Hot Topics in Infectious Diseases

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In infectious diseases, unlike many other fields. there has been significant interest in recent occurences such as:

- tainted spinach,
- lettuce and
- carrot juice.

To mark the 10 year anniversary of Infection Control Week at the University of Manitoba, this article will review 10 of the hottest topics in infectious diseases, public health and infection prevention and control, that have generated significant media attention over the past 10 years. The topics are organized alphabetically and not by level of interest or importance.

Alcohol hand sanitizers

The most fundamental means by which infection can be prevented is through hand hygiene. Hand hygiene is a general term that applies to either:

- hand washing,
- antiseptic hand wash,
- antiseptic hand rub, or
- surgical hand antisepsis.

Hand washing refers to the washing of hands with plain (non-antimicrobial soap). Plain soap contains detergent, but not antimicrobial agents. Their cleaning activity is related to their detergent properties which are capable of removing soil and other debris from the hands. Antimicrobial soaps that contain agents, such as chlorhexidine, are capable of decreasing the microbial flora in the hands.

A significant development in hand hygiene is the development of alcohol-based hand rubs. These hand rubs are alcohol containing preparations that consist of 60% to 95% ethanol or isopropyl alcohol (or others), which are highly effective in killing microorganisms on the hands of healthcare providers. The alcohol-based handrubs are very effective in sanitizing the hands of healthcare providers, particularly in killing gram-positive and gram-negative bacteria including multidrug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE). Alchohol-based hand rubs are effective against *Mycobacterium tuberculosis* fungi and most viruses; however, they are not effective against bacterial spores and protozoan oocysts. These agents are faster and more convenient to use than conventional hand washing and are particularly beneficial for use in offices and healthcare facilities, where hand washing stations are not readily available. The popularity of these agents has increased to the extent that they are now readily available to the consumer market.

"AROs"

The generic term antimicrobial resistant organisms (AROs), is most frequently used to encompass microorganisms, such as MRSA, VRE and bacteria that produce extended spectrum ß-lactamases (ESBLs). It is presumed that AROs have arisen by means of natural selection of organisms that have evolved and mutated to survive in the presence of antimicrobial agents,

which were once effective in controlling them. *Staphylococcus aureus* (*S. aureus*) was once uniformly susceptible to penicillin; however, with the wide scale use of this antibiotic, resistance eventually developed. The penicillin-resistent strains were easily controlled using cloxacillin (cloxacillin is an agent very similar to methicillin). Unfortunately, some strains of *S. aureus* have modified penicillin-binding proteins, rendering all ß-lactams essentially useless against this pathogen. With the emergence of MRSA, there has been an increased reliance upon non-ß-lactam agents for the management of MRSA infections. These include:

- parenteral vancomycin,
- clindamycin,
- trimethoprim/sulfamethoxazole (TMP/SMX) and
- quinolones.

MRSA has traditionally been observed to colonize or cause infections in patients who have had prior exposure to healthcare facilities, such as:

- hospitals,
- long-term care facilities and
- surgical centres.

However, more recently, a new variant of MRSA has been observed. This microorganism, which has been termed community-acquired MRSA (CA-MRSA), is a unique and distinct strain of MRSA. Unlike the hospital-acquired strains, which generally lead to colonization, the CA-MRSA strain is associated with deep necrotizing abscesses. This microorganism produces the Panton-Valentine leukocidin, which inactivates white blood cells leading to abscesses. Practitioners should suspect CA-MRSA infections when patients present with non-resolving furuncles or deep necrotizing abscesses. Agents which are used for the management of CA-MRSA infections include TMP/SMX and clindamycin.

VRE appeared within healthcare institutions in the late 1990s and early 2000s. *Enterococcus spp.*, is a microorganism that is generally susceptible only to ampicillin and vancomycin. Although the precise mechanism whereby VRE arose is uncertain, it is speculated that excessive use of vancomycin may be the reason. This may be a direct fallout from the management of MRSA infections. Over the past 10 years, after an initial sharp rise in the incidence and prevalence of VRE, there has been a gradual decline. This microorganism is traditionally observed in healthcare facilities and is not a community-acquired pathogen. It usually colonizes in the GI tract and can lead to deep and invasive infections in those who are profoundly debilitated.

Microorganisms producing ESBLs have been observed in residents of long-term care facilities and some who are hospitalized. The most frequent pathogens are *Escherichia coli* and some strains of *Klebsiella spp*. These organisms are uniformly resistant to most ß-lactam agents, but are susceptible to other agents, such as quinolones and TMP/SMX.

Bioterrorism

In 2001, anthrax was released into the American postal system. Concerns of bioterrorist activity were raised. Bioterrorism is the deliberate release of biological agents by terrorists against civilian populations. Unlike bombs, biological agents specifically target humans and other living creatures. In addition to causing disease, bioterrorist activities lead to societal fear and panic, which

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helps to destabilize society through its psychological impacts. However, not all pathogens, however, are suitable as bioterroristic agents. Table 1 demonstrates the key properties of candidate agents for bioterrorism. Agents which are suitable for bioterrorism are demonstrated in Table 2. The key to controlling bioterrorist activities include prompt recognition of syndromes or deaths due to infectious agents, even before an infectious agent is confirmed. Clearly, based upon the occurrences in 2001, bioterrorist activity could lead to grave consequences.

Table 1

Key properties of candidate agents for bioterroism

- Ease of acquisition and production
- Potential to be aerosolized.
- Particle size, 1 µm to 10 µm
- Dispersal over a wide geographic area
- Resistance to sunlight, desiccation and heat
- Potential for a lethal or a debilitating disease
- Person to person transmission
- Lack of effective therapy/prophylaxis

Clostridium difficile

This gram-positive, spore-forming, anaerobic bacillus received this name because it was difficult to grow. This microorganism causes disease through the release of toxins which can damage the bowel lining. The clinical manifestations include:

- Asymptomatic carriage
- Diarrhea
- Fulminant diarrhea
- Pseudomembranous colitis
- Toxic megacolon
- Possible death

Infection occurs when spores are ingested and an antibiotic is taken. The antibiotic disrupts the indigenous bowel flora allowing the *clotridium difficile (C. difficile)* spores to germinate and microorganism to multiply producing toxins.

Treatment is with metronidazole; however, vancomycin may also be used in specific circumstances. Recurrence rates range between 7% and 10% with a mortality rate that may be in excess of 8%. Some individuals have multiple relapses and the best technique for the management of these relapses is still not known. The increased incidence and prevalence of *C. difficile* disease came to our attention in recent reports from Quebec, where hospitalized patients were experiencing excess morbidity and mortality from this condition. Unfortunately, alcohol hand rubs unfortunately are not effective against the *C. difficile* spores.

Table 2

Potential candidates for biological terrorism

Bacteria

- *Bacillus anthracis*: Anthrax
- *Yersinia pestis*: Plague
- *Coxiella burnetii and* Q-Fever
- *Francisella tularensis:* Tularemia
- *Brucella spp*: Brucellosis

Viruses

- Smallpox
- Viral encephalitis
- Viral hemorrhagic fevers

Toxins

- Botulism toxins
- *Staphylococcal enterotoxin B*

The key to preventing *C. difficile* disease is:

- avoidance,
- judicious use of antimicrobial agents and
- aggressive attention to the environment to minimize the number of spores.

Attention to the environment will minimize the hospitalized patients' chance of coming in to contact with this pathogen.

E. coli 0157:H7

This bacteria came to attention in 1982 following an outbreak of bloody diarrhea, that affected people across the US. The source was traced back to contaminated hamburgers sold at a fast food restaurant. In 2000, in Walkerton, Ontario, seven people died and dozens of others were made very ill by consuming the municipal water which was contaminated with *Escherichia coli: 0157:H7*. Since that time, there have been numerous reports of *E. coli 0157:H7* disease-related to the consumption of food products, such as alfalfa sprouts and most recently, fresh spinach from the US. These foods likely became contaminated when animal feces were used as fertilizer or from runoff from farmer's fields with animal pastures. With regards to humans and the connection with ground beef, it is presumed that the *E. coli 0157:H7* contained in the cattle feces, contaminates the carcasses at the time of slaughter. When the ground beef is created, particles of animal feces are ground into the beef and subsequently if a meat patty is not adequately cooked (achieving a core temperature of 71 C), the microorganism may survive to be ingested and may subsequently lead to bloody diarrhea or the Hemolytic uremic syndrome. Thorough cooking of all ground beef products is mandatory.

Human Papilloma Virus

The human papilloma (HPV) virus has been implicated in a number of disease processes in humans, ranging from common skin warts to cervical dysplasia/cancer. It is estimated that as many as 50% to 75% of sexually active people acquire a genital HPV infection at some point in their lives. Most of these infections are asymptomatic, but can also lead to genital warts, condyloma acuminata, or squamous cell cancer of the ano-genital tract, which can carry a potential heavy burden of illness. A variety of different virus types exist, with variable propensity to cause cervical cancer (HPV 16, 18, 45, 31), or ano-genital warts (HPV 6, 11). While cervical cancer and ano-genital warts have been long recognized, intense interest in the HPV has arisen, as there are now several vaccines capable of preventing HPV-related disease. These novel vaccines provide an insight into what the future will hold for the prevention of infectious diseases and neoplasia.

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Influenza

Respiratory tract infections are common during the autumn, winter and spring months. For the majority of respiratory pathogens, the only means of prevention is direct avoidance as, a

vaccine does not exist. For influenza A and influenza B, a vaccine does exist. The strains of influenza virus selected for the vaccine are based upon the probability of those strains appearing or reappearing in the population. In addition to the vaccine, some antiviral agents may be of benefit in controlling or preventing influenza. In recent years, concern of an influenza pandemic has arisen. This fear has been further accentuated by how easily severe acute respiratory syndrome (SARS) spread across the world. Its ease of transmission will be related to the lack of human immunity against this presumably new influenza strain. With modern day global travel, a calamity of greater proportion than the influenza epidemic of 1918 is anticipated.

Avian influenza

Avian influenza is a viral infection that has been observed to spread quickly among birds by means of infected secretions and droppings. Some birds may carry the virus and infect other birds without becoming sick themselves. There is a current outbreak occurring in Asia and has been attributed to the H5N1 strain of the influenza virus. Although a number of human cases and subsequent deaths have occurred, these have been primarily in Asia and the Middle East. It is presumed that human acquisition is by means of direct contact with infected birds and their secretions, either during their:

- slaughter,
- defeathering,
- butchering and/or
- preparation for cooking.

Concern has been raised about the H5N1 strain as it rapidly mutates and can acquire genes from viruses infecting other animal species. It can cause severe disease in humans. It is speculated that if a human becomes infected with both the avian and human influenza strains, they could serve as a mixing vessel for the emergence of a novel sub type of the influenza virus with sufficient human genes to be easily transmitted from person to person. This event could mark the start of an influenza pandemic.

Prions

Transmissible spongiform encephalopathies, also known as prion diseases, are a group of progressive neurodegenerative disorders that affect both humans and animals.

Mad cow disease

Recently, mad cow disease has made the headlines. The implication of tainted cattle is potentially devastating for the Canadian beef industry.

CJD

Creutzfeldt-Jakob disease (CJD) has become an area of intense interest, despite the absence of an appropriate therapy. The management of persons with CJD is fraught with controversy and panic. Thankfully, numerous agencies, including Health Canada, have published the Infection Prevention and Control Guidelines for classic CJD.

Severe Acute Respiratory Syndrome (SARS)

The 2003 SARS outbreak in Toronto was a direct extension of an outbreak in Asia by means of an international traveller. SARS, with its attendant public fear and panic, has become a warning to all, that epidemics and possibly pandemics of infectious diseases, are possible.

SARS has highlighted the psychologic, health care and occupational impacts of infectious disease in the community and in the healthcare environment. It has demonstrated how quickly an infectious agent can spread within a healthcare facility, despite presumably optimal infec-

tion prevention and control measures. SARS has also brought to the forefront the importance of:

- hand hygiene
- routine practices for infection prevention and control
- the need for appropriate respiratory protection.

10. West Nile virus:

The West Nile virus first appeared in North America in 1999. It was associated with an outbreak of meningoencephalitis, leading to seven deaths in the New York area. Shortly thereafter in Canada, particularly in Ontario, multiple cases of the West Nile virus disease were observed. The clinical manifestations range from asymptomatic infection to meningoencephalitis, with some individuals suffering severe neurologic disease, such as:

- encephalitis,
- acute placid paralysis and
- movement disorders.

The virus rarely culminates in death, as most people infected with the virus are asymptomatic or have minor flu-like symptoms.

When West Nile virus infections were first identified in Canada in the early 2000s, a sharp peak in human cases was observed. Since 2003, there has been a gradual decline, to the extent that to date, < 100 cases have been reported to health authorities. The lifecycle of theWest Nile virus involves transmission from bird to mosquito to bird, with humans being incidental hosts. Therefore, municipalities have embraced mosquito control as the key mechanism to control the transmission of the West Nile virus. It is critical that public awareness campaigns be undertaken by public health departments and primary care providers to demystify this condition. The public must be aware that although the West Nile virus is in the community, the individuals who become critically ill are few and those with significant sequelae are rare.

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Concluding thoughts

The preceding 10 hot topics in infectious diseases are only very brief summaries of a large number of different conditions which may affect humans. Although we believe that the worst is behind us is, we do not know what emerging infectious disease(s) lies ahead. Hopefully, the lessons we have learned and continue to learn from the preceding 10 topics will allow us to better prepare for the future.

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