Epidemiology Concepts for Disease in Animal Groups

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Purpose:

The purpose of this module is to introduce the epidemiologic concepts applicable to understanding disease in animal groups to veterinary students and veterinary practitioners in a self-learning mode.

Learning Objectives:

After studying this module, you should be able to:

- Define the terms medical ecology, natural history of disease.
- Define the terms associated with communicable disease transmission, such as reservoir, vertical transmission, fomite and biological vector.
- Explain the significance of the epidemiologic triangle and give a specific disease example, including factors.
- Explain why individuals in a group manifest a spectrum of disease severity.
- Explain the difference between infection status and disease status.
- Describe the error that result from confusing infection status and disease status.
- Explain the significance of the "Iceberg" concept of clinical versus subclinical disease and give a specific example.
- Describe the four major errors that stem from misunderstanding the "Iceberg" concept.
- Explain the concept of endemic stability and how it relates to clinical outbreaks caused by endemic agents.
- Explain the concept of herd immunity and give a specific example of its relevance to a vaccination program.
- Interpret values of the basic reproductive ratio that are less than one, one and greater than one and give examples of interventions to reduce this ratio.
- Contrast what happens over the long term in propagating infections when the basic reproductive ratio is one or greater compared to when the ratio is less than one.
- Contrast the epidemic curve of a propagating epidemic with that of a point source epidemics.
- Explain the significance of the causal web in developing strategies to control or eliminate disease outbreaks.
Definitions:

**Medical Ecology:** For infectious disease, the study of the interaction of the components of the triad of infectious disease - the host, the agent and the environment.

**Natural History of Disease:** The natural course of disease from inception through resolution (complete recovery, chronic carrier or death) in the absence of treatment.

**Communicable Disease:** A disease that occurs due to transmission of an infectious agent from an infected animal or reservoir to a susceptible animal either directly or indirectly through a vector or the environment. In the narrower sense, communicable from animal to animal.

In the narrow sense, not all infectious diseases are communicable from animal to animal under common circumstances (e.g., most environmental mastitis) but some that are normally non-communicable become communicable under unusual circumstances.

**Portal of Exit:** The routes by which an infectious agent exits its host, such as by feces, urine, saliva, expired air, blood, semen or urogenital secretions. One route is usually primary, such as fecal for enteric infections, but the agent may also exit by other secondary routes, such as blood, saliva or urine during septicemia.

**Portal of Entry:** The routes by which an infectious agent can infect a susceptible animal. One route is usually primary, such as oral for salmonella, but agents can often enter by other secondary routes, such as conjunctival or rectal (iatrogenic transmission) for salmonella.

Communicable Disease Transmission Routes and Examples:

**Coital (Sexual):** *Trichomonas fetus,* venereal tumor, *Brucella ovis.*

**Conjunctival:** Leptospirosis, *Moraxella bovis,* *Brucella abortus.*

**Ingestion:**

**Fecal-Oral:** Most enteric pathogens - viruses (rota, corona), bacteria (salmonella sp., *M. paratuberculosis*), protozoa (Coccidia sp.), helminths.

**Milk:** Many bacterial agents that cause septicemia in the dam (leptospira, salmonella, *M. paratuberculosis*, *Brucella abortus*) can establish intramammary infections, are carried by white cells (BLV), or contaminate the teat skin and subsequently harvested milk or colostrum. Metazoans such as *Toxocara canis* are also transmitted by this route.

**Inhalation:** Respiratory viruses, Q-fever and other agents that survive in dusts and aerosols such as salmonella sp. and cryptosporidia.

**Intramammary:** Contagious mastitis pathogens (e.g., *Staph. aureus*, *Strep. agalactiae*, *Mycoplasma bovis*), environmental mastitis pathogens (coliforms).
**Intrauterine (Transplacental):** Many host adapted, endemic protozoal (e.g., toxoplasmosis, neosporosis), metazoal (e.g., *Toxocara canis*), bacterial (e.g., *Mycobacterium paratuberculosis*, *Brucella* sp.) and viral infections (e.g., BVD).

**Rectal:** Rectal palpation (iatrogenic) - BLV, BVD, Johnes, salmonella

**Transcutaneous:** Many vector-borne infections (e.g., anaplasmosis, the equine viral encephalidities), those associated with mammal bites (rabies), hookworm, iatrogenic infections from contaminated needles and biological products.

**Caution:** Although most infectious agents are transmitted by a primary route that is the most important to stop, do not overlook the potential for transmission by other routes that can defeat control programs once the primary route has been controlled. Pay particular attention to those involving a veterinary procedure that you may be held accountable for in the future. These include rectal palpation without changing sleeves, catheterization or endoscopy with contaminated equipment, transfusion, infusion or vaccination with contaminated fluids, and mass vaccination without changing needles or anything else that has the potential for transfer of biological materials between animals.


**Reservoir:** Any animal species, insect, soil or combination of these in which the infectious agent normally lives and multiplies so that it can be transmitted to a susceptible animal.

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**Main Forms of Transmission**

- **Direct Transmission:** Direct, immediate transfer of an infectious agent from an infected animal to a susceptible animal. This may be transplacental, by droplet sprays from coughing or urinating, by direct touching, such as during social behavior such as grooming, sexual activity, bites, or by direct contact with the normal reservoir of saprophytic agents, such as systemic mycoses in soil. Directly transmitted agents generally don’t have to survive in the environment for successful transmission to occur.

- **Vertical Transmission:** Infection that is transmitted from a parent to its offspring via infected semen or ovum, through the placenta, in the birth canal, via milk or due to direct contact, such as with contaminated teat skin. This is a form of direct transmission.

- **Horizontal (Lateral) Transmission:** Any form of infection transmission between individuals that is not vertical transmission.

- **Indirect Transmission:** Transmission of an agent by one of the following means.
  - **Airborne:** Transmission by microbial aerosols that tend to stay suspended for long periods rather than settle quickly like droplets or dust.
  - **Vehicle (Fomite) Transmission:** Transmission of an agent, static or multiplying, by a contaminated inanimate object such as water, food, biological products (e.g., vaccines, plasma), surgical instruments (e.g., endoscopes, balling guns, floats, speculums, stomach tubes, drenching guns), boots, clothes or water buckets.
  - **Vector Transmission:** Transmission of an infectious agent by an animal, usually an insect, in one of the following fashions.
**Mechanical:** Vector transports the infectious agent on its mouthparts or feet or passes it through its gastrointestinal tract. Multiplication, which can occur, or other development of the agent is not required for it to be transmitted and the agent can be transmitted immediately after the vector acquires it.

**Biological:** Multiplication or other development of the agent in the vector is required for it to be transmitted and this transmission can't occur until after an incubation period during which this happens.

**Resistance:** All of the body's defenses against infection. For most infectious disease resistance is relative, meaning that a sufficiently large infectious dose will overcome almost any level of resistance.

**Inherent Resistance:** Those host resistance factors that don't involve a humoral or cellular immune response. These include intact skin, the gastric barrier against enteric agents, the mucociliary barrier against the respiratory agents, the peristaltic action of ureters, the cervical mucus plug, the keratin of the mammary streak canal, tears of the eyes and so on.

**Immunity:** Resistance associated with cells or antibodies of the immune system.

**Active:** Immunity acquired by previous exposure to the antigens of the agent, either by previous infection or vaccination. Once acquired, this may be life-long.

**Passive:** Immunity acquired through transfer of antibodies from a source outside the animal, such as from colostrum, transplacental transfer or administration of hyperimmune serum. This is of short duration due to the half-lives of immunoglobulins.

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**Goals:**

**What is the "goal" of the infectious agent?**

The "goal" of most infectious agents is to maintain their existence by replicating and to propagate by spreading within ecological niches, such as an animal population. Many are have evolved sophisticated mechanisms to survive in all aspects of transmission between infected and susceptible animal hosts, much understanding of which is relatively recent. Many infectious agents are often in intense competition with other flora, such as in the host intestinal tract, and have evolved mechanisms enabling them to survive this competition. Infectious agents are also well equipped to adapt to new ecological niches, such as those presented by changing husbandry practices (e.g. use of recycled flush water for manure removal on dairies) or the movement of animals into new environments (e.g., llamas and alpacas from South American highlands to temperate low lands).

Many of infectious agents co-evolved with their animal hosts and were perpetuating successfully long before man imposed domestication on these hosts. Domestication has upset the "natural" medical ecology under which this co-evolution occurred and thus has changed the natural history of many infections. Man's changing husbandry and management factors continue to do so. For example, higher animal stocking densities increase effective contacts for many agents, particularly those transmitted by direct contact.

**Why does this matter?**

Many infectious agents have several mechanisms to exchange genetic material with unrelated species and to change the genetics of their progeny, have very short generation times compared to livestock and are rapidly and constantly changing as a result. While we deliberately select domestic animals, we also unwittingly select their infectious agents. We steadily apply selection pressure in the form of antibiotics, transportation, and new housing and feeding systems. Antibiotic usage selects those infectious agents that the antibiotics don’t work against. Animal management systems select those infectious agents that are able to survive and proliferate in them.

In one Holstein selection cycle (2 years), bacteria have 175 times as many opportunities for change as has occurred in over 100 years of dairy breeding. Given the dramatic milk yield increase that has occurred with 50 years of intense selection, where will the Holstein be after 17,500 years? That is equivalent to the opportunity that bacteria have for change every two years under optimal growth conditions.

**What is the goal of the clinician?**

Usually the goal of the clinician is to prevent clinical disease from ubiquitous agents (agents most likely already infecting a herd) and to eradicate non-ubiquitous agents from infected herds or to prevent their entry into non-affected herds. For the major infectious, communicable diseases in their species of interest, to accomplish these goals the clinician needs to understand the medical ecology and natural history of the disease sufficiently to:

- Prevent an animal or a group of animals from acquiring it (primary prevention).
- Control or eliminate such an infection in a group of animals once it is present (secondary prevention).
The following is a basic framework of questions for organizing this information:

- What is the reservoir(s) of the agent? What is the potential for susceptible animals to be exposed to this reservoir (Shedding level or environmental level vs. chance of contact or infectious dose)? What conditions favor spread from the reservoir? Which inhibit it?
- What is the typical period of communicability? What is the typical shedding pattern and level over this period? The longest period? What proportion of infected animals become chronic or latent carriers?
- How can subclinical carriers be detected? Incubating or latent carriers?
- What is the diagnostic performance of each of the available tests across the spectrum of infection and the stages (incubation, florid disease, convalescence) in the natural history of the disease?
- What is the primary mode of transmission? Secondary modes? What are the relative importance’s of these?
- If a mechanical or biological vector is involved, what factors influence its survival and transmitting ability? How can contact between the vector and susceptible animals be reduced or prevented? How long can mechanical vectors present a risk to susceptible animals?
- What are the environmental survival characteristics of the agent?
  - Is it significantly affected by freezing? By desiccation? By sunlight (UV)? How long does it typically survive at infectious levels in associated biological materials (e.g., feces, urine, saliva, nasal discharge, and cadavers)? In soil? In water? On surfaces?
- What practical sanitation procedures will eliminate it?
- What is the minimum dose that will typically cause infection (infectious dose)? Clinical disease? How does this compare to the typical level of exposure?
- What are the shedding levels of subclinically infected animals compared to clinically infected animals? How dangerous to susceptible animals are subclinically infected animals? Clinically infected animals?
- What host factors increase susceptibility? Resistance?
- What is the typical incubation period? What is its range (shortest to longest)?
- In a typical group of animals with the infection present, what are the proportions of subclinically and clinically infected animals during a clinical outbreak? During an endemic phase?
- What vaccines are available?
  - What is the efficacy of vaccination? How do the different types of vaccination affect the development of clinical and subclinical disease in its different forms? Of development and maintenance of carrier status? What risks do vaccines present (e.g., contamination with virulent strains, creation of carriers, confounding of diagnostic tests)? What is the interaction between vaccination and diagnostic tests? At the national level, what are the trade implications? What authorization is required to use them? If use is forbidden, what is the rationale?
- If economic decisions are involved, what are the relative costs of the infection in groups and the costs of prevention and control measures?

For some diseases, the most of the answers to the above questions are well established. For many, they are not and you will have to reason by analogy from other diseases and species where the answers are clearer. The goal of this module is to acquaint you with the underlying epidemiologic concepts that are useful in considering the above questions when working with disease problems occurring in animal groups (e.g., kennels, hospital wards, livestock herds, stables, fairs).
The Epidemiologic Triangle (Triad):

Disease is the result of complex interactions (some would say imbalance) between the triad of the agent (toxic or infectious), the host and the environment. The components of this interaction differ depending upon the specific circumstances of each group of affected animals. Particularly for agricultural animals, this triad is strongly influenced by husbandry and management factors, which are often the most important. For vector-borne diseases, vector factors are also linked to the other factors.

Recognizing the different components of this triad is important because they are the source of opportunities to reduce disease at multiple points in the transmission cycle. A common mistake is to focus on only one aspect of the triad for disease control or prevention and to overlook the others.

The Epidemioleic Triad

Agent Factor Examples:
- Dose
- Environmental hardiness
- Virulence (microbial)
- Infectivity (microbial)
- Toxicity (poisons)

Host Factor Examples:
- Innate resistance (e.g. gastric barrier, mucocilliary transport mechanism)
- Previous exposure
- Passive immune status (neonates)
- Vaccination status and response
- Age
- Gender
- Behavior (e.g. mutual grooming, dominance, pica)
- Production status (e.g., lactating vs. non-lactating)
- Reproductive status (e.g., pregnant vs. non-pregnant, sterile vs. intact)
- Genetics

The components of medical ecology
Intrinsic (non-changeable in the individual):

Age is very important because the risk of many diseases change widely over the animals life time due to underlying physiological changes that are associated with age. Neonates are very susceptible to many enteric and respiratory infections but resistance increases as the animals mature. As immune function declines with advanced age, susceptibility begins increasing again.

Clinical disease due to ubiquitous agents, such as the viral scour agents, can be reduced by delaying the neonate's exposure to the agent (innate resistance increases with age) and reducing the infectious dose by changing the environmental factors.

Due to genetics different breeds have different risks for diseases, such as hip dysplasia in German Shepherds. Within breeds, some infectious diseases occur due to underlying genetic defects (e.g., Holstein BLAD, Arab CID, Quarter Horse HPP).

Extrinsic (changeable in the individual):

Intact bitches are at risk of pyometra and mammary gland tumors than spayed (excluding stump pyometras) are not. Intact dogs behave differently than non-intact dogs, tending to roam more and thus being at higher risk of being hit by cars and of acquiring communicable infectious diseases.

Vaccination increases an individual’s resistance to disease but the protection is not absolute for most biologics.

Environmental Factor Examples:

- Animal stocking density
- Animal movement between groups
- Housing (e.g., ventilation, sanitation)
- Environmental conditions (e.g., temperature, humidity, wind velocity, precipitation)
- Nutrition (protein, energy and macromineral and micromineral adequacy)

Many infectious agents are susceptible to the ultraviolet (UV) in direct sunlight and to desiccation. Many infectious agents survive for long periods in damp environments.

Strangles (Strep. equi) in horses appears to occur more frequently during damp cold weather. This is likely because the agent is able to survive longer in damp environments.

Salmonellosis in all animals including humans occurs more frequently during summer than during other times of the year. This is likely because the agent is able to replicate to infectious doses in moist feedstuffs at summer temperatures.


These factors interact in complex ways that are often under the control of man.

EX: Increased animal density may lead to increased microbial load in the environment, a roof may prevent exposure of microbe to killing UV, low ventilation may increase humidity from animal respiration which in turn increases environmental survival of the organism which in turn increases exposure dose and infects more animals.

It has been said that:

"Bovine mastitis is a disease of man with signs in the cow."

"Bad management will overwhelm the best immunology."

The Spectrum of Disease Severity (Gradient of Infection):

Because each group member is affected by one or more of the epidemiologic triad factors differently, disease in a group is often manifested as a spectrum that can range from inapparent to subclinical to clinical to...
Subclinical means that signs of the disease cannot be detected without special tests.

Clinical means that the signs of the disease can be detected during a normal clinical exam.

Because the individual's body reacts to the disease, disease severity changes over time. During disease progression in a herd, individuals exposed at different points in time will be at different points in the natural history of the disease.

### Status and Spectrum of Disease Severity

<table>
<thead>
<tr>
<th>Exposure Status</th>
<th>Unexposed</th>
<th>Exposed</th>
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</thead>
<tbody>
<tr>
<td>Infection Status</td>
<td></td>
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<tr>
<td>Uninfected</td>
<td></td>
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<tr>
<td>Infected</td>
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<tr>
<td>Recovered</td>
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<tr>
<td>Disease Status</td>
<td></td>
<td></td>
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<tr>
<td>Subclinical (Inapparent)</td>
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<td></td>
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<tr>
<td>Clinical Disease (Apparent)</td>
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<tr>
<td>Morbidity (Sickness)</td>
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<tr>
<td>Mortality</td>
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<tr>
<td>Mild</td>
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<tr>
<td>Severe</td>
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<tr>
<td>Fatal</td>
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**Caution:**
Understanding the spectrum of disease that can be manifested in a group is important because an animal's position in this spectrum strongly affects how well most diagnostic tests perform on that individual and thus on the group overall. Tests generally perform better on animals with a higher level of severity.

Understanding the distinction between exposure, infection and disease status is important. A common error is to confuse the results of those diagnostic tests that are essentially measures of infection status, such as serological tests, with measures of disease status, such as biochemical tests.

**Examples of factors causing animals to manifest different disease severity**

<table>
<thead>
<tr>
<th>Lower in Severity Spectrum</th>
<th>Higher in Severity Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Dose</td>
<td>Higher Dose</td>
</tr>
<tr>
<td>Middle Aged</td>
<td>Neonate or Elderly</td>
</tr>
<tr>
<td>Lower Stress</td>
<td>Higher Stress</td>
</tr>
<tr>
<td>Adequate Cu, Se, Vitamins A, E</td>
<td>Deficient Cu, Se, Vitamins A or E</td>
</tr>
<tr>
<td>No other diseases</td>
<td>Other metabolic diseases, co-infections</td>
</tr>
<tr>
<td>Higher social dominance</td>
<td>Lower social dominance</td>
</tr>
<tr>
<td>Lower producing</td>
<td>Higher producing</td>
</tr>
<tr>
<td>Higher Specific Immunity</td>
<td>Lower Specific Immunity</td>
</tr>
</tbody>
</table>

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The "Iceberg" Concept:
In outbreaks of most disease in animal groups, both clinical cases (the tip of the iceberg) and subclinical cases (unobserved beneath the ocean surface) are present in the group. For many infectious agents, particularly those that are endemic, more of the infections in a group are subclinical (silent) than are clinical. For some exceptions, such as rabies, few if any subclinical infections occur and almost all if not all clinical infections end in death. This iceberg concept of severity distribution also holds for most induced, non-infectious diseases affecting a group, such as hypomagnesemia, ketosis and hypocalcemia. Disease in an individual is often evidence of a group phenomena because the factors that caused the disease in that individual are usually affecting others adversely as well.

For most groups, the response to the host-agent-environment interaction that results in disease is usually not an either/or, black or white phenomenon. Instead, it is usually a continuum, with different individuals expressing different degrees of severity at different times as determined by the unique combinations of agent-host-environment risk factors that they experience. For each problem outbreak, the “shape” of this iceberg (the proportion affected, the proportion of the affected that become clinical and the proportion of these that die) at any point in time depends on the specific combination of agent, host, environment, vector (if one is involved), and human husbandry/management factors acting in that specific situation.

Because these factors change over time (e.g., animal immune responses eliminate the infection, humans change their management practices, the environment changes both seasonally, day-to-day and year-to-year), this “shape” changes over time. This does make outbreak investigation and problem solving both challenging and rewarding for the clinician.

Examples of the "Iceberg" phenomenon of severity distribution:

- **Bovine paratuberculosis:** "If the clinically affected animal was born on the farm, a minimum of 25 other animals are probably infected and less than 30% of those will be detectable by currently available tests." Whitlock RH, Buergehl C Vet Clin North Am Food Anim Pract (1996) 12(2):345-356.

- **BLV:** "Bovine leukemia virus (BLV) infection of cattle is a common but inapparent retrovirus infection from which less than 5% of infected cattle manifest clinically with lymphoma."

- **Invasive streptococcal disease:** "In an outbreak of invasive streptococcal disease (the "flesh eating bacteria") involving 4 clinical cases associated with a school, 46 of 187 children were found to be carrying the agent in their pharynx. JAMA (1997) 277:38-43.

- **Human tuberculosis:** For human tuberculosis, approximately 1 in 10 infected people develop clinical disease. About 9 in 10 people infected with measles have clinical signs, about 2 in 3 people infected with mumps, and about 1 in 10 people infected with poliomyelitis. Although histoplasmosis is commonly regarded as a fatal disease, in some areas over 80% of the population have evidence of infection. (p. 48, Lilienfield & Stolley, 1994).

**Important Corollaries:**

- Because subclinical (silent) cases of most diseases are considerably more numerous than clinical cases in a herd, the economic cost of subclinical disease usually exceeds that of the clinical disease. For this reason, an important component of herd production medicine is using strategic sampling and testing (e.g., rumen pH sampling, MUN testing, urine pH testing, fresh cow milk culture, bulk tank milk culture) to assess the prevalence of subclinically affected individuals in a group for those conditions that affect production.
EX: In a feedlot study of bovine respiratory disease (pneumonia, Wittum, TE et al. JAVMA 209:814, 1996) 30% of the crossbred steers, all from a single source, were pulled for treatment of clinical respiratory disease. None died but being pulled and treated for clinical disease was associated with a 22 lbs. reduction in gain as well as the labor and drug costs. However, at slaughter a surprising 70% of the calves that had never shown signs of clinical illness had lung scaring indicating that they had had subclinical pneumonia. These subclinically affected calves, which represented 50% of the entire group, gained 43 lbs. less than their herdmates without lesions. Another lesson from this study is that vaccination is not absolutely protective as all of these steers received MLV IBR and BVD three weeks prior to feedlot entry and again at entry.

- The marginal cost (cost of one additional unit) of subclinical disease per infectious unit is usually greater than the marginal cost of clinical disease per infectious unit. Hypothetically this means that the economic cost of an animal going from no infectious units to a burden of one infectious unit is higher than the cost of increasing an already high infectious burden by one unit.

**Marginal Cost of Infectious “Units”**

EX: In a study of the effects of liver fluke burden on wool growth and body weight gain (Hawkins, CD and RS Morris, Vet Parasit 4:341-351, 1978), the marginal detrimental effect of increasing fluke burden declined as the burden increased.

EX: This phenomenon also occurs in the association between bovine mastitis, somatic cell counts and milk production. The relationship between milk production loss and the logarithm of the SCC is approximately linear, meaning that a unit increase in SCC at a low SCC is associated with a larger impact on milk production than is a unit increase in SCC at a higher SCC (Raubertas, RF and GE Shook, J Dairy Sci 65:419-425, 1982, Jones GM et al. J Dairy Sci 67:1823-1831,1984). This is the basis of the linear scoring system for assessing subclinical
mammary mastitis problems.

- Some evidence suggests that the higher the baseline production of the group, the greater are these marginal costs in the affected animals.

**Caution:** The following are four common but serious mistakes that are due to misunderstanding the "iceberg" phenomenon by veterinarians and owners make.

- Considering only the clinically (observably) ill animals in the midst of an outbreak.

  For example, if precautions are applied only to clinically ill animals, subclinically infected (normal appearing) but shedding animals can continue to infect other susceptible animals. People often don't recognize that normal appearing animals can be infected, which accounts for the saying that "most disease is bought and paid for".

  Instead of applying the intervention (treatment, isolation, culling) only to the clinically affected animals, it should be applied to all the susceptible, exposed animals in the group.

- Interpreting the absence of clinical cases as the absence of the disease in any form and, in the case of infectious diseases, the absence of infection.

  Many infections are able to enter a herd, such as by importation of a subclinical chronic carrier animal, and spread for weeks to years before the infection is finally diagnosed in a clinical case.

  **EX:** Johnes, salmonellosis, BLV, "hairy foot wart"

  Although productivity is lost due to the subclinical form of disease, the loss is usually difficult to recognize or to visualize. As a consequence, until the problem becomes clinical people often don't take action to prevent it.

- Interpreting evidence of the presence of infection by an agent as indicating that the agent is the cause of the disease problem without other corroborating evidence.

  In the midst of outbreaks, veterinarians often take samples only from the clinically affected animals. Direct evidence of an infection, such as isolation of an agent, or indirect evidence, such as a serologic titer, may be found. However, unless the agent is always virulent (rarely the case), unless other evidence shows that this agent is present less frequently in the non-affected animals than in the affected animals, or unless other specific evidence, such as pathognomonic histopathological or clinical signs, is present, one should be cautious in concluding based on isolation alone that the agent is responsible for the disease. Co-infections with ubiquitous agents are not uncommon and disease outbreaks often occur in groups in which the ubiquitous agents are circulating among susceptible animals, such as recently grouped animals.

  This error frequently results in sort of an "infectious agent of the month" club.

- Interpreting the decline of clinical cases over time as evidence that the veterinary or management interventions applied were effective.

  Recognize that this decline is the "natural history" of most infectious disease outbreaks without any interventions. For most outbreaks of infectious disease, the highest number of clinical cases usually occurs early in the natural course of the disease through the group and then declines as the animals respond to the infection and the pool of susceptibles declines. Clinical cases may disappear altogether even though the infection is still widespread in the herd. This natural decline is then mistaken as evidence of vaccine efficacy or drug efficacy if one has been used. In most outbreaks other management changes are also made so determining by observation alone which interventions were actually effective and which were not is difficult at best.

  (For an example of this "natural history" of a disease outbreak, see: Gay JM, ME Hunsaker (1993). Isolation of multiple Salmonella serovars from a dairy two years after a clinical salmonellosis outbreak. JAVMA 203:1314-1320)

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**The "Endemic Stability" Concept:**

Many endemic infectious agents do not cause clinical disease in newly infected hosts under normal circumstances of transmission and infection (low dose to an immunocompetent host). Disease is most often the result of the disruption of this relationship (e.g., high infectious dose, stressed host, failure of passive transfer). Disease associated with such agents is much less often due to the introduction or emergence of a more infectious or more virulent strain.

**Examples:**

*Pasteurella hemolytica A1,* the predominant bacterial pathogen of bovine respiratory disease, is normal commensal flora of the upper respiratory tract of a significant proportion of cattle.
Many of the diarrheal agents of cattle (rota virus, corona virus, cryptosporidia, coccidia) are endemic in almost all livestock herds and all individuals in these herds develop immunity against them yet outbreaks of clinical disease occur in relatively few herds. The key question is why these herds are affected and not the rest.


A dramatic example of the effect of change in the medical ecology (improved sanitation) is the emergence of poliomyelitis caused by the human polio virus. Susceptible infants infected with the virus do not develop poliomyelitis but some susceptible juveniles and adults do.

**Note:** Failed attempts to eliminate such infections can result in a larger than normal proportion of susceptibles and can precipitate a clinical outbreak. Likewise, other changes can upset endemic stability, precipitating the expression of clinical disease.

**Caution:** A common mistake is to interpret the sudden appearance of clinical cases as indicating that a new infectious agent has been introduced into a group when actually unrecognized changes in the disease ecology have resulted in clinical cases caused by a ubiquitous infectious agent that has been present in the herd all along.

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### The "Herd Immunity" Concept:

Transmission of most communicable infectious agents will not continue within an exposed group of animals if the proportion of resistant animals in that group is above a threshold level, typically 70 to 80%. This level depends upon the agent and factors influencing the likelihood of transmission, such as animal density and the typical dose of the agent. This resistance can be passive immunity (acquired antibodies), active immunity (previous infection or immunization) or innate resistance.

On the other hand, if the animal density or the agent dose is significantly high, all individuals in a population may effectively be susceptible to infection even with adequate vaccination.

**Examples:**

Based on evidence showing that outbreaks of rabies in dogs will not propagate if between 39% and 57% of dogs in an area are vaccinated, WHO recommends immunizing at least 70% of the dogs in a population. *Vaccine* (1996) 14:185-186.

Even though evidence shows that *Brucella* vaccination protects only approximately 60% of vaccinated animals from infection, evidence also shows that an outbreak of *Brucella* abortion will not propagate in a fully vaccinated herd.

For herd immunity to stop an outbreak of human measles, it is estimated 94% of the population must be immune. In human population centers of over 500,000 people, measles will cycle continually without vaccination because of the continually emerging pool of susceptibles.

**Caution:** A common error is to assume that because a vaccine or bacterin is approved by the USDA and is marketed, it is efficacious. For a surprising number of veterinary vaccines, evidence of efficacy is either lacking (which means that it may or may not be efficacious) or the evidence suggests that the vaccine is not efficacious. Many veterinarians and producers don't realize that evidence of field efficacy is not required as part of the USDA vaccine licensing process and subsequent evidence of lack of field efficacy does not jeopardize a license.


Basic Reproductive Ratio (R<sub>0</sub>) Concept:

R<sub>0</sub> ("R Zero"): The average number of susceptible animals that are infected by each infected animal. This is a measure of the ease of transmission of an infectious agent.

EX: For epidemics of airborne viral diseases such as Foot-and-Mouth disease in susceptible populations, the reproductive ratio is on the order of 70. This is due to the production of viral aerosols, particularly by swine, that can travel for long distances and in part accounts for the drastic measures taken against this disease.

EX: For a disease such as IBR in a dairy herd, the reproductive ratio is around 7. Rijsewijk & Wentink Vet Micro 53:169-180 (1996).

For communicable infections to progress, on average each infected animal must infect one or more susceptible animals. If each infects more than one, the outbreak increases exponentially. If on average each infects less than one, the outbreak decreases. If on average each infects one, in large populations the outbreak progresses at a constant rate.

Over the long run, an R<sub>0</sub> equal to or greater than one is required for an infectious agent to survive in a group. If it can be lowered to less than one (the veterinarian's objective), eventually the agent will be eradicated from the group. The goal of control and prevention strategies for infectious disease is to reduce R<sub>0</sub> below one if not to zero.

Reducing R<sub>0</sub> can be done at any point in the transmission cycle by:

- Reducing or eliminating the shedding of the agent by the infected host.
  
  EX: Treating or removing the infected host. However, detecting these infected hosts is not always straightforward, particularly if they have always been subclinical. Chronic subclinical carriers of leptospira can be treated with long-acting antibiotics. Cattle persistently infected with BVD can be detected by laboratory testing and removed from the herd.

- Reducing the duration of environmental survival of the agent

  EX: Sanitation (carrying out effective sanitation isn't as straightforward as it first appears), exposing the agent to sunlight, drying the environment.

- Reducing or eliminating vehicle contamination and fomite transmission

  EX: Preventing contamination of feedstuffs and water and adequate sanitation of items that come in contact with the animal's mouth or other portal of entry.

  In general, we need to practice better "food safety" for all animal feedstuffs because many of them will support replication of food-borne pathogens when moist and warm. Fomites such as livestock trailers are often overlooked for diseases such digital dermatitis ("hairy foot wart") in cattle.

- For vector-borne infections reducing the vector population or preventing exposure of susceptible animals to it.

  EX: Applying pesticides, removing animals from vector inhabited areas.

  Many vectors such as flies develop resistance to pesticides fairly quickly. Pesticides also affect many other beneficial insects, which often are more sensitive than the target species. For more effective long term reductions of vector populations, attack their life cycles at multiple points rather than attacking a single point as is commonly done.

- Reducing the exposure of susceptible hosts.

  EX: Decreasing animal stocking density for agents transmitted by contact, increasing ventilation of enclosed housing for airborne agents, preventing contamination of vehicles such as feed and water, isolation of infected animals during clinical illness and the carrier state, maintaining youngstock groups that are more uniform in age.

  Accomplishing this exposure reduction often requires management and housing changes that owners may not be willing or able to make. For example, an "all in, all out" policy is a very effective means of reducing transmission but it usually requires major changes in facilities and management practices to accomplish it.

- Increasing the resistance of the susceptible hosts.

  EX: Prior vaccination with an efficacious vaccine, maximizing transfer of maternal antibodies, adequate balanced nutrition (particularly of the trace elements and vitamins involved in immune system function).
Modern animal husbandry and the associated environmental modification often dramatically increase the $R_0$ for infectious agents that co-evolved and survived successfully with their hosts under entirely different environments. For example, we house animals in enclosed airspaces, which unless managed carefully can markedly enhance the transmission of aerosol-born agents. We group animals together much more densely than they are in nature, which increases the level of environmental contamination and markedly increases the opportunity for contact between infected and susceptible animals. We also manage the animal's environment in ways that enhances the survival of infectious agents, such as providing roofs that protects infectious agents from the UV in sunlight or recycling fecal-contaminated water that transports water-borne infectious agents back to susceptible animals.

**EX:** Consider the medical ecology of *Fasciola hepatica* in the native grazing environment (scarce water, infrequent flooding of forage, low density of animals) compared to irrigated pastures (regular source of water, high density of animals).

**EX:** A dramatic example of the effect of increasing $R_0$ through animal husbandry is the association between the concentration of wildlife, such as birds and cervids (elk, deer), at winter feeding stations and the associated infectious disease outbreaks.

In the past, too much emphasis has been placed on using vaccination as the sole means to control and prevent disease outbreaks and not enough on the many other factors under management control, such as animal housing design, animal contact control and basic sanitation practices. Basically, not enough emphasis has been placed on good animal husbandry.

Attacking the transmission cycle of a disease or the causal chain of a disease at several critical control points will enhance the biosecurity of a group of animals. Then, if intervention at one point fails, control will still be maintained by the interventions at the other points.

Although most vaccines reduce the number of clinical cases and the number of infections that would have occurred in a group during an outbreak, this prevention is not absolute. Most vaccines do not prevent all infections. Rather, in a group of animals most vaccines at best will reduce the number of animals infected, will reduce the proportion of those that become clinical cases among those that are infected and will reduce the amount and duration of shedding in those that are infected. But, as noted above, some vaccines don't even do this much.

**EX:** *Strep. equi* bacterins are estimated to reduce the number of clinical cases by approximately 50%.

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**Epidemic Curves:**

Plots of the number or proportion of animals affected in a group over time.

Epidemic curves are useful to determine what type of exposure occurred and what type of transmission is occurring in a disease outbreak. In turn, this information is useful to help determine what likely caused the outbreak and what interventions will likely stop it.

**Point Source Epidemics:** Point source epidemics occur when an index case or a "vehicle", such as contaminated feed, exposes most of the susceptible animals in a group at once. In the case of an infectious agent, this exposure was by a dose sufficient high to cause clinical disease in most exposed animals and if the exposure is to an index case the $R_0$ was initially very high. Thus, most cases occurred within the typical range of the incubation period and no further transmission occurred.
Propagating Epidemics: Propagating epidemics occur when infected animals transmit the infection to susceptible animals over time. Exposure of susceptibles occurs over time rather than all at once as above. These epidemics progress through a group over a period of time that is considerably longer than the typical incubation period.

Most likely a change in some host, agent or environment factor markedly increases the $R_0$ and infections that would have been subclinical and unrecognized now become clinical and recognized. Because clinical cases usually shed much more of the infectious agent than do subclinically infected animals, the level of environmental contamination increases, increasing the infectious dose to other individuals in the group. More of these now begin having clinical rather than subclinical infections and the outbreak grows.

The Causal Web Concept:

A causal web is the linkages between a set of agent, environment and host factors that have been shown to result in disease. Disease usually develops because of a chain of causes, rather than a single cause, that have acted one after another or together, often in complex ways. The purpose of developing a causal web is to provide "the big picture": a framework for thinking about the relationships between these causes and for developing strategies for controlling and preventing the condition in a group of animals. The relative importance of each component depends on the actual factors involved in the specific situation. Part of the detective work of solving disease problems in groups is determining which factors are most important in a particular situation and which of these are the easiest to change.

The following are two examples of causal webs modified from the bovine respiratory disease section of the Large Animal Medicine Notes "Epidemiology of Pneumonia in Feedlot Cattle" (S. Wikse).

Note that although the basic pathophysiological mechanism is similar in both, the critical control points are considerably different between older cattle housed outdoors in open feedlot pens and neonatal calves housed in enclosed barns. Note also that the relationships between the selected factors are fairly complex.

Causal Web (Path Model) of Risk Factors of Housed Calf Bronchopneumonia
Causal Web (Path Model) of Risk Factors of Feedlot Calf Bronchopneumonia
Why do clinical outbreaks of ubiquitous agents occur?
Infection occurs in an animal when the infectious dose exceeds its resistance, innate or acquired, against that infection. For many of the ubiquitous infectious agents, infection occurs at some point in almost every animal's life. Providing that the animal has sufficient resistance, most of these infections are subclinical and the animal develops immunity. However, if the dose received by the animal is sufficiently high, it will develop a clinical case rather than a subclinical infection. Outbreaks of clinical disease occur when more susceptible hosts than normal are infected with infectious doses that are sufficient to cause clinical disease.

For many infectious agents, clinical cases shed the infectious agent at higher levels for longer time than do subclinical cases. Thus, the infectious dose often increases as more animals develop clinical cases rather than subclinical cases and the environment becomes more heavily contaminated as a consequence. In turn, more infections occur in animals that were resistant to the lower infectious dose and more clinical cases develop. Until the transmission of the infectious agent is reduced, the infectious dose lowered, the resistance of the remaining unaffected animals is increased or the pool of susceptibles is exhausted the outbreak expands in a vicious spiral.

References and Further Information:

Anderson and May wrote this book and a number of other papers on the theory of the transmission of infectious agents, herd immunity and vaccination. Searching on either of their names will identify those papers.


Numerous examples of the causal webs for different types of diseases.


General description of the natural history of infectious disease processes, emphasizing the interaction between host and agent factors.

**Relevant On-Line Materials:**


**Other References:**


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