18 November 1977, Volume 198, Number 4318 SCIENCE

Biostatistics in Medicine

About 60 years ago, within a single decade, it was discovered that the course of three of the most complex and lethal of diseases—pellagra, pernicious anemia, and diabetes—could be turned around swiftly and precisely by the restoration of absent biochemical reactants. Thus a new era opened, and a few years later the discovery of the sulfonamides and penicillin made the fact of the revolution plain to everyone. Human disease was curable by the use of scientific methods.

The impact of this discovery is now only dimly remembered, but at the time it was overwhelming. Therapy had fallen out of fashion long since, as the result of another, earlier revolution. Two catastrophic observations had been made in the 19th century and were accepted with reluctance: the first was that many human ailments could reverse themselves without treatment; the second, that the stupendous therapeutic armamentarium of that time, which included everything from botanical extracts to applications of electrical currents and leeches, simply did not work. At around the time of Sir William Osler there began a long period of therapeutic nihilism, and it came to a close with the introduction of penicillin. Since the 1940's, medicine has been undergoing transformation from an art, as it was earlier termed, to a mixture of science and technology.

But the transformation is still in its early stages. There is a long list of formidable human diseases whose underlying mechanisms are not at all clear, and these are presently unapproachable by such precisely targeted techniques as the use of penicillin against streptococci. There is a long way to go. As a science, medicine has started, but it will not have arrived until biological problems posed by the senile dementias, arthritis, cancer, and so on are well on the way to being solved. What is new in medicine is the general awareness that these are biological problems and that they are ultimately solvable.

It is precisely because of the success of medicine in some of these problems that research on the unsolved diseases poses such complex ethical problems. It used to be agreed that therapy did not matter all that much, that most pharmacological agents were essentially trivial and at best marginal in their effects. We edged away from that attitude when the antibiotics turned up, and were finally wrenched away by the new anticancer drugs, the diuretics, the antihypertensives, and most of all by recent discoveries in neuropharmacology. The stakes have become very much higher, and the possible remedies for disease much more powerful and potentially dangerous.

In studying potential new therapeutic agents the design of experiments and the evaluation of results have become more difficult than ever before, partly because of what has already been learned about the natural history of the diseases under study. Excepting only cancer (and even here there are scattered reports of spontaneous cures) and certain inexorable forms of heart disease, most illnesses *can* reverse themselves. In schizophrenia and rheumatoid arthritis, for example, it is estimated that 35 percent of cases will recover no matter what is done. A great many patients with hypertension can have a normal life-span. Also, the remarkable potency of placebos in providing transient relief of symptoms in many illnesses has become an important complication for clinical research.

From here on, as far ahead as one can see, medicine must be building, as a central part of its scientific base, a solid underpinning of biostatistical and epidemiological knowledge. Hunches and intuitive impressions are essential for getting the work started, but it is only through the quality of the numbers at the end that the truth can be told.—LEWIS THOMAS, *Memorial Sloan-Kettering Cancer Center, New York 10021.*