patients with coagulopathy. We have been using a combination of high-concentrate thrombin preparation (5000 units/vial; Warner-Lambert) with gingival packing. About 5000 units of the thrombin preparation are applied directly to every dental socket and bleeding area. After application, fibrin precipitated on the bloody surface comes into contact with the preparation and the area is immediately filled with a firm coagulum and some intact thrombin powder stays on the surface of the coagulum. The coagulum appears firm, and blood oozing from the bottom of the tooth socket is coagulated by the residual thrombin. After this, gingival packing (eg, protection of the socket with a stent) was done.

CLINICAL APPLICATION OF HIGH-CONCENTRATE THROMBIN PREPARATION

| Age, sex | Teeth extracted* | Procoagulant activity of FVIII or FIX (%) | Local treatments required† | Replacement treatments required |
|---|---|---|---|---|
| *Haemophilia A* | | | | |
| 9, M | E \| | <1 | 1 | 0 |
| | ED\|D | <1 | 4 | 0 |
| 10, M | Bleeding of C \| E | 1·4 | 0 | 0 |
| 11, M | \|E | <1 | 2 | 11 |
| 20, M | \|8 | <1 | 0 | 32 |
| 46, M | \|8 | 3·4 | 4 | 0 |
| 72, M | 54321\|124 | 6·5 | 0 | 0 |
| *Factors VIII and V deficiency* | | | | |
| 30, M | 8 \| | 2<br>21·5 (V) | 4 | 0 |
| *Haemophilia B* | | | | |
| 9, M | D \| | <1 | 0 | 0 |
| | ED\| | <1 | 0 | 0 |
| | \|E | <1 | 1 | 0 |
| 23, M | \|58 | <1 | 2 | 3 |
| | 8 \| | <1 | 2 | 0 |
| *von Willebrand disease* | | | | |
| 26, M | \|4<br>6\|<br>\|678 | 30 | 3 | 0 |
| 39, F | 5\| | 36 | 0 | 0 |
| 25, F | \|8 | 2 | 0 | 0 |

*Location: A–E = deciduous, 1–8 = permanent; quadrants indicated to show upper L, upper R, lower L, lower R. †Number of treatments.

This approach resulted in rapid and complete coagulum formation. In three cases (see table) infusions of factor concentrates were required when topical coagulation was not satisfactory. This combined gingival packing following a single application of the thrombin preparation was kept in place for about two weeks until the wound healed. In all cases healing was excellent when the packing was removed.

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## A POTENTIAL HAZARD OF U 100 INSULIN SYRINGES IN DIABETICS ON CAPD

SIR,—Insulin-dependent diabetics on continuous ambulatory peritoneal dialysis (CAPD) often inject insulin directly into the peritoneal dialysate bag via an injection tube about 2·5 cm long which is separate from the connection site.[1] This technique is not only more convenient but also may be a more "physiological" route for insulin administration.[2] If a standard 1 ml syringe and a 21 gauge 40 mm needle are used the insulin enters directly into the dialysate and is easily mixed by inverting the bag. However, the new 100 U/ml diabetic syringe has a short non-detachable needle which barely penetrates the injection bung, and the insulin is retained in the dead-space between the bung and the bag. Thorough mixing becomes almost impossible, and such patients are very likely to receive suboptimal doses of insulin. We suggest that diabetic CAPD patients using the intraperitoneal route of insulin administration should continue to use a standard 1 ml disposable syringe and a 40 mm length needle to avoid this potential hazard.

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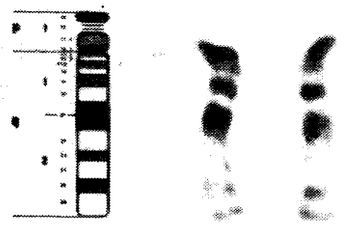
## PRADER-WILLI SYNDROME AND PRENATAL DIAGNOSIS

SIR,—A proportion of children with Prader-Willi syndrome have been reported to show a chromosomal deletion on the number 15 chromosome at the q11–13 band region.[1] Our laboratory has examined the amniotic fluid of a woman who presented to the pregnancy registration unit at this hospital at the age of 39. The family history revealed a sibling who had clinical signs and the diagnosis of Prader-Willi syndrome, but who did not exhibit the described deletion. It has even been suggested that this is an event which selectively affects the paternal chromosome 15 during gametogenesis.[2] Amniocentesis was done because of late maternal age and, besides routine karyotyping, an attempt was made to delineate the fine structure of chromosome 15. No deletion was found (see figure).



**Fine structure of chromosome 15.**

The mother was informed that no chromosomal defect could be seen and that the deletion associated with some cases of Prader-Willi was not present. She decided to continue the pregnancy. With careful techniques it may be possible to offer prenatal diagnosis for Prader-Willi deletion syndrome.

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## ANTENATAL DIAGNOSIS OF COMBINED XANTHINE AND SULPHITE OXIDASE DEFICIENCIES

SIR,—Combined xanthine oxidase and sulphite oxidase deficiencies result from a deficiency in the molybdenum-containing cofactor common to these enzymes. Affected children have severe encephalopathy, associated with myoclonic jerks, cerebral atrophy, and dislocated lens. Biochemically they present with an accumulation of sulphite and S-sulphocysteine due to sulphite oxidase deficiency, and a severe defective production of uric acid

1 Ledbetter DH, Riccardi VM, Airhart SD, et al. Deletions of chromosome 15 as a cause of Prader-Willi syndrome. *N Engl J Med* 1981; **304**: 325–29
2. Butler MG, Palmer CG. Parental origin of chromosome 15 deletion in Prader-Willi syndrome. *Lancet* 1983; i: 1285–86.

with raised urinary xanthine levels due to xanthine oxidase deficiency.[1] No effective treatment is available. We have diagnosed this condition in utero.

The index case[2] had early feeding refusal, and by 3 months of age had severe progressive encephalopathy. The diagnosis was suspected on the basis of low serum (<10 μmol/l) and urinary (0–0·4 mmol/g creatinine) urate levels, sulphituria, and S-sulphocysteinuria (1·4–7·2 mmol/g creatinine). Sulphite oxidase and xanthine oxidase deficiencies due to an absence of hepatic molybdenum cofactor were demonstrated.[3] She died at 3 years of age.

A normal boy was born after a second pregnancy during which amniotic fluid analysis at 18 weeks did not show S-sulphocysteine accumulation. The amniotic cell sulphite oxidase activity was in the normal range (see table).

AMNIOTIC FLUID ANALYSES

| — | S-sulphocysteine (μmol/l) | Sulphite oxidase (milliunits/mg soluble protein) |
|---|---|---|
| Controls | <2 (n=4) | 4·4–8·0 (n=5) |
| Pregnancy 2 | <2 | 8·4, 8·7 |
| Pregnancy 3 | 32 | None detected (n=2) |

During the third pregnancy the amniotic fluid, sampled at 17 weeks, contained increased levels of S-sulphocysteine. This was confirmed by an undetectable sulphite oxidase activity in cultured amniotic fluid cells (see table). The karyotype was 47XY trisomy 21. A prostaglandin-induced abortion was decided upon.

Our data demonstrate that positive and negative prenatal diagnosis is possible in sulphite oxidase deficiency due to an absence of molybdenum-containing cofactor. The demonstration of S-sulphocysteine accumulation in amniotic fluid seems to be a very reliable method for a rapid diagnosis of this condition.

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## DETECTING THE DUCHENNE CARRIER BY ULTRASOUND AND COMPUTERISED TOMOGRAPHY

SIR,—We were surprised that Professor Rott and his colleagues (Nov 19, p 1199) found greatly increased echogenic activity of the muscle in carriers of Duchenne muscular dystrophy (DMD). Their illustration resembles the changes we have seen in cases of muscular dystrophy and other neuromuscular disorders[4,5] and is at variance with the very slight changes we have observed with ultrasound in carriers and also with the minor and focal pathological changes one usually finds in the muscle.[6] Only about 10% of obligate carriers have overtly recognisable pathological change on light microscopy, whereas about 80% show significant deviation from controls in fibre diameter, fibre type proportion, or internal nuclei, which would not be expected to show up on ultrasound imaging.

Was the case illustrated representative of the five with increased echogenic activity and was the control scan done at the same time and with the same machine settings? The brightness of the image can be readily changed by altering the setting and because of this we always relate the increase in echo from the muscle to the corresponding decrease in bone echo. In children with advanced dystrophy the muscle echo increases markedly, whereas the bone echo disappears. In the carrier illustrated by Rott et al the muscle echo is markedly increased but the bone echo paradoxically also shows an increase in comparison with the control, which suggests an overall increase in brightness of the image.

If imaging techniques, such as ultrasound of muscle, are to be used to give genetic counselling in relation to X-linked muscular dystrophy we think it is essential to have very rigid biological controls and also some means of measuring the extent of change observed.

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## LISTERIOSIS AND PREGNANCY

SIR,—A 1980 *Lancet* editorial[1] and subsequent correspondence[2] alluded to a higher incidence of perinatal infection with *Listeria monocytogenes* than the 1 in 37 000 births reported by the Communicable Disease Surveillance Centre (1978). We can confirm this view: seven cases of perinatal listeriosis were diagnosed in the twelve months from June, 1982, at St Mary's Hospital, Manchester, where 4600 babies are delivered annually.

Infection by *L monocytogenes* is sought when the mother presents with an influenza-like illness, when there is evidence of intrauterine infection or cervical infection, or with unexplained intrauterine death. Only one of the positive cultures was obtained from a woman with a history of an influenza-like illness. Two cases were diagnosed by liquor culture from women with intrauterine infection following premature rupture of membranes and both were successfully treated. One case of intrapartum infection was attributed to listeria on account of culture from the gastric aspirate of the baby who developed signs of infection. Four cases were cultures from stillborn babies and in two of the cases mothers and placenta were listeria positive. In one case a mother delivered one macerated stillborn twin, which cultured listeria from fetal skin, and another perfectly normal healthy baby. In none of the four stillbirths were there any other apparent factors contributing to the fetal death.

If we are to continue to achieve reduction in the perinatal morbidity and mortality, organisms such as *L monocytogenes*, which have previously been considered rare and of low pathogenicity, need to be sought with greater vigilance. It is essential that any patient suspected of having listeriosis should be discussed with the microbiologist since different techniques are required for isolation and culture of the organism and routine incubation for listeria would be counterproductive. The organism is not unduly difficult to culture in the appropriate environment but behavioural patterns are not always classical. In the cases reviewed the morphology, cultural characteristics, and biochemical reactions of all the isolates were typical of their species, although not all of them produced haemolysis and in some cases motility was not obvious.

Even in the event of diagnosis of listeria after intrauterine death has occurred it is of no mean consolation to the parents to know that the cause of their tragedy may be avoided in future.

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