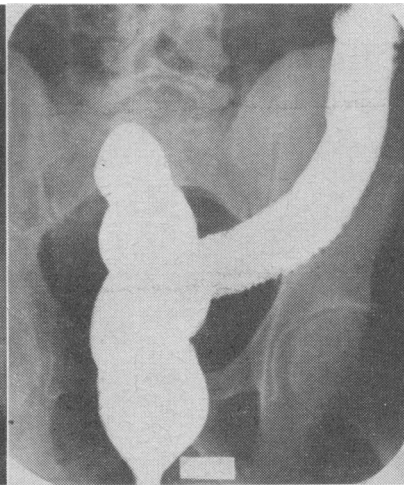


FIG. 6

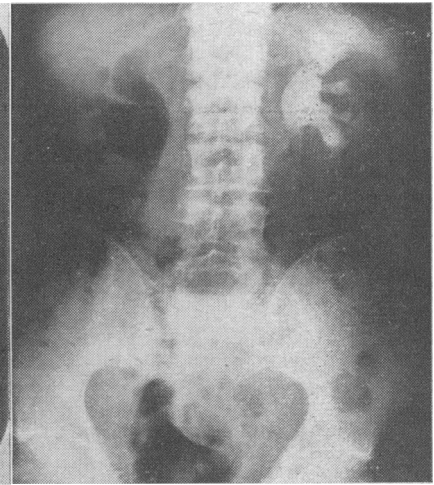


FIG. 7

FIG. 5.—Barium enema showing the abrupt transition between the sigmoid colon, which is the seat of diverticulitis, and the descending colon, which is normal although it shows some diverticular formation. FIG. 6.—Typical "saw-edged" appearance of the prediverticular stage of diverticulitis. FIG. 7.—Intravenous pyelogram in case of vesical calculi, showing a non-functioning kidney on right. Diverticulitis of the sigmoid colon was present; this had infiltrated into the lower end of the right ureter and filled the right kidney with air.

Patients discharged after treatment did not develop recurring symptoms. Diverticulitis is usually regarded as a persisting, recurring, and progressive condition, but study of these patients shows it to take the form of short-lived acute episodes that do not recur if the patient survives.

Analysis of the cases shows that they fall into five clinical groups (Table II).

TABLE II.—Clinical Groups

	No. of Cases	No. of Deaths
1. Altered bowel habit	25	
2. Rectal bleeding	16	
3. "Acute diverticulitis"	46	1
4. Obstruction	16	2
5. Perforation or fistula	35	13
	138	16

Group 1. Altered Bowel Habit, Often Accompanied by Abdominal Colic (25 cases).—Diarrhoea was the presenting symptom in 14 cases, constipation in 8, and alternating diarrhoea and constipation in 3. The high incidence of constipation is unexpected but interesting, and compatible with the idea of persistent colonic spasm.

Group 2: Rectal Bleeding (16 cases).—The bleeding was often profuse and blood transfusion was necessary in six of these patients. In one case, quoted previously, bleeding was from a large diverticulum in the pelvic colon, and excision of this diverticulum resulted in successful termination of the haemorrhage. In the other cases sigmoidoscopy showed the bleeding to originate from the mucosa of the sigmoid or recto-sigmoid.

Group 3: Acute Pain, Tenderness, and Rigidity in the Left Iliac Fossa (46 cases).—Acute pain of a continuous type in the left iliac fossa was the predominant symptom in 26 cases, diarrhoea was present in 9, and rectal bleeding occurred in 4. Central abdominal colic affected 25 patients, and constipation was marked in 7, alternating with diarrhoea in 1. Pain on defaecation combined with dysuria affected 4 patients.

Group 4: Intestinal Obstruction (16 cases).—Abdominal distension was the most marked feature in all these patients, together with vomiting. Colic was also present in each case, but constipation was rarely complete. The obstruction was complete or acute in only three, necessitating operation. In the other 13 cases the obstruction proved to be partial or subacute, and responded to conservative measures, including gastric aspiration, intravenous transfusion, antibiotics, and sedatives.

Group 5: Perforated Diverticulitis (35 cases).—Perforation led to generalized peritonitis in 23 cases, and localized leaking with abscess formation in 9. In three cases there was fistula formation—two vesico-colic and one vagino-colic. Operation was performed in 22 of these patients; and in most of the remainder it was not possible on account of the desperate general condition and of age. The great majority of the deaths occurred in this group.

Management of these 138 cases came under two headings, conservative and operative.

Conservative Treatment

Patients in the first four groups (103 cases) were for the most part treated conservatively in the first place. It is thought that these groups represent the first stage of the disease—namely, sigmoid and recto-sigmoid spasm—and that this is the principal pathological factor causing alteration in bowel habit, rectal bleeding, pain in the left iliac fossa, and subacute obstruction. The main points in conservative management were as follows:

Chemotherapy.—Most of the common anticoliform antibiotics—chloramphenicol, streptomycin, and tetracycline—were used with effect in short courses. The sulphonamides were also used successfully in many cases, both the

absorbable ones such as sulphadimidine and the insoluble members such as succinylsulphathiazole, especially in the presence of diarrhoea.

Sedatives.—Morphine or its derivatives were used in most cases, although theoretically they might be expected to increase the underlying state of spasm.

Neuromuscular Relaxants.—Pethidine was used in most cases in groups 1 and 3 and is probably the drug of choice when colic is present. "Trasentin" is also a very useful drug, but was employed in only a few cases in this series. Propantheline also merits wider trial in this group.

Blood transfusion was necessary in many of the group-2 cases, both for acute bleeding and for chronic anaemia. In some cases repeated transfusions were needed.

Gastric aspiration and parenteral fluids were given in all group-4 cases, and in the majority the intestinal obstruction settled on this regime.

The results of conservative treatment are excellent in the great majority of cases. This experience accords with that of Brown and Toomey (1960). There were no deaths in the patients of groups 1-4 where conservative management was deliberate. Eight deaths occurred in group-5 patients (perforated diverticulitis) treated conservatively, but in all these the conservative regime was obligatory; operation would have been carried out had the patients been fit enough.

Operative Treatment

Thirty-four cases underwent surgery, including 22 in group 5. The following operations were carried out:

Laparotomy (10 cases).—This served to confirm the diagnosis and extent of the disease in doubtful cases. In some, adhesions were separated and appendectomy was performed. There was one death.

Diverticulectomy.—For bleeding diverticulum in one case (see above).

Incision of a central abdominal abscess (1 case), followed by a faecal fistula which slowly closed.

Colostomy—with or without laparotomy (15 cases).—Five of these patients died. In 5 of the 10 survivors the colostomy was subsequently closed after an interval of months, as follows—18, 11, 6, 3½, and 2. The last-mentioned patient died of a leaking colostomy. Before closure, barium enema is of value to show the condition of the distal loop and ensure an adequate lumen.

Resection of a localized segment of diverticulitis with anastomosis (7 cases).—All these patients survived. In view of the pathology described, it is important to resect the complete colonic segment which is the seat of spasm. This usually means the sigmoid colon, which appears tubular and contracted with a thickened wall. It is not important to excise all the colon bearing diverticula. However, only few of the over-70 age-group are fit to withstand a major resection for a non-malignant condition (Bolt, 1960).

In some cases of perforated diverticulitis the sigmoid colon bearing the perforation can be exteriorized and excised, leaving a double-barrelled colostomy that can be closed at a second stage.

Among the group of 34 patients undergoing operation 7 (21%) died. In three patients in this group pelvic abscesses drained conservatively without operation: two discharged spontaneously—one per rectum and one per vaginam—and the third was drained through a sigmoidoscope. These three survived.

Mortality.—Among the 138 patients in this series 16 died as a result of the disease or its complications, an overall mortality of 11.6%. Of these deaths 13 occurred in the 35 patients of group 5 (37%). Only 5 of these followed operation; the remaining eight were never fit for operation.

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 (McCullum, 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

BY

F. T. PERKINS, M.Sc., Ph.D.

RISHA YETTS, B.Sc.

From the Biological Standards Control Laboratory,
Medical Research Council Laboratories, London

AND

WILFRID GAISFORD, M.D., M.Sc., F.R.C.P.

Director of the Department of Child Health,
University of Manchester

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