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Cultured human neurons, one of the targets of the potent signaling molecule nitric oxide (the NO of the cover). The diverse and important roles of NO are just beginning to be discovered; see the Editorial on page 1861 and the Molecule of the Year story on page 1862. [Photograph: Visuals Unlimited]

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Structural and Electronic Properties of La@C_{82}
K. Laasonen, W. Andreoni, M. Parrinello

Scanning Tunneling Microscopy of Electrodeposited Ceramic Superlattices

Dynamics of Soil Carbon During Deglaciation of the Laurentide Ice Sheet
J. W. Harden, E. T. Sundquist, R. F. Stallard, R. K. Mark

Evidence from the Lamarck Granodiorite for Rapid Late Cretaceous Crust Formation in California
D. S. Coleman, T. P. Frost, A. F. Glazner

Allometric Engineering: A Causal Analysis of Natural Selection on Offspring Size
B. Sinervo, P. Doughty, R. B. Huey, K. Zamudio

Components of Sterol Biosynthesis Assembled on the Oxygen-Avid Hemoglobin of Ascaris
D. R. Sherman, B. Guinn, M. M. Perdok, D. E. Goldberg

Cryobiological Preservation of Drosophila Embryos

Cellular Proteins Bound to Immunodeficiency Viruses: Implications for Pathogenesis and Vaccines

Protective Effects of a Live Attenuated SIV Vaccine with a Deletion in the nef Gene

Targeted Degradation of c-Fos, But Not v-Fos, by a Phosphorylation-Dependent Signal on c-Jun
A. G. Papavassiliou, M. Treier, C. Chavrier, D. Bohmann

Retinoids Selective for Retinoid X Receptor Response Pathways
J. M. Lehmann, L. Jorg, A. Fanjul, J. F. Cameron, X. P. Lu, P. Hafker, M. I. Dawson, M. Pfahl

Isolation and Structure of a Brain Constituent That Binds to the Cannabinoid Receptor

Direct Visualization of the Dendritic and Receptive Fields of Directionally Selective Retinal Ganglion Cells
G. Yang and R. H. Masland

Cloning of a Delta Opioid Receptor by Functional Expression

Prevention of Programmed Cell Death in Caenorhabditis elegans by Human bcl-2
D. L. Vaux, I. L. Weissman, S. K. Kim

Neutrophil Recruitment by Tumor Necrosis Factor from Mast Cells in Immune Complex Peritonitis
Y. Zhang, B. F. Ramos, B. A. Jakschik

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The Molecule of the Year

The Molecule of the Year is nitric oxide, NO, a molecule of versatility and importance that has burst onto the scene in many guises. In the atmosphere it is a noxious chemical, but in the body in small controlled doses it is extraordinarily beneficial. It helps maintain blood pressure by dilating blood vessels, helps kill foreign invaders in the immune response, is a major biochemical mediator of penile erections, and is probably a major biochemical component of long-term memory. These are just a few of its many roles, which are just beginning to be discovered, and they are discussed in the accompanying Molecule of the Year story (p. 1862). That NO plays so many roles is not surprising because the same biological second messengers usually are used in many diverse systems, but a gas was indeed a surprise for an endogenous role, and a labile and toxic gas even more so. As the first surprise of such an unlikely agent was overcome, the gas as a messenger seemed logical because it could pass through biological membranes readily and oxidize foreign substances.

NO's role in sexual dysfunction, that of impotence, supports further a new liberation from old mental straitjackets. The future is sure to bring more insights into the effect on complex processes such as IQ, bad behavior, and alcoholism by single genes or chemical reactions. Many people will be happy to learn that some forms of sexual dysfunction may not be caused by psychiatric disorders or the failure of a marriage but may instead reflect a deficiency in a chemical reaction that can be compensated for by medical treatment. New research on the role of NO may also lead to new insights into the loss of memory, which is so debilitating to so many.

This year's Molecule of the Year once again shows that scientific rewards can come from pursuing unconventional thinking. The recent presidential election focused on the persistent question of providing jobs and correcting ailing economies. Hopefully, the political and social scientists advising our leaders will pursue these problems with the same creativity that characterized the research on NO. The new, the unexpected, and the incongruous will be needed to address these social problems. In addition, our elected officials as well as the general public must face unpleasant realities, including the need for the United States to work hard to maintain its standard of living in a competitive world and the need to be open-minded enough to welcome unexpected solutions such as gaseous messengers.

Every year Science picks a Molecule of the Year along the lines described in our editorial of 22 December 1989. Molecule is a term we use to emphasize that we are honoring the discovery rather than the people who made the discovery, not because people are unimportant but because many other awards honor the discoverers, and most discoveries involve the contributions of many people. As in the case of "people prizes," there are many "runner-up" discoveries that are extremely important to humanity but, in our opinion, are not yet quite as developed as our winner. For example, one of our runners-up, the discovery of the structure of nitrogenase, has no immediate industrial application, but the way enzymes fix nitrogen is bound to be of great importance to agriculture. As more intense farming and cheaper fuel become the necessities of the future, better mechanisms for nitrogen fixation become more important. Enzymes certainly appear to have solved the problem better than man-made solutions so far. The hope is that the enzyme mechanism and the chemical knowledge can be combined to make a new solution that will benefit millions. The widespread use of supercomputers is not a sudden event, but the increased utility of this powerful tool in industry and science for applications such as aircraft design and oil exploration will solve many problems that were previously beyond approach.

All of the runners-up are discussed in the accompanying story. This year they are an impressive group ranging from discoveries that are already being applied, such as fetal diagnosis and treatment (in utero treatment of a fetus to correct its deficiencies and transplanting fetal tissue to adults with Parkinson's disease), to those that are now far enough along so that application seems inevitable, for example, antisense RNA. In addition, there are landmarks such as the mapping of chromosomes 1 and 21, which will certainly lead to medical discoveries, and the use of magnetic resonance imaging to diagnose medical problems and to locate areas of the brain identified with specific thought processes. Those who sometimes question the advances of science should think for a moment about the incredible developments that have slipped into everyday life without headlines. The Molecule of the Year and the runners-up are a good place to start for the discoveries that will inevitably make the future better than the past.

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The Taste of Birds: Pitohui

The announcement of a toxic alkaloid in the skin and feathers of three species of New Guinean Pitohui (Reports, J. P. Dumbacher et al., "Homobatrachotoxin in the genus Pitohui: Chemical defense in birds?" 30 Oct., p. 799) represents the first time that a chemical has been identified that may function to protect birds against predation. But it is not the first evidence for chemical defense in birds. Among European, African, and neotropical birds, the range of palatability of flesh and eggs covers from what humans have described as "ideal" at one end to "inedible" at the other (more than 200 species have been tested) (1). The hierarchy of human palatability rankings is similar to those produced by tests using hedgehogs, rats, ferrets, and cats as tasters. Flesh and eggs of the same species have often had different palatability rankings, and in neither case was palatability related to diet. For both flesh and eggs, however, palatability was correlated with ratings of the vulnerability to predation. Among vulnerable species that are also conspicuous (for example, auks, turacos, hoopoes, kingfishers, starlings, and woodpeckers), the flesh was consistently repugnant. Eggs tasted good, however, in species that escape egg predation by being protected by a cryptically colored parent (for example, many ducks and game birds). The estimated vulnerability to predation was correlated more closely with palatability than with diet, yolk color, egg texture, or taxonomic division. The most common bad taste was bitterness.

The work of Dumbacher et al. on the Pitohui thus complements strong evidence for chemical defenses against predation in other birds. The discovery of convergence in the chemical armory of Pitohui and of Phyllobates frogs suggests there will be much of interest to come from an analysis of noxious compounds in other birds.

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The report by J. P. Dumbacher et al. that pitohuis, conspicuously patterned black and orange-brown birds from New Guinea, contain a chemical substance that may make them unpalatable to predators reminded me of experiments carried out half a century ago by Hugh B. Cott testing the hypothesis that conspicuous colors and patterns of birds are aposematic (1). While he was stationed in the Middle East and England during World War II, Cott used hornets and domestic cats to assess the palatability of more than 50 species of birds. These trials demonstrated "a general inverse correlation between conspicuousness of the plumage and palatability of the flesh" (1, p. 517). Further, Cott noted that "the sematic colours [blue, red, rufous, white, and black] predominate[d] among the more distasteful species" (1, p. 517). In 1957 and 1958, Cott enlisted "a panel of tasters recruited from the staff of the Department of Game and Tsetse Control, Northern Rhodesia" (2, p. 357) and surveyed 200 species of birds belonging to 57 families. An association of conspicuousness with distastefulness was observed within taxonomic groups as well as across lineages. Cott's data are the basis for suggestions that the similarity in color and pattern of some birds that form mixed-species flocks might represent Batesian and Mullerian mimicry (3).

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REFERENCES

Ice Man: Victim of Prehistoric Schnapps?

Horst Seidler et al. (Reports, 16 Oct., p. 455) interpret the folded-over left ear of the prehistoric Tyrolean man recently found in an Austrian glacier as evidence that he succumbed to exhaustion and subsequent hypothermia. ("In this state of complete exhaustion the folding of an auricle would have not been consciously experienced.") This is a nice piece of scientific detective work, based on such a seemingly minor
Response: McManus’s hypothesis is not as improbable as it seems. His observations about the “folded-over ear” as a consequence of alcohol abuse have been described extensively (including radial nerve lesions resulting from lying in a nearly unconscious condition). However, our colleagues from the Institute for Alpine History Research at the University of Innsbruck have ascertained that no prehistoric bottle of spirits was found among the ice man’s provisions. We therefore consider exhaustion to be a more likely cause of death than exposure to cold caused by intoxication.

McManus does not suggest the use of drugs, but we refer the reader to a paper by R. Pöder et al. (1) discussing pieces of two *Piptoporus betulinus*, an agaric, fastened to a leather band among the possessions of the ice man. These fungi may have been used for spiritual and medicinal purposes. They contain a pharmacologically active substance, agaricine acid, an antibiologically effective agent. To our knowledge, no hallucinogenic effects have been described for *P. betulinus*.

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REFERENCES

EMF Research

H. Keith Florig, in his Policy Forum “Containing the costs of the EMF problem” (24 July, p. 468), addresses a segment of a broad problem that besets society today. How should one deal with fears that are not known to be justified? Florig estimates that the avoidance of weak electromagnetic fields (EMFs) now costs the United States about $1 billion annually, although there is no consensus that these fields, much small-
er than those occurring naturally in the body, can have any biological effects, let alone pose dangers.

Florig argues that more research on weak EMFs is economically justified inasmuch as that research is likely to either demonstrate that EMF dangers are real, allowing cost-effective decisions concerning mitigation, or show that the fields are harmless, thus eliminating avoidance costs. However, unless the new research differs in kind from that of the past 15 years, which I contend has created an imaginary problem where no real problem exists, one can expect only further obfuscation and higher costs to our society.

Past biological EMF research has often been misleading. Because there is no accepted model of the interactions of EMFs and the human body, experimental errors have been accepted as real effects. This is demonstrated by, and explains, the incoherence and lack of replication of the different positive reports and the almost universal lack of a dose-response relation.

Also the statistical significances of some of the biological work and many of the epidemiological reports have been seriously overstated. Such analyses are usually subjective; experience with simpler, falsifiable, physical science experiments has shown that significance levels are generally exaggerated.

There are further biases that emphasize false positives and suppress negatives. Results that are claimed to be positive are accepted for publication, while negative results are rejected as uninteresting—or as failures. And those who report positive results are more likely to have their funding renewed than those who "fail."

What should be done? Much advice, such as Florig's, is marred by conflicts of interest. Better, the National Academy of Sciences, chartered by Congress for the purpose of advising the government, should be asked to evaluate the evidence on EMF effects and to recommend appropriate action.

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Response: Adair implies that the hundreds of articles in the peer-reviewed literature reporting statistically significant observations of EMF bioeffects are the result of uncontrolled artifacts, statistical false positives, or observational bias. While such factors have undoubtedly clouded the scientific record, many credentialed observers believe that the chance that EMF hazards are real is far from negligible. A large number of biologists and epidemiologists

Continued on page 1960
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- Let the burner cool completely before removing the bulb.
- Unplug the power supply.

**PROCEDURE**

1. Move collector lens away from bulb (knob on lamp housing) or remove lens entirely. Separate socket from lamp housing (retaining screw).
2. Remove copper wire from post (thumb screw) then pull bulb upwards from socket (loosen lug nut at base; special wrench). Remove heat sink (silver cap on bulb; set screw).
3. Reverse steps 1-2 to reinstall new bulb, being careful not to put strain or stress on bulb when tightening fittings. (For 50W HBO burners, make sure flat sealed surface is facing to side.)
4. To align, remove an objective, rotate empty space into viewing position and place a white card flat on stage, revealing real and mirror arc images. Focus images using collector lens and align (see diagram) using centering screws on lamp housing.
5. Defocus images to evenly illuminate field; reinstall objective.

**TIPS**

- For greater stability, run for one hour before using.
- Never switch high pressure burners on and off quickly.

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contend that an equally plausible explanation of the record is that EMF bioeffects are simply more subtle than those of many other environmental agents and that, as lines of inquiry and scientific tools are sharpened through further research, uncertainties about possible EMF hazards will likely be reduced. Indeed, EMF bioeffects research funded by the Department of Energy and the Electric Power Research Institute has become much more focused over the last 5 years, reflecting knowledge gained through the previous decade.

Even if one concludes, like Adair, that the specter of EMF hazard is imaginary, there are still good reasons for expanding both the depth and breadth of EMF-related research. First, if the research record is indeed contaminated by artifact, an expanded research program that concentrates on experimental quality control and replication of existing positive studies would set the record straight. Second, public concerns and ad hoc expenditures on mitigation are driven primarily by several dozen nominally positive epidemiological studies of the relationship between EMF exposure and cancer. Further epidemiological investigation might "explain" these positive studies as arising from some non-EMF cause such as a yet-to-be-identified confounder.

Third, public and private officials faced with EMF risk-management decisions are more likely to delay spending on EMF mitigation if they believe that continuing research might reduce uncertainty in their decision. Finally, accelerated research on the public's need for EMF information, on fair ways to resolve powerline siting disputes, and on low-cost means for reducing EMF exposures can reduce both contention over powerline siting and the risk of product liability suits. This would save the costs of transmission project delays and courtroom battles and would go farther toward relieving public angst than would a halt to all research.

Adair's prescription for managing the EMF issue raises another broad problem that besets society today. In a democratic society, who should decide what fears are justified? Adair would vest that power in the scientific community (or more specifically in a small elite such as a National Academy of Sciences committee). Although the public and policy-makers depend on scientists for judgments about the probability and scope of possible EMF hazards, the legitimacy of the scientist's expertise stops there. Decisions about the appropriate level of funding for EMF research or about whether to control EMF exposures require making value judgments about willingness to pay, risk aversion, and equity among other things (1). Such decisions require input from all stakeholders.

Brain Tumor Treatment: Significant Contributions

In our report of 12 June (p. 1550), "In vivo gene transfer with retroviral vector-producer cells for treatment of experimental brain tumors" (1), we cited, among others, the papers of M. P. Short et al. (2) and Z. D. Ezieddine et al. (3), which described studies of in situ delivery of the lacZ gene into C6 gliomas and the effect of ganciclovir treatment on the growth of subcutaneously implanted tumors that bear a herpes thymidine kinase gene. We have received a complaint from X. O. Breakefield, a co-author of those reports, that our method of referencing did not give sufficient credit to their work.

It was the intent of the citations included in our manuscript to serve as an acknowledgement of the contributions of other workers reporting studies in this area of research. We regret that a more detailed description of the work contained in each of the cited papers was not possible within the space allotted by Science for the text of our report. The citation and terse description included were in no way intended to diminish the significance of contributions by any of the cited workers. We are pleased to again acknowledge that other investigators have suggested a similar strategy for the treatment of malignant tumors of the brain and note that none had reported the successful implementation of this strategy.

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REFERENCES

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