During expiration the flows required to close the Volumatic valve were slightly higher than those required to open the valve, but lie still in a range easily achievable by infants. The flows required to close the Nebuhaler valve were significantly higher than those required to close the Volumatic valve. In the vertical position the expiratory flows averaged 73.9 ml/second (range 69.8–81.5 ml/second) for the Nebuhaler and 24.3 ml/second (range 11.7–31.2 ml/second) for the Volumatic. These flows required for valve closure in Nebuhaler may not be achievable by infants. The reported values for peak tidal expiratory flow in normal infants (5 to 11 months of age) are 70 ml/second.⁵ During most of expiration the flow is likely to be considerably less, especially in infants with obstructive airway diseases. Infants with expiratory flow limitation during tidal breathing can not increase expiratory flows without increasing lung volume. Failure to close the spacer valve exposes the infant to the risk of rebreathing.

The intradevice and interdevice coefficients of variation for both types of spacer devices are acceptable. The higher coefficients of variation found during expiration in the Volumatic spacer device than found for Nebuhaler are interesting but of no clinical importance. Thus the intradevice or interdevice variability is not an additional factor to be considered when using airspacers in infancy.

Although up to 100 activations of a metered dose inhaler did not result in an increase in the pressure or flow required to open the spacer valve, prolonged use without adequate cleaning could result in the valve becoming 'sticky', thus requiring greater pressures and flows to operate the valve. Furthermore, the simulated inspiration and expiration in the present study were performed using room air. It is possible that humid expired air could cause the valve to become 'sticky'.

In conclusion, our results show that the flows required to open the valves in the Volumatic and Nebuhaler spacer devices are within the range of reported values that can be achieved even by flow obstructed infants. Flows required to close the valve, however, may not lie within reported physiological limits for normal tidal breathing of even healthy infants. Further studies, with particular reference to the flows generated during tidal breathing, and the orientation of the device, are needed to evaluate the possible role of aerosol holding chambers in the treatment of wheezy infants.

We thank Astra Pharmaceuticals and Allen and Hanburys for supplying the devices. The assistance of M Hibbert in performing statistical calculations is gratefully acknowledged.

FHS was supported by grants from the Swiss National Research Foundation (No 83.337.0.86) and the Swiss Academy of Medical Sciences.

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Accepted 10 March 1989

Polycystic ovary syndrome in a virilised, premenarcheal girl

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SUMMARY A premenarcheal girl aged 12 years presented with an abdominopelvic mass and virilisation. A large ovarian cyst was removed at laparotomy. A histological diagnosis of polycystic ovarian syndrome was made, with no evidence of an associated masculinising tumour.

Polycystic ovary disease was initially described by Stein and Leventhal in 1935 as comprising the triad of obesity, hirsutism, and amenorrhoea in women with bilaterally enlarged polycystic ovaries.¹ In more recent years the term 'polycystic ovary syndrome' has come to be applied to a broad range of clinical features including hirsutism, secondary amenorrhoea or other menstrual irregularities,

infertility, obesity, and enlarged ovaries. Frank virilisation is rare and the syndrome is usually seen in the third or fourth decades of life, but there are isolated reports of it in premenarcheal girls. This report describes a 12 year old girl with pronounced virilisation, a large ovarian cyst, and polycystic changes in both ovaries.

Case report

A girl presented at the age of 12 years and 5 months with several months history of persistent abdominal swelling. She was otherwise asymptomatic and she was premenarcheal.

On examination her height and weight were on the 75th centile for chronological age, and she had normal blood pressure. She had signs of virilisation, namely mild hirsutism, a deep voice, acne, and an enlarged clitoris. A large firm mass arising from her pelvis and extending to the level of her umbilicus was palpable. Her breast development was Tanner stage 2 and pubic hair stage 3.

Investigations showed that she had a normal female karyotype. Bone age was advanced at 15 years; skull radiographs were normal. Her endocrinological investigations are summarised in the table. The plasma testosterone concentration was considerably raised, and the androstenedione concentration was also raised. The other measurements were within normal limits for her pubertal stage. A large right sided ovarian cyst was shown on ultrasonography.

At laparotomy a large cyst, about 15 cm in diameter was found arising from the right ovary. The left ovary was slightly enlarged but otherwise normal. A right salpingo-oophorectomy and a wedge resection of the left ovary were carried out.

On histological examination by two independent pathologists no evidence of an androgen secreting tumour was found, and both ovaries had a polycystic appearance.

Immediately after operation the plasma testosterone concentration fell to 2.6 nmol/l, but then rose again over the next few months. High dose

dexamethasone failed to suppress androgen concentrations. Buserelin, a synthetic analogue of luteinising hormone releasing hormone, was given intranasally for three weeks and this resulted in a suppression of her plasma androgen concentration, which was sustained for some months. Her plasma testosterone concentration subsequently rose again, however, to 5.7 nmol/l and a further ultrasound scan showed polycystic changes in her remaining ovary. In view of these findings and her lack of breast development she was given a low dose combined oral contraceptive containing ethinylloestradiol 30 µg and desogestrol 150 µg (Marvelon, Organon). Six months later her plasma testosterone concentration had fallen to <0.7 nmol/l, and neither luteinising hormone nor follicle stimulating hormone were detectable in the serum.

Discussion

This patient had isolated polycystic ovary syndrome presenting with a pelvic mass and clinical signs of virilisation. An adrenal source of androgen excess was excluded by the failure of high dose dexamethasone to suppress plasma testosterone, and no ovarian tumour was found on histological examination. There was a temporary suppression of androgen concentrations while the patient was taking intranasal Buserelin: gonadotrophin releasing hormone agonists can suppress gonadotrophin secretion in patients with polycystic ovary syndrome.²

There are three unusual features about this case. Firstly, the degree of virilisation was greater than expected for a patient with polycystic ovary syndrome: the considerably raised concentrations of testosterone in this patient were more suggestive of an adrenal or ovarian tumour, but these were excluded.

The second unusual feature was the early age of onset of the disease and its timing in relation to puberty. Such a presentation at this age would again make an adrenal lesion or an ovarian neoplasm most likely. There are a few isolated reports of polycystic ovary syndrome occurring in premenarcheal girls without an associated ovarian tumour. Prunty *et al*, described a girl of 17 years who presented with primary amenorrhoea and severe virilisation.³ In 1972 Richmond *et al* reported a girl who presented at the age of 13 years and 2 months for investigation of hirsutism.⁴ She was premenarcheal with virilisation and acanthosis nigricans. Wedge biopsy specimens of both ovaries showed histological changes consistent with polycystic ovary syndrome but with no associated tumour. In this case the maximum plasma testosterone concentration on initial investigation

Table Summary of endocrinological investigations

	Patient's value	Normal range
Testosterone (nmol/l)	9.3	0.9-2.7
Androstenedione (nmol/l)	5.0	0.9-3.9
Luteinising hormone (IU/l)	9.0	5.6-13.6
Follicle stimulating hormone (IU/l)	6.0	2.4-7.7
Oestradiol (nmol/l)	0.21	0.03-0.22
17-OH progesterone (nmol/l)	2.0	0.4-4.2

was 4.9 nmol/l. Ovulation and regular menstruation were induced by treatment with clomiphene.

More recently, Rao *et al* reported a 12 year old girl with progressive hirsutism of nine months' duration.⁵ This patient was also premenarcheal with clinical signs of virilisation. Her plasma testosterone concentrations were initially measured on three occasions as being between 4.8 and 9.3 nmol/l. Both ovaries were enlarged on exploratory laparotomy, and bilateral wedge resections of the ovaries were carried out, which showed histological evidence of polycystic ovary syndrome but no tumour. In this patient the testosterone concentrations did not fall after operation, and she was treated successfully with an oral contraceptive.

Thirdly, polycystic ovary syndrome is usually characterised by some enlargement of the ovaries, but is rarely associated with large cysts. The patients in the reports above all had bilaterally moderately enlarged ovaries, but none had individual cysts of the size seen in our patient. This feature also suggests the possibility of associated malignancy, which was not found.

The pathophysiology of polycystic ovary syndrome is still not clearly understood. There are three main approaches to its treatment. Ovulation may be induced by various drugs including clomiphene citrate, human chorionic gonadotrophin, and pure follicle stimulating hormone; the older therapeutic approach of ovarian wedge resection is used much less often today. Antiandrogenic drugs such as cyproterone acetate may be used to reverse the

clinical features of masculinisation. Low dose oral contraceptives suppress gonadotrophin secretion and reduce ovarian secretion of androgen; they also reduce the adrenal production of steroids. In this patient an oral contraceptive successfully suppressed both testosterone and gonadotrophin concentrations.

In conclusion, this case and a few previously reported show that isolated polycystic ovary syndrome can be found in virilised premenarcheal girls. In such patients, however, an adrenal source of excess androgen or a virilising tumour of the ovary must be excluded.

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Accepted 15 February 1989

Successful treatment of a harlequin fetus

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SUMMARY We report the prolonged survival of a harlequin fetus who was treated with intensive supportive measures, emollients, and oral etretinate.

The Harlequin fetus is the severest of the congenital ichthyoses and is usually considered to be fatal.

Case report

A baby girl, who weighed 2360 g, was delivered at

38 weeks' gestation after a normal pregnancy. There was no relevant family history.

Her skin consisted of thick, yellow, leathery plaques separated by deep red cracks. There was ectropion of the eyelids and eclabion of the mouth. The ears were flattened and bound to the side of the head. The digits of the hands and feet were flexed and bound together by tight membranes. Examination of a skin biopsy by light and electron microscopy showed changes consistent with the clinical diagnosis of a harlequin fetus.

The baby was nursed in an humidified incubator and fluids were administered via an umbilical artery