XO/XY mosaicism in phenotypic males

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Abstract
Eight cases of 45 XO/46 XY mosaicism are described: four were phenotypic males. Karyotyping should be performed more frequently in short boys as growth hormone treatment and testicular biopsy, to screen for carcinoma in situ, are likely to be beneficial.

Though the phenotype of 45 XO/46 XY mosaicism is well recognised as variable, ranging from female with gonadal dysgenesis to virtually normal male,¹ most cases in the literature are reported as phenotypic females either as a variant of Turner's syndrome or with virilisation: only brief mention is made of phenotypic males with this karyotype.^{1 2} A recent report on a series of amniocenteses, however, reviewed 47 cases with XO/XY karyotype and known phenotype, of which 42 (89.4%) were apparently normal phenotypic males.³ This clearly suggests that the normal male phenotype with XO/XY mosaicism is underdiagnosed, as only short girls and those with ambiguous genitalia routinely have karyotypes in most clinics. We therefore reviewed our experience of children with the 45 XO/46 XY karyotype.

Methods and results
The karyotyping service serves a population of some 320 000 children. Karyotypes are routinely performed on all short girls and those with ambiguous genitalia, including most phenotypic males with hypospadias. There is no way of calculating the completeness of this

survey. Since 1981 to the present, 37 phenotypic females with 45 XO or other Turner mosaicism were diagnosed. Eight children were identified with the 45 XO/46 XY karyotype, of whom four presented as short boys, with some stigmata of Turner's syndrome and hypospadias or cryptorchidism (table). All the boys had phallic lengths within the normal range. Laparotomy was subsequently performed on two, for removal of mullerian duct remnants in one; unilateral streak ovary and mullerian tissue were identified in the other. All the palpable testes were scrotal and subject to regular expert examination.

Discussion
In our small series, four cases were detected in phenotypic males with some stigmata of Turner's syndrome and with minor abnormalities of external genitalia. A notable feature was growth retardation, supporting earlier reports.¹ Given the major bias of ascertainment suggested by Hsu,³ it seems probable that more short boys have covert XO/XY mosaicism. This raises several issues. It has recently been shown that girls with Turner's syndrome, including mosaic forms, respond to long term growth hormone treatment with enhanced predicted final height.⁴ Assuming the cause of growth failure is similar in these phenotypic males, then they also are likely to respond to growth hormone treatment. We propose a trial of growth hormone in these children. Thus as these children have a potentially treatable form of growth failure, these data suggest that karyotypes

Clinical features and karyotype

Case No	Age (years)	Presenting symptom	Height percentile	Bone age height	Bone age height SD	Karyotype	Gender of rearing	Clinical features
1	12	Short stature	<3rd	-2.28	-1.5	XO/XY	Male	Increased carrying angle, shield chest, right and left inguinal hernias, penoscrotal hypospadias, undescended testis (right), left mullerian duct and streak gonad
2	19	Short stature	<3rd	-1.24	-1.6	XO/XY	Male	Fish mouth, increased carrying angle, shield chest, mid-penile hypospadias
3	22	Short stature, pubertal delay	<3rd	-3.1	N/A	XO/XY	Male	Hypospadias, cryptorchid (left) with rudimentary ovarian tube, uterus, streak gonad, right testis in scrotum
4	3	Short stature	<3rd	-2.4	-0.6	XO/XY/47XY+18	Male	Shield chest, bilateral undescended testes, penoscrotal hypospadias, bifid scrotum
5	0.7	Ambiguous genitalia	25th	-0.2	-0.03	XO/X?Y	Female	Scotolised labia, virilised clitoris, single introital opening, shield chest, intra-abdominal testes
6	13	Short stature	<3rd	-1.43	-1.6	XO/XY	Female	Webbed neck, streak gonads with rudimentary uterus
7	26	Short stature, 1° amenorrhoea	3rd	-1.93	-0.5	XO/XY	Female	Increased carrying angle, streak gonads
8	12	Short stature	<3rd	+0.05	-1.9	XO/XY	Female	Webbed neck, shield chest, increased carrying angle, streak gonads

N/A: Not applicable.

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should be performed more frequently on short boys. Though it is debatable that all short boys should have a karyotype, certainly those with any stigmata suggestive of Turner's syndrome, with undescended testes, hypospadias, or with an unacceptable final height warrant one. More aggressive investigation may be necessary as Ayuso *et al* have reported the case of a phenotypic male with 46 XY karyotype from leukocytic cell lines but in whom the 45 XO cell line was observed in skin fibroblasts and gonadal tissue.² One last issue to consider is proper management of the testes. Obviously if the gonad is intraabdominal, it must be removed as it is likely to be a dysgenetic testis or streak gonad. Dysgenetic testes are presumed to be more prone to neoplastic transformation than streak gonads: Manuel *et al* calculated a tumour expectancy of over 70% by the third decade.⁵ It is not

clear, however, that palpable, descended testes really have such a high malignant potential.^{1 6}

Testicular biopsy before and after puberty, to detect carcinoma in situ, may be desirable and allow either early orchidectomy or bilateral irradiation if it is found.⁶

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Discovering anaemia at child health clinics

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Abstract

Children at three inner city child health clinics were offered haemoglobin estimation by fingerprick blood test when attending for immunisation against measles. Of the 98 immunised, 92 (94%) participated in the study, together with 58 other children. Anaemia (haemoglobin concentration <110 g/l) was found in 33 of 130 overall (25%), and in 17 of 44 Asian children (39%). The method of testing was acceptable to parents and staff.

Iron deficiency anaemia is common among toddlers.¹ The reason is usually dietary, and contributing factors include late weaning, use of ordinary cows' milk, and weaning on to a diet low in iron. It has important effects, including recurrent mild infections, poor weight gain, behavioural problems, and decreased mental performance, all of which may be helped by treatment with iron.²

It has been suggested that toddlers should be screened for iron deficiency,³ and the recent report of the Joint Working Party on Child Health Surveillance stated that screening for iron deficiency was probably desirable but further research is needed.⁴ The first question is whether routine blood sampling would be acceptable to parents. In this study we have looked at this, together with the feasibility of setting up a screening programme using haemoglobin estimation. We also calculated the incidence of anaemia in our community.

Subjects and methods

The study population comprised all children attending three inner city child health clinics

who were due to receive immunisation against measles and were aged 15–24 months during the six month study period.⁵

Invitation to participate was by letter accompanying the reminder about the immunisation appointment for children attending two of the clinics or by asking the parents when children attended for immunisation at the third. Facilities were available to explain the study to parents in various Asian languages. Signed parental consent was obtained. Children with known haematological disorders or diseases associated with anaemia were excluded.

We recognised that the study might have a detrimental effect on the measles immunisation rate. This was monitored during the study and it was decided to stop the study if an appreciable decrease occurred.

Capillary blood samples were taken by fingerprick, collected in 1 ml EDTA bottles and sent by routine collection to the hospital laboratory. Haemoglobin concentration (normal ≥ 110 g/l) mean corpuscular volume (normal 76–100 fl), and mean corpuscular haemoglobin (normal 27–33 pg) were measured.

A haemoglobin concentration of <110 g/l was considered as indicating anaemia, and the parents of these children were asked to attend the clinic and were given dietary advice (with the aid of the community dietician). Those with haemoglobin concentrations of <95 g/l were given oral iron supplements and further investigations including electrophoresis and estimation of serum ferritin concentration undertaken. All anaemic children were followed up to ensure that they responded to diet or iron. If another cause of anaemia or lack of response was found, appropriate follow up was arranged.

The study was undertaken with the usual

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