ASSESSMENT AND

GENETIC SUSCEPTIBILITY TO TOXIC CHEMICALS

by
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The range of human diseases and abnormalities contains, at one extreme, conditions regarded as inherited, e.g. sickle cell anaemia, phenylketonuria and haemophilia, and, at the other extreme, typically environmental diseases, such as anthrax and typhus. However, along this continuum are many disorders in which both genetical and environmental factors are apparently important. The genetic factors determine an individual's susceptibility to disease. The environmental agents are responsible for the manifesting of symptoms.

The elements of the situation were explained by Harris (1) in the form of two circles, a larger one enclosing a much smaller circle. The outer circle represents a population while the inner circle represents a subgroup of individuals genetically predisposed to develop a particular kind of disease. The two lines drawn from the centre to the periphery in a wedge shape divide the entire population into those individuals who happen to be exposed to environmental factors that tend to elicit the abnormality and those who are not exposed. Only the small segment of the population who are both genetically predisposed and subject to the unfavourable environmental situation actually develop the clinical disorder.

Pharmacogenetics and ecogenetics are scientific disciplines which are both devoted to the problem of the genetical predisposition to drugs and environmental agents. Pharmacogenetics was founded in the mid-1950s, when the differentiation of effects provoked by therapeutic doses of suxamethonium in a group of human beings was found to be genetically determined. In addition, the different variants of glucose-6-phosphate dehydrogenase (G-6-PD) were found responsible for the differentiation in susceptibility of red blood cells to haemolytic effects of some drugs. Evidence indicated that people who are carriers of some G-6-PD variants can manifest the haemolysis even after ingestion of substances which are normally fully harmless, e.g. fava beans.

Some years later, a wide variability was found in the extent to which individuals inactivate isoniazid and some