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Global Infection Prevention: A Strategy to Minimize Antibiotic Resistance

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Summary
Infection control throughout the world operates in an increasingly crowded planet challenged by poverty, hunger, malnutrition, and limited expertise globally to improve health in many communities, clinics, and hospitals. Rising rates of human, animal, and cargo traffic across international boundaries have increased opportunities for international transmission of pathogens. Often such pathogens are not responsive (i.e., resistant) to available antibiotics. Patients with these emerging infections initially seek help in clinics and hospitals. Therefore, early recognition and containment are strategies to prevent transmission to health care workers and other patients and thus society at large. Furthermore, with increasing rates of antibiotic-resistant microbes, clinicians have a shrinking repertoire of useful drugs for prevention and treatment. Currently, however, the era of alarming antibiotic resistance is challenged by fewer pharmaceutical companies investing in anti-infective discovery.

Current realities

Among the 7 billion global inhabitants, 1 billion cannot buy food, medicines, or vaccines, and they lack access to medical expertise. Of patients entering hospitals, 5%–10% in developed countries and 25%–50% in developing countries acquire an infection that was not present or incubating on admission. These are health care-associated infections, which are responsible for significant (incremental) morbidity, mortality, and costs above those expected from the underlying diseases alone. Often, these infections are caused by agents for which medicine has never had treatment (e.g., viruses) or those not susceptible to currently available antibiotics. The recent pandemic spread of SARS, H1N1 influenza, and ongoing global transmission of multidrug-resistant tuberculosis, community-acquired Methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug- resistant gram-negative rods (MDR GNR) have emphasized the fact that, in the words of author and columnist Thomas Friedman on the globalization of societies and nations, “the world is flat!” Antibiotic resistance, infection prevention and control, and antibiotic stewardship are global issues, not regional ones. A key point is that the most health-threatening microbes with antibiotic resistance enter our hospitals and clinics early on and can spread in the health care setting, often before they are recognized.

Scientific opportunities and challenges

There are five strategies that could be employed globally to minimize the transmission of antibiotic-resistant pathogens. Implementation would put an emphasis on early detection and control, ongoing practices to limit spread of all pathogens, and prevention. The five strategies are as follows:

1) Emphasize horizontal programs to limit spread of new (unknown) and old (known) health care pathogens. The effort expended will affect all organisms, thus influencing the total burden of infections rather than focusing only on a subset of the infections (e.g., only MRSA).

2) Develop real time international surveillance, rapid reporting, and a rapid response team to assist in the detection and control of an emerging pathogen. The sooner new organisms are identified, the earlier they can be controlled, specific patterns of transmission can be recognized, and a dedicated team of experts called into action.

3) Invest in technology such as that focused on rapid diagnostics and whole gene sequencing for organism fingerprinting. Rapid diagnostics can identify pathogens within hours, and whole gene sequencing is currently the most discriminating method for the fingerprinting of organisms needed to separate the offending pathogens from others in the same species.

4) Invest in vaccine prevention of key hospital and community pathogens. Prevention is always less expensive and more efficient in the long term than treatment.

5) Substantially commit to reducing poverty and hunger. The reduction of poverty will improve hygiene and natural immunity, thus reducing susceptibility to infections.

Policy issues

- An initial emphasis in all hospitals should be on horizontal prevention systems (i.e., programs reducing all pathogens) rather than vertical systems (i.e., focusing on specific agents such as only MRSA or only MDR GNR). Expecting greater than 95% compliance with hand hygiene will limit the spread of known and also emerging and unrecognized pathogens; it is inexpensive yet effective, especially for resource-poor countries. There is value in maintaining emphasis on clean water and soap (e.g., the "*Clean the World*" program to collect soap from hotels in the developed world and reprocess it for use in developing countries). An example of a horizontal program in surgery is one in which a multisite study of surgical skin preparations showed that 40% of *all* surgical site infections could be prevented with the use of chlorhexidine-alcohol versus the standard povidone alcohol preparations. Similarly, the use of daily scrubs of hospitalized patients with chlorhexidine-alcohol has been shown to reduce vancomycin-resistant enterococcal bloodstream infections by 73% and Acinetobacter bloodstream infections by 85%.

- A global center for real time surveillance and tracking of newly emerging, antibiotic-resistant infections is currently needed. This center should have the capacity for accurate fingerprinting of organisms to track them over time and space, and genetic analyses of virulence factors and specific genes coding for antibiotic resistance. As a result, there could be rapid reporting using updated maps of global movement of resistant organisms, which would allow a rapid response team of expert clinicians, epidemiologists, and microbiologists to be deployed to help control the transmission.

- A bold investment in vaccines for MDR organisms would eventually lead to less transmission and to reduced usage of antibiotics for therapy. For example, for decades the organism most frequently causing meningitis in children was *H. influenzae,* and rising rates of antibiotic resistance was a continual worry; yet with the deployment of the conjugate vaccine in the early 1990s, it has almost been completely eliminated. Similarly reduced rates of both infections and nasopharyngeal carriage have been observed after the use of pneumococcal and meningococcal conjugate vaccines in children, in part the result of herd immunity. Current vaccine priorities should include the following leading healthcare associated antibiotic-resistant pathogens: *S. aureus, Ps. Aeruginosa, C. difficile, K. pneumonine and* Acinetobacter. Priorities for community-acquired organisms should include a universal vaccine for *all* strains of influenza, and a vaccine for tuberculosis. These pathogens are responsible for a large proportion of deaths in the hospital and community.

- Finally, global policies should aim to reduce poverty and thus reduce malnutrition, preserve the immune system, and improve hygiene. In his book, *The End of Poverty*, Jeffrey Sachs estimates that extreme poverty could be eliminated by 2025 at the cost of 0.7% of the GDP of the more-affluent nations. In 1976, Thomas McKeown, in his book *The Role of Medicine* —

Dream, Mirage or Nemesis, described how death rates of both whooping cough and tuberculosis plummeted with improved hygiene and food supplies decades before the availability of vaccines and antibiotics. Global sponsors of such efforts today working in concert could include the World Health Organization (WHO), The World Bank, Centers for Disease Control and Prevention (CDC), the United Nations (U.N.), large multinational companies (e.g., Google), and world leaders from leading and emerging economies. Priorities must include the provision of safe water and food, and reduced exposure to zoonoses (i.e., pathogens transmitted from animals).

References

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