cases. Firor and Myers[3] pointed out one of the main reasons for acute appendicitis being so rare in the infant. Assuming luminal obstruction to be one of the major causes, they quoted the original observations by Treves that the appendix is characteristically funnel-shaped for the first 9 to 12 months of life. Thus blockage of the lumen by faecalith, oedema, or lymphoid hyperplasia is less likely to occur.

The presence of intestinal obstruction in this case led to surgical referral and intervention before perforation had occurred. Perforation increases the mortality rate to 85%: only four patients are recorded as surviving. Knowledge of fluid and electrolyte balance and techniques of neonatal anaesthesia have greatly improved recently and it is now less risky to operate on neonates. In cases of neonatal abdominal distension for which no definite diagnosis has been made, laparotomy should be considered at an early stage.

I thank Brigadier N G Kirby, Command Consultant in Surgery, BAOR, for his help in managing this patient and for his encouragement and advice during the preparation of this paper.

[1] Schaupp, W, Clausen, E G, and Ferrier, P K, *Surgery*, 1960, **48**, 805.
[2] Hardman, R P, and Bowerman, D, *American Journal of Diseases of Children*, 1963, **105**, 99.
[3] Firor, H V, and Myers, H A P, *Surgery*, 1964, **56**, 581.

British Military Hospital, Iserlohn, Germany
G L FOWKES, MB, FRCS, major, surgical specialist (present address: Inverell 2360, NSW, Australia)

Reduction in incidence of rash using polymer-free ampicillin

Rash is a common complication of ampicillin treatment with a particularly high incidence in certain diseases, including lymphatic leukaemia.[1] It has been suggested that two impurities of high molecular weight contribute to the rash. One is a penicilloylated protein and the care now taken to ensure that this impurity is removed during the manufacture of ampicillin has resulted in a significant reduction in rash incidence in man.[2] The second impurity is a polymer, whose role in the production of rash in man has not been investigated. In this study polymer-free ampicillin was given to patients suffering from lymphoproliferative disease with infective complications. The incidence of exanthemata was recorded and supplementary information obtained by skin testing.

Patients, methods, and results

Of the 10 patients studied, eight had chronic lymphatic leukaemia and two had lymphosarcoma affecting the spleen and marrow but with apparently normal peripheral blood. The indication for treatment was respiratory infection in seven patients and urinary tract infection in three. A 10-day course of polymer-free ampicillin was given, five patients receiving 2 g/day and the remainder 1 g/day. Four weeks after starting ampicillin skin tests were performed and repeated after 12 weeks in patients who developed a positive reaction or rash. Skin testing was carried out in three stages, starting with a preliminary prick test with minor determinants. Negative reactors were then given 0·01 ml intradermally of polymer-free ampicillin (10^{-2} mol/l) and ampicillin polymer (10^{-6} mol/l). Patients who reacted negatively were given 0·1 ml intradermally of polymer-free ampicillin (10^{-1} mol/l) and ampicillin polymer (10^{4} μg/l). Reactions were read at 20 minutes, 48 hours, and 72 hours. Biopsy specimens from those with positive skin test reactions and rashes were obtained when possible.

The results are shown in the table. One patient developed a maculopapular rash which was first noticed three days after stopping ampicillin. Microscopic examination of her skin showed non-specific inflammatory change, and she did not have a positive skin test reaction. Three patients were positive on skin testing to high-dose ampicillin polymer at four weeks. Biopsy in one case showed no evidence of hypersensitivity. In all three patients this phenomenon had disappeared by 12 weeks.

Comment

Commercial ampicillin is now virtually free of penicilloylated protein but still contains polymer. Our study was therefore an attempt to elucidate the role of polymer in the production of ampicillin rash. In a previously reported series 10 out of 12 patients with lymphatic leukaemia receiving ampicillin developed a rash.[1] In the present study only one patient out of 10 with similar disease given polymer-free ampicillin developed a rash. Although half our patients received a smaller ampicillin dose than those of Cameron and Richmond,[1] there is no evidence that the amount of ampicillin and the degree of rash are related.[3] It is unlikely that concurrent administration of prednisolone suppressed the reaction as corticosteroids have been found to be ineffective in preventing ampicillin exanthemata.[4]

The positive reactions on skin tests observed in three patients after four weeks were transient and had disappeared by three months. In their time relations and evanescence these positive reactions resembled the Jones-Mote reaction[5] but were histologically different. It is interesting that all three positive skin reactions were due to ampicillin polymer, but this does not clarify the underlying mechanism of their production. Clearly there were too few patients for firm conclusions to be drawn. The results do give clinical support for the efforts made by manufacturers to ensure the lowest possible level of polymeric materials in antibiotics.

We are grateful to Beecham Research Laboratories for the supply of polymer-free ampicillin.

[1] Cameron, S J, and Richmond, J, *Scottish Medical Journal*, 1971, **16**, 425.
[2] Knudsen, E T, Dewdney, J M, and Trafford, J A P, *British Medical Journal*, 1970, **1**, 469.
[3] Weuta, H Von, *Arzneimittel-Forschung*, 1972, **22**, 1300.
[4] Pullen, H, Wright, N, and Murdoch, J McC, *Lancet*, 1967, **2**, 1176.
[5] Jones, T D, and Mote, J R, *New England Journal of Medicine*, 1934, **210**, 120.

Department of Haematology, Royal Infirmary, Edinburgh
A C PARKER, BSC, MRCP, lecturer

University of Sheffield, Royal Hospital, Sheffield S1 3SR
J RICHMOND, MD, FRCP, professor, Academic Division of Medicine

Details of patients receiving polymer-free ampicillin

Case No	Age (years)	Sex	White blood count (×10⁹/l)	Absolute lymphocyte count (×10⁹/l)	Ampicillin (g/day)	Concomitant therapy	Skin test result	Rash
1	62	M	31·6	29	1	Chlorambucil 4 mg, allopurinol 150 mg		—
2	61	F	15·8	10·2	1			—
3	80	F	170	160	1		Positive at 4 weeks to high-dose ampicillin polymer	—
4	88	M	40·9	37·5	2	Prednisolone 10 mg		—
5	66	M	72	67	2			—
6	72	M	91	83	2	Chlorambucil 2 mg	Positive at 4 weeks to high-dose ampicillin polymer	—
7	49	M	223	210	1	Cyclophosphamide 100 mg, prednisolone 10 mg		–
8	61	F	83	80	1	Chlorambucil 8 mg, prednisolone 15 mg	Positive at 4 weeks to high-dose ampicillin polymer	–
9	66	F	5·1	2	2			–
10	66	F	5·1	2·2	2	Prednisolone 10 mg		+

Conversion: SI to traditional units—White cell and lymphocyte counts: 1 × 10⁹/l = 1000/mm³.