New Emerging Diseases in the 21st Century

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Περιεχομενα

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Η εμφάνιση και η επανεμφάνιση των μολυσματικών ασθενειών περιλαμβάνουν πολλούς αλληλένδετους παράγοντες. Η παγκόσμια αλληλοσύνδεση συνεχίζει να αυξάνεται με τα διεθνή ταξίδια, το εμπόριο, τις οικονομικές, πολιτικές και πολιτισμικές αλληλεπιδράσεις καθώς και με τις αλληλεπιδράσεις μεταξύ ανθρώπων και μεταξύ ανθρώπων και ζώων . Οι αλληλεπιδράσεις αυτές περιλαμβάνουν την ακούσια ή εκούσια ανταλλαγή των μικροβιακών παραγόντων και της μικροβιακής αντοχής και επιτρέπει την εμφάνιση νέων και μη αναγνωρισμένων μικροβιακών στελεχών της νόσου.

Με την έναρξη του 21ου αιώνα, ήδη έχουν αναγνωριστεί νέοι παράγοντες, και εχουν προκύψει νέα ξεσπάσματα νόσων. Η προσπάθεια για τον περιορισμό της εξάπλωσης των νεοεμφανιζόμενων λοιμωδών νόσων θα απαιτήσει συνεργασία μεταξύ πολλών κλάδων και φορέων σε όλο τον κόσμο. Το άρθρο αυτό προσδιορίζει τις εμφανιζόμενες μολυσματικές ασθένειες, συνοψίζει το ιστορικό υπόβαθρο, και εξετάζει τους παράγοντες που συμβάλλουν στην εμφάνισή τους.

Παράγοντες /στελέχη που έχουν κάνει μια σημαντική εμφάνιση, ιδίως τον 21ο αιώνα, ανασκοπούνται, μεταξύ των οποίων: οι αιμορραγικοί πυρετοί Έμπολα και Μάρμπουργκ , τα ανθρώπινα monkeypox, η σπογγώδης εγκεφαλοπάθεια των βοοειδών, το σοβαρό οξύ αναπνευστικό σύνδρομο (SARS), ο ιός του Δυτικού Νείλου, η γρίπη των πτηνών και ο H1N1.

Το άρθρο αυτό παρέχει για κάθε στέλεχος μια σύντομη ιστορική αναδρομή, περιγραφές περίπτωσεων και τις επιπτώσεις της υγειονομικής περίθαλψης.

Λέξεις κλειδιά: Γρίπη των πτηνών, σπογγώδης εγκεφαλοπάθεια των βοοειδών,ιός Έμπολα, νεοεμφανιζόμενες λοιμώδεις νόσοι , αιμορραγικοί πυρετοί, μολυσματικές ασθένειες, ιός Marburg, monkeypox, prion ασθένειες, SARS, ιογενείς λοιμώξεις, ιός του Δυτικού Νείλου, H1N1.

Εισαγωγή: Οι μολυσματικές ασθένειες ανά τον κόσμο θέτουν ένα σημαντικό φορτίο τόσο στα άτομα, όσο και στην υγειονομική περίθαλψη. Γενικά, οι μολυσματικές ασθένειες προξενούν μεγαλύτερες απώλειες στα νήπια, τα μικρά παιδιά και τους ηλικιωμένους, και έχουν επιπτώσεις, δυσανάλογα, στους μειονεκτούντες πληθυσμούς στις αναπτυγμένες χώρες. Με τον ερχομό της χρυσής εποχής των αντιβιοτικών και άλλων αντιμικροβιακών παραγόντων/στελεχών, πολλοί επαγγελματίες υγείας προσδόκησαν ότι οι μολυσματικές ασθένειες θα μπορούσαν να κατακτηθούν ή να ελεγχθούν. Αυτή η άποψη αποδείχθηκε υπερβολικά αισιόδοξη. Τα μικρόβια και οι ξενιστές τους υπάρχουν σε μια σχέση που επηρεάζεται από το περιβάλλον τους. Αυτή η σχέση, που βρίσκεται σε μια επισφαλή ισορροπία και εξελίσσεται συνεχώς, συμβάλλει στην προκύπτουσα φύση των απειλών από τις μολυσματικές ασθένειες.

Η εστίαση της προσοχής στις εμφανιζόμενες μολυσματικές ασθένειες – Emergence Infectious Diseases EIDs ξεκίνησε στα τέλη της δεκαετίας του 1960 και στις αρχές του 1970. Οι εμφανιζόμενες μολυσματικές ασθένειες έλαβαν μεγαλύτερο ενδιαφέρον με την εμφάνιση του ιού HIV / AIDS στις αρχές του 1980, και αυτή η προσοχή κατέληξε σε μια έκθεση σχετικά με τις εμφανιζόμενες και επανεμφανιζόμενες λοιμώξεις/ασθένειες το 1992 από το Ινστιτούτο Ιατρικής (IOM). Το 1995, ένα ειδικό περιοδικό, το Emerging Infectious Diseases, παρουσιάστηκε επίσημα από τα Κέντρα Ελέγχου και Πρόληψης Νοσημάτων- Centers for Disease Control and Prevention (CDC).

Ο καθορισμός των εμφανιζόμενων μολυσματικών ασθενειών ποικίλλει κάπως και εξαρτάται από το ποιος κάνει τον καθορισμό, ο χρόνος που γίνεται ο καθορισμός, και εάν ο καθορισμός πρέπει να είναι περιοριστικός ή συμπεριλαμβάνων/συνολικός.

Η ακόλουθη περιγραφή συμπεριλαμβάνει έναν συνολικό καθορισμό των εμφανιζόμενων μολυσματικών ασθενειών και παραδείγματα στις σχετικές περιπτώσεις

• Πρόσφατα εντοπίσθείσες ασθένειες που προκαλούνται από ένα ήδη γνωστό μικροοργανισμό.
• Πρόσφατα εντοπίσθείσες ασθένειες που προκαλούνται από έναν προηγουμένως άγνωστο ή μή αναγνωρισμένο μικροοργανισμό
• Γνωστές ασθένειες που πρόσφατα διαπιστώθηκε ότι προκαλούνται από ένα ήδη γνωστό μικροοργανισμό
• Ασθένειες και μικροοργανισμοί βρέθηκαν σε νέες γεωγραφικές περιοχές.
• Μικροοργανισμοί που βρέθηκαν να είναι ανθεκτικοί σε αντιμικροβιακές ουσίες.
• Μικροοργανισμοί των ζώων που έχουν επεκτείνει το φάσμα των ξενιστών τους σε πρόσφατα μολυνθέντες ανθρώπους
• Πρόσφατα εντοπισθέντες δεξαμενές ή φορείς για μικροοργανισμούς.
• Μικροβιακή εξέλιξη που οδηγεί σε μεταβολή της παθογένειας ή άλλων χαρακτηριστικών

Abstract

The emergence and re-emergence of infectious diseases involves many interrelated factors. Global interconnectedness continues to increase with international travel and trade; economic, political, and cultural interactions; and human-to-human and animal-to-human interactions. These interactions include the accidental and deliberate sharing of microbial agents and antimicrobial resistance and allow the emergence of new and unrecognized microbial disease agents. As the 21st century begins, already new agents have been identified, and new outbreaks have occurred. Solutions to limiting the spread of emerging infectious diseases will require cooperative efforts among many disciplines and entities worldwide. This article defines emerging infectious diseases, summarizes historical background, and discusses factors that contribute to emergence. Seven agents that have made a significant appearance, particularly in the 21st century, are reviewed, including: Ebola and Marburg hemorrhagic fevers, human monkeypox, bovine spongiform encephalopathy, severe acute respiratory syndrome (SARS), West Nile virus,avian influenza and H1N1. The article provides for each agent a brief historical background, case descriptions, and health care implications.

Key words: avian influenza, bovine spongiform encephalopathy, Ebola virus, emerging infectious diseases, hemorrhagic fevers, infectious diseases, Marburg virus, monkeypox, prion diseases, SARS, viral infections, West Nile virus, H1N1.

Introduction

Worldwide, infectious diseases place a considerable burden on individuals and health care. In general, infectious diseases exact a greater toll from infants, young children and the elderly, and disproportionately affect disadvantaged populations in developed countries. With the coming of the golden age of antibiotics and other antimicrobial agents, many health care practitioners anticipated that infectious diseases could be conquered or controlled. This view proved overly optimistic. Microbes and their hosts exist in a relationship influenced by their environment. This relationship, precariously balanced and continuously evolving, contributes to the emergent nature of threats from infectious diseases.

Focused attention to EIDs began in the late 1960s and early 1970s. EIDs received greater interest with the emergence of HIV/AIDS in the early 1980s, and this attention culminated in a report on emerging and re-emerging infections in 1992 by the Institute of Medicine (IOM) (Smolinski, Hamburg & Lederberg, 2003). In 1995, a dedicated journal, *Emerging Infectious Diseases*, was introduced by the Centers for Disease Control and Prevention (CDC).

The definition of emerging infectious diseases varies somewhat and depends on who does the defining, the time the definition is offered, and whether the definition should be restrictive or inclusive. The following description (Lashley, 2003, 2004; Lashley & Durham, 2002; Lederberg, Shope & Oaks, 1992) incorporates an inclusive definition of EIDs, and includes examples where relevant:

- Newly identified diseases caused by a previously known microorganism.
- Newly identified diseases caused by a previously unknown or unrecognized microorganism.
- Known diseases newly realized to be caused by a previously known microorganism.
- Diseases and microorganisms found in new geographic areas. .
- Microorganisms found to be resistant to antimicrobial agents.
- Microorganisms of animals that have extended their host range to newly infect humans.
- Newly identified reservoirs or vectors for microorganisms.
- Microbial evolution resulting in a change of virulence or other characteristics.
- Known diseases that have markedly increased in incidence.
- Organisms that have been deliberately altered to cause intentional harm such as weaponized *Bacillus anthracis* that was used to contaminate some mail in the United States in 2001.

In some cases, identification of the cause of EIDs has awaited the development of appropriate diagnostic technology. Some cancers and chronic diseases are due to microbial infection, and it is anticipated that even more will ultimately be shown to have a microbial contribution.

Emerging, or re-emerging, infectious agents or diseases began to be identified in the late 1960s and early 1970s, but it was not until the early 1990s that their potential impact began to attract significant attention. The most recent 2003 report from the IOM entitled "Microbial Threats to Health: Emergence, Detection, and Response" (Smolinski, Hamburg, & Lederberg, 2003) indicates that since the early 1990s, there has been an increasing number of new infectious agents and species identified, and outbreaks or resurgence of previously known illnesses have been detected. Beginning in 1992, with the emergence of Sin Nombre virus (cause of hantavirus pulmonary syndrome), the list of new pathogens and diseases continues into the 21st century with an outbreak of SARS due to a newly identified coronavirus; an outbreak of human monkeypox in the Western hemisphere; human cases of avian influenza in Asia; the identification of bovine spongiform encephalopathy-infected cattle in the United States; outbreaks of Marburg hemorrhagic fever in Angola and Ebola hemorrhagic fever in the Democratic Republic of the Congo; and the establishment of West Nile virus as endemic in North America. Selected new pathogens and the resulting infectious diseases identified since 1992 are listed in the Table below (Lashley, 2004). One should also keep in mind that emerging infectious diseases appear alongside the palette of the more common infectious diseases.

Table. Selected new pathogenic agents/ infectious diseases identified since 1992

Agent	Disease condition
Anaplasma phagocytophilum	Human granulocytic anaplasmosis
Australian bat lyssavirus	Encephalitis
Bartonella clarridgeae	Cat scratch disease
Bartonella elizabethae	Endocarditis, bacteremia
Brachiola vesicularum	Microsporidiosis
Ehrlichia ewingii	Ehrlichiosis
Encephalitozoon intestinalis	Enteritis, disseminated infection
Gymnophalloides seoi	Gastrointestinal illness
Hantaviruses - Sin Nombre virus - Whitewater Arroyo virus	 Hantavirus pulmonary syndrome Hemorrhagic fever
Hendra virus	Encephalitis, respiratory disease
Hepatitis G virus	Hepatitis (suspected)
Human herpesvirus-8	Kaposi sarcoma
Metapneumovirus	Acute respiratory infections, pneumonia
Metorchis conjunctus	Liver disease
Nipah virus	Encephalitis
Nocardia veterana	Pulmonary disease
SARS-associated coronavirus	Severe acute respiratory syndrome
Trachipleistophora hominis	Microsporidiosis
TT virus	Hepatitis (possible)
Vibrio parahaemolyticus serotype 03K6	Gastroenteritis

Contributing Factors to Emergence of Infectious Diseases

The 2003 IOM report (Smolinski, Hamburg & Lederberg, 2003) divided factors of emergence into 13 basic categories. These categories are listed below, with an example of each in parentheses. Further discussion on contributing factors may be found in "Emerging Infectious Diseases: Vulnerabilities, Contributing Factors, and Approaches" (Lashley, 2004).

- Microbial adaptation and change (e.g., the O157:H7 strain of *E. coli,* which is more virulent).
- Human susceptibility to infection (e.g., persons who are homozygous for methionine on codon 129 of the prion protein gene [*PRNP*] are more susceptible to development of Creutzfeldt-Jakob disease).
- Climate and weather (e.g., heavy rains can result in increased breeding sites for mosquito vectors and increases in mosquito-borne infectious diseases).
- Changing ecosystems (e.g., dam building has resulted in changing vector ecology and the emergence of Rift Valley hemorrhagic fever in Egypt).
- Human demographics and behavior (e.g., body piercing and potential hepatitis C infection).
- Economic development and land use (e.g., clearing forests in Venezuela has resulted in an increased cane mouse population, the probable reservoir host of the Guanarito virus and an outbreak of Venezuelan hemorrhagic fever).
- International travel and commerce (e.g., importation of Guatemalan raspberries and outbreaks of cyclosporiasis in the United States).
- Technology and industry (e.g., use of mass treatment with fluoroquinolones to treat *E. coli* infections in chickens, resulting in antimicrobial resistance in humans to other organisms).
- Breakdown of public health measures (e.g., breakdown in vector control, leading to increased abundance and distribution of *Aedes aegyptii*, the mosquito vector of dengue, and hence a spread of dengue hemorrhagic fever to the Americas).
- Poverty and social inequality (e.g., poverty can result in the eating of animals who have died from disease, resulting in human infections such as in the case of gastrointestinal anthrax in humans).
- War and famine (e.g., civil unrest and natural disasters). Any mass disruption and violence can result in disruption of public health services, especially preventive services, such as immunizations and vector controls.
- Lack of political will (e.g., the lack of reporting of global infectious diseases of interest for political and economic reasons, such as with SARS in China).
- Intent to harm (e.g., the intentional distribution of *Bacillus anthracis*, the etiologic agent of anthrax in the United States in 2001).

Many of these contributing factors are interrelated. For example, war creates crowded conditions leading to contaminated drinking water, unsanitary facilities, disruption of basic health services, and easier spread of infectious agents. War can also result in lack of food for those who are politically disenfranchised and in famine. Famine results in malnutrition, which then alters human susceptibility to infection. Victims of war are also prey for violence and sexual predators resulting in the spread of sexually-transmitted diseases, such as HIV. The interrelated nature of these contributing factors is also evident in the following section in the discussion of seven agents that have made a significant appearance as EIDs.

Selected Specific Emerging Infectious Diseases

Among the newer emerging infectious agents and diseases, many have already had great impact, while others show potential for impact in the near future. Agents that have made a significant appearance, particularly in the 21st century, are considered in more depth below. These agents include: Ebola and Marburg hemorrhagic fevers, human monkypox, BSE, SARS, West Nile virus, avian influenza and H1N1.

Hemorrhagic Fevers: The Ebola and Marburg Viruses

The Ebola and Marburg viruses are the only known members of the filovirus family. They can cause severe hemorrhagic fever with high fatality rates. There is no specific treatment. Ebola virus is better known to the public as a result of discussion in the popular media, such as in the book by Richard Preston, "The Hot Zone: A Terrifying True Story," (1994), and the movie "Outbreak," starring Dustin Hoffman (Warner Brothers Pictures, 1995). The natural animal reservoir of both is still unknown.

Ebola Hemorrhagic Fever.

Ebola virus infection was first recognized during a human outbreak in 1976 with almost simultaneous outbreaks in both the Sudan and Zaire (now the Democratic Republic of the Congo). It was named after a river in the Democratic Republic of the Congo (Peters & LeDuc, 1999) The Ebola virus is now known to have four subtypes: Zaire, Sudan, Reston, and Ivory Coast (Pourrut et al., 2005). After an outbreak in 1979 in the Sudan, Ebola appeared relatively quiescent until it appeared among macaque monkeys imported from the Philippines and housed at a primate facility in Reston, Virginia (Peters & LeDuc). In late 1994, a single case in a researcher who performed a necropsy on an ill chimpanzee led to the identification of a new subtype, Ebola-Ivory Coast (Arthur, 2002).

In Gabon, Africa, outbreaks of Ebola virus infection occurred from 1994 to 1997 (Georges et al., 1999). Another appearance was in 2000-2001 with an Ebola outbreak in Uganda that resulted in 425 cases with 224 deaths by January 2001 (CDC, 2001). In this outbreak, events and conditions associated with acquired disease were: funeral attendance for those who died with Ebola hemorrhagic fever, intrafamilial contact, and nosocomial infections. Schools were closed and a ban against funerals was enacted (World Health Organization [WHO], 2001).

In November, 2001, an Ebola outbreak again occurred in Gabon. and in the Democratic Republic of the Congo, and multiple outbreaks occurred in 2000-2004 in Gabon, the Congo, Sudan, and Uganda. Outbreaks continue in the Congo in 2005. At the same time, it was noted that Ebola outbreaks occurred in large mammals, mainly chimpanzees, duikers (a type of antelope), and gorillas, and that human outbreaks tended to follow those observed in animals. Airborne transmission of the Ebola Zaire strain to monkeys by aerosol has been demonstrated (Johnson, Jaax, White, & Jahrling, 1995) but is not known to occur from human-to-human. To date, no animal reservoir for Ebola virus has been identified (Pourrut et al., 2005).

Marburg Hemorrhagic Fever.

Marburg virus infection was identified in 1967, when laboratory workers in a pharmaceutical company in Marburg, Germany who were processing tissue from imported African green monkeys began to fall ill. The workers were admitted to the hospital with severe illness. The virus isolated was unrelated to any other known at that time. Other cases occurred at virtually the same time in Frankfurt, Germany and in what was then Belgrade, Yugoslavia (now Serbia) (Peters & LeDuc, 1999). It was determined that the monkeys in all three sites were from the same imported batch from Uganda. The full investigation ultimately led to the recognition of a new family of viruses, the Filoviridiae, of which Marburg virus was the first to be identified (Feldmann & Kiley, 2000).

Marburg virus was not recognized again until 1975 when three cases were reported from Johannesburg, South Africa. The index case (initial patient) was a young Australian man who had been on vacation doing a walkabout in what was then Rhodesia (now Zimbabwe) with a female companion. He died, but his companion, and the nurse caring for both of them, recovered (WHO, 2005a). In 1980, Marburg virus infection was next recognized when an index patient became ill in western Kenya, followed by secondary illness of the physician who tried to resuscitate him (Smith et al., 1982). From 1980 until 1998, outbreaks of Marburg virus infection were relatively few and involved a single or a few primary cases. In 1982, another single case was identified in South Africa. In late 1998, an outbreak of Marburg virus hemorrhagic fever occurred in Durba, in the Democratic Republic of the Congo. Many affected were illegal gold miners in abandoned mines. The remote location and local warfare prevented arrival of experts from the CDC and WHO for months. In October 2004, a very large outbreak began in Angola and was declared over in November 2005. As of November 2005, 374 cases of Marburg hemorrhagic fever were reported, and 329 were fatal (WHO, 2005b; 2005c).

Marburg hemorrhagic fever has affected many fewer persons than Ebola virus. Thus, the recent large outbreak that was declared over in November 2005 is of particular interest, especially since before this outbreak, cases in children were rare, and in this outbreak, children account for a high proportion of those affected. Transmission of these viruses occurs by direct contact with infected body fluids from animals and humans, such as blood, saliva, vomitus, respiratory droplets, urine and stool, and contact with virus-contaminated objects (e.g., needles, syringes). Persons who prepare, cook, and eat contaminated animals may become infected. Person-to-person transmission occurs, as does infection from direct inoculation. Transmission via semen may occur weeks after recovery (CDC, 2005a; WHO, 2001).

It is extremely important to use proper barrier nursing techniques to prevent secondary cases of Ebola and Marburg virus hemorrhagic fevers to caretakers and families, including use of standard, contact, and airborne isolation precautions. Updated information for infection control for patients with viral hemorrhagic fevers in U.S. hospitals may be found on the CDC website (CDC,2005a). There is also concern about use of the filoviruses as bioterror agents, especially if the viruses could be modified to efficiently spread via aerosol from person-to-person.

Monkeypox

Monkeypox results from an orthopoxvirus which has some similarities to the smallpox virus, variola. It is considered to be the most important orthopoxvirus infection in humans outside of smallpox, which has been eradicated in its natural state. Monkeypox was first identified in laboratory monkeys in 1958, and the first human case was reported in 1970 in a child in the Democratic Republic of the Congo. It is now considered endemic in parts of central and western Africa (DiGiulio & Eckburg, 2004a, 2004b).

In May of 2003, the first cases in the United States of what was later found to be monkeypox were reported among members of a family in Wisconsin (a woman and man in their early 30s and their young daughter). The family had bought two prairie dogs as pets 11 days before the mother developed fever, headache, sore throat, dyspnea, and malaise along with a small papule. The mother subsequently developed a more severe rash with more than 200 lesions. The outbreak was initially misdiagnosed as a possible staphylococcal infection (CDC, 2003a; Sejvar et al., 2004). The daughter presented with more severe illness that included rash, lymphadenopathy, malaise, enlarged tonsils, and fever. She eventually developed encephalitis, became unresponsive, and required intensive care. Initially it was believed that she might have contracted a viral encephalitis (such as from varicella or herpes simplex virus), but the diagnosis of monkeypox was confirmed. A fourth case was diagnosed in the distributor of exotic animals who had sold the two prairie dogs to the family first affected, thus establishing an epidemiological link between them (Reed et al., 2004).

Epidemiological investigation revealed that those two prairie dogs and others were co-housed with an infected Gambian giant rat from Ghana and other exotic rodent species. Additional infected prairie dogs had been sold at swap meets in Illinois, Indiana, and Ohio. In at least one case of monkeypox in this outbreak, an infected prairie dog at an animal clinic transmitted infection to a rabbit, who was the source of primary infection (CDC, 2003a). In this outbreak, 72 cases of monkeypox were reported to the CDC from Illinois, Wisconsin, Indiana, Kansas, Missouri, and Ohio. No specific treatment is known, but supportive and symptomatic care, use of antiviral medications such as cidofovir, and (potentially) vaccinia immune globulin may be useful (Frey & Belshe, 2004). No deaths occurred in this outbreak, and smallpox vaccine was administered both pre-exposure and post-exposure to persons at occupational risk (CDC, 2003b; DiGiulio & Eckburg, 2004b).

This outbreak is an example of how easily a microbe can traverse great distances. It also illustrates a challenge to public health protection, the import of live animals across borders as exotic pets without the necessary oversight (Lashley, 2004). In this outbreak of monkeypox, an embargo on the import, sale, and transport of rodents from Africa and on the sale or movement of prairie dogs was announced on June 11, 2003. However, there is a large illegal trade in animals brought into the United States, and this poses a danger for further instances of transmission of zoonotic diseases (animal diseases that can be transmitted to humans). Another concern is whether or not monkeypox virus has established a reservoir in North America (DiGiulio & Eckburg, 2004a).

In Africa, the mortality rate for monkeypox virus infection is between 1% and 10%, and can be higher in children or those who are immunosuppressed (CDC, 2003a). The usual mode of transmission is through the bite of or close contact with an infected animal. Acquisition of monkypox in Africa is associated with preparation and eating of infected rodents and monkeys (Fleischauer et al., 2005). Person-to-person transmission has been previously documented by

direct contact and respiratory droplet spread, and there is a theoretical risk for airborne transmission (CDC, 2003d). The risk for person-to-person transmission, while considered rare, is of particular concern to health care workers (Fleischauer et al., 2005).

One lesson learned is that when a clinician observes patients with atypical rashes, with or without encephalitis, monkeypox may need to be considered in the differential diagnosis. This is especially true if they have had recent travel to Africa or have exposure to exotic animals or pets (Sejvar et al., 2004). Another lesson is the need for appropriate use of effective infection control. Because severe illness, with no specific treatment, can result from monkeypox virus infection, it is also considered to be a possible agent for use by bioterrorists.

Bovine Spongiform Encephalopathy (BSE)

BSE is a transmissible spongiform encephalopathy (TSE). TSEs are progressively fatal, incurable neurodegenerative diseases that are considered to be prion diseases. Prion proteins that are altered, usually through conformational changes such as misfolding, cause three categories of disease in humans: sporadic, infectious/iatrogenic, and genetic/familial (Glatzel, Stoeck, Seeger, Lührs, & Azguzzi, 2005). Prion diseases include:

- Bovine spongiform encephalopathy (BSE), commonly referred to as "mad cow" disease.
- Kuru, which was spread horizontally among the Fore people of New Guinea who practiced ritualistic cannibalism, often in conjunction with certain death rituals. Kuru has died out in the Fores born since cannibalism has been banned.
- Scrapie, a neurological disease in sheep and goats.
- Creutzfeldt-Jakob disease (CJD) (sporadic, familial or variant), in humans.
- Chronic wasting disease of certain animals such as elk and mink.
- Certain genetically determined or familial disorders (e.g., fatal familial insomnia and Gerstmann-Sträusssler-Scheinker syndrome).

Variant Creutzfeldt-Jakob disease (vCJD) is considered to be causally linked to eating beef products contaminated with the prions that cause BSE (Belay et al., 2005). Classic CJD and vCJD are similar but vCJD occurs in younger persons, particularly under 50 years of age. Patients tend to present with behavioral changes or progressive neuropsychiatric symptoms, such as cerebellar ataxia, cognitive impairment, incontinence, dementia, and progression to mutism. The incubation period is long, usually years. Death is inevitable.

Most publicity and lay public concern about the TSEs has related to potential BSE transmission to humans from eating infected meat or meat products. Another area of concern, especially among health care professionals, is the actual and potential transmission through blood transfusions; transmission via corneal, dura mater, and other transplants; or other iatrogenic means (Lashley, 2002a). Concern has also arisen over potential transmission of prion diseases through inadequately sterilized instruments or devices.

The current BSE epidemic in the United Kingdom emerged in the 1980s, and epidemics have been reported in many other countries. Linkage to vCJD was first noted in a 1996 report (Will et al., 1996). In the United States, no identified cases of BSE occurred in cows until 2003, when it was identified in a dairy cow in Washington that had been imported from Canada. In June, 2005, BSE was confirmed in a 12 year old cow in Texas that was born in the United

States (Belay et al., 2005). In late July, 2005, a third cow was detected in the United States (BSE Update, 2005).

The 2003 case of BSE resulted in a number of economic sanctions against U.S. beef. Another result was the implementation of precautions and preventive activities to protect the food supply and enhance surveillance for clinical features of variant Creutzfeldt-Jakob disease (CDC, 2004). As of June 2005, 156 vCJD patients have been reported from the United Kingdom, 13 from France, 3 from Ireland, and one each from Canada, Italy, Japan, Portugal, and the Netherlands (Belay et al., 2005). One vCJD case has been identified in the U.S. This case was in a Florida woman who died in 2004, and who most likely acquired the disease when she lived in Great Britain (Belay et al., 2005).

Severe Acute Respiratory Syndrome (SARS)

Another example of the rapid emergence of a newly recognized human disease agent is the human coronavirus that causes SARS. SARS has been called the first pandemic of the 21st century (Skowronski et al., 2005). In late 2002, reports began to circulate about an "unusual" respiratory disease in southern China, first thought to possibly be an unusual strain of influenza. In February 2003, a physician who was incubating SARS traveled from Guangdong province to Hong Kong. He apparently transmitted SARS to local residents and other travelers, who then returned to their countries of Vietnam, Singapore, Canada, and Taiwan (Breiman et al., 2003). The WHO first reported an outbreak of "acute respiratory syndrome" in China in the February 14, 2003 issue of the *Weekly Epidemiological Record*, but a period of time passed before international notification occurred (WHO, 2003). The number of reported cases escalated worldwide through May 2003 and then began to decelerate. By mid-July, just under 8, 500 cases had been identified (CDC, 2003c). On July 5, the WHO announced containment of the SARS global outbreak; however, it also warned that SARS was not gone.

Rapid scientific attention resulted in the identification of a "novel" coronavirus as the causative agent (Drosten et al., 2003; Ksiazek, Erdman, & Goldsmith, 2003; Peiris et al., 2003). During the SARS outbreak, various definitions of the disease emerged, and a range of infectivity estimates were made. Isolation was deemed important, and it was noted that there was a very high attack rate among health care workers, as well as clustering of cases in community settings such as apartment buildings in Hong Kong. This demonstrated that SARS was highly contagious through close person-to-person contact. Airborne transmission was postulated as possible; SARS was also rapidly spread through air travel. Containment was difficult and it was uncertain whether a seasonal pattern would develop, much like that of influenza. It was believed that the SARS virus may have originated from wildlife, who are often in crowded markets and may be eaten.

Effects of this outbreak included uncertainties and fear that, in some cases, resulted in debates and policies against students returning to their U.S. universities from Asia after spring break, and travel restrictions to Hong Kong, parts of China (such as Beijing), Toronto, Canada, and Taiwan. Restrictions had political and economic consequences. Even Asian merchants in unaffected areas experienced a decrease in business, and in other areas, conventions and similar activities were canceled.

Identification of SARS cases in Singapore in September 2003 led to concerns about a possible resurgence in the upcoming winter. This concern proved valid. In early January 2004, China announced a case of SARS from Guangdong; reports of other cases soon followed (WHO,

2004). In response, Chinese health officials slaughtered 10,000 civet cats and other mammals and started a campaign against rats and cockroaches to prevent spread (Normile, 2004; Watts, 2004). On retrospective study, SARS-related virus antibodies were found in serum samples collected in May 2001, indicating that some persons were exposed prior to the 2003 outbreak (Senior, 2004; Zheng, Guan, & Wong, 2004).

West Nile Virus

West Nile virus is a single-stranded RNA flavivirus (Higgs, Schneider, Vanlandingham, Lingler, & Gould, 2005). The most frequent means of transmission is from the bite of an infected mosquito, especially *Culex* mosquitoes. Mosquitoes may be involved in a complex cycle when they acquire the virus from viremic wild bird reservoirs or other infected vertebrates, including horses and humans. Transmission may also occur through blood transfusion, tissue and organ transplantation, transplacentally from mother to child, and probably through breastfeeding. West Nile virus infection may also occur through direct inoculation, (e.g., among laboratory workers, or those who handle infected animals) (CDC, 2002). A disturbing report also indicates that nonviremic transmission with horizontal transfer of the virus can occur (Higgs, Schneider, Vanlandingham, Lingler, & Gould, 2005). Clinically, there are three basic outcomes following infection with West Nile virus, as follows:

1. No discernable symptoms. This outcome occurs in about 80% of those infected;
2. Development of West Nile fever, a mild illness with flu-like symptoms that is self-limited in immunocompetent individuals. This occurs in approximately 20% of those infected; and
3. Development of central nervous system infection, usually manifested as encephalitis or meningitis. Signs and symptoms include: fever, headache, gastrointestinal symptoms, stiff neck, alterations in consciousness and mental status such as lethargy, seizures, weakness, focal neurological deficits, movement disorders, and others. This outcome occurs in less than 1% of those infected, most frequently in those who are over the age of 50 years (Dean & Palermo, 2005; Granwehr et al., 2004; Watson, Bartt, Houff, Leurgans, & Schneck, 2005).

West Nile virus was first identified in 1937 from a person in the West Nile district of Uganda. Outbreaks were infrequent until 1996 when more significant outbreaks, with hundreds of persons manifesting neurological signs and symptoms, occurred in countries such as Romania, Russia, and Israel (Lashley, 2002b; Smithburn, Hughes, Burke, & Paul, 1940).

North America has only really been aware of West Nile virus since 1999, when a cluster of unusual cases of encephalitis in New York City heralded the arrival of West Nile virus in North America (CDC, 1999a; Lashley, 2002b). That year, 62 human cases were identified (CDC, 1999b). This introduction has been called the "perfect microbial storm" because certain factors were present at that point in time (Glaser, 2004, p.557). These factors included large, non-immune animal and human populations; multiple vectors; and a favorable environment for transmission and dissemination. West Nile virus spread quickly across the continent, and within 5 years established itself as endemic in the United States (Glaser, 2004). As of June 21, 2005, the number of human cases of West Nile Virus reported to the CDC was 2,539, with at least one case reported in each state. This is likely an under report, since West Nile virus infection is not a nationally notifiable disease (CDC, 2005b).

No specific treatment for West Nile virus is available. Prevention methods center around minimizing the opportunity for mosquito bites through the use of environmental controls, personal protection, surveillance, and reporting activities. "Emerging Infectious Diseases: Trends and Issues," by Lashley and Durham (2002), provides additional details about preventive methods. Personal protective behaviors associated with decreased risk of mosquito bites include wearing long sleeves and long pants, using insect repellant, avoiding exposure to mosquitoes, and avoiding outside leisure activities at dawn and dusk (Loeb et al., 2005). Health care providers should be able to educate consumers about protective measures. They should also be alert to the possibility of an outbreak of West Nile virus anywhere across North America, in eastern Europe, Israel, Africa, and elsewhere.

Avian Influenza

On the possibility of an avian influenza pandemic arising, Michael Osterholm, director of the Center for Infectious Disease Research at the University of Minnesota, has said "We're screwed" if it hits soon (Querna, 2005, para. 3). To some extent, the influenza virus has excited the imagination to a lesser degree than many other emerging viral diseases. However, it indeed fits into this category because of its ability to genetically change often and rapidly. This ability to mutate is one of the reasons that each year there are seasonal epidemics, and the necessity to produce vaccines targeted for the appropriate strain(s) in the upcoming influenza season.

Influenza virus types A and B infect humans and can cause widespread outbreaks. Type A tends to be the most severe. Influenza virus subtypes are referred to by their hemagglutinen (H) and neuraminidase subtypes (N) which are surface glycoproteins of the virus, such as the avian influenza virus subtype H5N1 (Moorman, 2003). The influenza virus is considered to have the potential for use as an agent for bioterrorism, most probably by alteration to a mutated form with greater infectivity, greater virulence, more efficient human-to-human transmission, and antiviral resistance.

There have been several great influenza pandemics, notably in the years:

- 1918-19: "Spanish flu" (caused 20 to 40 million deaths worldwide; a large proportion of deaths occurred in healthy adults 15 to 35 years of age)
- 1957: "Asian flu"
- 1968: "Hong Kong flu"
- 1977: "Russian flu"

In the United States each year, approximately 100,000 people are hospitalized with influenza, and about 36,000 die. Thomas Abraham warned of "a biological tsunami" brewing in regard to avian influenza (Abraham, 2005). There is fear that avian influenza could become pandemic in the very near future.

Avian influenza viruses are those carried by birds (usually wild birds)who then shed virus in saliva, nasal secretions, and feces. Birds or fowl become infected when they come into contact with secretions or excretions from infected birds, most often through fecal-oral transmission. Transmission also occurs through contact with surfaces or materials such as feed, water, cages, or dirt that are contaminated with the virus. Contaminated cages, for example, can carry the virus from one place to another.

The first documented direct transmission of an avian influenza virus (H5N1) to humans occurred in 1997 in Hong Kong. Limited human-to-human transmission was also thought to occur. Severe respiratory disease occurred in 18 healthy young adults and children and 6 died. Live poultry markets were the source of the virus strain in this outbreak. Many Asian people prefer to buy fresh foods at so-called "wet-markets," which are increasing in number. In both influenza and SARS, wet markets have been implicated as sources of virus transmission. This illustrates a cultural influence on emergence of infectious diseases.

Quarantine and depopulation (or culling of birds) are common controls for outbreaks of avian influenza. For example, the 1997 outbreak was controlled by slaughter of the poultry population. More than 1.2 million chickens and 0.3 million other poultry were killed and imports of chickens from Hong Kong and China were banned by other countries (Bridges et al., 2002).

In 1999, avian influenza viruses H9N2 were isolated in Hong Kong from children with mild influenza. One died. In 2003, the avian influenza virus strain H7N7 occurred in poultry farms in the Netherlands, spreading to Germany and Belgium. Infection, mainly conjunctivitis, occurred in humans, with 1 death. The 2003 outbreak was also controlled by the destruction of over 30 million domestic poultry. In British Columbia, Canada, an outbreak of avian influenza H7N3 occurred in poultry; human cases presented with conjunctivitis and mild flu-like symptoms (Monto, 2005; Tweed et al., 2004).

In 2003, the avian influenza virus strain, H5N1, emerged in 2 family members in Hong Kong after traveling in China. Also in 2003, an outbreak of avian influenza virus, H5N1, occurred in South Korea, and in 2004, it emerged in Vietnam and Thailand. Many countries banned the import of poultry products from the Asian countries affected. Other countries in which poultry were infected included Canada, Japan, Laos, North Korea, China, Cambodia, Malaysia, Rumania, and Indonesia. Human cases presented with severe respiratory infection and out of 108 known and confirmed cases recognized from January 2004 to June 28, 2005, 54 died. Probable human-to-human transmission was recognized (CDC, 2005c; Ungchusak et al., 2005). In rural Asia, many households maintain poultry for income and food, and increase the opportunity for human exposure (Stöhr, 2005).

Of concern is the possible mutation of the avian influenza virus to allow sustained person-to-person transmission. Noting the spread of avian influenza in 2004 to 2005, various conferences have addressed plans for surveillance and control, vaccine production, and treatment involving global cooperation among agencies such as the WHO, the Food and Agriculture Organization, and the World Organization for Animal Health (Avian influenza - Eastern Asia, 2005; Knobler, Mack, Mahmoud, & Lemon, 2005; WHO, 2005a).

A(H1N1) pandemic

In the 2009 flu pandemic, the virus isolated from patients in the United States was found to be made up of genetic elements from four different flu viruses – North American swine influenza, North American avian influenza, human influenza, and swine influenza virus typically found in Asia and Europe – "an unusually mongrelised mix of genetic sequences. This new strain appears to be a result of reassortment of human influenza and swine influenza viruses, in all four different strains of subtype H1N1.

Preliminary genetic characterization found that the hemagglutinin (HA) gene was similar to that of swine flu viruses present in U.S. pigs since 1999, but the neuraminidase (NA) and matrix protein (M) genes resembled versions present in European swine flu isolates. The six genes from American swine flu are themselves mixtures of swine flu, bird flu, and human flu viruses. While viruses with this genetic makeup had not previously been found to be circulating in humans or pigs, there is no formal national surveillance system to determine what viruses are circulating in pigs in the U.S.

In April 2009, an outbreak of Influenza-like illness occurred in Mexico and the USA; the CDC reported seven cases of novel A/H1N1 influenza. By April 24 it became clear that the outbreak of ILI in Mexico and the confirmed cases of novel influenza A in the southwest US were related and WHO issued a health advisory on the outbreak of "influenza like illness in the United States and Mexico". The disease then spread very rapidly, with the number of confirmed cases rising to 2,099 by May 7, despite aggressive measures taken by the Mexican government to curb the spread of the disease.[18]

On June 11, 2009, the WHO declared an H1N1 pandemic, moving the alert level to phase 6, marking the first global pandemic since the 1968 Hong Kong flu.

On October 25, 2009 U.S. President Barack Obama officially declared H1N1 a national emergency(The Daily Herald, 2010) Despite President Obama's concern, a Fairleigh Dickinson University PublicMind poll found in October 2009 that an overwhelming majority of New Jerseyans (74%) were not very worried or not at all worried about contracting the H1N1 flu virus.

A study conducted in coordination with the University of Michigan Health Service is scheduled for publication in the December 2009 *American Journal of Roentgenology* warning that H1N1 flu can cause pulmonary embolism, surmised as a leading cause of death in this current pandemic. The study authors suggest physician evaluation via contrast enhanced CT scans for the presence of pulmonary emboli when caring for patients diagnosed with respiratory complications from a "severe" case of the H1N1 flu.

March 21, 2010 worldwide update by the U.N.'s World Health Organization (WHO) states that "213 countries and overseas territories/communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 16,931 deaths.(WHO, 2009)

As of May 30, 2010 worldwide update by World Health Organization(WHO) more than 214 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including over 18,138 deaths.

The research team of Andrew Miller MD showed pregnant patients are at increased risk.(Businessweek , 2010) It has been suggested that pregnant women and certain populations such as native North Americans have a greater liklihood of developing a T helper type 2 response to H1N1 influenza which may be responsible for the systemic inflammatory response syndrome that causes pulmonary edema and death. (Vivian C, 2009)

EIDs and the Future

The emergence and re-emergence of infectious diseases involves many interrelated factors. Global interconnectedness continues to increase with international travel and trade; economic, political, and cultural interactions; and human-to-human and animal-to-human interactions. These interactions include the accidental and deliberate sharing of microbial agents and antimicrobial resistance and allow the emergence of new and unrecognized microbial disease agents. As the 21st century begins, already new agents have been identified, and new outbreaks have occurred. Solutions to limiting the spread of EIDs will require cooperative efforts among many disciplines and entities worldwide.

Most public health experts do not ask *if* one or more large scale pandemics will occur. They ask "*When?*" Avian influenza unfortunately holds the potential to be the disease that will illustrate that point. While there have been steps taken for effective prevention and strategies developed for dealing with a pandemic, globally these preparations are far from adequate. Many ethical and social issues have not been addressed in depth.

Paradoxically, while technology has allowed us to discover and treat new diseases and pathogens, it has also contributed to the evolution of the diseases themselves. Broad-spectrum antibiotics, immunosuppressive drugs, prosthetic and transplantation surgery have each created a niche for opportunistic pathogens. Indeed, each breakthrough in the prolongation of human life and ability to treat heretofore fatal diseases is inevitably followed by an interesting list of Infectious Diseases challenges. On a broader scale, the scope of Infectious Diseases will be increasingly challenged by societal pressures related to overpopulation, air travel, global warming, conflict, famine, deforestation and bioterrorism.

Long-term strategies are discussed in detail by the IOM report (Smolinski, Burger, & Lederberg, 2003) and others (Lashley, 2004). Among the keys to success will be adequate financial resources, knowledge sharing, rapid communication, and cooperation among health care professionals and experts in human behavior, politics, economics and other disciplines. For nurses, this must include the awareness of unusual symptoms or clusters of disease; provision of appropriate education; and acquisition of equipment and supplies needed to maintain infection control, and the authority to implement these, to assure the best possible patient and family care in the event of infectious disease.

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