

hypertrophy was seen only in the group with severe disease. At face value, the haemodynamic data from the Vancouver study accord with the general idea that the vasculature becomes rigid in severe disease, and that these altered vessels may not necessarily be more reactive than normal.

Repeated stretching of the small pulmonary vessels as a consequence of the higher lung volumes may be important in the development of intimal changes. In experimental models, stretching of vessels results in the laying down of longitudinal muscle¹⁰ and this process has been viewed as a component of normal repair.¹¹ The MRC results show that these intimal changes can best be related to the forced expiratory volume in one second (in other words, a measurement of the mechanical aspects of lung function), a finding that would support the possibility of increased vessel stretch in pathogenesis.

The MRC trial also shows that the clinical disorder recognised as hypoxaemic cor pulmonale is not very closely related to many of the physiological variables believed to be important in its aetiology—eg, right ventricular hypertrophy and polycythaemia were inconsistent findings and unrelated to the histological changes in the vasculature. Taken together, these studies clearly show that the early changes in the pulmonary vessels occur in the intima with the laying down of longitudinal muscle, and may be related to mechanical aspects of lung function. Changes in the circular muscle, as seen in chronic alveolar hypoxia, occur late in the disease, when vascular rigidity becomes apparent. These observations may explain the modest reversal of pulmonary hypertension with continuous oxygen¹² and the disappointing clinical response to vasodilators.¹³ Both studies again serve to emphasise the unsatisfactory nature of the term "right heart failure" as an explanation for oedema on the basis of hypoxic vasoconstriction and right ventricular pressure overload.

KLINEFELTER'S SYNDROME

IN an era of "high-tech" medicine, when the emphasis in genetic disease is focused on molecular biology and underlying pathogenesis, it is unfortunate that the clinical problems experienced by patients with relatively mundane yet common genetic disorders often tend to be overlooked. Individuals with sex chromosome anomalies, among whom men with Klinefelter's syndrome (47,XXY) feature prominently, fall in this category. Numerous birth surveys conducted in various parts of the world during the past two decades have revealed that approximately 1 in 1000

newborn males has a 47,XXY karyotype and an additional 1-2 per 10 000 show 46,XY/47,XXY mosaicism.¹

The critical importance of clear objective data about the clinical outcome in Klinefelter's syndrome is highlighted when a 47,XXY karyotype is discovered incidentally at amniocentesis. Not too long ago the prevailing textbook description of a "mentally retarded hypogonadal male with gynaecomastia" must have prompted many prospective parents to opt for termination of pregnancy. Increasing awareness that this florid depiction represents only a tiny minority at one extreme end of the spectrum has enabled parents, with the help of skilled counselling, to arrive at much better informed decisions. Studies in Denmark² and England³ have lately indicated that approximately 30% of well-informed couples decide to continue with the affected pregnancy. This percentage may well increase as a consequence of several ongoing longitudinal prospective surveys from which a clear and relatively benign picture of the 47,XXY phenotype is now emerging.⁴

Physical anomalies tend to be limited to a moderate increase in stature, largely attributable to long lower limbs, with mean adult height lying close to the 75th percentile. In contrast to the classical Pickwickian image, the mean weight of Klinefelter adolescents is slightly lower than that of controls. There is no conclusive evidence for an increased incidence of congenital malformations. Boys with Klinefelter's syndrome show a 10-20 point reduction in verbal skills,⁵ and it appears that this deficit persists through adolescence⁶ into adult life.⁷ Thus, delay in speech development, expressive language problems, poor short-term memory, or referral to speech therapy are factors that might reasonably prompt the alert paediatrician to request chromosome studies. Performance IQ scores do not differ significantly from those of controls and severe retardation necessitating special schooling is very uncommon.

Prospective parents of a boy with Klinefelter's syndrome are especially worried about the possibility of sexual dysfunction. Provisional results point towards an increased incidence of cryptorchidism, and testicular volume is almost always significantly reduced after puberty, with invariable infertility. Onset of puberty was delayed in 43% of boys in the large Danish study,⁵ with reduced penile size in 21%. Gynaecomastia was found in approximately a third of Klinefelter adolescents and adults, although it was usually mild to moderate and cosmetic surgery was seldom requested. The incidence of breast cancer in Klinefelter's syndrome is comparable to that in normal females. There is no well substantiated evidence for an increase in sexual abnormalities such as homosexuality, transvestism, or transsexualism. Sexual activity is often reduced in adults

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with Klinefelter's syndrome,⁹ although libido and potency may be increased by testosterone replacement therapy.¹⁰ This low level of sexual activity may well relate to a pronounced tendency for individuals with Klinefelter's syndrome to manifest passive pliant behaviour throughout life. In the neonatal period they are often subdued and sleepy ("well-behaved" babies); infancy and the toddler years are characterised by a lack of defiance. In childhood there may be major problems associated with shyness, poor self-esteem, loneliness, and emotional immaturity that often prompt referral to child psychiatry clinics.

Almost all attempts to establish the incidence of psychological or physical morbidity in Klinefelter's syndrome are bedevilled by biased ascertainment. For this reason, the data derived from studies of the cohorts of Klinefelter syndrome babies diagnosed in newborn surveys have provided immensely valuable objective information, of unique value for prenatal counselling. It will be several years before these investigations yield accurate results about the true incidence of social or psychological problems in adult life. Meanwhile, prospective parents and patients can take comfort from the Danish⁷ and Canadian⁸ studies which suggest that most Klinefelter syndrome males manage well in adult life with respect to occupation, social adjustment, and socioeconomic status, although there is no shortage of case-reports documenting loneliness, unemployment, and occasional criminal misdemeanours, usually of a petty non-violent nature.

A theme common to all the most recent studies is the need for support, counselling, and therapy. Boys with Klinefelter's syndrome are often clumsy and would usually benefit from gentle encouragement to participate in sporting activities that improve coordination. Special attention should be paid to language development, with early referral for speech therapy if necessary. If possible, excessive social stress should be avoided and self-confidence and assertiveness should be encouraged. Testosterone therapy, commencing in early adolescence, appears to be beneficial, not only for enhancement of sexual performance and prevention of osteoporosis but also for improvement of social interaction, mood, and general sense of wellbeing. With appropriate medication and support, the future for most individuals with Klinefelter's syndrome should bear little relationship to that depicted in the gloomier annals of yesteryear.

CUTANEOUS PHOTOSENSITIVITY

CUTANEOUS photosensitivity affects us all. It is the process of absorption of ultraviolet (UV) or occasionally visible radiation by molecules within the skin leading to chemical change and clinical effects. The absorbing molecules may be normal skin constituents such as DNA, RNA, or lipoproteins¹ (DNA is possibly the most important) or any of a host of drugs or chemicals of external origin.²

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Photosensitivity reactions resulting from absorption by endogenous skin molecules, excluding synthesis of vitamin D,³ are general with cutaneous tissue injury. Clinical features, well known acute inflammatory response, sunburn as tanning, hyperplasia, and, after recurrent ageing⁴ and cancer.⁵ Radiation absorption with superficial horny layer and by epidermal molecules. DNA repair processes reduce damage, but abnormality may increase it, as in albinism,⁶ caused by lack of melanin, and xeroderma pigmentosum where there is reduced repair of W-induced DNA damage.

Photosensitivity reactions resulting from absorption within the skin by chemicals of non-cutaneous origin are somewhat dissimilar, because the absorbing molecules are different. However, such reactions are also usually in clinical features may include cutaneous pain, oedema, urticaria, fragility, vesiculation and hypohidrosis and onycholysis.⁷ All of these changes, which disappear soon after withdrawal of the inducing chemical,⁸ may be seen for example in the manifestations of porphyria,⁹ in which there is cutaneous accumulation of photosensitising substances from the haem biosynthetic pathway.

Photosensitivity reactions may be modified by host response—eg, the common and annoying polymorphous light eruption,¹⁰ popularly but incorrectly called heat. This condition leads to recurrent, irritating eruptions of the exposed skin of about 10-20% of the population, usually young women, during summers and autumns. Much more disabling are the uncommon, chronic, eczematous photodermatoses affecting the unexposed skin of generally older men all year round. One is the "persistent light reaction," a chronic, widespread, eczematous dermatitis,¹¹ which develops after repeated episodes of photoallergic dermatitis,¹² in which allergic contact sensitivity to a specific UV-irradiated allergen, such as musk ambrette in aftershave preparations,¹⁴ and another eczematous condition is the clinically similar chronic actinic dermatitis,¹³ also known as the photosensitivity syndrome and actinic reticuloid syndrome,¹⁶ in which an allergen can be found.

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