

TERATOGENESIS

Preventing Birth Defects

from a Correspondent

THE first annual prize of L'Institut de la Vie was awarded to Dr William G. McBride of the Sydney Lying-in Hospital by an extremely distinguished panel of jurors. Dr McBride discovered the teratogenic effects of thalidomide. He refused to accept the prize money for himself and instead raised an appeal in Australia to increase the amount (250,000NF) by a factor of 25. He is half-way to his target, so that it was fitting that L'Institut de la Vie held a meeting in Paris on December 2-4 to discuss strategy in preventing birth defects when possible and in alleviating their physical, psychological and social effects.

The problem has at least three major aspects. First, it is plain that for many countries there are no reliable statistics of the frequency of even the commoner foetal and neo-natal defects. Dr McBride gave a lucid, but sobering, account of the obviously thorough and efficient screening of mothers, fetuses and neo-nates at his hospital. In New South Wales roughly 5 per cent of all children are seriously defective: 1.5 per cent have a major physical defect such as spina bifida, 1 per cent suffer from severe cerebral palsy and 2.5 per cent from mental retardation severe enough to prevent their taking an effective place in society. These figures are from an advanced, well nourished and healthy people, but even so the irreducible minimum of birth defects is clearly far from achievement.

Brillat-Savarin (*Physiologie du Gout*, 1825) said: "La destinée des nations dépend de la manière dont elles se nourrissent". His words were dramatically reinforced by Dr R. G. Whitehead (Kampala) who described the effects of protein malnutrition in a relatively undeveloped country. Protein malnutrition leads to a continuum of syndromes, from kwashiorkor, a disease caused principally by an excessive ratio of carbohydrate to protein in the diet, to marasmus, caused by plain starvation. The result of malnutrition in these forms is an increased susceptibility to disease and a prevalence of metabolic disorders associated with a reduced amino-acid pool. Although many of the effects on young children are reversible, permanent damage can be caused to the central nervous system, particularly if a foetus or young child is malnourished during one of several critical periods during development. It seems typical, in underdeveloped countries, that the problems posed by malnutrition are so severe that the occurrence of birth defects with more subtle causes is relatively insignificant. In any

case, the relevant statistics are almost non-existent.

The second aspect of the problem is the recognition of new teratogens, which can often only be done by epidemiological methods. Professor J. R. Miller (University of British Columbia) emphasized that it is essential to have fast, accurate and comprehensive recording of the occurrence of birth defects so that novel or unusual patterns can be quickly recognized. Clearly, the data storage and analysis must be carried out by a centralized computer system in each country. There are many pitfalls, however. For example, an outbreak of phimosis was traced to a single paediatrician who used the diagnosis to justify the circumcision of all male babies. More important is the fact that a very small incidence of some abnormality may have to be recognized very quickly if a tragedy of major proportion is to be avoided. It still seems that an experienced clinician is most likely to do this: Dr McBride suspected thalidomide after seeing six "thalidomide babies".

Third, once these problems are solved, come the questions of prevention and cure. One of the most successful cases is the identification of rubella as a teratogenic disease with the prospect of its impending eradication in developed countries. In a more dramatic vein, the technique of amniocentesis in which amniotic fluid containing foetal cells is removed from the mother offers many potential benefits in

cases where there is a high probability of a genetic or chromosomal abnormality. As Dr K. Hirschhorn (New York University School of Medicine) said, it should now be possible, in theory at least, to eradicate Down's syndrome (mongolism) by recognizing its karyotype in foetal cells, and aborting the fetuses concerned. Even so, some mothers still refuse abortion. Foetal cells removed by amniocentesis can also be cultured and assayed for enzymatic deficiencies in cases where inborn errors of metabolism are suspected. Again, some degree of indirect genetic engineering by therapeutic abortion is possible, and the impression is that progress in this sphere is extremely rapid. It should become possible to obtain samples of foetal blood to determine blood group and it might also be possible to induce the synthesis of enzymes not already present.

The impression left by the meeting is that clinical medicine is advancing rapidly in combating teratogenesis, but that there are still no useful contributions from the more theoretical biologists who were well represented. Fundamental research is obviously essential, but the gap between basic science and clinical science seemed unusually wide. One point, which was rather unemphasized, was that the biggest single contribution to the removal of birth defects would be the reduction of malnutrition, which can only be done by population control.

What Colour is the Sky on Venus?

THE National Aeronautics and Space Administration is not yet anticipating sending astronauts to Venus, let alone a poet or a painter. But in spite of the distance of at least 4×10^7 km that separates the Earth from one of its nearest planetary neighbours, some quite detailed information and reasonably based speculation about the nature of the Venusian atmosphere are now forthcoming.

A further contribution to the discussion will be published in next Monday's *Nature Physical Science* (January 3) in which A. C. Aikin of the NASA/Goddard Space Flight Center discusses ion clusters and the Venus ultraviolet haze layer. In his article he cites observations of electron concentrations in the Venusian atmosphere as a function of height and discusses the possible composition of the complementary positive ion concentration.

If, as is thought, CO_2^+ is the principal ion, then Aikin argues for the importance of clustering of this ion by the addition of CO_2 or of almost any other molecule which may be present. He suggests that these condensation nuclei eventually build up to micron-sized

particles by coagulation of clusters. The object of such detailed speculation is to offer an explanation for the observed ultraviolet haze layer on Venus, if not also the yellow cloud layer at lower altitudes. The compositions proposed would suggest an atmosphere much more inhospitable than anything yet produced on Earth.

Aikin stresses the likely importance in all this of the reactions of electrically charged particles. The advantage that these have over neutral species is the long range of their interactions so that high rates of reaction, even at low number density, are produced. (The rapidity of such "condensation" effects was, of course, put to good use by Wilson when he invented his cloud chamber.) Similar effects certainly play a part in the behaviour of the Earth's atmosphere, especially during thunderstorms. Although the composition of the Venusian atmosphere may be very different from that of the Earth's, initial arguments must be based on the supposition that some features of both are similar. Only further investigation by space probes can show whether arguments based on such similarities can be sustained.