Enzyme therapy by transplanting hepatic or bone marrow cells in immunosuppressed animals with model diseases, was partly successful (D. Sutherland, University of Minnesota, Minneapolis) although, with the exception of acute hepatic failure (where only temporary action is required), rejection remains a formidable obstacle for use in man. There has been, however, some success with bone marrow transplants in immune deficiency disease. Furthermore, transplants of HLA-identical fibroblasts increased levels of the relevant enzymes in patients with Hurler's, Hunter's and Sanfilippo type A diseases for up to several years and there was no evidence of graft rejection (M. F. Dean, Kennedy Institute of Rheumatology, London; D. Gibbs, Clinical Research Centre, Harrow). A more hopeful alternative would, of course, be transplantation of cells after they have been corrected for the malfunctioning or missing gene by one of the available methods.

A subtle and perhaps more efficient method of restoring enzyme activity in a large group of disorders is the administration of massive doses of specific vitamins (see review by C. R. Scriver, in *Treatment of Inborn Errors of Metabolism* (eds Seakins, Saunders & Toothill) 127, Churchill Livingstone, Edinburgh and London, 1973) which through a variety of mechanisms (for example the coenzyme may form part of the active site of the enzyme, affect apoenzyme synthesis and degradation or influence the specific activity of the enzyme by altering its conformation), result in beneficial biochemical and clinical changes (G. E. Gaull, Mount Sinai School of Medicine, New York). Much of the understanding of vitamin action has come from work with vitamin B and aspartate-β-decarboxylase (A. Meister, Cornell University Medical College, New York). A similar (but limited to mannosidosis) approach may be ingestion of Zn which can activate the partially missing α-mannosidase (G. A. Grabowski, University of Minnesota, Minneapolis). The almost certain effects of Zn on the absorption and metabolism of other trace metals could, however, prove unacceptable. In yet another approach advantage is taken of the equilibrium thought to exist between the various pools of substrate in the body. For instance, plasmapheresis coupled with a phytanic acid-poor diet lowered serum phytanic acid considerably and slightly improved muscular strength in a patient with Refsum's disease. Plasmapheresis alone reduced trihexosylceramide levels to normal for a several day period in a patient with Fabry's disease (H. W. Moser, The John F. Kennedy Institute, Baltimore). The latter finding was also observed after repeated injections of plasma α-galactosidase A isozyme in two brothers with the same disease (R. J. Desnick, Mount Sinai School of Medicine).

Although some of these attempts at therapy have already benefited patients and some may have saved lives, most of the clinical trials were not preceded by animal experimentation, because animal models of human genetic diseases are extremely rare. The setting-up of such models is essential if therapy is to become more effective. An interesting example of a mouse with multiple lysosomal enzyme deficiences was demonstrated by P. Pentchev (National Institutes of Health). Even so, direct clinical trials are often a necessity. For instance, work with animal models is of little use in determining the likely immunogenicity of enzymes or cells prepared from human sources or whether cells from seemingly healthy donors may be contaminated with viruses, infectious viral components or with malignant cells. Some of these contaminants are impossible to measure or even anticipate and recipients, especially if immunosuppressed, may therefore be at risk. Similarly, artificial carriers such as liposomes, although controllable in terms of infectious contaminants, may exaggerate antigenicity through an adjuvant action

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A hundred years ago

In the interests of British science we have refrained now for some time from referring to the evil days which have fallen upon one of the most reputable of our learned societies. The time, however, has now come when silence is impossible. At the meeting of the Royal Astronomical Council yesterday, the Astronomer-Royal, in consequence of the recent action of the Council—an action inevitable when the present constitution of that body is considered—resigned his seat at the board. We cannot too much regret that this Society, the traditions of which are second to none in Europe, should have been utilised for some years past by an advertising clique who have everything to gain by their connection with a body of honourable students of science. The withdrawal of men long known for their astronomical work from the Council commenced some time since. It has now culminated in the resignation of the Astronomer-Royal, and we are informed that other resignations are to follow; indeed, a man of scientific repute risks somewhat in being found amongst the Councillors. Surely the Fellows of the Royal Astronomical Society of London are strong enough to remedy such a state of things as this.

At a recent meeting of the Medical Society of Berlin Prof. Virchow gave (by previous request) his views on the subject of the Plague of Astrakan. . . .

At the beginning of most pestilential epidemics a Committee of doctors has generally declared that it was not the plague. They pronounced it petechial typhus. This was the case immediately before the outbreak of the plague at Rescht, when the disease had been long confined in Kurdistan and Mesopotamia. M. Tholozan was the first to say it was plague, and that the case was that, not of a great epidemic, but of a latent disease, spreading slowly and attacking only a few. It is indubitable that we have there a true centre, whence the disease gradually spread, and I do not see why we should go to India, where the disease has not prevailed for many years past. Proceeding logically, we shall accept this course: From Kurdistan and Mesopotamia to Persia and on to beyond the Caspian. Even if the present cases on the other side of the Caspian were accompanied by pneumorrhagia, I would not hesitate to say they belonged to the plague proper, and that the disease is the same as that in Mesopotamia. The symptoms are very different from those of petechial typhus, the disease which the Turkish doctors affirmed. If near Salonichi (Xanthi) there be really petechial typhus accompanied by *Metastasis bubonica*, I fear it is the plague. It remains to keep our eyes open and see what happens after the return of the Russian army from the infected country (an occurrence which may well rouse grave apprehensions).

What has been done for our protection is little apt to tranquillise us. A blockade comprising all the frontier as well as the coast, from the Baltic to the Black Sea, seems to me illusory.

One example of severe quarantine has occurred in this century in the case of the plague at Noja, in Bari (Kingdom of Naples), in 1815. Trenches were dug, and three cordons of sentinels were formed (the third round the entire province), with orders to kill whoever tried to break the blockade and did not stop at the first summons; and some individuals were actually killed. But I cannot think an entire country is able to protect itself thus. Examination of passports would be excellent if those who deliver passports and certificates of health were angels. But the Russian functionaries are men, and think like men. The impossibility of always getting true certificates of origin has been seen in the case of the cattle plague. I consider, however, that pressure should be exerted on Russia to form a blockade of the infected districts. And especially it should be seen to, that the returning Russian army does not bring any pestilential germs with it. As to restrictions on communications by land, the greatest of these are ineffectual for the end desired.

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