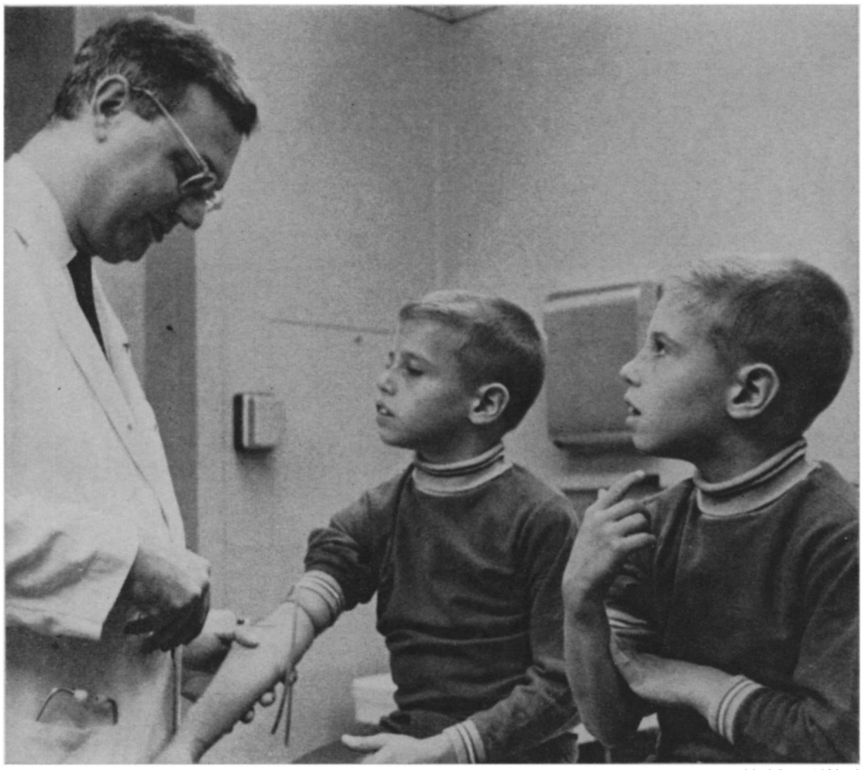


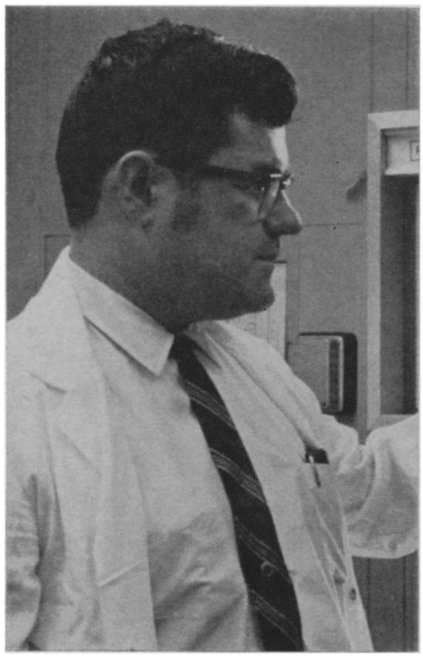
Hubbard/NIH

Dr. Vesell draws blood sample from identical, if unhappy, twins.

PHARMACOGENETICS

Individual drug responses

Ten-fold variation found in metabolism; twin study shows heredity important



Dr. Page, partner in the studies.

Physicians prescribe drugs on the basis of scant and sometimes misleading advertising. This indictment of the medical profession comes from the Department of Health, Education and Welfare after a year-long study of prescribing practices.

Assistant Secretary Dr. Philip R. Lee has reported that 35 percent of the members of a group of patients hospitalized for chronic illness had adverse reactions to at least one drug. He believes many such reactions are needless.

Lack of objective data on drugs is one reason for poor prescribing; ignorance about individual patients' responses to drugs is another. In continuing studies of twins, Drs. Elliot S. Vesell and John G. Page of the National Heart Institute find that many of these differences are controlled by inheritance. Dr. Vesell explains that some people are fast drug metabolizers—they use up a drug quickly; others are slow metabolizers. If those who metabolize slowly receive standard doses of a drug on a regular basis, the drug or its active breakdown products accumulate in their bodies, possibly causing toxic reactions. Such toxicity may kill (SN: 6/29, p. 614).

Soon, he suggests, "physicians may determine individual rates of drug metabolism before beginning long-term therapy." Dr. Vesell and others have found some commonly used drugs to be almost entirely under genetic control in their rates of destruction within the body. They include dicumarol, an anticoagulant; dilantin, for the control of epilepsy; antipyrine, an antifever agent, and phenylbutazone, an analgesic and anti-inflammatory compound. "We have every reason to believe there are others and that this principle is the rule, rather than the exception," he says.

To test the hypothesis of genetic control of drug levels and hence of responsiveness to drugs, Drs. Vesell and Page recently recruited healthy twins from the Washington, D.C., area and performed a group of experiments.

In the first experiment, seven pair of identical and seven of fraternal twins, none of whom had taken any drugs for the preceding month, were given phenylbutazone orally.

Their handling of the drug was analyzed to measure the contribution of hereditary and environmental factors to a particular result. The formula permits a range of values from zero—no hereditary influence, to one—strong influence. Fraternal twins with half their genes in common showed a value of 0.45—close to half. Identical twins registered an even 1.

Because many of the identical twins lived apart and had different habits in eating, smoking and using normal medications, their common responses could not be linked to environment.

Studies of metabolism of antipyrine, involving the initial group of 14 pair of twins plus an additional four pair, showed similar results. Although metabolism time varied among sets of twins, each pair of identical twins handled antipyrine in virtually the same time, whereas variations occurred among fraternal twins.

Differences among the 36 volunteers, considered individually rather than in pairs, were three-fold, further illustrating the importance of determining metabolic rates before instituting therapy. In one person, the half-life of antipyrine was 5.1 hours; in another, 16.7 hours. Variations in response to dicumarol, a commonly used anticoagulant, were ever greater; the range was 10-fold in the rate of elimination of this drug in a twin study about to be published by Drs. Vesell and Page. *B.J.C.*