glucose-6-phosphate support incorporation equivalent to that of glycerol phosphate after two hours' incubation. Table II gives the percentage of incorporation into lipid of total counts present in the incubation system (corrected for differences in protein content) with each of the substrates, and also the percentage of incorporation when the value for glycerol phosphate is set arbitrarily to 100. Again the same defect in utilization of glucose and glucose-6-phosphate is noted in diabetic tissue, and it also appears that glycerol phosphate promotes less incorporation (about 76%) of ^{14}C -palmitate into neutral lipid in diabetic tissue when compared with normal.

TABLE II.—Efficiency of Glycolytic Intermediates to Support Lipogenesis in Diabetic Tissue

Substrate Addition	% Incorporation of ^{14}C -Palmitate into Neutral Lipid			
	% of Total Counts/mg. Protein/2 Hours		% Relative to Glycerol Phosphate	
	Diabetic	Control	Diabetic	Control
Glucose	19.3 ± 2.7 (9)*	77.9 ± 16.4 (7)	30	93
Glucose-6-phosphate ..	27.3 ± 3.4 (9)*	80.0 ± 12.0 (9)	44	95
Glycerol phosphate ..	62.4 ± 13.1 (8)	84.0 ± 12.7 (8)	100	100

Fat-free homogenates (50 μl .) from diabetic and normal tissue were incubated as described in Methods section for two hours at 37° C. in test-tubes. Extraction of neutral lipid was performed by a modification of Goldfine's (1966) method. Results are means ± S.E.M. Number of experiments are given in parentheses.

* Significance of difference against glycerol phosphate is < 0.002.

DISCUSSION

The preliminary data in this paper show that in patients with maturity-onset diabetes their subcutaneous adipose tissue, which is a major site for removal of blood glucose, is unable to utilize this sugar efficiently owing to an intracellular defect in metabolism at a step after glucose-6-phosphate and before glycerol phosphate. This is most likely to be at the reaction catalysed by phosphofructokinase. The fact that this defect was observed in homogenates indicates that neither membrane transport of glucose nor the action of insulin antagonists is involved in producing this effect. It is tempting to suppose that the failure of adipose tissue to metabolize glucose in maturity-onset diabetes is responsible for the delay in clearance

of a glucose load from the blood stream, and that this secondarily stimulates an excessive secretion of insulin to overcome the hyperglycaemia. This hypothesis would imply that the tissue changes observed in this study may be present from the start of the disease and also that other tissues, such as striated muscle and liver, may be unable to accommodate the extra glucose, perhaps because they too have a similar defect. These suggestions are currently being explored.

Alternative and perhaps more likely explanations for our findings are that maturity-onset diabetes is associated with tissue changes, such as raised levels of intracellular fatty acids or citrate, which secondarily give rise to the alterations in glucose utilization observed in the present experiments. The effect is, however, unlikely to be due merely to a raised concentration of intracellular fatty acids, because the pathway from glycerol phosphate to triglyceride is maximally inhibited by free fatty acids (500 μM) (Galton, 1968), whereas in Table II lipid synthesis from glycerol phosphate was depressed by only 24% in diabetic tissue compared with normal.

Whichever interpretation turns out to be correct it is probable that the failure of adipose tissue to metabolize glucose could contribute to the impaired tolerance to glucose in maturity-onset diabetes.

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Medical Memoranda

Ruptured Spleen Associated with Chicken-pox

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Chicken-pox is usually a mild disease in children, but in adults it may be much more severe and even fatal (Bagdade and Melmon, 1966). This is especially so if the patient's resistance has been lowered by corticosteroids (*Brit. med. J.*, 1957; *Lancet*, 1957), cytotoxic agents (Cheatham, 1953), irradiation (Cheatham *et al.*, 1956), or by the presence of another disease (Eisenbud, 1952; Kaplan and Tully, 1953; Hayes *et al.*, 1965). Though lesions of the abdominal viscera have been seen at necropsy on a number of occasions (Schleussing, 1927; Johnson, 1940; Oppenheimer, 1944; Claudy, 1947; Eisenbud, 1952; Kaplan and Tully, 1953; Cheatham *et al.*, 1956; Hayes *et al.*, 1965; Bagdade and Melmon, 1966), I have been unable to find reports of their having caused serious complications in non-fatal cases. It therefore seemed worth while to report the

occurrence of spontaneous rupture of the spleen in chicken-pox.

CASE REPORT

The patient, a man aged 25, was admitted to Monsall Hospital, Manchester, seven days after the onset of a typical chicken-pox rash. His sister aged 10 was convalescing from the disease at the time. He complained of a stabbing pain in the left hypochondrium, which began shortly before he noticed the rash. During the previous six hours the pain had become much more severe. On examination he was very pale and shocked. His systolic blood pressure was 90 mm. Hg. He had generalized abdominal tenderness and there was considerable rigidity over the upper abdomen. A blood film showed normal red and white cell morphology but scanty platelets. A diagnosis of intraperitoneal haemorrhage was made and he was transferred to Crumpsall Hospital, where a laparotomy was performed the same day.

At operation there were 6 pints (3.4 litres) of blood in the peritoneal cavity. The haemorrhage appeared to arise from a small subcapsular haematoma at the hilum of the spleen. The serosal surface of both the spleen and the other abdominal viscera showed

many small vesicles and pustules. A splenectomy was carried out and a transfusion of 8 pints (4.6 litres) of blood was given. After the operation he made a rapid recovery from both the varicella infection and the surgical intervention. He was discharged from hospital nine days after the operation, and when seen in the follow-up clinic one month later he was well and without complaints.

PATHOLOGICAL EXAMINATION OF SPLEEN

The spleen weighed 165 g. There was a subcapsular haemorrhage 2 cm. in diameter on the gastric surface of the spleen close to the hilum. Many small raised nodules, the largest 0.3 cm. in diameter, were present on the serosal surface, and similar nodules were scattered throughout the splenic pulp.

In histological sections the raised nodules on the surface of the spleen showed varying degrees of necrosis from very early lesions, in which the only abnormality was some loss of nuclear staining, to areas of complete necrosis and pustule formation (Fig. 1). Haemorrhage in some of the necrotic areas formed small subcapsular haematomas (Fig. 2). Areas of necrosis were also present in the parenchyma of the spleen; in some areas these were localized to hyperplastic germinal centres, but in other places there were infarct-like areas involving both the red and white pulp. Necrosis of the walls of central arterioles was seen in some of the more severely affected areas. In addition, occasional small tuberculoid granulomas were present. The latter did not contain acid-fast bacilli in appropriately stained sections. A search was also made for the typical type A intranuclear inclusions of the varicella-herpes group. These inclusions were not seen, but in some of the necrotic areas, particularly in the germinal centres, inclusions were present in the nuclei of reticulum cells. These inclusions stained purple with eosin-methylene blue and replaced much of the normal nuclear material.

FIG. 1.—A pustule is present on the surface of the spleen at this point. (H. and E. $\times 100$.)

FIG. 2.—Capsule of the spleen is thickened, and haemorrhage is present in a necrotic area beneath it. (H. and E. $\times 100$.)

COMMENT

Previous descriptions of the splenic lesions in chicken-pox are all based on the findings in cases coming to necropsy. Vesicles and nodules were seen on the surface of the spleen and abdominal viscera by Claudy (1947) and Cheatham *et al.* (1956). Focal necroses were found histologically in the spleen by Schleussing (1927) and Hayes *et al.* (1965), while vascular necroses with infarct-like areas of necrosis were a prominent feature in the case described by Oppenheimer (1944). The type A intranuclear inclusions identified in the sinusoidal endothelial cells by some authors (Kaplan and Tully, 1953; Cheatham *et al.*, 1956) were not seen in the present material, but less definite inclusions were present in the nuclei of reticulum cells. The typical inclusions are found much more commonly in epithelial than in endothelial or mesenchymal cells (Hayes *et al.*, 1965), and thus, despite their absence here, there is little doubt from the appearance of the abdominal viscera at operation and from the histological findings in the spleen that the present case was one of visceral chicken-pox. Such cases are usually fatal (Rotem, 1961).

Rupture of the spleen is usually due to direct external violence—indirect injuries rarely cause rupture (Aird, 1957)—but there was no history of trauma of any kind in this case. Aird (1957) also discussed spontaneous rupture of the diseased spleen and gave many references to associated diseases. The commonest infection in this country resulting in spontaneous rupture is infectious mononucleosis, and in this disease the marked cellular infiltration of the capsule has been implicated. In the present case areas of necrosis were particularly prominent in the capsule and subcapsular regions, and haemorrhage into necrotic areas had given rise to small subcapsular haematomas. It is probable that extension of such a haemorrhage with necrosis of the overlying capsule was responsible for the larger haematoma from which severe blood loss occurred. Haemorrhagic manifestations associated with low platelet counts and other less consistently abnormal blood coagulation tests have been reported in chicken-pox (Charkes, 1961; Blair *et al.*, 1965). There was no evidence here of bleeding elsewhere which might suggest a haemorrhagic diathesis, though the platelets were reported as scanty on the blood film examined at Monsall Hospital.

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