exhausted within a few decades. Coal-mining will remain an important industry, though some uneconomic pits will still need to be closed, and fewer miners will be needed, because the new coal-fields have easier geological features and will be more productive.

Coal-mining deserves its reputation as a dangerous and unhealthy occupation. Nevertheless, fatal accidents have declined gradually and are now about 0·3 to 0·4 per 1000 men a year. This is far below the level for commercial divers and deep-sea fishermen, but a coal-miner still has three times the risk of being killed at work as the average man, and non-fatal accidents, often very severe, remain common.

Counting all causes of death, in 1961 the Registrar General gave a standardised mortality ratio (SMR) of 114 for miners[1]—14% above average. The accuracy of such statistics depends on how occupations are registered after death, and the true SMR may well be lower.[2] Jacobsen[3] studied 17 000 men who were working in selected pits in 1953 and over the next 14 to 18 years found them to have an SMR of 82. Nevertheless, that finding should not be taken to mean that coal-mining prolongs life: the influence of selection operates at three stages. First, there is self-selection—feeble young men seldom consider becoming miners. Medical examination at entry also leads to a rejection of about 2% of juveniles and 3% of adults, and only a minority of these are turned down because of poor sight. Thirdly, there were 17 000 men employed at one point in time. Those miners who had considered their health to be adversely affected by their work had already left, so the population was made up of survivors. Men who leave mining have ventilatory tests below average.

The mortality over 20 years of men living in the Rhondda Fach in 1950-1 has now been updated[4] and the findings differ from Jacobsen's. Non-miners had an SMR of 99, whereas miners and ex-miners without pneumoconiosis or with mild pneumoconiosis had SMRs ranging from 116 to 120, and those with high categories of progressive massive fibrosis had an SMR of 195. In those with mild pneumoconiosis, mortality was higher in ex-miners than in those still at work, indicating again the need for caution in reaching conclusions from working populations. Nevertheless, while miners do not live as long as non-miners in the Rhondda there is little difference between the two groups in Leigh, Lancashire.[4] Which area is close to the general experience remains uncertain, but Jacobsen's figures suggest that the Rhondda is exceptional.

Mines in the Rhondda differ most obviously from those in England in having a very high prevalence of pneumoconiosis; but this does not appear to explain the difference in mortality, which is also high in miners without pneumoconiosis in the Rhondda. Possibly there may be an inverse relationship between the presence of bronchitis and the prevalence of pneumoconiosis.[5] An excess of bronchitis in men without pneumoconiosis might then explain their high mortality, and might also mask an adverse effect of simple pneumoconiosis on survival. On the other hand, persistent production of sputum does not influence the development of pneumoconiosis,[6] and if this proves to be true also for airways obstruction the theory becomes invalid.

Whatever the relation between simple pneumoconiosis and disability its development is undesirable because its presence determines the appearance of progressive massive fibrosis. Progressive massive fibrosis increases mortality wherever it occurs, whether in Leigh or in the Rhondda. The prevalence of pneumoconiosis is falling. When the National Coal Board carried out its first complete survey of mines in 1959-63 the prevalence was 12·3%. The fourth survey of 1974-7 showed a fall to 7·5%, and certifiable disease (category 2 or more) had dropped from 5·4% to 2·1%.[7] The fall in Welsh pits has only been from 26% to 20%. The much worse figures in Wales are at least partly the result of mining harder coals. There is a fivefold difference in the prevalence of progressive massive fibrosis between collieries mining high-rank and low-rank coals.[8] Nevertheless, the latest National Coal Board report[8] also suggests that the hardness of the coal in itself may not be so important as the dust levels associated with its extraction. Dust levels in Welsh pits are now comparable to those in England, so that in time it will become clearer whether the rank of coal or quantity of dust is the more important.

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Recognisable patterns of male infertility

Most of the causes of female infertility can now be diagnosed accurately and many of them treated. In consequence the male contribution to infertile partnerships has attracted more notice recently. By conventional standards most men attending infertility clinics appear endocrinologically normal. Usually the oligospermia is unexplained, and simple measures such as ligation of a varicocele or advice about close-fitting underwear and excessively hot baths may be enough to improve the quality of the semen. Sometimes ensuring that the female partner is ovulating regularly is all that is needed for conception. In a few cases, however, there is evidence of a clearly defined hormonal disorder—or perhaps of a more subtle endocrine abnormality. Here the outlook has been improved with better understanding of the regulation of testicular function raising hopes of advances in treatment.

The traditional teaching has been that the functions of the Leydig cells and the seminiferous tubules are controlled separately by luteinising hormone (LH) and follicle-stimulating hormone (FSH) respectively. This is an oversimplified view. FSH appears to be a prerequisite for the acquisition of LH receptors by Leydig cells,[1] while spermatogenesis seems to require testosterone as well as FSH.[2] The action of androgens depends on classical steroid hormone mechanisms, including binding to specific cytoplasmic and nuclear receptors.[3] These androgen receptors can suffer varying degrees of deficiency. Complete absence of the cytoplasmic receptor will result in resistance to the action of androgens, when (despite normal amounts of testosterone) the external and internal genitalia will fail to develop in genetic males with testes. Androgen resistance occurs in utero and is lifelong. From this extreme —the complete testicular feminisation syndrome—there is a range of related syndromes in which the resistance to androgen action is less strong, producing a series of intersex states with varied degrees of masculinisation. One well-recognised variant, often known as familial incomplete male pseudohermaphroditism type I, appears to be an X-linked recessive

condition resulting in males with poor phallic development, bifid scrotum, undescended testes, hypospadias, defective Wolffian duct derivatives, a blind vaginal pouch, and at puberty gynaecomastia and only partial virilisation.[4 5] These patients are sterile. Another variant was recently described[6] in three infertile but otherwise normal men. They were either azoospermic or severely oligospermic, and all had higher-than-normal circulating concentrations of testosterone but diminished androgen binding as measured in fibroblasts grown from biopsy samples of genital skin. Two of the patients had raised serum concentrations of LH. This clinical syndrome may be one explanation for a finding of azoospermia in men with high blood concentrations of testosterone, but we do not yet know how common the syndrome is.

In the second type of familial incomplete male pseudohermaphroditism[7] the defect is a lack of the enzyme 5α-reductase, which converts testosterone to the much more active dihydrotestosterone. Testosterone as such is active only in certain tissues such as the epididymis, vas deferens, and seminal vesicle and in bone and skeletal muscle. Derivatives of the urogenital sinus, the prostate and penile urethra, require 5α-dihydrotestosterone; and so deficiency of 5α-reductase causes perineoscrotal hypospadias and the development of a blind vaginal pouch. The male internal genitalia are normal, and the considerable rise in testosterone that occurs at puberty promotes the development of a masculine appearance and psychosexual orientation.[8] Children with this syndrome are commonly assigned the female sex at birth, and the remarkable and successful change from the female gender to a clearly male physique and orientation in the early or mid teens seems to contrast with the accepted teaching (largely derived from experience of gender designation in patients with congenital adrenal hyperplasia[9]). Gender identity is usually said to be fixed in the first few years of life by environmental factors, but an additional hormonal factor now seems likely—possibly testosterone rather than dihydrotestosterone. Spermatogenesis often occurs in 5α-reductase deficiency,[10] showing that this too is testosterone dependent; but the prostate remains rudimentary and body hair is relatively sparse. A similar but acquired and reversible biochemical syndrome, with infertility, may be seen in men with untreated gluten enteropathy.[11]

Both LH and FSH are thought to be under the control of the hypothalamic decapeptide gonadotrophin-releasing hormone (GnRH); yet their secretory patterns may be very different. GnRH seems to be discharged into the portal-hypophyseal vessels episodically; possibly the pulse frequency affects LH and FSH differentially since LH is cleared more rapidly than is FSH. Patients with an endogenous deficiency of GnRH present with failure to enter or complete pubertal development; often this is an isolated deficit, but sometimes there may be associated midline developmental defects leading to anosmia, cleft palate, and colour blindness (Kallman's syndrome). The endocrinological abnormalities are presumed to be secondary to lack of GnRH since the pituitary-gonadal axis can be stimulated by exogenous GnRH[12] and long-term treatment with eight-hourly subcutaneous injections may induce potency, virilisation, and spermatogenesis.[13] When, however, such patients are given unmodified GnRH continuously they develop a refractory state,[14] and this pituitary resistance is even more evident when treatment is given with long-acting analogues, developed in an effort to simplify treatment.[15 16] If these agents are to have any use (other than, paradoxically, as contraceptives[17]) more effective regimens must be devised.

The major site of action of FSH is the Sertoli cell, where it causes production of cyclic AMP, a specific androgen-binding protein,[18] and the conversion of androgens to oestrogens.[19] How these changes relate to spermatogenesis is not clear; but FSH seems important in its initiation and, with testosterone, its maintenance. Normal spermatogenesis promotes the secretion of a selective FSH suppressor "inhibin," which is thought to be a peptide of Sertoli cell origin acting on the pituitary.[20] High concentrations of FSH signify a fault in inhibin production, associated with severe and usually irreversible damage to germ cells, even though the functions of the Leydig cells may be unimpaired. Indeed, estimation of FSH has proved to be the single most useful diagnostic blood test in the investigation of male infertility, since it predicts this end-stage damage.[21] No advances have been made in treating the underlying disorders of spermatogenesis.

Prolactin plays an important part in testicular function in some species; in man the circadian rhythm in plasma testosterone concentration, which cannot be accounted for by changing patterns of LH release, has been correlated with prolactin secretion.[22] Hyperprolactinaemia may cause a form of impotence that responds well to treatment with bromocriptine.[23] This happens even in patients with normal testosterone concentrations, while subnormal concentrations may rise into the normal range with treatment.[24] Most reported studies have been on patients with severe hyperprolactinaemia and pituitary tumours, and much less is known of the importance of prolactin in patients with gonadal dysfunction as their primary complaint. Hyperprolactinaemia alone seems unlikely to cause oligospermia despite occasional reports to the contrary[25 26]—and in most oligospermic men it is still true that no endocrine abnormalities can be defined.

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