ance of tinea. The effect of such focal immunosuppression on experimental infections deserves study. Thus, the use of topical nitrogen mustard should greatly facilitate the induction of model infections with fungi as well as with bacteria and viruses.

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Hepatic Injury in Dermatitis Herpetiformis

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Abstract. Liver function tests were performed in 60 patients with dermatitis herpetiformis. Abnormalities of bilirubin or elevated liver enzyme levels were found in 17% of the patients. 13% had abnormal liver enzymes or elevated bilirubin levels not due to haemolysis. In 8% of patients bilirubin levels were elevated as a result of dapsone-induced haemolysis. The incidence of liver function abnormalities was higher (19%) in those on a normal diet than those on a gluten-free diet (9%). The abnormalities were not associated with the presence of immune complexes, anti-mitochondrial or anti-smooth muscle antibodies.

Key words: Dermatitis herpetiformis; Dapsone; Gluten-sensitive enteropathy; Coeliac disease; Liver disease

Both adult and childhood variants of coeliac disease have been shown to be associated with hepatic damage (4, 6). These two studies showed an improvement of abnormal values in liver function tests with a gluten-free diet (GFD). Dermatitis Herpetiformis (DH) is known to be associated with gluten-sensitive enteropathy (1, 3). There are rarely overt symptoms or signs of malabsorption and the intestinal lesion is often milder than in coeliac disease. The mechanism of liver damage in coeliac disease is unknown and there is uncertainty as to its relation, if any, to the severity of the intestinal lesion.

In this study we have investigated patients with DH for evidence of liver damage, and compared the results of those taking a gluten-free diet with those on a normal diet.

There has been a report of cholestatic jaundice in patients taking dapsone and so we compared those patients receiving dapsone with those who were not (11).

PATIENTS AND METHODS

60 consecutive patients attending a dermatitis herpetiformis clinic were studied. The diagnosis had been made on clinical grounds, response to dapsone, and the demonstration of IgA in the uninvolved skin. 34 were on a gluten-free diet, but 13 of these still required dapsone or an alternative drug, 1 was taking sulphapyridine and 2 sulphamethoxypyridazine. 26 were on a normal diet, 20 took dapsone and 1 sulphamethoxypyridaxine, 5 took no medication—4 because the rash was trivial and one was newly diagnosed.

The following liver function tests were performed: estimations of bilirubin, albumen and activities of alkaline phosphatase, aspartate transaminase (AST) and gamma glutamyl transpeptidase (GGTP).

Reticulocyte counts and, when indicated, haptoglobin levels were estimated to assess the extent of haemolysis.

Immune complexes were estimated by the C_{1q} binding method, and non-organ-specific antibodies screened for in those with abnormal liver function tests.

Jejunal biopsies were obtained by a Crosby capsule and morphology and lymphocytic infiltration assessed in those patients who agreed to this investigation.

Table I. *Details of patients with abnormalities in liver function tests*

Patient	Sex	Diet	Drugs	Other diseases	Liver function tests*		
					Bilirubin	AST	GGTP
Normal values					<17 μmolG/l	30 μ/l	<25 F <40 M
1	F	Gluten-free diet	Azathioprine. Prednisone	Chronic active hepatitis	51 (13)	17	32 (27)
2	F		Trifluoperazine. Maprotiline	Thyrotoxicosis. Depression	5	11	42 (27)
3	M		Dapsone	Dapsone-induced haemolytic anaemia	36 (31)	14 (34)	10
4	F	Normal diet	Dapsone	Dapsone-induced haemolytic anaemia	25 (30)	36 (16)	15
5	F		Dapsone	Dapsone-induced haemolytic anemia	27 (38)	20	14
6	F		Sulphamethoxy-pyridazine	Depression	4	18	29 (25)
7	M		Propranolol. Dapsone. Carbimazole	Thyrotoxicosis Ischaemic heart disease	7	9	63 (35)
8	M		Dapsone	Dapsone-induced haemolytic anaemia	35 (30)	18	39
9	F		Dapsone. Propranalol	Thyrotoxicosis	15 (32)	13	36 (42)
10	M				20 (18)	24	20

* Values on repeat in parentheses.

RESULTS

Liver function test abnormalities were found in 10 patients (17%); 5 had more than one abnormality (Table I) and 5 patients had evidence of dapsone-induced haemolysis.

The incidence of abnormal liver function tests was higher (19%) in those on a normal diet than in those on a GFD (9%) (Table II). This difference was independent of dapsone therapy.

Patients taking a GFD

Three patients (9%) had abnormalities of liver function tests. One of these had elevation of both AST and bilirubin. She had chronic active hepatitis proven by histological examination of the liver and positive anti-smooth muscle antibody. She was receiving treatment with azathioprine and prednisone for this. Another patient had a persistently elevated GGTP. She occasionally took gluten and was taking trifluorperazine. The third patient still required dapsone, and had elevated bilirubin and AST. He had a dapsone-induced haemolytic anaemia demonstrated by elevated reticulocyte count and depressed haptoglobin levels. This probably accounts for the elevated bilirubin level.

The latter 2 patients did not have anti-smooth muscle antibody. None had immune complexes, anti-mitochondrial antibody or anti-reticulin antibody.

Patients on a normal diet

Seven patients (27%) had abnormal liver function tests. 5 had elevated bilirubin levels, and in 4 of these this could be attributed to a dapsone-induced haemolytic anaemia. 5 patients (19%) had abnormal liver enzymes, one had an elevation of AST, and in 3, elevations of GGTP were present.

None of these patients had anti-smooth muscle, anti-mitochondrial antibody, or immune complexes. 1 patient had anti-reticulin antibody.

The incidence of abnormal liver enzymes was higher in patients on a normal diet than those on GFD, whether on dapsone or not (Table II), and hence could not be attributed to dapsone therapy.

The effect of dapsone on liver function tests

The effect of dapsone on liver function tests is shown in Table II. The incidence of abnormal liver function tests was 20% in those patients taking dapsone and 11% in those not requiring it. 5 (17%)

Reticulocyte count	Haptoglobins if haemolysis suspected	Jejunal morphology + lymphocyte count
<2.0%	0.5–2.0 g/l	Lymphocyte count <250 per 1 000 epithelial cells
0.7		Flat. Lymphocyte count: 838
1.4		Convolutions. Lymphocyte count: 490
4.5	<0.5	
2.0	<0.5	Flat. Lymphocyte count: 490
3.8	<0.2	
0.9		
1.3		
3.1	<0.5	Flat with cubical epithelium. Lymphocyte count: 332
4.5	0	Leaves + convolutions. Lymphocyte count: 340
0.8		Leaves + convolutions. Lymphocyte count: 340
0.8		Leaves + convuolutions. Lymphocyte count: 390

of those patients taking dapsone had haemolytic anaemia causing elevated bilirubin levels. 4 patients taking dapsone had elevations of liver enzymes, 2 AST and 2 GGTP (Table I).

DISCUSSION

This study demonstrates that hepatic injury does occur in patients with dermatitis herpetiformis. The total incidence (17%) was lower than in adult coeliac disease (39%) (4), and in untreated childhood coeliac disease (30-60%) (6). However, 57% of the DH patients were on a GFD and this is known to lead to an improvement in abnormal liver function tests in coeliac disease (4, 6). DH patients on a normal diet have a 19% incidence of hepatic injury, while in those on a GFD the incidence is 9%; this difference is not related to dapsone therapy. Thus although the incidence in DH is lower than in coeliac disease, there is still a marked difference between those on a GFD and those on a normal diet. This suggests that the hepatic injury is linked to the gluten-sensitive enteropathy.

The lower incidence of liver abnormalities in patients on a GFD and their improvement with a GFD suggests that the hepatic injury is a direct result of a damaged, hyperpermeable gut mucosa, and this is supported by similar findings in children with mucosal damage due to other causes (6). The mediators of the liver damage are unknown. However, in our patients with hepatic injury the gut lesion was severe (i.e. flat) in only half. Thus a severely damaged gut is not a necessary prerequisite for hepatic injury. The enteropathy in DH has been reported to be patchy in the upper small intestine (1) and thus a single jejunal biopsy may not necessarily give a true indication of the severity of the intestinal defect.

The incidence of hepatic damage in DH, adult coeliac disease, and childhood CD is the same as the incidence of the anti-reticulin antibody in these three disorders (10), all showing gluten-sensitive enteropathy. It is usually assumed that enteropathy in childhood coeliac disease is more severe than in adult coeliac disease and is mildest in DH; the anti-reticulin antibody reflects this. However, there is no correlation between the presence of anti-reticulin antibody and hepatic damage in individual patients, as anti-reticulin antibody was present in only one of these patients.

Malnutrition has been postulated as the mechanism of hepatic injury in coeliac disease (4, 6) but our patients have no evidence of this.

The reason for the hepatic injury is not clear. Coeliac disease, dermatitis herpetiformis and chronic active hepatitis are all associated with a high incidence of HLA B8 (8), and it could be that the observed hepatic dysfunction is a manifestation of subclinical chronic active hepatitis. There are several reports of coeliac disease or DH co-existing with chronic active hepatitis or primary biliary cirrhosis (2, 5, 7). One of our patients had histological-

Table II. *Abnormal liver enzymes in patients with dermatitis herpetiformis in relation to therapy*

Therapy	Number of patients	% with abnormal liver enzymes
GFD (total)	34	9
GFD alone	21	10
GFD + dapsone	13	8
Normal diet (total)	26	19
Normal diet alone	5	20
Normal diet + dapsone	21	19
Total	60	17

ly proven chronic active hepatitis with anti-smooth muscle antibody. The others did not possess anti-smooth muscle or anti-mitochondrial antibodies.

It has been proposed that immune complexes are formed in the intestine in coeliac disease (9). We did not find any immune complexes in the DH patients with hepatic injury, although the present techniques may be insufficiently sensitive to detect them. Hence it seems difficult to postulate that these are the mediators.

Our results contrast with those of Stone & Goodwin (11) who showed a 50% incidence of obstructive jaundice in patients taking dapsone for acne. None of our 30 patients taking dapsone had an elevation of the alkaline phosphatase level. This may be due to the lower doses used in DH (50–150 mg daily), compared with 150–200 mg daily for acne patients. The incidence of haemolytic anaemia was approximately the same in both series, viz. 1 out of 6, or 17%. It is unlikely that the abnormalities of AST and GGTP observed in our patients were due to the dapsone, as in several cases they returned to normal without any reduction in their dapsone dosage.

Despite the difficulty of adhering to a GFD the lower incidence of abnormal liver function in patients with DH on a GFD in contrast to a normal diet is yet another reason for advising this treatment, where it seems practical.

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A Spontaneously Healing Collodion Baby: A Light and Electron Microscopical Study[1]

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Abstract. Skin biopsies from a collodion baby, spontaneously healing at the end of the third month, were taken on the 1st and 15th day after delivery and examined by light and electron microscopy. The microscopical features observed were different from those known to occur in collodion babies evolving into lamellar ichthyosis and may

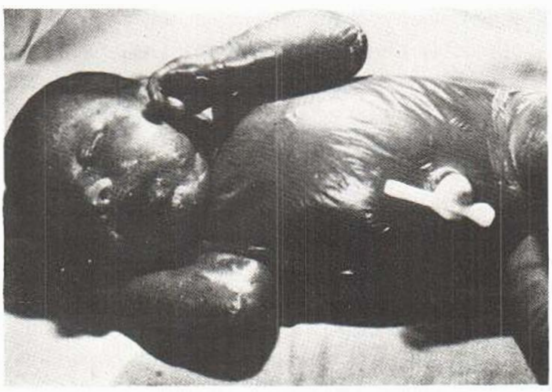

Fig. 1. Clinical appearance of the propositus on the first day after delivery: typical collodion baby.

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