INFECTIOUS DISEASES AND ECOSYSTEM RECOVERY

A presentation to the Puget Sound Partnership Leadership Council
March 27, 2015

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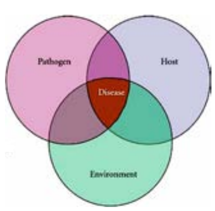
Thank you for inviting us to speak about infectious diseases and ecosystem recovery. There are many causes of disease (traumatic, toxic, metabolic, etc.) but for today we are going to be focusing on four categories of agents that cause infectious disease: bacteria, fungi, parasites and viruses. We will, however, touch on how other types of diseases such as trauma like boat strike or contaminants and toxins interact with infectious diseases.

In an oversimplified world, or at least for most people that love to watch A&E over Memorial Day, disease is bad and its mechanism of action is simple. You get exposed to a pathogen, you get infected, and either you get better or you die. Or, in the case of The Andromeda Strain, everybody dies (except the hero and the crying baby).



In reality, it's not that simple. On a daily basis we are bombarded with a variety of infectious agents, but they all don't make us sick. In fact, we probably actually are exposed to many and they even replicate in our body and we can spread them, but they don't cause disease. Or, our immune system wipes them out before they do cause disease. Disease, or dis-ease as the name implies, is really about an unhealthy state that is caused not just by an infectious agent (as we're discussing today) but also is modulated by our own bodies and the environment.

Let's take the example of Ebola virus disease, something that has been in the news a lot lately with the recent outbreaks in West Africa. According the World Health Organization, Ebola virus disease kills 50% of the people that become infected. But its not that simple, you see depending on the situation, the case fatality rate can vary from

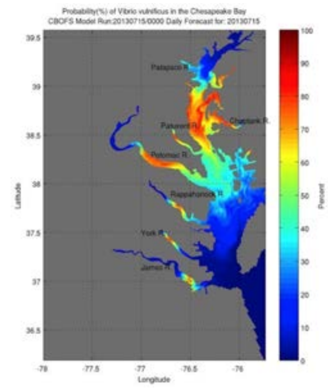
25-90%. So what are the factors that determine that? Those 3 from the Venn diagram. The virus itself matters. A recent science report showed the virus did not mutate much during the long human-human transmission this past year, but there are different types of Ebola virus and those have differing potentials to cause disease in people. The person or host also plays a role. What is their state of nutrition, what is their immune status, etc. And finally, the environmental plays a role. In the case of Ebola, the level of supportive health care can determine if you survive or die.

Let's look at those in a little more detail.

As an example of pathogen, let's discuss avian influenza (AI), or bird flu. These viruses are categorized by 2 proteins that occur on the surface of the virus, the Hemagglutinin and Neuraminidase proteins, better known in the media as the H and N proteins. In the world of bird flu (and actually including a few bats), there are 18 H proteins and 11 N proteins. The genes of AI viruses can reassort with ease so if we do a little high school math and calculate out the permutations, 11 x 18 gives use 198 different viruses. That makes it a nightmare for people working on vaccines, but it also means that not ALL of these viruses can cause disease in a specific host. At the risk of bumping over into the host discussion that Dr. Rhodes is going to present, I want to point out that only the H5 and the H7 viruses can be highly pathogenic (or cause bad disease) in poultry. And even some of the H6 and H7 viruses don't cause bad disease. Wild birds, on the other hand, can carry almost every single AI virus and have it not cause disease. As I said before, there are a few that have been only found in bats and as we know from the pandemic H5N1 outbreak a few years back, sometimes these viruses can kill wild birds. So there's an example of how the pathogen itself can help determine disease. Linda will give you examples of how the host modulates disease and how the environment plays a role.

The ability for the host to discriminate "self" from "foreign" relies on the immune system. All animals & plants have innate immunity, which relies on recognition of features shared by many pathogens such as the proteins in a bacterium's "tail" (or flagellum). Because innate immunity is ready-to-go against common features, it responds quickly & to a broad range of pathogens. However, it has no way to improve its response, in either magnitude or specificity. Adaptive immunity is found only in vertebrates (animals with backbones), & it is the basis for vaccination. Adaptive immunity "learns" to recognize specific features of a pathogen, such as a particular protein on the surface of the plague bacterium. "Learning" takes time, so there is a lag in response during the first encounter. However, subsequent responses are fast, much greater in magnitude, & are remembered for a long time (years).

The third factor affecting disease occurrence is environment. This can include physical & weather conditions, availability of food & nutrients, presence of anthropogenic contaminants, availability of suitable habitat, etc. Here is an example of how temperature can affect skin infections. *Vibrio vulnificus* is a free-living, aquatic bacterium that can cause soft tissue infections through broken skin; the higher the concentration of *V. vulnificus,* the great the likelihood of infection. The concentration of *V. vulnificus* correlates well with seasonal water temperatures, & the number of infections due to *V. vulnificus* among fishers & fish handlers also correlates well with mean water temperatures.



The relationship between the abundance of *V. vulnificus* & water temperature is so good that it is the basis for a forecasting model developed for Chesapeake Bay (right).

Studying disease patterns (epidemiology) can provide information about the pathogen-host-environment relationship for a particular disease. There are a few fundamental observations that have emerged from epidemiology that are important when assessing a disease. First, infection does not necessarily mean disease. Detecting clinical disease is usually just the “tip of the iceberg” for infection by the pathogen. Infected but not clinically sick individuals can be reservoirs for the pathogen, or even serve as vectors if they can transmit the pathogen. Second, understanding the route of transmission is important because it affects disease patterns & management decisions. Horizontal transmission can be directly between hosts or may use a third party, such as an intermediate host or a vector. Vertical transmission is from a parent (usually mother) to offspring.

Here’s an example of how a difference in transmission generates different patterns. In a plot of a single source of pathogen with poor or no transmission (e.g., cholera in London well), a high number of cases (or deaths) can occur in a short period of time. In contrast, a plot with direct horizontal transmission can have fewer cases but over a longer period of time. If there is an incubation period between infection & disease, the number of cases (or deaths) may have a periodic fluctuation over time.

The immune status of others can be an environmental feature as well as a host feature for a horizontally transmitted pathogen. If nearly everyone is susceptible, the problem can spread throughout population, often rapidly. If some individuals are resistant (either genetically or through vaccination), the disease hits a “dead end” with the resistant individuals, which can slow or reduce the spread. If most individuals are resistant, the spread can be reduced enough to actually protect the few susceptible individuals. This is known as community or “herd” immunity.

So with any disease or pathogen, there are some important questions you want to be thinking about:

#1 Is disease a single animal problem or can it cause a population-level impact?

#2 Can the pathogen affect people or domestic animals?

#3 How do multiple pressures affect disease outcome?
#4 Can disease have catastrophic impacts on the ecosystem?

Let's take an example of the first: Is disease a single animal problem or can it cause a population-level impact?

Ichthyophonus is a fungus that can infect many species of fish, but it has tended to cause epidemic kills among forage fish, especially herring. It is transferred by ingesting infected tissue or water, so can be easily transmitting among schooling fish such as herring.

Ichthyophonus reduces individual fitness, which can increase susceptibility to predation. After periods of low nutrition (e.g., winter) herring infected with *Ichthyophonus* are slower to rebuild energy stores. Ichthyophonus heart infections can cause poor swimming ability, which reduces prey consumption and possibly increase risk to predation. Because herring have schooling behavior, direct horizontal transmission can be high.

Among Puget Sound stocks of Pacific herring, there is good evidence for a reduction in the maximum age between the mid-1970’s & later 1980’s, & the latter pattern has persisted. The increasing prevalence of *Ichthyophonus* with age suggests that this fungal infection may compromise the long-term survival of individuals, perhaps playing a role in shifting the age structure. Note that correlation is not necessarily causation, but it is intriguing that we see *Ichthyophonus* prevalence increase as fish increase in age.

Let's look at the 2nd question, Can a disease be transmitted to people or to domestic animals? Animal can transmit some diseases to people and people can transmit some diseases to animals. Likewise, wild animals can transmit some diseases to domestic ones and domestic animals can give some diseases to wildlife.

A simple example of this is sealpox, a virus that can be transmitted from wildlife to humans. Here you see a lesion, or example of what the virus can do when it infects a seal. If an infected seal were to bite a human, it could cause a similar lesion in the person at the site of the bite. That is a very straightforward case of direct transmission.

Let me give you a second example. How many of you are familiar with the issue of brucellosis in the Greater Yellowstone Ecosystem (GYA)? Brucellosis is caused by a bacterium *Brucella abortus*,that originally was transmitted from cattle into bison and elk. Then the US spent millions to eradicate the disease from domestic livestock. Now we face the issue of bison and elk (originally infected by domestic cattle) transmitting the bacterium back to domestic cattle, creating regulation nightmares for farmers and the

USDA and complicating exportation of US meat and dairy products. *Brucella abortus* can infect wildlife, domestic animals and humans.

How many of you are familiar with *Brucella* in harbor seals? In 1994 scientists discovered a species of *Brucella, B. pinnipedialis* in Puget Sound seals. This bacterium is very similar to the *Brucella* found in the GYA. And, like that organism, it can cause disease in humans as well as in domestic animals like sheep and cattle. It doesn't seem to be a problem limiting our seal population in the Salish Sea. We have one of the most dense harbor seal populations in the world. But now that we have a better idea of how it is transmitted in seals we think there is little reason to be concerned for human or domestic animal health, but we really need to identify and study these pathogens to be able to evaluate risk to people and domestic animals.

I won't ask how many of you have had the displeasure of having *Giardia*. We did a study a few years back and found *Giardia* in almost half of the harbor seals sampled. We also found it at 90% of the haul out sites studied. Interestingly, it was a strain we think is specific to seals. You see you can molecularly type these protozoal parasites and understand their epidemiology. Pretty cool. Does it cause disease? We don't know. Can it infect humans? We don't know. Even more interesting, though, there was one site in south sound where we found a canine variant in the seals. The culprit? This guy…
Well not this dog exactly. This funny looking creature is my dog and I pick up his poop when he goes on the beach. But we think domestic dogs transmitted it to seals.
I give you this example to remind you that diseases can go both ways. Disease can also go from people to animals. A few years ago we had a harbor seal in rehabilitation that was infected with MRSA, a resistant bacterium. When we typed it we found that a rehabilitator who was a carrier of this bad bug probably infected the seal.

Ok, so we told you disease is not usually just about getting exposed to a pathogen. Let us now give you some real life examples of that.

Viral hemorrhagic septicemia virus (VHSV) is an epidemic-causing pathogen of both marine & freshwater fish. It produced a major epidemic in the Great Lakes in the mid-2000's, affecting many species & triggered a ban of fish transport in states & provinces bordering the Lakes.
Epidemic kills have also been observed along the west coast, involving forage fish.

VHSV is shed into water by infected fish, regardless of whether they are symptomatic, asymptomatic, or even recovered from an infection. This means there are many sources of virus. However, the strain of virus is important for its ability to cause disease in different hosts. Notice that Pacific herring are vulnerable to all known strains of VHSV.

Here's a comparison of disease among multiple pressures on Prince William Sound herring & Puget Sound herring. In Prince William Sound, herring experienced the Exxon Valdez oil spill in 1989, just before spawning. Four years later, a massive population crash occurred, & no recovery has occurred yet. Factors identified as contributors include VHSV infection, poor nutritional status, & a change in age structure toward younger (3 year old) spawners, possibly associated with oil spill exposure.
In Puget Sound, herring populations are on a slower declining trajectory, but also have not recovered. Puget Sound herring are also infected with VHSV & carry a surprising body burden of persistent organic pollutants. Disease can cause epidemic kills, but can also be one in a suite of factors impacting a population.

Let's talk about another one of the Partnership's Dashboard indicators… southern resident killer whales. We understand that killer whale declines are multi-factorial and include declines in prey … salmon, increased vessel noise (remember, that killer whales live in an acoustic environment. They use sound to communicate and to hunt. Increased noise challenges their ability to echolocate prey), and contaminants. We know that SRKWs are some of the most contaminated marine mammals in the world.

So where do diseases fit in? Say you have a killer whale that has high contaminant levels, food is scarce and ambient boat noise is further reducing the animal ability to find food. This animal is going to have trouble finding food so it begins to metabolize stored adipose tissue (the site where these contaminants are stored), which potentially decreases the animal's resistance to infectious agents that by themselves might not be that pathogenic. You then have an animal exposed to a pathogen that is in the environment that doesn't often cause disease, let's say the bacterium *Edwarsiella tarda*, but this time it causes dissemination infection and even death in that animal.

Ok, let's take a look at the 4th question you'll want to think about: Can disease have a catastrophic impact on the ecosystem? Or, maybe less head line grabbing, but the same concept: Is the disease going to alter the ecosystem dramatically from the way that we currently know it?

If disease, either alone or in combination with other pressures, can change the abundance of herring & other forage fish, there would be consequences throughout the pelagic food web. This is because herring & forage fish are positioned at the middle of the energy flow from plankton to top level predators. Because the main problematic pathogens for herring, *Ichthyophonus* fungi & VHS virus, can infect & cause disease across many species, there is substantial risk of cross-species infection, especially among forage fish.

Pacific herring are a major, if not the majority, component of diets for important commercial & recreational fish species, comprising over half of the diet of Chinook &

coho salmon. And higher-level predators, such as resident killer whales, depend on species that depend on herring. Loss or reduction in herring would exert a "bottom-up" force on fish-eating fish, birds, & mammals. Pacific herring feed on plankton, including many early stages of other fish (zooplankton). This makes herring a "top-down" force in regulating the abundance of other fish species, which is important for ecosystem balance. Furthermore, herring move from estuaries & near-shore areas to deeper marine & even continental shelf regions throughout their life cycle. This makes herring a major transporter of biochemical energy between widely spaced ecosystems - & we haven't even begun to understand their role out in the open ocean.

Let's look at a final example – one that has been in the news lately and I'm sure on all of your minds every time you walk the beach at low tide… sea star or starfish wasting disease. And let's ask ourselves those 4 questions. I think it will provide a nice example of how you, the Partnership's Leadership Council, will want to think about diseases as you work to restore the Puget Sound and Salish Sea.

First, let's ask, is this a single animal problem or a population level impact? That's not a hard question to ask now, but early on in the outbreak, this is the question that scientists and veterinarians were asking. What if you were walking on the beach at the start of this outbreak and you see one sick sea star near some healthy ones, as in this picture? Well animals die all the time and are eaten by scavengers. It's the way the ecosystem works. An overzealous, unaware kid on the beach could have trampled this one sea star. You probably can't say if this is an individual animal problem or a population-level problem. But then as the outbreak spreads, affecting about 20 different species and a huge geographic range, we see, hey, this is having a population-level impact.

Next ask if this disease can this affect people? Is my son going to get this when he's walking on the beach or is my dog going to waste away after he eats a sick starfish? Will it kill a farmer's pigs if he feeds them a bunch of dead sea stars that somebody collects to get off the beach? About 25 scientists and I published a paper recently showing that a virus called SSaDV was involved in this outbreak and from what we know about this virus and the family this virus comes from, we're not worried about people and domestic animals.

But we do need to be thinking about other species, especially other species of echinoderms. After all, we have a very important red urchin fishery here in Washington State. The virus was found in several species closely related to sea stars, purple sea urchins and eccentric sand dollars, but it has never been implicated in disease. Its potential, however, bears keeping in mind.

Okay so you're probably already thinking, is SSaDV really the whole story? Well I don't think there is one author on that paper who believes the virus itself is the whole story. After all, we identified this virus in museum samples from 1942. Sure we know that associated parvoviruses can mutate easily and alter their virulence, but we don't have evidence right now that that is what happened. More than likely, this virus is interacting with other co-factors to cause the epidemic. And, fortunately right now people are investigating the role of warming waters, ocean acidification, pollution and other potential co-factors might have played in the outbreak.

Linda and I would like to close by leaving you with a few recommendations:

1. Acknowledge that disease is a major factor in structuring ecosystems – some say it is as powerful a force as predation. You are already doing this just by inviting us to present today.
2. Integrate disease intelligence gathering into other collection and monitoring efforts. If we are out capturing herring for genetic work, we should also be considering taking disease samples.
3. Consider creating a small PSEMP working group on disease. This would integrate the various scientists that study diseases in invertebrates, fish, birds and mammals and the could provide you with a heads up when there are concerns and serve as a sounding board for questions you and others working on ecosystem recovery have.

Photo Credits: A & E Media (Andromeda Strain), Putignani & Menchella, 2010. Interdisc Persp Infect Dis #753512 (Venn diagram host, pathogen, environment diagram), John Jacobs, NOAA Coop, Oxford Lab (Chesapeake Bay model map), wasting Ochre sea star (J. Gaydos)