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Jan Koch-Weser, M. D.:

ON <u>SYSTOLIC</u> HYPERTENSION, more common than <u>diastolic</u> hypertension and at least as <u>dangerous</u>

What it is, what it does, and what to do about it.

PUBLISHER'S NOTE: Jan Koch-Weser, M.D., Director of the Merrell International Research Center in Strasbourg, France, has been in the thick of the battle against hypertension for the past two decades. As Head of the Hypertension Unit at the Massachusetts General Hospital from 1966 to 1975 he was instrumental in developing and evaluating many of the most effective antihypertensive drugs and drug combinations in use today. He was among the first to emphasize the increasing opportunity to select for each hypertensive patient the drug or drugs most appropriate to the etiologic and hemodynamic characteristics of his disease. At the Merrell International Research Center, Dr. Koch-Weser is now concentrating his efforts on the creation of new therapeutic agents for the ongoing battle against cardiovascular diseases.

-Richard Stanton

No other disease has received more therapeutic attention during recent years than hypertension. Three factors account for this opportunistic concern. First, cardiovascular diseases are by far the most common cause of disability and death in civilized societies. Second, abnormally elevated blood pressure is one of the most important factors responsible for cardiovascular morbidity and mortality. Third, normalization of blood pressure by appropriate treatment largely or completely climinates the adverse effects of hyper-

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Regulation of the Chemical Industry

Recently I visited six of the major industrial laboratories in the United States, including three chemical establishments. I found much that was interesting and at the forefront of science and technology. At the same time, there was much evidence of the impact of federal regulations on industrial research, particularly in the chemical companies. Expenditures for long-range research have declined markedly, but funds for defensive research and development, including toxicology, are sharply higher.

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In almost all conversations, chemists alluded to federal regulations. Attitudes ranged from the view that the chemical industry is in mortal peril to the thought that the present trauma will lead to beneficial results both for society and for the industry. Directors of research contritely admitted past shortcomings in the chemical industry's behavior with respect to its products. They particularly regretted inadequate consideration of the long-term fate of substances and were unhappy about careless errors by some users of chemicals. They now recognize that if misuse leads to untoward effects, they will share the onus. Thus there is now a willingness to monitor the use and fate of chemical products all the way to final disposition.

An important trend is an expansion of efforts devoted to toxicology. Companies that already have toxicology laboratories have expanded them. Other companies have established new facilities. In addition, a Chemical Industry Institute of Toxicology has been created, financed by contributions from 36 companies. Precise figures are not available, but the total professional personnel involved industry-wide is now of the order of 1500. The demand for trained toxicologists has far exceeded the supply.

Chemical companies have long been aware of the problems created by toxic substances in the workplace. Some of the lessons were learned inadvertently decades ago at the expense of workmen. This led to the establishment, for example, of the Haskell Laboratory of DuPont in 1935. Much of the early work of such laboratories was devoted to studies of acute toxicities. Although some attention was given to effects of chronic exposure, the possible risks of carcinogenicity were not probed deeply.

At the moment, the magnitude of the carcinogenic hazards posed by industrial chemicals is not well known. But the public has gained the impression that the risks are substantial, and the tendency of the government is to take no chances. Thus chemical companies live in fear of sudden drastic action. Many long-term studies are now in progress or have been completed. A typical experiment on a single chemical involves following 800 animals for 2 years and performing pathological examinations on 40 different tissues per animal for a total of 32,000 specimens. In instances where no excess cancer is found in comparison with controls, the outcome is clear. But what of instances similar to the saccharin case in which an extremely large dose seems to produce some cancer? Is there or is there not a threshold dose? Are there detoxifying mechanisms by which the animal or human disposes of small amounts of chemicals which in large doses are carcinogenic? How applicable to humans are studies on microorganisms or rodents?

Uncertainty is compounded by the language of relevant legislation. For example, the opening policy statement of the Toxic Substances Control Act asserts that the regulations are "not to impede unduly or create economic barriers to technological innovation while fulfilling the primary purpose . . . to assure that such innovation and commerce . . . do not present an unreasonable risk." With such a compounding of uncertainty, it seems obvious that in future thousands of toxicologists will obtain their livelihood in the laboratories while bevies of lawyers will grow rich on litigation. But perhaps the outcome will be more constructive. From the studies we may develop general principles about the functioning of living systems. The chemical industry may emerge more capable of discharging its responsibilities to society and accordingly stronger and more acceptable.

-PHILIP H. ABELSON



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