Mean ($\pm$ SD) basal skin flow changes (% plus or minus) during local and contralateral hand cooling tests before and during naftidrofuryl treatment

Test	Before treatment	During treatment	P value
Local cooling	-21.5 $\pm$ 26.9	-9.0 $\pm$ 18.5	P = 0.001
Normal range	+ 7.5 $\pm$ 19.6		
Contralateral hand cooling	-49.2 $\pm$ 19.5	-25.4 $\pm$ 12.1	P < 0.001
Normal range	-23.4 $\pm$ 10.4		

test. Individual cooling test results that were within the normal range before the treatment were not much changed by naftidrofuryl. Five patients had epigastric discomfort while taking naftidrofuryl. This was the only side effect.

Comment

The mechanisms causing RP can be divided into systemic microvascular reflexes and local mechanisms (local hyperreactivity of the blood vessel walls and increased local blood viscosity)—the relative importance of each differing in individual patients—and an already decreased basal flow when such mechanisms are normal.² Earlier studies^{3,4} suggest that naftidrofuryl helps in various peripheral vascular disorders without causing hypotension and flushing. It enhances the tissues' oxidative potentials after conditions of raised anaerobic tissue metabolism.⁵ This study shows that naftidrofuryl has a beneficial effect on the basal skin flow and both the reflex and the local mechanisms underlying RP. Its effect on the microvascular reflexes was most pronounced, indicating that a better clinical effect might be expected in patients in whom these are impaired. A controlled clinical trial is therefore warranted in patients selected on these grounds. They will be found mostly among patients with RD, RA, and possibly SLE.²

I thank Lipha Pharmaceuticals Ltd for placebo capsules.

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Plasma lipoproteins in renal transplant patients

Changes in plasma lipoprotein patterns in chronic renal failure and after renal transplantation were reported by us,¹ and our observations have been confirmed by others.² We have re-examined the plasma lipids in 17 of our original patients four years after our initial investigation.

Patients, methods, and results

Of our 32 original patients in 1971, 17 were available for study in 1975, exactly four years later. Six of the remainder had died, five had rejected their allograft and been returned to haemodialysis, and four were unavailable for study. Out of the six who died, two had myocardial infarcts, two had renal failure due to rejection, one had haemorrhage from a duodenal ulcer, and one had a subarachnoid haemorrhage. The group consisted of seven men and 10 women with an average age of 41 years (21-56). Each patient was seen and examined after a 12-hour fast in a renal transplant follow-up clinic. Venous blood samples were analysed by semiautomated techniques

for cholesterol and triglycerides and lipoprotein patterns electrophoretically according to techniques previously described.¹

The comparative body weights, prednisolone dose per day, and plasma cholesterol and triglyceride concentrations of the 17 patients studied in 1971 and 1975 are shown in the table. During this follow-up period the dose of corticosteroids had been gradually reduced so that in the second study period the average ($\pm$ SD) dose (11 $\pm$ 1.1 mg/day) was virtually half that used in the initial period (21 $\pm$ 2.3 mg/day). Concomitantly the plasma cholesterol and triglyceride concentrations had significantly fallen and were within the normal range. Furthermore, the lipoprotein patterns had returned to normal in 11 cases, only two remaining in class IIa and four in class IV. There had been no significant change in glomerular filtration rate over this period (63.5 $\pm$ 6.1 ml/min and 73.9 $\pm$ 7.6 ml/min).

Comparative mean ($\pm$ SD) plasma triglyceride and cholesterol concentrations, glomerular filtration rates, body weights, and prednisolone dose/day in 1971 and 1975 in renal transplant patients

	1971 (n = 32)	1975 (n = 17)
Triglycerides (mmol/l)	2.4 $\pm$ 0.2	1.4 $\pm$ 0.1*
Cholesterol (mmol/l)	6.5 $\pm$ 0.3	5.2 $\pm$ 0.2*
GFR (ml/min)	63.5 $\pm$ 6.1	73.9 $\pm$ 7.6
Weight (kg)	61.4 $\pm$ 2.6	60.2 $\pm$ 2.7
Prednisolone (mg/day)	21 $\pm$ 2.3	11 $\pm$ 1.1*

*P < 0.001 (paired t test).

Conversion: SI to traditional units—Triglyceride: 1 mmol/l $\approx$ 86 mg/100 ml. Cholesterol: 1 mmol/l $\approx$ 39 mg/100 ml.

Comment

Vascular disease is the commonest cause of death in patients with chronic renal failure on haemodialysis. Cardiac and vascular accidents account for over 30% of all deaths in patients with renal transplants, taking second place only to infections.³ Our initial study in 1971¹ was prompted by a similar clinical observation. Like other authors, we found substantial hypertriglyceridaemia in the non-nephrotic renal failure group, whereas in the transplanted individuals taking an average prednisolone dose of 21 mg/day cholesterol, triglyceride, and non-esterified fatty acid levels were significantly raised. Insulin concentrations remained normal throughout. Postulating that these raised values could well be related to the corticosteroid treatment, this further study was undertaken four years later when the corticosteroid dose in the original patients had been reduced from a mean of 21 mg to 11 mg/day. A pronounced improvement was observed. Most patients had normal concentrations of cholesterol and triglycerides, and lipoprotein patterns had returned to normal.

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Prenatal diagnosis of a galactosaemia heterozygote by fetal blood enzyme assay

Although dietary exclusion of galactose greatly improves the prognosis of galactosaemia, in all six pregnancies referred to us where the mother had given birth to an affected child the parents requested diagnostic amniocentesis so that they could choose to have only unaffected children. We describe such a mother who refused to accept the risk of having another affected child but who presented at 20

weeks' gestation, when delay for culture of amniotic cells prior to assay might render unethical the termination of an affected but viable fetus. Rapid diagnosis of a heterozygote fetus was established by direct enzyme assay of fetal blood collected at fetoscopy.

Patients, methods, and results

The mother, aged 26, had given birth to one infant with probable galactosaemia, who had neonatal jaundice and died aged 4 months, and another with galactosaemia, now aged 5 years, thriving, and developing normally on a low galactose diet. Amniotic cells were collected from clear amniotic fluid at the Mothers' Hospital (Salvation Army), London E5, by suprapubic amniocentesis at 20 weeks' gestation, cultured, and assayed for galactose 1-phosphate uridyl transferase (EC 2.7.7.12 "transferase") activity as previously described.^{1,2} Fetoscopy was carried out at King's College Hospital 14 days after amniocentesis. The placenta was anterior but by simultaneous use of a real-time ultrasound scanner it was possible to avoid damaging it. A small placenta-free area was found on the left lateral uterine wall and the fetoscope was inserted there through a 2-mm abdominal incision.³ Fetal vessels on the chorionic plate were difficult to see because of yellowish-brown discoloration of the amniotic fluid, probably from bleeding after the earlier amniocentesis. The precise location of the needle tip was therefore uncertain, but four samples of 0.1-0.2 ml of blood mixed with amniotic fluid were aspirated.

Two of the blood samples contained 90% fetal erythrocytes, identified by the Kleihauer technique, but had haemoglobin concentrations of 3-4 g/dl, suggesting that dilution had occurred by amniotic fluid. Fetal blood samples had transferase activities of 18.2 and 18.4 $\mu\text{mol UDPgal formed/h/g haemoglobin (units)}$, which were similar to or higher than those of similarly diluted heterozygote values of both maternal (18.2 units) and two unrelated carriers (13.2, 13.4 units) and within the range of 21 control heterozygotes (table). Amniotic fluid supernatant had barely detectable transferase

Whole-blood galactose 1-phosphate uridyl transferase activities ($\mu\text{mol UDPgal formed/h/g Hb}$)

Subjects	Mean	No of subjects	SE of mean	Range
Controls	28.3	66	0.642	20.3-42.1
Non-galactosaemic patients*	31.7	36	1.029	20.8-47.1
Heterozygotes (N/G)†	16.5	21	0.612	12.6-21.4
Heterozygotes (D/G)‡	5.8	2	—	5.1-6.4
Galactosaemia	2.5	7	0.462	0.7-3.9

*Patients in whom a diagnosis of galactosaemia was suspected but excluded.

†Normal/galactosaemia.

‡Duarte/galactosaemia.

activity. Cultured amniotic cells assayed 24 days after amniocentesis had a transferase activity of 47 $\mu\text{mol/h/g protein (units)}$ as compared with 70 and 76 units for simultaneously assayed control amniotic cells from two other pregnancies. Previous mean values for amniotic cells from 13 normal pregnancies were 63.3 units (SE of mean 4.04).

On these results the fetus was considered to be a heterozygote. The mother was delivered of a normal female infant (birthweight 2860 g) at 39 weeks. Transferase activity was estimated as 14.1 units in cord blood and 9.1 units at the age of 2 months at the Hospital for Sick Children, Great Ormond Street, in Dr A D Patrick's laboratory, and the infant confirmed to be a galactosaemia heterozygote (heterozygote range in this laboratory 9-15 units).

Comment

Fetal blood sampling has been used hitherto for prenatal diagnosis of disorders which cannot be detected by studies on amniotic cells, such as haemoglobinopathies and Duchenne muscular dystrophy.⁴ This case illustrates how fetal blood sampling can be used for rapid prenatal diagnosis of other disorders when the mother presents in an advanced stage of pregnancy. Fetal blood sampling by fetoscopy has reached a high degree of reliability. When performed at between 18 and 22 weeks' gestation 50-500 μl of pure fetal blood, uncontaminated by maternal blood or amniotic fluid, has been obtained in 19 out of our last 20 consecutive fetoscopies (95%).⁵ In two-thirds of the cases the placenta was predominantly anterior. The difficulty encountered in the case reported here due to bleeding caused by penetration of the anterior placenta by the amniocentesis needle emphasises the need to perform amniocentesis under direct ultrasound control to avoid placental damage.

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ESR in gonococcal arthritis

Two distinct syndromes of gonococcaemia have been differentiated. One is serious, with often fatal endocarditis. The other, more benign, is characterised by fever, arthralgia, and skin eruptions. The latter syndrome complicates about 2% of cases, affecting 0.4% of cases in men and 2.3% in women. Barlow¹ traced only 24 recent British cases. I report a further case, in which the ESR response paralleled clinical and bacteriological cure.

Case report

A man aged 24 was admitted to a general surgical ward on 18 October with a two-week history of vomiting, epigastralgia, malaise, and cough. His temperature was 39.9°C (103.8°F) and he had epigastric tenderness. Blood leucocytes were $16.6 \times 10^9/\text{l}$ ($16\,600/\text{mm}^3$) (polymorphs 88%). There were no heterophile antibodies. Abdominal and thoracic x-ray examination, urine analysis, and throat bacteriology were normal. Serum amylase concentration was 160 IU/l. Liver function tests were normal. Three conventional blood cultures were sterile. His left knee became warm, swollen, and painful on 24 October. X-ray pictures of it were normal. Knee aspirate cultured on conventional media was sterile. RA and LE latex tests were negative. Plasma uric acid, antistreptolysin O titre, ECG, and radiographs of the sacroiliac region were normal. A transient fever occurred on 25 October. Repeat aspiration on 1 November produced purulent fluid with $27.4 \times 10^9/\text{l}$ ($27\,400/\text{mm}^3$) white cells (93% neutrophils). The blood leucocyte count was $12.5 \times 10^9/\text{l}$ ($12\,500/\text{mm}^3$). In early November he developed a transient, sparse crop of peripheral pustules accompanied by fever and right wrist arthralgia. On 16 November biopsy of left knee synovium showed thickening, oedema, and infiltration by inflammatory exudate. In late November urethral investigation was suggested. He had neither genital symptoms nor signs but urethral Gram-negative intracellular diplococci were found on a smear and confirmed by Thayer-Martin medium culture. Subculture for sugar fermentations was unsuccessful. Treatment with 5 megaunits of benzylpenicillin initially and 1 megaunit six-hourly for 48 hours and ampicillin 500 mg with probenecid 500 mg by mouth for a further five days produced a rapid clinical cure of the arthritis. The fever did not recur. Urethral tests for gonococci were negative on two subsequent occasions. His first and only sexual partner proved to have cervical gonococci and was treated.

ESR before and after antibiotic treatment in case of gonococcal arthritis

	Day of treatment			
	Before	Second	Fourth	Seventh
ESR (mm in first hour)	75	7	13	6