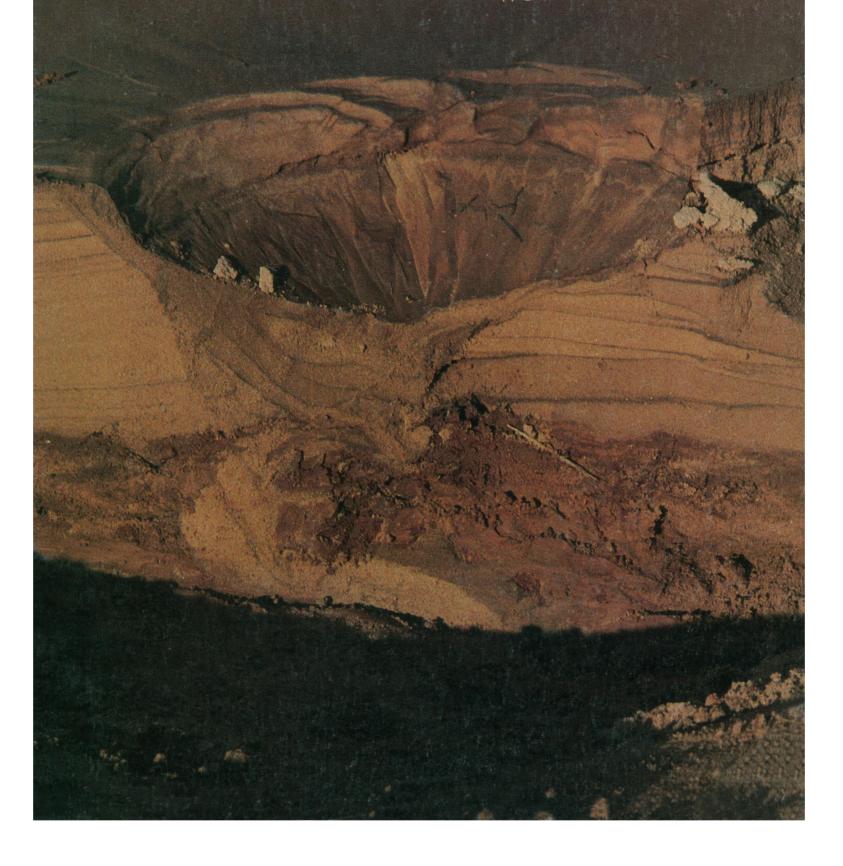
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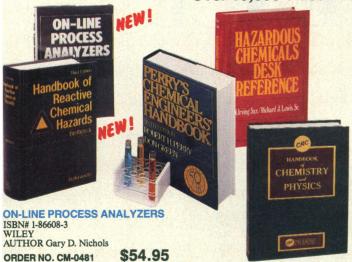
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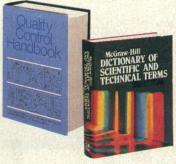
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COVER Vertical section through 15-cm-high sand boil caused by liquefaction during the 24 November 1987 Superstition Hills, California, earthquake. Alternating layers of fine (dark) and coarse (light) sediment indicate that discharge rate through the feeder dike in the reddish-brown soil beneath the sand boil was variable. See page 56. [Photograph by T. C. Hanks, U.S. Geological Survey, Menlo Park, CA 94025]

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This Week in

Science

Therapeutic purines and analogs

LMOST half a century ago the idea was formulated that nucleic acid bases—which were needed by all cells but were taken up more readily by those that were dividing rapidly—might be exploited for use in stopping the growth of cancer cells and infectious agents. A search was therefore begun for cytotoxic and therapeutic analogs of purines and pyrimidines. This search has had dazzling clinical as well as basic science payoffs. Gertrude Elion describes highlights of the work on purine analogs for which she and George Hitchings shared—with James Black—a Nobel Prize in 1988 (page 41). The first clinical success came in the early 1950s: children with leukemia responded well to the drug 6-mercaptopurine, and today 6-mercaptopurine remains part of the combination chemotherapy that cures most children with this disease. Later, azathioprine, an immunosuppressive agent, was developed and put to use in the treatment of autoimmune diseases and as a suppressor during organ transplantation. More recently, acyclovir, an antiviral has been used for treating genital herpes and shingles and for suppressing viral infections in immunocompromised patients. The research has explored both normal and aberrant pathways of purine metabolism and thus has also led to the development of drugs for metabolic diseases such as gout.

Old cold life oases

HE growth of communities of marine organisms, the so-called "life oases," around cold seeps on ocean floors is not a new phenomenon: fossils and geochemical evidence from two islands in the Canadian Arctic trace life oases at cold seeps back to the Early Cretaceous (some 140 million years ago) (page 53). The seep communities on Ellef Ringnes Island and Prince Patrick Island were, like modern seep communities, based around chemosynthetic bacteria that used methane as their energy source; the methane oozed through

faults onto the ocean floor. As the bacteria oxidized methane, they produced carbon dioxide with a distinctive isotope signature; the carbon dioxide was incorporated into carbonate rocks. A crust of carbonate formed at the oceansea floor interface, and gas pressure from below caused cracking; seeping hydrogen sulfide created a corrosive environment conducive to pyrite precipitation. The food web that developed around the bacteria included various grazing and filtering organisms—tube worms (with telltale pyrite-coated tubes), bivalves, gastropods, brachiopods, fishes, and others. Although the sources of the methane and hydrogen sulfide are unclear, Beauchamp et al. note that since hydrocarbon-rich fluids once seeped to the surface in this area there may still be oil or gas beneath the

Liquefaction of Superstition Hills

N 24 November 1987, an earthquake struck the Imperial Valley of California. An array of instruments that had been installed 5 vears earlier in the nearby flood plain of the Alamo River monitored both the changes in the pore-water pressure in the natural silty sand layer and the shaking of the earth above and below the layer (page 56). Surprisingly, and in contrast to laboratory experiments in which liquefaction occurs at the same time as strong shaking, pore-water pressures rose only slowly as the shaking intensified, and the sandy laver completely liquefied only well after the strong earthquake motions had ceased. Water and muddy sediments erupted from the earth, turning the site into a quagmire (cover). Holzer et al. suggest that complete liquefaction may have been delayed until uneven pore-water pressures were redistributed in the ground. An understanding of the dynamics of liquefaction is important for evaluating contemporary earthquake hazards and for paleoseismologic analyses, because ancient sand boils are used for dating prehistoric earthquakes and estimating their magnitudes.

New vaccine strategy

→HE flagella of Salmonella have been used as the carriers of epitopes (foreign determinants) in a new type of vaccine (page 70). Flagella are prominently positioned on the bacterial surface and are, themselves, highly immunogenic. Into the hypervariable region of the (previously cloned) gene for the flagellin protein, Newton et al. inserted a synthetic oligonucleotide corresponding to an epitope of cholera toxin. The flagellin protein tolerated the insertion and assembled properly. Chimeric flagellin was expressed at the surface of attenuated Salmonella organisms and, in mice, induced an immune response specific for the epitope. This delivery system may be able to present many different types of epitopes for immune responses and is already being assessed for use with epitopes derived from several other bacteria and viruses.

Sensing scents

T LECTROPHYSIOLOGIC studies of single olfactory cells—both iso-Ilated cells and cells in tissue slices—are elucidating how odors are detected (page 79). The cells, from salamanders, were exposed to an "odorant cocktail" containing micromolar or higher amounts of several aromatic compounds. As the cocktail "puff" arrived at the cell surface (in about 20 milliseconds), electrodes at individual cells recorded an inward current that occurred in response to potassium ions in the mixture; after a delay of hundreds of milliseconds, constituents of the cocktail generated their ion current. Firestein and Werblin point out that the response kinetics—both the delay in the response and the shape of the doseresponse curve—are consistent with involvement of a second messenger in olfaction: instead of acting directly on membrane ion channels, the odorants may stimulate an enzyme cascade that is instrumental in gating the ion channel in the membrane. The biochemistry and biophysics of odor detection by olfactory cells and of light detection by photoreceptor cells may be very similar.

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Scare of the Week

he fable of the boy who cried wolf is as pertinent today as it was in Aesop's time. We are being subjected to the scare of the week. Some of these scares may reflect real dangers, but they are becoming obscured by a cacophany of false or exaggerated ones. Two that hit the headlines recently illustrate quite different problems.

The first was a highly publicized announcement by the Natural Resources Defense Council that Alar-treated apples would cause thousands of cancer deaths to children. The reaction was predictable: school districts quickly canceled apple distribution and the fruit piled up on grocery shelves. The facts came more slowly. Only 5% of apples are treated with Alar, and in that 5% the levels of Alar are well below conservative Environmental Protection Agency tolerances. Even in a worst case scenario the probability of cancer among the affected group would change from 25% to 25.025%. When health commissioners announced the facts, the country returned to normal and apples were returned to school districts and grocery shelves. However, serious psychological and financial damage was sustained.

It is time to recognize that public interest groups have conflicts of interest, just as do business groups, even though their public positions are orthogonal. Businesses prefer to be out of the limelight; public interest groups like to be in it. Because they are selling products in the marketplace, businesses downplay discussions of hazard. Because public interest groups acquire members by publicity, they emphasize hazards. Each group convinces itself that its worthy goals justify oversimplification to an "ignorant" public. Businesses today have product liability and can incur legal damages if they place a dangerous product on the market. Public interest groups have no such constraints at the moment; it may be time to develop appropriate ones so that victims of irresponsible information have redress. Public interest groups, as well as apple growers, contribute importantly to our society, but both groups should be accountable for their acts.

The second scare was the banning of Chilean grapes after a terrorist threat and the finding of traces of a little cyanide in two grapes. On the surface it resembles the Alar scare: the amounts of cyanide were found to be negligible, so the job losses and the ensuing ill will created among Chilean farmers seemed disproportionate in retrospect. The difference is that eating too much cyanide can cause instant death, whereas Alar presents a possible danger only over a lifetime of consumption and that scare required no instantaneous action. Although the Chilean grape scare may have been more justifiable, a reevaluation suggests that a less extreme reaction would have been more appropriate.

The overreaction in these cases has as its background the present climate in our society in which complete safety without cost is seen as a feasible goal. The possibility of danger, therefore, is perceived to result from chicanery, negligence, or incompetence. In such a climate, officials respond with extreme measures. Because increased costs in either the affected products or in taxes are not obviously linked to these official actions, the system becomes tilted to overreaction. A certain balance is necessary to prevent the costs of legitimate safety measures from becoming prohibitive. A graphic illustration of this problem surfaced recently with the arrest in Los Angeles of a person who admitted having made about a hundred bomb threats to airlines, all false, each of which had been investigated by authorities. If every threat causes flights to be canceled or fruit to be removed from grocery shelves, terrorists and psychotics will soon be able to grind society to a halt. On the other hand, the alternative of broadcasting each threat, caveat emptor with a vengeance, would soon cause all warnings to be ignored.

To thread our way between real dangers and false alarms, we must often let officials decide which terrorist threats deserve wide publicity, and the public must be understanding of risk as well. Because these officials cannot always be right they deserve to be judged on an overall record, not from the certainty of hindsight. The public must recognize that a risk-free society is not only impossible, but intolerably expensive. At some point the real danger of too much pesticide must be balanced against the value to poor people of cheaper fruit. There are numerous deaths from falls down stairs in the home every year, but we do not advocate that all staircases be replaced by elevators. Scares of the week are in the same category. We cannot afford to be complacent about real threats, but we must remember that to be alive is to be at risk.—Daniel E. Koshland, Jr.

7 APRIL 1989 **EDITORIAL**

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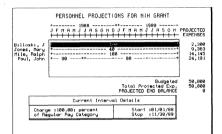
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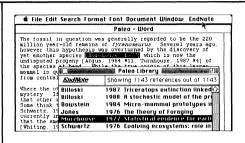
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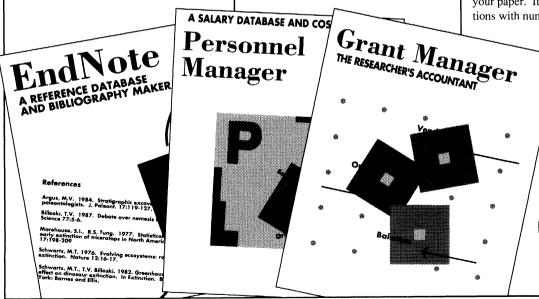


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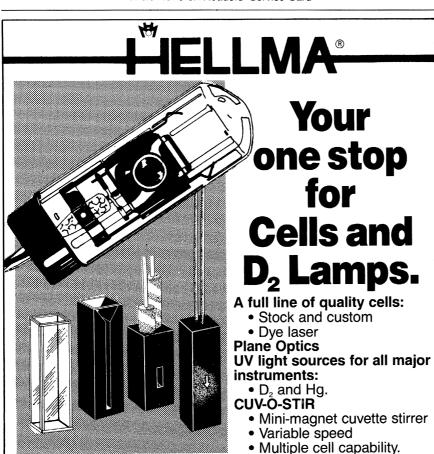
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with (and training in) such scientific decision-making modes, we would begin to have a population of young people who understood science and who knew why they should believe in scientific findings as contrasted with so much of the pseudoscience that appears in the popular media. Of course, this would require that their teachers also understand scientific decision-making methods.

A population so trained would be far more supportive than the public is today of science in all of its manifestations; they would also be much better able to function in a democratic society.

> THOMAS MOORMAN 1850 Folsom Street, Boulder, CO 80302

The Chevron Doctrine

Daniel E. Koshland, Jr. (Editorial, 3 Feb., p. 585), argues that laws that are deliberately worded vaguely should be interpreted so as to give the authorities who administer them a certain amount of discretion. Readers may be interested to learn that federal courts already employ such a "background rule" when interpreting laws that delegate particular tasks to executive agencies. Under the so-called Chevron doctrine (1), unless an agency's interpretation is contrary to the clear intent of Congress, reviewing courts will generally defer to an agency's interpretation as long as it is reasonable. This reasonableness standard permits agencies to administer "blank check" laws with some room for judgment. Thus, to the extent that Congress enacts such laws with this "background rule" in mind, Koshland's laudable proposal has in effect already been implemented.

IVAN K. FONG Chambers of Judge Abner J. Mikva, U.S. Court of Appeals for the D.C. Circuit, Washington, DC 20001

REFERENCES

Chevron U.S.A. v. Natural Resources Defense Council, 467 U.S. Rep. 467, 837, 843 (1984).

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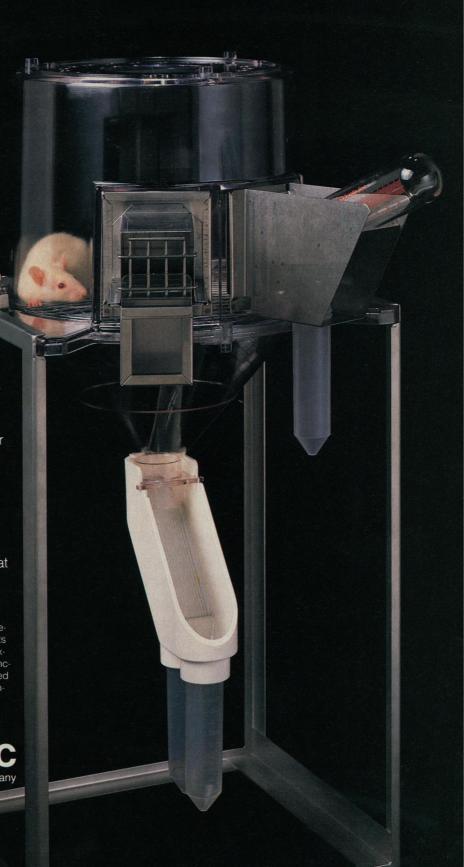
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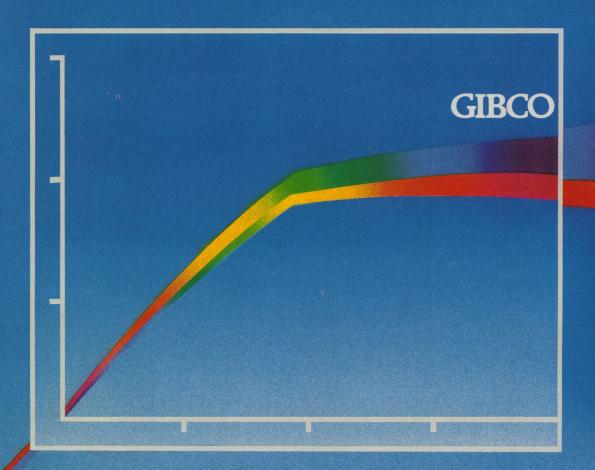
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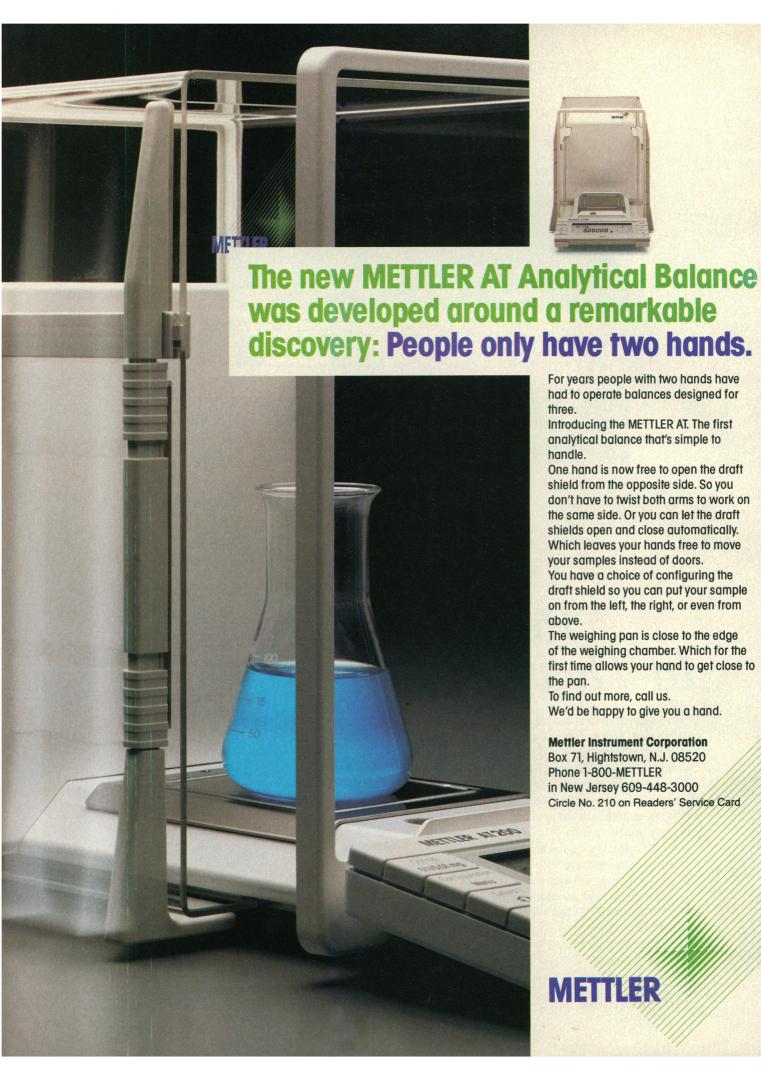
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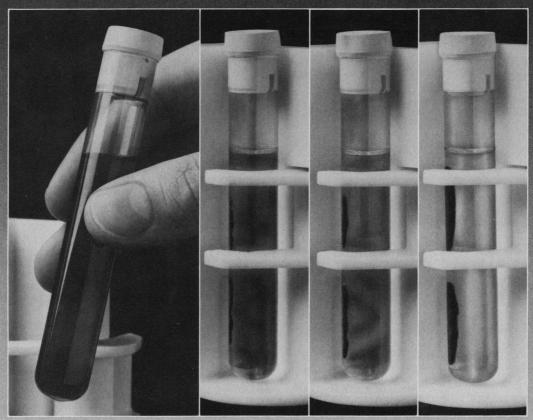
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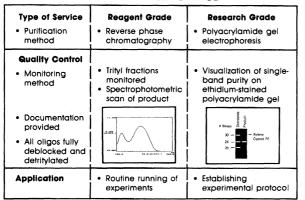
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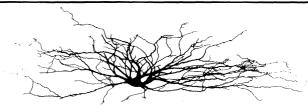
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The symposium will be cochaired by Dr. David H. Sachs of the National Cancer Institute and Dr. Samuel Strober of Stanford University Medical Center. Presentations will be structured around the following topics: basic mechanisms of self-non-self discrimination; clinical status of transplantation; transplantation tolerance; and pathways of allorecognition and their inhibition. Presentations by noted experts will be followed by open discussion.

The speakers are D. Sachs, F. Bach, J. Sprent, R. Germain, P. Terasaki, R. Storb, J. Najarian, J. Thomas, B. Roser, H. Waldmann, S. Strober, J. Batchelor, C. Carpenter, B. Hall, K. Lafferty, J. Borel, F. Sanfilippo, P. Peterson, R. Bollinger, A. Monaco, J. van Rood, D. Scharp and M. Hardy.

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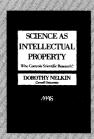
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