

or transverse positions of the fetal head in the second stage of labour, nor with Potter and MacDonald,<sup>8</sup> who found no increase in the rate of instrumental delivery in a group of nulliparous patients who were given epidural blocks.

The increase in the malposition rate in the epidural group is probably due to the decrease in tone of the pelvic floor muscles. This will interfere with the normal mechanism of labour in that the occiput will not be so easily rotated anteriorly when the presenting part is pushed against the gutter normally formed by the unrelaxed levator ani muscles.

Nearly all the patients with a malposition at the end of the second stage of labour in our series had a Kjelland's rotation forceps delivery. Although an epidural block facilitates such manipulation because of the excellent analgesia and pelvic floor relaxation, further study is needed into the possible trauma to mother and child that might be incurred if 20% of all patients with epidural analgesia have rotation forceps deliveries. In this series, only one baby in the epidural group was admitted to the special care baby unit. This baby had a cephalohaematoma after a ventouse delivery. Two babies in the non-epidural group were admitted with birth asphyxia and both had been delivered spontaneously.

The factors associated with a lower instrumental delivery rate after epidural analgesia seem to be multiparity (although this was only relative to the incidence in primigravid patients), a second stage of at least an hour, and a return of sensation to both perineum and abdomen. Topping-up an epidural analgesic at the end of the first stage of labour increases the incidence of instrumental delivery. But the timing of the initial induction of analgesia seems to have no effect on the final outcome. The increased malposition rate after epidural analgesia was not affected by any of the factors studied and remained around 20%. Possibly a lower strength of local anaesthetic (say 0.125%)<sup>9</sup> might lower the incidence of vaginal operative delivery and malposition and this is worthy of further study.

Epidural analgesia therefore seems to be associated with an incidence of instrumental delivery in primigravidae of about 70% and in multiparae of about 40%. These rates may be slightly reduced by some of the changes in the management of labour mentioned above, but the associated incidence of malposition will remain high. The psychological and physical disadvantages of such an "interference" rate have not yet been fully evaluated but must be considered before a decision is made to give the patient the benefits of epidural analgesia. In the absence of any strong medical indication for regional analgesia, the patient should be made aware of the increased chance of instrumental delivery so that she herself may choose between such a method of pain relief and the considerably reduced chance of a spontaneous delivery.

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## Fetal proteinuria in diagnosis of congenital nephrosis detected by raised alpha-fetoprotein in maternal serum

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### Summary

High concentrations of alpha-fetoprotein ( $\alpha$ -FP) were found at 14, 19, and 21 weeks gestation in the serum of a woman with a history of unexplained fetal death in her previous pregnancies. The  $\alpha$ -FP concentration of the liquor also was high at 21 weeks and the pregnancy was terminated. Though the fetus was macroscopically normal, measurement of albumin,  $\alpha$ -FP, IgG, and  $\alpha_2$ -

macroglobulin in the fetal urine showed a selective proteinuria, and congenital nephrosis was diagnosed after examination of the fetal kidneys by electron microscopy.

Possibly some fetuses reported to be "false-positive for neural tube defect" may have had renal lesions of this nature. Examination of fetal urine may be the simplest initial diagnostic procedure in any future case.

### Introduction

It is important for the role of maternal serum alpha-fetoprotein ( $\alpha$ -FP) screening that a thorough examination be made of any fetus without neural tube defect which is the product of a pregnancy associated with high  $\alpha$ -FP levels. It is also important for genetic counselling that a definite diagnosis is reached.

We present the results of studies made on an apparently normal fetus after termination of a pregnancy in which extremely high maternal serum and amniotic fluid  $\alpha$ -FP concentrations had been found.

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### Case report

This 24-year-old patient's first pregnancy ended in spontaneous abortion at 14 weeks' gestation. Her second pregnancy seemed to be proceeding normally until 36 weeks' gestation, when she began to lose weight and felt fetal movements no longer. Fetal death in utero was confirmed and labour was induced at 38 weeks. The male infant weighed 3140 g and appeared normal. The internal organs were macerated. The placenta was extensive and weighed 850 g.

In her third pregnancy serum taken for routine  $\alpha$ -FP screening had an  $\alpha$ -FP concentration of 128  $\mu$ g/l at 14 weeks' gestation (normal median value 30  $\mu$ g/l). At 19 weeks the  $\alpha$ -FP concentration was 690  $\mu$ g/l (normal median value 65  $\mu$ g/l), and at 21 weeks the level had reached 875  $\mu$ g/l (normal median value 85  $\mu$ g/l).

Ultrasonic scanning showed a single fetus with normal biparietal diameter for gestation and no obvious defect. The possibility of amniocentesis and its implications were fully discussed with the parents. Both expressed their wish that this should be carried out. Pale yellow blood-free liquor was obtained with an  $\alpha$ -FP concentration of 288 mg/l (normal median value 8 mg/l). The pregnancy was terminated by extra-amniotic infusion of dinoprostone  $E_2$ . An apparently normal female fetus was delivered in an intact sac.

### INVESTIGATIONS

Both blood and urine were obtained from this fetus and 14 macroscopically normal fetuses. All urine specimens were screened for the presence of haemoglobin F, and only specimens that were entirely free of blood contamination were accepted. Their volumes ranged from 0.1 to 2.5 ml.

$\alpha$ -FP in fetal serum, urine, and liquor was measured by "rocket" electroimmunodiffusion using Behringwerke standard.  $\alpha$ -FP in maternal serum was measured by radioimmunoassay using a double antibody technique and Nishi standard. Albumin and IgG were measured by single radial diffusion and  $\alpha_2$ -macroglobulin by "rocket" electroimmunodiffusion using Behringwerke standards. Specimens were screened for haemoglobin F by counterimmunoelectrophoresis.

Specimens of kidney from the aborted fetus had been fixed in formalin but were refixed in buffered osmium before embedding in Epon. Specimens from control cases were embedded after fixation in 2% glutaraldehyde in cacodylate buffer with post-fixation with osmium. Thin sections from the selected glomeruli were examined with a Zeiss EM9 electron microscope.

### Results

**Protein estimations**—Compared with 14 other fetuses, the fetus from our patient had slightly lower serum concentrations of albumin,  $\alpha$ -FP, and IgG than might be expected for gestation (table I). The urine of the fetus contained grossly higher concentrations of these proteins than any urine specimen from the control fetuses (table II). The proteinuria of the fetus was selective, with less excretion of IgG than of albumin and  $\alpha$ -FP and no macroglobulin.

**Pathology**—The fetus weighed 450 g and measured 17.5 cm crown to rump and 30 cm crown to heel. Chromosomes were normal. No abnormality was found in any of the internal organs on histological examination. Intensive examination of the kidney sections by electron microscopy, however, showed fusion of the foot processes of the podocytes in the deeper glomeruli from the juxtamedullary region

TABLE II—Mean protein concentrations in fetal urine. Ranges are given in parentheses

Cases	Control fetuses 1-14	Fetus under study
Albumin (mg/l)	55 (15-168)	11400
$\alpha$ -FP	11 (3-28)	1042
IgG	12, 16*	140
$\alpha_2$ -macroglobulin	Not detectable†	Not detectable
Urine values as % of serum values:		
Albumin	0.31 (0.07-1.24)	62.0
$\alpha$ -FP	0.41 (0.15-1.40)	68.1
IgG	1.4, 1.6	11.0

\*Only two values were above limit of detection (10 mg/l).

†All values were below limit of detection (2 mg/l).

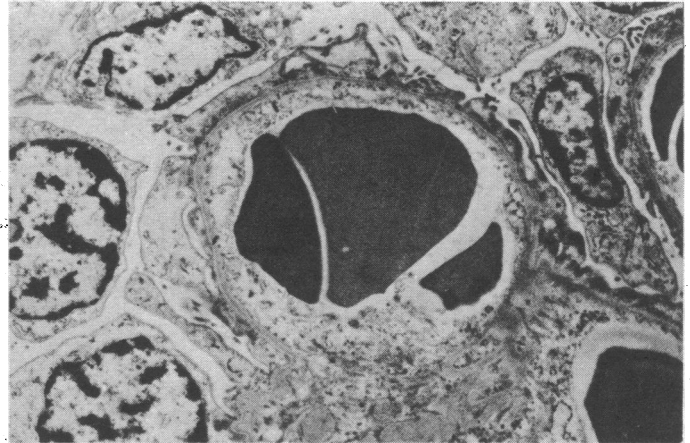


FIG 1—Capillary loop showing fusion of foot processes and increase in mesangial matrix. ( $\times 4804$ .)

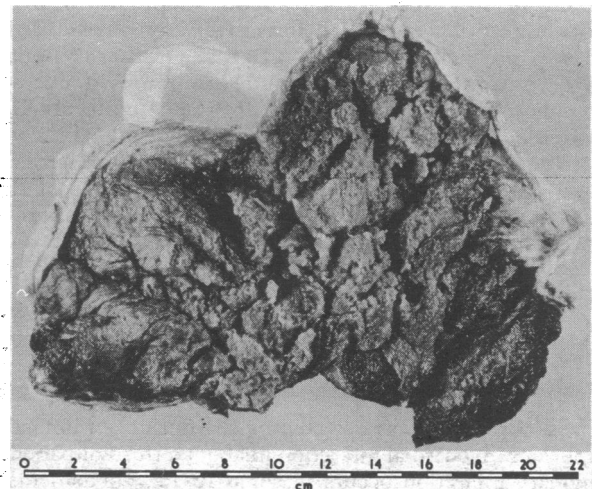


FIG 2—Maternal side of placenta.

TABLE I—Protein concentrations in fetal serum

Case No	Gestation (weeks)	Albumin (g/l)	AFP (g/l)	IgG (g/l)	$\alpha_2$ M (g/l)
Control fetuses:					
1	14	11.3	3.35	0.31	0.24
2	14	12.8	3.30	0.26	0.19
3	14	15.8	2.85	0.50	0.26
4	14	18.2	4.70	0.25	0.28
5	16	19.9	2.50	0.64	0.29
6	16	20.2	4.83	0.59	0.30
7	17	13.6	2.50	0.61	0.30
8	17	18.3	2.00	0.96	0.25
9	17	19.2	2.98	0.86	0.40
10	17	21.2	2.45	0.57	0.28
11	18	19.2	2.28	1.52	0.40
12	18	22.1	2.40	1.02	0.42
13	18	23.7	2.88	1.33	0.49
14	22	28.2	2.06	2.26	0.60
Fetus under study	22	18.4	1.53	1.27	0.55

and, in occasional glomeruli, a considerable increase in mesangial matrix (fig 1). These features were not seen in the control cases examined and the abnormal appearances were identical to those recently described in congenital nephrosis.<sup>1</sup> The placenta, weighing 280 g, resembled a placenta membranacea (fig 2). Histologically the villi were fewer and less branched than usual while the stroma showed an increase in Hofbauer cells and fibroblasts. Cytotrophoblast was present but the cytoplasm was condensed and the nuclei structureless and often pyknotic. The cord was thick, oedematous, and twisted.

### Discussion

Congenital nephrosis is accompanied by high maternal and liquor  $\alpha$ -FP levels and induced abortions have been performed

in Scandinavia on the basis of  $\alpha$ -FP measurements in mothers known to be at risk.<sup>1,2</sup> Features suggestive of this diagnosis in the present case, in which there was no previous history, were the large abnormal placenta<sup>3</sup> and the fetal proteinuria. Although raised urinary  $\alpha$ -FP levels have been reported in a fetus with congenital nephrosis,<sup>2</sup> gross selective intrauterine proteinuria has not, to our knowledge, been reported.

The pathological diagnosis in this case could not be made by conventional histological methods but only by electron microscopy of the deeper, more mature glomeruli. Since this is a difficult diagnosis complicated by the process of glomerulogenesis, there is a real danger that such cases will be dismissed as being false-positive for neural tube defect. An attempt should therefore be made to collect fetal urine from any apparently normal fetus aborted because of high liquor  $\alpha$ -FP values.

Urinary protein concentrations similar to those reported here will at least give a provisional diagnosis and encourage painstaking electron microscopic examination of the kidneys.

Congenital nephrosis is invariably fatal, usually in the first months of life, and, although it is relatively uncommon in Britain, other sporadic cases without family history will probably be identified by  $\alpha$ -FP measurements.

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## Preventing thromboembolism after myocardial infarction: effect of low-dose heparin or smoking

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### Summary

**A trial of low-dose subcutaneous heparin to prevent thromboembolic complications after myocardial infarction was carried out in 78 patients. Of the 37 heparin-treated patients only two (5%) developed evidence of leg vein thrombosis, while 14 (34%) of the 41 controls did so, and five controls developed pulmonary emboli. Leg vein thrombosis developed in 12 (50%) of the 24 controls who did not smoke cigarettes but in only two (13%) of the 17 controls who were cigarette smokers. Non-smokers who have a myocardial infarction should be given low-dose heparin subcutaneously to prevent leg vein thrombosis and pulmonary embolism.**

### Introduction

Leg vein thrombosis, as detected by the fibrinogen uptake test, complicates myocardial infarction in about a third of patients.<sup>1-3</sup> Pulmonary infarction occurs in some 10-15% of patients and probably causes death in about 3-6%.<sup>4-6</sup>

These complications can be effectively prevented by prophylactic heparin in therapeutic doses,<sup>2,7</sup> but this carries the risk of haemorrhagic complications. These complications are avoided with low dose heparin prophylaxis given subcutaneously, but it is not yet established whether such treatment prevents leg vein thrombosis after myocardial infarction.

In a previous study,<sup>8</sup> we reported that cigarette smoking was also associated with a decreased incidence of leg vein thrombosis after myocardial infarction. The present study was therefore made to examine the efficacy of low-dose heparin prophylaxis

and to re-examine the relation of thrombosis to cigarette smoking.

### Patients and methods

All patients admitted to the coronary care unit at Westminster Hospital were considered for the study. The protocol excluded patients with severe hypertension or evidence of an active peptic ulcer or who had had a cerebrovascular accident, but no such patients were admitted during the period of the trial. The patients were allocated to a control or a heparin prophylaxis group on the basis of random number selection from a sealed envelope.

All the patients were examined for leg vein thrombosis on alternate days for two weeks by clinical observation and by the fibrinogen uptake test. The clinical results were recorded by the doctor (PM) in charge of the coronary care unit, but the fibrinogen scans were recorded by the technician in our lung function laboratory and he did not know whether the patients were receiving heparin prophylaxis or not.

The fibrinogen uptake test was performed according to the method of Kakkar *et al*.<sup>9</sup> Leg vein thrombosis was diagnosed only if there was a difference in count of 20% between adjacent positions on the same leg or similar positions on the two legs. The initial dose of <sup>125</sup>I-labelled human fibrinogen (Radiochemical Centre, Amersham) was given as soon as possible after admission and, if necessary, repeated after 10 days to maintain the level of radioactivity.

### Results

Eighty-one patients entered the study. Three were subsequently withdrawn because the diagnosis of myocardial infarction was not confirmed. Only one of the patients died before the end of the two-week study. She was a control patient who developed leg vein thrombosis and clinical evidence of a pulmonary embolism. She died on the seventh day, probably as a result of further pulmonary embolism, but no necropsy was permitted to confirm this. The two groups (table I) were equally matched for known high risk factors—that is, age over 70 years and presence of cardiac failure. There were more patients with varicose veins in the control group, but none of these developed a leg vein thrombosis.

Of the 37 patients given heparin prophylaxis only two (5%) developed evidence on the fibrinogen uptake test of a leg vein thrombosis. One had had a cardiac arrest and a cut down done on a vein, and the fibrinogen test was subsequently positive on that side, prob-

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