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> Cover: Rabbits, rats and mice have long been used by scientists to determine the relative toxicity of chemical compounds, from cosmetics to food additives to industrial solvents. Pending acceptance by government regulators, test tube alternatives may reduce the number of animals required for such tests.



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## Letters

## Bedtime behavior

Yawning research ("Are we boring you?" SN: 12/5/87, p.360; Letters, 1/9/88, p.19) sounds like an excuse to have a good time at someone else's expense. It should be obvious that yawning is genetic behavior for social animals. It's an animal's way of telling the pack, "Hey, I want to sleep." Without yawning to synchronize sleep patterns in a group of individuals, one or more of them would keep the others awake. Animals that don't sleep don't survive, which brings us to us.

I suspect that Dr. Provine will find that after-sleep yawning occurs much less often than does before-sleep yawning. Morning yawning is no doubt the before-language way of saying, "I'll get up if you'll get up."

William T. Holmes Poway, Calif.

## Collaboration yes, construction no

"The Road to Magnetic Fusion?" (SN: 11/7/87, p.294) accurately presented the ra-

tionale for internationalizing the U.S. magnetic fusion program and discussed congressional concerns about the unprecedented level of international collaboration that would be required for the joint construction of the International Thermonuclear Experimental Reactor (ITER).

I would, however, like to correct one key error in the article. While the outcome of the quadripartite meeting in Vienna on October 18 and 19 was truly significant, it was never intended to reach "agreement ... for construction of the next large step ...." The quadripartite group agreed that each delegation would recommend to its authorities participation in a major ITER conceptual design and validating R&D activity over the next three years. I believe this agreement represents a major step in international scientific collaboration. It is intended to provide all of the information needed for subsequent decisions on international construction of a facility which may be the key to ensuring an adequate supply of energy for the entire

To put the ITER activity in context, I would

like to point out that the current fusion programs are already engaged in extensive international cooperation. All fusion programs are working to strengthen the coordination of national planning efforts to ensure best use of the resources available worldwide for fusion research.

John F. Clarke Associate Director for Fusion Energy Department of Energy Washington, D.C.

## Calculus solutions

In "Calculus Reform: Catching the Wave?" (SN: 11/14/87, p. 317), the author points out that about 90 percent of the typical problems in an undergraduate calculus text can be done using some of the current electronic calculator-computers. The point of the exercises, however, is not the answer, but the method used to find the answer. The student would learn nothing from such computer solutions, just as he or she would learn little

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that the test has been studied for more than a decade, its results have been documented in peer-reviewed journals and it has been designated a standard method by the American Society for Testing and Materials, a nationally respected organization devoted to developing test standards.

Sen. William Proxmire (D-Wis.), in a letter to EPA Administrator Lee Thomas, recently expressed his dismay that "the Agency may not be doing everything it possibly can to replace traditional methods of testing with alternatives."

The EPA has also been criticized for continuing to require the so-called  $LD_{50}$  test as a measure of mammalian toxicity. The test has been described by Gerhard Zbinden, an internationally renowned toxicologist and director of the Institute for Toxicology in Zurich, Switzerland, as "a ritual mass execution of animals." Each  $LD_{50}$  test requires that 40 to 200 animals be exposed to a range of concentrations of a potential toxin in order to determine the dose at which 50 percent of the animals will die.

"Clearly, such experiences reinforce industry's perception that there is no clear regulatory procedure....for replacing animal tests with appropriate alternatives," Spira says. "These ambiguities produce a counter-incentive for industry to invest significant resources to develop, validate and implement alternatives."

Theodore M. Farber, director of the EPA's toxicology branch, confirms that the  $LD_{50}$  is still required. However, he says, "We have formed a committee that will be looking for some acceptable alternatives to the  $LD_{50}$ . We are also actively looking at the Low Level Eye Irritation test." Alternatives might be identified and validated for at least limited use as early as this spring or summer, he says.

Bureaucratic sluggishness is not the only factor slowing acceptance of in vitro alternatives; difficult scientific hurdles remain. Uppermost among them is the need to design objective validation criteria for new test methods.

For example, to test the validity of two new *in vitro* tests that make use of different tissue cultures, each culture might be exposed to a standardized selection of common irritants — from the most innocuous to the most corrosive — and the results compared to traditional animal test results. But because each new test measures a slightly different variable, comparisons can be difficult to make.

"We can generate numbers in vitro," says Frazier, of CAAT. "The question is, what do those numbers mean?"

Moreover, says Dennis M. Stark, director of research and testing alternatives at Rockefeller University, with so many laboratories developing their own *in vitro* tests, "Any list [of standards] that comes out of a laboratory is going to look self-

serving." So here, too, he says, the role of the federal agencies will be a critical one.

Stark says a recent meeting with Gary Flamm, the director of the FDA's office of toxicological sciences, left him convinced that the agency was serious about promoting *in vitro* alternatives. Flamm "seemed very interested in moving this thing from ground zero. He listened to us and seemed interested in getting things done."



A laboratory mouse getting a forced oral dose of a suspected toxin as part of the LD<sub>50</sub> test.

However, Stark warns, "Companies are apt to keep doing the  $LD_{50}$  because of fear of litigation, even if the FDA doesn't insist." He has suggested that the FDA start accepting  $LD_{50}$  results using fewer animals whenever the data are supported by in vitro tests. "This would help reduce the number of animals being used, but it would still use some animals so that corporate lawyers would feel more secure," he says. In addition, such combinations of tests would move the *in vitro* validation process forward by adding to the database of *in vitro* results.

Ultimately, some argue, even regulatory revisions may be insufficient. Christopher Kelly of the National Testing Corporation in Palm Springs, Calif., a developer of *in vitro* toxicology tests, says that nothing short of congressional action is needed to ensure *in vitro*'s acceptance.

"Regulators only do what the law tells them to do," he says. "All in all, nothing is going to change until the law changes." He notes that one bill, HR 1635, now pending in Congress, would insist that if there is a valid *in vitro* test available, it must be used.

Others, including Spira, say that even such a law may not be strong enough. Unless specific reductions in the number of animal tests are spelled out, he says, with real penalties for failure to use *in vitro* tests, "creeping routinism" will ensure that unnecessary animal tests continue to prevail.

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by copying the solution from a fellow student. The answer is to give problems that require thought as well as manipulation, and to require the student to write out all the steps, just as was once done in high school geometry. It will also require the teacher or problem assistant to read the solution with care. This will entail more effort than is often currently devoted to teaching calculus, but the students deserve no less.

Harry H. Denman Professor of Physics Wayne State University Detroit, Mich.

I was pleased to read of the "calculus reform" movement. I hope, however, that the movement does not stop at calculus and extends into high school and grade school. For many years math has been taught as if every student were a math major and could appreciate and understand its intrinsic beauty. In reality, math is a tool that is used to solve practical problems and has no other value to the vast majority of its students. The standard teaching approach, which stresses theoretical development, does not offer the student a tangible goal toward which the development is leading. Students generally have no idea where the math is taking them. They are just following directions.

If a new math concept were introduced to students by presenting a problem whose solution would be greatly aided by the new concept, then the development of the math toward that solution would have some meaning to them.

Math teaching is dominated by those who see and appreciate the pure beauty inherent in the subject. The students, however, do not share this vision, and so math has developed its fearful reputation. Mathematicians frequently lack the basic pragmatism toward the problem-solving role of math that others, such as engineers, have developed.

We are alienating our students from math at a time when its importance in our society is blossoming. Students need a better understanding of what math can really do for them.

Paul W. Dueweke Palo Alto, Calif.

Ho hum. Another conference on the crisis in teaching college calculus. When will people face the truth? Little kids, learning at home, are able and eager to learn college math and science, if given chances to do so. But we don't offer them.

Many of the most interesting, important and useful features of science (nature) and its language, mathematics, are kept in a few college courses. Unless a person takes these courses, he or she never gets a chance to learn them. Moreover, they are given to prepare for careers in physical science or engineering. Of many tragic results, parents with training in these fields can't talk to their own children about them.

The above can be changed with materials to learn enjoyably "college level" math and science at home, at any time of life. Until we face these facts, and do constructive things about them, the futile conferences will continue.

Robert G. Hoffmann Indianapolis, Ind.

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