

NEW AND RE-EMERGING INFECTIOUS DISEASES

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Infectious diseases traverse the usual boundaries established by medical specialists. All organ systems may be involved, and all physicians caring for patients may have to deal with infected patients.

Infectious diseases remain leading cause of morbidity and mortality throughout the world primarily because known measures of control and therapy are not applied. In technically advanced countries, the pestilences of antiquity no longer occur. Yet, even in these areas infectious diseases remain important contributors to illness and death.

Among clinical specialty areas, that of infectious diseases is remarkable in being non-systemic in orientation. The specialist in infectious diseases must be prepared to deal with involvement in any organ, system, or region of the body. A patient comes to see a physician because of a sore throat, not because of infection caused by *Streptococcus pyogenes*. In assessing illness, he must be capable of taking into account age, sex, and genetic constitution; nutritional, hormonal, and metabolic status; the consequences of trauma, surgery, and other physical or chemical agents; and the effects of neoplastic, degenerative, and hypersensitive states. In this re-

quirement, the specialty of infectious diseases becomes the last disciplinary domain of general medicine.

Ironically, many of the forces that contribute to the appearance of new diseases and emergence of old ones are created by human activity - in many instances by what we consider extraordinary achievements. We have underestimated the complexity of our environment and the capacity of other species adapt and evolve. We have overestimated the power of tools, such as antimicrobials, pesticides, and vaccines to free us of disease. We have failed to recognize that events in plants and animals can teach us and affect our health. We have paid little attention to the geoclimatic influences on health. We have too often ignored the social, economic, and political contributions to disease. Several general concepts can help focus your attention to infectious diseases.

Disease emergence is complex; often several factors must change sequentially or simultaneously to allow a disease to emerge. Infectious diseases are dynamic. New infections will continue to appear, possibly at increasing rates.

Known infectious diseases will change in distribution, severity and frequency.

Most new infections are not caused by novel pathogens.

Human activities are the most potent factors leading to the appearance of new infectious diseases and the change in known infectious diseases. Social, economic, climatic, and political forces shape disease patterns and influence emergence.

Interventions to control infections can paradoxically increase the burden of disease.

Understanding disease emergence requires looking beyond the organism to the milieu, the ecosystem, and society. A global perspective is essential.

The pathogens identified in most of the newly named diseases, such as Legionnaires' disease, toxic shock syndrome, Lyme disease, and AIDS are not novel pathogens that appeared *de novo* just prior to the recognition of disease. In most instances of new diseases, the pathogens have been present for centuries or longer. The process that leads to the recognition and naming of a disease often involves social and economic, as well as scientific events. Factors that favor recognition of a disease as new are several: clustering of cases in time or space; increase in prevalence; distinctive signs, symptoms or laboratory findings; short incubation; rapid progression; high mortality and so on.

History teaches that from time to time it is worthwhile looking back at where we have been to better understand where we are and where we may be going. During the last 20-30 years, some of the most evident, striking, and interesting changes in patterns of disease have occurred among those due to transmissible agents. The increasing human population facilitates transmission of disease from person to person with epidemiologic changes or increased virulence, and the expansion of the population into new ecologic niches brings people in contact with new potential disease pathogens and the emergence of new disease problems.

What types of change have occurred in the patterns of infectious diseases? The most dramatic is the occasional recognition of so-called new diseases. Some of these are, in fact, old illnesses for which a cause has been recognized. Diarrhea due to *Campylobacter*, unheard of 30 years ago and now considered among the most common causes of bacterial enteritis, serves as an example.

Some diseases, on the other hand, do seem to be truly new or at least more common than was previously thought. AIDS is the most obvious and lamentable example. In addition, some old diseases are now appearing in new geographic locales.

Malaria is being seen increasingly in the United States civilian population, which is no surprise since millions of Americans each year are traveling to tropical countries. We must also remember new populations at risk, such as renal and cardiac trans-

plant recipients who, due to immunosuppression, are susceptible to opportunistic infections.

Some old organisms have apparently adopted new tactics. Toxic shock syndrome is the result of a previously unknown toxin, produced by the familiar pathogen, *Staphylococcus aureus*. To further confuse us some old infections are appearing in new clinical guises, such as atypical measles in adolescents and young adults who received measles vaccine prior to 1967. Infant botulism, first recognized as a clinical entity distinct from food-borne botulism in 1976, presents the picture of the infant between the ages of one and six months collapsing with a neuromuscular illness, flaccidity, and hypotonia due to *Clostridium botulinum* growing in the intestinal tract and liberating a potent toxin.

What are the causes for these changing patterns of infectious diseases? At least three factors can be implicated:

- 1) changes in lifestyle, including sexual behaviour, travel patterns, dietary trends, leisure activity, and composition of the work force, have impacted on disease patterns as have
- 2) immigration and
- 3) the effects of medical progress.

Changing patterns of infectious diseases

<i>Type of change</i>	<i>Example</i>
New diseases	AIDS Cryptosporidiosis
New geographic range for old disease	Malaria in American travelers Chagas' disease in Central America immigrants
New populations at risk	Listeriosis in renal transplant recipients Giardiasis in day-care centers
New tricks for old „bugs“	Toxic shock syndrome <i>Pseudomonas</i> folliculitis
New faces for old diseases	Atypical measles Infant botulism
New ecologic niches for old „bugs“	Sneaker-associated <i>Pseudomonas</i> osteomyelitis Hot tub folliculitis
New modes of transmission	Rabies following corneal transplantation Creutzfeld-Jakob disease in recipients of human growth hormone

As recently as 20-30 years ago, none of the entities shown on the left-hand side of the balance was part of our medical vocabulary. While acquiring many new afflictions, we got rid of one very old one - smallpox.

IN	OUT
AIDS	Smallpox
Babesiosis	
Lassa fever	
Lyme disease	
Toxic shock sy	
Infant botulism	
Kawasaki disease	
Rotavirus diarrhea	
Chlamydia pneumonia	
Hepatitis C, D, E, G	
Legionnaires' disease	
Campylobacter enteritis	
and others	

Kawasaki disease, which is probably of infectious etiology, produces in children symptoms of fever, skin and mucous membrane lesions, lymph node enlargement, and sometimes aneurysms of the coronary arteries. Recent evidence has implicated retroviruses as a possible etiology for this fascinating entity.

Legionnaires' disease, first recognized during the 1976 epidemic in Philadelphia, is now known to be a cause of sporadic as well as epidemic pneumonia. Another new entry to our medical vocabulary is amebic meningoencephalitis, a rare but devastating infection of the central nervous system. It affects people swimming and diving in freshwater lakes and is caused by free-living amebas of the genus *Naegleria*.

In recent years we have also come to know the causes of some older diseases such as antibiotic-related colitis arising from a toxin produced by the bacterium *Clostridium difficile*. We have also learned that cat scratch disease is traceable to a small gram-negative bacterium.

Changes in sexually transmitted diseases

We now recognize many more than the traditional five venereal diseases taught 20-30 years ago. The weight of all of these afflictions has tipped the balance. A variety of microorganisms can be transmitted during sexual contact. They differ markedly in their taxonomy, virulence factors, growth requirements, and response to therapy. They are grouped together because sexual transmission plays an important role in their overall epidemiology. None of the sexually transmitted diseases (STD) is acquired solely via coitus. In some cases (e.g., shigellosis and candidiasis), sexual transmission

plays a relatively minor role, although for other conditions, such as infection with *Chlamydia trachomatis*, sexual transmission is the major route of acquisition.

NOW	YEARS AGO
AIDS	
Scabies	
Amebiasis	
Giardiasis	
Shigellosis	
Salmonellosis	
Hepatitis B, G/?/	
Chlamydia infection	
Campylobacteriosis	LGV
Ureaplasma urethritis	Syphilis
Cytomegalovirus infection	Gonorrhea
Herpes genitalis	Chancroid
and others	Granuloma inguinale

Changing Lifestyles and New Populations at Risk

Cryptosporidium is a protozoan parasite of the gastrointestinal tract that only recently has been identified as a cause of human gastrointestinal disease. It is common in immunologically normal persons in whom it produces a self-limiting illness, as was described in the day-care-center outbreak.

The advancing average age of the population and the growing use of nursing homes has generated another new population at risk. Nursing home outbreaks of influenza, tuberculosis, varicella-zoster, a variety of diarrheal illnesses, and meningitis have all been reported.

Whirlpools, spas, and hot tubs, which were virtually nonexistent a few years ago, are now widely enjoyed by many people privately at home and in a variety of health and leisure clubs. With new pleasures come new problems, for example *Pseudomonas folliculitis* as the new entity.

Other unusual infections that have been associated with hot tubs and whirlpools include Pontiac fever due to *Legionella pneumophila* and *Acanthamoeba keratitis*.

Leisure offers another options also. Trips to the mountains and woods bring contacts with the beauties of mother nature, but also contacts with one of nature's less appealing creatures - the tick - the vector of the *Borrelia* causing Lyme disease.

Impact of Travel

Free people are traveling abroad with increasing frequency including exotic parts of the world where malaria, schistosomiasis, and filariasis are endemic. In addition to more pleasant souvenirs, some are returning with infections that first appear on arrival and that, because of their rarity in our country, are often not thought of by physicians.

Impact of Medical Progress

Medical progress continues to bring many benefits, but it has also brought with it new infectious disease complications and new modes and patterns of disease transmission.

Opportunistic infections in organ transplant recipients

Bacterial infections complicating foreign body implants:

- heart valves, prosthetic joints, cerebrospinal fluid shunts, hemodialysis and peritoneal dialysis access sites, intrauterine devices, fetal scalp monitors, central venous catheters
- Fungemia complicating total parenteral nutrition
- Bacteremia due to contaminated blood products
- Mycobacterial abscesses following augmentation mammoplasty implants
- Post-cardiac bypass mononucleosis syndrome
- Pneumonia due to contaminated inhalation therapy equipment
- AIDS following transfusion and organ transplantation
- Hepatitis B /G?/ and HIV infection after artificial insemination
- Creutzfeldt-Jakob disease in recipients of human growth hormone
- Creutzfeldt-Jakob disease following human dura mater grafting
- Rabies and Creutzfeldt-Jakob disease after corneal grafting
- Acanthamoeba keratitis in contact lens wearers

New Pathogenic Agents

Creutzfeldt-Jakob disease is one of two diseases

now known to be caused by transmissible agents called prions. The other is scrapie, a disease of sheep. They are very small agents capable of replicating in mammalian cells but containing no nucleic acids. They appear to be small proteins many times smaller than the smallest viruses. Diseases in which prions have been implicated are classified as slow infections characterized by very long incubation periods of months, years, or even decades in which the host is without symptoms. Thus, we see that one dramatic change in the last 20-30 years is our recognition of an entirely novel form of infectious agent and a change in our understanding about the pathophysiology of infectious diseases and the rate at which infections may evolve.

What can we learn from these changing patterns of infectious diseases? Surely we have ample proof of the dynamic nature of medicine. It would be prudent for those involved in medical education to be cognizant of these dramatic changes that have occurred in so brief a time as they struggle to make curricula relevant. Who could have imagined AIDS or prions? Perhaps as we study and learn from the changing patterns of disease, we shall find the clues and lessons that will enable us to achieve greater successes.

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