WHAT DO EPIDEMIOLOGISTS DO?

Epidemiologists monitor diseases in populations. To monitor infectious viral diseases, they identify infected individuals (including animals) in three ways: (1) by noting the presence of classic symptoms of the disease, (2) by sequencing viral genomes in samples collected from infected individuals, and (3) by detecting antibodies to specific viral peptides in the individual's blood using **enzyme immunoassay (EIA)**.

Epidemiology is a growing field that ranks #3 in *U.S. News*' 2017 "Best Science Jobs," with a median salary of $69,450 and a 1.9% unemployment rate. Epidemiologists tend to have a Bachelor of Science (BS) undergraduate degree and a Master of Public Health (MPH) degree.

For example, in the Nipah virus outbreak of 1998-1999 in Malaysia, epidemiologists suspected that pigs were the source of the human outbreak because most patients were pig farmers and the viruses isolated from samples from sick pigs and patients with encephalitis (a swelling of the brain and a result of the Nipah infection) had identical nucleotide sequences. To stop the outbreak, the sick pigs were killed and buried. The outbreak ended, supporting the conclusion that the pigs had indeed been the source of this outbreak.

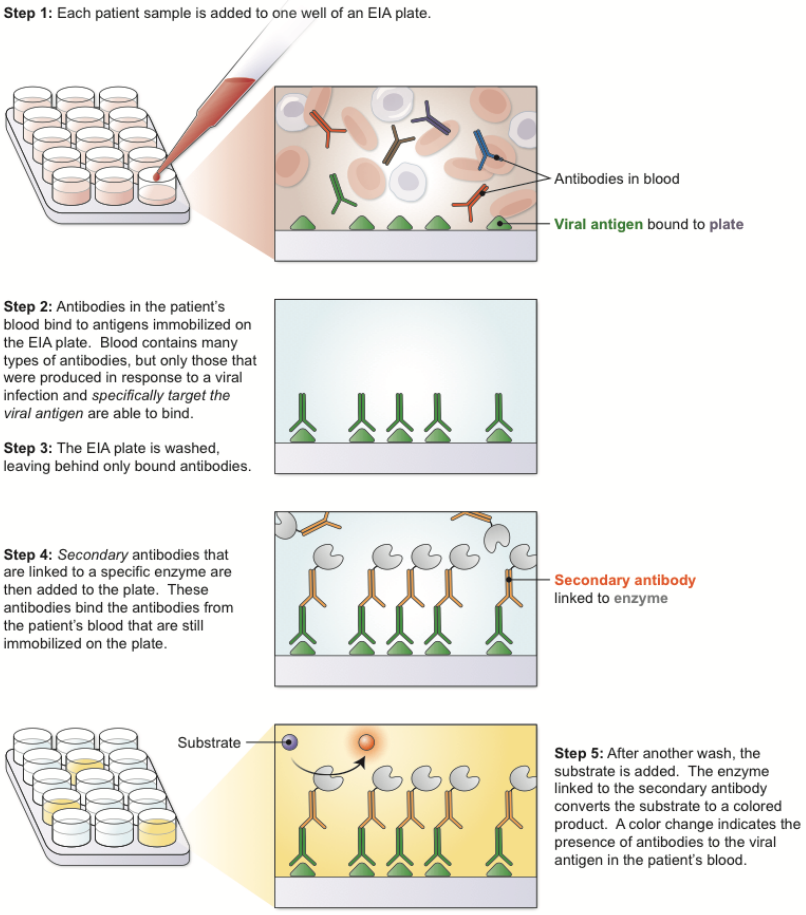

Figure 1: EIA method for detection of Nipah virus antibodies.

Identifying viral genetic material in an individual's blood sample indicates that the individual is currently infected, and sequencing the genetic material can reveal the identity of the virus. Although EIA requires knowing the identity of the virus, it will indicate whether the individual was infected at some point in their life, even if they have already cleared the virus. **EIA** involves coating a cell culture plate with a specific **antigen**: a portion of a viral protein that is recognized by an **antibody**. A sample of an individual's blood is next added to the plate. If the individual has produced antibodies to the virus, the virus-specific antibodies will bind to the viral antigen on the plate. A second antibody that binds to all of the patient's antibodies is then added. This second antibody is linked to an enzyme that changes the substrate into a colored product. A change of color in a given well following the addition of substrate indicates that patient's blood sample contained antibodies to the viral antigen.

Some epidemiologists are especially focused on detecting and monitoring **emerging** diseases. An emerging disease is one that is either new within a population or is rapidly increasing with respect to the number of cases or the geographic range affected. Epidemiologists are concerned with an emerging disease's potential to become an **epidemic** (also known as an outbreak), which refers to the sudden spreading of the disease over a wide but isolated area, or a **pandemic**, which refers to an epidemic that spreads worldwide. To assess the potential risk of a disease becoming an epidemic or pandemic, epidemiologists need to understand various characteristics of the disease, including its incubation period, how it spreads, and the risk factors involved in acquiring the disease. They need to collect data on the disease's **incidence**, **prevalence**, **morbidity**, **mortality**, **case fatality ratio**, and **basic reproductive number**. These terms are described briefly below.

Incidence is the number of *new cases* of an infection within a specified period; it is typically measured as number of cases per thousand or million individuals per time period (week/month/year). Those infected do not necessarily exhibit symptoms. For example, in 2014 an estimated 30,500 cases of hepatitis C virus (HCV) infection were reported in humans in the United States, making the incidence 30,500 new cases/309 million people/1 year, or about 101 cases per million people per year.

Prevalence is the percentage of *total cases* of infected individuals in a particular population. It's important to measure both incidence and prevalence, because a highly lethal disease may have a high incidence but a low prevalence because many of the infected individuals have died. Conversely, diseases that persist may have a high prevalence but a low incidence (many people are infected, but there are relatively few new infections per year). For example, in 2015, approximately 3.5 million people in the U.S. were infected with HCV out of a population of approximately 309 million, meaning nearly 1% of Americans are infected.

Morbidity is the percentage of infected people who display symptoms. For example, only 20% of people infected with West Nile virus have any symptoms; therefore, the morbidity rate is 20%. Morbidity values depend on the interplay between viral fitness and host health and immunity. For most viruses, symptoms tend to be worse in the very young and very old or those with otherwise compromised immune systems. Furthermore, individuals who were infected with a larger dose of virus (the *viral load*) are more likely to exhibit symptoms.

Mortality is the percentage of people infected who die as a result of the infection. Mortality is calculated by dividing the number of deaths by the total number of cases of infection, including those who do not display clinical symptoms. For example, 1 in 10,000 people infected with mumps virus dies. If left untreated, nearly everyone who becomes infected with rabies dies, giving the virus a 100% mortality rate. Mortality rate is typically expressed as a percentage or as number of deaths per 1000 cases per year.

Case fatality ratio (CFR) is the percentage of people with symptoms of infection who die as a result of the infection. For instance, the severe acute respiratory syndrome outbreak in China in 2003 resulted in 8,422 individuals reporting symptoms, of which 916 died, or a CFR of about 11%.

Basic reproductive number (R_0) is the number of secondary infections in a population of susceptible hosts expected to occur from interactions with a single infected individual (i.e., the index case); it is a measure used to determine the likelihood of a virus becoming an epidemic. The calculation to determine R_0 takes several factors into account.

R_o is calculated using the formula $R_o = C \times P \times D$

C = the number of contacts the index case makes per unit time (day, week, month, etc.)
P = the probability of transmission per contact with the infectious person
D = the duration that the infected person is infectious to others

The R_0 calculation for HCV is 1-3; for measles, 12-18; for mumps, 4-7; and for the Ebola outbreak of 2014 it was 1.5-2.67. If R_0 is greater than 1, an epidemic is considered likely, because the number of cases likely to occur after the index case is high. If R_0 is less than 1, it is less likely that an epidemic will occur because it should be possible to eradicate the infectious agent before it spreads to too many people.

Epidemiologists must identify the infectious agent, understand how it is transmitted, and be able to summarize complex sets of data and effectively communicate them to agencies like the Centers for Disease Control and Prevention and the World Health Organization to help determine what type of intervention, if any, is necessary.

In this activity, you will examine some of the data collected by epidemiologists studying a Nipah virus outbreak. You will perform the relevant calculations, make claims about whether the Nipah outbreak in Malaysia will become an epidemic, and determine the natural reservoir for Nipah virus.

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