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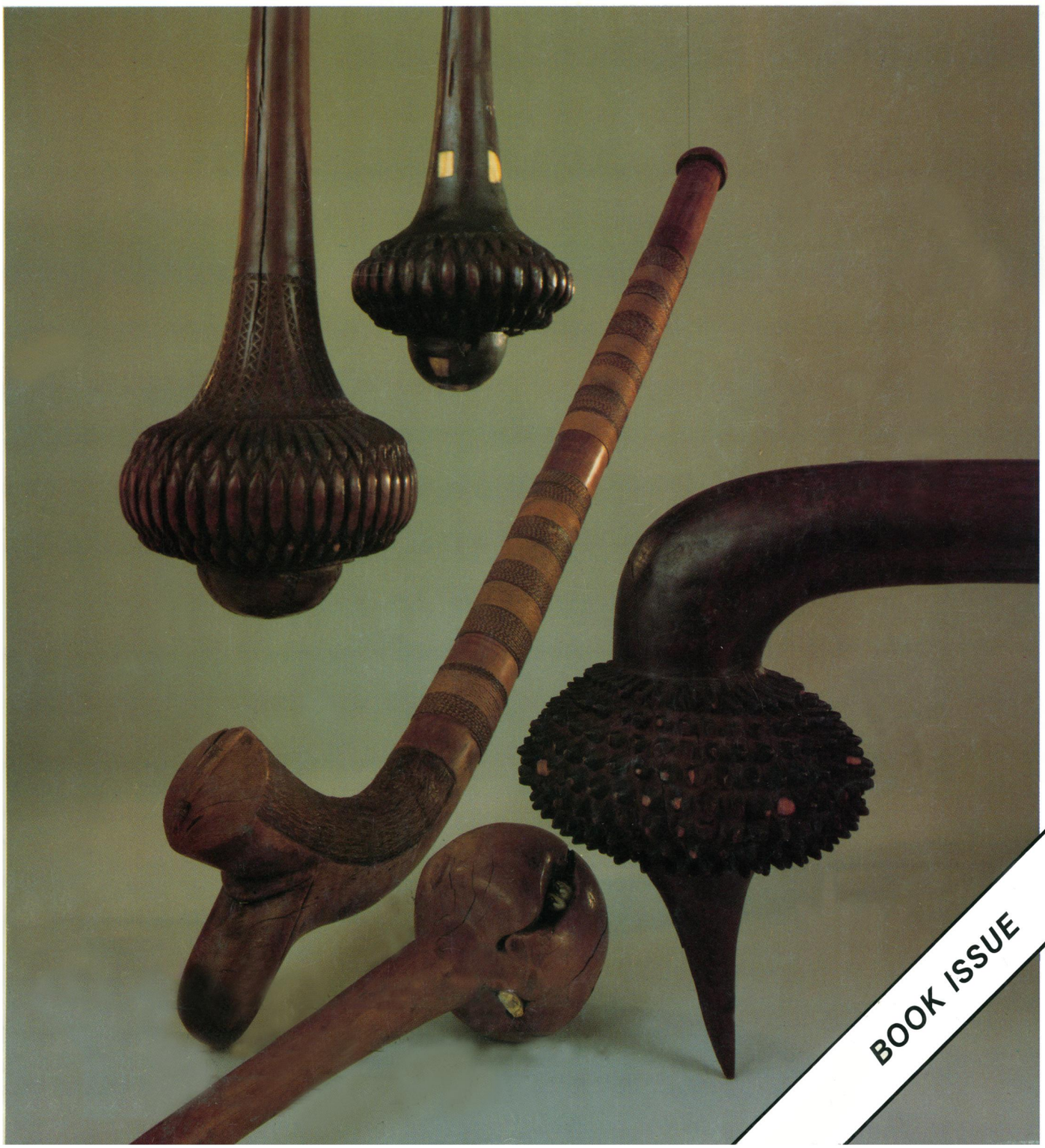

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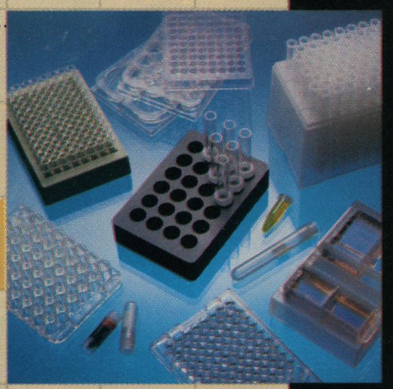

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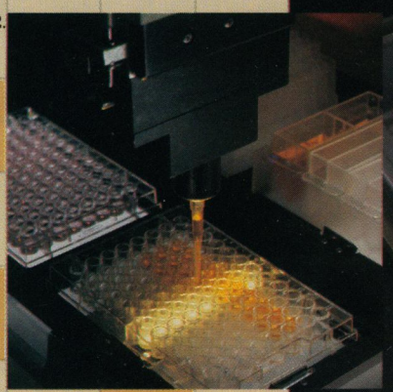

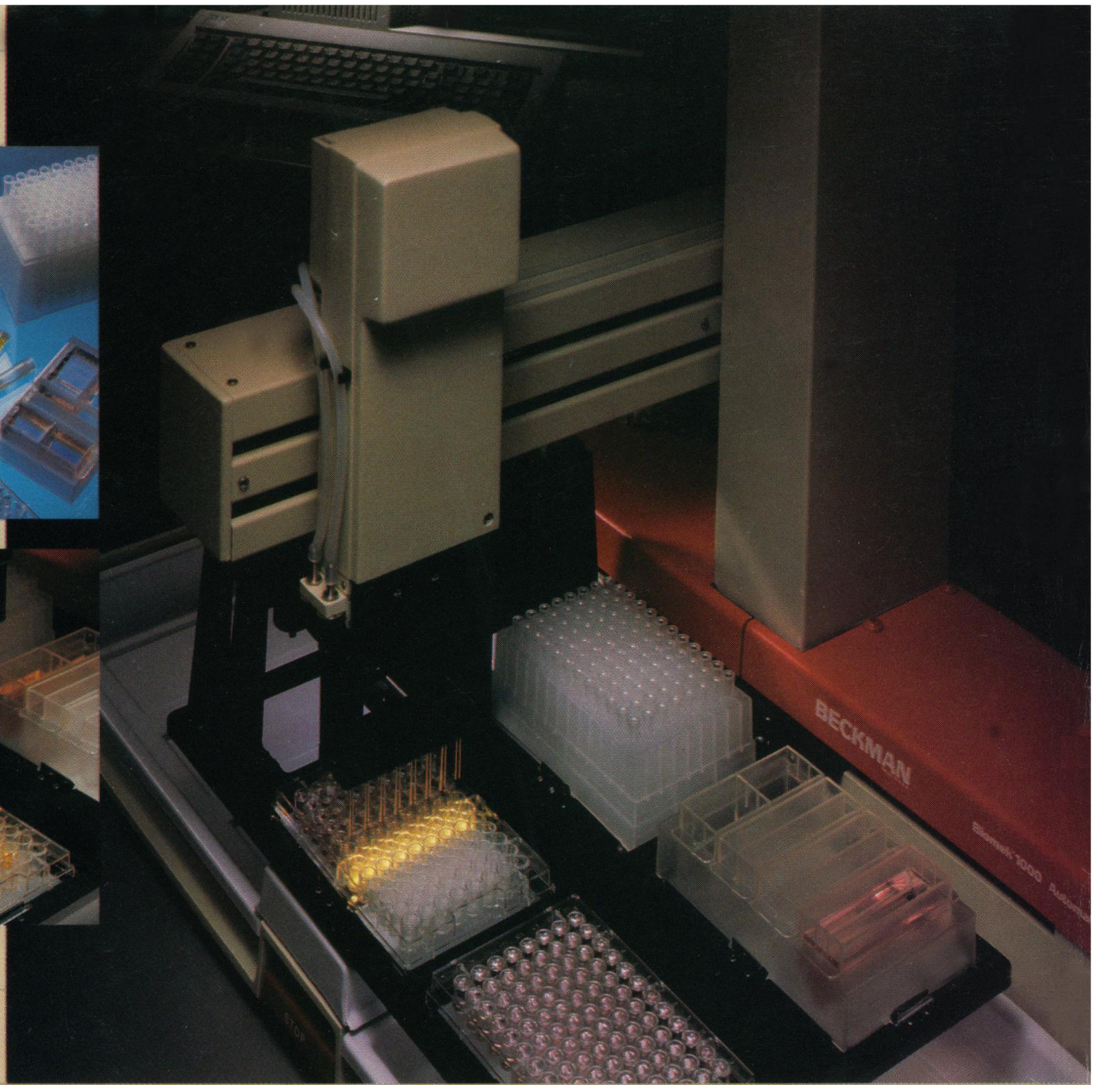

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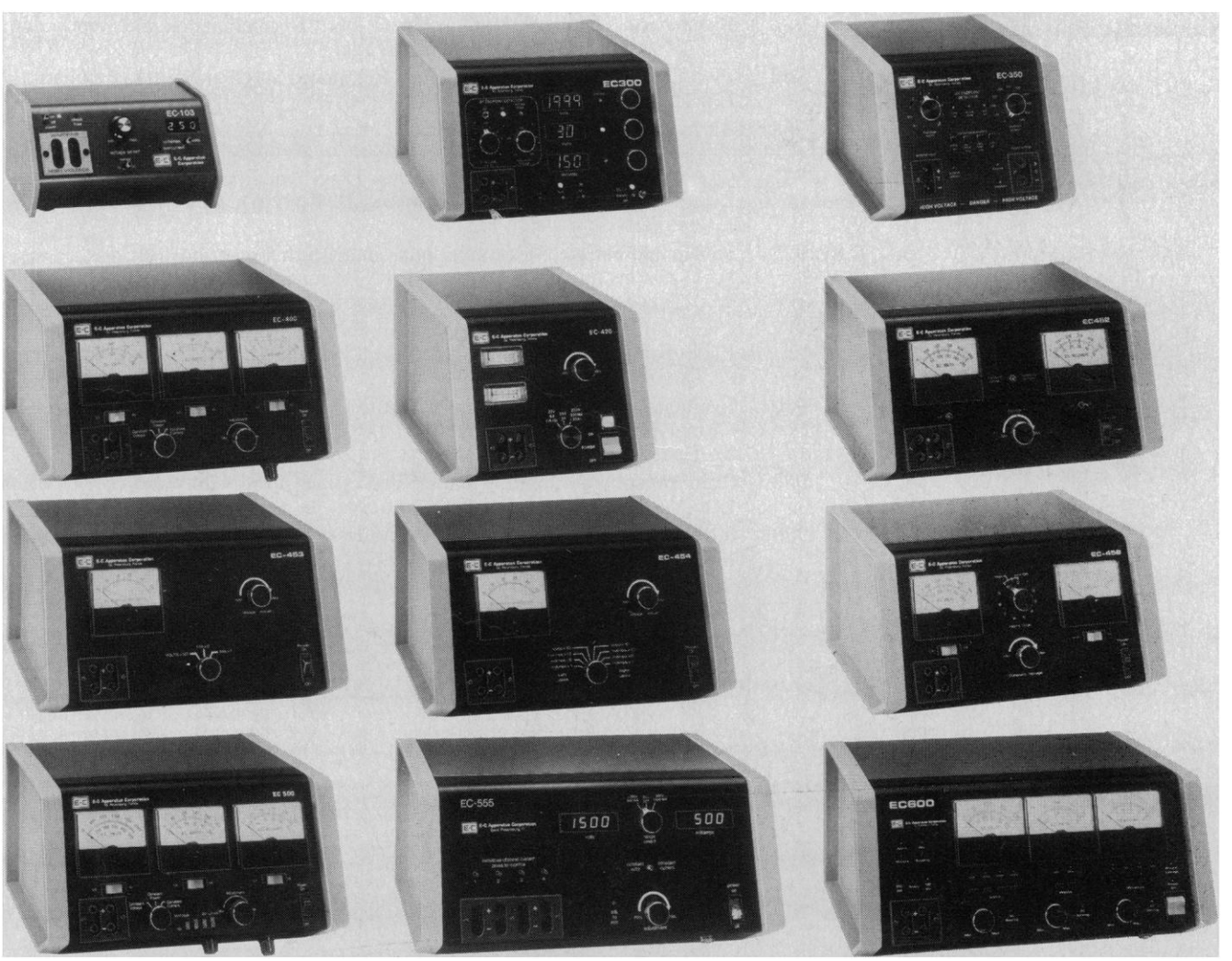

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COVER Fijian war clubs presented to the U.S. Exploring Expedition on its visit to Ovalau in 1840. "Short round-headed throwing or missile clubs such as the two at the top and one in the foreground were used to stun an enemy. . . . The larger two-handed clubs have different functions. The center club was said to slice and snap through bone, while the painted battle hammer on the right made a neat hole in the skull." The collection of Fijian artifacts made during the Expedition is "one of the three most important in the world and the only large one that can document a specific time period." [Courtesy of the National Museum of Natural History; from A. L. Kaeppler, "Anthropology and the Exploring Expedition," in *Magnificent Voyagers*, reviewed on page 1020]

Book Reviews

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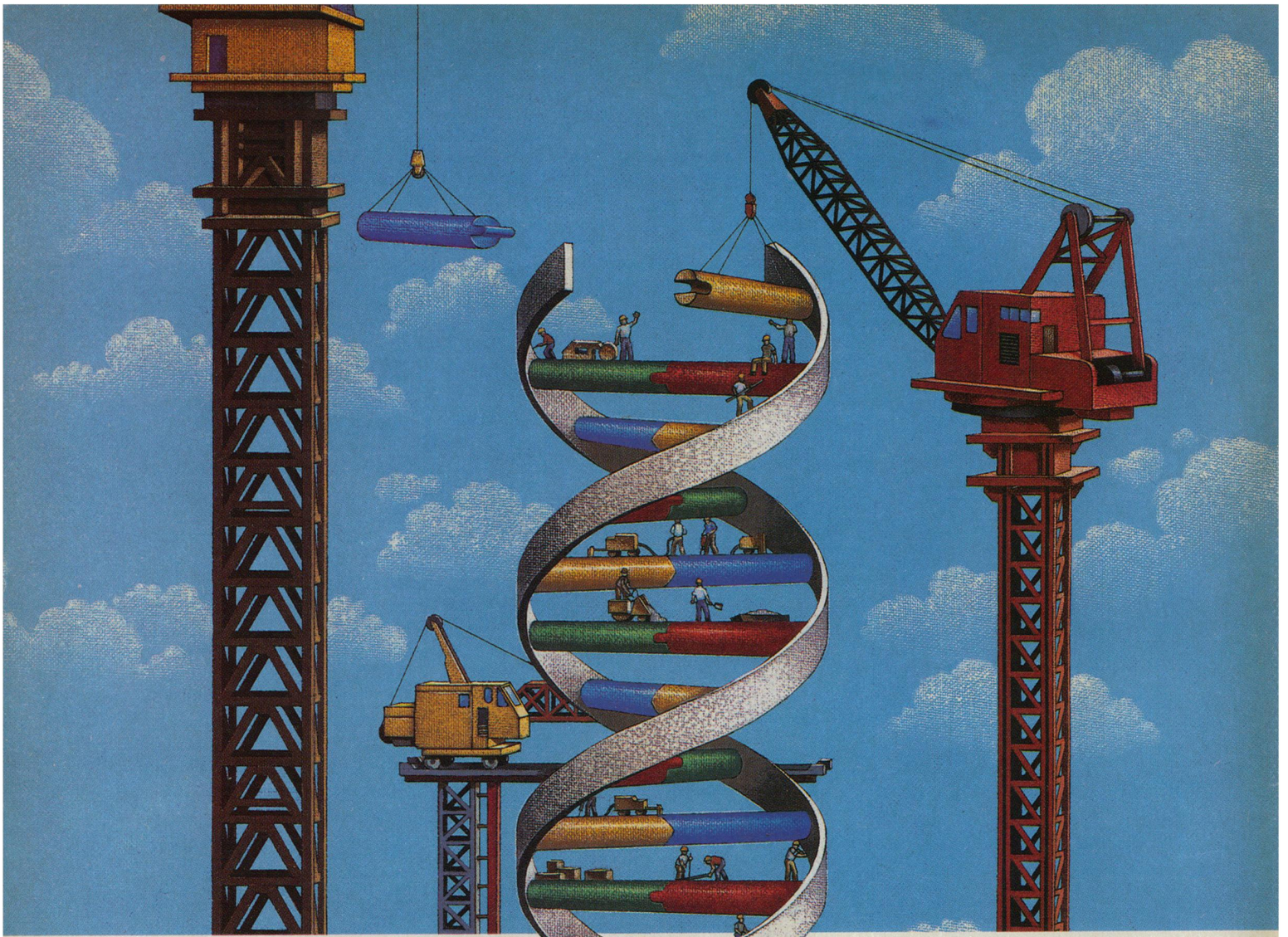

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This Week in
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Lastest twists in the DNA story

DNA is a contortionist's dream; its twists include the double helix that forms as paired strands of bases spiral, the supercoiling or knotting of the helical axis as it is suspended in space, and the catenanes—linked chains, figure eight's, and the like—that form as discrete molecules interlock (page 951). Wasserman and Cozzarelli describe the biochemical topologic method through which catenanes, knots, and other contortions of the molecule are being studied. How pieces of DNA are arranged in these twists can now be disentangled visually as a result of a new coating procedure that makes the strands thick enough for viewing in the electron microscope. From the types of knots and catenanes that can be produced in the laboratory or are found inside cells, the "history" of a DNA molecule can be deduced and enzymatic mechanisms by which it formed proposed. The topologic approach, combining mathematics and molecular biology, makes possible the formulation of theories about important cellular processes such as DNA replication and recombination.

Atmospheric data in cold storage

THE notion that the amount of acid in the atmosphere—falling to the earth as acid rain or snow—has been intensifying is supported by data from a glacial ice core containing a 115-year record of precipitation (page 975). The core was taken from an uninhabited region of Greenland that is free of local sources of acid contamination. In alternating seasons, air masses arrive from North America and from Eurasia carrying chemicals introduced into the atmosphere both by natural processes and by the activities of humans. Mayewski *et al.* found that anthropogenically produced sulfate began increasing in the early 1900's but was masked by sulfate emitted from volcanoes that were active at that time. Sulfate deposition is now about three times what it was at the turn of the century. Nitrate deposition showed strong seasonal variations; over this regular nitrate signal, the nitrate deposition increased in 1955 and intensified in 1975. Nitrate from both anthropogenic and natural (burning of fossil fuels and biological materials) origins has increased twofold just since 1975. Other chemical markers (such as oxygen isotopes that indicate that annual temperature has remained relatively stable in the region) have not similarly increased during the period recorded in the core.

Demyelinating disease process

PATHOLOGY in demyelinating diseases such as multiple sclerosis is thought to result from a combination of viral effects and immunologic reactions against cells of the central nervous system (page 991). A possible link between these two has been discovered by Suzumura *et al.* using a mouse system in which viral infection in the brain produces chronic central nervous system demyelination. Brain cells do not normally express antigens of the major histocompatibility complex (MHC). However, when mice are experimentally infected with a neurotropic virus, cells in the brain secrete a substance that induces MHC antigens on two types of neural cells, oligodendrocytes and astrocytes. Once the brain cells express the unexpected antigens, cells of the immune system become involved, immune reactions begin against cells bearing the MHC antigens, and demyelination ensues.

Suppression of endotoxin shock

A hormone such as dexamethasone may be useful for controlling the shock reaction that is caused by severe bacterial infections, if hormone use is judiciously timed (page 977). Shock results when bacterial endotoxin induces host macrophages to secrete the hormone cachectin and cachectin binds to and alters the metabolism of various tissues in the body. Beutler *et al.* used a cachectin-specific DNA probe to analyze cachectin messenger RNA molecules in macrophages and a cachectin-specific antibody to detect cachectin itself. The macrophages of mice known to be sensitive to endotoxin contained a pool of cachectin-specific messenger molecules and reacted to exposure to endotoxin by producing more messenger and cachectin. Macrophages from mice that resist endotoxin produced only limited quantities of messenger upon exposure to endotoxin and produced no cachectin. With dexamethasone treatment before endotoxin exposure, macrophages from sensitive mice could be prevented from producing additional messenger and cachectin. Thus, if dexamethasone is administered to infected individuals at an early time in the infection before the series of reactions leading to cachectin production get under way, shock may be suppressed.

Phenols induce plant tumors

A group of phenolic compounds made by plant cells may be the stimuli that induce bacteria to produce tumors on wounded plants (page 983). Flowering plants that have crown gall disease are infected through wounds by *Agrobacterium tumefaciens*. Bolton *et al.* screened 40 chemical compounds derived from plants for their ability to activate the virulence genes of *A. tumefaciens*. Because the activity of the virulence genes cannot be measured directly, activity of a "reporter" gene (one for which a protein product could be detected) was measured: the reporter was inserted into the DNA so that its production was under the control of the regulators of the virulence genes. Seven phenolic compounds, alone or in combinations, induced the virulence-genes region. These and similar compounds probably are released by injured plant cells and may induce the virulence genes of infectious bacteria. That diverse phenolic compounds can induce these genes explains the relatively wide host range of *A. tumefaciens* as a plant pathogen.

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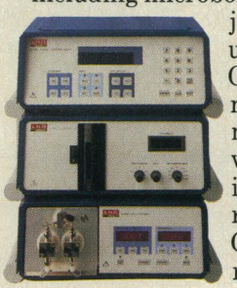

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Risk Research: When Should We Say "Enough"?

In response to legitimate concerns, government often undertakes programs of applied research to investigate suspected hazards. Such programs should not be started without some reasonable expectation that useful understanding can be obtained at an affordable price. Once started, when is government justified in stopping? If a risk is clearly demonstrated, the answer is straightforward. But suppose that after significant effect a risk is not demonstrated. When should we say "enough"? In programs of applied risk research, the failure to ask or answer this question can lead to serious social consequences.

A good example is provided by the suggestion that exposure to the 60-hertz electromagnetic fields from power lines, wiring, and appliances may pose health risks.* For several years the Department of Energy, the Environmental Protection Agency, the State of New York, and others, including the Electric Power Research Institute, have invested heavily in research examining this issue. The research has not demonstrated that a hazard exists, but it has demonstrated that under a variety of specific circumstances low-frequency fields can produce changes in living systems. Some of these appear to involve nonlinear transductive coupling at cell surfaces in relatively weak fields. The results are complicated by experimental evidence which suggests that if there should turn out to be adverse health impacts, stronger fields might not be "worse" than weaker fields, and various resonant and dynamic process may be important. A large number of laboratory animal screening studies have, with a few ambiguous exceptions, failed to turn up indications of adverse health impacts. A series of epidemiological studies purporting to link long-term 60-hertz magnetic field exposure with certain cancers are decidedly inconclusive. At the moment, the scientific evidence neither clearly indicates that there is a significant risk, nor clearly indicates that there is little or no risk posed by 60-hertz field exposures. It does not even offer many suggestions about what we should do if we want to "play it safe," since unlike most chemical hazards, in this case we probably cannot assume that "if it's bad, more is worse."

Having created a large inconclusive data set, and in the process having got a lot of people concerned, government research programs in this area are now being cut back or eliminated because of budgetary constraints. At the same time, growing public concern has prompted several state regulatory agencies to arbitrarily impose regulations on power line fields. The courts are also involved. Last November a county court in Texas ordered a utility to pay $25 million in punitive damages on the grounds that in building a 345-kilovolt line within 60 meters of a school the utility had acted "with callous disregard for the safety, health and well-being of . . . the children. . . ." The utility has been ordered to relocate the line at a cost that may exceed $40 million. In short, we have invested enough to produce a body of science that, in its current state, will support vigorous adversarial debate and rancor for years to come and are now truncating government research funding before producing enough science to resolve the question of risk.

Research can never demonstrate that a risk does not exist. It can establish probabilistic bounds on possible risks, and, if those bounds are sufficiently low, we should then say "enough." For this to happen two things are needed. First, government agencies need to explicitly consider the question of "stopping rules" before they embark on mission-oriented programs of risk research. As the research progresses they need to continue to refine those rules in the light of what has already been investigated and learned; what it is likely to cost to learn more; what the risks might be; and what kinds of findings are still needed before it makes sense to stop. Second, we need to evolve some common understanding between society, risk regulators, and the courts about how to establish acceptable probabilistic upper bounds on possible risks. Without these two developments, well-meaning government investments in risk-motivated applied research may sometimes do more harm than good.

—M. GRANGER MORGAN, Department of Engineering and Public Policy, Carnegie Mellon University, Pittsburgh, PA 15213

*See reviews in *Biological Effects of 60 Hz Power Transmission Lines* (Report of the Florida Electric and Magnetic Fields Science Advisory Commission to the Florida State Department of Environmental Resources, Tallahassee, FL, March 1985); M. G. Morgan, H. K. Florig, D. R. Lincoln, I. Nair, *IEEE Spectrum* **22**, 62 (February 1985); W. R. Adey, *Physiol. Rev.* **61**, 435 (1981).

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dream to read all the books in the library. She could, however, be stern. Thus, displeasing a librarian ranks alongside displeasing Genghis Khan on my list of nightmares. The issue number appears on the Table of Contents page, only one flip away from the cover, and as I have recently put magazine designers on the same pedestal as librarians, I shall stay with the current arrangement for awhile. Besides, Miss Gildersleve kept adding books as fast as I could read them, so a little connivance in getting librarians to read our Table of Contents may be just retribution.

In response to other letters, we are earnestly trying to solve the problem of the mailing label marring our covers.

—DANIEL E. KOSHLAND, JR.

Punctuated Equilibrium: From the Other Side

It is most irregular, but I appear to be the medium by which the shade of Francis Galton wishes to respond to Stephen Jay Gould (Letters, 25 Apr., p. 439). Finding both secretaries and word processors in markedly short supply on the other side, Galton respectfully requests that Gould and others reread Galton's earlier letter to *Nature* (4 May 1871, p. 105), merely substituting "punctuated equilibrium" for "Pangenesis." Galton feels that his views, thus amended, will be shared by many evolutionary biologists.

Since some readers may not have ready access to copies of *Nature* from over a century ago, Galton's letter is repeated below (*1*).

> I do not much complain of having been sent on a false quest by ambiguous language, for I know how difficult it is to put thoughts into accurate speech, and again, how words have conveyed false impressions on the simplest matters from the earliest times. Nay, even in the idyllic scene which Mr. Darwin has sketched of the first invention of language, awkward blunders must of necessity have occurred. I refer to the passage in which he supposes some unusually wise ape-like animal to have first thought of imitating the growl of a beast of prey so as to indicate to his fellow-monkeys the nature of expected danger. For my part, I feel as if I had just been assisting at such a scene. As if, having heard my trusted leader utter a cry, not particularly well articulated, but to my ears more like that of a hyena than any other animal, and seeing none of my companions stir a step, I had, like a loyal member of the flock, dashed down a path of which I had happily caught sight, into the plain below, followed by the approving nods and kindly grunts of my wise and most respected chief. And now I feel, after returning from my hard expedition, full of information that the suspected danger was a mistake, for there was no sign of a hyena anywhere in the neighborhood. I am given to understand for the first time that my leader's cry had no reference to a hyena in the plain, but to a leopard somewhere up in the trees; his throat had been a little out of order—that was all. Well, my labour had not been in vain; it is something to have established the fact that there are no hyenas in the plain, and I think I see my way to a good position to look out for leopards among the branches of the trees. In the meantime, Vive Pangenesis!

This is highly metaphorical, of course, and I'm not sure that I fully understand it all yet. But I can report that Galton seemed agitated over trusted leaders who took pride in having others pursue their ambiguous, untested ideas for over a decade to an inconclusive end.

ROBERT B. ECKHARDT
Department of Anthropology and *Graduate Program in Genetics, Pennsylvania State University, University Park, PA 16802*

REFERENCES AND NOTES

1. It can also be found, with the background to the matter, in W. B. Provine, *The Origins of Theoretical Population Genetics* (Univ. of Chicago Press, Chicago, IL, 1971).

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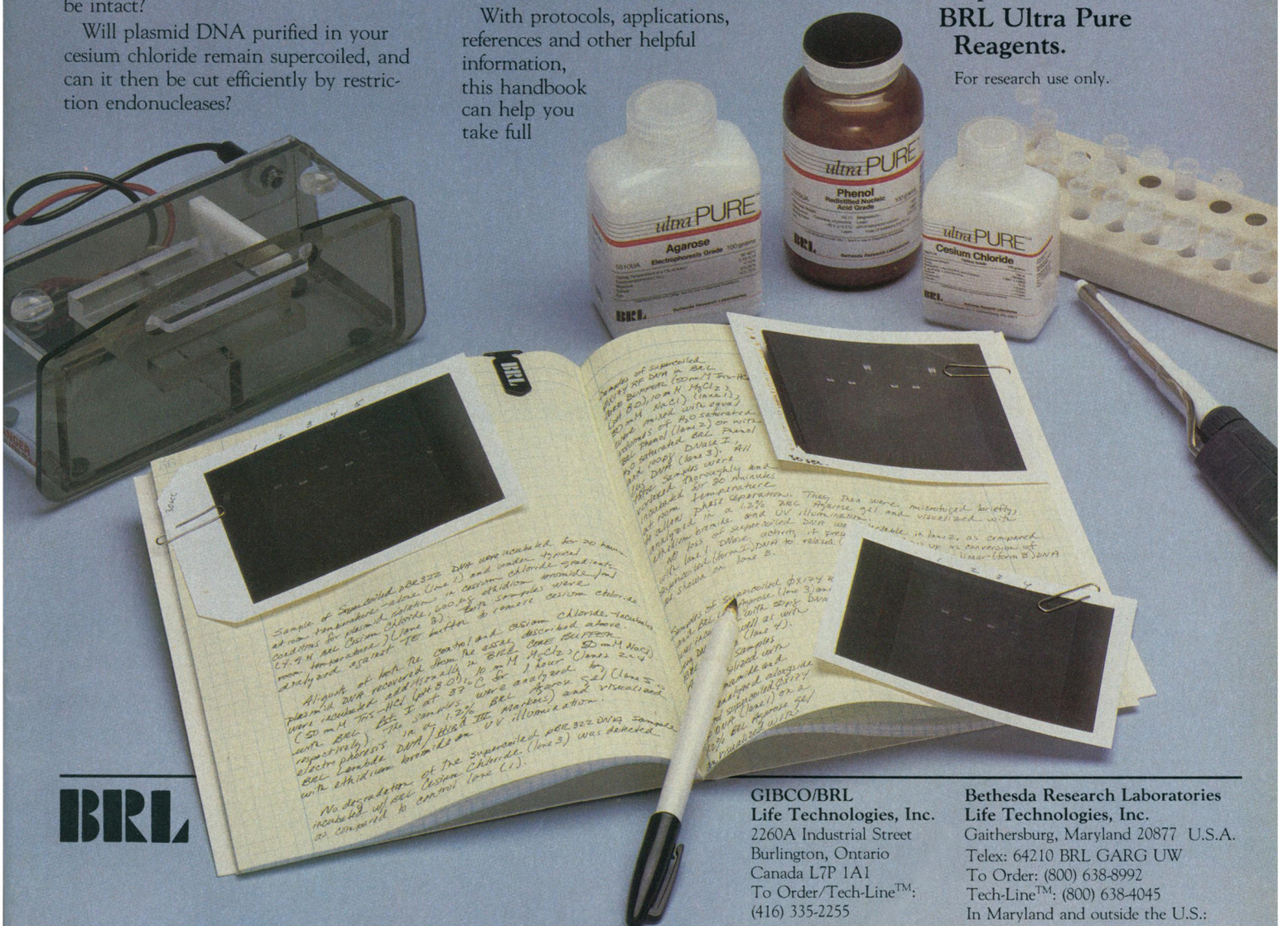

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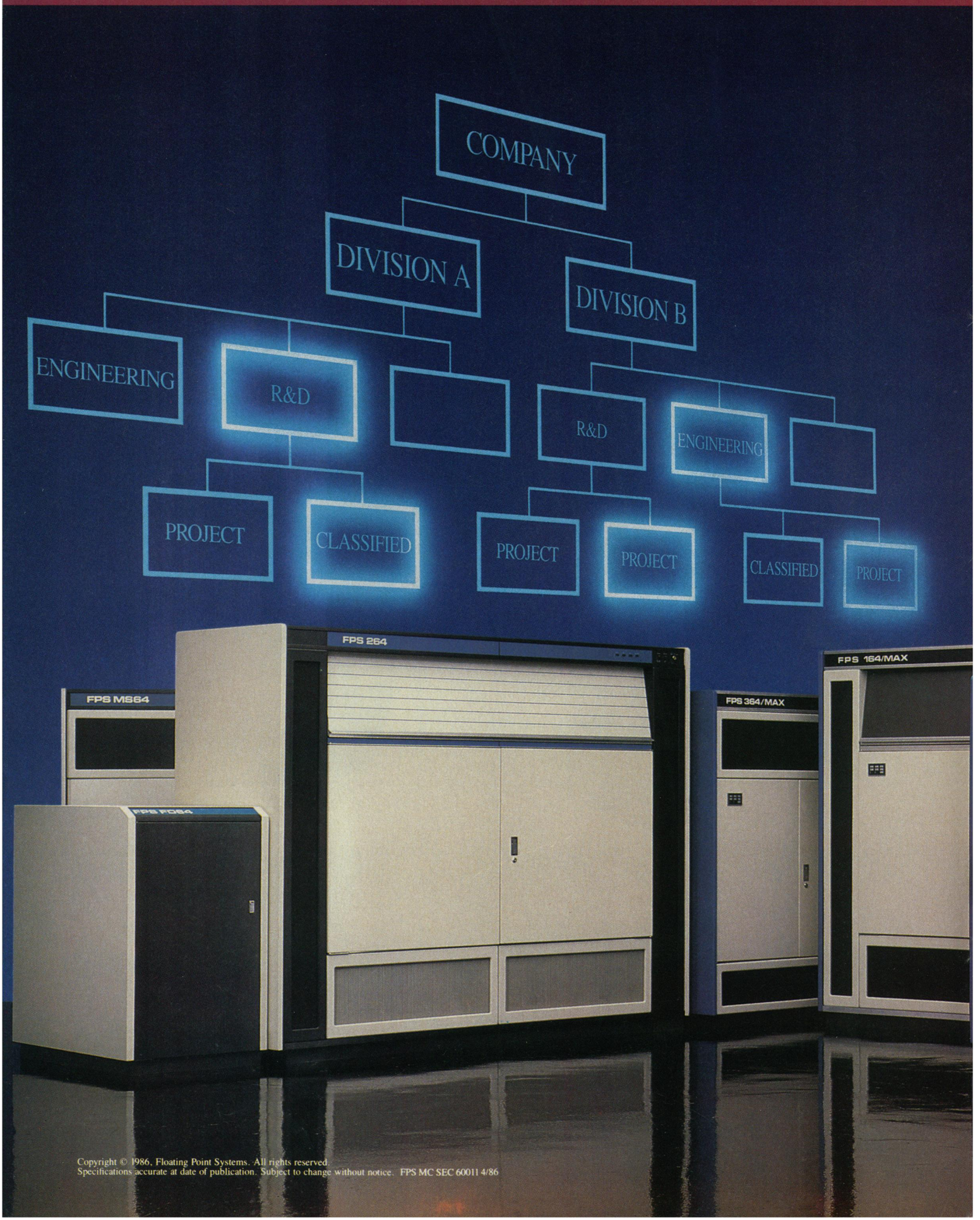

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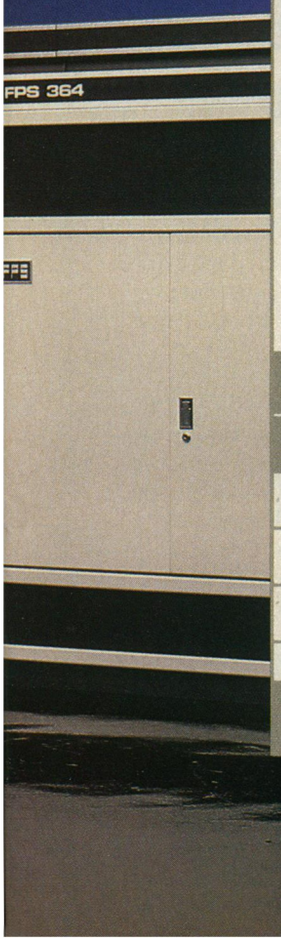

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National Cancer Institute

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Biological Resources

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Contact: Dr. G.E. Houts
Molecular Genetic Resources
6201 Johns Road, Suite 8
Tampa, Florida 33614
(813) 886-5338

Citing Contract #N01-CP-51007

Cost: $0.05/Unit
(Plus Shipping Outside Contiguous United States)

Cell Culture Identification Service. Using Isozyme Analysis, Immunofluorescence and Karyotypic Analysis (Chromosome Banding)

Contact: Dr. Ward Peterson
Children's Hospital of Michigan
3901 Beaubien Boulevard
Detroit, MI 48201
(313) 494-5705

Citing Contract #N01-CP-21017

Cost: $200/Analysis

Viruses: Avian, Feline, Murine, and Primate Viruses Prepared in Tissue Culture

Contact: Ms. P. Massagee
BCB Repository
Microbiological Associates, Inc.
5221 River Road
Bethesda, MD 20816
(301) 657-8169

Citing Contract #N01-CP-11000

Cost: Inquire

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Contact: Coordinator for Research Resources
Biological Carcinogenesis
Branch, DCE, NCI, NIH
Landow Building, Room 9A22
Bethesda, MD 20892
(301) 496-1951

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Contact: Coordinator for Research Resources
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Branch, DCE, NCI, NIH
Landow Bldg., Room 9A22
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(301) 496-1951

Cost: Shipping Charges Only

Cotton-Top Marmosets *(S. oedipus)* for Use as Models for Carcinogenesis—Holding, Inoculation, Observation, and Pathology Services are Available.

Contact: Dr. Neal Clap
Marmoset Research Program
Oak Ridge Associated Universities
P.O. Box 117
Oak Ridge, TN 37831
(615) 576-4103

Citing Contract #N01-CP-51006

Cost: $10.00 per diem (or higher for procedures involving additional care, etc.) $10.00 per blood sample

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Resource materials are available from bovine leukemia virus-infected cattle and sheep and control animals. These include blood, serum, plasma, bone marrow, leukocytes, bone marrow smears and virus-producing lymphocytes.

Contact: Jorge F. Ferrer, M.D.
Chief, Section of Viral Oncology
New Bolton Center
University of Pennsylvania
382 West Street Road
Kennett Square, PA 19348
(215) 444-5800
Extension 286

Citing Contract #N01-CP-51003

Cost: Inquire

Chemical Resources

Analytical resources for the collection, separation, and elucidation of the components of cigarette smoke and cigarette smoke condensates: A contractor with experience in the development of analytical methods for the determination of constituents of cigarette smoke and of specialty instrumentation for inhalation toxicology is available to assist qualified investigators with particular interest in studies on human and animal model exposure to environmental and sidestream smoke. A large inventory of reference experimental cigarettes, Standard Low Yield Reference Cigarettes, and an extensive chemical data base on smoke and smoke condensate components is available.

Contact: Thomas B. Owen, Ph.D.
Chemical and Physical Carcinogenesis Branch, DCE, NCI
Landow Building, Room 9C-18
Bethesda, Maryland 20892
(301) 496-5471

Cost: Inquire

Chemical Carcinogen Reference Standard Repository: Reference quantities of over 700 compounds are available. In addition to the newer Fecapentaenes and food mutagens, numerous representatives of the following classes of compounds are available: polynuclear aromatic hydrocarbons (PAH), PAH metabolites, radiolabeled PAH metabolites, nitrogen heterocycles, nitrosamines/nitrosamides, aromatic amines, aromatic amine metabolites, radiolabeled retinoids, azo/azoxy aromatics, inorganics, nitroaromatics, pesticides, pharmaceuticals, natural products, dyes, dioxins, chlorinated aliphatics and miscellaneous groups. Data sheets provided with the compounds include chemical and physical properties, analytical data, hazards, storage, and handling information. Catalog available upon request.

Contact: Coordinator for Chemical Research Resources
Chemical and Physical Carcinogenesis Branch, DCE, NCI
Landow Building, Room 9B-10
Bethesda, MD 20892
(301) 496-5471

Cost: Subject to chemical class code and quantity (see catalog) plus handling and shipping charges.

Environmental Cancer

NCI's Chemical Carcinogenesis Research Information System (CCRIS) database will be available online through the National Library of Medicine's new Toxicology Data Network (TOXNET) system beginning January, 1986. Through an interagency agreement between NCI and NLM, the CCRIS database will be built, maintained and updated in TOXNET's sponsored databases in the broad areas of chemistry, toxicology, and hazardous waste information. The CCRIS database contains evaluated data and information on carcinogens, mutagens, tumor promoters, cocarcinogens, metabolites of carcinogens and carcinogen inhibitors derived from published review articles, ongoing current awareness survey of primary literature, NCI/NTP's short- and long-term bioassay studies, the IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, and special studies and reports.

Contact: Dr. Thomas P. Cameron
Office of the Director
Division of Cancer Etiology
National Cancer Institute
Landow Building, Room 1D34
Bethesda, MD 20892
(301) 496-1895

Cost: Inquire

The Special Assistant for Environmental Cancer, Office of the Director, announces the availability of a limited number of copies of the following reports, which have been prepared under contract to NCI:

Survey of Compounds Which Have Been Tested for Carcinogenic Activity, PHS-149, 1974-1975, 1976-1977, 1979-1980, and a Cumulative Index

Monographs on Organic Air Pollutants

Species-to-Species Comparison of Carcinogen Metabolism

Survey of Organic Drinking Water Contaminants: Carcinogens, Mutagens, and Tumor Promoters

Inhibitors of Chemical Carcinogenesis

Contact: Ms. I.C. Blackwood
Office of the Director
Division of Cancer Etiology
National Cancer Institute
Landow Building, Room 1D34
Bethesda, MD 20892
(301) 496-1625

Cost: Free to investigators interested in environmental cancer

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Monographs on Human Exposure to Chemicals in the Workplace
(Not included in free distributions)

Monographs on 68 chemicals will be for sale by the:

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U.S. Department of Commerce
Springfield, VA 22161
(703) 487-4650

Cost: Inquire

Epidemiology Resources

The Immunodeficiency—Cancer Registry (ICR) is a unique registry of cancer cases that occur in patients with naturally occurring immunodeficiencies. Case material collected by ICR comes from case reports appearing in scientific literature and voluntary reporting by physicians. Criteria for inclusion in the registry are clinical or laboratory evidence of a primary immunodeficiency syndrome prior to the onset of malignancy. Data contained in the ICR are available to the extramural research community for the planning, design, and conduct of research efforts. Limited assistance is available to investigators interested in utilizing the registry.

Contact: Dr. Alexandra H. Filipovich
Immunodeficiency—Cancer Registry
Box 610 Mayo
University of Minnesota
Minneapolis, MN 55455
(612) 376-2174

Citing Contract #N01-CP-31011

The Tumor Virus Epidemiology Repository (TVER) contains sera and other biological samples from more than 13,000 patients and controls obtained in 12 different countries. The TVER was established primarily to support collaborative research on the role of Epstein-Barr virus (EBV) in Burkitt's lymphoma, nasopharyngeal carcinoma, and related diseases. Part of the collection includes sera that were obtained from nonhuman primates inoculated with EBV.

The TVER is able to adjust its collection to facilitate the development of new collaborative studies. In addition, some samples are available for reagents and independent research. The most extensive collections are serum samples from patients with Burkitt's lymphoma (sera from more than 1,000 patients).

Contact: Dr. Paul H. Levine
Environmental Epidemiology Branch, DCE, NCI, NIH
Landow Building, Room 3C25
Bethesda, MD 20892
(301) 496-4375

Cost: Free to Collaborating Investigators; Others, Shipping Charges Only

The National Institute of Allergy and Infectious Diseases and the National Cancer Institute have developed a repository of biological specimens from homosexual men. The specimens were collected through contracts with five major U.S. universities for studies of the natural history of acquired immune deficiency syndrome (AIDS).

Information about applying for collaborative use of these specimens and pertinent epidemiological data is now available from the Project Officer or the NCI Co-Project Officer. For further information, write to: Project Officer, AIDS Repository, Epidemiology and Biometry Section, National Institute of Allergy and Infectious Diseases, Westwood Building, Room 739, National Institutes of Health, Bethesda, MD 20892 or to Dr. A.R. Patel, Extramural Programs Branch, EBP, Division of Cancer Etiology, NCI, Landow Building, Room 8C-16, Bethesda, MD 20892.

Human fibroblast cultures from individuals at high risk of cancer, members of cancer-prone families, and normal family members.

Contact: Dr. Margaret Tucker
Family Studies Section, EEB, DCE, NCI, NIH
Landow Bldg., Room 3C29
Bethesda, MD 20892
(301) 496-4375

Cost: Free to collaborating investigators
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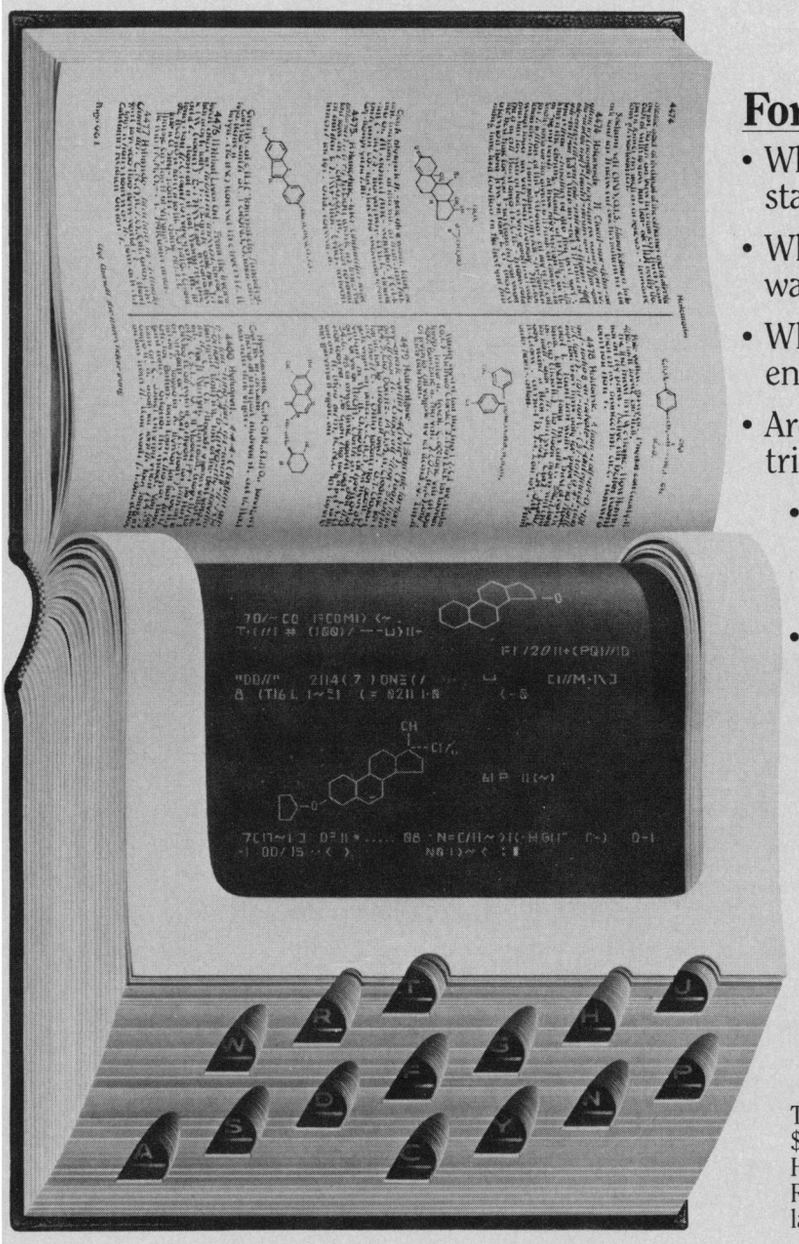

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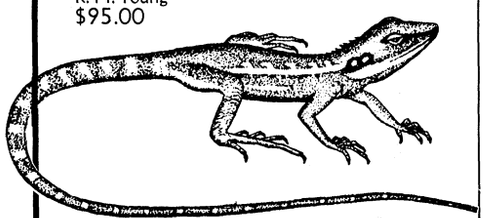

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Contributors include J. R. L. Allen, C. Atkinson, T. Bown, I.B. Campbell, J. Francis, R. Kemp., M. Kraus, R. I. Macphail, C. Percival, G. Retallack, and V.P. Wright.
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