nucleic acid polymerases or are incorporated into the macromolecules. An abnormal base inserted, for example, in DNA by this route will result in a false template for replication. The resulting abnormalities can eventually result in cell death, but the sites of the critical lesions in the molecule and the extent to which they can be repaired are still unknown.

Another variant of this kind of cancer therapy depends on antibiotics such as actinomycin and adriamycin, which interfere with the functions of nucleic acids by binding to them. The altered state of the DNA interferes with the enzyme activity required for its transcription or replications. R. C. Gallo described the possibilities of RNA-dependent DNA polymerase (reverse transcriptase) being a target for chemotherapy. This enzyme is concerned in the first step that leads finally to the insertion of the genetic information of RNA tumour viruses into host DNA. Rifampicin and adriamycin both inhibit reverse transcriptase and are selectively toxic for virus-transformed cells. At the congress it was suggested that drugs like rifampicin could be useful in preventing the spread of RNA tumour viruses by stopping them from infecting and transforming fresh cells. In this context, reports of leukaemic patients who after a bone marrow graft developed leukaemia in cells of donor origin suggest that such an infection is possible in man.

For most cancers a tactical problem is to find drugs that can act on cells that are not replicating. Another topic at the conference was the need for identification of other enzymes which might prove suitable points of attack. Certain groups of isoenzymes are known to be disturbed in many types of cancer, and (at least in theory) they might provide such a new target. Isoenzymes are often a resurgence of fetal enzymes and give the cancer cell a chemical difference from its normal counterpart. However, there is little evidence that drugs might act selectively on certain isoenzymes without affecting non-cancerous homologues.

The state of current knowledge of the isoenzymes of lactic dehydrogenase and proteases was discussed at the conference and served to emphasize our current inability to take advantage of differences in their patterns as prime targets for cancer chemotherapy. Indeed, it is uncertain whether any of the enzymes known to have isoenzyme disturbance in cancer are placed in strategically vital biosynthetic pathways. On the other hand, the particular enzyme complement of cancer cells, as well as their permeability, may be exploited as a method of increasing selective drug activation in tumours. The azo-reductase activity of hepatoma cells can convert non-toxic azomustard to a short-lived active compound within the cancer cell.

Though organic chemists can design with some certainty analogues of metabolites which are likely to inhibit a particular enzyme in vitro the likelihood of a compound being a successful antitumour agent is slim. We still cannot predict the fate of the compound or the interplay of factors which determine the amount of active drug that reaches the target. Probably we shall still have to rely on large random screening programmes to find new classes of drugs, but the investigation in depth of the mode of action of the more successful antitumour agents may lead us in fact to find new targets, on which a further period of rational design can be profitably applied.

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**Alcoholic Cardiomyopathy**

It may seem surprising that the role of alcohol in the genesis of chronic heart muscle disorder is still in any dispute, but the reasons for the continuing uncertainty can be stated simply. There are more drinkers than abstainers in our society, and those who drink excessively are notoriously untruthful about their alcohol intake. The clinical and pathological features of cardiomyopathy attributed to an excessive alcohol intake do not differ in any discernable way from the features of dilated (congestive) cardiomyopathy in professed non-drinkers. Alcohol is a myocardial depressant when administered acutely, and this effect is not in question. Other drugs such as barbiturates also cause demonstrable myocardial depression when given in this way but have not been incriminated as causes of cardiomyopathy. If the heart is already ailing from any cause then the action of a myocardial depressant is hardly likely to be beneficial. If a patient with heart muscle failure (dilated cardiomyopathy) is also an alcoholic then further depression of myocardial activity could result from the alcohol, but this in itself would not constitute proof of an alcoholic origin for the heart disease. Equally, any improvement which followed abstinence from alcohol would not afford proof of cause and effect. Conversely, even if alcohol were in truth the causal agent of the cardiac disorder, then persistence of abnormality after withdrawal of the alcohol might be expected because the myocardial damage, left ventricular dilatation, and functional failure might be irreversible. A further problem is that full-blown cardiomyopathy is uncommon in alcoholic patients with cirrhosis of the liver; this suggests that alcohol may be no more than a conditioning agent acting on an already sick and susceptible end-organ. Animal studies have not fully elucidated the problem, and the biochemical mechanism through which alcohol might produce a cardiomyopathy remains completely unknown.

Finally, a cardiomyopathy possibly induced by alcohol should not be confused with cardiomyopathy caused by two known associations of alcoholism, though both are rare and the second one probably now extinct. Alcoholism is nowadays uncommonly associated with nutritional deficiency, but when this occurs inadequate vitamin B₁ in the diet can lead to heart failure. In this wet beri-beri there is fluid retention and cardiac dilatation but a high output state. The hyperkinetic heart failure responds quickly to vitamin B₁ and is haemodynamically and clinically totally different from the hypokinetic low output state and poor contractile function of congestive cardiomyopathy. A different cause of heart failure was the addition of cobalt to beers to improve the stability of the "head." This was shown some years ago to be responsible for heart failure and death in men who had habitually drunk several gallons of beer daily. The addition of cobalt to beer has now been banned, and this form of heart failure is unlikely to recur.

Despite the doubt whether it is an entity, alcoholic cardiomyopathy is a widely accepted clinical concept, and the subject has been well reviewed by Regan. In a recent study of patients with cardiomyopathy associated with a high alcohol intake Demakis and his colleagues from Chicago looked at the natural course of 57 patients followed for an average of 40-5 months. Their progress was related to the persistence or not of the excessive alcohol consumption. Fifteen (26%) improved— and 11 of these 15 patients had abstained from alcohol but four had continued to drink. In twelve there had been no change and thirty (53%) had deteriorated, but only four of these had abstained from alcohol. Twenty-four (42%) of the patients
State of Health

Too much weight should not be given to comparisons based on international statistics, but we have no cause for pride or complacency in the position held by England and Wales in the European health league. Our infant mortality of 17.2 is the 11th of 33 countries quoted in the annual report of the Chief Medical Officer of the Department of Health; while the perinatal mortality of 22.3 is in 18th position, a loss of two places from the preceding year. The figures for Scotland and Northern Ireland were even worse. While there has been a decline in the incidence of stillbirths and infant mortality in recent years, the fall has been faster and further in many other countries.

This report is the first prepared by Dr. Henry Yellowlees since he became C.M.O. in 1972, and much of the data it contains are based on work done while Sir George Godber was still in control. Despite the efforts made by Sir George to discourage smoking, lung cancer is now second only to breast cancer as the commonest site for fatal tumours in women; stomach cancer is still second to lung cancer among men. Nevertheless, cancer is not the greatest killer. In rough figures, ischaemic heart disease accounts for 25% of all deaths, stroke for 15% and other circulatory disorders for another 10%; all cancers account for about 20%; and respiratory disorders for 15%.

Alcoholism seems to be a growing problem. Since 1968 the numbers of admissions to hospital for alcoholism have risen from 6,000 to 10,000 a year; there are now probably over 400,000 alcoholics in England and Wales. The number of drug addicts under treatment has also continued to rise.

The most cheering news is confirmation that the birth rate has reached its lowest level ever in peace time. Compared with the peak of 850,000 births in 1966, only 676,000 babies were born in 1973. Part of the fall in birth rate may be due to postponement of childbearing; among women who married aged 20-24 the proportion remaining childless one year later is now over 80%; but there is also some evidence suggesting that the size of completed families is indeed falling.

Whatever the population trends, the number of doctors in the N.H.S. is still rising by about 3% a year, mostly in the hospital service. Among family doctors there has been a further fall in the number born in the Irish Republic and Northern Ireland and a further rise in those born overseas, who now make up 16.5% of unrestricted principals in England and Wales. In comparison only 11.8% of principals are women; they form 32% of entrants to medical school, 15% of all hospital staff, but only 7.9% of consultants.

It is within the hospital service that the N.H.S. relies most heavily on overseas graduates. There are now nearly 10,000 doctors in hospital posts who were born overseas, and they make up 60% of all senior house officers and 56% of all registrars. For the next 10 years, says Dr. Yellowlees, it will be possible to sustain the programme of expansion of N.H.S. medical staff only by the employment of more doctors from abroad. Nevertheless, international trends may cut off the supply long before that.8

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