much more than just information transfer, especially in science. New information needs to be connected to preexisting knowledge in the student's mind. Students need to develop models to see how science works. Instead, my students were relying on rote memorization. Reflecting on my own education, I believe that I also often relied on rote memorization. Information transmitted in lectures stayed in my brain until I had to draw upon it for an exam. I once heard somebody describe the lecture method as a process whereby the lecture notes of the instructor get transferred to the notebooks of the students without passing through the brains of either (*3*). That is essentially what is happening in classrooms around the globe.

Since this agonizing discovery, I have begun to turn this traditional information-transfer model of education upside down. The responsibility for gathering information now rests squarely on the shoulders of the students. They must read material before coming to class, so that class time can be devoted to discussions, peer interactions, and time to assimilate and think (*4*). Instead of teaching by telling, I am teaching by questioning.

I now structure my time during class around short, conceptual multiple-choice questions. I alternate brief presentations with these questions, shifting the focus between instructor and students. The questions address student difficulties in grasping a particular topic and promote thinking about challenging concepts. After posing the question, I give the students 1 to 2 minutes to think, after which each must commit to an individual answer. They do this by submitting their answers using handheld devices called "clickers" (see the figure). Because of the popularity of these devices, questions posed this way are now often referred to as "clicker questions." The devices transmit the answers to my computer, which displays the distribution of answers. If between 35% and 70% of the students answer the question correctly, I ask them to discuss their answers and encourage them to find someone in the class with a different answer. Together with teaching assistants, I circulate among the students to promote productive discussions and guide their thinking. After several minutes of peer discussion, I ask them to answer the same question again. I then explain the correct answer and, depending on the student answers, may pose another related question or move on to a different topic. This approach has two benefits: It continuously actively engages the minds of the students, and it provides frequent and continuous feedback (to both the students and the instructor) about the level of understanding of the subject being discussed.

I often meet people who tell me they have implemented this "clicker method" in their classes, viewing my approach as simply a technological innovation. However, it is not the technology but the pedagogy that matters (*5*). Unfortunately, the majority of uses of technology in education consist of nothing more than a new implementation of old approaches, and therefore technology is not the magic bullet it is often presumed to be. Although clickers offer convenience and (at least for now) an amount of trendiness that appeals to students, the method can be implemented with flash cards, which are inexpensive and never prone to technological glitches (*6*).

Data obtained in my class and in classes of colleagues worldwide, in a wide range of academic settings and a wide range of disciplines, show that learning gains nearly triple with an approach that focuses on the student and on interactive learning (*7*, *8*). Students are given the opportunity to resolve misunderstandings about concepts and work together to learn new ideas and skills in a discipline. Most important, students not only perform better on a variety of conceptual assessments, but also improve their traditional problem-solving skills (*9*). Also, data show that such interactive engagement helps to reduce the gender gap that exists in introductory physics classrooms (*10*).

So, evidence is mounting that readjusting the focus of education from information transfer to helping students assimilate material is paying off. My only regret is that I love to lecture.

References and Notes

1. D. Hestenes, M. Wells, G. Swackhamer, *Phys. Teach*. **30**, 141 (1992).
2. A version of (*1*) revised in 1995 by I. Halloun, R. Hake, E. Mosca, and D. Hestenes is available in (*4*).
3. D. Huff, *How to Lie with Statistics* (Norton, New York, 1954).
4. E. Mazur, *Peer Instruction: A User's Manual* (Prentice Hall, Upper Saddle River, NJ, 1997).
5. M. K. Smith *et al.*, *Science* **323**, 122 (2009).
6. N. Lasry, *Phys. Teach.* **46**, 242 (2008).
7. A. P. Fagen, C. H. Crouch, E. Mazur, *Phys. Teach.* **40**, 206 (2002).
8. N. Lasry, E. Mazur, J. Watkins, *Am. J. Phys*. **76**, 1066 (2008).
9. C. H. Crouch, E. Mazur, *Am. J. Phys*. **69**, 970 (2001).
10. M. Lorenzo, C. H. Crouch, E. Mazur, *Am. J. Phys*. **74**, 118 (2006).

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MICROBIOLOGY

Mosquitoes Cut Short

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Can the life-shortening effect of a bacterium on mosquitoes control the transmission of dengue?

Forty years ago, as the first drug- and insecticide-based global malaria eradication plan was being abandoned, the concept was raised of using evolutionary genetics to fight vector-borne diseases like malaria, dengue, and river blindness (*1*). The idea was to exploit selfish genetic elements, entities that can spread through host populations by distorting normal Mendelian inheritance, thereby enhancing their own transmission. Theoretically, such elements could be used to drive antipathogen effector genes through mosquito populations. On page 141 of this issue, McMeniman *et al*. (*2*) report a major step in a lateral development of this approach. They have infected the mosquito species that transmit dengue viruses to humans with an inheritance-distorting bacterium that kills mosquitoes likely to be infectious.

Wolbachia are maternally inherited bacteria found in a diverse range of arthropods. Because only female hosts can keep a lineage of *Wolbachia* alive, the bacteria have acquired mechanisms to ensure the overrepresentation of infected female offspring. One of these strategies is called cytoplasmic incompatibility, in which uninfected females that mate with *Wolbachia*-infected males fail to produce offspring. This reproductive asymmetry can allow the bacteria to spread through a population even if they reduce host fecundity (see the figure). Rapid invasion of fruit fly (*Drosophila*) populations by *Wolbachia* has been seen in real time in nature, raising the prospect of using these bacteria to spread disease-controlling genes through mosquito populations.

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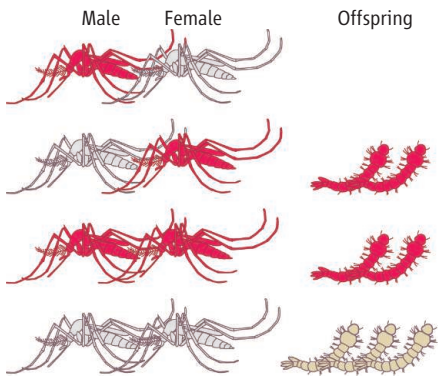
Yet in a cruel twist of fate, the mosquito that transmits dengue (*Aedes aegypti*) and the mosquito that transmits human malaria (*Anopheles* spp.) are not naturally infected by *Wolbachia*, even though many other mosquitoes are. But 3 years ago, microinjection of *Ae. aegypti* embryos with *Wolbachia* that were derived from *Ae. albopictus* was reported (*3*). The resulting infections had strong cytoplasmic incompatibility, highly efficient maternal inheritance, and in the laboratory increased from 20 to 100% of mosquitoes in just eight generations. Since then, the question has been how to translate this advance into dengue control.

One way would be to genetically engineer *Wolbachia* to carry a foreign gene (transgene) whose product attacks the flavivirus that causes dengue. A less intuitive alternative is to either provide *Wolbachia* with a gene whose product kills its host mosquito, or to find a *Wolbachia* strain that kills its host naturally. One strain, *w*MelPop, halves the life span of its natural host, *D. melanogaster*. McMeniman *et al*. now report the successful infection of the mosquito *Ae. aegypti* with *w*MelPop, and show that it also halves the life span of the new host. There are no data yet showing that *w*MelPop will spread in populations of *Ae. aegypti*, but the very strong cytoplasmic incompatibility is sufficient to prevent the loss of *w*MelPop from laboratory populations, despite its lethality.

Can the life-shortening effect of *Wolbachia* on mosquitoes achieve dengue control? Most vector-borne pathogens require many days to develop within the vector before becoming infectious to humans. For the virus and protozoan parasites that cause dengue and malaria, respectively, this extrinsic incubation period is about 2 weeks, although it is very temperature sensitive and for dengue, can be as short as 1 week (*4*). Because mosquitoes generally die quickly, the extrinsic incubation period of many infectious agents is longer than the average life span of the mosquitoes that transmit them. This means that only old mosquitoes are potentially dangerous to humans.

By killing old mosquitoes, *w*MelPop could thus impact on dengue transmission. But determining whether it can remove enough infectious mosquitoes to be useful will be a challenge. McMeniman *et al*. found that the mean longevity of *w*MelPop-infected mosquitoes is at least 3 weeks. Mosquitoes acquiring dengue from their first human meal would therefore be infectious for about a week. However, if *w*MelPop also halves life spans in the field, where background mortality rates are higher, substantial reductions in transmission could occur. For the right set of parameters, dengue control is possible in theory (*5*).



Ready for combat? A bacterial strain of *Wolbachia* has been adapted to infect the mosquito vector that transmits dengue virus to humans. The bacterial infections (red) are only transmitted through females to offspring, and cut mosquito life span by up to 50%. This may block disease transmission to humans.

A critical factor is *Wolbachia* virulence. All else being equal, the greater the impact on mosquito life span, the greater the disease control. But there are important downsides. Excessively virulent bacteria strains will spread very slowly, if at all; there are limits to what even cytoplasmic incompatibility can drive. Moreover, the reproductive advantage of cytoplasmic incompatibility largely accrues from *Wolbachia*-infected individuals mating with each other (see the figure). To ensure that such matings are sufficiently frequent, control programs will need to initially release large numbers of *Wolbachia*-infected, mating-viable individuals. The required numbers increase markedly with virulence (*5*). High virulence will also start its own evolutionary games: selection for *Wolbachia*-resistant mosquitoes and for more benign *Wolbachia*. Moreover, *Wolbachia* virulence is environmentally sensitive (*6*), as are pathogen extrinsic incubation period (*4*) and other determinants of disease transmission. Epidemiological models with explicit evolution are needed to determine the virulence required to give maximal and evolutionarily stable disease control in diverse ecological settings. Appropriate phenotypes could be selected from what is available naturally, or engineered by inserting appropriate virulence transgenes into the *Wolbachia* genome. It seems unlikely that one phenotype will fit all circumstances. There may even be geographic locations where no phenotype provides adequate disease control. Evolutionary epidemiological models would also help determine whether life-shortening *Wolbachia* could contribute to controlling other vector-borne diseases, not least malaria.

Other strategies for targeting old, potentially infectious adult mosquitoes are being developed. These include engineering densoviruses (natural viruses of mosquitoes) (*7*) and biopesticides that are based on entomopathogenic fungi (*8*). Such biopesticides effectively reduce malaria transmission in the laboratory by killing older insects (*9*), and theoretical models demonstrate good malaria-control potential in endemic areas (*10*, *11*). But interventions aimed only at older mosquitoes control disease transmission, not mosquito densities. This is in stark contrast to chemical insecticides which, as currently used, suppress mosquito densities by killing individuals of any age. Large-scale removal of mosquitoes is popular with local people but opens up niches for new vector strains or species and comes at the very high price of massive selection for insecticide resistance.

Would the release of life-shortening *Wolbachia* select for dengue viruses that develop more rapidly in *Ae. aegypti*? This possibility is highly relevant for any interventions that alter mosquito age structure (*12*). The high rates of mortality typical of mosquitoes must already be imposing intense natural selection for shorter extrinsic incubation periods. The apparent lack of response to this selection implies that prolonged development substantially enhances pathogen fitness (*13*). Even if life-shortening *Wolbachia* impose sufficiently strong selection to offset these fitness gains, the resulting evolution of more rapidly developing dengue viruses would presumably generate otherwise less fit pathogens. The impact of such evolution on public health will be important to understand. It may be less problematic than the evolution of insecticide resistance, the main evolutionary consequence of last century's vector-control strategies.

References

1. C. F. Curtis, *Nature* **218**, 368 (1968).
2. C. J. McMeniman *et al.*, *Science* **323**, 141 (2009).
3. Z. Xi, C. C. H. Khoo, S. L. Dobson, *Science* **310**, 326 (2005).
4. D. M. Watts, D. S. Burke, B. A. Harrison, R. E. Whitmire, A. Nisalak, *Am. J. Trop. Med. Hyg.* **36**, 143 (1987).
5. J. L. Rasgon, *Adv. Exp. Med. Biol.* **627**, 114 (2008).
6. K. T. Reynolds, L. J. Thomson, A. A. Hoffmann, *Genetics* **164**, 1027 (2003).
7. J. Carlson, E. Suchman, L. Buchatsky, *Adv. Virus Res.* **68**, 361 (2006).
8. M. B. Thomas, A. F. Read, *Nat. Rev. Microbiol.* **5**, 377 (2007).
9. S. Blanford *et al.*, *Science* **308**, 1638 (2005).
10. E. J. Scholte *et al.*, *Science* **308**, 1641 (2005).
11. P. A. Hancock, M. B. Thomas, H. C. J. Godfray, *Proc. R. Soc. London B.* **276**, 71 (2009).
12. Y. Michalakis, F. Renaud, *Nature* **435**, 891 (2005).
13. J. C. Koella, *Microbes Infect.* **1**, 303 (1999).

10.1126/science.1168659