To what can the rise of drug resistance in *M. tuberculosis* in many parts of the world be attributed? Historically tuberculosis is a socially sensitive disease[6] which flourishes under the overcrowded conditions found among the poor in developing and the poor and homeless in — the irony of the phrase is painful — the developed countries. Because after a few weeks of treatment patients feel better, they often take their medication irregularly or not at all until they relapse — a perfect strategy for developing drug resistance. The alarmingly heightened susceptibility to TB of individuals infected with human immunodeficiency virus has added a new dimension to the problem. One critical question is whether higher frequencies of drug-resistant variants emerge as a consequence of immunodeficiency, and the diminution of the immune response as a major selective force against the pathogen.

As demographers and epidemiologists peer into their crystal computers and ponder on the world in the year 2015, they foresee major changes. The trend first perceived in Europe and currently underway in the advanced developing countries is predicted, in time, to affect all developing countries. This Demographic Transition translates into more people living longer, population ageing and urbanization[7,8]. In developing countries there is often a period in which death rates decline before a decrease in fertility rates, resulting in a bulge in the population. The health correlate to the Demographic Transition is the Epidemiological Transition, which is characterized by increased life expectancy, increased prevalence of chronic degenerative diseases and decreased mortality, particularly from infectious diseases[9–12]. Two health problems, then, have to be addressed — the triad of infectious diseases, malnutrition and population pressure; and chronic diseases such as cardiovascular disease and cancer. The industrialized countries passed through the Epidemiological Transition only gradually, but, in the words of Foege and Henderson[13], "The developing countries will not have the luxury of dealing with the two kinds of problems sequentially. For the remainder of this century, the developing countries will be dealing with both simultaneously". And in these countries, we should remind ourselves, live three-quarters of the human population of the planet.

One policy implication of health transition thinking is the reallocation of scarce health resources to the area where the new action is likely to be, namely to chronic illness, with a de-emphasis on infectious diseases. The recent AIDS, cholera and dengue epidemics, however, indicate that such a policy decision may be premature; we remain vulnerable to new and emerging infectious diseases[14]. The paper by Zhang *et al.* reminds us that there is also a constant threat from mutations of infectious pathogens which confer resistance to previously effective drugs and to the immunological surveillance that we take for granted.

This is unlikely to be a problem peculiar to tuberculosis. *Streptococcus pneumoniae*, which has no β-lactamase, the common enzyme for degrading penicillin-like drugs, has found another way to resist destruction by these drugs[15]. And in the case of *Staphylococcus aureus*, a major source of hospital infections which mutated to become resistant to methicillin and was held at bay for thirty years only by vancomycin, new isolates resistant to this drug have been reported[16]. Malarial parasites have emerged in Asia with multiple resistance to a variety of antimalarial drugs (P. de Raadt and T. Godal, personal communication). As in the case of multidrug-resistant *M. tuberculosis*, there are few, if any, useful back-up drugs in the pipeline.

Without a significant effort to control the appropriate use of, and compliance with, existing antibiotic regimens, and increased support for basic research and development of new drugs and vaccines, we may be working our way back to a frightening future. □

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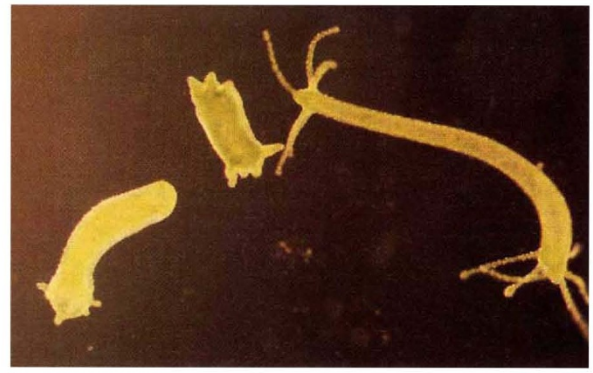
Hydra and the homeobox

THE more people look for homeobox genes, the more such genes turn up. For instance, A. Miles and D. J. Miller have isolated a homeobox gene from the coral *Acropora formosa* that bears sequence similarities to the *Drosophila* pair-rule gene *even-skipped* (*Proc. R. Soc. Lond.* B248, 159–161; 1992). Now, no fewer than five homeobox-class genes are reported in multi-headed mutants of another cnidarian, the hydra *Chlorohydra viridissima* (M. Schummer *et al. EMBO J.* 11, 1815–1823; 1992). Intriguingly, at least two of the genes are sequentially expressed in the regenerating head end of the animal, and in the same order as their cognates in *Drosophila* and mice. The observations imply that even in these simple, non-segmented animals (which lack a mesoderm), homeobox-class genes are involved in the specification of anterior–posterior polarity. The hydra genes are dubbed *cnox1, 2, 3* and *4* (short for cnidarian homeobox) and *msh*, and the homeoboxes of the first two show distinct resemblances to *labial/Hox-1.6* and *Deformed/Hox-1.4* respectively. Just as *Hox-1.6*-family members are expressed more anteriorly than those of the *Hox-1.4* family, the expression of *cnox-1* peaks before that of *cnox-2* during hydra head regeneration. *cnox-3* is similar to *Distal-less*, and *msh* is similar to the *msh/Hox-7* gene family. Schummer *et al.* point out that the ready regeneration of the mutant multi-headed hydra makes an excellent model system for testing ideas about head development in higher animals. H.G.



Getting a head — regenerating hydra after 30 hours, after peak expression of *cnox2* and before peak expression of *cnox3*.

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