BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 9 JUNE 1979

# What is to be done with the XYY fetus?

As prenatal chromosome analysis has become routine the selective termination of pregnancy has become widely accepted as a means of avoiding the births of at least some infants with Down's syndrome. When fetal chromosomal anomalies other than Down's syndrome are discovered in the course of prenatal diagnosis the justification for abortion depends on a careful assessment of the probable degree of handicap. Termination of pregnancy may be offered with confidence for chromosome anomalies consistently associated with multiple malformations and severe retardation—for example, 13 trisomy and 18 trisomy. Nevertheless, some other chromosomal anomalies may not always cause gross abnormality, and in the sex chromosome aneuploidies there may be a wide range from near normality to severe handicap. The degree of handicap is difficult to predict accurately in individual cases—though in practice termination is usually requested. One such sex chromosome aneuploidy, 47XYY, is a clear example of this problem.

When the XYY genotype was first recognised[1] it was thought to be of little practical importance. Nevertheless, the subsequent discovery of an excess of 47XYY men in maximum security hospitals[2] and several widely reported murder trials[3] have created a popular stereotype of the XYY man as a tall, mentally retarded, violent criminal. Most women would choose not to have such a son, and superficially the case for termination of the XYY fetus is strong. Indeed, the evidence drawn from a few highly selected individuals is striking: congenital malformations of the kidneys,[4] slowing of nerve conduction,[5] signs of minimal brain damage,[3] and EEG abnormalities[6] have all been described in association with the XYY genotype. In maximum security special hospitals about 3% of men are XYY,[7] and they are characterised by tallness,[2 7] reduced mean IQ,[3 8] and youth.[9] Their crimes are usually directed against property rather than people but are repeated and serious enough to have led to their incarceration. Furthermore, the evidence does not suggest that the social and domestic environments in which XYY men have been brought up are responsible for their behaviour.[10 11]

Examination of population frequencies shows, however, that this stereotype is representative of no more than a fraction of all XYY men. The birth incidence is thought to be about 1 1000 males,[12] and since there is no evidence of increased mortality the adult population frequency will be the same. Price[9] studied men in the four special hospitals in Britain during the three years 1972-4, and found 21 individuals with the XYY genotype out of a total of 885 men successfully karyotyped. This frequency of just over 2% is 25 times greater than the expected population rate. But there were about 20 million men of the relevant age groups in Britain at that time, so that in addition to the 21 XYY males in special hospitals there were another 20 000 in the general population. Clearly, only about one XYY man in every 950 is an inmate of a special hospital at any particular time. Chromosome surveys in psychiatric hospitals,[13] prisons, detention centres, borstals, and approved schools[14] have not shown any great excess of XYY males, and the risk that an XYY male will enter a special hospital at some time in his life seems to lie between 1%[15] and 3·5%.[12]

These statistics are reassuring, but the high frequency of XYY males in special hospitals remains to be explained. Possibly[9] any XYY man who finds himself in an ordinary psychiatric hospital is likely to be transferred to a special hospital, because normal psychiatric services cannot contend with a mentally ill and retarded male in late adolescence who is also above average size. But how far do XYY males as a whole differ from their XY peers? The answer to this question depends in part on the outcome of studies of XYY men found in the normal adult population.[8 16 17] In one "double-blind" study[16] psychologists appeared to be able to distinguish all the XYY men from normal XY controls, but in none of these studies did the men show any gross excess of criminality or of violent behaviour. In an Edinburgh study[18] 14 XYY boys have been randomly ascertained from the newborn population and are being followed prospectively without the parents knowing the precise chromosomal diagnosis. Relatively minor deviations from normal have been detected over one to 10 years. The boys tend to be taller, and to have a slight reduction in mean IQ score at the age of 4 (98·4 using the Stanford Binet scale compared with a control group with the rather high mean IQ of 115·7). Behavioural problems have been found in four of 11 XYYs compared with two out of 18 controls, but aggression was not an important feature, though it did occur occasionally in response to frustration. Delayed speech development was a little commoner than in controls, but speech improved with time. Broken bones and infections occurred more commonly in XYYs.

Unhappily, similar prospective studies at Harvard[19] were terminated after violent criticism from individuals representing "science for the people." Research into the genetic basis for behavioural disturbance was said to be unwarranted and to divert funds from more deserving programmes for social improvement. Furthermore, the investigators were forced to

obtain fully informed consent from the parents, who then knew that their child was an XYY. The attitude of the parents to their child was inevitably influenced by the widely publicised criminal stereotype.

A doctor dealing with a newborn XYY infant should probably avoid telling the parents about the child's XYY constitution until he is perhaps 2 to 4 years old,[18 20] thus allowing the parents and child to form a normal early relationship. But what is the correct course of action if XYY is discovered prenatally, when there is still a possibility of abortion? Many clinicians familiar with the facts would be strongly tempted not to tell the parents, and would allow the pregnancy to proceed to term. Medicolegal and other reasons[21 22] would compel others to tell the parents, but they would emphasise what they consider are the relatively small risks. Undoubtedly yet other clinicians would feel that the risks are high enough to justify abortion and would say so. But what if the parents then refuse to agree to an abortion? No general rule of counselling can be applied. The fertility and age of the couple, their expectations, resources, education, and emotional stability are all relevant. But the dilemma remains: what is to be done with the XYY fetus?


1 Sandberg, A A, *et al*, *Lancet*, 1961, **2**, 488.
2 Jacobs, P A, *et al*, *Nature*, 1965, **208**, 1351.
3 Borgaonkar, D S, and Shah, S A, in *Progress in Medical Genetics*, vol X, ed A G Steinberg and A G Bearn, p 135. New York, Grune and Stratton, 1974.
4 Machin, G A, *Clinical Genetics*, 1978, **14**, 370.
5 Wright, M O, *Clinical Science and Molecular Medicine*, 1973, **45**, 337.
6 Fenton, G W, *et al*, *British Journal of Psychiatry*, 1971, **119**, 185.
7 Jacobs, P A, *et al*, *Annals of Human Genetics*, 1967-8, **31**, 339.
8 Witkin, H A, *et al*, *Science*, 1976, **193**, 547.
9 Price, W H, in *Sex Offenders—a Symposium*, ed John Gunn. London, Special Hospitals Research Unit, Report No 14, 1979.
10 Price, W H, and Whatmore, P B, *British Medical Journal*, 1967, **1**, 533.
11 Ratcliffe, S G, and Evans, H J, *Lancet*, 1975, **1**, 1144.
12 Hook, E B, *Science*, 1973, **179**, 139.
13 Newton, M S, *et al*, *Clinical Genetics*, 1972, **3**, 215.
14 Jacobs, P A, *et al*, *Journal of Medical Genetics*, 1971, **8**, 49.
15 *Lancet*, 1974, **2**, 1297.
16 Noël, B, *et al*, *Clinical Genetics*, 1974, **5**, 387.
17 Zeuthen, E, *et al*, *Acta Psychiatrica Scandinavica*, 1975, **51**, 3.
18 Ratcliffe, S G, Axworthy, D, and Ginsborg, A, in *Birth Defects Original Article Series*, in press.
19 Hook, E B, in *Genetics and the Law*, ed A Milunsky and G J Annas, p 73. New York, Plenum, 1976.
20 Hamerton, J L, *American Journal of Human Genetics*, 1976, **28**, 107.
21 Goldenberg, R L, and Finley, S C, *Lancet*, 1978, **2**, 465.
22 Powledge, T M, and Fletcher, J, *New England Journal of Medicine*, 1979, **300**, 168.


# Saving asthmatics

Despite the familiarity of asthma to both doctors and patients it may be frightening and dangerous. Each year 1500 people die from asthma,[1] one-third of them below the age of 55 years.[2] How many of these people might have been saved? The answer to that question would be more obvious if treatment had already made an impact on the number of deaths from asthma. But in fact, apart from a period in the 1960s when the number of deaths was even higher, the mortality statistics have been largely unchanged for over 30 years. The unchanged death rate is a depressing reality to be set against the claims made for major advances in treatment including corticosteroids, cromoglycate, and selective β-adrenoceptor stimulants. Why young patients still die cannot yet be explained completely. The answer must await fuller understanding of the pathogenesis of severe asthma, but some practical improvements are surely possible.

Many patients who die from asthma do so outside hospital. Often death is unexpected, seeming to follow a fairly brief period of deterioration.[3] In such cases the patient may have been well but suddenly developed a fulminating attack of asthma, or he or she may have appeared to be well but in fact had had severe limitation of pulmonary function with little ventilatory reserve with which to withstand a further deterioration. Fulminating attacks undoubtedly occur,[4] and if susceptible patients (with "brittle" asthma) can be identified they require specialised supervision if fatal attacks are to be avoided. Most deaths occur, however, in patients whose illness has been underestimated by both themselves and their doctors. Major physiological abnormalities may be present when patients with asthma feel well and have no abnormal physical signs.[5] Furthermore postmortem studies of death from asthma have shown extensive pathological changes, including widespread mucus plugging in many cases, suggesting a relatively longer period of deterioration before death.[3 6] More recently, Bellamy and Collins[7] found that most of 44 adult patients admitted to hospital with acute severe asthma had been poorly controlled for a mean period of five weeks before a more rapid deterioration had finally led to their admission.

Most patients admitted to hospital with asthma—and probably many of those who die outside hospital—seem, then, to have a background of poor control before their more severe episodes. Improvement in this background control holds out the best prospects for reducing the numbers of potentially fatal attacks. Certainly when available treatments are applied vigorously they are effective, as shown by a hospital mortality rate of less than 1% in a series of patients admitted with severe asthma—most of those who died were thought to have been poorly assessed and inadequately treated.[8]

Good control of asthma is based on three principles: education of patients; careful supervision; and prompt recognition and treatment of deterioration. Patients should be taught to take prophylactic medicines regularly and to seek medical advice promptly if any deterioration occurs. They should be assessed regularly in a clinic or surgery where the degree of airflow obstruction may be measured. The peak flow meter is cheap, portable, robust, and easy to use, and as essential as a sphygmomanometer in the practice of medicine. If peak expiratory flow rate is measured each time the patient attends, any deterioration may be spotted early and its severity assessed. If deterioration occurs in spite of adequate treatment, or patients fail to respond to their usual bronchodilators, then the problem will not be solved by changing to another bronchodilator. A short course of oral corticosteroids may be required, and longer-term maintenance may be needed with inhaled cromoglycate or beclomethasone.

If an acute severe attack of asthma does develop the patient must be encouraged to seek help quickly, and in some areas emergency self-admission services have proved effective.[9] During a severe attack breathlessness will prevent sleep or movement from a chair, the pulse rate will be over 120 a minute, and the peak expiratory flow rate will be lower than 100 litres a minute. Other features such as cyanosis or pulsus paradoxus may also be present.[10] Before sending the patient to hospital the doctor should give an intravenous injection of 300 mg of hydrocortisone and an intravenous injection of 250 mg of aminophylline, both injections given slowly.

In the light of our present knowledge our best hopes for preventing death from asthma lie in better assessment, closer supervision, and more enthusiastic treatment. Asthma is another common condition in which there is a clear case for