Conclusion

From the figures alone we cannot be encouraged in the hope that the large psychiatric hospitals will readily be emptied of their long-stay populations, by whatever means. In Salford, at least, it is a population ever longer-staying, not by any means all old, increasingly difficult to discharge, and dying only slowly. And we replenish it year by year with new patients. We must examine the people concerned to discover what the "need" really is and to make rational provision, but the hospital and social services must work closely together to achieve this.

A further paper uses these and other data to estimate future demand for beds (Fryers, 1973).

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Placental Lactogen Levels in Diabetic Pregnancy

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Summary

A prospective study has been carried out of placental lactogen levels in pregnancy complicated by diabetes mellitus. The levels were higher than those in normal pregnant subjects; the higher levels were related to increased placental and fetal weight but more closely to the former; and lower levels were found when there was clinical evidence of placental dysfunction. Those patients requiring the largest insulin increment for the control of their diabetes in the pregnancy have placental lactogen levels in the higher range.

Introduction

The chemical and biological similarity between human placental lactogen (HPL) and human growth hormone suggests that it plays a part in the altered carbohydrate metabolism of pregnancy (Grumbach *et al.*, 1966; Beck and Daughaday, 1967; Saman *et al.*, 1968; Kalkhoff, 1969). It may also be a useful diagnostic marker for fetal well-being in pregnancies complicated by diabetes mellitus (see table). The present study, which is based on a large number of samples from 34 consecutive pregnant diabetic patients, was designed to assess the relation of HPL levels to insulin requirements during pregnancy, and to define further its place as an index of fetal risk in diabetic pregnancies.

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Subjects, Materials, and Methods

A total of 219 measurements were carried out in 34 patients with abnormal glucose tolerance tests during pregnancy. Twenty-nine patients received insulin, three of these becoming insulin dependent only during the pregnancy. Sixteen of the patients were primiparous and there was one set of twins. There was no maternal or perinatal mortality. Diabetic control was achieved as described by Brudenell and Beard, 1972.

Infant weight at delivery was expressed as a percentile above or below the normal mean corrected for gestational age, sex, and parity, and placental weight as the number of grammes above or below the normal mean after correction for gestational age.

Insulin increment was calculated as the percentage increase in the dose at delivery over that required at 20 weeks. Thirteen patients had increments above 100% and 13 patients increments below 100%.

A group of 11 patients with evidence of placental dysfunction in addition to diabetes was distinguished. This included four cases of pre-eclamptic toxæmia, seven with infants whose birth weight was below the 25th percentile for their period of gestation, and three in which fetal distress, confirmed by cardiotocometry and pH estimations, occurred in labour.

Blood samples were collected at each antenatal visit from 20 weeks' gestation onwards, and weekly during routine admission from 32 weeks until delivery. Specimens were collected between 11 a.m. and noon, and plasma HPL levels measured using a semiautomated radioimmunoassay (Letchworth *et al.*, 1971). All results were analysed after logarithmic transformation, and the significance of differences between means assessed by Student's *t* test.

Results

For the whole group mean HPL levels were above those of the normal population after the 28th week (fig. 1). The levels were related to both placental and fetal weight ($P < 0.001$ and < 0.05). The levels were lower in those subjects with placental dysfunction than those without ($P < 0.001$) (fig. 2). In the former

FIG. 1—HPL levels in pregnancies complicated by diabetes mellitus (hatched area). The normal range is shown by solid lines. The 95% confidence limits are shown.

FIG. 3—HPL levels in 13 diabetic pregnancies with insulin increments above 100% (---), and in 13 diabetic pregnancies with increments below 100% (-.-.-.-).

FIG. 2—HPL levels in pregnancies complicated by diabetes mellitus (hatched area). (a) 23 cases in which there was no evidence of placental dysfunction. (b) 11 cases with evidence of placental dysfunction. Normal range is shown by solid lines.

group 63% of levels were below 5 μg/ml after the 34th week, in contrast to 21% in patients without evidence of placental dysfunction. Higher levels were found in patients with an insulin increment greater than 100% than in those where the increment was less than 100% ($P < 0.005$) (fig. 3).

Discussion

Previous studies on HPL levels in pregnancies complicated by diabetes are summarized in the table. The present results agree with those authors who found raised levels, a finding which probably reflects the increased placental mass characteristic

Previous Studies on HPL Levels in Pregnancies Complicated by Diabetes

Author	HPL Levels	No. of Patients
Beck <i>et al.</i> , 1965	Normal	27
Saxena <i>et al.</i> , 1969	High	12
Josimovich <i>et al.</i> , 1970	Normal	..
Singer <i>et al.</i> , 1970	High	13
Zuckerman <i>et al.</i> , 1970	High	6
Samaan <i>et al.</i> , 1971	Normal	24
Genazzani <i>et al.</i> , 1971	Normal	8
Spona <i>et al.</i> , 1971	Normal	39
Spellacy <i>et al.</i> , 1971	Low	33
Haour <i>et al.</i> , 1971	High	12
Selenkow, 1971	High	84

of the condition, and which is further confirmed by the clear-cut relation between HPL levels and placental weight. The finding of a significant but less striking relation to fetal weight is likely to be a secondary association.

The levels of HPL are reduced in the cases of diabetic pregnancy in which the fetus is at greatest risk. Interpretation of these levels, however, depends on a knowledge of the range of levels associated with the complication, as previously found with pre-eclampsia (Letchworth and Chard, 1972a). Levels are higher than those in a normal pregnancy, and a level which is apparently "normal" may, in a diabetic, be low, and thus of prognostic significance. As an arbitrary limit, 5 μg/ml provides a clinically useful division for the separation of diabetic pregnancies into those with and those without placental dysfunction. However, there is considerable overlap between these groups and it may be expected that the results of serial values will be of still greater value (Letchworth and Chard, 1972b). Full evaluation of this possibility will require the accumulation of further data.

The observation that insulin requirements are related to HPL levels is compatible with the known diabetogenic effect of this hormone. The relation is probably direct, but other factors—notably, the placental steroids (Kalkhoff *et al.*, 1970; Costrini and Kalkhoff, 1971)—may also be involved in the altered carbohydrate metabolism of pregnancy.

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Clinical and Laboratory Double-blind Investigation on Effect of Fibrinolytic Therapy in Patients with Cutaneous Vasculitis

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Summary

The effects of phenformin and ethyloestrenol and phenformin and stanozolol on the clinical state, plasma fibrinolytic activity, and fibrinogen-fibrin-related antigen (F.R.-antigen) were compared with placebo in 13 patients with cutaneous vasculitis. Eight patients showed considerable clinical improvement when taking phenformin and an anabolic steroid; an impaired fibrinolytic activity before treatment favoured clinical improvement.

Introduction

Cutaneous vasculitis refers to a miscellaneous group of conditions in which one of the primary histological defects is inflammation of the skin blood vessels; fibrinoid necrosis and vascular occlusion may follow. The clinical picture depends on the site, size, and number of vessels affected, and so one may see any combination of purpura, papules, nodules, necrosis, and even ulceration. The pathogenesis, however, is unknown but recent investigations (Cochrane, 1968; Katz et al., 1968; Cream, 1972) have suggested that immunological phenomena such as precipitation of immune complexes may be important. As a result of the immunological reaction occurring within the blood vessel wall or lumen a series of

events follow which may culminate in the formation of a thrombus. Investigations of blood coagulation factors are limited (Isacson et al., 1970) and appear at the moment to be of little help in the understanding of the development of the vasculitic lesion. Studies of fibrinolysis, however, have been more detailed and interesting. Cunliffe (1968) reported three patients who had a persistently reduced fibrinolytic activity as shown by a prolonged euglobulin lysis time, and which returned to normal in two cases as the vasculitis spontaneously healed.

Cunliffe and Menon (1971) further investigated 52 patients with a vasculitis predominantly affecting the skin. Of these, 32 patients had a significantly reduced plasma fibrinolytic activity. The same authors reported in an uncontrolled study that in nine out of 10 patients who received oral fibrinolytic therapy with phenformin hydrochloride and ethyloestrenol clinical improvement occurred over a period of 6-36 weeks. Isacson et al., (1970) reported a decreased blood fibrinolytic activity in four of 11 patients with chronic vasculitic lesions of the lower legs. Parish (1972) also reported eight patients six of whom had a decreased blood fibrinolytic activity. In contrast to these findings, however, Kurban and Ryan (1969) and Vaithianathan and Takats (1968) were unable to detect a reduced fibrinolytic activity in patients with a vasculitis.

Published data on the treatment of cutaneous vasculitis with fibrinolytic therapy from other centres are not available. Clearly, therefore, the field was set for a more detailed, preferably double-blind study of oral fibrinolytic therapy in patients with chronic vasculitis. At the same time it appeared prudent to measure fibrinogen-fibrin-related antigen (F.R.-antigen) in these patients with a demonstrable disorder of their fibrinolytic mechanisms.

Patients and Methods

Each of the 13 patients who entered the trial had a vasculitis of at least six months' duration and the clinical details are

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