there are some things we should not know, but based more than anything on fear and ignorance. In such an atmosphere medicine and science will suffer. Research programmes will fail to find support, and parliament may be rushed into wholly restrictive legislation. A permanent open ethical committee with powers to advise on issuing and withdrawing licences (if only indirectly) could show that research can be regulated without being banned, that knowledge can be pursued without being put to morally intolerable uses. After the last war there was a cliché to the effect that man's scientific knowledge had outstripped his moral sense. At that time it was uttered in the context of the physical sciences. The bomb had, rightly, frightened us all. Now that same cliché is more and more to be heard in the context of the biological sciences. We must take it seriously. Only within an ethical framework widely seen to be secure and sensible can we continue, as we must, to push back the frontiers of science.

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Slugs and snails against sugar and spice

Changes in the ratios of boys and girls might have profound consequences

What are little boys made of?
Slugs and snails and puppy dogs' tails.
What are little girls made of?
Sugar and spice and all things nice.

This early nineteenth century nursery rhyme is not as far fetched as it might seem. Scientists in France and Canada have claimed a high success rate in prescribing diets for women who wish to choose the sex of their offspring. Women who want boys are given diets rich in sodium and potassium (meat and salt), while those hoping for a girl eat diets rich in calcium and magnesium (milk and milk products).[1]

This idea of being able to conceive a child of the desired sex is not new.[2] The early Greeks believed that the spermatozoa that determined the different sexes were stored in different testicles and that tying off the left testicle would produce boys. Even in the eighteenth century French noblemen were told that removing the left testicle would guarantee a male heir.

In most populations with reliable systems of registration of births more boys are born than girls. In Europe and North America the sex ratio of babies at birth is about 105—that is, 105 boys to every 100 girls. Other countries have higher ratios—for example, Hong Kong (109), Greece (113), and Korea and the Gambia (116). Populations with lower sex ratios—that is, a smaller majority of males—are the people of Chile (103) and the Asian people of South Africa (101).[3] Many reports suggest that black populations have consistently lower sex ratios than non-black populations,[4] but in a north Nigerian province where good records are kept the Hausa people have a sex ratio of births of 107.[5]

For any population the sex ratio at birth is usually fairly stable from year to year, but temporary changes are sometimes recorded. For example, in 1978 the sex ratio of births in the Republic of Ireland fell to 104 (the lowest for 20 years) and in Northern Ireland to 101 (the lowest so far recorded).[6] The reason for these changes remains a mystery. In some countries the ratio at birth varies seasonally,[7] which could be related to changes in diet throughout the year or to temperature: sexual activity may be less frequent when the temperature soars.

The proportions of male births have increased during and immediately after wars,[8] and again the change in diet caused by food rationing and the release from stress on coming home could have had effects. Indeed, the wives of men in occupations of high stress—such as fighter pilots, astronauts,[9] and the abalone divers in Australia[10]—bear more girls than boys. Some other occupations may affect the workers and the general population by exposing them to pollution. A survey of male anaesthetists showed that they had more girls than boys,[11] while in two steel towns in Scotland with high air pollution male births were significantly raised shortly before the onset of lung cancer epidemics.[12,13] Fishing communities in Scotland have shown high sex ratios more often than expected, which might be explained by chance or by a high fish diet.[14] People working in the alcohol trade have more daughters than sons[15]; and butchers had more daughters in the 1960s and early 1970s when cattle were given oestrogens but more sons when androgens were being used.[16]

The stress of disease may affect the sex ratio—for example, women with schizophrenia produce more girls than boys,[17] whereas women with multiple sclerosis tend to have more boys.[18] In two west African populations a large excess of male births came from conceptions the year after an epidemic of measles,[19] and patients who develop prostatic cancer have more sons than daughters.[20]

It is hard to see the connection between all these changes in the sex ratios of births, but the key may lie in the study of hormones. Insemination on different days of the menstrual cycle leads to variation in sex ratios, and there is a small but significant excess of girls after hormonal induction of ovulation for fertility problems in women. Men attending a Hungarian fertility clinic were treated with three different drugs and their wives produced 44 boys to nine girls, 62 boys to 30 girls, and 17 boys to 27 girls.[21] Diet, stress, and disease might have indirect hormonal effects and change sex ratios in the offspring.[22,23]

Sex preselection before conception is becoming possible,[24,25] and "gender choice" kits have been produced by an American pharmaceutical company.[26] There may be important medical, social, and demographic results. In families at risk for linked diseases it would be better to opt for a girl rather than have selectively to abort males. More families stop having children after a boy is born than after the birth of a girl, and sex preselection might thus lower the birth rate, but in most families with one child the offspring would be a boy. In less developed countries sons are the providers for old age, and there are reports of the termination of pregnancies in which the fetus is of the unwanted sex. In China, where the government is encouraging families with one child, the sex ratio of the population is rising to over 115—perhaps because of infanticide of girls.[27] Recently Asian women have been reported to abort female fetuses because of the dowry problem, and the state of Maharastra has introduced legislation to ban amniocentesis except for detecting genetic disorders. About 78 000 female fetuses were aborted in India between 1978 and 1982.[28]

There might be profound social changes if the sex ratio of

nations was changed dramatically because of parents being able to select the sex of their offspring. An excess of males might lead to increased competitiveness for the rarer females, and homosexuality might increase. In addition, fewer girls would reduce the birth rate in the next generation because population growth depends on the number of fertile females within a community. On the other hand, an excess of women in the population might inhibit male competitive aggressiveness and result in a more peaceful society. Would social institutions have to change radically to allow—or even encourage—a resurgence of polygamy? Or could the numerical dominance of women be transformed into a social dominance with the emergence of Amazon style societies?

This is all speculation, but one thing is certain. Should the sex ratio become even more biased toward maleness (as seems most likely) then the traditional old maids will evolve into old bachelors of the future.

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Alfred Nobel and the drug hunters

Pharmacologists have won many Nobel prizes

A Nobel prize is the greatest honour that a scientist can receive. It recognises unique achievements in the physical or biological sciences and confers superstar status on recipients. Indeed, in Sweden Nobel laureates are given the sort of media treatment that in Britain we reserve for royalty on a good day. Nobel prizes are therefore always special, but the 1988 harvest for physiology or medicine must be declared a vintage year.

Over the years pharmacologists have figured prominently in the award of Nobel prizes, but Gertrude Elion, George Hitchings, and Sir James Black are all drug hunters. Nobel prizes have been previously awarded to therapeutic innovators, and the very first prize, in 1901, was given to Emil von Behring for developing antisera against diphtheria and tetanus. Banting and Macleod (though not Best) shared the 1923 prize for isolating insulin, while Whipple, Minot, and Murphy were awarded the prize in 1934 for the first successful treatment for pernicious anaemia. Gerhard Domagk won the 1939 prize for discovering the antimicrobial actions of the drug prontosil but was forbidden to accept it by Hitler; he eventually received the medal (though not the money) in 1947. The discovery and development of penicillin by Fleming, Chain, and Florey, which led to their being awarded the 1945 Nobel prize, now feature in the school history syllabus. It has overshadowed (at least in Britain) the work of Selman Waksman, an emigré Russian who spent his academic life at Rutgers University. Waksman, a soil microbiologist, conducted a well planned scientific search for antibacterial substances elaborated by soil micro-organisms. His discoveries included streptomycin, neomycin, and actinomycin, and he was awarded the Nobel prize in 1952. Daniele Bovet, the last drug hunter to be awarded the prize, received his award in 1957 for introducing H_1 antihistamines.

All three recipients of this year's Nobel prize for physiology or medicine earned their awards while working in the pharmaceutical industry. Curiously, individual innovators in the industry rarely achieve much public recognition. By its nature pharmaceutical innovation is often multidisciplinary, but there is often one inspirational leader. Paul Janssen is probably the best known through the company that bears his name: his discoveries include haloperidol, loperamide, fentanyl, ketoconazole, and astemizole. Few, however, would be able to name the discoverers of thiazides (Karl Beyer of Merck Sharp and Dohme), salbutamol (David Jack of Glaxo), cyclosporin A (Jean Bovel of Sandoz), or captopril (Miguel Ondetti and David Cushman of Squibb). One result of the 1988 prize may be the wider acknowledgment of individual contributions within the pharmaceutical industry.

The discoveries made by the winners of the 1988 Nobel prize for physiology or medicine have had a direct influence on the day to day work of almost every prescribing doctor. Their combined output includes acyclovir, allopurinol, azathioprine, cimetidine, mercaptopurine, propranolol, thioguanine, and trimethoprim. The trio have thus had far reaching effects on cardiology, oncology, nephrology, infectious diseases, and gastroenterology. And as the development of the first clinical immunosuppressive agent (azathioprine) opened up transplantation surgery so has the discovery of cimetidine virtually closed down gastric surgery. This Christmas basic and clinical scientists from a range of disciplines can bask in reflected glory.

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