by its characteristic pattern of pulsatile arterial flow and constant venous flow. The waveforms were defined as abnormal if shifts in frequency at the end of diastole were absent in recordings obtained from three different points on the maternal abdomen. A sample of fetal blood was taken from the umbilical vein by cordocentesis, and the oxygen tension and pH were determined (figure).

The degree of fetal smallness was expressed as the number of standard deviations by which the observed abdominal circumference differed from the normal mean for gestational age, and the severity of hypoxia was expressed as the difference between the oxygen tension observed and the normal mean for gestational age.⁴ The correlation between the degree of fetal smallness and the pH of blood from the umbilical vein ($r = -0.095$) or the severity of fetal hypoxia ($r = -0.02$) was not significant. Seven fetuses had normal oxygen tensions and pH, 25 were hypoxic, five were acidotic, and 22 were both acidotic and hypoxic.

Comment

Increased impedance to blood flow in the umbilical artery, as shown by the absence of frequencies at the end of diastole, seems to be a good marker of fetal asphyxia. As all the patients in this study had been referred, and therefore preselected, we cannot comment on the

prevalence of this marker in fetuses that are small for gestational age.

The absence of significant correlation between the degree of smallness of the fetus and hypoxia or acidosis shows that uteroplacental insufficiency is not the only cause of small fetal size. Moreover, many babies that are growth retarded because of uteroplacental insufficiency have birth weights that are within the normal range for gestational age.⁵ If waveforms of flow velocity in the umbilical artery prove to be as useful a marker of prenatal asphyxia in well grown fetuses as they are in small fetuses they may replace measurement of fetal size for the antenatal prediction of fetal asphyxia. Missed diagnoses of fetal hypoxia might account for some "unexplained" stillbirths.

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Recurrent early miscarriage and polycystic ovaries

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The aetiology of recurrent miscarriages (three or more consecutive spontaneous abortions) is poorly understood. A recent trial suggested that the cause may be immunological,¹ but the polycystic ovary syndrome may also have a role. Spontaneous abortions occur in about 30% of pregnancies after induction of ovulation in women with the syndrome regardless of the treatment used. Because polycystic ovaries are also found in women who ovulate^{2,3} we investigated a possible association between polycystic ovaries and recurrent miscarriages in women with spontaneous ovulatory cycles. As defects in the luteal phase, which may occur in women with polycystic ovaries, may be related to miscarriage we also assessed progesterone secretion.

Subjects, methods, and results

We studied 56 consecutive patients presenting to the recurrent miscarriage clinic; all ovulated spontaneously. We recorded their menstrual histories,

their heights and weights, and whether they had acne or hirsutism. Ultrasonography of the pelvis was performed, and polycystic ovaries were identified.² Blood was taken for measurement of luteinising hormone concentration. A control group of 11 parous volunteers with no history of disturbance of their ovulatory cycles or recurrent miscarriages were examined similarly. Early morning urine specimens were collected daily throughout an ovulatory cycle from 30 women who had had recurrent miscarriages, and the concentration of pregnanediol-3 α -glucuronide, the major urinary metabolite of progesterone, was measured. Values were compared with those obtained in five controls and in 20 cycles in nine normal, non-parous women (table).

Forty six (82%) of the 56 women who had had recurrent miscarriages, had polycystic ovaries compared with two (18%) of the 11 parous women ($\chi^2 = 15.5$, $p < 0.001$). Age, body mass index, and length of the ovulatory cycle were not significantly different among all the groups of women. Six of the 46 patients with recurrent miscarriages and polycystic ovaries had mild or moderate hirsutism and 13 had acne, whereas only one of the 10 women with recurrent miscarriages and normal ovaries had hirsutism (and acne).² None of the parous control women was hirsute or had acne. The serum luteinising hormone and mid-luteal pregnanediol-3 α -glucuronide concentrations were normal in all of the women with recurrent miscarriages.

Median (range) values for clinical features and hormone concentrations in women with recurrent miscarriages and controls

	Women with recurrent miscarriage		Controls	
	Normal ovaries (n=10)	Polycystic ovaries (n=46)	Parous (n=11*)	Non-parous (n=20†)
Length of menstrual cycle (days)	28 (26-32)	30 (21-57)	29 (26-33)	28 (26-30)
Body mass index (kg/m ²)	21 (19-24)	22 (18-42)	23 (20-25)	
Luteinising hormone‡ (IU/l) (normal range 0.8-11.5)	4.9 (2.8-7.0)	5.9 (1.7-11.1)	4.3 (2.1-6.9)	
Pregnanediol-3 α -glucuronide§ (μmol/l)	16.5 (5.9-29.0)	15.6 (5.0-69.2)	18.7 (16.5-35.6)	16.8 (4.1-21.8)

*Except for measurements of pregnanediol-3 α -glucuronide, where n=5.

†Twenty cycles in nine controls.

‡Excluding measurements obtained in mid-cycle—that is, in presence of follicle ≥ 16 mm in diameter.

§Derived from average of three mid-luteal measurements in each subject.

Comment

The prevalence of polycystic ovaries in the women who had had recurrent miscarriages was high (82%). Although the number of parous control women was small, their prevalence of polycystic ovaries (18%) was similar to that observed in a much larger population of normal women (22%).³ The normal serum luteinising hormone and urine pregnanediol-3 α -glucuronide concentrations suggest that the endocrine abnormalities typical of women with polycystic ovaries who do not ovulate did not occur in the women we studied who ovulated spontaneously. This, however, is consistent with our previous findings that luteinising hormone concentrations are usually normal in women with polycystic ovaries who ovulate but are hirsute, and that three quarters of the women in the normal population who are diagnosed as having polycystic ovaries have normal serum luteinising hormone concentrations.^{2,3}

A raised serum luteinising hormone concentration may be a risk factor for early miscarriage.⁴ Women with polycystic ovaries who conceive after induction of ovulation with pulsatile luteinising hormone releasing hormone have an increased rate of early loss of pregnancy compared with hypogonadotrophic patients. Serum luteinising hormone concentrations were higher, particularly during the follicular phase, in women with polycystic ovaries who had an early pregnancy loss compared with those whose preg-

nancies progressed to term.⁴ Serial blood sampling and ultrasonography are required to establish whether patients who have recurrent miscarriages have inappropriately high luteinising hormone concentrations at some particular point in their menstrual cycle.

Another possibility is that the increased risk of early miscarriage in women with polycystic ovaries results from an abnormal endometrial environment in early pregnancy.⁵ Endometrial changes may in turn be linked to the abnormal production of immunoglobulins by decidual cells thought to occur in women who have recurrent miscarriages.

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Response of human skeletal muscle to the anabolic steroid stanozolol

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As part of a larger trial assessing the value of stanozolol in preventing postoperative deep vein thrombosis¹ we studied whether stanozolol increased the size of human skeletal muscle fibres.

Patients, methods, and results

We studied 16 patients undergoing elective abdominal surgery, eight of whom received 10 mg stanozolol orally each day for 14-21 days before operation as part of the larger trial.¹ Patients were matched in pairs for age, sex, and body build (percentage overweight for height was calculated from tables giving expected weight for height). None of the patients had a history of abdominal operations, recent weight loss, endocrine disorder, or treatment with corticosteroids, and none had a malignant condition. Consent was obtained from the patients and the trial was approved by the hospital ethical committee.

A biopsy specimen of rectus abdominis at least 1 cm long was taken at operation (avoiding tendinous insertions) before diathermy or retractors were used. These were processed according to a routine protocol, and serial cryostat sections were stained with haematoxylin and eosin, reduced nicotinamide-adenine dinucleotide diaphorase, Gomori's trichrome, and adenosine triphosphatase preincubated at pH 9.4, 4.63, and 4.35.² An image based analysis system (IBAS 1, Konitron Bildanalyse System) was used to measure the smallest diameter of the myofibres (the greatest distance across the lesser aspect of the fibres in the

section stained with adenosine triphosphatase and preincubated at pH 9.4).² At least 200 type I fibres and 200 type II fibres were measured in each sample except one, in which only 151 type I fibres were present. All of the fibres within fascicles chosen at random were measured. The variability in measurements between operators was found to be less than 3%. A paired Wilcoxon rank test was performed on the mean diameters of the fibres in the two groups.

The diameters of type I fibres were significantly larger ($0.02 < p < 0.005$) in the patients treated with stanozolol compared with the controls (table). There was no significant difference ($p > 0.05$) between the type II (a and b) fibres in the treated and control groups. Type IIc fibres were present in varying and small numbers in the samples (0.4% of the total), but no statistical analysis was performed on these.

Comment

These results show an increase in the bulk of type I (oxidative) fibres in response to the anabolic steroid stanozolol. Changes in the size of muscle fibres are most common in type II fibres, which atrophy with disuse, malnutrition, and excess glucocorticoids and show hypertrophy after "strength building" exercise. Arduous long term physical exercise leads to an increase in the bulk of type I fibres, both by hypertrophy of fibres and by transformation of fibre type³; and the oxidative capacity of the muscle increases concurrently.⁴ The bulk of fibres may also increase in certain diseases such as Duchenne muscular dystrophy, in which the composition of the hypertrophied muscle is abnormal.

The muscle we examined is not usually used in exercise. If, however, an increased bulk of type I fibres in other skeletal muscle increased its aerobic potential it might fatigue less readily. Any resulting increase in exercise might lead to secondary hypertrophy of type II fibres, improving performance and, incidentally, masking a predominant direct effect on type I fibres in

Mean diameters of type I fibres
(μ m) in pairs of patients and
controls matched for age, sex,
and body build

Patient no	Patients treated with stanozolol	Controls
1	44	33
2	46	47
3	56	44
4	40	39
5	62*	57
6	51	43
7	57	43
8	41	40

*Only 151 fibres were available for measurement in this sample.