Herd Immunity

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KEYWORDS

• Herd immunity • Contagious disease • Basic reproductive number • Infectiousness • Immune • Susceptible

KEY POINTS

- Herd immunity is an important concept of epidemic theory regarding the population-level effect of individual immunity to prevent contagious transmission of pathogens.
- Understanding herd immunity requires consideration of the factors that affect infectiousness, agent transmission, and immunity, as well as an understanding of the human and animal behaviors that result in undesirable outcomes.
- The basic reproductive number is a measure of contagion in a population that helps to predict the proportion of immune individuals needed to prevent an epidemic.
- Vaccination programs to eliminate or eradicate pathogens from a population require that the threshold level of herd immunity be achieved.
- Some age-associated epidemics of disease, such as pneumonia in calves before weaning, may be explained by the loss of herd immunity caused by waning maternal antibodies.

INTRODUCTION

Herd immunity is an important concept of epidemic theory regarding the population-level effect of individual animal immunity to prevent transmission of pathogens. Herd immunity exists when sufficient numbers of animals in a group or population have immunity against an agent such that an outbreak fails to materialize when the agent has been introduced by an infected individual, because the likelihood of an effective contact between diseased and susceptible individuals has been reduced.[1] Herd immunity applies to a restrictive set of conditions that are discussed later. When these conditions apply, methods to achieve herd immunity serve an important role in preventing disease epidemics and are an important component of programs for disease elimination or eradication.[1] Loss of herd immunity may also explain age-associated epidemics of disease related to loss of passively acquired maternal immunity.[2] Herd immunity is not just about the immunization process. Understanding herd immunity requires consideration of infection dynamics, modes of transmission, as well as the acquisition of immunity by individuals in the population.

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INFECTION DYNAMICS

Infection dynamics considers the state of infectiousness of individuals, rather than whether or not the animal is infected, the stage of the disease process, or even whether disease ever manifests clinically.[3] Diseases are not transmitted, but pathogens are. Infection refers to the invasion and replication of an agent in a host. Infectiousness, or the state of being infective, refers to the capability of an infected individual to transmit the agent to others. Being infected is not the same as being infectious, because the state of infectiousness does not necessarily coincide with the entire period of the infection process. The expression of clinical signs of disease is a poor correlate of infectiousness because:

- The state of infectiousness may occur before, after, or during the period of clinical signs, depending on the agent
- Infection may not be apparent clinically (eg, subclinical infections)
- Similar clinical signs may be caused by more than 1 infectious agent
- Clinical signs of disease commonly require not only infection with the agent but also the occurrence of other component causes[4,5]

Therefore, in this article, the discussion about factors leading to herd immunity largely considers infected individuals who are infectious without regard to their current state of health.

The Risk of Infection Given Exposure

Infectious agents are acquired by a host during contact with a reservoir in a manner that facilitates infection. The reservoir can be environmental sources, animals, insect or other vectors, or humans. Infectious agents can invade a host through inhalation, ingestion, or direct penetration of skin or mucous membranes. Once exposure occurs, the factors that influence the transition to infection are related to the dose, the agent, and the host. Exposure to a larger number of organisms increases the likelihood of infection. Methods to decrease the number of organisms or their vectors, such as washing pen surfaces, using disinfectants, or applying insecticides, help to reduce the probability of infection. Agent-related factors, or infectivity factors, are characteristics of the agent that typically enhance its ability to invade the host by attachment of the pathogen to host cells. One of the most important host-related factors, or susceptibility factors, is immunity acquired after vaccination or prior infection with the pathogen. Immunity may be complete or partial, and may wane with immunosuppression; for example, because of malnutrition, chemotherapy, or some viral infections, such as bovine viral diarrhea virus (BVDV). Other susceptibility factors include whether or not hosts express receptors that pathogens use for invasion, or whether hosts have physiologic factors that affect host clearance of microorganisms. For example, impaired mucus clearing of the lungs may increase the risk of respiratory bacterial pathogens.[3]

The Risk of Infectiousness Given Infection

The degree and duration of infectiousness are essential parameters for describing an infectious process, and critical for explaining or predicting the spread of an infectious agent within a population. The degree of infectiousness depends on characteristics of the agent and host. There may be variation in the number of organisms produced by an infected individual. The dose load of agent may wax and wane with the stage of infection or by the disease state of the host. For example, individuals infected with a respiratory disease agent may be minimally infectious until they begin to cough.

Similarly, individuals infected with an enteric agent may be more infectious during the time when they have diarrhea, partly because they may be shedding more organisms and partly because there may be more opportunities for fecal-oral contact. The duration of infectiousness may be caused by characteristics of the agent, the nature of the infection, and the various host-pathogen interactions that affect the host's ability to eliminate the infection.[3]

Some infected individuals present a greater risk for transmission of infectious agents than others. Many infectious diseases show transmission heterogeneity, a superspreading effect whereby many of the infections are transmitted by a minority of individuals.[6–8] This heterogeneity of transmission may occur because of behaviors of the host or because spatial relationships lead to greater opportunities for effective contacts.[8] In some cases, superspreading occurs because of the large infectious dose produced, termed supershedding.[9] Sometimes superspreading is caused by characteristics unique to certain individuals; for example, because of genetics,[8] or persistent infection, as with BVDV.[10] Transmission heterogeneity has been observed with enterohemorrhagic *Escherichia coli* O157 (EHEC O157) infection of cattle. At a given point in time, cattle infected with EHEC O157 shed the organism at varying concentrations in feces.[9,11,12] Therefore, at any point in time, some infected cattle may be contributing vastly more EHEC organisms into the environment, and possibly to other cattle, than others.[13]

Duration of Infectiousness

The possible outcomes following infection are resolution of the infection, persistence of infection, or death caused by disease. These factors also influence the duration of infectiousness. The resolution of infectiousness depends on many factors, including the pathogenicity of the organism, host immunity, and the use of antimicrobial therapy. Pathogens that are highly virulent may paradoxically reduce duration of infectiousness by killing the host. Some pathogens, such as BVDV, have bimodal distributions of infectiousness because most hosts have a brief transient period of infection, whereas other infected hosts have prolonged, sometimes persistent, states of infectiousness. For some agents, a single host may have multiple periods of being in an infective state. Hosts infected with agents with a latent state (eg, the herpes viruses) may have recurrent periods of infectiousness between latent periods.[3] The immune response following exposure to a pathogen may be sterilizing, partial, or it may wane with time. Sterilizing immunity is not accomplished with most pathogens and may not be essential for population-level protection against transmission of infection.[14]

QUANTIFYING CONTAGION IN POPULATIONS

Secondary Attack Rate

The secondary attack rate is a statistic sometimes calculated in outbreak investigations. The secondary attack rate is the probability of infection among susceptible individuals in contact with an infectious host, and is a function of the factors affecting infectiousness and transmission given infectiousness.[3] This approach is used for quantifying the contagiousness or transmissibility of pathogens from infected individuals to susceptible individuals.

Basic Reproductive Number

Similar in concept to the secondary attack rate, the basic reproductive number, R_0, is the average, or expected, number of secondary cases that occur in a completely

susceptible population following introduction of a single infectious case. The term case refers to an infectious individual regardless of disease status. R_0 is a fundamental statistic in epidemiology for the purpose of studying infectious disease dynamics to summarize a complex set of factors affecting the rate of transmission in a population. The simplest interpretation of R_0 is that if the value is greater than 1, then an outbreak of disease will occur; if R_0 is less than 1, then an outbreak is unlikely or expected to be of low magnitude. The value of R_0 is used to model the potential size of an outbreak and to estimate the proportion of the population that must be immunized to eliminate an infection from the population.

R_0 is a function of biological, behavioral, and environmental factors that affect the rate of contagion. R_0 is a dimensionless statistic, not a rate over time or a measure of disease severity. Neither is its value modified through vaccination. The basic reproductive number is rarely calculated directly. Estimations of R_0 are often modeled as a function of:

- The duration of infectiousness after infection
- The likelihood of infection given contact between an infectious and susceptible host (or vector)
- The contact rate[15]

Because of its complexity, R_0 is sometimes misunderstood and misapplied. One of the most common errors is the belief that R_0 represents a constant value for a given pathogen. Some pathogens are more contagious than others in exactly the same setting. However, the characteristics of the pathogen that favor transmission is only 1 of several factors explaining contagion of any particular pathogen. Any factor that changes the contact rate affects the value of R_0, including population density, seasonality, or social organization.[15] For example, the R_0 value for BVDV in susceptible calves housed in a feedyard drylot is likely to be higher compared with similar calves living in extensive range conditions because of the difference in population density.

Reproductive Ratio

Similar in concept to R_0 is the reproductive ratio, R, also known as the effective reproductive number.[4] The reproductive ratio is the average number of transmissions of infection that occur from each infectious case.[3] In contrast with R_0, which refers to contagion in a completely susceptible population, R can vary over time as immunity changes in a population, and it is sometimes estimated from population-based data. If the susceptible individuals are added to the population, then R increases. If the proportion of susceptible individuals decreases because of immunity from vaccination or exposure, then R decreases. In circumstances in which R is less than 1, transmission cannot be sustained and transmission of infection wanes. If R is greater than 1, then transmission is sustained and major or minor epidemics occur until the proportion of susceptible individuals decreases to the point that R becomes less than 1 and the epidemic of infectiousness wanes.[3,4]

Threshold Level

The threshold level is a concept that incorporates the effects of transmission dynamics with the geographic distribution of animals to determine the minimum density of susceptible animals that would support an outbreak of disease, or, correspondingly, the density of susceptible animals required to prevent a disease outbreak.[16] The threshold level is defined mathematically by Kendall's pandemic threshold theorem. At greater than the threshold density, 1 infected animal can, on average, infect more than 1

susceptible animal and an outbreak can occur.[16] The threshold level has not commonly been applied to animal diseases. However, as an example, it has been estimated that a minimum density of 12 dogs/km^2 is required for an epidemic of canine parvovirus to occur.[16]

Dissemination Rate

Livestock animals are typically managed as subpopulations (ie, groups of animals that cluster within farms that may be more or less biosecure against pathogen introductions). However, animals, people, and equipment may move from farm to farm, or the wind or water might work to disseminate pathogens from one place to another. The dissemination rate describes the risk for pathogens to move from one farm to infect animals on another farm. The dissemination rate depends on:

- Characteristics of the environment, including weather, animal density, and geography
- The type of farming operation, such as the species, class of animal, and opportunities for fomite transmission
- Animal movement, such as for marketing, or from one pasture to another
- The behavior of the farmer, including decisions that affect biosecurity or their own movements, or contact with animals from other sources
- Disease control strategies beyond the farm, such as requirements for quarantine, inspection, or movement restrictions
- Host factors, including their level of immunity, presence of other concurrent diseases, age, breed, and pregnancy status
- Characteristics of the pathogen that affect its survival in the environment and contagion between hosts[16]

Large, multifarm epidemics of disease are often brought under control by taking efforts to manage the factors that decrease the dissemination rate, such as changing behaviors of farmers by creating awareness, and modifying the factors that facilitate farm-to-farm transmission, such as preventing the mixing of animals at markets. The estimated dissemination rate is calculated by dividing the number of farm outbreaks in the population occurring in a defined time period by the number of farm outbreaks that occurred in the time period before (**Fig. 1**).[16]

MODELING EPIDEMICS

Epidemic models help to show the relationships between factors that result in an epidemic of infective cases, as well as showing the nature of the epidemic. There are many forms of epidemic models, with differing levels of complexity. The Reed-Frost model is a simple epidemic model that is useful for demonstrating epidemic theory and herd immunity.[17] The Reed-Frost model (**Fig. 2**) uses a contact rate and the numbers of infected, susceptible, and infected individuals at intervals equivalent to the incubation period to predict the form of a propagated epidemic over time. Propagated epidemics are epidemics that proceed through secondary cases of infection, compared with common or point-source epidemics, which occur as primary cases of infection caused by exposure to a source common to all.[16] The Reed-Frost model assumes that animals move from susceptible to infected in 1 incubation period and are then immune in subsequent periods. The process of moving from susceptible to infected occurs as a chain of binomial distributions.[16]

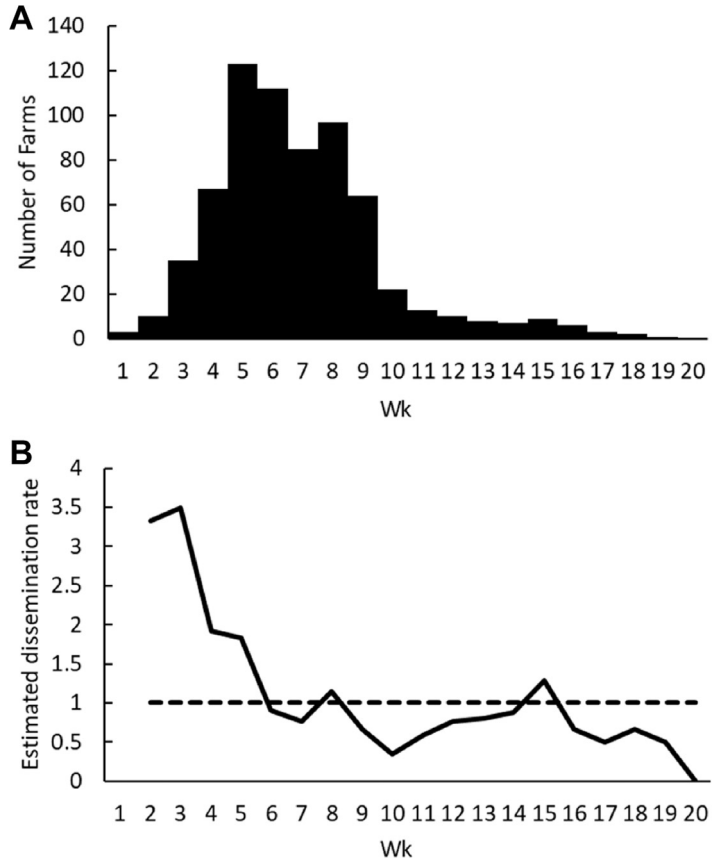

Fig. 1. (*A*) An epidemic curve of farms with a disease and (*B*) the corresponding estimated dissemination rate.

HERD IMMUNITY

The goal of vaccination programs is either to prevent the expression of clinical signs of disease following infection or to prevent the transmission of infection in the first place.[4] The strategy of vaccinating for clinical protection is useful for endemically stable pathogens that are common to many animals but only rarely cause disease. Health is improved because the probability for infected animals to show clinical signs of disease is reduced. However, the pathogen may continue to circulate in the population. For pathogens of high economic cost, such as foot and mouth disease, or important to human health, such as rabies, it may be more desirable to eliminate the agent from the population. The strategy of using vaccines to prevent transfer of infection is required to eliminate or eradicate an agent from the population. In this situation, the vaccine should be sufficient to induce herd immunity.[4] Herd immunity is the resistance of a group or population to attack by a disease to which a large proportion of the group is immune, thus lessening the likelihood of an infectious individual to make effective contact with a susceptible individual.[1] Herd immunity can function to prevent the successful introduction of infection into a population of animals or minimize the extent, or speed, of transmission after it has entered the population.[18]

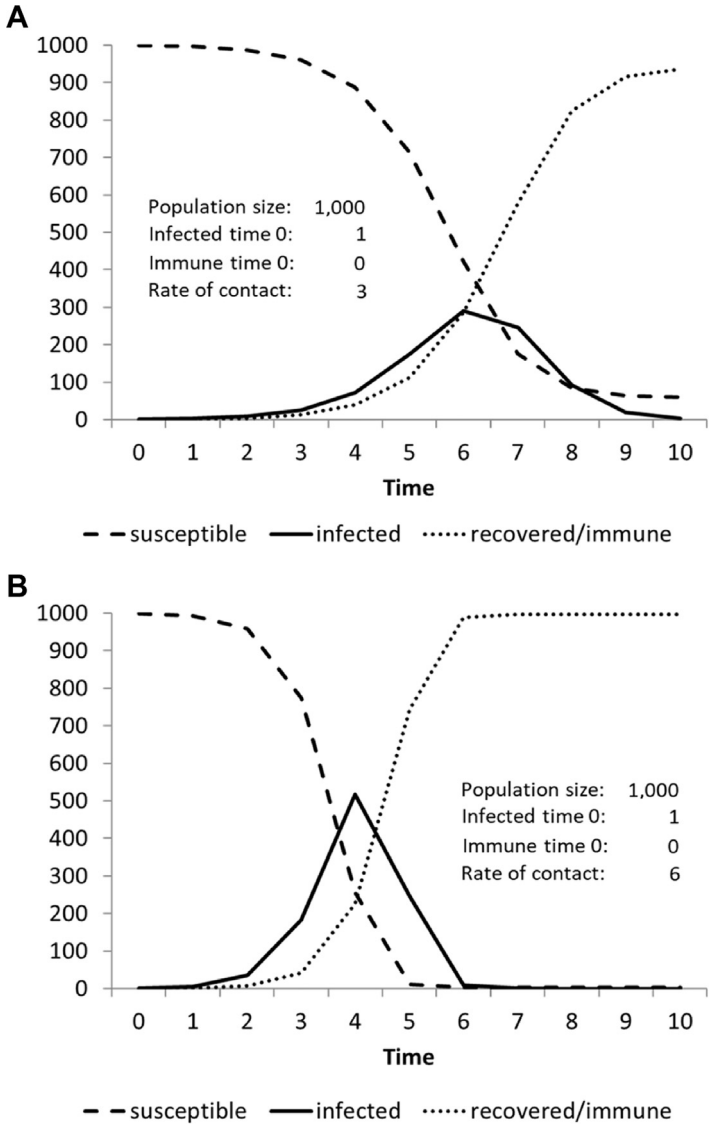

Fig. 2. (*A*) A Reed-Frost model of an epidemic following introduction of a single infective individual in a population of 1000 susceptible individuals with a contact rate of 3 per time period and (*B*) 6 per time period. Note the change in peak and duration of the epidemic depending on the contact rate.

Analogy of Herd Immunity

The following analogy is intended to help explain herd immunity and how the concept is applied to the population-level control, elimination, and eradication of disease. Where I live, the grass in my yard is lush and green in the spring. If I toss a burning match into the grass, the yard will not burn because the green grass is not susceptible to burning. In the early summer, the grass in my yard is still mostly green, but some brown, dried blades of grass are beginning to appear. If I toss a match into the grass

now, a few of the dried blades might catch fire, but the yard will not burn because there are too many green blades of grass to allow the fire to spread. It is at this point that my yard is showing the value of herd immunity. Even though some of the grass is susceptible, the amount of grass immune to fire prevents the destruction of my yard. Later in the summer, the grass in my yard is dry, brown, and burnable. It has lost herd immunity. If I toss the burning match now, the grass will burn and the fire will spread because most of the grass is now susceptible to burning. The ensuing epidemic of fire might even consume my home. Eventually, everything in my yard that was susceptible to burning has been consumed and the fire burns itself out. But that is not the end of the story, because I live in a community where other people have yards. When my grass was burning, hot embers may have been disseminated to my neighbors' yards by the wind. One neighbor keeps his yard the same way I do, so his yard and house also burn. A second neighbor is worse at keeping his yard than I am. His yard has very little grass, so even though the grass he has is dry and burnable, the fire cannot spread from one blade of grass to the next. His yard and home are spared because of a low contact rate. A third neighbor keeps his yard well watered so, even though some of the grass are dry and burnable, most of the grass is still lush and green. He has maintained herd immunity and his yard is spared. Understanding this fire danger in the summer, and wanting to avoid it, the whole neighborhood could be protected by changing some risky human behaviors (such as tossing burning matches) that introduce fire, making certain that yards are less likely to burn by keeping them watered to maintain herd immunity, or by having so little grass in the yard that the basic reproductive number is less than 1.

Demonstrating Herd Immunity with the Reed-Frost Model

Fig. 3 shows what happens to the epidemic curve as the proportion of the population that is immune to the disease increases. In contrast with the circumstances represented in Fig. 2, with a population that is entirely susceptible at the time the pathogen is introduced, Fig. 3A shows that the form of the epidemic curve changes because it takes longer for the infection to spread through the population when at least part of the population is immune. The epidemic may fail to materialize if a sufficient proportion of the population is immune (see Fig. 3B).

The degree of contagion of the agent is a direct determinant of the proportion of immune individuals required for herd immunity. R_0 can be used to estimate the proportion of immune individuals required to reach the threshold for herd immunity. The relationship between R_0 and the proportion of immune individuals required to achieve herd immunity to the extent that an epidemic is prevented (p_c) is noted by the formula[19]:

$$p_c > (R_0 - 1)/R_0 \text{ or } 1 - 1/R_0$$

For example, if $R_0 = 5$, then the proportion of immune individuals required to achieve the threshold of herd immunity must exceed $1 - 1/5 = 80\%$. If $R_0 = 20$, then more than 95% of the population must be immune to achieve this level of herd immunity.

There are challenges to achieving herd immunity. The proportion of immune individuals in a population needed to achieve the threshold of herd immunity assumes randomness in the contacts between infected and susceptible individuals. However, heterogeneity in transmission is a reality in most human and animal populations. Highly susceptible subpopulations that sometimes experience epidemics of infection become a challenge to eliminating or eradicating important

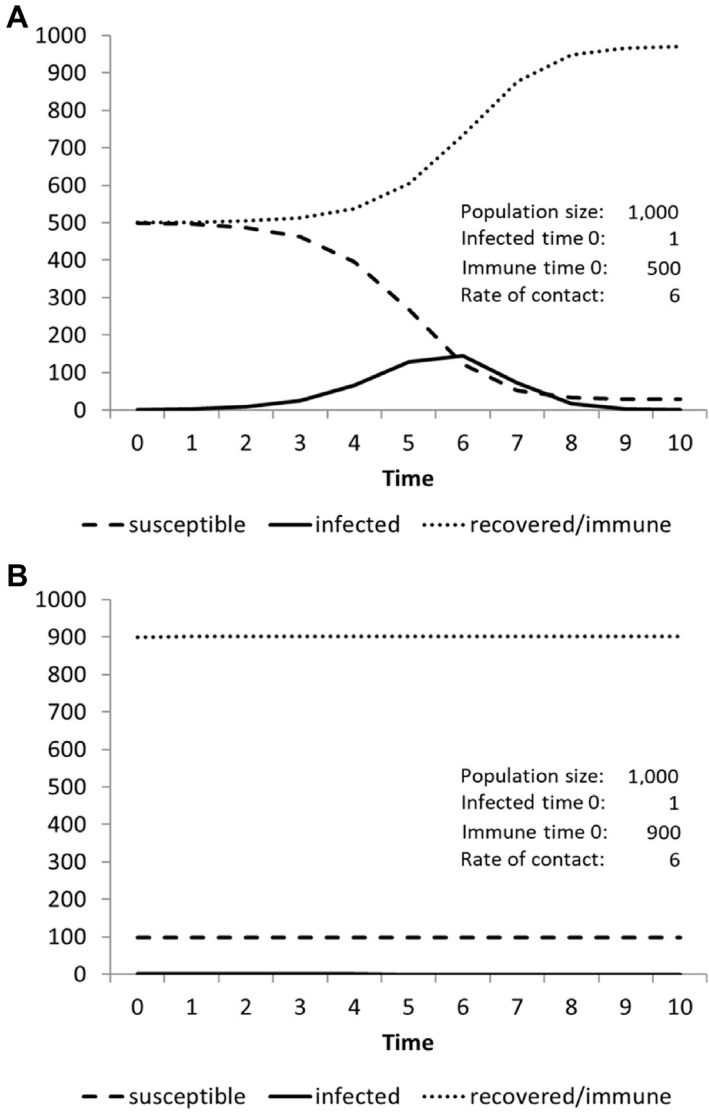

Fig. 3. (*A*) A Reed-Frost model of an epidemic following introduction of a single infective individual in a population of 1000 with 500 immune individuals and (*B*) 900 immune individuals at time 0 with a contact time of 6 individuals per time period. Note that the herd immunity threshold is exceeded when 900 of the 1000 individuals are immune and no epidemic took place.

human or animal pathogens, such as the lack of uniform distribution of vaccine in the population.[1,19–21] Further, vaccination does not ensure immunization. Even in well-executed mass-vaccination programs, immunization may only be achieved in 70% of those vaccinated once, and maybe 90% following a second round of vaccination.[21] Poor timing of vaccination, poor cooperation between farmers and veterinarians, and poor vaccine storage and preparation all contribute to lower-than-desired levels of herd immunity. Vaccination programs that result in low levels

of herd immunity may even help to perpetuate the persistence of the pathogen in a population either by providing greater opportunities during the vaccination process for comingling and continued transmission, or because the vaccination program makes clinical signs of the disease less evident and therefore more tolerable to farmers, politicians, and other decision makers who become less zealous about pursuing pathogen elimination.[21]

Herd Immunity in Livestock Populations

It is not possible to achieve herd immunity against all pathogens. Herd immunity applies to restrictive circumstances such that:

- The pathogens are fairly species specific
- The pathogens are spread contagiously by fairly direct means
- Host exposure or vaccination confers fairly strong immunity[1]

For example, even though it is possible to confer strong immunity through vaccination, it is not possible to achieve herd immunity against agents such as *Clostridium tetani* or *Bacillus anthracis* because they are fairly noncontagious infections primarily spread via environmental exposure. For these diseases, there is no protection afforded to nonimmunized individuals by others in the population being immune. Because *Streptococcus agalactiae* is spread by contagion and is an obligate pathogen of the bovine mammary gland, this agent meets some of the requirements necessary to achieve herd immunity. Nevertheless, it has not been possible to induce strong immunity to this agent through either infection or vaccination.[22]

However, herd immunity still applies to many important contagious infections of cattle and small ruminants. For example, rinderpest virus, declared eradicated from the world in 2011, had the characteristics for achieving widespread herd immunity, including having a single viral immunotype and vaccine induction of long-standing protective immunity.[20,23] Rinderpest virus has additional characteristics, such as causing few inapparent infections and lacking a chronic carrier state, which helped make it an ideal candidate for eradication efforts.[20]

Vaccination has been used to achieve herd immunity in regionally targeted programs to eliminate some pathogens. For example, foot and mouth disease has been eliminated from some populations by ring vaccination around infected herds, and rabies virus has been geographically restricted by providing vaccine baits as barriers to virus transmission in wildlife.

Outbreaks of pneumonia in calves before weaning may be explained by the loss of herd immunity that occurs with the synchronous loss of passively acquired maternal immunity by calves of similar age.[2] The half-life of maternally acquired immunoglobulin G is approximately 16 days, so the remaining maternal antibodies are negligible by the time a calf is 3 to 4 months of age.[24] In herds with a short calving season, calves lose their maternally derived immunity over a similarly small window of time that seems to coincide with the period of greatest incidence of pneumonia. It is common for pneumonia to occur as sudden epidemics when most calves are 3 to 4 months of age, the age at which herd immunity might be lost.[2]

SUMMARY

Population-based vaccination programs are typically designed to either mitigate clinical signs of endemically stable diseases or to prevent transmission of important contagious pathogens for the purpose of eliminating or eradicating the organism

from the population. Herd immunity in the population is required to achieve the latter strategy. Herd immunity occurs when a sufficient proportion of the population is sufficiently immune to prevent ongoing transmission of the pathogen to susceptible animals. Achieving herd immunity requires an understanding of the factors that affect infectiousness, agent transmission, and immunity as well as an understanding the human and animal behaviors that result in less-than-favorable outcomes.

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