2

Virus Transmission and Epidemiology

OUTLINE

Journal Club, 02/02/2024
Marika D'Avanzo – University of Naples Federico II

Previously on Journal Club…

Viruses can be beneficial

Viruses were first recognised and studied as disease causing agents. Only within the last couple of decades scientists have realised that viruses have shaped evolution of all life in fundamental ways.

One example of the role of viruses in evolution involves the co-option of retroviral envelope proteins in the development of placenta. The envelope glycoproteins of enveloped viruses are essential for viral entry into host cells. They bind to susceptible cells and induce fusion of the virion envelope with the cell plasma membrane; they are proteins that specialise membrane fusion. Genomic studies have revealed that placental mammals have “domesticated” the envelope glycoproteins of retroviruses to facilitate implantation of embryos into the maternal endometrium, a process central to formation of the placenta. So the evolution of placental mammals required retroviruses!

Another example of the benefits of viral infection involves plants. In a 2007 paper (Màrquez et al., 2007) the authors analysed a type of grass that tolerates high soil temperatures (up to 65 °C) in Yellowstone National Park. They showed that the heat tolerant plants were colonized by a fungus that was in turn infected by a virus. The authors demonstrated that both the fungus and the virus were necessary to confer heat resistance to the plant.

HIV transmission

Unprotected Sexual Contact: HIV is most commonly transmitted through unprotected sexual intercourse with an infected person. This includes vaginal, anal, and oral sex.
Mother-to-Child Transmission (Perinatal Transmission): it can occur during pregnancy, childbirth, or breastfeeding. Effective antiretroviral therapy can reduce the risk of mother-to-child transmission.
Blood and Blood Products: This risk has been significantly reduced in many countries due to screening of blood donations and improved safety measures.
Sharing of Needles and Syringes: Injecting drug users who share needles and syringes are at risk of HIV transmission if one of them is infected.
Occupational Exposure: Healthcare workers may be at risk of HIV transmission through accidental needlestick injuries or exposure to infected blood.
Organ Transplantation and Blood Transfusion: if the donor's blood or organs are infected and not properly screened.
Contaminated Medical Equipment: reusing or inadequately sterilizing medical equipment, such as needles or surgical instruments.
Mucous Membrane Exposure: if HIV-infected body fluids (such as blood, semen, vaginal fluids, rectal fluids, and breast milk) come into contact with the mucous membranes, found in the mouth, genitals, and rectum.

HIV is not transmitted through casual contact, or through respiratory droplets. Using barrier methods (such as condoms) during sexual activity, practicing safe injection practices, and accessing HIV testing and treatment are crucial in preventing the spread of HIV.

Spillover event

Spillover infection, also known as pathogen spillover and spillover event, occurs when a reservoir population with a high pathogen prevalence comes into contact with a novel host population. The pathogen is transmitted from the reservoir population and may or may not be transmitted within the host population.

Due to climate change and land use expansion, the risk of viral spillover is predicted to significantly increase.
Spillover is a common event; in fact, more than two-thirds of human viruses are zoonotic.

Examples of Spillover Zoonosis	
Disease	Reservoir
Hepatitis E	Wild Boar
Ebola	Fruit Bats
HIV/AIDS	Chimpanzee
COVID-19	Bats

Infectious diseases epidemiology

Infectious disease epidemiology is the study of the complex relationships among hosts and infectious agents. Epidemiologists are interested in virus spread or transmission, with or without disease.

Viral epidemiologists try to predict the potential for development of epidemics and define the kinds of interventions that could contain a virus outbreak.

Factors that can impact virus transmission and spread include:

1. Prevalence of the agent within the population;
2. Mode or method of transmission of the agent;
3. Duration of the infection and the window of transmissibility;
4. Numbers of susceptible and nonsusceptible individuals in the population;
5. Population density;
6. Patterns of travel or associations (schoolchildren and their families form interconnected networks);
7. Living conditions;
8. Climate and/or season.

Predicting the course of an outbreak is particularly challenging if a novel virus is involved, as we do not have information about modes of virus transmission, duration of infection, window of transmissibility, or stability of the virus in the environment. Factors that may impact the outcome of infection are differences in age, gender, nutrition, and genetic susceptibility (from asymptomatic infection to severe, life-threatening disease).

Key terms used by epidemiologists

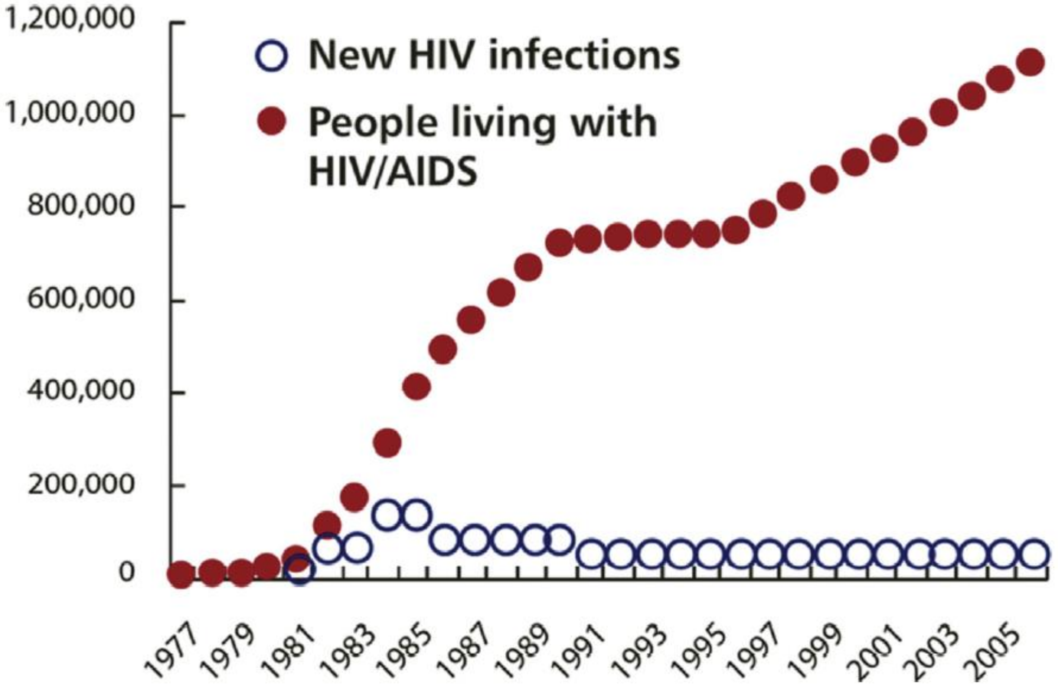
INCIDENCE RATE

A count of the number of new infections during a specific time period. A specific population and a time frame are defined. The number of new cases is the numerator of the ratio, the size of population and time frame the denominator (person-years).

PREVALENCE

The total number of cases present or counted. In the case of a persistent infection such HIV, the numerator includes patients infected for many years or decades. Prevalence is expressed as a ratio such as “cases per million.” There is no time parameter in this ratio.

Key terms used by epidemiologists



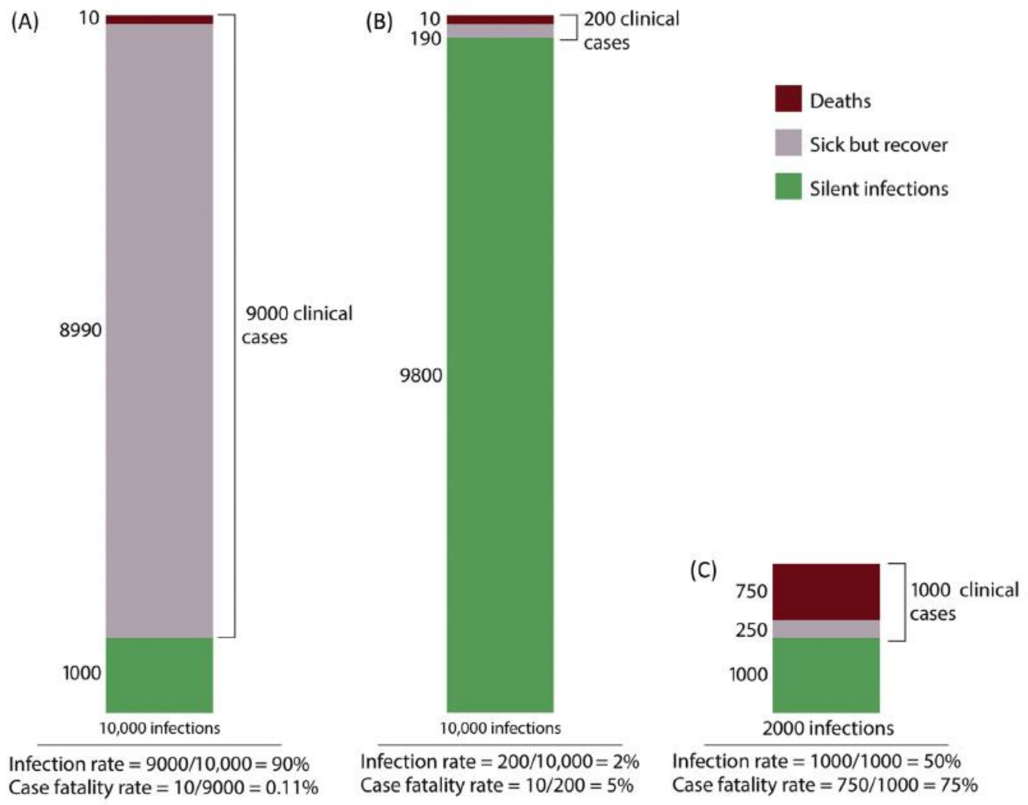
Incidence versus prevalence of HIV infections. The number of new HIV infections per year in the United States has remained steady but most infected individuals live years to decades with treatment, hence the yearly increase in prevalence. Source: Campsmith, et al., 2008. CROI 2009. JAMA 300 (5), 520529.

For an acute viral infection, such as measles, the incidence rate may be similar to the prevalence of the virus, given that virus is present and transmissible for a relatively short period of time. When considering persistent or chronic infections, such as those caused by the HIV or hepatitis C virus (HCV), incidence and prevalence can be quite different.

In the case of HIV, education about safer sex practices can decrease incidence (new infections), while the availability of antiviral drugs results in significantly longer survival times, thus increasing prevalence.

Interestingly, it has been shown for HIV that drug treatment decreases incidence while at the same time increasing prevalence, because treatment not only prolongs life but decreases transmission by drastically reducing viral loads in infected patients.

Methods to count viral infections and disease



Infection ratio versus fatality ratio. The infection ratio is the number of clinical cases per case of infection. The case fatality ratio is the number of deaths per clinical cases. Panel A: virus with high pathogenicity but low virulence. Panel B: low pathogenicity. Panel C: high virulence.

Accurate determination of incidence rates or prevalence depends on the ability to count infections and values obtained depend on the methods used for counting (case definition of a disease or the diagnostic tools available to detect a viral infection can lead to changes).

Passive surveillance is done when healthcare workers report cases of disease. The weak link in passive surveillance is the filing of the initial report, as in practice only a small fraction of cases of common, reportable viral diseases are actually reported. Even so, passive surveillance is useful for monitoring infectious disease trends.

Active case detection, another way to collect information on disease outbreaks, seeks to classify an illness and determine the causative organism, to assess the extent of an outbreak and its economic and health impact, to stop the outbreak and to inform the public.

Serological surveys are an important tool because many viral infections stimulate the production of detectable antibodies in blood, providing a history of both clinically apparent and clinically inapparent infections and telling if severe disease is a rare outcome on a background of a many inapparent infections or it represent the total number of infected.

Infection vs disease

Serosurveys are needed to determine the case infection ratio, the number of clinical cases over the number of infections. To evaluate and express the severity of clinical disease, the case fatality ratio or the number of deaths per 100 clinical cases is used. The case infection ratio of a virus might be 0.001 (1 in 10,000 infected individuals develops disease) but the case fatality rate for the same virus might be 1 (every clinical case results in death). While they may not be able to differentiate between natural infection and immunization, serosurveys can assist in determining the pathogenicity of a virus.

Pathogenicity is a measure of the proportion of infections resulting in an evident disease. Measles virus is highly pathogenic (95% of infected individuals experience disease).

Virulence is a measure of the severity of the disease and it is the number of deaths per number of infections. A virus can have low pathogenicity (few infections lead to a disease episode) but high virulence (when disease does occur it is often fatal) or the opposite might be true (most infections lead to disease, but disease is mild).

Many viral infections are completely inapparent. Outbreaks of novel viral diseases can be very stressful for society if we are not able to distinguish between pathogenicity and virulence. Very similar viruses can vary greatly in pathogenicity, virulence, and transmissibility, thus very small genetic differences between closely related virus strains can have huge biological effects. Influenza viruses can vary greatly in their pathogenicity, virulence, and transmissibility, based on just one or very few amino acid differences.

Developing model of virus transmission

Models of virus transmission can be used to determine the types of interventions (for example, vaccination, quarantine, drug therapy) that will most effectively reduce transmission and limit the scope of an outbreak.

Required knowledge is the number of susceptible individuals in the population, the proportion of infectious individuals, and the rate of contact between the two groups. In the case of an acute virus, a patient may be infectious for days or weeks. The recovered patient usually has detectable antibody and no longer participates in the transmission chain. Vaccinated individuals are unlikely to be in the transmission chain and high vaccination rates can protect unvaccinated individuals. In contrast, transmission of persistent viral infections can occur in the presence of antiviral antibody.

Most herpes virus infections are persistent and individuals are infected for life. People and animals may transmit herpesviruses, with or without displaying symptoms. Patients latently infected with the chickenpox virus (HHV3 or varicella zoster virus) are only infectious if they develop the painful rash called “shingles” as the fluid vesicles contain large amounts of infectious virus. In contrast, HHV2, the virus that causes genital herpes, can be spread in the absence of a visible lesion.

For long-term persistent infections like for HIV, hepatitis B virus, and HCV, they can be asymptomatic even when large numbers of virus particles are present in blood and body fluids.

Incubation, latent or infectious periods

The time between acquiring an infection and the onset of illness is the incubation period. The time between acquiring an infection and the ability to transmit the agent is the latent period. The period during which the infected person can potentially transmit the infectious agent to others is the infectious period.

If the incubation period is longer than the latent period, asymptomatic individuals unknowingly transmit virus. In a persistent infection such as HIV, a long incubation period provides months to years during which an active infection may go undetected. Following the Ebolavirus outbreak of 2014/15, it came as a surprise that some survivors continued to shed virus (for example, in semen) for many weeks.

Understanding the distinction between clinical illness and the ability to transmit virus is key to developing effective quarantine measures.

Virus transmission

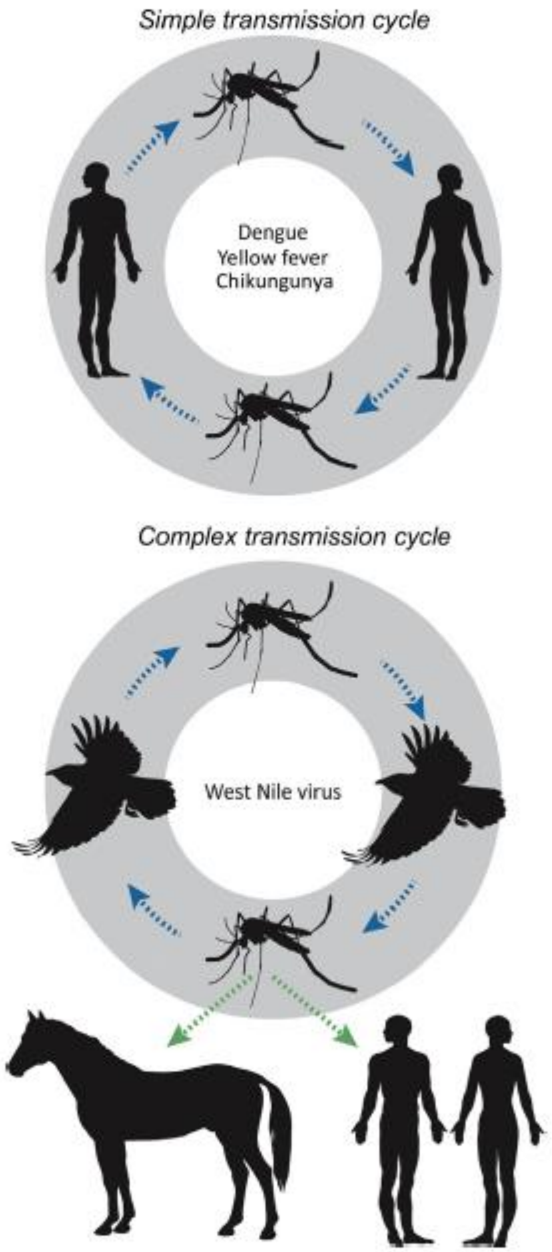
Some viruses are very host specific, infecting only a single species. For example, polio, measles mumps, rubella, and chickenpox viruses infect only humans. For viruses maintained in a single host population, transmission modes can vary.

Mechanisms for transmission include direct transmission from one animal to another (respiratory, fecal-oral, sexual, blood, or from parent to offspring (vertical transmission, occurring across the placenta, perinatally during birth, and via colostrum or milk), or via contaminated food, water, or fomites.

Other viruses spread across species boundaries by routes such as respiratory or via contaminated food, water, or fomites. Influenza viruses can be transmitted between humans and pigs at county fairs and petting zoos. Spread is not always from pigs to humans, spread from humans to pigs has been well documented. Avian influenza viruses can be transmitted to humans involved in the slaughter and processing of poultry. Rabies virus is transmitted via bites through contaminated saliva.

Veterinarians are at risk for contracting zoonotic viruses during exams or necropsies and research virologists can acquire viruses from infected laboratory animals or infected cultures.

Virus transmission



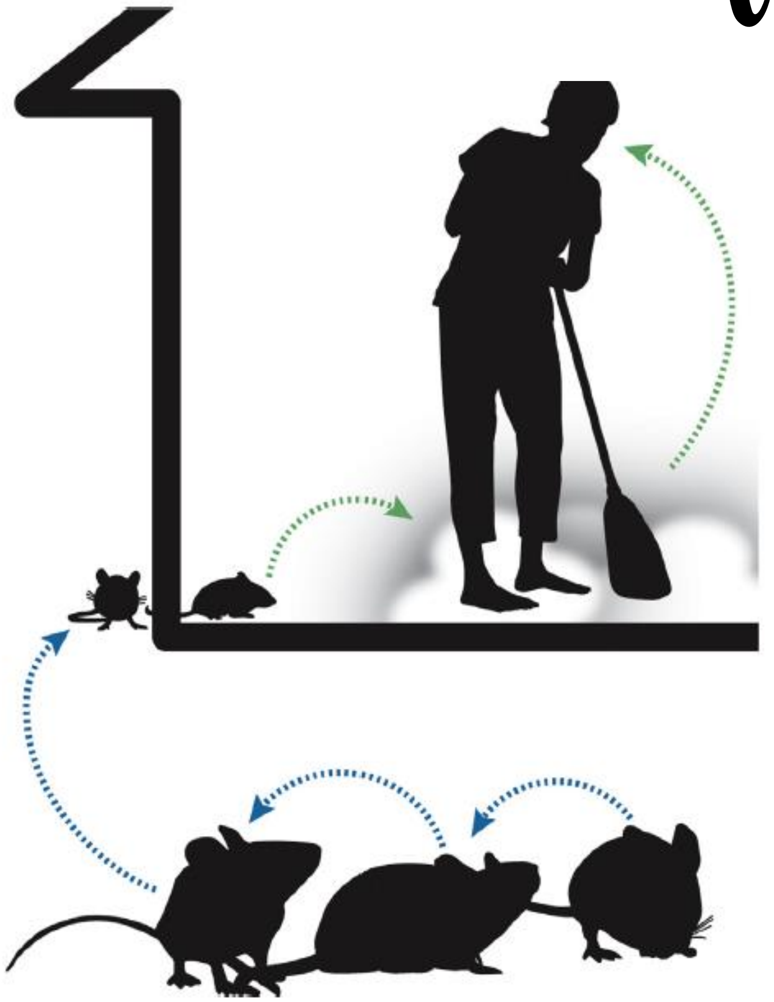
Some viruses must infect different hosts to be maintained in nature, such as yellow fever virus and dengue virus. The natural transmission cycle is from infected mosquitos to humans.

Viruses transmitted by insects are collectively called arboviruses (arthropod-borne). West Nile virus, arbovirus, is largely maintained in a transmission cycle between mosquitos and birds. Humans can be infected, but usually are dead end hosts because we often transmit virus back to mosquitos and human-human transmission is very rare.

Transmission from an animal to insect vector requires that sufficient virus be present in the blood. Once ingested by the insect, most arbovirus replicate in the insect to facilitate spread back to the human, animal, or avian host. Many are maintained for long periods in their insect hosts: mosquitos can transmit virus to their offspring (transovarial transmission). Thus even in the absence of susceptible vertebrate hosts, the virus persists in nature.

Virus transmission via insect vectors depends on the species of insect vector, the host preference of the blood-feeding vector, and environmental factors (temperature, rainfall) that may limit or facilitate vector spread.

Virus transmission



Hantavirus transmission. The normal hosts are rodents. They excrete virus in urine and feces. When rodent activity is high, structures may become contaminated. Humans can be infected by inhaling contaminated dust.

Another notable mechanism of transmission of some zoonotic viruses is through dried feces or urine. Rodents are natural hosts for a number of viruses that are potential human pathogens. These viruses do not seem to harm their rodent hosts but can cause severe disease if humans are infected through inhaling contaminated dust.

In the United States, hantavirus was first discovered as the cause of a small outbreak of severe pulmonary disease that occurred in 1993. The outbreak was linked to an explosion in the deer mouse population that year. Since that time over 600 cases of hantavirus pulmonary syndrome have been reported in the United States.

Recommendations to avoid infection include appropriate rodent control and cleaning methods. Rodent infested areas should be sprayed and mopped with disinfectant as it is important to avoid generating dust that can be easily inhaled.

Basic reproductive rate

R_0 is defined as the average number of new infections initiated by a single individual in a completely susceptible population during the individual's infectious period. R_0 is a function of both virus characteristics and contact patterns within a community.

Measles virus is highly infectious with an R_0 of 12-18. R_0 is calculated by assuming that every contact is susceptible. However prior infection and/or vaccination reduces the number of susceptible individuals in the population.

The effective or net reproductive number (R) is the actual average number of secondary cases and it equals the product of R_0 and the proportion of susceptible individuals in the population. R is smaller than R_0 because not all individuals in real populations are susceptible.

When $R > 1$, we expect the incidence of infection to increase, but when $R < 1$, the infection burns itself out. When $R = 1$, the number of infections is constant. Thus infection control programs can be modeled to determine the most effective methods available (vaccination, quarantine, use of antiviral drugs) to control an outbreak.

We must also consider the human factor, the ability, and willingness of a population to adhere to recommended control methods and guidelines.

In summary, understanding the epidemiology of an outbreak requires knowledge of the particular virus, the host, the place (geography), and the time (season).

Take home messages

- A variety of environmental, biological, and societal/behavioral factors impact virus transmission.
- Viruses (even closely related viruses) differ in their virulence, pathogenicity, and transmissibility, and these attributes are not linked. A virus may be highly transmissible but has low pathogenicity. A virus may have high pathogenicity but low virulence. Recall that pathogenicity is a measure of how many clinical cases are seen among infected individuals. Virulence is a measure of the severity of disease.
- Serosurveys are important for gathering information about the total number of infections within a group. Including those instances where infection was inapparent.
- A variety of factors impact the outcome of an infection. These include the age, sex, immune status, nutritional status, and overall health of the individual or animal.
- Modes of virus transmission include respiratory, fecal-oral, direct contact, insect vectors, vertical.

Thanks for your attention :)

GAME CODE: **577463**