Prevention of measles: vaccine efficacy and potential effectiveness of a vaccination programme on entry to school

A measles outbreak in a primary school was investigated to measure vaccine efficacy, examine whether medical records on entry to school predicted subsequent illness with measles, record lost schooldays for each child with measles, and see if the outbreak could be terminated by offering vaccination to any remaining susceptible children.

Subjects, methods, and results

As all cases of measles in the outbreak were in children aged under 8 only the 136 children aged between 3 and 8 in seven open plan infant and nursery classes were considered to be at risk. Vaccination state is most accurately recorded on the infant vaccination record, which for many children had been transferred to their school medical record. Questionnaires, inquiring about illness with and vaccination against measles, were distributed to parents of 124 children present at school on one day, and 84 replied within 48 hours. The infant vaccination records for four children in whom the vaccine was reported to have failed before 1985 were not present in their school medical records, so local clinics and general practitioners were contacted to establish their true vaccination state.

During the outbreak there were 35 cases of measles, which were either diagnosed by a general practitioner or defined as rash for three or more days and fever with cough or coryza or conjunctivitis. All cases were in unvaccinated children, thus the observed efficacy of measles vaccine was 100% (table). In the measurement of vaccine efficacy reported illness with measles before 1985 in four vaccinated and nine unvaccinated children was ignored¹; examination of clinic and practice records for these four vaccinated children confirmed that only one child had developed measles, diagnosed by a doctor, when aged 51 months after vaccination at 23 months.

On entry to school, history of illness with or vaccination against measles, or both, had been noted in many school medical records, and this information together with the infant vaccination record, if contained in the school medical record, was used to assess each child's probable immune state to measles at the

Efficacy of measles vaccine during outbreak in primary school*

Vaccine state before 1985 outbreak†	No of children ill during outbreak	No of children not ill during outbreak
Vaccinated (n=51)		51
Not vaccinated (n=58)	35	23

*Excludes 27 children whose vaccine state was unknown, none of whom had measles.

†From parents' questionnaire or infant vaccination record, or both.

time of their medical examination on entry to school. Forty two children were classified as probably susceptible, 73 as immune (42 after vaccination and 31 after illness with measles), and 21 as immune state unknown. The subsequent number of cases of measles in those susceptible was 35 (83%), including nine cases at school before the 1985 outbreak; in those who had been vaccinated two (5%); in those who had measles before school entry two (6%); and in the immune state unknown group five (24%). For a few children the later information obtained from the questionnaire changed the assessment of vaccine state at the time of the outbreak.

Each child with measles was absent for an average of eight schooldays. Seven weeks after the first case had occurred only five children were identified as possibly still susceptible. They were offered immediate vaccination; two did not respond, one who had previously been advised against measles vaccination refused again, one accepted the vaccine, and the other was found to have been vaccinated before beginning school. During the rest of the term there were no further cases of measles.

Comment

From 1980 to 1983 over 37 000 cases of measles were notified yearly in England and Wales in children aged 5-9 years.² This age group accounts for 38% of all notifications of measles, and transmission of measles increases three times each year, when school terms begin.³ Many districts are responding to the 1984 measles control initiative⁴ by offering measles vaccination at school entry.

Our investigation showed the efficacy of measles vaccine in a primary school and that most of the high morbidity from measles might have been avoided if the susceptible children, most of them readily identifiable, had been vaccinated at school entry. To be successful a vaccination programme to control an outbreak of measles in a school should be implemented within 10 days of onset of the primary case.⁵

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C reactive protein concentration as screening test for bacterial infection in febrile children

Interest has focused on C reactive protein concentrations¹ as an early predictor of bacterial sepsis in children.^{2,4} We compared a semiquantitative assay of C reactive protein with total and differential white cell counts in the early diagnosis of childhood infection.

Patients, methods, and results

All children admitted with fever (temperature $>37.5^{\circ}\text{C}$) to the paediatric medical unit from 1 October 1983 to 31 July 1984 were studied. After history taking and a full physical examination, blood was taken for full and differential white cell counts and for measuring C reactive protein concentrations. Other relevant serological, haematological, and bacteriological tests were performed as dictated by the history and presenting signs. Urine culture was performed in all children. Bacterial infection was diagnosed by culture of pathogenic bacteria from appropriate specimens—for example, three consecutive urine specimens or suprapubic aspirate. Appreciable consolidation on chest x ray films, particularly with lobar distribution, was also considered diagnostic.

Total and differential white cell counts were performed by standard laboratory techniques, a count of $\geq 10 \times 10^9/\text{l}$ with $\geq 60\%$ neutrophils being regarded as indicating bacterial infection. Assay of C reactive protein concentrations was performed on 250 μl of serum using ICL scientific rapid latex agglutination slide test in serial dilutions to give a positive result at a C reactive protein concentration $\geq 15 \text{ mg/l}$. Statistical analysis was by χ^2 test.

Of the 430 febrile children admitted, 129 were excluded from analysis, because of previous antibiotic treatment in 79 and acute otitis media (unconfirmed bacteriologically) in 50. The remaining 301 children were aged from 1 week to 14 years (median 1.25 years). Children under 2, who have the greatest risk of serious bacterial infection, were analysed separately.

The table shows the results of assay with C reactive protein concentrations compared with the results of white cell count for both infected and non-infected children, with their respective specificities and sensitivities. Hence a raised C reactive protein concentration at admission accurately predicted bacterial

Comparison of diagnostic accuracy (No (%) of children) of assay of C reactive protein concentrations and white cell count in febrile children

	C reactive protein concentrations	White cell count
	$\geq 15 \text{ mg/l}$	$\geq 10 \times 10^9/\text{l}$ $\geq 60\% \text{ polymorphs}$
Children with bacterial infection:		
All ages (n=121)	58 (48)	57 (47)
<2 years (n=75)	32 (43)	29 (39)
	$<15 \text{ mg/l}$	$<10 \times 10^9/\text{l}$ $<60\% \text{ polymorphs}$
Children with non-bacterial infection:		
All ages (n=180)	173 (96)	126 (70)
<2 years (n=113)	112 (99)	87 (77)

infection in 89% of children (97% aged <2 years) whereas a raised blood count predicted 51% (53% aged <2 years). These results are significant ($p<0.001$, all ages). The absence of bacterial infection was correctly predicted in 73% of children (72% <2 years) by normal C reactive protein concentrations and in 66% by a normal blood count (65% <2 years). These results are not significant.

Comment

This study confirms the lack of specificity and sensitivity inherent in total and differential white cell counts. Some studies have used a total count $\geq 15 \times 10^9/l$ as suggestive of bacterial infection.⁵ On this criterion, though specificity was increased (87% all ages; 63% <2 years), sensitivity was so reduced as to make the test worthless (32% all ages; 27% <2 years).

Overall, 61% of white cell counts (62% <2 years) agreed with the ultimate diagnosis, but this was greatly superseded by the accuracy of assays of C reactive protein concentrations (77% all ages; 77% <2 years) ($p<0.001$ both groups).

Paediatricians rely heavily on laboratory investigations in managing febrile children, especially younger children with few clinical signs. The specificity with which C reactive protein concentrations predicted bacterial sepsis enabled appropriate treatment to be started early and motivated staff to consider deep seated infection in the febrile child with minimal clinical signs.

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Inflammatory bowel disease: a common cause of bloody diarrhoea in visitors to the tropics

Bloody diarrhoea in visitors to, and those temporarily resident in, tropical countries is usually assumed to be infective in origin—bacillary or amoebic dysentery and, less commonly, colonic schistosomiasis.¹ Our investigation challenges this widely held concept.

Summary of 129 patients and geographical location and time of onset of bloody diarrhoea and other symptoms

Aetiology of colitis	No of cases	Mean age in years (range)	Sex		Ethnic group			Place of onset of bloody diarrhoea				No (%) with abdominal pain	No (%) with fever	Mean duration in days between onset of symptoms and diagnosis (range)
			M	F	Europid	Asian	African	Asia	Africa	Middle East	South America			
Acute infective:														
<i>Shigella</i> spp	25	31 (15-74)	13	12	25			12	10		3	12 (48)	17 (68)	10 (1-49)*
<i>Campylobacter</i> spp	12	33 (23-61)	7	5	11	1		7	3	1	1	8 (67)	9 (75)	6 (3-60)
<i>Salmonella</i> spp	1	52	1		1			1					1 (100)	3
<i>Entamoeba histolytica</i>	27	30 (15-62)	22	5	26	1		18	9			6 (22)	1 (4)	28 (5-84)†
Inflammatory bowel disease	32	37 (20-72)	22	10	25	7		8	14	6	4	9 (28)	4 (13)	84 (21-200)‡
Non-specific proctitis	12	29 (20-48)	8	4	9	2	1	6	5	1		2 (17)	4 (33)	20 (3-56)§
Colonic carcinoma	2	39 (23-55)	1	1	1	1		1	1			1 (50)	0	85 (21-150)
Cause not determined	18	34 (20-53)	11	7	15	3		6	10	2		9 (50)	9 (50)	14 (1-120)

* Excludes two patients with history of about three months; † Excludes five with history of four months to one year; ‡ Excludes 10 with history of one to 30 years; § Excludes four with history of four months to four years.

Patients, methods, and results

Case notes of all 129 inpatients (admitted consecutively) at the Hospital for Tropical Diseases, London, between 1978 and 1984, whose presenting complaint was bloody diarrhoea acquired in or immediately after return (within two weeks) from a tropical environment were abstracted (see table). All were United Kingdom residents; in most the onset of symptoms coincided with a first visit to a tropical country, and none had previously had bloody diarrhoea.

Investigations included fresh faecal microscopy and culture, rectal mucosal scrapes (under direct vision) and biopsy, endoscopy, large intestinal radiology (in a minority small intestinal also), and serum indirect fluorescence antibody tests² for invasive amoebiasis. Infective colitis was diagnosed on stool cultures, and amoebic colitis on the presence of haematophagous *Entamoeba histolytica* trophozoites or ulcerated rectal mucosa plus a positive indirect fluorescence antibody test result. After exclusion of these, inflammatory bowel disease was considered: non-specific ulcerative colitis was diagnosed on the basis of macroscopic rectal changes with characteristic histological or typical radiological abnormalities, or both, and Crohn's disease on typical histological or characteristic radiological appearances, or both. Macroscopic inflammation of rectal mucosa plus normal radiological appearances, and non-specific chronic inflammation (in rectal biopsy specimens) were categorised as non-specific proctitis. Colonic carcinoma was confirmed histologically.

The table summarises the results. Nine patients with ulcerative colitis and 12 with amoebic colitis had suffered severe weight loss. There were no deaths. Thirty of those with inflammatory bowel disease had ulcerative colitis and two Crohn's disease. Distribution of ulcerative colitis was total (14 cases), proctosigmoid (12), or distal (splenic flexure to rectum) (4); four patients with total colitis deteriorated despite sulphasalazine and corticosteroids and required colectomy. In those with Crohn's disease both ileum and colon were affected. In 23 patients *E histolytica* trophozoites were detected in fresh faecal samples or rectal mucosal scrapes: in seven the scrapes were positive after faecal smear and rectal biopsy had proved negative. The indirect fluorescence antibody result was positive in 15 out of 19 cases (79%) of amoebic colitis in whom it was estimated (in four in the absence of *E histolytica* trophozoites). Metronidazole (800 mg thrice daily for five days) and diloxanide furoate (500 mg thrice daily for 10 days) produced rapid recovery in all. *Shigella dysenteriae* (eight cases), *S flexneri* (12), *S sonnei* (three), and *S boydii* (two) were important pathogens; 19 patients received oral rehydration only, and six (with severe constitutional symptoms) an antibiotic also. Five with a campylobacter infection were also given an oral antibiotic (erythromycin). Four patients with non-specific proctitis responded to sulphasalazine and corticosteroid enemas. A 23 year old Indian woman had a carcinoma at the descending colon-sigmoid junction which was diagnosed by colonoscopy after negative radiological findings.

Comment

In many of these patients acute infective and amoebic colitis accounted for the bloody diarrhoea. Nevertheless, one quarter had inflammatory bowel disease, which seems to be uncommon in most populations indigenous to tropical countries,¹ presenting for the first time in relation to tropical exposure. A change in the colonic luminal microfloras is probably important. The underlying aetiology of inflammatory bowel disease might be infective,^{1,3} and exacerbations may be mediated by viruses and other pathogens.⁴ The agents responsible for travellers' diarrhoea differ geographically,^{1,5} which also may be relevant.

Clinically it is impossible to differentiate the three major causes of bloody diarrhoea with certainty. Some patients with inflammatory bowel disease had gone for very long periods without a firm diagnosis; most with acute infective colitis, however, had a short history. Differentiation between amoebic colitis and inflammatory bowel disease may be especially difficult. If amoebic colitis is undiagnosed and corticosteroids are administered or colectomy undertaken, or both, severe morbidity and even death may ensue.¹ Initial investigations were not always adequate to diagnose amoebic colitis; rectal scrapes and indirect fluorescence antibody tests were necessary.

Continuing diarrhoea in travellers after return to the United Kingdom is a