NEW AND EMERGING WATERBORNE INFECTIOUS DISEASES

Louis H. Nel and Wanda Markotter
Department of Microbiology and Plant pathology, University of Pretoria, South Africa

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Contents

Summary

Waterborne diseases are classified as those transmitted through the ingestion of contaminated water and water acts as the passive carrier of the infection agent. Most commonly, waterborne infections are caused by human and animal fecal pollution of water and this go hand in hand with scarcities of water supply and poor water sanitation.

Organisms that jump species or which are already present in a non-pathogenic form and now become pathogenic through specific modification, mutation or recombination would usually cause new diseases.

Many bacterial diseases however, fall in the category of re-emerging diseases due to resistance to antibiotics. Apart from these reasons, the past few decades have seen increases in global traveling, population explosions (leading to poverty and breakdown of public health systems) and incursions into virgin ecosystems with an increased opportunity for zoonoses and related events that lead to broader host ranges and wider distribution of pathogens.

Taken together all of these factors play some role in the present time emergence and re-emergence of infectious diseases around the globe. Bacteria, protozoa and viruses are the cause of many emerging and new waterborne infectious diseases and these diseases will be discussed in more detail in the following sections.

1. Infectious Diseases

Infectious diseases are caused by microbial pathogens that have parasitized and plagued their cellular host species since time immemorial. Known microbial pathogens of man include agents of fungal, protozoan, bacterial, clamydial, rickettsial, viral, viroidal and infectious proteinaceous nature.

Spectacular advances in public health practices, including some hugely successful immunization programs, have perhaps led to some complacency with respect to serious infection in the developed world. However, globally 45% of all deaths and 63% of early childhood deaths are still caused by infectious diseases (WHO, 2000).

Of these infectious diseases, six can be identified as the leading high mortality rate diseases: AIDS, acute respiratory infection, diarrheal diseases, malaria, measles and tuberculosis. Although all of these diseases can be controlled by improvements in the quality of water and sanitation, immunization, education and early diagnosis, the scale of the problem as well as political and monetary priority or ability hamper such ideals.

The origin of many of these disease-causing infectious agents is not clear, but following on large population growths with concomitant densely populated geographical regions, humans have become a reservoir for some of these, with now well-established human-to-human transmission cycles.

A relevant example of such an infectious disease is Acquired Immunodeficiency Syndrome (AIDS), a disease caused by the Human Immunodeficiency Virus (HIV), which is today exclusively and directly transmitted from human to human.

However, a great many infectious diseases are zoonoses, meaning that they are naturally transmitted between vertebrate animals and man – in fact more than 200 such zoonotic diseases are known. Our example of HIV/AIDS (as a disease with an established human reservoir), also serves as an example of a disease with a zoonotic origin.

The ancestral viral agent of this disease has been shown to be Simian Immunodeficiency Virus (SIV), which was transmitted from non-human primates to man on several occasions and subsequently led to the evolvement of HIV1 and HIV2 respectively, following two such zoonotic events.

Human-to-human, as well as zoonotic transmission of infectious microbial agents can occur through several different routes. Infectious diseases are typically transmitted through the skin or eyes (direct contact, insect vectors, bite wounds, sexual contact).

In other cases the agents are airborne and infect the epithelial cells lining the respiratory tract from where further systemic infection may proceed.

However, very important additional sources of infectious microorganisms are contaminated food and water – with a route of infection through the mouth and alimentary tract, or through the respiratory system, as will be discussed in the following sections of this chapter.

2. New, Emerging, Re-emerging and Resurgent Infectious Diseases

Numerous definitions have been formulated in describing new, emerging, re-emerging and resurgent infectious diseases. Generally however, new diseases are synonymous with emerging diseases and can be regarded as diseases first described in the period from the 1970s to1990s.

Most of these diseases are caused by specific modifications of agents that are already present in the environment (e.g. in a different host reservoir). These agents then evolve, mutate or are otherwise epidemiologically affected by changing conditions or other selective advantage.

Typically, re-emerging diseases are those diseases that have persisted at a subdued level in the population and recur as a result of antimicrobial drug resistance or any other changes which might favor dramatic increases in disease incidence. Re-emerging diseases can also be described as resurgent, pertinently referring to an abrupt increase in incidence or geographic distribution of the particular disease.

An appropriate definition was formulated in the 1992 Institute of Medicine Report as follows (http://fas.org/promed): "emerging infections are those whose incidence in humans has increased since the 1980s or threatens to increase in the near future.

Emergence may be due to the spread of a new agent, to the recognition of an infection that has been present in the population but has gone undetected, or to the realization that an established disease has an infectious origin. Emergence may also be used to describe the reappearance (or "reemergence") of a known infection after a decline in incidence."

At least 29 pathogenic microbes and infectious diseases have been recognized since 1973, whereas over 20 diseases have re-emerged due to various factors since the 1980s.

The emergence and re-emergence of diseases are clearly related to changes in the infectious pathogen, the vector or transmission system and the host population.

Apart from drug resistance already mentioned, some other epidemiologically important changes are: mutation which leads to increased virulence; changes in the distribution or activity of vectors; globalization and increased travel; war; population explosions; climatic and ecological changes; geographical displacement of species; movement into previously uninhabited areas; poverty and breakdown of healthcare systems; changes in agriculture and industrialization.

3. Waterborne Infectious Diseases

Most waterborne infectious disease is related to fecal pollution of water sources, resulting in the so-called fecal-oral route of infection. Importantly, these infections can be both human-to-human (poor water sanitation) and zoonotic (animals and humans sharing water resources, combined with poor sanitation).

Many microorganisms can survive (e.g. virus particles) or survive and flourish in water with minimal nutrients (e.g. aquatic bacteria and protozoan parasites). Therefore, safe and healthy drinking water is crucial as far as this aspect of public health is concerned.

At least 20% of the world's population does not have access to safe drinking water. This, combined with poor sanitation services, directly contributes every year to three to five billion cases of diarrhea and 3 million deaths.

In addition, some important water-borne infectious diseases have more recently been introduced by advanced practices such as the aerosolization of water, common in showers (for personal hygiene) and through spraying in markets, nurseries and the like (towards maintaining large scale air cooling).

4. Viral Agents

A variety of pathogenic viruses is waterborne and is sometimes also referred to as diarrhea viruses. Although diarrhea does not seem to be as dramatic a disease as AIDS, smallpox, rabies, polio and the like, these viruses are of great economic and medical importance.

Viral diarrhea continues to be a major cause of morbidity and mortality worldwide, resulting in uncounted millions of child deaths every year. The list of waterborne viruses includes Adenoviruses (types 40 and 41, specifically),

Astroviruses, Caliciviruses, Enteroviruses (different Picornavirus genera), Hepatitis E like viruses and Reoviruses (including Rotaviruses).

Virus	Disease and geographical incidence	Reasons for emergence	Clinical features	Detection and control/prevention
Astroviruses	Astrovirus enteritis, Worldwide	First discovered in 1975, and at present second only to Rotavirus and Norwalk-like viruses as cause of childhood diarrhea.	Incubation period 24-36h: self-limiting watery diarrhea, lasts for 2-3 days. Nausea/vomiting, abdominal pain and low grade fever	Detected in stools by immune electron microscopy (IEM) and immunofluorescence (IF) of infected tissue cultures. Treatment supportive with oral rehydration fluid (ORF) or intravenous rehydration (IR). No vaccine available.
Caliciviruses	Calicivirus enteritis, Worldwide	Norwalk-like viruses were identified in 1972, Increased incidence. Zoonotic caliciviruses are likely to emerge from the worlds' oceans.	Abrupt onset Symptoms are diarrhea with nausea and vomiting. Upper respiratory symptoms and fever less common.	Detected in stools by electron microscopy (EM) and IEM. Treatment supportive with ORF or IR. No vaccine available.
Enteroviruses	Aseptic meningitis and various other syndromes. Worldwide	Rapid genetic evolvement of new strains. Development of resistance to anti-viral drugs	Incubation time 3-5 days Often self-limiting, mild or asymptomatic. Typical symptoms can be blisters on the oral cavity, palms and soles, ulcers, and fever. Complications lead to aseptic meningitis, encephalitis, myocarditis, pericarditis, pneumonia, and paralysis.	Diagnosis in throat or faecal samples or specimens from the affected part of the body: e.g. cerebrospinal fluid (CSF), biopsy material, and skin lesions. Serology can be used but it is complicated because of the large number of serotypes. Treatment focuses on management of complications No vaccine for non-polio enteroviruses.
Hepatitis E-like viruses	Hepatitis. Frequent epidemics in China, Asia, Africa, Mexico and Central America	New waterborne infectious viral agent, New waterborne viral agent - First characterized in the 1990's. Strong evidence for zoonoses.	Incubation time 15-60 days; case- Symptoms similar to other types of viral hepatitis - include malaise, anorexia, abdominal pain, arthralgia, and fever Pregnant women have higher mortality rates	Diagnosis based on the epidemiological characteristics of the outbreak and by serological exclusion of hepatitis A and B viruses. Confirmation by IEM in faeces or liver biopsy. Supportive treatment No effective vaccine.

Table1. Waterborne new and emerging diseases of viral origin.

Although all of these viruses have the potential to become re-emerging viruses given the appropriate conditions and circumstances, only particular members of the Astroviruses, Enteroviruses, Hepatitis E-like viruses and the Caliciviruses can at present be regarded as emerging or re-emerging and will be discussed further. Concise information on the disease, nature of emergence, clinical syndromes, detection and treatment/control is presented in Table 1.

4.1. Caliciviruses

This is a group of small nonenveloped single-stranded RNA viruses. The calicivirus name originates from the cuplike appearance of stained particles under the electron microscope. Several lines of evidence suggest that caliciviruses emerge from ocean reservoirs, with subsequent zoonotic and interspecies movement. Among the known Calicivirus pathogens of humans are the Norwalk and Norwalk-like viruses and the Sapporo and Sapporo-like viruses.

The Hepatitis E virus (HEV) was also formerly classified as a Calicivirus, based on physicochemical and biological properties. However, the genome organizations of HEV and the Norwalk-like viruses are different and virus codon usage is very different from that of other Calicivirus genogroups. On the basis of homologous regions across the genome and the production of subgenomic RNA during HEV replication, it has also been suggested that HEV might be related to a non-enveloped alpha-like virus, by genetic recombination. New recommendations of the International Committee on the Taxonomy of Viruses (ICTV) now place HEV into a separate family, called HEV-like viruses.

The human caliciviruses cannot be cultured *in vitro*, but they are very widely distributed throughout the world and infection is common, especially in children. Although it is thought that pathogenic caliciviruses are likely to continue emerging from the worlds' oceans in various forms, only the Norwalk-like viruses are at present and from a public health point of view, of emerging importance. Norwalk virus was first identified in 1972 after an outbreak of gastrointestinal illness in Norwalk, Ohio. Later, other viruses with similar features were described and called Norwalk-like viruses. These viruses are common causes of nausea, vomiting, diarrhea, and abdominal cramps with occasional headache and low-grade fever.

The disease starts 24-28 h after exposure and last about 16-60 h. While Norwalk-like viruses cause sporadic and epidemic gastroenteritis in all age groups of humans, loss of fluids and electrolytes are particularly serious in the very young and elderly. Transmission is by the fecal-oral route, but many documented cases are linked to the consumption of raw shellfish, especially oysters and clams. Shellfish become contaminated via stool from sick food handlers or from raw sewage dumped overboard by recreational and/or commercial boaters. Contaminated water, ice, eggs, salad ingredients, and ready-to-eat foods are other sources of infection. The only source of calicivirus is feces from infected persons, thus shellfish-related outbreaks will continue to occur where appropriate standards for proper disposal of human sewage are not in place or enforced. It has been shown that caliciviruses can pass through water purification filters and remain infectious at standard levels of chlorine in drinking water.

4.2. Enteroviruses

Enteroviruses, as the name suggests, are positive sense RNA viruses of the family *Picornaviridae* that flourish mainly in the intestinal tract. The genus *Enterovirus* is now divided into five major groups: polioviruses, group A coxsackieviruses, group B coxsackieviruses, echoviruses and (newer) enteroviruses. Enteroviral illnesses are very common, but do not usually or often result in serious disease. In fact, non-polio enteroviruses are second only to rhinovirus (also a picornavirus and etiological agent for the common cold), as the most common viral infectious agent in humans. In addition to the three different polioviruses, there are 61 non-polio enteroviruses that can cause disease in humans: 23 Coxsackie A viruses, 6 Coxsackie B viruses, 28 echoviruses, and 4 other enteroviruses. Polio is certainly not an emerging disease and in fact, eradication of polio by worldwide immunization now seems to be achievable. However, many other members of the enterovirus family can be considered truly emerging, whereas other are of emerging importance because of potential resistance to anti-enteroviral drugs available for therapeutic intervention of viral replication.

The fecal-oral route is thought to be the predominant mode of enterovirus transmission, although some exceptions occur. In the cases of coxsackie A21 (spread mainly by respiratory secretions) and enterovirus 70 (shed in tears and spread via fingers and fomites), indirect transmission is seen with poor sanitary conditions and will then also occur via contaminated water. Transmission of the virus occurs easily and the majority of infections are symptomless or mild in nature, the most common effect being a non-specific illness, with fever. However, some serotypes of enteroviruses may cause serious clinical syndromes like acute paralysis, encephalitis, meningitis, myocarditis, hepatitis and chronic infection (particularly in immunocompromised individuals).

Some enterovirus serotypes have been responsible for serious, large epidemics throughout the world in recent years. Notably, since 1996, echovirus infections have been responsible for several large epidemics of aseptic meningitis in Japan, Europe and the Middle East. These epidemics involved different highly infectious serotypes of the virus, *viz* types 4, 9 and 30, but also new genetic variants of these viral serotypes. Similarly, Enterovirus 71 (EV71) has caused major disease outbreaks in North America, Europe, Malaysia, Japan and Australia since 1995 and involved more than a million cases in Taiwan in 1998. In the latter epidemic, case fatality among children under 5 years of age was 20%, with pulmonary complications and meningoencephalitis the primary causes of death. Evidence based on the molecular characteristics of EV71 virus isolates suggests rapid evolvement and genetic diversification that may also involve alteration in the untranslated regions of the viral genomes. Such mutations not only have implications of a continuation of future epidemics, but also of changes in viral virulence.

4.3. Astroviruses

These are small, uniformly round viruses with a star like appearance that were first discovered in 1975. Astroviruses are commonly spread through fecal-oral contamination. Following a 1-4 day incubation period, the clinical symptoms present as watery diarrhea that lasts for 2-3 days. Recent evidence has shown the prevalence of this virus to be much higher than previously thought. The Astroviruses now appear to be endemic throughout the world and they cause gastrointestinal disorders not only in humans (there are at least 7 human astrovirus serotypes), but also in many other vertebrates. While the disease is most often mild and does not result in severe dehydration, it can be more serious in immuno-compromised children and adults, and elderly institutionalized patients. It appears to have a very low pathogenicity in adults, but the Astroviruses are second only to Rotavirus and Norwalk like viruses as a cause of childhood diarrhea. The virus can be present in municipal drinking waters because of the inability of prescribed chlorine levels to inactivate the virus.

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Biographical Sketches

Prof Louis H Nel holds BSc (HONS) and MSc (all cum laude) in microbiology from the University of the Free State and a PhD in molecular virology from the University of Pretoria. He is currently employed by the University of Pretoria where 17 students have been awarded their MSc and/or PhD research degrees with him as the promoter over the past four years. Since the year 2001, Prof Nel has published 23 papers in Science Citation Indexed Journals and /or chapters in books.

Prof Nel furthermore regularly acts as critic for leading journals and as referee for local and international project proposals. In this regard he is consulted throughout southern Africa and the larger continent as a leading expert on Lyssavirus research, in particular. However, he has also made significant contributions to national working groups like the Legionella action group and working groups of the Water Research Council and of the South African government (Dept of Science and Technology). His extensive international contributions include those related to the IAEA and the FAO (UN), by whom he is regularly approached as an expert consultant in the molecular diagnosis of infectious diseases.

Miss. Wanda Markotter started her undergraduate degree in Molecular Biology in 1993 at the University of Pretoria. In 1996 she completed an Honours degree, cum laude, in Microbiology at the University of Pretoria and received an M Sc degree in Microbiology in 2002.

Wanda is at present employed as a junior lecturer in the Department of Microbiology and Plant pathology at the University of Pretoria and has been involved in teaching postgraduate and pre-graduate course in molecular biology of bacteria and viruses as well as molecular techniques. Her research focus is on viral diseases that affect both humans and animals. She is also involved in various scientific organizations such as the Molecular and Cellular biology group (MCBG), Infectious disease Society of Southern Africa, Southern and Eastern Africa rabies group (SEARG) and the World academy of Young scientists (WAYS).