



At last, "I am a  
pharmacologist."

"Convention doesn't  
make it true."



## Bridging two disciplines

"Though I felt like a pharmacologist,  
I was never sure I looked like one . . ."

by Barbara J. Culliton

Bernard Brodie is a gambling man.

Just before Christmas of his senior year at college, with his last \$40 in hand, he sat down to a game of poker, won \$1,000 and paid the tuition for his last semester at McGill University. That was in 1930.

Since then, with his gambler's luck, a remarkable store of scientific intuition, a touch of genius—and 15 hours a day of hard work—Bernard Brodie has lead the infant discipline of pharmacology to adulthood as one of the most important and rapidly expanding fields of biomedical research. Guided by Brodie whose insights show no regard for traditional theories, drug studies evolved from an imprecise and descriptive activity to a sophisticated science. He has made his mark by supplying the two essential ingredients to fruitful scientific inquiry: ideas and manpower.

"**Brodie intuitively** knows where the interesting things are, branching out freely in any direction in pursuit of a hypothesis, and he's always had the ability to select damn good younger colleagues," according to Dr. Sidney Udenfriend whom Dr. Brodie describes as one of his more brilliant proteges. Dr. Udenfriend is one of some 300 scientists trained in Brodie's sprawling laboratory of chemical pharmacology which occupies two floors at the National Institutes of Health. There, a favorite laboratory activity is playing

consequences. Having come up with a hypothesis to explain some chemical or physiological phenomenon, Dr. Brodie and co-workers gamble—following the consequences of its being true instead of looking for reasons why it cannot be true.

One round—played by Dr. Brodie and two graduate students—developed the hypothesis that special enzymes in the liver metabolize drugs that simulate foreign organic compounds ingested in food and that these enzymes evolved as the need for them developed. Hence, not all species need enzymes to metabolize foreign compounds. Many fish and aquatic amphibia, for example, dispose of most foreign material by excreting them through permeable gill membranes. Land-living reptiles, however, with their impermeable skins, need and have enzymes to convert foreign substances to components their systems can handle. From reptiles, the enzymes next appeared in birds and mammals. "The animals, in fact, inherited them from the reptiles, for nature usually retains a good thing," Dr. Brodie says.

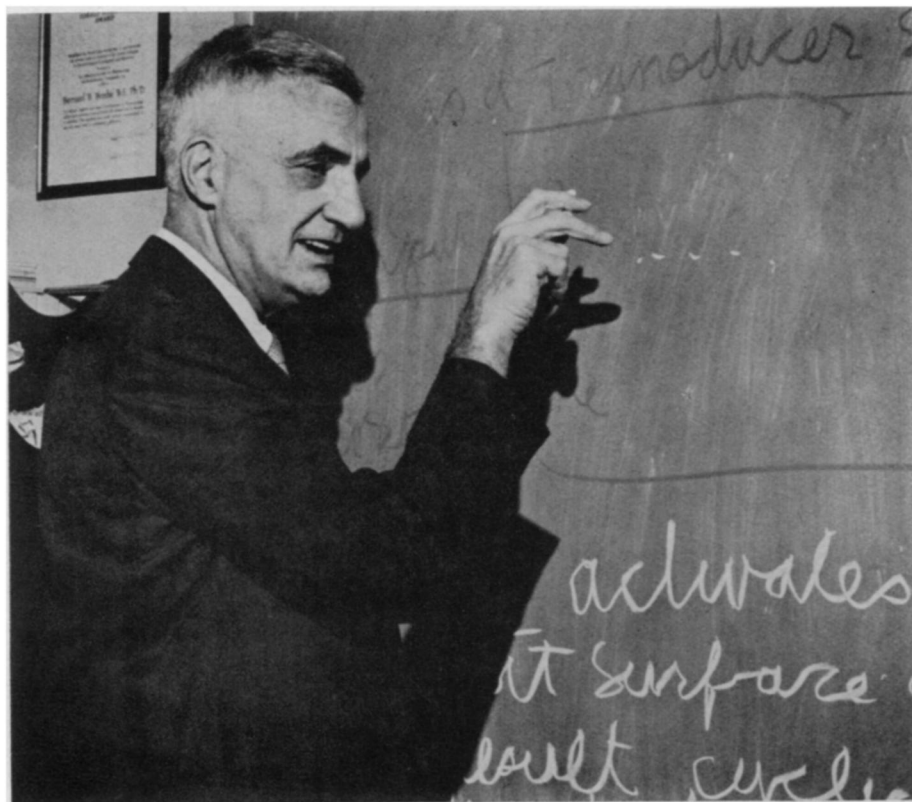
**But consequences** didn't end there. Out of these academic studies of the evolution of enzymes came a finding of considerable practical value. "In trying to prove that 'ontogeny recapitulates phylogeny,' graduate student Roger Maickel and an English visitor

discovered that the newborn of mammals lacked drug-metabolizing enzymes," Dr. Brodie points out. At first newborns drink their mother's milk which is free of organic substances that have to be metabolized and so they have no need of enzymes. From this it follows that drugs should be given to babies only under exceptional circumstances.

**For all** the pharmacologists he's trained, Bernard Brodie—otherwise known as Steve because everyone named Brodie is called Steve—was not trained in his own field. His doctorate is in chemistry from New York University. He went into pharmacology afterward because, he says, he was lucky enough to have teachers who advised him while he was still young.

"My mentor, in organic chemistry, advised me to go into pharmacology because I was unable to remember simple structures or the Geneva nomenclature and because I was accident prone. He introduced me to Dr. George B. Wallace, that kind and gentle teacher who was willing to take into his department an ugly duckling because he foresaw that one day biochemistry and pharmacology would have to come together. From him I learned about intuition in science and the value of the working hypothesis."

Later, Dr. Brodie worked under Dr. James A. Shannon, now director of



Gary Laurish

"... the value of a working hypothesis."

NIH, whom Brodie calls "the most logical man I have ever known." It was Dr. Shannon who impressed on him the value of applying chemistry to pharmacology, saying "You can answer almost any question in pharmacology if only you can determine a drug accurately." To this end, Steve Brodie has devoted his life, developing methods of measuring precisely what happens to a drug once it is inside the body and showing that it is drug metabolism—rather than dosage or localization in tissue or absorption or excretion rates—that accounts for the enormous variability in response between individuals and among species. Challenging what he calls toxicologists' foolish axiom that animal data can be extrapolated to man, Dr. Brodie and his proteges have identified innumerable environmental and genetic factors that influence drug metabolism.

**The results** of Dr. Brodie's 30 years of experimentation are influencing profoundly the course of animal drug studies and the shape of medicine to the point that, with certain drugs, the time may be approaching when physicians will be able to give patients a highly individualized regimen for medication. But if the years have been long, the days have been even longer and the 15 hours a day, or more specifically a night, that the hard-driving, white-haired, Dr. Brodie labors make him a

difficult man to work for. He seldom comes into his lab before noon and often works until three or four o'clock in the morning, thinking, testing or writing one of the nine or ten drafts that precede every finished paper. "You can only take his schedule for so long," says one of his former co-workers. "Usually it's our wives who complain first, but after a while it's just too much for most of us." And so, after a few years Brodie's young proteges branch out on their own and a new crop of scientists come to train.

Mrs. Brodie, however, has learned to be a tireless night-person like her husband. Adjusting her life around his, Anna Brodie often spends her nights typing manuscripts or serving coffee to her husband's colleagues working in their Bethesda, Md., home.

**Admired** as he is, and generally acknowledged to be the nation's leading pharmacologist, Bernard Brodie is not an altogether popular man. Ironically, the very intuition that marks him as a brilliant scientist is the thing that sometimes disconcerts his colleagues. For Dr. Brodie, who believes that various disciplines can interact and that long-held ideas are not necessarily sacred, has the habit of moving freely from field to field as his ideas lead him. "When he challenges a traditional view in neurophysiology, turns himself into an expert in the field in a year's reading

and talking and ends up being right, he doesn't exactly endear himself to the acknowledged leaders in that area," a colleague says. However, endeared or not, the thrust of Dr. Brodie's drug studies has been felt in such diverse disciplines as physiology, clinical medicine, psychiatry and biochemistry. For the pervasive, interdisciplinary scope of his work—rather than for any single discovery—he has been honored by his profession some 17 times.

**Last March** he was awarded an honorary degree from the University of Barcelona for his broad contributions to pharmacology and, particularly, for his work on reserpine, a commonly used psychiatric drug. In 1965, the Czechoslovak Academy of Sciences elected him to honorary membership and in 1966 he became one of the first men in his field to be elected to the National Academy of Sciences.

An inveterate participant at the august sessions of such societies, tweedy, soft-spoken Dr. Brodie says he really doesn't listen well at meetings and slips out for a glass of B&B and some English food whenever he gets the chance. Like certain variations in drug response, his taste for English food must be inherited, for though he lived in Canada as a boy, he was born in Liverpool, in 1909.

Of all the honors he has received, one from the American Society for Pharmacology and Experimental Therapeutics was, perhaps, the most welcome. Accepting the Torald Sollmann Award on Aug. 13, 1963, Steve Brodie said it had a "special and rather personal meaning—I have been accepted by a company of my peers.

"I came into the world of pharmacology virtually a stranger," he told the assembly, "with some knowledge of chemistry and physical chemistry but none whatever of biology . . . . Despite my ignorance, members of the Society always treated me as a person without bias who might possibly have something to add to a discussion. As a consequence of my kind reception, I finally began to feel like a pharmacologist. But, though I felt like a pharmacologist, I was never sure I looked like one. Old friends . . . tried to assure me that it was hard to tell the difference, but I sometimes showed the little chip on my shoulder when, after a spirited discussion, I would hear as I walked away, 'But, after all, he is not a real pharmacologist.'

"Now I am convinced the Society cannot be wrong; I am a pharmacologist. I wish to thank, from the bottom of my heart, those persons who had anything to do with nominating me for this award for the assurance that I am what I have pretended to be." ♦