FOREWORD
TO THE FIRST EDITION

Claude Bernard wrote, "We are all fallible when facing the immense difficulties presented by investigation of natural phenomena." It is evident that some are more fallible than others. It is also evident that some branches of medical research offer more difficulty than others in avoiding fallibility.

Knowledge essential for effective clinical practice has not been easy to acquire. Only patients can instruct physicians; but where observations cannot be made on patients, recourse must be had to studies on other species. Such studies are based on animals living free in nature or, more usually, restricted in captivity. The overwhelming majority of the studies are artifactual, particularly when carried out on caged mammals. The studies involve inducing infections, toxic states, or nutritional disorders under conditions presumed to resemble those that occur in human disease, but they clearly never resemble them closely.

Although today we consider bedside teaching essential, there was no formal clinical teaching anywhere on the European continent, except at Leiden, until 1745. In that year (many of the Leiden faculty had moved to Vienna), ward rounds were begun in Vienna under van Swieten. Kanilfeld began this kind of teaching at Pavia in 1780, von Plenciz at Prague in 1781, Frank at Gottingen in 1784, and Hufeland at Jena in 1793. De Rechefort, who should be remembered for having introduced electroshock in the treatment of depression, is known for having originated clinical teaching in France around 1780. The rich early history of bedside teaching in Great Britain revolves mainly about the great hospital medical schools, starting with Guy's in 1723. Unlike the medicine throughout much of Europe, German medicine remained tied to dogmas until beyond the middle of the nineteenth century, except for the teaching by Frank at Gottingen and Hufeland at Jena.

Despite the growth of interest in bedside medicine in most of Europe, its teaching was inexact and ill-directed until the remarkable developments of the post-Napoleonic years at Paris and the corresponding period at Vienna. The discovery of percussion by Anenbrugger in Vienna and its promotion by Corvisart in France was followed by the discovery of auscultation by Laennec and the subsequent growth of physical diagnosis under the French physicians Louis, Bayle, and Andral, the last of whom brought the microscope and the chemistry laboratory into the service of bedside medicine. Physical diagnosis reached new heights a little later under Skoda in Vienna.

Despite these notable advances, clinical medicine could not develop assurance by bedside studies alone. It was not until Bichat and Cruvilhier in France, and later Rokitansky in Vienna, gave bedside observation the support of pathological anatomy that clinical medicine reached greatness. Bedside medicine and postmortem anatomy fed each other's growth and development, a symbiosis that unfortunately has been lost sight of in recent decades. (The close relation between pathology and medicine was recognized at Harvard as recently as 1912, when Henry Christian went from hospital pathologist to Hersey Professor of the Theory and Practice of Physic at Harvard and Physician-in-Chief of the Peter Bent Brigham Hospital.)

Gross pathology could not, however, establish etiology (except in trauma) and was also deficient in elucidating progressive states of disease. The development of pathological histology and bacteriology in the second half of the nineteenth century helped in these directions, for these disciplines remained basically patient oriented. Nevertheless many erroneous ideas resulted from the artifacts inherent in their use. The development of physiology and physiological chemistry, largely in Germany, also began slowly to enter the picture, but their influence on bedside medicine was for years small and their contributions were intermingled with some very stubbornly maintained erroneous theoretical formulations.

Among the interesting findings in chemistry was one made in 1903 by Winterstein, one of the great chemists of the time. He showed that there was no such thing as pure cholesterol more than a day or two old, when made pure it changed quickly to several dozen other compounds. This has been repeatedly verified since that time. A decade later the Russian Anitshkow stated that when he fed cholesterol to rabbits they developed atherosclerosis and that the dietary cholesterol caused the atherosclerosis; his report was received in some quarters with astonishment but for the most part only with indifference. This error was resurrected two decades later in the United States. Timothy Leary's monograph on atherosclerosis (Arch Pathol 17:434, 1934) praised the Russian theory and presented in its support a series of important-sounding irrelevancies, embel-

lished with some gross errors. He wrote:

> Any metabolic agent capable of producing atherosclerosis must have been an article of diet from early times, since atherosclerosis has been found in mummies. The substance is a necessary part of every animal cell, forming, from Starling's concept, the stable groundwork of the cell cytoplasm. As far as anyone knows no cholesterol is synthesized by the human body. All of the supply is ingested. The most urgent demands for it come at times of most rapid cell formation. Egg yolk is intended for the embryo. Milk is intended for the infant. It is interesting to note that Wells, in his "Outline of History," records that it was relatively late in the evolution of primitive man that he developed what Wells calls "the rather unnatural use of animal's milk as food." The high blood cholesterol found in pregnant women marks the mobilization of this substance for the needs of the fetus in utero. Man is the only animal that ingests eggs and milk* throughout its lifetime. Man is also the only animal, as far as is known, which dies in early life from coronary sclerosis, and which acquires atherosclerosis almost universally in advanced life.

This restatement of Anitshkow's theory evoked even less approval, if that is possible, than the first. Leary, like Anitshkow, ignored the fact that what he fed was a mixture of two or three dozen compounds and not cholesterol per se. The journalistic tone of his concluding statements and his grossly inadequate understanding of nutrition and biochemistry evoked scorn as often as indifference.

We know that much of the cholesterol in the blood and tissues is synthesized in the body, some of it in the blood vessels themselves. Today we also know that cholesterol purified every day before being administered to animals does not cause atherosclerosis and that oxides that form when cholesterol is exposed to air for a time do. The recent review by Mann (N Eng J Med 297:644-650, 1977) should dispose of the diet-cholesterol theory of atherosclerosis. It probably will not; the "mysterious viability of error" commented on by Francis Bacon in 1605 can be counted on to prevail in official dicta for years to come. The notion has become a petrifact, a word used by Spengler to describe stubbornly defended error. It may never be demolished, however strong the evidence against it. The petrifact has continually received vociferous support in irresponsible statements by journalists and spokespeople for foundations and official agencies. These statements maintain that high dietary cholesterol intakes in the industrialized nations have initiated an explosive worldwide epidemic of heart disease. Statements of this sort are reprehensible (however, unintentionally so). Although the number of cases of coronary heart disease has increased in this century, A. E. Harper (J Nutr Ed 9:154, 1977) has shown that when the statistics

*The popularity of milk is far from new. It should be remembered, for instance, that Clement of Alexandria (third century A.D.) called the Christians *galaktophogoi*. For a discussion of the symbolism of milk in Christian dogma, see Eisler, R. Orpheus the Fisher. London: Watchkins, 1921, p. 62 et seq. [footnote added].

are corrected for the aging of the population, there has been no increase in the disease. In fact, there has been a steady decrease that started long before significant numbers of the susceptible population began to be concerned about the notion that cholesterol in the diet causes atherosclerosis.

How can errors due to indifference to artifactual factors be avoided? History provides the answer to this question. Physicians since the time of Bonet and, more strikingly, of Morgagni have used postmortem examination of their patients as a first step in clinical investigations because the examination of patients dead reveals more than the examination of patients living. Meyer Texon has used this approach and thereby provided us with a mass of unselected postmortem material on the subject. The demonstrated occurrence of the atherosclerotic lesions at bends, branchings, bifurcations, and fixed points of arteries—all areas of distorted blood flow—calls attention to the primary role of hemodynamic factors in the genesis of atherosclerosis. (An observant naturalist might have reached the same conclusion, having been struck by the fact that the only place the carp develops significant atherosclerosis is at a bend of 135° in its aorta. This experiment of nature should not have been so long ignored.) Although the ways in which hemodynamic forces stimulate the smooth muscle cells of the media to increase in number, rearrange themselves, and migrate remain incompletely defined, it must be concluded that the development of atherosclerosis is a hemodynamic phenomenon. The next step, already initiated by Texon, is the experimental production of atherosclerosis in various species according to the principles expanded in this book. After that, attempts can be made to mitigate these effects.

Meyer Texon's book, as a nonartifactual study of human atherosclerosis, stands out as a basic text of all research on the subject.

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