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## Disease-a-Month

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## Global infectious diseases—The new norm for the United States?

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From 1900 to the end of the 20th century, and into the present, there has been a significant shift in the top ten causes of death in the United States (Tables 1 and 2).<sup>1–3</sup> Where once infectious diseases were leading health care concerns, these have been largely replaced by cardiovascular disease and cancer. Unfortunately for a large proportion of the planet, infectious diseases remain the leading causes of death,<sup>1–11</sup> disability, in some cases preventable blindness,<sup>12,13</sup> and other serious sequelae. Because of our location, significant public health and medical infrastructure, and widespread immunizations against a wide array of pathogens, the US has been fortunately isolated from many infectious diseases, with the notable exception of tuberculosis (TB), HIV/AIDS, Lyme, West Nile, pneumonia, and influenza-related illness, as well as hospital-acquired infections. Of note, West Nile virus infections in the United States resulted in more than 140 deaths in 2006.<sup>14</sup>

Unfortunately most of the world still bears an enormous burden related to infections. Instead of recognizing that billions of people worldwide are exposed to important and emerging infectious diseases,<sup>8,9,15–17</sup> our training has relegated this topic mostly to “tropical medicine” or public health or labeled the threat as a “zebra” item.<sup>18,19</sup> While most of us remember from our early medical training the old adage “If you hear hoof beats, think horses, not zebras,” the US, and our attention, including medical training, can no longer afford to follow this adage or relegate these so-called “zebras” to the dismissed column, as many of them are important global health concerns. The world has come to our country as much as we have traveled to the world. And by extension—the world's diseases have come to our clinics, emergency departments, and health care facilities.

Globalization, population shifts, and the changing ecology, including encroachment of previously unexplored regions, have altered the longstanding epidemiology of infectious diseases, causing spread where once continents and oceans contained the pathogen. New pathogens are occurring—some through unknown means and others through natural adaptation. It has long been recognized that influenza viruses exchange genetic material, either emerging as a new strain, as we continue to see with H5N1,<sup>20–25</sup> H1N1,<sup>26–31</sup> and now the latest H7N9.<sup>32–35</sup> But this likely holds true for other viruses, as recently demonstrated with a novel coronavirus, most recently referred to as Middle East respiratory syndrome (MERS CoV).<sup>10,11</sup>

Social determinants of health—poverty, overcrowding, lack of infrastructure in many developing nations and in our own cities, which leads to poor sanitation, inadequate clean water, under-immunization and lack of health care access, environmental changes resulting in

**Table 1**

Leading causes of death in 1900 and 1997 in the US and in 1992 in Peru.

Major causes of death (attributable)	The United States, 1900	Peru, 1992	The United States, 1997
1	Respiratory disease	Respiratory infections	Heart disease
2	Tuberculosis	Cancer	Cancer
3	Gastrointestinal disease	Gastrointestinal disease	Cerebrovascular disease
4	Heart disease	Heart disease	Pulmonary disease
5	Infectious/parasitic diseases	Tuberculosis	Accidents
6	Kidney diseases	Cerebrovascular disease	Pneumonia/influenza
7	Early infancy diseases	Urinary system disease	Diabetes
8	Cerebrovascular disease	Nutritional deficiencies	Suicide
9	Cancer	Early infancy	Homicide
10	Liver disease		HIV AIDS

expanding zones for mosquitoes and the pathogens they transmit, cultural concerns about modern medicine, and restrictions on vector control including public opinion, cost, safety, impact on the ecology, and population migration—have all contributed to a resurgence in certain infectious diseases and a spread to areas previously unaffected, including the United States.

Disease transmission primarily occurs through person-to-person contact [respiratory (Figs. 1, 2),<sup>6,22</sup> fecal oral, or blood exchange], through fomites, instruments (drug paraphernalia or inadequately cleaned medical/surgical equipment) and vectors (mosquitoes or worms). While not everyone is exposed to instruments, or mosquitoes, avoiding people can be a challenge—respiratory contagion being an issue of enormous concern in the containment of infections. The spread of pulmonary infections occurs readily from upper and lower respiratory tract infections (Fig. 2).<sup>6,22,36,37</sup>

Respiratory illness spread in the following ways<sup>6,22,36,37</sup>:

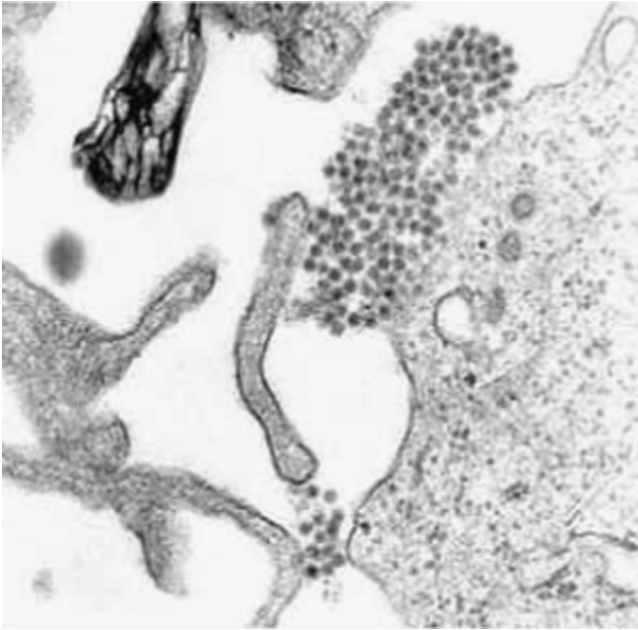
- Droplets
- Proximity (less than 6-ft social distancing especially)
- Environment (overcrowding, for example)
- Fomites
- Mucosa
- Prior immunity (or lack thereof)
- Poor hygiene
- Inherent transmissibility of pathogen ( $R_0$ )

Although great strides have been made over the last 20 years, including the ability to describe the etiology of a variety of disease states by the same pathogens and symptom syndromes that previously remained mysteries without clear-cut etiologies, including parvovirus B19, cytomegalovirus (CMV), Epstein–Barr virus (EBV) and others, pathogens and the vectors that facilitate their

**Table 2**

Top five causes of death for persons 65 years of age and older.

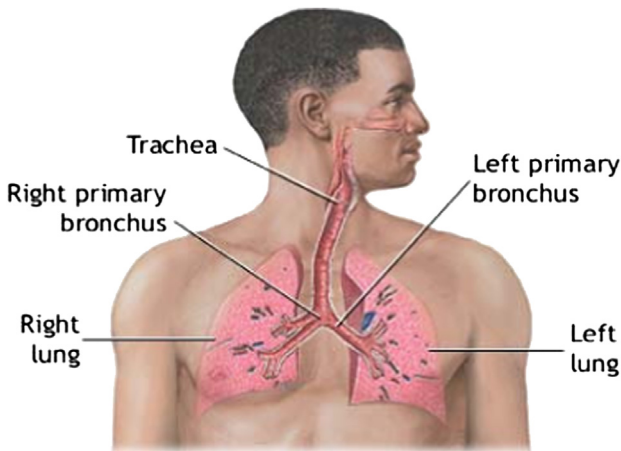
Whites	Blacks	American Indians	Asian or Pacific Islanders	Hispanics
1. Heart disease	Heart disease	Heart disease	Heart disease	Heart disease
2. Cancer	Cancer	Cancer	Cancer	Cancer
3. Stroke	Stroke		Stroke	Stroke
4. COPD	Diabetes	Stroke	Pneumonia/influenza	COPD
5. Pneumonia/influenza	Pneumonia/influenza	COPD	COPD	Pneumonia/influenza



**Fig. 1.** Routes of entry for respiratory infections

transmission remain a persistent danger. Dr. Lederberg was prescient when he opined about the challenges for humans that viruses pose.<sup>38</sup> Against this backdrop of new, reemerging, potentially travel related, and newly adapted, more virulent pathogens, one can appreciate there are numerous emerging infectious threats that are suitable for an entire edition of *Disease-a-Month* to address.

Clearly there are many pathogens to discuss, and train for in the US, but we would be remiss to ignore the most significant infectious diseases—ones that impact large populations and cause serious illness, such as malaria,<sup>39</sup> dengue, tuberculosis,<sup>40,41</sup> HIV/AIDS, and influenza, among the most important.



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**Fig. 2.** Respiratory infections (upper and lower tract) can readily be spread airborne.<sup>6,22</sup>

As this article goes to press, we are entering influenza season. It is not news, nor should it be necessary for the CDC to remind the public and health care professionals that over 30,000 people die every year in the United States from just two vaccine preventable diseases (VPD)—influenza and pneumococcal pneumonia. As physicians and health care providers, we recognize any success at reducing infections from 1900 to 2000 is largely due to vaccines, sanitation, and better hygiene. In spite of this, some of our colleagues continue to express that they do not get the flu shot. It is critically important that we not only encourage our patients to obtain appropriate vaccinations, we should be good role models and obtain the vaccines ourselves.

The scope of the first two editions (Parts I and II) focus on emerging, novel, and/or expanding infectious diseases in general, travel-related infections, and then specifically on dengue.

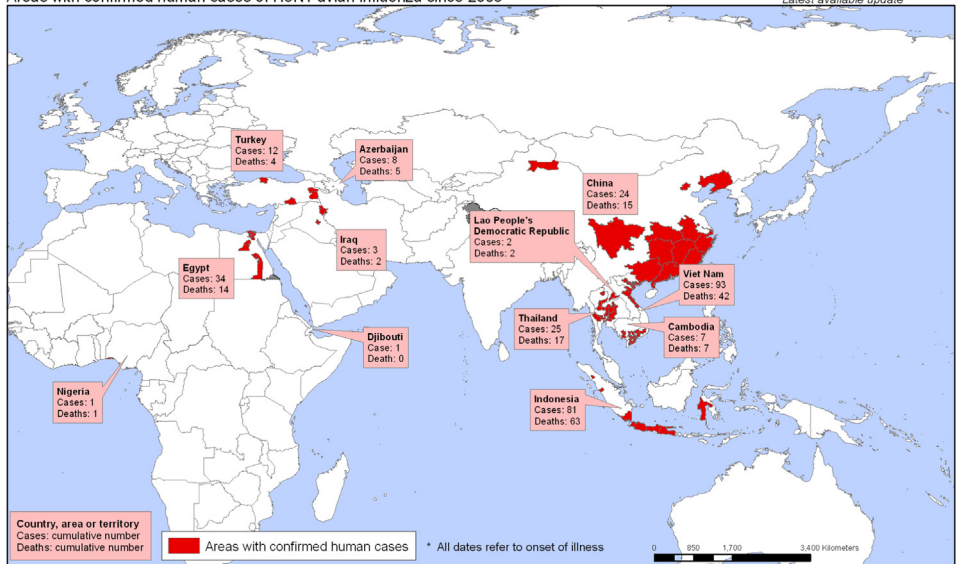
Dengue is one of the most important global pathogens—a viral hemorrhagic fever illness that imperils over 3 billion people,<sup>17</sup> affects through various forms of illness hundreds of millions of persons worldwide, including deaths, is spreading beyond its normal confines, and has been increasingly diagnosed in the United States.

A separate edition of *Disease-a-Month*, Part II will concentrate on the most recently identified coronavirus MERS CoV and a novel reassortant avian origin human influenza A virus H7N9 with an update of the H5N1 avian influenza into 2013, other influenza viral illnesses, a discussion on the currently available antivirals, as well as ones being developed to treat influenza, and an update on influenza vaccines, including the ones most recently approved by the US Food and Drug Administration (FDA)—the quadrivalent inhaled vaccine, in addition to looking at adjunctive therapies, including studies investigating the use of anti-inflammatory medications and the various “statin” drugs.

In 2012, a novel coronavirus MERS CoV causing Middle East respiratory syndrome was discovered, which is distinct from the previously problematic novel coronavirus referred to as severe acute respiratory syndrome coronavirus (SARS) that appeared in 2002–2003.<sup>11</sup> MERS CoV to date seems to carry a higher case-fatality rate, but it is currently less capable of person-to-person transmission than SARS. However we are still early in the outbreak and much is left to learn.<sup>10,11</sup>

Areas with confirmed human cases of H5N1 avian influenza since 2003 \*

Status as of 11 April 2007  
Latest available update



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO / Map Production: Public Health Mapping and GIS  
Communicable Diseases (CDS) World Health Organization

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Fig. 3. WHO map of countries involving confirmed human cases 2003–2007.<sup>42,43</sup>

Figure 3 illustrates the number of countries where confirmed H5N1 infection has occurred, according to WHO, from 2003 to 2007, excluding the 100,000,000 birds afflicted over that time as well as other non-human species.<sup>38</sup>

In the following section, we will discuss a variety of clinically important emerging and reemerging pathogens, the extent of morbidity and mortality that they pose, the clinical challenges we face as health care professionals, including travel-associated illness (TAI), and the opportunities to prevent, contain, and recognize the growing number of infections occurring worldwide from well-entrenched diseases such as multidrug-resistant tuberculosis (MDR TB) to novel ones such as novel human coronavirus now referred to as Middle East respiratory syndrome human coronavirus (MERS HCoV), that pose a very real threat of creating widespread epidemics, even pandemics.

It is worth noting within the scope of important emerging and reemerging disease, we could just as easily dedicate an entire edition to multidrug- and extreme drug-resistant tuberculosis (MDR TB and XDR TB, respectively), to the critically important hospital-associated infections such as by *Clostridium difficile* and *carbapenem resistant enterococci* (CRE), or to the emerging transplant-associated viral illnesses. As long ago as 1998, concerns had been raised about the rising threat of *C. difficile*.<sup>44,45</sup> Some of these will be addressed in a future edition of *Disease-a-Month*.

Regardless of which emerging pathogen we discuss—avian influenza H5N1, H7N9, MERS CoV, swine flu, or other viruses—it is important to recognize that preparedness efforts as a response to a potential pandemic caused by swine or avian influenza, SARS, or MERS can also enhance awareness and promote advances in diagnostic and treatment capabilities toward other significant infectious disease worldwide.<sup>22,43,46</sup>

It is also important to note these efforts are not part of a zero sum game. Enhancing capacity for one pathogen threat can improve the capability to address a wider array of infectious diseases. Recognizing we can never defeat pathogens, as there will always be infectious threats as long as mankind explores new regions, microbes retain their ability to adapt to our best science, poverty, poor sanitation, persistent overcrowding in housing and health care facilities, along with cutbacks in research, health care resources, and public health underscore the importance of continued vigilance for and training about emerging infectious diseases to maximize what capabilities we still have.

While the mainstay of containing emerging threats often rests upon public health expertise—that is the big picture. Science can provide timely antimicrobials, even vaccines to help thwart the spread of infections. But disease and health care occur at the street level where person-to-person transmission occurs. Hospital and emergency department (ED) overcrowding remains a significant problem in containing the spread of infections. While some health care facilities (HCF) have improved access to masks and hand sanitizers as well as cough/sneeze etiquette posters, these can have limited value if manpower shortages, cultural imperatives, for example, going to a health care facility with many members of the family, and language and education barriers work against social distancing, personal hygiene, and other containment strategies. Some practices and health care facilities have implemented old pediatric strategies of placing potentially contagious patients into separate areas. Clearly this is a space-, manpower-, and resource-intensive strategy, but one that may reduce transmission of illness from those who are affected. A serious discussion on how to cohort and isolate potentially contagious people, as well as strategies to alleviate overcrowding, much of which stems from the misuse of ED and HCF for primary care problems, is vitally necessary.<sup>47</sup>

The change in immigration—from the 1900s where illness often was a disqualification to entry to the 2000s where often very sick and contagious individuals freely enter—needs serious solutions. It seems this discussion, including how to reduce risk at critical population portals—airports, emergency departments, and elsewhere—rarely occurs unless there is threat of a SARS or novel swine flu infection, such as happened in 2003 and 2009, respectively.

Additionally, public health is often underfunded, though it is a critical component in both a domestic and global safety net to capture and share information as well as resources towards containing outbreaks. There still remains, in many regions, a disconnect between public health medicine and private health care.

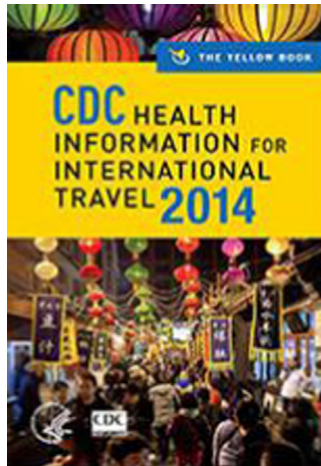


Fig. 4. CDC Health Information for International Travel 2014.<sup>50,51</sup>

Thinking out of the box, from academia, industry, and health care facility leaders, and multidisciplinary collaboration to identify pre-epidemic opportunities to reduce the risk of disease transmission are critically important now, perhaps more than ever, especially considering the number of existing global infections—hospital-acquired and endemic or in the wild that are reemerging (polio and dengue) or transforming into more virulent forms (e.g., *C. difficile*).<sup>48,49</sup> This will take political and fiscal courage as well as significant effort. Improving how we train our future health care professionals, especially to consider travel-related illnesses and global infections that are likely to show up in the US, as well as providing the tools to more rapidly identify these diseases is an important task to be considered in medical education.

As we will discuss in the MERS CoV section, the exchange of information through global and regional public health as well as the use of social media, including ProMED discussion sites, has been a valuable resource for health care professionals on the front lines of treating emerging pathogen-related illnesses.

A useful reference, especially for guiding patients before their journeys, is the CDC Health Information for International Travel 2014 (Fig. 4).<sup>50,51</sup> Utilizing social media and other approaches to promote strategies that can reduce transmission of diseases—whether respiratory, sexually transmitted, even drug-use related—to diverse populations within our communities offer promise. The anti-vaccine movement has deftly utilized the media and demonstrated the power of, if you will excuse the pun “going viral”—we, too, must adapt and improve our proactive use of these communications tools.

Lastly, a reminder that we live in a global world should serve as a caution that the US is no longer isolated from even the most remote places or protected from outbreaks abroad. With the magnitude of population movement—returning service men and women from war-torn, impoverished regions and areas with multiple, significant endemic illnesses, immigration, business travel, and vacationing—we all need to abandon the dangerous notion of “over there.” As SARS demonstrated to North America in 2003 and Swine Flu in 2009, global emerging infections such as dengue are here to stay for the foreseeable future and the US will be visited sooner or later by another one. Will it be MERS CoV, Avian H7N9, or something completely novel? And most importantly, will we be prepared?

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