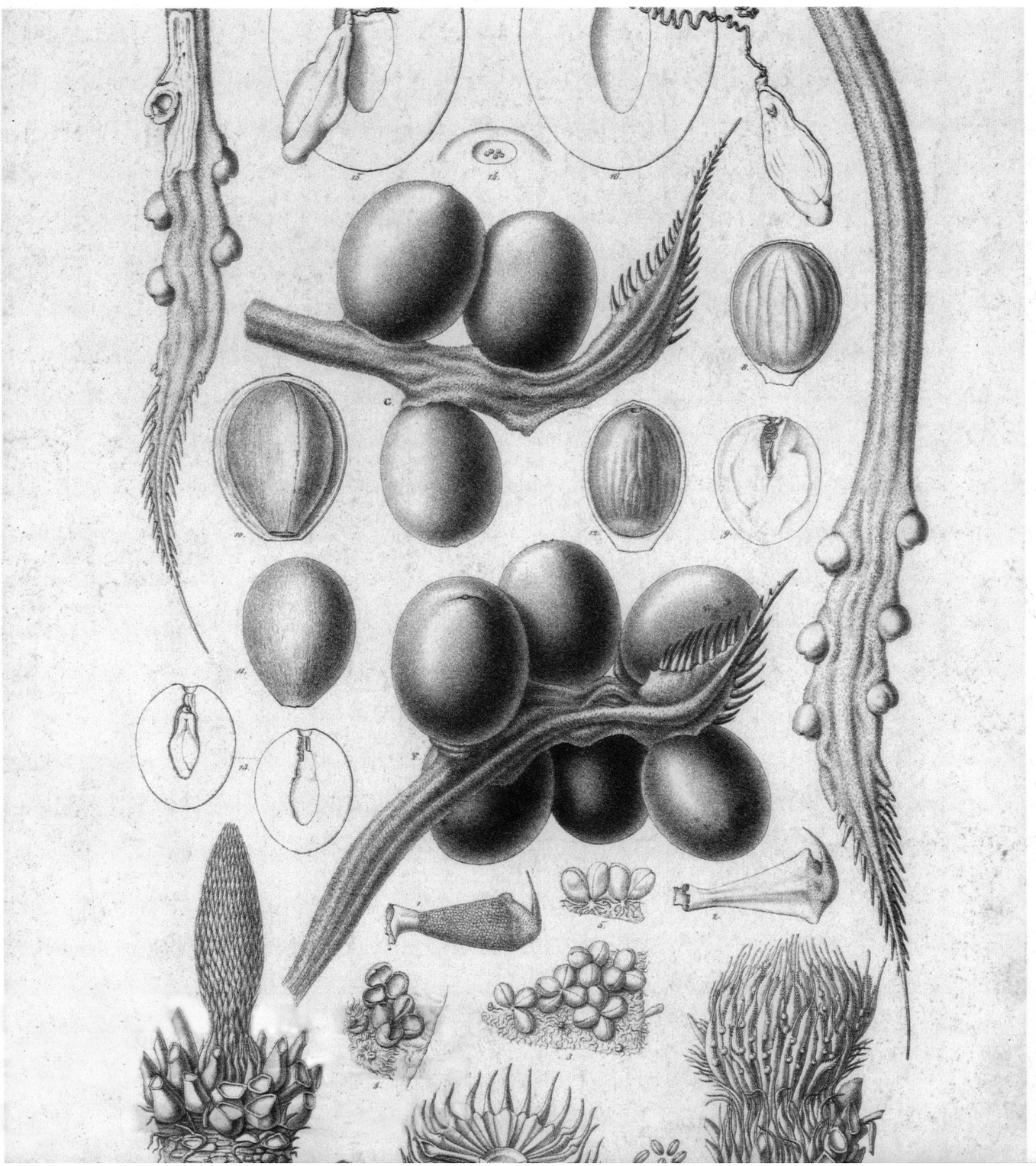
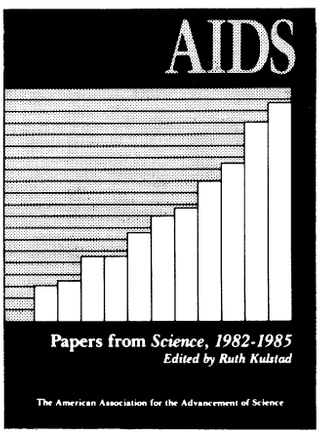
American Association for the Advancement of Science

SCIENCE

31 July 1987 $2.50
Vol. 237 ■ Pages 465–564





A One-Volume Library of Essential AIDS Research

AIDS: Papers from *Science*, 1982–1985

Edited by Ruth Kulstad

Some of the most frequently cited papers on acquired immune deficiency syndrome (AIDS) that appeared in ***Science*** between August 1982 and September 1985 are included in this volume. Arranged chronologically, these 108 research papers and ***Science*** news reports show how far AIDS research has come and provide an indication of the directions in which it might go. This fully indexed collection is useful not only for the experimental data and conclusions, but also as an excellent source of references to AIDS work in other major journals worldwide.

An overview of research in AIDS to date is provided in the introduction by Dr. Myron Essex, chairman of the Department of Cancer Biology, Harvard University School of Public Health.

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ON FUNDAMENTAL CANCER RESEARCH

Genetic Mechanisms and Cancer

November 8 - 11, 1987
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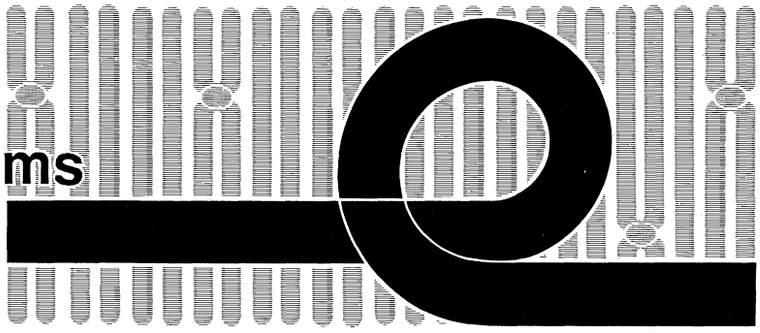

Co-chairpersons: M. Siciliano, L. Strong

SESSIONS/TOPICS	SPEAKERS
Bertner Memorial Lecture	F. Ruddle (Yale)
Organization of the Human Genome	C. Cantor (Columbia), H. Lehrach (EMBL), R. White (Utah)
Chromosome Changes and Somatic Cell Variation	J. Rowley (Chicago), G. Adair (Texas)
Regulatory Genes Affecting Somatic Cell Variation	H. Blau (Stanford), K. Fournier (Hutchinson), R. Roeder (Rockefeller), C. Wu (NCI)
Mutation and Repair	E. Friedberg (Stanford), P. Hanawalt (Stanford), L. Thompson (Livermore), R. Humphrey (Texas), R. Albertini (Vermont)
Gene Amplification	G. Wahl (Salk), M. Gottesman (NCI), F. Alt (Columbia), G. Brodeur (Washington University)
Inherited Cancer	A. Knudson (ICR), F. Li (NCI), G. Saunders (Texas), W. Cavenee (Ludwig Institute-Montreal), L. Strong (Texas), J. Gusella (Harvard), S. Naylor (Texas)
Action of Cancer Genes	A. Levine (Princeton), D. Hanahan (Cold Spring Harbor)

GOALS

The goals of the symposium are to evaluate current progress in understanding genetic mechanisms and cancer and to identify new directions for clinical and experimental work.

WORKSHOP IN MOLECULAR GENETICS: TERMINOLOGY AND TECHNIQUES

A three-hour refresher course on methods and concepts of the study of cancer genetics will be presented on Sunday afternoon, November 8, 1987. A reception follows at which faculty members will be available for an extended discussion period. There is no additional fee for the workshop but preregistration is required by **October 15, 1987.**

CALL FOR POSTERS

Abstracts may be submitted for the 1987 Research Symposium Poster Session. Abstracts should be typed double-spaced on plain, 8 1/2 by 11-inch paper and must be received no later than **August 17, 1987.** Participants will be notified of their poster's acceptance by mail. Submit abstracts to: Anthony J. Mastromarino, Ph.D., Office of the Vice President for Research-Box 101, UT M. D. Anderson Hospital and Tumor Institute, 1515 Holcombe Blvd., Houston, Texas 77030. Phone: (713) 792-3391.

INFORMATION

For additional information, please contact Conference Services-HMB 131, M. D. Anderson Hospital, 1515 Holcombe Blvd., Houston, Texas 77030, phone: (713) 792-2222. Registration fee is $200 if received by 10/15/87; $225 after 10/15/87. It includes admission to the workshop in molecular genetics, scientific program, book of abstracts, refreshment breaks, continental breakfasts, lunches, receptions, and banquet.

CME Continuing medical education credits will be available.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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■ The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objects are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

COVER Lithograph depicting seed (center) and other parts of *Cycas circinalis* Linn. (false sago palm), a neurotoxic plant. Heavy use of cycad seed for food and medicine has been linked to Guam amyotrophic lateral sclerosis and parkinsonism-dementia, a prototypical disease for study of neurodegenerative disorders of old age. Now considered rare and endangered, cycads are primitive "gymnosperms" that flourished 150 to 200 million years ago. See page 517. [Figure 176C in C. L. Blume, *Commentationes Botanicae. Imprime de Plantis Indae Orientalis. Rumphia* (Lugduni-Batavorum, Amsterdam, 1848), Part IV, pages 11–18]

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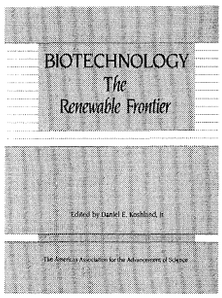
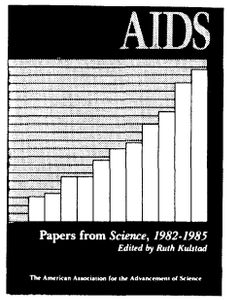


Biotechnology: The Renewable Frontier, *D.E. Koshland, Jr., ed.* Like its predecessor, this volume covers the latest and most important topics in biological R&D. It illustrates the extraordinary cross-disciplinary aspects of modern biology and its tremendous impact on the future with sections ranging from new techniques, immunology, developmental biology, cancer, hormones, sensory phenomena, and more.

1986; case $29.95, $23.95 for AAAS members; paper $17.95, $14.35 for AAAS members; 384pp



AIDS, *R. Kulstad, ed.* Research papers and reports on acquired immune deficiency syndrome (AIDS) published between August 1982 and September 1985 show how far AIDS research has come and provide an indication of the direction in which it might go. An overview of research in AIDS is provided by Myron Essex, chairman of the Department of Cancer Biology, Harvard University School of Public Health.

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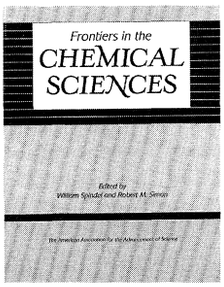

Frontiers in the Chemical Sciences, *W. Spindel, R.M. Simon, eds.* Focuses on the themes of fundamental chemical change and extreme molecular complexity. Details progress in all areas of chemistry, including new work in ultrafast reactions, catalysis, conduction organics, enzyme mechanisms, and materials and analysis.

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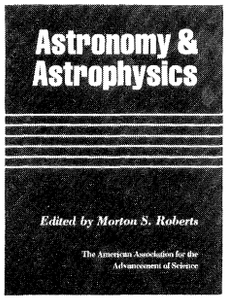

Astronomy & Astrophysics, *M.S. Roberts, ed.* From the solar system to the pulsars at the very edge of the observable universe, this volume reveals a broad, coherent, and contemporary picture of our astronomical universe. Topics range from the solar system, the structure and content of the galaxy, galaxies and cosmology, and instrumentation.

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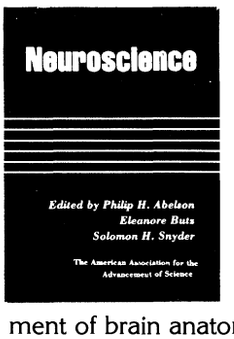

Neuroscience, *P.H. Abelson, E. Butz, S.H. Snyder, eds.* Neuroscience research ranging from genetic engineering to clinical therapy is presented. Provides an integrative treatment of brain anatomy, physiology, and chemistry and addresses fundamental questions concerning nervous system functioning.

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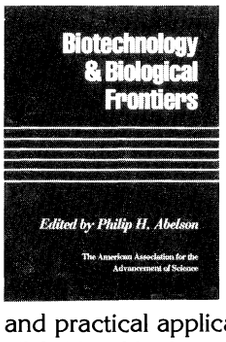

Biotechnology & Biological Frontiers, *P.H. Abelson, ed.* Covers the most important topics at the forefront of biological R&D and deals with both fundamental research techniques and practical applications. For researchers and students in all fields of biology, agriculture, and the health sciences.

1984; case $29.95, $23.95 for AAAS members; paper $14.95, $11.95 for AAAS members; 550pp

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Predicting the weather

No weather forecast can exceed in accuracy the most inaccurate component of the prediction equation (page 493). Thus, although weather forecasting is today based on sophisticated numerical models and an improved understanding of atmospheric processes and new supercomputers and data-collection instruments are used, it is still only possible to make predictions with reasonable accuracy a few days in advance. Tribbia and Anthes describe the roots of contemporary prediction strategies (that go back to the beginning of this century), the current status of and limits to weather forecasting, the computational methods used, and the physical laws applied to predictions. The inherent unpredictability of atmospheric, land, and oceanic processes will continue to limit the accuracy of forecasts. But despite these problems, the regular collection of atmospheric, oceanographic, and allied data is providing insights into the earth's climatic past, present, and future.

Sickling red cells

ERYTHROCYTES from patients with sickle cell anemia contain a defective form of hemoglobin, the transporter of oxygen from lungs to tissues (page 500). The abnormal hemoglobin polymerizes upon partial deoxygenation in tissues to form a viscous gel that deforms (sickles) cells and makes them rigid. Organ damage results because rigid cells may occlude blood vessels causing less oxygen to be transported to tissues. Gelation has an unusual time course that is characterized by a pronounced delay period before polymers appear. For studying the role of the delay time in gelation in vivo, Mozzarelli *et al.* developed a technique for detecting polymers at partial saturation with carbon monoxide (a gas that affects gelation in the same way oxygen does). Lasers were used to control the saturation of hemoglobin with carbon monoxide and to measure the kinetics of gelation in single cells. The analysis indicated that most cells (about 80%) of sickle cell anemia patients would not sickle in the circulation, because the delay time is long compared to the cell's transit time through the body and return to the lungs for reoxygenation. These findings may explain the low proportion of sickled cells in the venous circulation of patients and clarify how vessels occlude and tissue damage ensues in sickle cell anemia.

Observations of Pluto and Charon

ASTRONOMERS observed a number of "mutual events" of Pluto and its satellite Charon in 1986 (page 512). Telescopes at observatories in Hawaii and Texas were equipped with detectors monitoring changes in the brightness of the Pluto-Charon system; data were collected by Tholen *et al.* during "superior events" (during which Charon passed behind Pluto, making observations of Pluto possible with relatively little contamination by light from Charon) and "inferior events" (during which Charon passed in front of Pluto). From the patterns of albedo values, it appears that the hemisphere of Charon facing Pluto has a neutral color, whereas the other side has a reddish color similar to Pluto's. Density measurements indicated that Pluto consists of more rock than water ice. Orbital features of Charon and the radii of Pluto and Charon were calculated with greater accuracy than has been possible. This year and next, there will be more mutual events; some will be total, not partial like the 1986 events, offering even better opportunities for obtaining data about the system's orbital and physical properties.

Toxic seeds and degenerative diseases

INDIGENOUS peoples of Guam and Rota, the Chamorros, once had high incidences of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer-type dementia (the syndrome ALS-PD) (page 517). Since World War II, the incidence has progressively declined. Genetic factors and viral agents have been ruled out as causes of ALS-PD, and explanations have been sought in changing cultural practices resulting from Americanization. Toward the end of World War II, the Chamorros had to rely heavily on *Cycas circinalis* (cover)—the false sago palm seed—for food and medicine. The seeds contain an unusual toxic amino acid, called L-BMAA. When synthetic L-BMAA was fed to macaques, Spencer *et al.* found that cells of the nervous system underwent structural and functional changes, and motor dysfunctions, and behavioral changes like those seen in motor neuron diseases and parkinsonism were induced. These findings suggest an explanation for the hitherto enigmatic clustering of symptoms and lend support to the hypothesis that toxic amino acids (in this case from a source outside the body, but in other cases possibly from an endogenous source) may be associated with development of parkinsonism, Alzheimer's, and perhaps other degenerative diseases (see also Research News, p. 483).

Sphingomyelin and spiroplasma growth

MORE than 25 years ago the first isolations were made of a tick-borne agent that causes cataracts and brain infections in experimentally infected mice; a culture medium has now been defined in which this agent, *Spiroplasma mirum*, can readily grow and multiply (page 525). A crucial component of the formulation developed by Hackett *et al.* was sphingomyelin, a membrane lipid. Sphingomyelin may help stabilize the organisms, and the requirement for it may explain the tropism of *S. mirum* for certain sphingomyelin-rich tissues (especially neural and hepatic tissues) of infected mice. Sphingomyelin was essential for spiroplasma growth at 37°C (the temperature of a mammalian host), while some (albeit slow) growth took place without it at 30°C (the temperature of a tick). Investigations of the biology and pathologic effects of this spiroplasma can now be undertaken.

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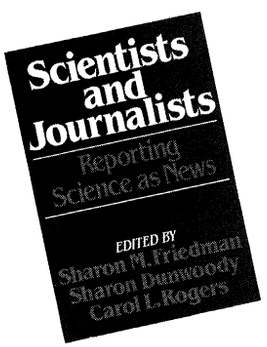

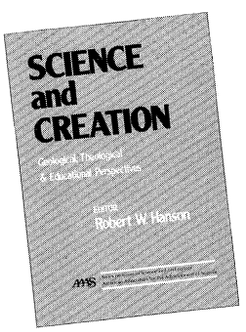

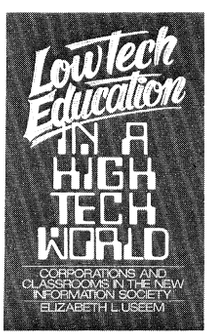

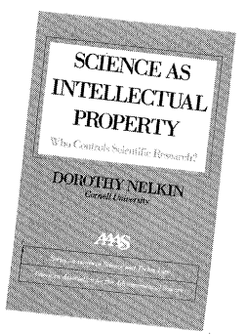

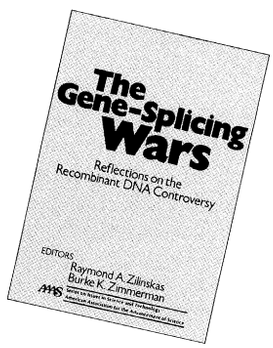

Scientists and Journalists: Reporting Science as News

Edited by Sharon M. Friedman, Sharon Dunwoody, and Carol L. Rogers

The public is interested in science and depends largely on the mass media for the latest information. But how well do scientists and journalists connect to communicate to the public? This book examines the human aspect of the links between scientists and journalists through the eyes of both.

1985, 352 pp., hardcover; $24.95, AAAS members $19.95

Science and Creation: Geological, Theological, and Educational Perspectives

Edited by Robert W. Hanson

The creation/evolution controversy is examined by scientists, theologians, educators, and historians. These authors view the controversy as a false dichotomy and as an attempt to force a choice between two ideas that are not mutually exclusive. Includes case studies from several states.

1986, 240 pp., hardcover; $24.95, AAAS members $19.95

Low Tech Education in a High Tech World: Corporations and Classrooms in the New Information Society

Elizabeth L. Useem

Are students in the U.S. developing the skills necessary for a high technology society, or will it be technological boom, educational gloom? Useem examines education in California's "Silicon Valley" and Boston's Route 128, two of the country's leading high tech centers, and suggests ways for education and industry to forge a stronger partnership for the future.

1985, 256 pp., hardcover; $19.95, AAAS members $15.95

Science as Intellectual Property: Who Controls Scientific Research?

Dorothy Nelkin

Who controls research? A growing number of legal and administrative disputes raise critical issues of professional sovereignty, scientific secrecy, and proprietary rights. Nelkin offers cases illustrating the dilemmas that arise as the interests of scientists, the rights of citizens, and the security needs of government and industry come into increasing conflict.

1984, 130 pp., softcover; $10.00, AAAS members $8.00

The Gene-Splicing Wars: Reflections on the Recombinant DNA Controversy

Edited by Raymond A. Zilinskas and Burke K. Zimmerman

Questions of safety and ethics about recombinant DNA techniques continue to surface. This book takes a look at historical, political, industrial, scientific, and international aspects of these issues. The authors show how lessons learned from the experience can be used to cope with similar issues in the future.

1986, 256 pp., hardcover; $24.95, AAAS members $19.95

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Cancer Phobia

For more than 10 years, the public has been subjected to a media barrage leading to widespread, misinformed fear of chemicals. Through the use of questionable evidence, many major substances have been labeled carcinogens. If data are adjusted to eliminate effects of cigarette smoking, there has been no overall increase in cancer due to other factors. The highly publicized cancer epidemic that was predicted earlier has not materialized.

With increasing use of synthetic chemicals, it was desirable to screen them for possible carcinogenicity by tests on shorter lived animals such as mice and rats. The general procedure is to subject the mice or rats to massive doses of the chemical to be tested, usually by feeding, gavage, or inhalation. Preliminary experiments determine a maximum tolerated dose. This amount, repeated over a 2-week period, usually leads to a noticeable but tolerated reduction in weight. A chronic dose regimen is then employed in experiments that last for the animal's lifetime. The levels used vastly exceed those to which humans are likely to be exposed.

Many of the experiments that have been cited as proving a potential carcinogenicity of a chemical for humans have been performed on inbred strains of mice that have a natural incidence of liver tumors. In humans, there are taboos against inbreeding, which often leads to genetic impairments. Thus the use of inbred mice, though convenient experimentally, is suspect. More important is the fact of high natural incidence of liver tumors in the test mice. The usual response of these animals to massive doses of a chemical is to develop an even higher incidence of liver tumors. When this happens, the chemical is labeled a potential carcinogen in humans. It so happens that in humans primary liver cancer is rare with the exception of alcoholics and those who have suffered from hepatitis. With these exceptions, incidence of liver cancer in the United States decreased substantially during the times when use of industrial chemicals expanded greatly. Thus extra liver tumors in a naturally tumorigenic mouse is of dubious relevance to humans.

Results from the massive doses are extrapolated linearly to low doses, and the assumption is made that humans are as sensitive as the most cancer prone of the species of animals tested. Use of a linear extrapolation to low doses implies that humans do not have repair mechanisms against injury.

Countless millions of animals have been sacrificed in testing chemicals. Comparatively little effort has been devoted to studying the mechanisms of chemical carcinogenesis. An important exception is work conducted at the Chemical Industry Institute of Toxicology (CIIT). The CIIT, which has achieved an excellent reputation among toxicologists for its careful work, has examined the detailed mechanisms of the interaction of formaldehyde with nasal passages of rats and has shown that the linear model is not correct in predicting nasal cancer in the rats. Rather, a more relevant measure is the extent of interaction of formaldehyde with the nasal DNA. The amount of binding of formaldehyde to DNA decreases much faster than the concentration of formaldehyde in the nasal passsages and is a better predictor of carcinogenesis.

Another important study of CIIT has been an investigation of the mechanism of the carcinogenesis of branched-chain hydrocarbons in male rats. These hydrocarbons are key components of unleaded gasoline. The studies showed that the hydrocarbons interfere with the mechanism for excreting a low-molecular-weight protein by the male rat. Research at CIIT indicates that this may be the cause of kidney cancer in male rats exposed to gasoline. A similar mechanism with related cancer does not exist in female rats, in male or female mice, or in humans. This type of result calls into question the practice of the regulatory agencies in selecting for extrapolation to humans data from the most sensitive animal.

Animals differ by more than a factor of 1000 in the levels required for lethal response to dioxin. Rodents and humans are known not to be identical in their biochemistry. To attain a realistic estimate of the hazard—if any—presented by a chemical, specific information about its metabolism and physiological effects is needed. The two examples involving formaldehyde and hydrocarbons illustrate the power of an approach in which detailed mechanisms of chemical carcinogenicity are examined.—PHILIP H. ABELSON

much more vertical than that in the humanities. If this point is granted, the need for a reconsideration of college curricula will necessarily follow. I am naturally delighted that Marshall Brown, "a professional humanist," reads *Science*, and I agree that it is not the appropriate journal in which to engage humanists in the important debate on curricula; I shall certainly try to go further. Brown states as "Fallacy 1" my thesis that "Science is vertical whereas other fields are horizontal." He then goes on to state that "Humanities courses are not sequential, but they are cumulative." I couldn't find a better way to explain just what I mean by the distinction between vertical and horizontal learning. This is the heart of the matter.

Later in my article I wrote, "Which will be easier to learn without instruction in later life, *more* Shakespeare or molecular biology?" (emphasis added). The word, "more," carries the firm implication that students will at least be exposed to some. Brown somewhat misquotes me as saying that "One can 'learn' Shakespeare more easily than molecular biology 'without instruction in later life.' " There is no danger that a humanist will not be exposed to enthusiastic teaching of Shakespeare (and other literature, for which "Shakespeare" serves as proxy), but perhaps he or she could sacrifice some part of it for a course in calculus or general biology or elementary chemistry. Finally, Brown criticizes me for claiming that "Students should learn science, not how scientists think." Can anyone really be educated in this modern world without a reasonable knowledge of some of the major generalizations of science? And I deny that one can learn how scientists think without having a good portion of the meat of science to chew on.

In his letter, Alexander Astin agrees that we need more science in undergraduate curricula, but contends that "learning is no less cumulative and no less hierarchical when it comes to such 'soft' fields as foreign languages, communication . . . and artistic technique . . . ." I am enthusiastic about teaching foreign languages, and learning in foreign languages is certainly vertical as compared with that in history or literature, although probably still less vertical than that in physics or molecular biology. But fortunately much of the cultural value of foreign literature, at least for nonspecialists, can be obtained from translations. Even George Steiner used translations in preparing his highly regarded treatise *Tolstoy or Dostoevsky* (Knopf, New York, 1959). Mathematics may be the language of science, but regrettably no one has yet found a way to translate it. The distinction between vertical education in science and horizontal education in the humanities is not absolute, but on balance the distinction stands.

Astin writes, "A more fundamental consideration in trying to adjudicate competing claims on curricular time should be social and national need: what are the critical problems of our time, and which disciplines are in the best position to shed light on these problems?" My Policy Forum contained a list of some of the intellectual and practical problems of our day that depend on science; isn't it fascinating to find a humanist arguing for the practical application of knowledge and a scientist arguing for better understanding? No one is asking that our students give up history and psychology and economics. Certainly scientists want a base in these areas for future learning. My suggestion is that humanists should spend 80% of their time in college, rather than 94% of it, with these subjects and increase their effort (or at least their time) in science from 6% to 20%. This may, of course, be what Astin had in mind anyway when he agreed to more science in our curricula.

C. Tyler Burt asks that "our future elite . . . should have 4 years of peace to delve into the pure world of thought. . . ." Peace? Avoiding instruction in science is "peace"? Science and mathematics have no place in "the pure world of thought"? Burt's letter illustrates why we need curricular reform.

Finally, and thankfully, Jeffry Mallow has written that Loyola University will ask their students to learn more mathematics and science. Yale has also expanded its science requirements. May they lead us out of the wilderness. Science isn't easy, but there is still no royal road to learning.

F. H. WESTHEIMER
Department of Chemistry,
Harvard University,
Cambridge, MA 02138

Erratum: The first sentence of the second paragraph of Richard A. Kerr's Research News article "Halocarbons linked to ozone hole" (5 June, p. 1182) should have read, "Using a technique borrowed from galactic astronomy, the Stony Brook researchers believe that they have detected roughly 0.5 to 1.5 parts per billion of chlorine monoxide within the deepening hole. . . ." The article incorrectly referred to "0.5 to 1.5 parts per million."

Erratum: In the article "Space station price climbs higher" by Eliot Marshall (News & Comment, 17 July, p. 242), Herbert Friedman, a member of the National Research Council panel studying the space station, was incorrectly identified as a former presidential economic adviser. He is emeritus scientist, Naval Research Laboratory and Martin Marietta Fellow of the National Air and Space Museum.

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