are to be found. This leaves a troubling sense of trying to please everyone. Choices must be made. Affirmation of the traditional model of general practice demands the rejection of those changes which threaten it. Yes to availability, continuity, and advocacy for the individual must mean no to fund holding and managerial ambitions.

In a fractured and distressed society,[8] general practice has undeniable strengths.[9] Accessible to all and free at the time of need, general practice promotes equity and solidarity. It offers value for money and inhibits the inappropriate and expensive use of specialists.[10] General practice remains dependent on the human touch and counteracts the reliance on technology and fragmented specialist care which can sometimes result in a lack of compassion. The increasing availability of knowledge through information technology is challenging traditional medical paternalism. General practice is pioneering the shift from an authoritarian to a democratic model with doctor and patient as coproducers of health.[7] Modern fragmented technomedicine induces unrealistic and dangerous expectations while at the same time promoting dependency. Biological variation and the stresses and misery of human life are converted into diagnoses with consequent demands for specialised investigation and treatment.[11] The general practitioner can counteract both the somatisation of unhappiness[12] and help increasingly sophisticated consumers to recognise that the achievements of medical science remain limited. Unfortunately the profession is also fractured and distressed, and this may explain why, despite all this, the college stops short of making a final judgment. Times of turmoil are times of opportunity but not if tough decisions are indefinitely postponed.

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Declining sperm counts

Environmental chemicals may be to blame

See pp 467, 471, 506

The controversy over whether sperm counts have declined over the past 50 years is reopened by two papers in this issue of the *BMJ*. In a carefully analysed study of cohorts of unselected men in Britain born between 1951 and 1973, Irvine and colleagues demonstrate a progressive decline in sperm concentration and total sperm number per ejaculate of about 2% a year over 11 years.[1] A smaller study by Bujan *et al* finds no change in sperm counts of sperm donors in the Toulouse area of France over a 16 year period.[2]

The controversy over sperm counts began with a meta-analysis by Carlsen *et al* which showed a decline in a sperm concentrations from 113×10^6/ml to 66×10^6/ml between 1940 and 1990.[3] These findings were supported by Auger *et al* in a study of 1351 fertile men in Paris.[4] Commentators have criticised both the retrospective design and the mathematical analysis used by Carlsen *et al*.[5,6] Irvine *et al* have used data from one laboratory and employed appropriate mathematical analysis to reach their conclusion that sperm counts have declined.[1] Bujan *et al* suggest that the difference between their findings and those of Auger *et al*[4] may be related to the differing environmental conditions of rural and urban populations.[2]

The reported decrease in sperm concentration may seem difficult to reconcile with the absence of any detectable decrease in male fertility.[5] But important impairment of fertility is often not evident until sperm concentrations decline below 5×10^6/ml.[7] This is consistent with one hypothesis advanced to explain the decline in sperm count. Sharpe and Skakkebaek proposed that exposure of the fetal testis to oestrogens or oestrogenic compounds decreased the multiplication of Sertoli cells.[8] These cells control the inner environment of the seminiferous tubules in which spermatogenesis occurs,[9] and there is strong evidence that each Sertoli cell can support only a limited number of germ cells.[10] Hence a decrease in the number of Sertoli cells reduces the output of fertile spermatozoa. Our growing knowledge of how the number of Sertoli cells can be manipulated[11] may provide clues to how environmental factors affect sperm output.

Oestrogens and pesticides are implicated

The concept that exposure of the fetal testis to oestrogens can interfere with adult sperm production is supported by other data. The sons of women who were given diethylstilboestrol in pregnancy between 1945 and 1970 have been found to have decreased sperm counts and semen volume and an increased incidence of cryptorchidism and hypospadias.[12] The Danish Environmental Protection Agency has recently released a report raising concern over possible links between environmental chemicals that have oestrogenic effects and the increasing incidence of cryptorchidism, testicular cancer, and declining sperm counts.[13]

Another environmental pollutant with the potential to influence testicular function in utero is the main metabolite of DDT, p,p-DDE, which has been shown to act as an antiandrogen.[14] Countries such as Brazil and Mexico used nearly 1000 tonnes of DDT in 1992.[15] The metabolic products of DDT and related molecules seem to have the capacity to act through oestrogenic or antiandrogenic mechanisms on the developing male reproductive tract.[15]

The time delay between exposure to an agent and development of reproductive dysfunction can often pose problems of

linkage. Until recently, for example, the cause of Young's syndrome remained obscure. Young's syndrome occurs in men with bronchiectasis and is characterised by azoospermia due to epididymal obstruction.[16] No link has been found with mutations of the cystic fibrosis gene.[18] The syndrome was particularly prevalent in Britain and Australia between 1960 and 1980[16] but is now rarely seen.[17] In 1993 Hendry *et al* noted that many men with Young's syndrome had a history of Pink's disease in infancy.[18] Pink's disease disappeared around 1960 with the removal of mercury from teething powders, and the disappearance of Young's syndrome some 30 years later raises the strong possibility that exposure to mercury in infancy may have caused both Pink's disease and Young's syndrome through mechanisms yet to be elucidated.

Such examples, and our growing understanding of the vulnerability of the male reproductive system to environmental factors, highlight the need for vigilance. Regulatory and research agencies need to determine the most appropriate methods of assessing the actions of agents on the reproductive system, and should undertake whatever studies are necessary to confirm or refute the emerging hypotheses. Delay may compromise the fertility of future generations.

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Flavonoids and heart disease

Evidence of benefit still fragmentary

See p 478

A longstanding tenet of nutrition holds that people with diets rich in fruits and vegetables enjoy better health than people eating few fruits and vegetables. Consequently, research has sought the components or compounds responsible for this apparent health benefit. Much of that research currently focuses on dietary antioxidants, fuelled by our growing appreciation that damaging oxidative processes are a common biochemical link between otherwise pathophysiologically distinct diseases.[1] For example, the development of early atherosclerotic lesions is now thought to be specifically promoted by low density lipoprotein particles that have been oxidatively modified,[2,3] and oxidative damage to nucleic acids may have an important role in carcinogenesis.

Dietary antioxidants, which complement the actions of enzymatic antioxidants, are now widely recognised as including α tocopherol (vitamin E), ascorbic acid (vitamin C), and β carotene (a precursor of vitamin A). Perhaps flavonoids should now be added to this list. The article by Knekt *et al* in this issue of the *BMJ* (p 478)[4] joins two other epidemiological reports[5,6] in suggesting a role for the flavonoids, and for quercetin in particular, in the prevention of coronary artery disease.

This Finnish study relates subjects' usual diet, as reported for the year before entry to the study, to mortality from heart disease over the subsequent 26 years.[4] The findings show a modestly protective effect, after consideration of other important dietary factors such as saturated fat. (Though not commented on by the authors, flavonoids also seem to be associated with fewer deaths from diseases other than atherosclerosis.) The case for a specific cardioprotective role of quercetin comes from the data showing that apples and onions, important sources of quercetin in the Finnish diet, were the foods most strongly related to mortality risk.[4] It is unfortunate that these food-specific analyses were not adjusted for total energy consumption, since an overall increase in calorific intake could easily be a marker of high physical activity or body size, both of which are themselves inversely correlated with risk of heart disease.

As intriguing as these flavonoid findings are, the epidemiological evidence is not entirely consistent. In the atherosclerosis risk in communities study, consumption of apples was not related to thickness of the carotid artery wall (Kritchevsy, unpublished data), nor was flavonoid intake associated with heart disease in either the nurses health study or the male health professional study (Eric B Rimm, personal communication). It may be that the contribution of a particular food to cardiovascular health depends on the composition of the rest of the diet. The data of Knekt *et al* show a relatively low intake of vitamin C in the Finnish diet, and, since quercetin may lead to sparing of vitamin C, flavonoids may be most important in populations with marginal vitamin C intake.

Interpretation of this information by practising clinicians (for themselves or for curious patients) is challenging. One needs to know the biochemical composition of flavonoids, their pharmacology and range of physiological effects, their potential for toxicity, and their established health benefits. Structurally, flavonoids are polyphenols of about the molecular weight of cholesterol; as such, they are small, lipid soluble compounds like α tocopherol and β carotene. However, unlike these two established dietary antioxidants, flavonoids are ubiquitous in the plant kingdom and include