

emphasise another potential danger of additives in parenteral solutions and to underline the desirability of using prepared solutions of known concentration.¹

Full details of this patient's condition may be obtained from GG.

¹ Ellis, B W, *et al*, *British Medical Journal*, 1976, **1**, 1388.

² Kay, R G, *et al*, *Annals of Surgery*, 1976, **183**, 331.

³ Polson, C J, and Tattersall, R N, *Clinical Toxicology*. London, Pitman, 1969.

⁴ Gallery, E M, Blomfield, J, and Dixon, S R, *British Medical Journal*, 1972, **4**, 331.

⁵ Spencer, H, *et al*, in *Zinc Metabolism*, ed A S Prasad. Springfield, Thomas, 1966.

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Reiter's disease after *Salmonella typhimurium* enteritis

I report possibly the first case of Reiter's disease after *Salmonella typhimurium* enteritis.

Case report

A 12-year-old girl was admitted to hospital in February 1976 with an acute polyarthritides. Two weeks previously she had developed frequent loose bloody stools, for which she had been given a kaolin and neomycin mixture, the diarrhoea settling after one week. She then remained well until three days before admission, when her mother noticed that her right eye looked inflamed. She also had terminal burning on micturition but no frequency. Two days before admission she developed painful swelling of the left knee, right elbow, and right wrist.

She did not look ill but her temperature was 38.8°C. She had bilateral conjunctivitis and mild pharyngitis. The left knee was hot, red, and swollen with an obvious effusion, and pain limited flexion to 40°. The right wrist and elbow were also hot and swollen with limited movement. There was no rash or lymphadenopathy, and the urethral orifice did not look inflamed. She had a tachycardia of 130/min and a moderate midsystolic ejection murmur. Haemoglobin was 14.0 g/dl; white cell count $10.9 \times 10^9/l$ ($10\ 900/mm^3$), 82% neutrophils; and erythrocyte sedimentation rate 50 mm in the first hour. Stool culture grew *S typhimurium*, phage type U129-014. Aspirate from the left knee joint was cloudy, contained polymorphs but no organisms, was sterile on culture, and had a protein content of 51 g/l. Radiographs of affected joints, feet, and sacroiliac joints were normal. Antistreptolysin titre, tests for rheumatoid and antinuclear factors, gonococcal complement fixation test, Wassermann reaction, and tine test were negative. Throat swab and urine and blood cultures were sterile. Chest x-ray appearances and electrocardiogram were normal. HLA typing yielded A2, AW19, B7, and B27.

She was treated with bed rest and small doses of aspirin, and when the stool culture report was obtained ampicillin was started. The conjunctivitis and dysuria cleared rapidly but she developed tenderness of the left heel and inflammation of the left ankle and right knee joints. During the next 10 days her joint symptoms fluctuated and over the next month gradually settled. One month after admission fever, abdominal pain, and diarrhoea developed and *S typhimurium* was again isolated from her stools, but her joint symptoms did not relapse.

One year after the initial illness she was well and fully mobile and her stools were free of salmonellae. She had some residual synovial thickening in the right knee joint.

Comments

In 1916 Hans Reiter described a soldier who developed the triad of conjunctivitis, urethritis, and polyarthritides after an attack of bloody diarrhoea. Since then the disease has been described in many adults after shigella dysentery and also after non-gonococcal urethritis. A few cases have occurred in children, mostly after diarrhoeal illnesses.¹ In salmonellosis a bacterial arthritis may occur, the organism usually

being cultured from the joint fluid.² In addition a non-bacterial reactive arthritis has been described^{3 4} and shown to be associated with HLA-B27, which is commonly found in Reiter's disease.⁵ Vartiainen and Hurri³ described 12 patients in whom polyarthritides followed infection with *S typhimurium*, one of them also having conjunctivitis and iritis. Berglöf⁴ described a man with *S typhimurium* infection who developed polyarthritides, conjunctivitis, urethritis, and prostatitis and had x-ray changes in the sacroiliac joints. Neither paper mentioned Reiter's disease. So far as I know there have been no published case reports of Reiter's disease with salmonella infections, but in both my case and Berglöf's the association of diarrhoea with polyarthritides, conjunctivitis, and urethritis must warrant this title.

I thank Dr H V L Finlay for permission to report this case and for advice and encouragement.

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² David, J R, and Black, R L, *Medicine*, 1960, **39**, 385.

³ Vartiainen, J, and Hurri, L, *Acta Medica Scandinavica*, 1964, **175**, 771.

⁴ Berglöf, F-E, *Acta Rheumatologica Scandinavica*, 1963, **3**, 141.

⁵ Aho, K, *et al*, *Annals of the Rheumatic Diseases*, 1975, **34**, suppl No 1, p 29.

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Tetrabenazine in Sydenham's chorea

Tetrabenazine is a reserpine-like compound which has an established place in the treatment of Huntington's chorea.^{1 2} We report two cases of rheumatic chorea in which involuntary movements were dramatically improved by this drug.

Case reports

Case 1—A 10-year-old girl was admitted to hospital with a five-month history of difficulty in walking, slurred speech, and inability to dress herself. Her speech was severely dysarthric, and there were widespread coarse choreic movements of all limbs, which made it impossible for her to stand or to use her arms for any purposive movement. She was fearful but there were no signs of intellectual impairment. The cardiovascular system was normal and full blood count, erythrocyte sedimentation rate, measurement of electrolyte concentrations, liver function tests, antistreptolysin O titre, and chest radiography showed nothing abnormal. Treatment was begun with tetrabenazine 25 mg three times daily. Within 24 hours there was a dramatic improvement in speech and involuntary movements and after a few days she could walk and dress herself. Depression or other unwanted effects were not observed. The movements almost completely resolved after about two weeks and the medication was discontinued one month later. When last seen three years after her illness she was maintaining good health but small choreic movements were still evident.

Case 2—A 12-year-old boy was admitted to hospital with a three-week history of stiff and painful joints in the arms and legs. This resolved in two and a half weeks, but was replaced by severe, widespread, coarse choreic movements in all limbs. Feeding was impossible and he could barely walk with the aid of one person. A faint cardiac systolic murmur was detected at the apex. The anti-streptolysin O titre was raised at 600 IU/ml. Full blood count was normal and erythrocyte sedimentation rate was 44 mm in the first hour. Chest radiography and electrocardiogram were both normal. Initial treatment consisted of penicillin and diazepam which had little effect on the chorea. After one week diazepam was stopped and tetrabenazine 25 mg twice daily was given. This resulted in a dramatic lessening of involuntary movements within 24 hours, and after one week's treatment they were minimal and he could walk and feed himself unaided. Tetrabenazine was discontinued after three months. Depression was not observed and he was free from chorea until four months after discharge when he had a further episode of joint pain and chorea which again responded to tetrabenazine.

Comment

The important features shown in these two cases were the rapidity and specificity of the action of tetrabenazine. The movements were

lessened by some 80% within one day without any discernible adverse effects. Such an effect has received little attention. Dalby³ describes one case of rheumatic chorea which responded well and Swash *et al*² make passing mention of the effectiveness of this treatment in a case of recurrent rheumatic chorea. Some have expressed reservations about tetrabenazine in Huntington's chorea,⁴ suggesting that the risks of depression and drug-induced Parkinsonism outweigh the advantages of its anti-choreic action. This viewpoint has not been universally accepted.^{1,2,5} Such unwanted effects would be more likely to develop during long-term treatment, but in Sydenham's chorea the movements seldom last in a severe form beyond three months, so side effects would be expected infrequently.

The authors would like to express their thanks to Dr L S Illis, Wessex Neurological Centre, Southampton, for permission to report the data in Case 1.

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² Swash, M, *et al*, *Journal of Neurology, Neurosurgery and Psychiatry*, 1972, **35**, 186.
³ Dalby, M A, *British Medical Journal*, 1969, **2**, 422.
⁴ Huang, C Y, *et al*, *Medical Journal of Australia*, 1976, **1**, 583.
⁵ Thavasothy, R, *British Medical Journal*, 1970, **2**, 237.

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Familial autoimmune haemolytic anaemia

Familial autoimmune haemolytic anaemia (AIHA) has rarely been reported in man.¹⁻³ We describe two sisters who developed the disorder at the same age; one responded partially to low-dose prednisolone, while the other required splenectomy. HLA typing of these patients and of three siblings provided supportive evidence for an association between HLA-1 and 8 and AIHA.⁴

Present series

Case 1—A 66-year-old woman of previous good health presented in 1970 with a four-month history of dyspnoea, palpitations, peripheral oedema, and increasing weakness. She was icteric and pale with an enlarged liver and spleen (3 and 5 cm respectively below the costal margin). Haemoglobin was 6.4 g/dl; WBC $4 \times 10^9/l$ (4000/mm³); and reticulocyte count 35%. The peripheral blood film contained spherocytes, and a marrow aspirate showed normoblastic hyperplasia. Serum bilirubin concentration was 52 $\mu\text{mol/l}$ (3 mg/100 ml) (normal 2-17 $\mu\text{mol/l}$; 0.1-1.0 mg/100 ml), and, though result of the antinuclear factor (ANF) test was positive, LE cell preparations were negative. Autologous erythrocyte survival was 11.5 days (normal 25-35), with a spleen to liver ratio of 4:1. The direct antiglobulin test (DAGT) result was positive (table). There were no intracorpuscular red-cell abnormalities, and no evidence of intravascular haemolysis was found. By mistake she was given only 4 mg prednisolone daily instead of the usual 40-60 mg but made a slow partial recovery, which was probably spontaneous. In view of her clinical improvement together with a fall in the DAGT titre

and disappearance of free serum antibodies it was decided to continue that dosage of prednisolone indefinitely. She remained clinically well despite an 11.5% reticulocytosis and a DAGT titre of 1/40. The most recent haemoglobin was 13.5 g/dl and the serum bilirubin 35 $\mu\text{mol/l}$ (2 mg/100 ml).

Case 2—This patient, a 64-year-old full sister of case 1, presented in 1975 with a two-year history of increasing dyspnoea and fatigue. She was pale and icteric and her spleen and liver were enlarged 8 and 3 cm respectively below the costal margin. Haemoglobin was 6.1 g/dl; WBC $4.9 \times 10^9/l$ (4900/mm³); and reticulocyte count 16.8%. A peripheral blood film contained occasional spherocytes, and a marrow aspirate showed normoblastic hyperplasia. Bilirubin concentration was 48 $\mu\text{mol/l}$ (2.8 mg/100 ml), ANF was absent, and similar investigations to those in case 1 showed no evidence of intracorpuscular abnormality or of intravascular haemolysis. The DAGT result was positive (table). Autologous erythrocyte survival was 14.6 days, with a spleen to liver ratio of 2.8:1. She was begun on high-dose steroids (60 mg prednisolone daily), her clinical state initially improving, with a fall in the DAGT titre to 1/80. The development of diabetes on a steroid dosage required to control haemolysis necessitated splenectomy. Steroids were then stopped completely. When last seen she was clinically well with a normal haemoglobin concentration and reticulocyte count, but the DAGT titre remained positive at 1/400 (anti-IgG) and 1/64 (anti-complement).

Family study—The results of antiglobulin testing, red-cell genotyping and HLA typing in cases 1 and 2 and of three entirely normal and apparently full sisters (cases 3-5) are shown in the table. Both sisters with AIHA had HLA antigens 1, 8, and 7.

Comment

Experiments on New Zealand black mice have yielded strong evidence that AIHA can be hereditary.⁵ Though it is now recognised that autoimmune disease in man is often familial—for example, pernicious anaemia and thyroid disease—the paucity of reports of familial AIHA implies that its occurrence is likely to be coincidental. The finding of the sharing of common HLA antigens (1 and 8), shown to be increased in incidence in cases of AIHA,⁴ however argues for a genetic susceptibility to develop this disorder. Furthermore, the two oldest normal siblings (cases 3 and 4) did not possess such HLA antigens. Though the third normal sibling (case 5) had HLA antigens 1 and 8, she had not reached the age at which cases 1 and 2 presented.

We hope that this report will stimulate further such documentation.

We thank Dr S H Davies and Professor R H Girdwood for permission to report on these patients under their care; Dr Jean Whitaker for co-operation in providing blood specimens; Mr George Willis and technical colleagues for serological testing; and Mrs E Scott for typing the report.

- ¹ Seip, M, *et al*, *Acta Paediatrica Scandinavica*, 1969, **58**, 275.
² Pollock, J G, *et al*, *British Journal of Haematology*, 1970, **18**, 171.
³ Roth, P, *et al*, *Schweizerische medizinische Wochenschrift*, 1975, **105**, 1584.
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Red-cell typing, leucocyte typing, and serological findings in five sisters

Case No	Age in years	ABO and Rh types	HLA type	Antiglobulin test results at presentation	
				Direct*	Indirect
1	66	O; CCD \bar{e} (R ₁ R ₁)	A1, 28; B7, 8	1/320; complement only	"Non-specific" cold (4°C) autoagglutinin and "warm" (37°C) autoantibody (no specificity determined)
2	64	B; C \bar{D} \bar{E} \bar{e} (R ₁ r)	A1, 3; B7, 8	1/320; complement + IgG	Warm (37°C) autoantibodies of anti- \bar{e} plus unidentified specificity
3	74	O; CCD \bar{e} (R ₁ R ₁)	A2, 28; B12, 17	Negative	Negative
4	68	B; C \bar{D} \bar{E} \bar{e} (R ₁ R ₂)	A2, 28; B12	Negative	Negative
5	62	B; C \bar{D} \bar{E} \bar{e} (R ₁ R ₂)	A1, 28; B8	Negative	Negative

*Direct test performed with broad-spectrum reagent; when result positive, then serum also tested against monospecific anti-IgA, IgM, and IgG and C3.