

high tension for both the 1- and the 3-million-volt instruments in Toulouse. The Swiss have, until recently, preferred huge open-air million-volt generators, but they are now providing more compact twin pressure-enclosed supplies, one member of which contains a generator connected through a pressurized tube to a second container, which houses the accelerating tube. The Japanese manufacturers, Hitachi, Shimazu, and Japan Electron Optics Laboratories, have each designed their own Cockcroft-Walton machines and have chosen from the start to place each generator in its own single pressurized housing, which also encloses the accelerator tube. The High Voltage Engineering Corporation of Burlington, Massachusetts, has made a very satisfactory and stable three-phase insulating core transformer power supply operating at 500 kv for the lens column built by RCA for the University of Virginia in Charlottesville; this power source was described as inherently suitable for electron microscope applications up to 3000 kv. The possibilities of using Van de Graaff generators or superconducting linear accelerators for electron microscopes also received attention.

Various methods of optimizing the design of conventional magnetic lenses for high-voltage microscopy were proposed by Z. S. Basinski of Ottawa, J. L. Farrant of the Commonwealth Scientific and Industrial Research Organisation, Australia, and A. Strojnik of Cornell University. Progress in developing superconducting lenses for electron microscopes was reported by M. I. Dietrich (Siemens A.G., Germany), by H. Fernández-Morán (University of Chicago), and by a group at the Oak Ridge National Laboratories in Tennessee. Several persons expressed the view that superconducting lenses offered much promise for instruments operating at 5 megavolts. Status reports were presented from several of the more than ten new high-voltage facilities which have gone into operation or will do so during the coming year in Britain, Sweden, Japan, Australia, and the United States.

A new method for measuring energy losses of electrons traversing samples was presented by J. S. Lally (U.S. Steel Laboratories) in a session on diffraction contrast. In collaboration with C. J. Humphreys (Oxford University), who has been a visitor at the U.S. Steel Laboratories, Lally showed by experiment, supported by theory, that the crystal

orientation which maximizes penetration of high-voltage electrons through heavy materials is not the same as the orientation offering the best penetration at 100 kv. Beam effects in diffraction contrast from crystals were discussed by W. K. Bell (University of California, Berkeley), and by A. Methereil (Cambridge University). The fundamental mechanisms of inelastic scattering at high voltages were reviewed by P. B. Hirsch (Oxford University).

The final session of the meeting was devoted to the least mature aspect of high-voltage microscopy—image contrast of molecular structures. The fundamental scattering mechanisms and phase relationships determining contrast at this level were discussed. Increased penetration with higher accelerating voltage was anticipated, but the lack of a corresponding large loss in

contrast was a surprise. The feasibility of achieving "atomic" resolution at high voltage was the subject of lively debate and much skepticism. The direct read-out of molecular structure from visualization and recognition of single atoms in single molecules has been the dream of some electron microscopists, but the conference ended with this prospect unresolved.

H. STANLEY BENNETT  
*Department of Anatomy, University of North Carolina, Chapel Hill 27514*

H. P. JENERICK  
*Institute for General Medical Sciences, National Institutes of Health, Bethesda, Maryland 20014*

I. WARSHAW  
*National Science Foundation, Washington, D.C. 20550*

## Chronic Non-Psychiatric Hazards of Drugs of Abuse

A conference on Chronic Non-Psychiatric Hazards of Drugs of Abuse was held in San Francisco, 29–30 October 1969. The conference was co-sponsored by the Center for Studies of Narcotic and Drug Abuse of the National Institute of Mental Health and by the recently formed Environmental Mutagen Society.

The conference focused on biological hazards of drugs of abuse and excluded their psychiatric and psychopharmacological effects. The major categories of hazards considered were toxicity, carcinogenicity, teratogenicity, and mutagenicity. The object was to review existing toxicological information on these drugs and to identify productive strategies for future research. A particular effort was made to interpret current data on biological hazards due to LSD.

Hazards posed by drugs of abuse were viewed against the perspective of therapeutic and prophylactic drugs, as well as from the wider perspective of environmental chemical pollutants. Drugs of abuse, however, present unusual toxicological problems. Their use, which has increased dramatically over the last decade, is generally restricted to young adults. Such drugs are self-administered in a variety of ways, including ingestion, injection, and inhalation; they are generally administered in unquantitated doses. They are often administered in highly impure or contaminated states in combination with

a variety of other drugs and chemicals, and for prolonged periods of time. Finally, intercurrent infection and malnutrition are sometimes prevalent in user populations. In part, as a result of the restricted availability of these drugs, their chronic biological effects have been less well studied than other categories of drugs or environmental pollutants. The concept of matching benefits against hazards, generally considered appropriate in toxicological evaluation of therapeutic drugs, pesticides, or food additives, is complicated by other concerns implicit in the concept of "drug abuse."

Chemical structures of major categories of drugs of abuse were reviewed. The chemical crudity of most synthetic and semisynthetic formulations, and also the possibility of important biological activity of misidentified or unidentified chemical contaminants were emphasized. For example, the anesthetic Sernyl is commonly sold on the streets as synthetic marihuana. Background information on psychiatric, sociological, and pharmacological aspects of drug addiction and dependence were considered. Barbiturate dependence merited particular concern in view of the high mortality associated with abrupt withdrawal of this drug.

Biological interactions between different drugs of abuse and between them and other environmental pollutants were considered in relation to hepatic

microsomal enzyme function. For example, barbiturates are potent inducers of detoxifying microsomal enzymes; conversely, microsomal enzyme functions are inhibited by cannabiniol constituents of marihuana and by 3,4-methylenedioxyamphetamine (structurally related to piperonyl butoxide, a pesticide synergist and potent microsomal enzyme inhibitor).

While population surveys are helpful in establishing shifts in usage patterns of various drugs of abuse, they are unlikely to be useful in monitoring or detecting chronic hazards. Epidemiological approaches were discussed both generally and in specific relation to mutagenic effects. Detecting such hazards typically requires very large population samples, which practical considerations limit. However, valuable epidemiologic data on drugs of abuse, as well as on a variety of other environmental influences, could well accrue from a uniform nationwide registration for congenital anomalies. For example, if LSD was a powerful teratogen, this might manifest by a significant clustering of birth defects in younger mothers in metropolitan districts. No such fluctuations have been observed. However, present systems of data collection are only marginally capable of detecting gross effects.

The scientific literature on carcinogenicity, teratogenicity, and mutagenicity of drugs of abuse is almost nonexistent, with the notable exception of that on cytogenetic effects of LSD. Carcinogenicity was discussed with particular reference to problems of biotransformation of precarcinogens and carcinogens, the need for enhancing the sensitivity of standard animal tests, and their high degree of human relevance. Feeding or other appropriate administration of high test doses to rodents, from early infancy onward, may help to reduce the insensitivity of current carcinogenicity tests which must use numbers of rodents incomparably smaller than the large human populations at presumptive risk. The recent Bionetics study on pesticides (sponsored by the National Cancer Institute) demonstrates that such techniques do not produce false positives. With regard to teratogenicity testing, while standard protocols are available, these could be made less empirical if modified in light of data on metabolic transformation and on the duration of sensitivity of any particular developing organ to any drug.

Inframammalian models for muta-

genicity testing—bacteria, *Neurospora*, *Drosophila*, and in vitro cytogenetics—were considered to yield useful information. Mammalian methods, however, provide information with a higher degree of presumptive human relevance. Such systems, which are both sensitive and practical, include in vivo cytogenetics, the host-mediated assay, in which bacteria or *Neurospora* are tested in a mammalian milieu, and the dominant lethal assay. A combination of mammalian and ancillary submammalian tests are likely to detect all chemicals producing point mutations or chromosome anomalies.

Early cytogenetic studies on LSD were reviewed and found difficult to interpret because of poor experimental design, inadequate controls, drug contaminants, and unresolved sampling problems. These studies reflect difficulties, sometimes inevitable, in the use of humans, notably the likelihood of previous or concurrent exposure to other drugs. It was considered that these problems would be avoided by well-planned serial in vivo animal studies. Recently, more adequate human studies have suggested that pure LSD administered under controlled conditions may not produce cytogenetic effects. Needless to say, such findings have no bearing on the psychiatric hazards of these drugs.

The confusion in regard to LSD underscores the critical need for programmatic development of information on genetic and other hazards of drugs of abuse, quite apart from other drugs and chemical pollutants, with currently available methods that are sensitive, relevant, and practical. Standard uniform reference samples of crude and synthetic drugs of abuse should be made more easily available to toxicologists. The possibility of integrating various methods—for example, the use of single animal groups for concurrent tests such as carcinogenicity tests, in vivo cytogenetics, the host-mediated assay, the dominant lethal assay, and psychopharmacological studies—should also be explored.

The proceedings of the conference will be published by the National Institute of Mental Health in monograph form.

SAMUEL S. EPSTEIN

*Children's Cancer Research Foundation, Inc. and Harvard Medical School, Boston, Massachusetts 02115*

JOSHUA LEDERBERG  
*Stanford University Medical Center, Stanford, California 94305*

## Personnel Placement

### POSITIONS WANTED

**Austrian Engineer**, 9 years of English-language industrial experience, available for technical, scientific, and commercial translations from/into German. Professional, prompt. Rudi Payer, Williamstown, Ontario, Canada. 4/24; 5/1, 8, 15, 22

**Biochemist**: Ph.D., 1965. Research experience in soil-plant nutrition, pesticides, steroids and drugs metabolism. Publications. Seeking teaching, research. Oversea appointment considered. Available September 1970. Box 162, SCIENCE. X

**Biologist**, desires temporary position (1970-71). Ph.D., 13 years' total teaching. General biology, invertebrate zoology, elementary physiology, evolution. Box 163, SCIENCE. X

**Botanist/Mycologist**. Ph.D. (1969). Age 41. NSF postdoctoral. Interested aquatic, soil ecology. Seeks teaching and/or research position September 1970. Box 164, SCIENCE. X

**German Pharmacist**, Dr., rer. nat., seeks research position (drug action or metabolism, pharmaceutical synthetic or analytical chemistry). Two years of postdoctoral industrial experience (analytical field). Box 165, SCIENCE. X

**Husband/Wife Team**: 1968 Ph.D. Statistics: extensive computer experience, biomedical data acquisition systems, discriminant analysis. 1965 Ph.D. experimental psychology: effects teratological agents on behavior, operant conditioning. Publications, grants. Seeks appointment medical school or other. September 1970. Box 166, SCIENCE. X

**Immunologist**, Ph.D. Five years' teaching/research (clinical/experimental) experience, including 2 years' postdoctoral training in fluorescent microscopy. Publications. Desires appointment, university-government. Box 167, SCIENCE. X

**Inorganic**: Analytical/Radiochemist, Ph.D. 1968. Desires learning position in marine sciences. Would like postdoctoral or laboratory position. South Atlantic or Gulf coasts preferred. Box 168, SCIENCE. X

**Marine Invertebrate Zoologist/Science Policy**. Completion of doctorate, August 1970. Seeks challenging, interdisciplinary position in human biology/human ecology academic setting. Teaching experience, publications, Public Health Service Fellow. Box 169, SCIENCE. X

**Molecular Biology**: M.S. Microbiology; 4 years' experience including tissue culture, RNA, DNA, nucleoproteins, enzyme extractions, isotopes, bacteriophage, tumors. Research or teaching. Box 170, SCIENCE. X

**Physicist**, Ph.D., extensive experience in nuclear, electronic and general instrumentation. Position wanted in biomedical/bioengineering research or research and development. Box 171, SCIENCE. X

**Plant Ecologist**, Ph.D. expected 1970. Five years' full-time college teaching: ecology, biogeography, botany, taxonomy, biology, plant anatomy, science teaching methods. Desires teaching/research in small college/university. Available Fall 1970. Box 172, SCIENCE. X

**Retired Ph.D.**, human anatomist, comparative anatomist, neuroanatomist, biologist. Numerous publications. Active teaching-research. Desires medical school or small college association in South, Southwest, or West. Attractive financial arrangement available, Box 173, SCIENCE. 5/1

**Physiologist**, Ph.D. 1963. Training with strong chemical orientation. Histochemical, tissue culture, electron microscope and immunoelectrophoretic techniques and T.B. Antigen fractionation and characterization. Seeks research position in and around Baltimore-Washington area. Box 174, SCIENCE. X