may be initiated is equally important. Though some of the drug interactions involving warfarin were apparently widely known to the doctors taking part in this study the awareness of the less well publicized interactions fell steeply. Probably some of these interactions are of minor clinical importance and the risks should not be overstressed until the relative importance of each interaction has been evaluated. It is of interest that half the practitioners were aware of the adverse interaction between salicylates and warfarin though this usually occurs only at doses of salicylates (> 3 g) well beyond the doses usually prescribed or taken as selfmedication. On the other hand, the clinically-important interaction involving clofibrate was known to only one doctor in three.

ANTIDIABETIC AGENTS

The low degree of awareness of potential interactions⁷ involving these drugs suggests that, though the occurrence of drug interactions occurring in patients on these agents is potentially high, they may be clinically less significant.

MONOAMINE OXIDASE INHIBITOR DRUGS

The doctors who replied were most aware of the adverse interactions involving this group of drugs. Indeed, five of the six best known interactions involved this group. This high degree of awareness reflects the publicity that these interactions⁸ have received. Hence the risk of the initiation of unintentional drug interaction may be least with this group of drugs though the clinical effects of the interactions may be the most important. The low reporting of clinical interactions may reflect the effectiveness of education in this area.

COMBINED PREPARATIONS

In the present study the awareness of the interacting sub-

stance, such as barbiturate or sympathomimetic agents, was reduced when the substance was "hidden" in the fixed-dose proprietary preparations. This emphasizes the need for doctors to be aware of the components of the combined preparations that they use.

The findings relating to interactions actually experienced have the limitations common to all voluntary reporting systems. If a doctor is not aware of the existence of an adverse drug interaction he will be unlikely to recognize and report it. Nevertheless, the information in this study about the reactions experienced is of some interest in assessing the relative importance that the practitioners attach to the clinical problem of drug interactions.

Doctors clearly wish to have relevant information about clinically important drug interactions but the advice must be practical and authoritative. The distribution of extensive information about drugs that doctors hardly ever prescribe reduces the effectiveness of important information. Since the completion of this study tables of several clinically important adverse drug interactions have been circulated to all the practitioners in the region. As an additional measure warning labels, with detailed information about drugs that interact, are being designed to attach to the hospital and general practice records of patients on specific drugs.

We wish to thank the practitioners of the north east of Scotland for their co-operation with this study.

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Occasional Survey

Acute Terminal Ileitis and Yersinia Infection

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Summary

Acute terminal ileitis was for many years thought to be due only to Crohn's disease, though most patients found at laparotomy to have this condition did not progress to the chronic form of Crohn's disease. A case of acute terminal ileitis due to Yersinia pseudotuberculosis is presented here to draw attention to another, perhaps predominant, cause of this condition.

Introduction

Though *Yersinia pseudotuberculosis* has been known to be a cause of terminal ileitis and mesenteric lymphadenitis for some 20 years¹⁻³ yersinia ileitis is still rarely recognized. Only 20 or so such cases were diagnosed in the United Kingdom during 1959-72⁴ and none have been reported in the British literature since then. The condition may be misdiagnosed as acute Crohn's disease, and since the prognosis and treatment of the two conditions differ it is important that the differentiation be made.

Case Report

A 12-year-old boy was admitted to this hospital on 2 March 1973 with a two-day history of feeling unwell and pain in the right iliac fossa. He had vomited twice before admission and had not opened his

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bowels for four days. There were no urinary symptoms. He was feverish (temperature 39.2°C, pulse 130/min), tender and rigid in the right iliac fossa with rebound tenderness, and tender to the right on rectal examination. The chest was normal radiographically but an abdominal x-ray film showed several fluid levels, particularly in the right iliac fossa, indicating a local ileus, possibly associated with appendicitis, and this provisional diagnosis was made. Investigations before operation were: W.B.C. 18,400/mm³ (82% neutrophils, 18% lymphocytes); E.S.R. 33 mm in the first hour; total proteins 5.6 g/100 ml (albumin 2.4 g). Other serological values were within normal limits.

Under anaesthesia a mass was felt just below and to the right of the umbilicus. Laparotomy showed free serous fluid, a thickened and slightly congested retrocaecal appendix, an inflamed, erythematous, indurated 8 cm of terminal ileum with serosal hyperaemia extending on to the caecum, and enlarged lymph nodes in the small-bowel mesentery. *Yersinia* infection was considered and appendectomy was performed. Half of the organ was preserved for culture and half for histological examination. Biopsy specimens of two enlarged lymph nodes were removed for histological examination and culture and free peritoneal fluid was also sent for culture.

Postoperatively he remained feverish. Benzylpenicillin was given on the second postoperative day, and two days later his temperature and pulse returned to normal. On the sixth postoperative day the W.B.C. was normal. Thereafter his recovery was uneventful and he was discharged 10 days after the operation. Barium meal and follow through examination weeks after the operation showed no abnormality in either the small or the large bowel. When reviewed in the outpatient clinic one month after the illness had begun he had made a complete recovery.

PATHOLOGICAL FINDINGS

Histologically the appendix showed a non-specific hyperplasia of the lymphoid follicles with moderate submucosal fibrosis. Epithelioid granulomata were not seen and there was no evidence of an acute intramural inflammatory process. The lymph node showed pronounced sinus hyperplasia with no epithelioid granulomata or other specific features.

Yersinia antibody titres (from the Public Health Laboratory, Leicester) were diagnostic of *Y. pseudotuberculosis* infection with a type 1 titre of 1/10,240. *Y. pseudotuberculosis* was isolated from the appendix and was sensitive to ampicillin, tetracycline, co-trimoxazole (Septrin), gentamicin, and cephalothin sodium but not to sulphonamides. There was no growth of the organism from cultures of the lymph node, peritoneal fluid, or faeces.

Discussion

YERSINIA INFECTION

Knapp and Maschoff¹ were the first to isolate *Y. pseudotuberculosis* from a mesenteric node of a patient with the clinical picture of acute appendicitis. Since then it has been isolated from many cases of mesenteric adenitis, with or without associated terminal ileitis, predominantly in Europe^{5,6} but recently in Canada, the United States, Australia, New Zealand and Japan.⁷⁻¹¹

Y. pseudotuberculosis and the closely related *Y. enterocolitica* may cause several clinical syndromes, the most common of which is mesenteric adenitis, which may be associated with intussusception as well as terminal ileitis.^{5,12} Of a series of mesenteric adenitis cases in the United Kingdom some 18% were due to *Y. pseudotuberculosis*.⁶ In a larger series in Scandinavia 13% were due to this organism while a further 63% were due to the enterocolitica strain.¹³ Both strains may cause terminal ileitis.^{14,15} In the United Kingdom during 1972 18 cases of *Y. pseudotuberculosis* infection were reported but there were none of *Y. enterocolitica* infection.¹⁶ Other, less common presentations are erythema nodosum and septicaemia. The organism is widely spread throughout the animal kingdom, and this is most probably the reservoir and source of the infection in man.^{17,18} The primary infection is thought to be in the ileal mucosa.¹⁹ Infection with this organism is usually considered to

have a good prognosis, though a recent report²⁰ indicated occasional chronicity, and some severe complications have been noted.^{5,21-23}

Diagnosis of *Yersinia* infection is made on the positive identification of the organism, which may be cultured from the mesenteric nodes, appendix, peritoneal fluid, ileal contents, blood, and, occasionally, the stools and urine.²⁴ Serological identification is, however, the most reliable method of diagnosis as the organism is difficult to grow.²⁴

ACUTE TERMINAL ILEITIS

For many years after it was first described acute terminal ileitis was considered to be an acute form of Crohn's disease. In a review article, however, Gump *et al.*¹⁹ found that only between 10 and 20% of the cases progressed to the chronic disease with further attacks. Of the rest, some would have been due to unrecognized *Yersinia* infection.²⁵ Sjöström, in a study of acute terminal ileitis, cultured *Y. enterocolitica* from 21 out of 29 cases,²⁶ while in other studies *Y. pseudotuberculosis* has been implicated.^{8,9}

The clinical features of acute terminal ileitis due to *Yersinia* infection closely resemble those of acute appendicitis. Laparotomy should be performed even if the disease is suspected, as coexistent acute appendicitis cannot be excluded.¹⁰ Under anaesthesia a mass may be palpable and at laparotomy the appendix may be inflamed, but is more often normal, and there is usually mesenteric lymphadenopathy. The terminal ileum is thickened and inflamed for a variable distance and is usually the only part of the bowel affected. The differential diagnosis includes in particular acute Crohn's disease, but other forms of ileocaecal disease such as tuberculosis or amoebiasis must be considered. Histological findings in *Yersinia* infections are non-specific, and postoperative barium studies should show no abnormality. In most cases the infection settles and antibiotics are unnecessary. The most appropriate antibiotic seems to be tetracycline.

With acute terminal ileitis due to Crohn's disease there may be a significant past history or evidence at laparotomy or later from barium studies of other segmental intestinal involvement suggestive of Crohn's disease. Histological examination of a resected lymph node or the appendix is often unhelpful but may sometimes be diagnostic. In most cases of Crohn's ileitis there is involvement of the caecum.²⁶ With Crohn's ileitis the prognosis should be guarded; it may settle without active treatment but steroids or azathioprine may be needed, and chronic disease may follow at a later date.

In all cases of acute terminal ileitis found at laparotomy the following is therefore recommended. Appendectomy, culture and histological examination of the resected organ, biopsy and culture of any enlarged mesenteric nodes, and culture of any free peritoneal fluid. Serological tests for *Yersinia* should be done to confirm the diagnosis and to enable the course of the illness to be followed. Blood, faeces, and urine cultures are also helpful. Barium studies should be performed postoperatively if Crohn's disease is suspected. Fistula does not appear to be a hazard after appendectomy, for even in Crohn's disease a fistula develops from the diseased terminal ileum rather than from the appendix stump.^{19,27} Furthermore, it is best to perform an appendectomy because most cases are opened as suspected appendicitis through a McBurney-type incision and there is less confusion if the appendix is removed. Incision into the ileum for biopsy and culture has no place, even though there have been several reported cases without complications,^{8,9} as *Yersinia* infection is better diagnosed on other grounds and such a procedure would predispose to the formation of fistulae in cases of Crohn's disease.

I should like to thank Professor B. N. Brooke for allowing me to report this case and for his very helpful advice in preparing this paper.

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Conversations with Consultants

Independence at Midwich

FROM A SPECIAL CORRESPONDENT

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"There is," they assured me confidently, "plenty of wealth under the grime of Midwich." Dr. Rother, a specialist physician, estimated the average industrial wage at well over £50 a week. How did this affluence affect the hospital service? It meant low quality staff and a high turnover, though perhaps surprisingly nursing recruitment was not too bad. Many nurses, however, came from overseas and Mr. Test had reservations about the suitability of some of them for staffing his obstetric unit. There was no praise for Salmon, which in their opinion had needlessly divided administrative responsibility for nursing. Too many nurses now spent too much time at unnecessary lectures. If Test's ward sister was away there were times when his beds were covered for only eight out of 24 hours by a fully qualified nurse, which, with many post-operative patients to be cared for, was a hazardous situation.

One in Four G.P.s from Abroad

Walking up from Midwich station to meet the three consultants from the infirmary I had noticed a fair proportion of immigrants among the home going crowds. Was this proportion reflected in the town's doctors? Dr. Rother estimated that one in four of the local general practitioners had qualified abroad, as had most of the S.H.O.s and registrars. They told me, too, that advertisements for consultant posts were now attracting few applicants, with overseas graduates predominating. Mr. Test mentioned the outcome of a recent consultant appointment committee where the successful applicant—an experienced man who had qualified on the Indian sub-continent—had, soon after being offered the post, written to say he was leaving Britain to take a well-paid appointment in the Middle East. He contrasted this situation with his own appointment a decade or so ago from over 70 applicants.

*This and the succeeding names are fictitious.

Mr. Taw, surgeon at the Midwich Infirmary, forecast that within a decade one third of consultants in the area would have qualified abroad. They seemed resigned to a dependence on overseas staff—"we are north of that magic line between Bristol and the Wash," observed one wryly. While acknowledging the good medical standards of some of the overseas doctors the three men were adamant in wanting an E.C.F.M.G.-type examination, including a test of English, as a means of raising standards. Wasn't the clinical assessment scheme for screening would-be entrants to the N.H.S. working? Their response was unenthusiastic—it was for too short a period and the consultant often had insufficient time to assess the attached doctor properly. Referring to the language problem Dr. Rother said he found that whereas many foreign doctors spoke good English they frequently failed to grasp its important nuances when it mattered—in talking with patients.

Overpaid Administrators

In contrast to comments by other consultants in this series none of this group had any complaints about the administration blocking or modifying their requests for equipment and suchlike. In fact, Test admitted that the planning mistakes that had emerged during the operation of his new unit could be laid at the door of doctors—including himself—who had given bad advice. They were not, however, greatly impressed by the general standard of lay administrative staff, who always had secretarial staff (a sore point) and were, in their opinion, overpaid for their level of qualification.

£15,000 a Year

"So how much are you worth," I inquired. Without hesitation Taw answered, "A wholetime consultant deserves £15,000 a year." Examples of well-paid acquaintances in other professions were wheeled out. The group were convinced that not a single general practitioner in their area earned less than £10,000, criticizing en passant G.P.s' unavailability "after