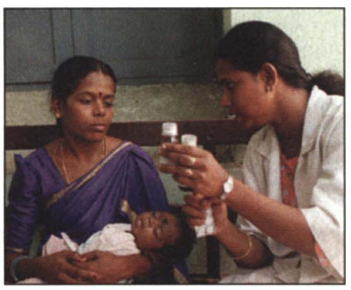
Mother-to-Child HIV Transmission and ARVs

ANTIRETROVIRAL (ARV) THERAPY IS USED FOR both treatment and prevention of HIV infection. It decreases patients' viral loads, dramatically improves their health, and delays death (*1*). ARVs also successfully reduce mother-to-child transmission of HIV (MTCT). Combined with avoidance of breast-feeding, ARV can almost completely prevent MTCT. A simple regimen is based on nevirapine (NVP) and was pioneered in Uganda (*2*). Efforts to make this intervention generally available to HIV-positive pregnant women are under way (e.g., by the UN Programme on HIV/AIDS, the World Health Organization, and UNICEF).

Initially, treatment costs were prohibitive to all but the wealthiest patients. Side effects and complex regimens have further constrained ARV use in resource-poor countries, where the HIV/AIDS epidemic is hitting hardest (*3*). The advent of generic drugs, often as simplified combination pills, has led to dramatic drops in costs. Bringing treatment to the millions who are currently denied access to it is considered a moral imperative by many. Brazil has taken the initiative by making ARVs available free of charge.



An Indian AIDS patient holds her child as she listens to a nurse at the Tamil Nadu Government Lying-In Hospital in Madras, India.

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Despite its effectiveness in reducing viral replication, ARV therapy does not cure—it delays the onset of AIDS. Most patients will eventually develop drug resistance and thereafter progress to AIDS and death. Although ARVs have turned HIV into a chronic disease (*4*), the impression that it no longer kills is misleading. An important reason for the development of drug resistance is lack of adherence to demanding drug regimens (*5*). In tuberculosis (TB) control, the Directly Observed Treatment (Short-course chemotherapy) [DOT(S)] strategy has successfully improved compliance and prevented resistance (*6*). This strategy has also been advocated for ARVs (*7*). Unfortunately, whereas TB therapy is curative and DOT(S) is required for months, ARV therapy is not a cure and is required indefinitely.

Although ARV therapy benefits patients, its impact on sexual transmission is unclear and not necessarily positive. As long as strains are drug susceptible, patients' viral loads can be suppressed, presumably reducing their infectiousness. However, infectiousness may increase again once resistance develops. The relative infectiousness of resistant strains remains largely unexplored. The empirical evidence that resistant strains can be transmitted effectively is overwhelming (*8*, *9*). Mathematical modeling suggests that widespread use of ARV therapy may lead to >50% primary resistance within decades (*10*). In addition to interfering with treatment, this could affect MTCT prevention. For example, NVP is one of the three compounds of Triomune, a drug marketed in India (*11*). Resistance to Triomune may render NVP useless, which would be disastrous. In India, over 20 million children are born annually. If HIV prevalence among pregnant women grows to 5% (modest by African standards), then—assuming that NVP reduces vertical transmission by 10% (e.g., from 30% to 20%, with continuing breast-feeding)—it could prevent 100,000 HIV infections annually in India alone.

It has been argued that prevention and treatment should be complementary in the struggle against HIV (*12*). But if drug resistance becomes widespread, MTCT prevention will fail, and more children will die of AIDS. Then, instead of being complementary, treatment will hinder prevention. Should this be accepted as an inevitable consequence of the benefits that ARVs give to millions of adult HIV patients? This dilemma could be avoided if some ARVs are exclusively reserved for preventing MTCT. These drugs should not be affected by (cross) resistance to drugs used for treatment. There are similar examples: For 40 years, rifampicin has been largely reserved for TB and leprosy. Had it not, short-course chemotherapy would now be impossible.

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References and Notes

1. J. Stephenson, *JAMA* **277**, 614 (1997).
2. L. A. Guay *et al.*, *Lancet* **354**, 795 (1999).
3. A. Telenti, G. Paolo Rizzardi, *Rev. Med. Virol.* **10**, 385 (2000).
4. W. M. Valenti, *AIDS Read.* **12**, 64 (2002).
5. P. Garcia de Olalla *et al.*, *J. Acquir. Immune Defic. Syndr.* **30**, 105 (2002).
6. M. W. Borgdorff, K. Floyd, J. F. Broekmans, *Bull. World Health Org.* **80**, 217 (2002).
7. P. Farmer *et al.*, *Bull. World Health Org.* **79**, 1145 (2001).
8. R. M. Grant *et al.*, *JAMA* **288**, 181 (2002).
9. See www.hivandhepatitis.com/recent/resistance/070802c.html.
10. N. J. D. Nagelkerke *et al.*, *Bull. World Health Org.* **80**, 89 (2002).
11. *Clin. Infect. Dis.* **33**, ii (2001).
12. G. P. Garnett, L. Bartley, N. C. Grassly, R. M. Anderson, *Nature Med.* **8**, 651 (2002).

Balancing Public Health and Civil Liberties

THE MODEL STATE EMERGENCY HEALTH Powers Act (MSEHPA), written by request of the Centers for Disease Control and Prevention, has galvanized the debate around the appropriate balance between public health and civil liberties (*1*). R. Bayer and J. Colgrove are widely known scholars who seek to

Letters to the Editor

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offer a neutral commentary ("Public health vs. civil liberties," Policy Forum, 13 Sept., p. 1811). However, some of their points require clarification.

Focusing on a vocal minority of critics, the authors imply that MSEHPA has not been well received. Yet, 36 states have introduced legislation based, at least in part, on some provisions of the Act, with 20 states (and the District of Columbia) passing bills. The Secretary for Health and Human Services recommends that states use MSEHPA as a checklist to ensure legal preparedness for bioterrorism.

The authors suggest that the Act provided a range of "extraordinary measures" that "radically enhanced the power of the state." Yet, MSEHPA is based largely on existing state laws. Its powers regarding persons (e.g., testing, treatment, and isolation) and property (e.g., nuisance abatements and "takings," i.e., the acquisition of private property by the state for legitimate governmental purposes) are a traditional part of state public health law. Nothing within MSEHPA is "extraordinary" or a "grave threat."

MSEHPA safeguards personal liberty by providing clear standards governing state power rather than relying on officials' discretion; ensures procedural due process rather than arbitrary actions without hearings; respects cultural, religious, and ethnic differences instead of tolerating discrimination; and entitles individuals to adequate information, basic treatment, and humane conditions during an emergency.

What is the appropriate balance between individual rights and public goods in response to bioterrorism? Critics contend that no conflict exists. Past experiences, however, show that fighting serious health threats sometimes interferes with individual interests (*2*). Law alone cannot ensure that power is appropriately exercised; preparedness and competencies of judges, health officials, and citizens are essential. The Act offers clear criteria, fair procedures, and robust entitlements that are conspicuously absent from existing, antiquated infectious disease statutes.

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References
1. L. O. Gostin *et al.*, *JAMA* **288**, 622 (2002).
2. L. O. Gostin, *Public Health Law: Power, Duty, Restraint* (Univ. of California Press and Milbank Memorial Fund, Berkeley and New York, 2000).

Response

WE AGREE WITH GOSTIN AND COLLEAGUES that "fighting serious health threats sometimes interferes with individual interests." Indeed, this conflict has been at the heart of American public health and is reflected in the views of groups concerned with privacy rights and civil liberties who objected to provisions of MSEHPA in both its original and revised forms. Our intent was not to judge the validity of the claims made by MSEHPA's supporters or critics about the extent to which the act would or would not violate individual rights or about the extent to which the proposed legislation entails an advance over the current legal regime in terms of the rights that would be accorded to individuals in the face of a public health emergency. Rather, it was to describe an enduring tension that lies at the heart of public health in the United States and the resulting challenges that face those who attempt to strike a balance between privacy rights and the common good when crafting policy and law. It is, however, worth noting that organizations such as the New York Civil Liberties Union that have a historic commitment to liberty and privacy remain unconvinced by the analysis of the current legal regime undertaken by Gostin and colleagues, and by the remedy they offer (*1*).

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Reference
1. New York Civil Liberties Union, "Testimony of Robert Perry on Behalf of the New York Civil Liberties Union before the Assembly Standing Committee on Health and the Assembly Standing Committee on Codes Concerning the Model State Emergency Health Powers Act," 14 March 2002.

Unisexual Clones: Lizards and Corals

THE FASCINATING AND WELL-CONCEIVED Report by S. V. Vollmer and S. R. Palumbi ("Hybridization and the evolution of reef coral diversity," 14 June, p. 2023) shows that interspecific hybridization in corals can produce F_1 offspring that "can reproduce asexually and form long-lived, potentially immortal hybrids with unique morphologies." A similar phenomenon occurs in terrestrial vertebrates, among reptiles, but the unisexual clones are treated as species by taxonomists.

The vast majority of lizards are bisexual (dioecious, gonochoristic) species. Ova will not develop until or unless they are fertilized, and the animals have Mendelian patterns of inheritance. There are also, however, a few morphologically recognizable unisexual (all-female) species that reproduce by obligatory parthenogenetic cloning. Some of these are triploid species that do not suffer from imbalances of gene activity. Phylogenetic analyses reveal that the clones are of hybrid origins and the switch from sperm-dependent to sperm-independent reproduction occurred in one generation. When successful, the ancestral bisexual species and their clonal derivatives continue to perpetuate themselves independently as distinct entities and all constitute separate species on different evolutionary tracks, even though the clonal lineages do not survive long in geological time. Interested readers can access this literature through Reeder *et al.* (*1*).

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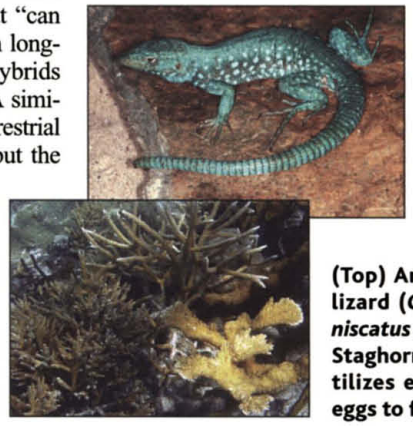
Reference
1. T. W. Reeder, C. J. Cole, H. C. Dessauer, *Am. Mus. Novit.* **3365**, 1 (2002) (available at http://research.amnh.org/scipubs/).

Response

THE FUNDAMENTAL EVOLUTIONARY BIOLOGY of the coral hybrids we studied in the Caribbean is very similar to the existence of unisexual and parthenogenetic animals like Cnemidophorus lizards, skinks, and live bearing fish [see Bell (*1*) for a comprehensive list]. In all cases, the hybrid clones produce a descendant line identical to their single ancestor, and independent hybrid lines give rise to potentially competing "experiments" in interspecies hybridization (*2*). Successful lines thrive, but perhaps not for long if the niche to which they were by chance adapted disappears. Perhaps the biggest difference is that the vertebrate hybrids must be able to develop parthenogenetically—they still produce eggs that must successfully complete full development (*1*). By contrast, colonial animals like corals can propagate without parthenogenesis through colony fragmentation and regrowth. Each new "generation" need not pass through the germ line, and for these hybrid corals, the soma reigns supreme. Furthermore, because even sexually competent corals can clone



(Top) Aruba Island whiptail lizard (*Cnemidophorus lemniscatus arubensis*). (Bottom) Staghorn coral (middle) fertilizes elkhorn coral (right) eggs to form a hybrid (left).

CREDIT: (TOP) PAUL FREED/ANIMALS ANIMALS; (BOTTOM) HECTOR RUIZ/UNIVERSITY OF PUERTO RICO, MAYAGUEZ