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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Paediatric Research Unit, the Prince Philip Research Laboratories, Guy's Hospital Medical School, London SE1 9RT

A H FENSOM, BSC, PHD, biochemist

P F BENSON, MD, FRCP, reader in clinical biochemical genetics

Department of Obstetrics and Gynaecology, King's College Hospital, Denmark Hill, London SE5 8RX

C H RODECK, BSC, MRCOG, lecturer

S CAMPBELL, FRCOG, professor

Queen Elizabeth Hospital for Children, Hackney Road, London E2 8PS, and the Mothers' Hospital (Salvation Army), London E5 8EN

J D M GOULD, MB, BSC, senior registrar (present address: Hospital for Sick Children, Great Ormond Street, London WC1N 1EH)

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

Comment

This patient fulfilled the criteria of Wright's² category of "probable gonococcal arthritis" (mucosal gonorrhoea, recent exposure, and response to antigonococcal treatment). He was genitally asymptomatic, a feature of men with the gonococcal-arthritis syndrome.³ This diverted attention from the source of the infection and delayed diagnosis. Diagnosis can be further hindered by arthritis after effective genital therapy⁴ and extragenital infection.⁵ The response to penicillin is excellent. The strains producing gonococcaemia are almost always very penicillin sensitive. The ESR is invariably raised in these patients.² In this patient it became normal after effective treatment (table).

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British Military Hospital, Münster, BFPO 17

DERMOT MURRAY, MB, MRCP, Lieutenant-Colonel, RAMC

Oral contraceptives and diabetes mellitus

Many women who take an oral contraceptive have a disturbed carbohydrate metabolism which has been likened to the steroid diabetes seen during corticosteroid administration.^{1,2} Although the metabolic changes are reversible in most women after they stop the contraceptive, long-term usage might increase the risk of clinical diabetes mellitus. We present the findings of two major prospective surveys of oral contraception in the United Kingdom—namely, the Royal College of General Practitioners' study and the Oxford/Family Planning Association study—both of which began in 1968 and have been fully described elsewhere.^{3,4}

Studies and results

The table shows the distribution of reports of all cases of diabetes mellitus diagnosed for the first time during the course of the Royal College of General Practitioners' study up to June 1978. Cases first diagnosed during pregnancy have been excluded together with the associated periods of observation. The cases are categorised according to their contraceptive state at the time of diagnosis. There is no material difference in the frequency of reporting of diabetes mellitus between contraceptive takers (women who have used oral contraceptives continuously during the period of observation), ex-takers, and controls. Bias arising from differences between the contraceptive categories in respect of diagnostic criteria, patient reporting, or loss of patients to

follow-up is unlikely to have concealed a real excess in incidence of diabetes in takers.³ Risk factors for diabetes were not recorded when the 46 000 women were recruited for observation in 1968-9, and cannot now be obtained for the total study population. But we have investigated whether a family history of diabetes or a history of bearing heavy babies was associated with the contraceptive method in the 48 diabetic patients under analysis. We were able to obtain further information in respect of 37. A family history of diabetes occurred in 56% (10 patients) of those who had ever used contraceptives and 53% (10 patients) of controls. A baby weighing more than 8 lb (3629 g) occurred in 67% (12 patients) of "ever-users" and 63% (12 patients) of controls, while a baby weighing more than 9 lb (4082 g) occurred in 33% (6 patients) and 32% (6 patients) respectively. These data, though less than ideal, do not suggest that use of an oral contraceptive was influenced by a knowledge of the risk of diabetes in our study population.

The distribution of all newly diagnosed cases of diabetes mellitus referred to hospital during the Oxford/Family Planning Association study up to December 1977 is shown in the table. The cases are categorised according to their contraceptive state at entry to the study. The data are few, but they do not suggest any increase in the hospital referral rate for diabetes mellitus in oral contraceptive users compared with users of other contraceptive methods. Although the overall rate appears to be only about half as great as in the RCGP study, we believe that ascertainment of cases is complete. This finding may indicate that not every new diabetic in the age group concerned is referred to hospital, although there are several other differences in the study populations and methods which could account for the discrepancy.

Comment

Muck⁵ observed a total of 133 women who had used oral contraceptives for three to 12 years. A pathological reduction in glucose tolerance occurred no more frequently in this group than in a control group. Clinical diabetes was diagnosed in only one patient and subclinical diabetes in two patients taking oral contraceptives. Similar negative results were observed in 82 women who had taken oral contraceptives for one to four years.²

While it is still desirable to monitor oral contraceptive takers whose medical and family history suggest an increased likelihood of developing diabetes, the present results, based on substantial long-term oral contraceptive usage, do not support the belief that this contraceptive method increases the risk of diabetes mellitus.

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Royal College of General Practitioners, Manchester Research Unit,
8 Barlow Moor Road, Manchester M20 0TR

SALLY J WINGRAVE, BA, MBIOL, research assistant

CLIFFORD R KAY, MD, FRCP, director

University of Oxford, Department of Social and Community
Medicine, 8 Keble Road, Oxford OX1 3QN

MARTIN P VESSEY, MD, FFCM, professor

Reported first occurrences of diabetes mellitus in women studied in two surveys of oral contraception

RCGP STUDY (By method of contraception at diagnosis*)

	Takers		Ex-takers		Controls		Ratio of standardised rates	
	No observed	Standardised rate (TWY)	No observed	Standardised rate (TWY)	No observed	Standardised rate (TWY)	Takers: controls	Ex-takers: controls
	12	0.19	9	0.19	27	0.24	0.80 (0.43-1.25)†	0.79 (0.56-1.60)†
Periods of observation (WY)	67 990		42 623		111 252			
OXFORD/FPA STUDY (By method of contraception at entry*)								
	Oral		Diaphragm		IUD		Total	
	No observed	Standardised rate (TWY)	No observed	Standardised rate (TWY)	No observed	Standardised rate (TWY)	No observed	Standardised rate (TWY)
	4	0.08	5	0.17	1	0.06	10	0.10
Periods of observation (WY)	54 900		25 276		17 868			

*Indirectly standardised for age, parity, cigarette consumption, and social class.

†95% confidence limits.

TWY = Thousand women-years. WY = Women-years.