results from growing numbers of the U.S. population attaining ages at which coronary death rates are highest.

Second, the same demographic process brings increasing proportions of the world's populations, especially in developing countries, to middle and later adult ages, at which coronary rates soar. The effect of this profound demographic change is compounded by adverse changes in diet, physical activity, and use of commercial tobacco products. These changes together are expected to produce major increases in coronary heart disease morbidity and mortality in coming decades and have done so in places as diverse as Scotland and Singapore. The World Bank is examining these trends and the potential for programs to combat them, especially in developing countries, as a major priority (*2*).

Third, the impressive outcomes of clinical trials with the cholesterol-lowering drugs called statins (*3*) are rightly hailed by Brown and Goldstein. But it should not be overlooked that the people studied in those trials were largely survivors of an earlier heart attack; those whose initial manifestations of coronary disease were fatal cannot be helped by medical interventions. Further, even under the exceptionally favorable conditions of closely monitored treatment in clinical trials, relative to medication use in the general patient population, the majority of expected deaths (based on rates in the placebo group in each trial) were not prevented in any of the trials. Hence the recent recommendation to the National Heart, Lung, and Blood Institute by its Task Force on Research in Epidemiology and Prevention to place the highest priority for coronary disease prevention on prevention of the risk factors—such as elevated cholesterol concentration—in the first place (*4*). This is a public health challenge of the first order.

Well-founded optimism is welcome, but misplaced confidence could undermine the intensified public health efforts needed to address the continuing epidemic of coronary heart disease and its risk factors, both in the United States and throughout the world, for the foreseeable future.

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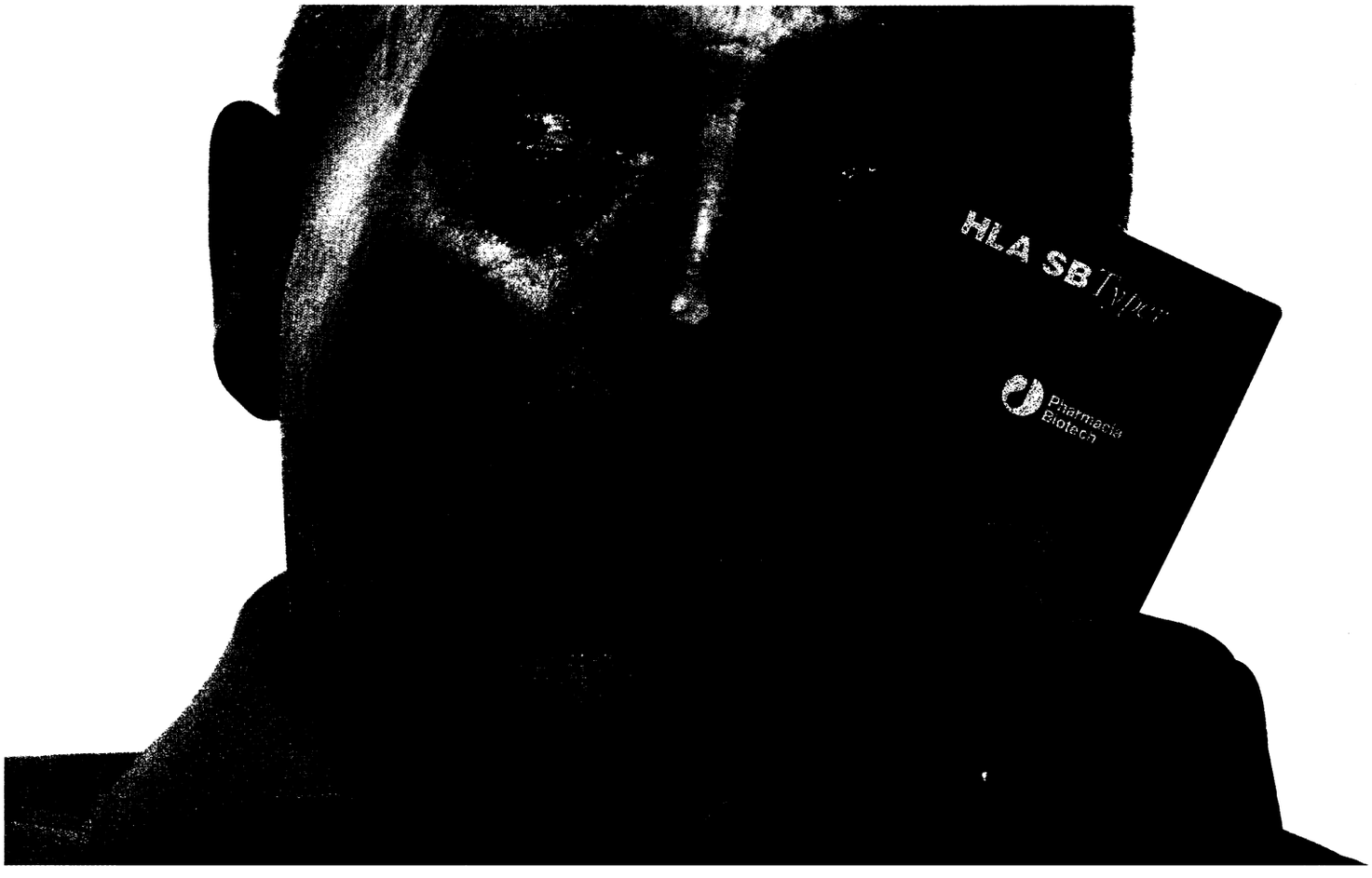
Release of RHD Virus in Australia

The defenders of the rabbit hemorrhagic disease (RHD) virus release program (Dan Drollette, News & Comment, 12 Apr., p. 191; ScienceScope, 19 April, p. 341) appear to have confused the concepts of "host switching" and "host range" (*1*). Alvin Smith and I have raised the concern that the host range of this agent, first described in 1984, is not known. Our concern has been that widespread release of this virus to a continent apparently lacking experience



with it would reveal unfortunate new information about the host range of the agent. While it is possible that the RHD virus might switch hosts, suddenly developing an ability to replicate in another species, we agree that this would be unlikely, although the possibility is enhanced by the ecological conditions in Australia.

The question of host range, while generally applicable, has particular relevance because of our knowledge of caliciviruses as a family. Some caliciviruses, although within a genome group different from that of the rabbit calicivirus, are known to have a broad host range (*2*, *3*). Because it took 50 years to learn what is now known about the host range of some calicivirus strains, it is reasonable to believe that the host range for the RHD virus, described in 1984, is not yet known. The possibility that the RHD virus might find a host among the large number of previously unchallenged species in Australia seems reasonable.

Scientists from the Commonwealth Scientific and Industrial Research Organization (CSIRO) have addressed this concern by conducting challenge experiments in 28 species of animals. These experiments have not been published.

Smith is described as an isolated critic. However, he has isolated more species of caliciviruses than anyone else, from approximately 30 species of animals (*2*). His work led to the hypothesis that the vesicular exanthem of swine virus (a calicivirus) outbreaks in pigs in the southwest United States from the 1930s to the 1950s were related to San Miguel sea lion caliciviruses. This hypothesis was substantiated by his own work and recently proved independently by others (*4*).

The plans for studying the RHD viral agent in Australia clearly failed. Release of a lethal agent into the wild without knowledge of its route of transmission was a mistake. On the other hand, Brian Cook of CSIRO makes a valid point, quoted in Drollette's article, that the Australians face a difficult challenge, namely, weighing the potential "risk of a virus which might cross over into another species against the inevitability of losing more of our native speices." This is an appropriate concern and certainly justifies the efforts toward studying the RHD virus as a potential biological control agent. However, approval of the RHD virus program after an accidental release would set a poor precedent for future studies of biologic control.

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References and Notes

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If the escaped RHD virus can be declared an official "biological agent" by the Australian government, that would remove liability, but to receive such "approval" the virus must be shown to be species-specific, infecting only the European domestic rabbit *Oryctolagus cuniculus* (*1*).

CSIRO scientists, ostensibly investigating host range, gave 30 species of domestic, wild, and laboratory animals a low virus count (1000 rabbit lethal $dose_{50}$) so as not to "force a response," according to Harvey Westbury, senior veterinary virologist of the Australian Animal Health Laboratory

(quoted in Drollette's article). But this dosage is below the immunogenic and infectivity threshold in 28 of the 30 species tested (four animals per test)—only about 1/30,000 of the dose a predator would receive eating a single infected rabbit liver. To test human susceptibility, Australian authorities examined serum samples from only six people (all were laboratory workers and were antibody-negative) and did not examine high-risk individuals such as ranchers, biologists, and hunters who handle infected rabbits. One laboratory worker tested during an RHD outbreak in Mexico was positive for the RHD antibody (*2*).

Sudden appearance (*3*) and high mortality (95%) indicate that that RHD almost certainly did not originate in rabbits and is not species-specific. The cause of death (disseminated intravascular blood clots with fibrin-depleted blood oozing from orifices and into tissues) is not described for any other calicivirus. The likelihood of this "hemorrhagic" factor emerging in other species infected with caliciviruses is unknown. The mechanisms of virus movements across land and ocean channels are unknown.

Rabbit calicivirus has yet to be grown in cell culture. Therefore, vaccines and some diagnostic reagents are ground-up livers from diseased rabbits. Koch's postulates are unfulfilled, and, consequently, there is confusion about etiology (*3*, *4*).

Adequate surveys to determine disease or infection in nonrabbit species that have been exposed naturally have not been carried out. Serologic testing of extremely small numbers of nonrabbit species, exposed experimentally and naturally, has yielded antibodies [in the mouse, kiwi, dog, fox, and human (*5*)], yet without proof (mice excepted), Australian officials have stated that infection did not occur. Despite much evidence suggesting otherwise (*6*), Australian government agencies declared RHD to be species-specific for rabbits and not infectious to other animals or humans. [Four of the five known calicivirus groups cause disease in humans (*7*)]. These same agencies have notified the Australian people that it would be safe for them to eat rabbits exposed to RHD and to feed these rabbits to their pets (*1*).

I discussed these critical factors with Drollette, but he did not mention them in his article. These factors were considered by the recently elected Australian government in rethinking the official position on the targeted March-April 1996 release of this new hemorrhagic disease virus. Additional studies have been ordered before reconsideration of RHD virus as a "biological agent" and a sanctioning of its deliberate spread. If these studies are carried out to truly test the host specificity and zoonotic potential of this new and deadly virus, then scientific credibility could be restored.

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Corrections and Clarifications

In the third sentence of the next-to-last paragraph of the report "Structure of the atmosphere of Jupiter: Galileo probe measurements" by A. Seiff *et al.* (10 May, p. 844), "300 μbar" should have read, "0.3 μbar."

Figure 8 (p. 514) of the Research Article "Observations of Saturn's ring-plane crossings in August and November 1995" by P. D. Nicholson *et al.* (26 Apr., p. 509) was printed upside down.

The caption of table 1 of the report "Fluorescent hydroxyl emissions from Saturn's ring atmosphere" by D. T. Hall *et al.* (26 Apr., p. 516) should have pointed out that the orientation of the Faint Object Spectograph that acquired spectra at five target locations above Saturn's ring plane can be seen in a figure provided by the authors at the following URL site: http://www.sciencemag.org/science/scripts/display/short/272/5261/516.html.

Letters to the Editor

Letters may be submitted by e-mail (at science_letters@aaas.org), fax (202-789-4669), or regular mail (*Science*, 1200 New York Avenue, NW, Washington, DC 20005, USA). Letters are not routinely acknowledged. Full addresses, signatures, and daytime phone numbers should be included. Letters should be brief (300 words or less) and may be edited for reasons of clarity or space. They may appear in print and/or on the World Wide Web. Letter writers are not consulted before publication.