Fighting Antibiotic Resistance

In his letter about antibiotic resistance, H. L. Cooper (29 July, p. 590) advocates further study of the example set by Hungary, where the use of penicillin was considerably reduced in order to fight the spread of antibiotic-resistant bacterial mutants that survive when the wild-type strain is eliminated. It is expected that, in the absence of penicillin, the mutants eventually will be replaced by the competing, better-adapted wild types. While the minimal use of antibiotics is clearly desirable, the "asymptotic" success of such a strategy would depend on its acceptance on a worldwide scale and its extension to the great variety of antibiotics now in use. The use of antibiotics cannot be expected to reach zero.

One might consider a different approach, an attempt at a "Darwinian" reversal of fortune for drug-resistant mutants, which would seem to deserve a wider study, although it has been tried previously unsuccessfully in isolated cases. If this approach survives criticism and the necessary tests, it might complement other attempts that are not likely to lead to a complete solution to the crisis. Assume that a bacterium A, sensitive to an antibiotic α, mutates into bacterium A', for which there is no antibiotic (*1*). If a patient suffering from an A' infection could safely be "inoculated" with A, and if the competition indeed led to the elimination of A', one could then apply α to eliminate A in turn, although admittedly the situation is not simply "time-reversed" from the one which gave rise to the mutant. Success would depend on the relative viability of A and A' in that particular niche (*2*). One can envisage four investigative stages to decide for any (A, A') combination how well the competition works and in which success at one stage would encourage pursuit of the next one.

Stage 1: In vitro experiments carried out in a culture medium that approaches a natural niche, with A and A' injected in different amounts and in different order, with different time intervals between the injections. Thus, one could find to what extent A' loses out against A, with the results depending on their relative growth rates (*3*). It might be possible to replace A by a defective harmless pathogen of the same species, perhaps genetically engineered.

Stage 2: Studies with animal models to determine whether, after an A' infection, the addition of A, given at different times after the onset of the A' infection, succeeded in reducing A' below a threshold where it can be successfully fought by the immune system.

Stage 3: Inoculation with A of volunteer patients suffering from an A' infection that is not life-threatening and in whom suitable doses of A, routes of inoculation, and the time needed to eliminate an A' infection could be studied (*4*). The "age" of the A' infection might be important; it might be approximately deducible in some cases, for example, for patients infected in hospitals, for children infected by siblings, and so forth.

Stage 4: Patients suffering from a life-threatening A' infection might volunteer for inoculation by A, especially if it could be replaced by a harmless pathogen derived from it.

If inoculation with A should aggravate an existing infection unduly, the antibiotic α might have to be applied prematurely, aborting the attempt at a cure.

While some isolated, related procedures have been tried in the past (*5*), a systematic study (stages 1 and 2) of different (A, A') combinations seems desirable to find out whether there are some for which the approach discussed seems promising. A search for "Darwinian reversal" would also be of interest to evolutionary biologists.

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References and Notes

1. Although bacterial mutants usually arise spontaneously, some may be induced, for example, by diagnostic x-rays, which are copiously used for patients with lung infections.
2. The procedure may not work for those mutants A' that can transfer their drug resistance to A, depending on the rate of transfer.
3. Evidence of considerably slower growth of mutants than that in the wild-type strain is reported by M. Demerec [*Genetics* **36**, 585 (1951)] and by J. R. Saunders [*Brit. Med. Bull.* **40,** 54 (1984)].
4. Such "experiments" may have been unwittingly done when patients infected by A' were by chance infected later by A; if this indeed led to the elimination of A', one might have concluded that α, although ineffective at first, later became "miraculously" effective.
5. M. Scolaro, R. Durham, and G. Pieczenik chose a similar approach to treat a virus infection [*Lancet* **337**, 731 (1991)]. However, they took a bold shortcut, using blood from a patient infected with a nonpathogenic human immunodeficiency virus (HIV)–1 strain to inoculate HIV-infected volunteers.
6. I thank C. W. Anderson, D. M. Atwood, S. J. Gould, S. Lacks, A. D. Woodhead, and G. C. Williams for illuminating discussions.

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Women in Science

In their Policy Forum "The paradox of critical mass for women in science" (7 Oct., p. 51) Henry Etzkowitz *et al.* address the significant fact that academia's gender imbalance will not change solely by getting more women to enter science disciplines. They state, "[a] key factor in overcoming the problems posed by the paradox must be university-wide policies and programs. . . ."

This is a "paradox" that the Association for Women in Science (AWIS) has tried to overcome for 23 years. Etzkowitz *et al.* are on target in recognizing that increasing the

number of women entering science, that is, broadening the pipeline, will not by itself change the nature of how science departments are organized and how the women in the pipeline fare once they are in those departments.

AWIS, along with others, has tried to confront the gender imbalance primarily by addressing the practitioners of science. AWIS' Mentoring Future Scientists project and a national leadership conference, "Taking the Initiative: Women in Science and Engineering Leadership" held in May 1994 are two recent examples. Although these and other programs have been successful, it has become increasingly apparent that the lack of gender equity in science needs to be approached from more than one angle. Specifically, the policies and structures surrounding science need to change to accommodate a younger generation of scientists, both female and male, for whom the current scientific model does not work.

We are therefore pleased to announce a 2-year pilot project, "Women Scientists in Academe: Warming Up a Chilly Climate," that will develop a model program offering workable options for institutions committed to enhancing the academic climate for women science faculty.

AWIS will work with three institutions to promote the integration of women scientists into the academic environment. We will identify both common denominators and specific differences among science departments at each institution and design strategies for increased retention, promotion, and tenure of female faculty.

AWIS' work supports the contention of Etzkowitz *et al.* that it is only through change in the institutional climate for women scientists that women will achieve a critical mass in science without the "paradox."

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Etzkowitz *et al.* point out the difficulties women still face in all scientific disciplines. The system simply cannot change until more women become fixtures in science, and we are not doing enough to encourage women to choose and stay in these disciplines. The problem is one for all of us: We are excluding a large contingent that could be making significant contributions, if given appropriate encouragement and support.

Another online discussion group, which Graduate Women in Science (an affiliate of the AAAS) started last April, was established to support women in all scientific disciplines. Any woman researcher (graduate student, career track, or retired) may join the discussion by sending an e-mail letter to sheri__cole@som-bsb.ucsd.edu. Our aim is to reach all women scientists who feel the need for a connection to other women scientists, all over the globe. We discuss topics of interest to women scientists, such as "how to have it all; career, family, and personal life"; "time management"; "successful management skills"; and "how to choose a graduate adviser and survive graduate school." This group has been a valuable mentoring tool for women beginning their careers, providing pertinent information about issues that continue to haunt career women.

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"The paradox of critical mass for women in science" gives a confused picture of this problem and its policy implications. The term "women-friendly subfields" of science gives the clear implication that other fields are unfriendly or hostile to women. As a physicist, I know with certainty that my field, although it has few women, is no more unfriendly to women than those fields in which women are now numerous. Great efforts are being made in physics, as in all areas, to encourage their participation.

Much of what is said by Etzkowitz *et al.* suggests that the familiar ways in which scientists have practiced their crafts—long hours, competitiveness, and great commitment, for example—contribute to repelling women with broader interests. That may be, but it is rather general among fields and applies in many areas outside of science, including business, law, and medicine.

Criticism of the traditional practice of scientific research is tantamount to a demand that the general practice of science be changed. That might be beneficial or not to science and to scientists, but it does not address the question of why some fields have many more women than others. Nothing in the Policy Forum by Etzkowitz *et al.* tells us what the determining factors are in women's attitudes to the various fields. In the general absence of an understanding of this problem, any drastic actions are imprudent.

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The message of Etzkowitz *et al.* is summarized in their marvelously turgid last sentence: "Equal representation of women and men in scientific professions would counter the elitist image of science and hopefully earn in-

creased support for allocation of public resources to science." What an insult, both to women scientists and to taxpayers! Etzkowitz *et al.* have written, hopefully or not, a parody of political correctness run amuck.

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First Up and Out

I was surprised to read that the space probe Ulysses is the first to fly up and out of the ecliptic plane as it circles the sun on a polar orbit, as stated by Peter Aldhous in an otherwise fine Research News article "Long-awaited probe gets new view of the sun," (16 Sept., p. 1659). The honor of first climbing that peak actually goes to Voyager 1, which did so after its Saturn flyby in 1981. Following orders, it reached an altitude of 4 billion miles by February 1990, and then took the first "family portrait" of the solar system looking down.

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Corrections and Clarifications

In the report "Functional consequences of post-translational isomerization of Ser^{46} in a calcium channel toxin" by S. D. Heck *et al.* (11 Nov., p. 1065), the affiliation of several authors was incorrect. S. D. Heck, C. J. Siok, P. R. Kelbaugh, P. F. Thadeio, M. J. Welch, R. D. Williams, A. H. Ganong, M. E. Kelly, A. J. Lanzetti, D. Phillips, M. K. Ahlijanian, and N. A. Saccomano, should have been listed as at Pfizer Research Incorporated, Groton, CT 06340, USA. All other affiliations were correct.

In the report "Homozygous human TAP peptide transporter mutation in HLA class I deficiency" by H. de la Salle *et al.* (8 July, p. 237), figure 2B (p. 239) was printed incorrectly. The correct figure appears below.