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DNA Breakthrough Points Way to Therapy by Virus

PLANNING for social progress demands a vigilant search for the opportunity to link effective means with deserving goals. We are ridden with problems against which we are simply too ignorant to mount a frontal attack, for example, how to temper the ravages of aging. In such an area we must content ourselves with piecemeal advances in isolated sectors and work patiently to strengthen the whole framework of human understanding.

In the course of this process of basic research, opportunities often arise where least expected. Each fundamental breakthrough should provoke the question, "What can now be done that was not possible before?" This is an opportunistic search for newly answerable problems, but in the most difficult and most important areas we have no way to program fundamental discovery.

THE REPLICATION of DNA in the test tube opens the way to a number of new approaches to the study and treatment of disease. It is virtually certain that, in the long run, our mastery of cancer and of senility will be reached with the help of this steppingstone.

Meanwhile, there are some very concrete advances that we can map out with existing insights. For the moment, these would be most relevant to diseases that are connected with a hereditary defect and that have a simple biochemical basis.

The plan is founded on an unlikely combination of biological studies ranging from the genetics of bacteria to virus-induced warts in rabbits and the recent advances in molecular biology. It is a scheme that we might call "virogenic therapy." This is an extension of the already well-founded use of tempered live viruses as vaccines to stimulate immunity against their wild cousins. To see the analogy we must, however, focus on the earliest steps of a vaccination, since the later step of provoking immunity is just one special case of virotherapy.

IN ITS essentials, a virus particle is a large DNA molecule protected by a protein coat. (For precision, we have to note that some viruses are RNA, but the basic principles are the same.) The DNA codes for the production of a number of special proteins related to the survival of the virus, including that coat protein but also including a number of new enzymes.

The infection of a cell by a virus is therefore tantamount to adding some new genes to that cell. The consequences depend on the specific quality of the virus as it has evolved in nature or been contrived in the laboratory. It may kill the cell and ultimately the whole animal. Alternatively, it may be essentially innocuous, adding a few additional proteins to the long list of those already synthesized by the cell.

In this context, the purpose of vaccination is seen to be to provoke the further synthesis of the virus's own coat protein. This in turn will provoke the host to develop immunity against that coat and enable the host to recognize and destroy further incursions by the same virus or its virulent cousins.

Dr. Stanfield Rogers of the Oak Ridge National Laboratories has pointed out that we should find viruses that code for other proteins needed by a given patient, for example, insulin by a diabetic or the phemylalanine-oxidizing enzymes by a PKU-infant.

SUCH VIRUSES might be found by a massive screening program to test the enormous variety of viruses that continuously evolve in nature. This kind of approach paid off very well in finding the antibiotics like streptomycin. The odds of finding an insulin-coding virus are obviously rather slim, but such a program would justify itself anyhow with its by-product of encyclopedic knowledge of virus-cell biochemistry. That encyclopedia might one day save the human species from extinction under attack by a virulent mutant of some now harmless obscure virus.).

An even more aggressive approach is based on recent work like that of Kornberg and Khorana on the enzymatic and chemical manipulation of DNA. It would be fanciful now to think of synthesizing an entire viral DNA according to our intended design, which, anyhow, we still do not know in sufficient detail. We can, however, think of extracting the DNA molecules that code, say, for insulin and chemically grafting these to the DNA of an existing tempered virus. These new hybrid viruses would then have to be very carefully studied, and perhaps modified even further, to select those appropriate for virogenic therapy in man.

This program needs to be discussed in a newspaper column as well as in scientific journals because its success is mainly a question of public policy. Existing institutions are not well suited in either style or scope to the innovative development side of "R. & D." for health.