which premature death can be prevented at modest cost.

In "nontraditional" areas of premature death prevention, notably some associated with modern technology, far greater costs are incurred for each premature death prevented. The estimates range up to hundreds of millions of dollars per death from exposure to chemical carcinogens (*2*). When expressed in this way, the cost of reductions in radiation exposure being imposed to prevent cancer may reach hundreds of billions of dollars per premature death averted. Two current examples serve as illustrations.

At Three Mile Island, 2.3 million gallons of waste water slightly contaminated with radioactivity has accumulated in the course of cleanup activities. The water contains tritium and traces of other radionuclides in amounts that could be discharged to the Susquehanna River without exceeding the limits prescribed by federal regulations. However, this has not been done because of opposition by nearby communities. The National Council on Radiation Protection and Measurements evaluated (*3*) the effects of discharging the water into the river and found that the dose to the maximally exposed individual would be 2 microrems, which is equivalent to that received in about 4 minutes from natural sources of radiation such as cosmic rays and radionuclides in the earth's crust. The collective dose (the mean dose times the number of persons) was calculated to be about 1 person-rem (prem). However, because of community opposition to this method of disposal, the utility proposed instead that the water be evaporated, at an additional cost of about $5 million. Exposure of the public would not be lower than if the water were to be discharged to the river, but it might be perceived to be more acceptable. If one assumes that the risk of radiation-induced cancer is, at a maximum, about 2 per 10,000 prem, it can be calculated that the cost of averting a fatal cancer by the method of discharge to the river is about $25 billion.

A similar calculation can be done for changes being proposed in the design of low-level radioactive waste disposal facilities. The Environmental Impact Statement filed by the Nuclear Regulatory Commission (NRC) estimated that the dose to people living in the vicinity of disposal sites constructed and operated according to the regulations of that agency would be about 0.003 millirem per year (*4*). If we assume that 100 persons will be so exposed, this translates into a 50-year collective dose of 0.015 prem. In response to public pressure, some states have specified that more protection be provided than is required by the NRC. The additional protection involves expenditures of more than $100 million over the life of the facility (*5*), which is equivalent to many *trillions* of dollars per premature death averted!

No doubt there are people who find it repugnant that actions taken to prevent premature death should be based on the cost of doing so. But there is no alternative in a society in which there are limited resources and so much to do. Hiring an additional school nurse, construction of a new firehouse, or implementation of an educational program to encourage immunization of children all require that funds be made available in competition with other needs. The enormously disparate costs of reducing risks that originate in different ways should be better understood by the public, the media, and our government officials.

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Malaria Vaccine Trials

We disagree with some statements in the insert "Vaccine trials disappoint" (News & Comment, 29 July, p. 522), particularly the view expressed in the title.

In the recent trials, one out of three volunteers immunized with a synthetic peptide vaccine, consisting of 12 amino acids [$(NANP)_3$] combined with tetanus toxoid, were protected against infection by the most dangerous malaria parasite, *Plasmodium falciparum*. In two out of three volunteers, there was a delay in the appearance of parasites in the blood, which indicates inactivation of a large proportion of the sporozoites inoculated by the mosquitoes during the challenge (*1*). This was one of the first synthetic vaccines against an infectious agent tried in humans. In several of the volunteers, the titers of serum antibodies had not diminished 1 year later. Equally important, the vaccine was safe, and there was a correlation between the titers of serum antibodies to the NANP peptide and to sporozoites.

In a separate trial, a recombinant vaccine containing multiple NANP repeats also protected one out of three volunteers (*2*). These results are encouraging when one considers that five infected mosquitoes were used for the challenge. Except in highly endemic areas, the proportion of infected mosquitoes is less than 1% and, in many areas, it is less than 0.01%.

This is not to say that there are no more problems to be solved. It will be necessary to include T cell epitopes in the vaccine and to use better adjuvants, also a priority for most other subunit vaccines now being developed. Reports that the immune response to weak antigens is enhanced by incorporating a lymphokine in the adjuvant (*3*) are also encouraging. Blood-stage vaccines are also being developed, and one was recently shown to be partially effective (*4*). A combined sporozoite–blood-stage vaccine should have greater potency.

Another implication to which we take exception is that a sporozoite vaccine would have to be "100% effective" since "a single sporozoite . . . can cause a full-blown infection." To our knowledge, it has not been shown that the severity of the malaria infection in humans is independent of the parasite inoculum; there is, in fact, epidemiological evidence to the contrary. More important, it has been established in a rodent model that vaccination with attenuated sporozoites generates cytotoxic T cells that play an important role in protection (*5*), most likely by releasing gamma interferon. This lymphokine inhibits the development of the liver stages at exceedingly small doses (*6*). Therefore, if a few invading parasites escape the effect of antibodies, they can still, in principle, be destroyed during the next stage of development by effector mechanisms stimulated by a sporozoite vaccine.

The Agency for International Development malaria program, as a whole, has contributed greatly to ongoing studies aimed at developing a vaccine for the most important infectious disease of the developing world. Without the financial support of AID, these studies could not have been performed in academic institutions. The merits of individual projects in the AID network and other malaria programs should be evaluated by peer review and not by unsubstantiated commentaries in scientific journals.

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