JAMA EDITORIALS

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## TRANYLCYPROMINE SULFATE

It has been six months since tranylcypromine sulfate (Parnate) was taken off the market by its manufacturer. This action occurred after strong pressure from the FDA, but under firm protest by the company. Widespread publicity associated with the event, much of it ill-advised and unnecessarily hysterical, embarrassed some physicians and caused their patients undue anxiety. Subsequent to the withdrawal of the drug, conflicting statements emanated from both the company and the FDA, whereupon the manufacturer requested a public hearing. From statements voiced by eminent physicians, it was evident that medical opinion was divided regarding the potential benefit of the drug as related to its potential hazards. Shortly before the hearing was to be held, the FDA announced that, after further review and study, it was permitting tranylcypromine to return to the market. The condition attached was that the manufacturer give emphatic attention to all potential hazards associated with the drug, particularly those associated with paradoxical hypertension and the enhancing of the hazards of tranylcypromine by other drugs in common use and by some common kinds of food and drink. (The Council monograph on tranylcypromine, appearing in this issue on page 763, has been updated to incorporate all available pertinent data on the agent.)

Retrospectively, the medical profession may well be somewhat confused and find it difficult to understand the course of events in this case. Comments and questions similar to the following have been understandably made. It has been suggested that it might have been better to have made a thorough investigation before the drug was removed from the market rather than afterward. One wonders whether pushing the panic button was justified. One also hopes that there now is or soon will be available at FDA an operational plan for requesting removal of a drug from the market with a minimum of furor and fuss.

It is easy to criticize, but one must realize that the new Drug Amendments of 1962 and the regulations they have engendered have thrust tremendous administrative responsibilities on an agency which is inadequately staffed and which has been compelled to recruit personnel who have not yet had time to become adequately experienced. It is understandable that they became extremely concerned about a drug, the toxicity of which apparently was enhanced by concurrent and/or consecutive use of other agents and even by cheese and beer, to a degree not heretofore so well documented, at least in man. It is to the credit of the new medical director of the FDA, Joseph F. Sadusk, Jr., MD, that the tranylcypromine controversy which he inherited, appears to have been resolved by an objective appraisal of the medical and scientific data available. His recent discussion at the AMA Annual Meeting in San Francisco was a fair and unbiased presentation of the situation and quite properly placed a share of the responsibility upon the physicians by reminding them of their professional obligation to be fully aware of the *facts* concerning the potential benefit-to-risk ratio of the drugs they prescribe. He warned that unless physicians meet this responsibility, useful therapeutic agents might not be available in the future simply because they produce adverse side effects.

But what about the physician? Where can he obtain reliable information? The drug monographs published in THE JOURNAL under the auspices of the AMA Council on Drugs (collected and kept current in *New and Nonofficial Drugs*) are an excellent source of such information. These monographs are the digests of the meeting of the minds of AMA drug department staff, consultants, and AMA Council on Drugs' physicians and scientists. Another source is the package insert accompanying each drug. This may be obtained from any pharmacist or from the pharmaceutical company producing the product. It is not fully appreciated that the information in the package insert is the result of discussion among industry and FDA physicians and scientists. A third source of information is a telephone call to the AMA Department of Drugs which has on file a great deal of up-to-date drug information.

Finally, the history of medicine has demonstrated clearly that the medical profession—when it has the facts—can be trusted to utilize hazardous substances in the best interests of the patient. It would be well for the FDA to bear this in mind and to use its regulatory power with discretion in *any* area in which *a significant segment* of the medical profession agrees that a drug, even though potentially hazardous and having a certain risk in its use, can be used effectively to the best interests of

patients. It appears from Dr. Sadusk's disposition of the tranylcypromine problem that he is aware of this, and that he realizes the difference between an *educational* problem (requiring an appropriate educational approach for solution) and an *imminent public health problem* (requiring prompt, decisive, regulatory action).

DEPARTMENT OF DRUGS

## A NEW MEANS OF HEAT RELIEF

In industries such as steel, aluminum, and glass manufacturing and deep mining, workmen may be exposed to heavy thermal stress. When heat is accompanied by high humidity, due either to subtropical climate or to the addition of water to the atmosphere as may occur from wet drilling in mines, normal body cooling through sweat evaporation is impaired, and the risk of heat casualty is increased.

A simple, low-cost method for providing a microenvironment of cool, clean air for the man at work, based upon the use of the Ranque-Hilsch vortex tube, has now been devised. The vortex tube is lightweight and operates on standard industrial compressed air as the sole source of power. The device has no moving parts and requires very little maintenance. Described as a simplified radial-inflow turbine, it converts compressed air into a hot and a cold stream.[1] One model of the vortex tube that is now in regular use in the southern United States weighs only 19 oz. Carried by the worker on a belt at his waist, it is supplied by compressed air through a pressure hose. It consumes 25 cu ft of air per minute at 100 lb per square inch pressure. It is capable of producing a cold stream of 20 cu ft of air per minute at a temperature 55 F below the temperature of the supply air. The cool air is dispersed over the man's upper trunk through lightweight perforated plastic tubing worn beneath ordinary work clothing, and a stream may be delivered to the breathing zone inside a simple fabric hood when exposure to radiant heat is especially severe, or when respiratory protection as well as heat relief may be desired. With proper attention to the quality of the compressed air that enters the vortex tube, the stream emitted from the tube is safe for breathing.

Physiological observations made on men at work on hot jobs in an aluminum reduction plant showed that the use of the vortex tube for individual air cooling resulted in a three-fold reduction in sweat loss, a 25% reduction in heart beat cost, and a 50% reduction in the expected rate of increase of body temperature under the observed conditions. These studies are reported in the September issue of the *Archives of Environmental Health*.[2] A slightly different version of the vortex tube designed for man cooling in laboratories that may be contaminated by radioactive compounds provides for the delivery of cool air inside transparent protective clothing was reported in a US Department of Commerce bulletin.[3] Vortex tube units with accessory equipment are now commercially available from several suppliers of personal protective clothing. The vortex tube alone costs less than $75.

The special advantages to the workman whose tolerance for heat has been reduced through aging or physiological impairment are clear. The selective use of the device may be of particular interest to use of the vortex tube may be of particular interest to the physician who wishes to see a patient who has cardiovascular disease continue in his regular work, even when the man is employed on a hot job.

1. Fulton, C.D.: Ranque's Tube, *Refrigerating Engineering Magazine*, pp 1-7 (May) 1950.

2. Lienhard, W.F.; Hughes, J.P.; and Brassette, T.A.: Man Cooling by Vortex Tube Device, *Arch Environ Health (Chicago)* 9:377-386, (Sept) 1964.

3. Alexander, J.M., Croley, J.J.; and Messick, R.R.: *Use of Vortex Tube for Cooling Wearers of Industrial Protective Clothing*, AEC Research and Development Report DP-861, Office of Technical Services, US Dept of Commerce, (Oct) 1963.

## MYELOFIBROSIS (PANMYELOSIS) IN HIROSHIMA

Myelofibrosis—a disease (or diseases) with variable degrees of anemia, splenomegaly, fibrotic bone marrow, and myeloid metaplasia—eludes precise definition. Theories on pathogenesis range from necrobiosis (due to the toxic action of benzene, radioactive phosphorus, radium, and other agents) and primary bone-marrow failure (in which myeloid metaplasia is viewed as a compensatory process), to the current, widely held theory that it is but one of a group of myeloproliferative disorders. Proponents of this latter view regard intramedullary and extramedullary changes as stemming from a common "myelostimulatory factor." Depending on the phase of the disease, or the form it takes in a particular patient, the myeloproliferative disorder might be manifested as polycythemia vera, myelogenous leukemia, erythroleukemia of di Guglielmo, or myelofibrosis.

The so-called myelostimulatory factor, having also eluded precise definition, has remained, to a large extent, an abstraction, a convenient rack which can accommodate many hats. However, Anderson, Hoshino, and Yamamoto,[1] in their study of Hiroshima victims, have found evidence to implicate ionizing irradiation in most of their cases of myelofibrosis.

Records at the Atomic Bomb Casualty Commission for the years 1950 to 1959 show the autopsy prevalence of myelofibrosis to be 4½ times more common in bomb-exposed than in nonexposed persons, and 18 times greater than elsewhere in Japan. In the immediate area of the bomb, the incidence was inversely proportional to the distance from the hypocenter, a pattern also noted for leukemia. Be-