Epidemics-in-waiting

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Could the next SARS-like virus reach epidemic proportions? Quantifying the likely threat of emerging diseases isn't easy, but evolution is a crucial factor that may tip the balance in favour of such human parasites.

One of the oldest tenets of evolutionary biology is that it is easier to change a little than a lot. We also know that evolutionary change is more easily selected for in a large population than in a small one. On page 658 of this issue, Antia et al.[1] combine these facts to reach a previously unappreciated conclusion about emerging infectious diseases: some types of infectious parasites that attack the human population may pose a serious threat even if they are not initially able to cause epidemics. The reason is that certain parasites are specially poised to evolve so that they can cause epidemics.

In epidemiological models, an infectious agent can be characterized by its basic reproductive rate, R_0. This is the average number of new infections caused by the first infected individual in the population. The epidemic threshold is $R_0 = 1$, above which the disease spreads (neglecting random effects) and below which it eventually dies out. R_0 is not, however, a measure of virulence or of the harm inflicted on the host by infection. In humans, for example, R_0 is virtually zero for some diseases with a high mortality rate (such as rabies, and hantavirus respiratory infections); but R_0 is well above unity for other diseases that also have high mortality rates (such as measles in undernourished populations, AIDS and smallpox).

Antia et al.[1] point out that, because of evolution, parasites with an R_0 value that is hovering just below one can be epidemics-in-waiting. An obvious reason for this is that it takes less change to achieve an R_0 of more than one if the initial R_0 is just below one. A less obvious reason — and the focus of Antia and colleagues' paper — is that the length of time a parasite persists in the population before disappearing increases with R_0; parasites with R_0 nearly at unity can persist for a considerable time by chance. The longer the parasite persists, the greater will be its opportunity to evolve to a higher R_0. This is merely a population size effect: each additional host infected before the parasite dies out provides yet another opportunity for a mutation that might push R_0 over the epidemic threshold.

The model is tractable because of its reliance on the single parameter R_0, but the biology behind it is potentially complicated.
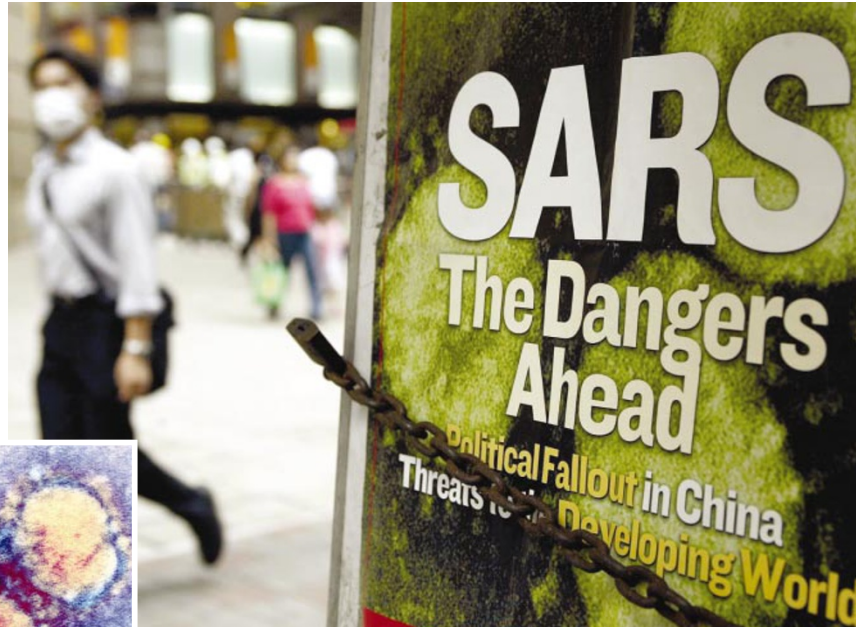

Figure 1 **Danger ahead?** The virus (inset) causing severe acute respiratory syndrome, or SARS, emerged in southeast Asia in late 2002. As the infection spread, face masks became a common sight on the streets of Hong Kong and elsewhere. Antia et al.[1] describe a way to help identify other viruses with epidemic potential.

R_0 encapsulates the long chain of events involved in the parasite's association with its host — its first contact, entry, growth in the initial tissue infected, infection of secondary tissues, and so on, until the final stage of its dissemination to make contact with other hosts. A mutation that increases R_0 may arise at any stage in this chain, provided that it ultimately leads to an increase in the number of infections. For instance, an increase in R_0 may evolve through changes in surface molecules that improve parasite infection of new hosts directly, or it may evolve through improved growth within the host (possibly increasing virulence) so that more parasite progeny are disseminated from the host, resulting in higher numbers of secondary infections.

The rabies and hantavirus examples mentioned above are characterized by good within-host growth of the parasite but poor dissemination to new hosts. The 1976 outbreak of Ebola virus in southern Sudan (which spread from an initial infection of a cotton factory worker to the owner of the local jazz club, then to others at the club, giving at least eight generations of transmission[2]) is a case in which within-host growth

was good and the dissemination–infection stage brought the parasite perilously close to the epidemic threshold. However, a parasite could also begin its foray into humans by being fairly infectious but poor at surviving the onslaught of our immune system (as seems to have been the case with the Ebola virus that, in 1989, destroyed an imported Philippine monkey colony in Reston, Virginia[3]). Mutations that increase R_0 might then improve within-human growth. This type of emerging pathogen is the most easily missed and potentially the most dangerous. Efforts to understand the relationship between parasite adaptation to hosts, virulence and transmission have developed into a small industry in evolutionary biology. The relationship is complicated because it involves group versus individual selection, population bottlenecks and trade-offs[4,5].

Antia and colleagues' result[1] contributes to a growing awareness of the evolutionary and ecological factors surrounding the emergence of new diseases. We have already had warnings that virulence itself may evolve in response to changes in cultural practices[6], and that immunocompromised patients

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may act as stepping stones to foster evolution of new pathogens capable of attacking people with healthy immune systems[7]. With the possibility of using grafts from non-human species to replace tissues in humans, we also need to be aware of the potential for activation and genetic recombination of otherwise dormant retroviruses in the human genome or in the graft.

Antia *et al.* do not, however, emphasize cultural factors in disease emergence. Instead, they provide a way of identifying which agents are most worthy of attention — those closest to the epidemic threshold. An example suggested by Antia *et al.* is the threat of monkeypox in a world with little resistance to its relative smallpox, because of a lack of either vaccination or exposure. Furthermore, the result draws attention to the neglected topic of parasite dynamics in the pre-epidemic stages. This was brought into focus earlier this year when it was realized that the initial spread of severe acute respiratory syndrome (SARS; Fig. 1) depended heavily on the social connectivity of the first (index) case in a community. Such results and realizations give us a better understanding of how to contain infectious diseases, through early prevention rather than cure. Ultimately, we should learn where and when to apply our efforts to block transmission and so prevent an epidemic.

Currently, the resources and public attention devoted to an infectious disease depend on a combination of social, biological, economic and political factors specific to that disease. Disease virulence, transmissibility and incidence are included in such considerations. The complacency of the pre-HIV and pre-bioterrorism eras has yielded to a growing acceptance of the need to monitor pathogens and even pre-pathogens in our environment. It is not beyond imagination that, even with existing technology, methods could be developed for monitoring emerging pathogens, potentially distinguishing between strains with differing R_0 values. The means, provided by Antia *et al.*[1], of identifying these epidemics-in-waiting could become a critical tool in a global defence strategy against emerging pathogens. ∎

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Light at a standstill

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Nothing travels faster than light, but how slow can light go? Pulses of light have already been slowed to speeds of just a few metres per second, but now they have been brought to a complete halt.

Frozen light is a reality. As they report on page 638 of this issue, Bajcsy and colleagues[1] have trapped, and held, a pulse of light for a few hundredths of a millisecond, which is a long time in optical terms. To those unfamiliar with the realm of quantum optics, the notion of stationary light may seem rather strange. But ultraslow light — travelling at just a few, instead of 300 million, metres per second — is easily available in many labs these days. So bringing a light pulse to a full stop was the next logical step.

And it is of interest for many reasons. This is the latest development in a continuing paradigm shift in optics, occasioned by the marriage of quantum coherence in atoms and molecules with coherent light[2–5]. The ability to trap and hold light also holds promise for application to such diverse areas as quantum informatics, nonlinear optics and even the foundations of quantum mechanics. Perhaps most important of all, it is simply fascinating science.

To put the achievement of Bajcsy *et al.*[1] into perspective, let me briefly mention some of the key steps and issues that have led to the creation of frozen light pulses. The landmark slow-light experiment[6] — down to a speed of just 17 metres per second — was carried out in an ultracold gas. The advantage of such low temperatures is that they eliminate the spread in atomic frequencies that is caused by atomic motion: this optical Doppler effect could otherwise obscure, even spoil, the measurements of slow light. It is not necessary, however, to use trapped ultracold atoms and get rid of the Doppler effect to slow light down: this has been proved by the slowing of light to less than 100 metres per second in a hot gas of rubidium atoms[7].

It could be argued that the know-how to make slow light has been around since the late nineteenth century. The velocity of the peak of an optical pulse is called the group velocity because it takes a 'group' of two or more frequencies of light to make a pulse. Atoms and molecules tend to interact with light more strongly at certain frequencies, and this is manifest in a variation of the material's index of refraction, which causes different waves to move with different velocities. Of course, this affects the group velocity of the pulse — and is the reason that light is dispersed by a prism or water droplets to make a rainbow.

The good news is that strong dispersion is easy to achieve: the light frequency should be tuned close to the resonant frequency of the atoms, and then the group velocity may be slowed by a factor of a thousand or more. The bad news is that minimum pulse velocity also means maximum absorption of the light by the material: the pulses move very slowly, but they are so strongly absorbed that they penetrate only a few wavelengths' distance through the material.

But the last decade of the twentieth century saw revolutionary changes in optical science. We now have 'phase-coherent' materials, which give the huge dispersion associated with resonance but do not absorb light. These materials are truly a new state of matter, aptly called 'phaseonium', and their electromagnetically induced transparency[8] has proved useful in slowing light down to just a few metres per second. It has been shown[9,10] that the quantum state of a light beam can be stored in phaseonium vapour and then retrieved by a later pulse of light. This works because in slow-light propagation, part of the light beam is converted into atomic excitation (that is, it is mapped onto atomic spins). This transfer of the information contained in the light's quantum state onto the atoms (writing), together with its subsequent retrieval (reading), is a vital tool in the emerging field of quantum information, including cryptography and computing. However, although the concept of storing light by 'drawing' its quantum blueprint in the atomic medium is interesting, this is not the same as freezing light.

In fact, there are several possible routes to frozen light. For example, my own group is investigating the passage of slow-light pulses through a moving phase-coherent medium, such that the pulse would appear stationary to a fixed camera in the laboratory[11]. The route chosen by Bajcsy *et al.*[1], following the theoretical outline of ref. 12, does not involve a moving medium. Instead, a light pulse is trapped inside a gaseous, phase-coherent medium by changing the optical properties of the medium. There are two steps to the process: first, two laser pulses, the 'control' and 'signal' fields, are injected into a medium in which all the atoms are in the lowest-energy, ground state; then, with both control and signal fields in the medium, the control pulse is turned off. This results in the atoms' absorbing the signal field and storing the quantum state of the signal. Following the example of previous work, the next step