Dr. Ed Kaplan is the William N. and Marie A. Beach Professor of Management Sciences at the Yale School of Management; a Professor of Public Health; Director of the school's Methodology and Biostatistics Core; and an Investigator in the Law, Policy and Ethics Core. But what Kaplan is probably best known for is showing that a needle exchange program in New Haven, Connecticut helped limit the spread of HIV. (His findings survived reviews by the General Accounting Office, the Centers for Disease Control and Prevention, and the National Research Council.) In February 2003, Kaplan was elected to the National Academy of Engineering “for assessment of needle-exchange programs and for generally bringing engineering perspectives to the design of public health policies.”

In addition, Kaplan is the Area Editor for Policy Modeling and Public Sector Operations Research at Operations Research, and on the editorial boards of the Journal of AIDS, Journal of Mathematics Applied in Medicine and Biology, and Health Care Management Science. He also served on the Institute of Medicine’s Committee on HIV Prevention Strategies. Professor Kaplan is an expert in operations research and statistics who has developed novel methods for quantitatively evaluating HIV intervention programs.

You gained some notoriety for reporting that contrary to the CDC’s previous ring policy, a mass vaccination program would be the best way to respond to a smallpox outbreak. For the record, why does this beat other methods?

Given that there is essentially no immunity in the country at present, and given that at the time an attack is detected, one would not know whether it was big or small (in the sense that a large versus a small number of persons were initially infected), our analysis suggests that fewer deaths would result from post-attack mass vaccination than ring vaccination. Furthermore, mass vaccination could be completed swiftly -- the time required is determined by the number of personnel available to perform the vaccinations, whereas an approach based on tracing contacts would proceed more slowly at the pace of the epidemic, since new contacts in need of vaccination would only be reported as new cases are detected. Thus, a mass vaccination program could reach a very large percentage of the population in a short period of time -- say 10 days -- whereas a tracing approach would continue for several generations. Given that the Council of Economic Advisors as estimated that a smallpox attack could cost the U.S. about $177 billion per week, a rapid response is certainly in order.

The government has bсужден this somewhat, opening the door for mass vaccinations. But a modified ring remains CDC policy. Why the reluctance to adopt your findings further?

Actually, if you listen carefully to what the CDC Director says, she has for some time now stated that vaccinating the country within 10 days post-attack is in fact the readiness goal. Within this overall plan it is certainly...
sensible to prioritize the close contacts of cases, particularly household contacts that can be located almost immediately. What we are opposed to is taking time away from vaccinating the public to search for contacts - - the tradeoff is rapid vaccination of the general public to raise immunity versus a slower vaccination of "higher yield" contacts to stop the spread from the inside out. In the event of a large attack, the logistics of tracing would become overwhelming, as the CDC's plan has recognized from the beginning -- after all, the plan did state that if ring vaccination and case isolation failed to stop the spread of disease within a few generations, a "broader" strategy (i.e. mass vaccination) would be implemented. So clearly the CDC recognizes the potential for becoming overwhelmed in a large attack by the demands of tracing -- otherwise, instead of shifting to mass vaccination, there would just be more surveillance and containment. However, our point is that at the time an attack is detected, one would not know if it was large or small. If one knew the attack was large, one would move to mass vaccination right away. If one knew the attack was small, one could just do surveillance and containment. Unfortunately, though there are two types of the errors (mass vaccinate against a small attack, or do tracing against a big attack), the consequences of these errors are not symmetric. In particular, the worst mistake to make is to start with a limited response when the attack is in fact large. There only needs to be a very small chance that the attack is large for mass vaccination to be the optimal (that is, death minimizing) response, thus our recommendation is to react immediately with mass vaccination to hedge against the worst case.

As for reluctance to adopt our findings further, old ideas die hard. CDC planners fervishly believe that the smallpox eradication program functioned in a particular way, and that the results obtained then would apply now. I would argue that in fact the eradication program was able to do what it did precisely because there were very high levels of vaccination at the time the final push to eradication began in many places (coupled with survivorship from past disease), and that in fact the number of persons vaccinated per case was much larger than what people are pretending to be the case -- for example, World Health Organization data show that between 500 and 5,700 persons were vaccinated per smallpox cases during the eradication campaigns in several countries. This hardly sounds like limited vaccination to me.

Furthermore, I would argue that there is a world of difference between a small naturally-occurring outbreak, and a potentially large, deliberate and strategically placed outbreak by terrorists who are trying to kill us. I would much rather err on the side of caution than simply assume that a limited vaccination program could control a bioterror attack.

**How prepared is the U.S. logistically for a biological attack? Where does the system need the most improvement?**

The U.S. is not prepared well at all in my view. The real problems are at the local level. Though there are plans to get vaccines and/or medicines from the National Strategic Stockpile to an area under attack within, say, 6 to 12 hours, with few exceptions there no plans at the local level. For smallpox, such planning would involve vaccination clinics with sufficient personnel to staff them. As we all know, the number of persons vaccinated in different cities and town is woefully inadequate to respond at present. But even for non-contagious agents such as anthrax, the key question remains not how long it take to get Cipro or doxycyclin from a stockpile to a city, but how long it takes to get the medicines into people's mouths. As an example, we estimate that just a single kilogram (2.2 pounds) of weapons-grade anthrax released from the top of a tall building in a tall city could infect 1.5 million people, and that each day of delay in distributing antibiotics to the entire population would cost 10,000 lives! Thus, we think the pre-attack distribution of medicines or vaccines, albeit on a voluntary basis, warrants greater consideration than has been admitted until now.

There has also been a pre-occupation with smallpox. Go to the CDC's
Anything coming out of the world response to SARS that you think is worth noting in relation to how we might respond to a potential biological attack?

The only treatment for SARS at the moment is supportive care in the hospital, and the way to prevent further spread is via isolation and quarantine. Were we attacked with a contagious agent for which there is no vaccine or treatment, isolation and quarantine would also be the only real approach. The continued popping up of SARS clusters shows just how hard it is to catch everyone. Now, to be rash (pun intended), one could argue that this should be easier with smallpox due to the obvious symptoms of that disease, but the general point remains -- as long as some of the carriers of an infectious disease are able to escape detection (or for that matter fail to comply with quarantine), continued spread can be expected. Please note that I am not being critical of the way CDC and the WHO are responding to SARS -- the virus has been identified, and great effort is being made to contain the spread of this disease. It does show, however, how difficult pure containment can be.

How difficult is it to differentiate a naturally occurring, albeit new disease such as SARS from an intentional act of terrorism? What would you look for, mathematically, when assessing this?

SARS apparently started small. So might intentional acts of bioterror (e.g. the anthrax mail cases), but the potential for much larger initial conditions (i.e. initial numbers of infections) exists (e.g. smallpox or anthrax via a ventilation system in a large building -- think of Pennsylvania Station as an example). Situational awareness becomes very important at this point -- once one starts to see cases, it is important to estimate when the attack occurred, how many people were initially infected, and also where the attack took place. If the attack is with an agent for which its incubation/progression distribution is known (as is the case for smallpox, and also anthrax thanks to the work of Ron Brookmeyer from Johns Hopkins), it actually is possible, statistically, to get a rather good handle on these quantities from the timing of the first reported cases -- not only is there information contained in the number of such cases, there is also information in the temporal spacing of the cases. The closer together the first cases cluster, the more likely it is that there was a large rather than small attack. Of course, if we are dealing with a new natural SARS-like disease, then we are faced with learning about the incubation times in real time. Even here there are good statistical procedures that can help once one realizes the biases inherent in the data observed -- if one is observing data, say, 7 days after the time of exposure, than only those cases with incubation times of at most 7 days can be observed! Nonetheless this could become an issue if there is a bioterror attack with a new agent, or a modified version of an agent we think we understand.

You've had enormous variety in your education and fields of research. Is bioterrorism of the moment for you, or does this feel like the sort of topic a person with three masters, a bachelors and a PhD settles down with for the next couple decades?

This does not feel like something I am settling down with for the next couple of decades. In fact, I got started in this area because I was asked to do so by people at NIH. I do, however, believe that our research team has a lot to contribute now. There has been very little formal analysis conducted that embeds logistics into epidemiological models, yet doing so is of obvious importance. Epidemiology reveals what diseases can do to people. Logistics reveals what people can do to diseases! Our work with smallpox and anthrax illustrates these linkages -- for example, the importance of understanding the interplay between queues of people waiting to receive vaccines or treatments and outcomes such as death.
and disease -- and since logistics is ultimately about response operations in this context -- how many people are needed to vaccinate, dispense medicines, provide care; how much time does it take to perform various operations; what are the capacity requirements for quarantine and isolation -- the models help figure out what to do NOW so that one can respond IF one needs to. And what to do NOW is what people are arguing over, so as long as we believe we have useful contributions to make in this area, we'll keep at it.

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