trial had industrial lung disease, and it is possible that such subjects may be less likely to respond to prophylactic chemotherapy than those who have not been exposed to a dust hazard. One of the sulphonamide series may not, in fact, have been the best drug to choose: the administration of drugs (such as penicillin) by injection was thought to be impracticable with working subjects, while the possible undesirable side-effects of chloramphenicol (Franklin and Garrod, 1953) and aureomycin—apart from the expense of these two drugs—would hardly justify their use over prolonged periods for prophylaxis, although good results have been claimed recently for the continuous administration of aureomycin in preventing acute respiratory infections in patients with congestive cardiac failure (McVay *et al.*, 1953). The dosage of sulphonamide may have been inadequate to establish a sufficiently high blood level, and the production of sulphonamide-resistant organisms may have been stimulated, but larger doses would probably have produced toxic effects.

In conclusion it may be said that at present there is no evidence that a suitable drug for the prophylaxis of the acute exacerbations of chronic bronchitis exists, but that if and when such evidence became available, as a result of a controlled trial, much disability might be prevented. In seeking such a drug much help would be obtained if more were known about the epidemiology, clinical types, bacteriology, and pathology of chronic bronchitis.

Summary

The acute exacerbations of "winter bronchitis" that occur in pneumoconiosis, emphysema, and "chronic bronchitis" are a serious problem.

A controlled clinical trial is described in which subjects with various forms of chronic bronchitis were studied in three centres during the winters of 1951–2 and 1952–3. In all, 83 subjects were included. Of these, 42 were given 0.5 g. of sulphadimidine three times a day during the winter months and 41 were given inert tablets in the same way.

A clinical assessment of the subjects was made at monthly intervals. Acute exacerbations of respiratory symptoms were classified as follows: (1) an acute "unmodified" attack of bronchitis; (2) a modified and less severe attack of bronchitis; (3) an attack of bronchial spasm; and (4) a head cold or "influenza."

No evidence was found that sulphonamide was effective in preventing the acute exacerbations of "winter bronchitis," but the trial was relatively insensitive.

We acknowledge our indebtedness to Dr. C. M. Fletcher (previously director of this unit), at whose instigation the trial was planned; to Dr. J. C. Gilson (director) for his advice and criticism; to our colleagues in the unit, especially Dr. I. Davies and Dr. M. C. S. Kennedy (M.R.C. Silicosis Treatment Centre, Stoke-on-Trent), who helped in the running of the trial; also to the general practitioners who referred patients. We are grateful to the Imperial Chemical (Pharmaceuticals) Ltd. for the supply of the tablets used, and to the Austin Motor-Car Company for facilities afforded.

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ACUTE APPENDICITIS IN CHILDHOOD

BY

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A review of a personal series of 118 cases of acute appendicitis treated in conjunction with the children's department of the Royal Victoria Infirmary has led to the appreciation of certain aspects of this disease which it is felt are not widely known. Any factor which may lead to the delay in admission of over 24 hours is worthy of close study. In 63 children peritonitis was already present, a figure which cannot be viewed with any complacency. Comment on some of the difficulties of diagnosis in this disease has been made recently (*British Medical Journal*, 1953).

Pathology

Study of the pathological lesion of the appendix in 101 cases in which this was recorded shows that an obstructive element occurred in 74. This obstruction was produced by faecaliths (32), kinking (20), and stricture (10). In 12 cases obstruction was reported, but the exact nature of this was not stated. One case of acute appendicitis was a complication of a carcinoid of the appendix which had caused some occlusion of the lumen. The high incidence of a degree of obstruction to the lumen of the appendix is to be noted, and is contrary to the experience of Bunton (1953). In many cases in which occlusion of the lumen was present it was noted that the infective process tended to stop at this point, only the distal portion of the appendix being involved in the disease process. It would therefore seem that the acute infection starts within the lumen of the appendix, and subsequently, either by tension or by spread into the walls, produces perforation. Perforation often occurs at the site where a faecalith is impacted; a faecalith causing this complication, and measuring 2 cm. in length, is shown in Fig. 1. A faecalith may be present in very young children, as was shown by one child aged 18 months.

FIG. 1.—Faecalith associated with acute appendicitis in a child of 9 years, producing obstruction of the lumen and perforation at the point of impaction.

Catarrhal or intramural appendicitis occurred in 26 cases. In this type of lesion the infection would appear to start in the wall, as commented upon by Bunton, and subsequently spread throughout the length of the appendix and sometimes on to the caecal wall. There is, however, in this series, insufficient evidence to suggest that it is possible to make a clinical differentiation of one type of appendicular lesion from another. The omentum was found limiting the spread of the infection in only 18 cases. Another variable factor in acute appendicitis is the infecting organism and its toxicity. While *Bact. coli* is undoubtedly present in most

cases, other organisms can be responsible for the disease, and variations may arise from difference of virulence as well as the factors which have already been referred to.

The position of the appendix is shown in Fig. 2, and it will be seen that in only 40 patients was it found lying in the classical subcaecal position. The development of the disease in relation to the day of admission is indicated in Fig. 3. The abscess present on the first day was due to a recurrent attack of acute appendicitis. Eight of the 21 cases

admitted on the second day had already developed localized peritonitis before 36 hours. Although Bunton reports that respiratory infection is common in association with acute appendicitis, this series conforms more to the American opinion that this is not a common feature; only 14 of these children had a history of upper respiratory infection.

Diagnosis

The age incidence is shown in Fig. 4. It will be seen that there are 19 cases of acute appendicitis under the age of 5 years. In view of the differences in pathology and position it is not surprising that the clinical picture of appendicitis varies greatly from case to case, and the spread of the disease process may also show considerable differences in

FIG. 2.—Position of the appendix in relation to day of admission. The circles indicate points where maximum tenderness would be expected to have occurred in first 24 hours of the disease.

FIG. 3.—Development of the disease in relation to day of admission.

FIG. 4.—Graph A shows age incidence of acute appendicitis in this series. Graph B shows age incidence of cases in which the initial symptom was vomiting.

relation to time. Localized tenderness is undoubtedly the most useful early physical sign, and Fig. 2 shows the points where tenderness could have been elicited in the early stages of the disease. Once peritonitis has developed the diagnosis becomes apparent, but it is clear that, if admission in the first 24 hours is to be obtained, rigidity should not be awaited. What can be achieved by intelligent appreciation of physical signs was well shown in one child of 15 months from whom, of course, little help could be obtained. The physician who saw the patient recognized that there was one point of maximum tenderness in the abdomen, observed by the reaction of the child to pressure over this point; and this patient is the youngest with unperforated appendix to be admitted to the department. This physician had received her training in the children's department of this hospital.

Delay in Diagnosis

Factors which may lead to late admission are shown in Fig. 5. While pain is by far the commonest initial symptom, vomiting came first in 34 cases in this series. It will be seen that there was a marked tendency for patients with the initial symptoms of vomiting to be admitted somewhat later than was the case with pain. While on occasion the vomiting preceded the pain by a matter of only a few hours, this was not always the case, and in one patient there was an interval of 72 hours before pain developed. During this time vomiting had been persistent, but nevertheless the true diagnosis was not arrived at until peritonitis had developed. Another factor which may cause some delay of admission is illustrated in Fig. 2. This shows the position of the appendix in relation to the day of admission. It will be observed that in only three cases admitted after the fourth day was the appendix lying in the classical subcaecal position.

Diarrhoea is an uncommon initial symptom, occurring in only three cases, but it was an associated symptom in 19 of the 31 cases in which the appendix was found lying in the

pelvis. A child with acute appendicitis often sleeps fitfully owing to exhaustion. Professor Ian Aird (1949) stated that a child should not be wakened at night for an operation; this teaching would appear to be out of keeping with the dangers of delay, and to lull the medical adviser and the parents into a false sense of security.

Previous abdominal pain had been present in 28 cases in this series. At least some of these attacks of pain may have been associated with mild appendicitis. On several

FIG. 5.—Illustrates initial symptom in relation to day of admission.

occasions these patients had been admitted to hospital and were discharged without operation. In view of the high incidence of obstructive lesions in acute appendicitis it would seem justifiable to remove the appendix when such a lesion is diagnosed in the period before the onset of acute inflammation. An observation making such a diagnosis possible in some cases was reported by me (Hindmarsh, 1948). This observation has been amply confirmed by experience and its value well established. Such lesions of the appendix also produced chronic abdominal discomfort which may simulate other disease processes, particularly in adults.

Treatment

The pre-operative treatment of the more seriously ill patients is of great importance, and the operation should be delayed several hours to allow dehydration to be overcome. Such dehydration is due not only to vomiting and toxæmia but also, if generalized peritonitis is present, to loss of body fluids into the small intestine and into the peritoneal cavity. Once the condition of the patient has improved satisfactorily operation is proceeded with. An opportunity is also given to start streptomycin when rupture is suspected and intravenous aureomycin when generalized peritonitis is present.

Types of Operations Performed in This Series of 118 Cases

Operations Performed	Number	Mortality
Appendicectomy	78	Nil
Appendicectomy with drainage	32	1
Drainage of abscess:		
Primary	6	Nil
Complication	10	"
Interval appendicectomy	8	"
Total	134	1

In 110 cases appendicectomy was performed at the first operation. A muscle-splitting incision is favoured in early cases, and was used on 57 occasions in this series; but if a mass is palpable on clinical examination and the length of the history suggests that the appendix is gangrenous and at the point of perforation, a longer incision than this is to be preferred. In this school we favour the Rutherford

Morison incision, and this was used on 43 occasions. This is a muscle-cutting incision in the R.I.F. which can be extended either upwards or downwards, depending upon the position of the appendix found at exploration. In Rutherford Morison's original description the incision was much longer than is now the usual practice. The skin incision is no more than 3 in. (7.5 cm.) in the first instance, and is extended only as required. Paramedian incisions are used only when there is any doubt in the diagnosis, or when a pelvic mass can be palpated prior to operation, as in pelvic appendicitis, as this incision gives the most direct approach to the disease process. The paramedian incision was used in only 16 patients in this series.

There were 24 cases of abscess; 16 of these had the appendix removed with drainage. In six drainage alone could be instituted owing to the appendix not being readily accessible. One was treated conservatively for two to three days and subsequently drained. I would certainly agree with Deaver (1952) that there is no urgency to drain a well-localized abscess, but if such conservative treatment is adopted chemotherapy should be given. In the two other cases treated conservatively one was complicated by the presence of whooping-cough, and the risk of anaesthesia was thought to be great enough to risk delayed operation, and in the other the abscess was very well localized, with a history of six days' duration.

I agree with Gross (1953) that Fowler's position is to be recommended in cases of peritonitis, and we feel that the low percentage of subdiaphragmatic abscess recorded by the Boston Children's Hospital may be partly due to this position.

The indications for drainage are similar to those suggested by Scott and Ware (1945), of the Boston Children's Hospital, and it is only used, therefore, when a good deal of peritoneal exudation develops round a forming abscess cavity, or when it is suspected that a faecolith may have escaped from the appendix and has not been recovered. It has been the practice in this series to lay the drain down the lateral wall of the abdominal cavity into the pelvis in such cases. In no case was this responsible for post-operative obstruction, which has occurred in only one case after operation when no drain was used.

Recently there has been some discussion on the advisability of burying the appendix stump with a purse-string suture (Cleland, 1953). There was no incidence in this series, or in a much larger series in adults, in which burying the appendix led to any threatened intussusception. If the stump is carbolized an abscess in the caecal wall as reported by Cleland is unlikely to develop. When the caecum is thickened and oedematous it may not be possible to carry out invagination, and indeed it was not done in the fatal case. This child of 9 years developed a central abdominal abscess, drainage of which led to a faecal fistula, and, in spite of the prolonged administration of intravenous fluids, blood transfusion, and antibiotics, she wasted away and died eight weeks after admission. At necropsy it was shown that the appendix stump was communicating with this abscess, and it is probable that the acute pain that she developed nine days after the first operation was due to a leakage from the caecum. It would therefore seem that if for some technical reason the appendix is unable to be buried an unabsorbable suture should be used.

In the post-operative period gastric aspirations and intravenous therapy are continued in all cases of localized and generalized peritonitis. These are continued until flatus is passed or bowel movement occurs. There was no case of persistent paralytic ileus in this series.

Antibiotics

Antibiotics were not used in cases admitted without peritonitis. These cases made a straightforward recovery, and all but one were discharged within seven days. Penicillin and streptomycin were favoured when localized peritonitis was present. This treatment is continued for five to seven

days, depending upon the patient's response. The average stay in hospital in this type of case was 14 days. In generalized peritonitis aureomycin (since it became available) was given intravenously during the time an intravenous drip was continued, unless the sensitivity of the organism called for another antibiotic. This is continued for 10 days, and is then discontinued even if the patient is febrile. The patient is not discharged until two days after the discontinuation of antibiotics, to allow any abscess to declare itself: use of antibiotics in a febrile patient tends to mask the clinical signs of the developing abscess and the abscess cavity becomes surrounded by dense fibrous tissue which makes the subsequent diagnosis and treatment more difficult. The average stay in hospital in cases of generalized peritonitis was 21 days. In some cases, however, ultimate discharge from hospital was delayed for up to two months.

When appendicectomy was not performed it was the practice to get the patient back two months later for interval appendicectomy. It is interesting to note that two cases in which an abscess was drained were readmitted with a further acute attack while awaiting interval appendicectomy. This has occurred in other cases treated by my colleagues.

Subdiaphragmatic abscesses developed in two cases—one to the left side and one to the right. One case of left paracolic abscess and six cases of pelvic abscess occurred—two of which discharged spontaneously. There were two cases in which abscesses developed deep to the wound and had subsequently to be drained. There was also the case of central abdominal abscess which has already been referred to. Wound infection developed in only six cases. It would not seem necessary, therefore, to leave the superficial layers of the wound open, as suggested by Abel and Allen (1950). None of these cases required subsequent operation, as removal of some of the cutaneous stitches usually allowed the abscess to discharge spontaneously.

Comment

When 63 cases out of 118 are admitted with localized or generalized peritonitis the situation must give rise to great concern. It is clear that responsibility for the factors which have allowed this state of affairs to develop must be established. According to the records, in only 11 cases was failure to suspect appendicitis by the medical practitioner responsible for the delay. It must be admitted, however, that among these patients were some of the most seriously ill children. The usual tentative diagnosis had been one of gastro-enteritis, which was treated with antibiotics. In most cases, however, it is clear that the parents failed to realize that persistent pain and vomiting, particularly where the latter was the first symptom, was caused by acute appendicitis. Often, too, a parent administers a dose of castor oil or other purgative which leads to delay in seeking medical advice. A great deal can be done by education of the public, as has been shown by Abel and Allen, and it would seem that such education will be required before any marked improvement can occur in the time of admission of such children.

I agree with my colleagues in the children's department that where abdominal pain has persisted for several hours the presence of appendicitis or some other serious condition should be strongly suspected, and expert assessment made at home or in hospital as soon as possible. Our aim should be for all children with acute appendicitis to receive treatment within the first 24 hours of the disease.

Summary

A series of 118 cases of acute appendicitis in childhood is recorded.

More than half were admitted with localized or generalized peritonitis.

Vomiting as an initial symptom occurred in 34 cases, particularly in children of 5 years and under.

Other factors which may delay diagnosis are discussed.

Treatments carried out in this series are described.

Delay in admission is mostly due to delay in seeking medical advice.

I acknowledge the assistance I have received from the ward sisters and residents in the paediatric department, particularly Dr. J. H. Jackson, whose endeavours have been largely responsible for saving a number of seriously ill children. My thanks are due to Dr. F. J. W. Miller and Dr. S. D. M. Court, who have co-operated in caring for the dangerously ill child. I am grateful for the co-operation of my surgical colleagues, and to the anaesthetists whose care has aided the smooth post-operative recovery of patients. I also thank Mr. D. P. Hammersley for the diagrams and Professor A. G. R. Lowdon for his interest and advice. I would like to acknowledge my gratitude to the late Sir James Spence for the pleasure of collaborating with his department.

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A TRIAL OF MERCAPTOMERIN IN SEVERE CONGESTIVE HEART FAILURE

BY

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High claims have been made for mercaptomerin ("thiomerein"). In this preparation an organic mercurial compound is linked with sodium mercapto-acetate, which replaces the theophylline of earlier mercurial diuretics such as mersalyl and "unephral."

One important advantage claimed is the suitability of the preparation for self-administration by the patient in his own home (Krehbiel and Stewart, 1951). Mercaptomerin is less toxic and less irritant than mersalyl, and this permits of subcutaneous injection. Self-administration would therefore be no more onerous than with insulin. The advantages of this to both general practitioner and patient in a chronic condition like congestive cardiac failure need not be emphasized.

There is evidence, however, that non-irritant mercurial preparations may also be relatively inactive, since both their therapeutic and their toxic actions require dissociation of the compound (Handley and LaForge, 1947). The potency of all new mercurial diuretics must therefore be fully proved before their non-irritant properties on subcutaneous injection can be accepted as an advance.

A trial of mercaptomerin has been carried out in which three aspects were studied: the diuretic efficiency, the duration of the diuretic response, and the incidence of local toxic reactions.

Methods

Patients admitted to hospital in severe congestive heart failure were used in the trial. All had marked oedema. They were given a diet constant in fluid, salt, and calorie content. Doses of 2 ml. (40 mg. of mercury per ml.) of a mercurial diuretic were given at 48-hour intervals, mercaptomerin and mersalyl being used alternately. This was continued until eight doses had been given—four of each (Fig. 1).

The diuretic response was determined by measurement of the output of urine. The volume excreted in all the 48-hour periods following the mersalyl injections was