are now assessing its use as a screening test in a large population of hypertensive subjects.

We gratefully acknowledge the co-operation of Dr A M Joekes and Dr F D Thomson of St Paul's Hospital for allowing us to study four of these patients.

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(*Accepted 21 October 1977*)

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Contact dermatitis attributed to ethylenediamine

Patients with allergic dermatitis from ethylenediamine form a group with the potential of developing severe generalised rashes from certain systemically administered drugs such as aminophylline.

Patients, methods, and results

A total of 159 consecutive patients with a clinical diagnosis of contact dermatitis were patch-tested with 21 common allergens obtained from Trolab, Denmark. The allergens were applied for 48 hours using the A1-test and inspected at 48 and 96 hours. Some 106 patients had one or more positive patch tests; 33 patients were sensitive to nickel; ethylenediamine was the second commonest allergen identified. The clinical features of the 20 patients sensitive to ethylenediamine are summarised in the table.

Comment

The group of patients sensitive to ethylenediamine had a long history of dermatitis before referral for investigation. The sensitivity to ethylenediamine was unexpected; therefore the inclusion of this substance in a patch test series is justified. Exposure to ethylenediamine may occur in the industrial preparation of dyes, rubber accelerators, fungicides, synthetic waxes, resins, insecticides, and asphalt wetting agents. Another occupational group where sensitisation has been reported is pharmacists and nurses who handle aminophylline suppositories. Aminophylline is a combination of theophylline and ethylenediamine. Since none of the patients had industrial exposure to ethylenediamine we suggest that they represent a further group who suffer dermatitis from applied medicaments.

The investigation of allergic contact dermatitis in such patients is difficult. Patients frequently have incomplete recall of applied preparations if several have been used in the management of a chronic condition. Patients rarely distinguish between cream and ointment bases and this information cannot always be obtained from their medical records. Patients use indiscriminately topical medicaments obtained from relatives or friends. Little information is volunteered by the manufacturers of cosmetics as to the contents of their products. The data sheets of medicaments do not identify the full composition of the product.

Patch testing on normal skin using a proprietary preparation containing corticosteroid can give a false-negative result. This has been studied by Epstein and Maibach,[2] who recommended ethylenediamine 1% in petrolatum as the test substance. Provost and Jillson[3] studied a similar group of American patients in whom the use of Mycolog cream, in which ethylenediamine is a stabiliser, was shown to be a source of the allergen. Tri-Adcortyl cream is the British equivalent of Mycolog cream. It contains triamcinolone acetonide, neomycin, gramicidin, nystatin, parabens, and ethylenediamine. Neomycin and parabens are well known sensitisers. Tri-Adcortyl ointment does not contain ethylenediamine.

All our 20 patients sensitive to ethylenediamine had used Tri-Adcortyl cream although four patients did not remember. The

Clinical features of patients sensitive to ethylenediamine

Case No	Age (years)	Sex	Occupation	Duration of exacerbation (months)	Site or type of dermatitis	Duration of previous skin disease (years)	No of topical prepns used	Systemic drugs	Personal atopic history	Other sensitivities
1	9	F	Schoolgirl	12	Feet	1	>4	Nil	Nil	Mercaptobenzthiazole, Thiuram-mix, Cobalt, Neomycin
2	15	F	Schoolgirl	4	Hands, feet	1	>4	Nil	Nil	Dichromate
3	19	F	Receptionist	½	Hands	Lifelong	>4	Nil	Hay fever	Nickel
4	19	F	Office work	9	Hands	3/4	>4	Trimeprazine tartrate	Atopic aczema	Nickel, Cobalt
5	21	F	Housewife	2	Generalised	Lifelong	>4	Chlorpheniramine maleate	Asthma, atopic eczema	Nickel
6	33	F	Housewife	2	Hands	2	>4	Nil	Nil	Nil
7	43	F	Housewife	4	Hands	17	>4	Nil	Nil	Thiuram-mix
8	54	F	Housewife	6	Feet, hands	2	3	Nil	Nil	Nickel, Thiuram-mix
9	56	F	Fishworker	3	Hands	½	3	Chlorpheniramine maleate	Nil	Nickel, Thiuram-mix
10	61	F	Housewife	2	Face, hands	3	3	Trimeprazine tartrate	Atopic eczema	Neomycin
11	72	F	Housewife	1½	Pruritus vulvae	1½	>4	Hydroxyzine HCl	Nil	Caine-mix, Wool-alcohols
12	10	M	Schoolboy	½	Feet, arms	1/6	3	Nil	Hay fever	Neomycin
13	34	M	Not recorded	>12	Axillae	>3	2	Nil	Nil	Deodorant
14	39	M	Oil-related industry	3	Thighs	3½	>4	Trimeprazine tartrate	Nil	Balsam of Peru
15	42	M	Engineer	>12	Pruritus ani	6	>4	Nil	Nil	Soframycin, Neomycin, Nickel
16	42	M	Chemist	9	Pruritus ani	2	>4	Nil	Nil	Balsam of Peru
17	53	M	Hairdresser	4	Seborrhoeic dermatitis	1	2	Methyldopa, cyclopenthiazide, promethazine HCl	Nil	Nickel
18	56	M	Fisherman	½	Feet	1/6	2	Nil	Nil	Nil
19	66	M	Retired seaman	2	Stasis dermatitis	15	Unknown	Hydroxyzine	Nil	Neomycin, Nystatin cream
20	74	M	Retired railway employee	½	Seborrhoeic dermatitis	2	2	Orciprenoline Sulphate	Nil	Neomycin

patients who had used only two topical preparations recalled an initial response and then a subsequent deterioration with generalisation of itch when using this preparation. This is circumstantial evidence that the continued use of Tri-Adcortyl cream may induce the sensitivity. Provost and Jillson reported two patients, sensitive to ethylenediamine, who developed a widespread dermatitis after systemically administered aminophylline. Exfoliative dermatitis was the outcome in another patient described by Petrozzi and Shore.[4] Several antihistamines are related to ethylenediamine and the use of these should be restricted. In particular, Fisher[1] suggested that tripelennamine hydrochloride tablets or topical ophthalmic preparations with antazoline phosphate should be avoided. Hydroxyzine hydrochloride and mepyramine maleate are also considered to be potential hazards. Calnan[5] has reported one patient with allergy to ethylenediamine, piperazine, and hydroxyzine.

Many topical preparations contain potential sensitising agents. If manufacturers listed the composition of their products more completely, the investigation of unresponsive dermatoses would be simplified. The sensitivity to ethylenediamine has been described because of its importance.

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(*Accepted 26 October 1977*)

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Thalassaemia minor, iron overload, and hepatoma

Although haemochromatosis has been described in association with several chronic haemolytic anaemias, such patients have usually received many blood transfusions. Iron overload has been rarely reported in thalassaemia minor in the absence of exogenous iron.[1] Hepatocellular carcinoma occurs in some 8-22% of patients with primary haemochromatosis[2] but is rare in secondary iron overload. This report describes a patient with thalassaemia minor who developed iron overload and died of a hepatoma.

Case report

In January 1975 a 74-year-old retired docker was admitted with an acute exacerbation of his longstanding chronic bronchitis. Eighteen years previously he had had a Polya gastrectomy for peptic ulcer. At no time had he received oral iron or blood transfusion and he was not a heavy drinker. A distant ancestor was French. He was grey, pale, and weighed 46 kg. A smooth non-tender liver was palpable two fingers below the costal margin. The haemoglobin (Hb) concentration was 6 g/dl, mean corpuscular volume (MCV) 87 fl (87 μm^3), and mean corpuscular haemoglobin (MCH) 26 pg. The blood film showed moderate anisocytosis, poikilocytosis, and hypochromia with many schistocytes and target cells. HbA_2 was 4% and HbF 4·2%. Serum folate was 0·6 μg/l (0·6 ng/ml) and serum vitamin B_{12} 110 ng/l (110 pg/ml). The bone marrow showed megaloblastic erythropoiesis. The anaemia was attributed to nutritional deficiency related to partial gastrectomy and thalassaemia minor. The serum iron concentration was 37 μmol/l (207 μg/100 ml) and total iron binding capacity 40 μmol/l (225 μg/100 ml). Liver biopsy showed normal architecture with severe iron deposition (grade IV). Treatment included transfusion of six units of blood, parenteral B_{12}, and folic acid.

Three of the patients' four children and six grandchildren had thalassaemia minor with microcytosis and raised HbA_2.

On his second admission in November 1976 he presented with continuous sharp right upper quadrant pain for the previous month. He weighed 42 kg and was icteric. The liver had enlarged into the right lower quadrant and was hard, knobbly, and tender. The haemoglobin concentration was 12·6 g/dl, MCV 61 fl, MCH 22 pg, and MCHC 34 g/dl (34%). The serum iron concentration was 19 μmol/l (106 μg/100 ml), folate 5·4 μg/l, and B_{12} 1320 ng/l. The ferritin concentration was very high at 3593 μg/l. The concentration of total bilirubin was 40 μmol/l (2·3 mg/100 ml), direct bilirubin 19 μmol/l, aspartate transaminase 69 U/l, and alkaline phosphatase 271 U/l. The prothrombin ratio was 1·2. Hepatitis B antigen was not detected. Alpha-fetoprotein test was positive. Liver scan showed multiple filling defects. Liver biopsy showed both severe iron overload (grade IV) in Küpffer and parenchymal cells, without cirrhosis and hepatocellular carcinoma. The liver iron concentration was 9·83 μmol (550 μg)/100 mg dry weight (mean normal liver iron 1·4 μmol (78 μg)/100 mg) and hepatoma iron 0·9 μmol (50 μg)/100 mg. The patient died with bronchopneumonia three weeks later.

At necropsy the liver weighed 3050 g; the parenchyma was largely replaced by nodules of tumour up to 15 cm diameter, some of which were necrotic. There was a dramatic blue coloration of parenchyma with potassium ferrocyanide. Microscopy confirmed the biopsy findings. Hepatoma had invaded the hepatic vein and become deposited in lung parenchyma. Tumour emboli were found in the pulmonary artery and left ventricular wall. Large amounts of iron were present in the pancreas, spleen, and marrow. The bone marrow was widened and contained red marrow throughout its length.

Discussion

Excessive iron storage has rarely been described in thalassaemia minor. Williams and Siemsen[1] reported a patient with thalassaemia minor who developed haemochromatosis in the absence of any exogenous iron, as occured in the present case. Inappropriate absorption of iron has not been shown in thalassaemia minor[3] and a study of iron metabolism of the descendants of the present case may help to define the aetiology of the overload.

Hepatoma is rare in iron overload secondary to chronic anaemia.[4] Barry *et al*[5] reported a patient with hereditary spherocytosis who had iron overload without cirrhosis and developed a hepatoma. The present case is unique because of the development of iron overload without exogenous iron or transfusions; the absence of fibrosis in a heavily iron-loaded liver; and the association between thalassaemia minor, iron overload, and hepatoma.

We thank Dr A L Turnbull for his advice, Dr G Laird for permission to report his patient, Dr D Pollock and Dr A Casswell for their help, and Miss Myra Barnett of St Bartholomew's Hospital for measuring the ferritin and liver iron concentrations.

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(*Accepted 25 October 1977*)

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