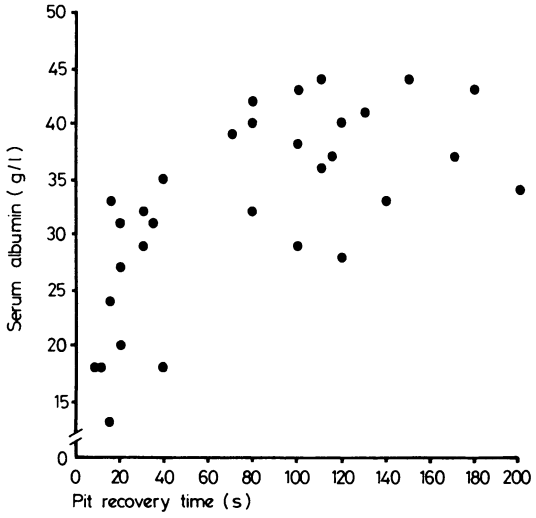
assessed clinically, the recovery rate was measured, and venesection was performed without stasis for serum albumin estimation. All were seen before the diagnosis was ascertained. If the oedema over the tibia could be depressed deeply in one to two seconds by thumb pressure, and if a pit was observed to be visibly recovering two to three seconds after the release of pressure, the oedema was termed fast; if not it was termed slow. A device consisting of a perspex disc (45 mm diameter) with a Teflon-lined central ring containing a freely moving hollow perspex cylinder (15 mm diameter) was taped to the skin over the lower third of the tibia, with the patient semi-recumbent. The cylinder was depressed by firm digital pressure to a depth of 5 mm for 10 seconds, and the subsequent millimetre of recovery, measured visually on a Vernier scale, was timed after allowing two seconds for initial elastic recoil. The mean of two readings at different sites was taken. The consistency of the method was first established: no observations in a given patient differed from the mean by over 10%.



Relation between serum albumin concentration and pit recovery time in the 31 patients.

Thirty-one patients (15 men, 16 women) had enough oedema to be measured by the device; the results are shown in the figure. There was a significant relation between the pit recovery time and serum albumin concentration. By plotting log albumin concentration against log pit recovery time a regression coefficient was found ($P<0.001$). Clinical impressions of fast pitting oedema correlated with pit recovery times of 40 seconds or less.

Comment

Oedema has traditionally been divided into three main categories according to the mechanism of formation[1]: (*a*) congestive oedema, due to increased hydrostatic pressure, as in congestive cardiac failure and venous or lymphatic obstruction; (*b*) hypoalbuminaemic oedema, due to reduced plasma oncotic pressure, as in nephrotic syndrome, malnutrition, and malabsorption; and (*c*) capillary oedema, due to increased permeability of capillaries, as in vasculitis (including glomerulonephritis), and idiopathic oedema in women.

In hypoproteinaemic oedema the tissue fluid protein content is less than 1 g/l,[2] while in congestive cardiac failure it is 4-5 g/l.[3] In capillary oedema the protein content of the oedema fluid is higher, and is over 10 g/l[4] in glomerulonephritis. Moreover, the localised oedema produced by subcutaneously infused fluid can be dispersed more rapidly in patients with hypoalbuminaemia.[5]

The viscosity of tissue fluids is related to their protein content, and the mobility of pitting oedema presumably depends on this. The reduced protein content of the oedema fluid in hypoproteinaemia therefore explains the relation between the serum albumin concentration and the rate of recovery of pitting. This phenomenon could have a useful clinical application in that hypoproteinaemic oedema may be diagnosed by simple observation. When oedema pits with little resistance and recovery is visible in the initial seconds, hypoproteinaemia probably plays a part in the pathogenesis of the oedema and may be its major cause. In other types of oedema the pit tends to form less readily and recovers more slowly. Chronic oedema may not pit due to fibrosis and induration, but may pit rapidly due to laxity of the tissues.

We suggest that the nature of the pitting should be assessed in oedematous patients as it provides a physical sign which can be of value in making a clinical differential diagnosis.

We thank Mr A Johnson of the MRC Statistical Research Unit and Dr L J Grant for their help.

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Different periods of fasting have no effect on oral glucose tolerance

It has been suggested that the length of the pretest fast influences the result of an oral glucose tolerance test.[1] In that study the patients who exhibited least carbohydrate tolerance were woken at 0500 for a meal. It seemed possible, therefore, that factors other than the duration of the fast itself might have influenced the results obtained. To study the effect of fasting itself we altered the time of the test from 0900 to 1400. We also altered the longest period of fasting from 12 to 16 hours, thereby eliminating a disturbed sleep pattern as an integral part of the study.

Patients, methods, and results

A total of 23 consecutive adult patients admitted to the general medical wards without a past, present, or family history of diabetes who volunteered to participate in the study after its routine had been explained to them form the basis of this report. Each had three oral glucose tolerance tests performed after randomly selected fasting periods of four, eight, and 16 hours. The tests were all performed at 1400, on each of three days; each test was separated by not less than two days or more than five days. All were eating a normal hospital diet during the study. Fifty grams of glucose was given by mouth and venous blood samples taken at 0, 30, 60, 90, and 120 minutes. The blood glucose concentration was estimated on each specimen by Technicon method N-2b. One patient was discovered to have chemical diabetes and her results have been excluded from the table, which contains those for the other 22. The differences between the results were tested for significance by Student's *t* test.

The 30-minute values after the 4-hour fast were significantly higher than those obtained after either the eight-hour ($t=2.0195$, $0.05>P>0.02$) or the 16-hour ($t=2.0772$, $0.05>P>0.02$) fasts. No other differences were significant.

Mean (± SD of mean) blood sugar concentrations (mmol/l) for three oral glucose tolerance tests in 22 patients

Pretest fast (h)	Time (minutes)				
	0	30	60	90	120
4	4·30 ± 0·46	7·15 ± 1·24	7·14 ± 1·97	5·71 ± 1·43	4·81 ± 0·988
8	4·20 ± 0·31	6·45 ± 0·97	7·42 ± 1·62	6·33 ± 1·9	5·32 ± 1·56
16	4·28 ± 0·66	6·46 ± 0·88	6·52 ± 1·8	6·18 ± 2·04	5·42 ± 2·4

Conversion: SI to traditional units—Glucose: 1 mmol/l ≈ 18 mg/100 ml.

Discussion

While oral glucose tolerance may be less in normal people in the afternoon,[2] standardisation of the time of the three tests on each patient allows a valid comparison to be made between the results obtained in each of the tests. Unlike Walsh *et al*[1] we did not find that the duration of the pretest fast influenced the degree of carbohydrate tolerance. It is true that the values obtained at 30 minutes after the four-hour fast

were just significantly higher than those obtained at 30 minutes after either an eight-hour or a 16-hour fast. Nevertheless, the subsequent values obtained after the four-hour fast were similar to those after the other periods of fasting. Thus in the biological sense there was no impairment of carbohydrate tolerance after the four-hour fast.

We think that waking the patients at 0500 in the study of Walsh *et al*[1] may have influenced the results they obtained. We suggest that in further studies hormone concentrations, particularly those of plasma cortisol, should be measured in addition to blood glucose concentrations. We think that our results indicate that by itself the duration of the pretest fast does not affect tolerance of oral glucose.

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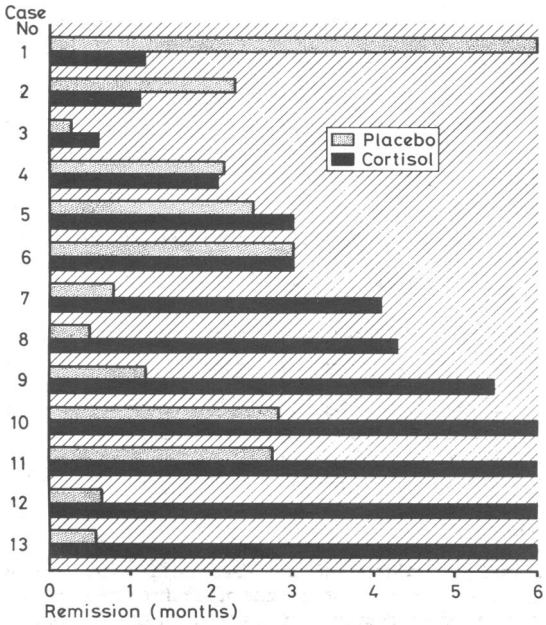
Idiopathic nephrotic syndrome: prevention of early relapse

In children with the idiopathic nephrotic syndrome early relapses are often due to adrenocortical suppression after prednisone.[1 2] We have shown that such early relapses can be avoided by partial cortisol substitution.

Patients, methods, and results

Eight boys and five girls (aged 4·7-14·6 years) who had had glucocorticoid-sensitive idiopathic nephrotic syndrome for up to 10·3 years were studied after their parents had given informed consent. The clinical definitions and prednisone regimen have been described elsewhere.[3] A two-hour ACTH test[4] was performed 1-12 days after treatment. Children with subnormal responses[4] were allotted to group 1 (drug sequence A-B) or group 2 (sequence B-A). Drugs A and B were tablets of identical appearance and taste, A containing 5·0 mg cortisol and B without the active agent. Their identity was not known to anyone concerned in the study. Children weighing 30 kg or more took two tablets at 7 am and one tablet at 2 pm; smaller children were given half the dose. When infection or detectable proteinuria (urine was checked at home every morning with Albustix) occurred the daily dose was doubled and given in equal parts every six hours over the next three days or until the symptoms had disappeared. The first drug was continued for six months or until relapse. As soon as the child again had post-prednisone adrenocortical suppression after a relapse, the second drug of the sequence was started. In six children the ACTH test was performed on completion of each drug period.

Twenty-one of the 26 drug periods had to be interrupted because of relapse (see figure). At three months eight children remained in remission during the cortisol period only, one child in the placebo period only, and one child during both periods. The difference was significant at the 5% level ($\chi^2 = 4·0$). At six months five remissions continued, four of them during the cortisol period. Three of these children were followed for a full year and all relapsed. The fifth six-month remission was observed in case 1 during a placebo period; subsequent 2·4-year follow-up indicated that the idiopathic nephrotic syndrome had been cured. The following variables were compared between the cortisol and placebo periods with Student's paired *t* test: the extent of pre-prednisone proteinuria; pre- and post-prednisone plasma concentrations of albumin, protein, cholesterol, and urea nitrogen; length of prednisone treatment; and post-prednisone and post-substitution ACTH test responses. No differences were significant. The effectiveness of cortisol substitution was independent of age and sex.



Length of remissions in 13 nephrotic children with post-prednisone adrenocortical suppression. Periods of partial cortisol substitution and placebo medication are compared.

Comment

The results of this double-blind cross-over study indicate that partial cortisol substitution prevented half the relapses predictable within three months of remission. This supports the hypothesis that post-prednisone hypocortisolism is responsible for many of the early relapses in the idiopathic nephrotic syndrome.[1 2] Many frequent relapsers are in a continuous cycle of relapse-prednisone treatment-adrenocortical suppression-relapse.[2] Children with adrenocortical suppression should be identified and temporarily provided with partial cortisol substitution. This has to be partial; otherwise the suppression will persist. Our present regimen seems to be appropriate.

We thank the Sigrid Jusélius Foundation for generous support and AB Medica OY, Helsinki, for the drug preparations.

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Persistent orthostatic hypotension after epidural analgesia

Some degree of hypotension normally occurs during epidural blockade, but is transient. In the case reported here, however, severe orthostatic hypotension persisted for many weeks. This complication of epidural analgesia has not been reported.

Case report

A 26-year-old primipara was admitted ten days after the expected date of delivery. She had been well throughout pregnancy, with normal blood pressure, no postural symptoms, and no evidence of gestational diabetes. Labour was induced by artificial rupture of the membranes, and soon after the patient requested epidural analgesia. A catheter was inserted through a Tuohy needle at the level of L 2-3, the epidural space being identified by loss of resistance. The anaesthetist was experienced in the technique, and the dura was not punctured. A test dose of 2 ml lignocaine (1·5%) was administered with the patient in the left lateral position, followed by a further 10 ml.