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Social Groups and Social Group Immunology: A Literature Review

by

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Introduction:

Social groups are a common phenomenon among animal species including humans. While there are many evolutionary advantages to this, there is also the increased risk of infection due to being in close proximity to other individuals. Thus, this paper looked at the possibility that social grouping might be evolutionarily unfavorable from an immunological stand point on the basis that individuals would be closely related, have similar immune systems, and therefore risk widespread infection in a community with the introduction by a single pathogen.

The idea that a closely related group of animals would increase the devastation caused by a single infection isn't new. In fact, it's seen in domesticated plant species – especially crops – on a regular basis. To increase the performance of crops, traits that increase yield and rate of growth have been selected by breeders. However, this reduces the variation among the plants and results in increased vulnerability of whole groups of plant species to pathogens. This requires that two assumptions about the crops are true: the trait that makes the crops vulnerable is widespread among the plants enough to affect more than one individual and that the pathogen is able to quickly spread between all of the individual plants that are susceptible (Allard et al., 1993).

An example of a domesticated crop that abides by the two assumptions above (since not every domesticated plant species does) are Cavendish bananas. They were cultivated due to their resistance to a disease that wiped out Gros Michel bananas and nearly ended the banana industry years before but are now facing a similar epidemic, Panama disease. The genetics of the Cavendish bananas, due to selection by the industry, are similar between each plant and thus the disease is spreading rapidly enough through the banana crops that there is a chance these bananas could be entirely wiped out (Kema et al., 2017).

Social groups are defined as groups of individuals of the same species living in close quarters with one another, interacting on a regular basis with one another. Each individual in the group often has a very specific niche or responsibility and has to abide by predetermined behavioral rules. This helps increase the survivability of each individual in the group while also ensuring the group is capable of staying together peacefully. However, each individual often gives up its individuality and works strictly for the good of the group in a behavior known as cooperation (Wilkin and Brainard, 2016).

To maintain a social group, animals have to develop unique behavioral characteristics. One of the most important are ways to communicate with other members of the group. Communication can take several forms but primarily, relies on body language and, in primates, facial expressions. These communications are necessary to relay position in the group to other members (especially when challenged) or to let the group know where to find resources (Wilkin and Brainard, 2016).

Most other behaviors related to communication include displays of aggression. Aggression can be actual violence against other members of the group or can be harmless displays meant to intimidate one of the two involved parties to back them down. This helps maintain social order within the group so as to prevent anarchy. Furthermore, it often occurs in response to competition over resources. This can happen within the species (whether between individuals of the same group or between two different groups) or between multiple species. Within the group, the resources are often then divided by rank which is reinforced by aggressive behavior (Wilkin and Brainard, 2016).

Competition is the greatest cost to social grouping behavior; more individuals result in more resources needed. However, as seen with honeybees, there are other forces that outweigh this cost. The primary reason is that there is also competition between groups and the survival of a group over another group increases the survival of the individuals in the successful group. In the honeybee experiment, it was found that the group increased their ability to compete by increasing the quality of the food the foragers found and their ability to find more resources. Interestingly enough, individual survival wasn't increased (measured under the hypothesis that larger hive sizes would decrease the amount of time it took for an individual forager to find resources) as the worker bees still spent the same amount of time foraging (Seeley and Visscher, 1988).

Another way in which social grouping directly increases the survivability of individuals involves behaviors to reduced risk of predation. As to how this happens, there are a couple of hypothesizes. One such is called the dilution effect in which the more potential targets for a predator to choose from reduces the odds that an individual would be the one preyed upon. The other explanations is known as the many eyes hypothesis which states that individuals in a group can be less vigilant since there are more animals capable of spotting predators early (Roberts, 1996). This acts as a strong selective force for evolution in favor social groupings since it would increase the protection of the involved individuals.

An interesting anti-predator behavior that has developed as a result of social grouping is mobbing (when a group of prey attack en masse the perceived predator.) The interest in this behavior lies in its intentions: is it altruistic or selfish? A study done on Arabian babblers suggesting it may be a selfish behavior to increase the survival of each individual in the prey group though the study recognized there are likely many factors which increase the odds that the mobbing behavior would occur (Ostreiher, 2003).

Social grouping provides an advantage to animals in terms of energy and heat conservation too. In an experiment done on rat pups, it was found that they would huddle together and compete for the warmest position in the pile – the bottom underneath all of the other pups. Competition for the warmest spot led to circulation of position by the rat pups, which in turn raised the temperature of the entire nest to a thermoneutral temperature. The pups, as a result, expended less energy during thermogenesis (creation of heat) and lost less heat to the environment (Alberts and Indianna, 1978).

There are many other advantages to social groupings that, in combination with the few examples listed here, demonstrate that the behavior is evolutionarily favored in some respect. However, there are also limiting factors known to prevent overpopulation by a species, even if that species doesn't exhibit social group behavior. These include the well-known factors such as resource availability, space in a territory, and the chances of reproduction. A not so commonly known factor that limits population size – especially in social animals – is parasitism. The larger the group is, the more likely a majority of the group's members have parasites. This seems to set an optimal group size for animals (Cote and Poulinb, 1995).

The evolution of social behavior is further supported by the appearance of natural chemicals produced in the brain that both promote social behavior but also seem to induce preferences for individuals already part of the group. One such chemical is oxytocin, which seems to act on the amygdala (a section of the cerebral hemisphere associated with experiencing and expressing emotions) to induce increased affection and affiliation with familiar individuals in rhesus macaque groups but at the same time territorialism and aggression towards unfamiliar individuals (Amaral, 2002 and Kavaliers and Choleris, 2011). This is interesting because it shows a possible evolutionary preference for social grouping in animals expressing oxytocin.

Similar to oxytocin, arginine vasopressin is also produced in the brain and seems to promote the formation of social bonds with familiar individuals as well as to increase aggression towards unfamiliar individuals. In fact, because arginine vasopressin and oxytocin are so similar, they are able to bind to each other's receptors and still induce a signal (Kavaliers and Choleris, 2011). This increases the chances of the signal being produced and amplified suggesting that it is a necessary signal to receive and respond to in terms of survival.

Oxytocin and arginine vasopressin are not only involved in behavior but have roles in physiology of animals as well. One particular way in which these two chemicals seem to affect physiology is through the development of different muscles. Oxytocin seems to influence the development of cardiac muscle and smooth muscle while arginine vasopressin affects skeletal muscle (Costa et al., 2014).

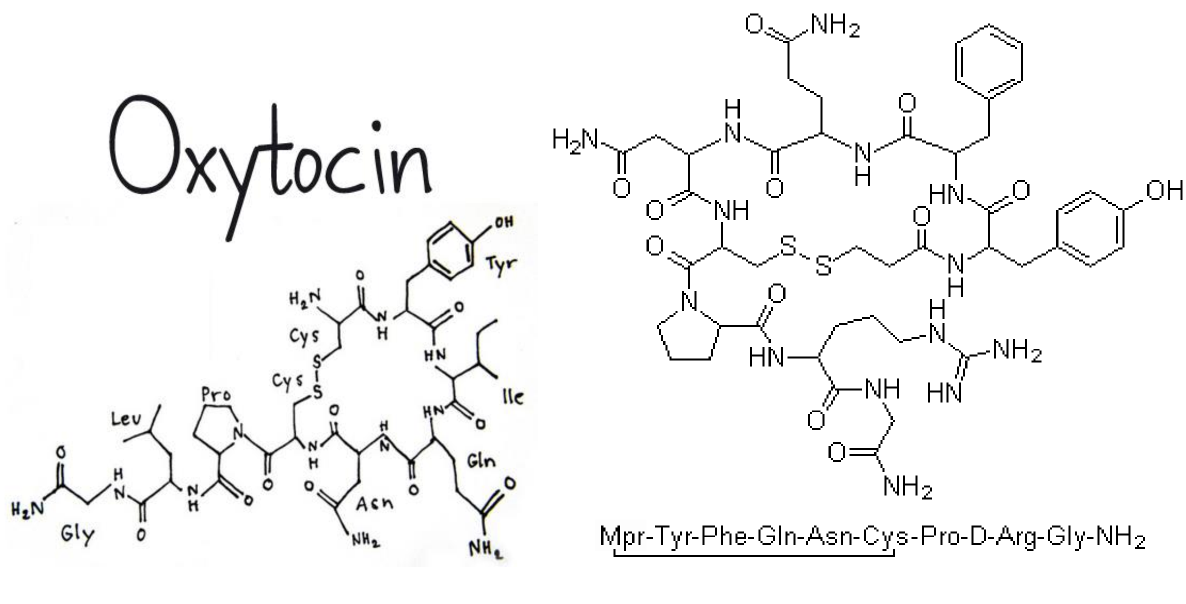


Figure 1: Right, Oxytocin from http://brighterbrains.org/hub/wp-content/uploads/2014/11/oxy.jpg. Left, Arginine Vasopressin from http://www.labgogo.com/Product/structure/16679-58-6.jpg.

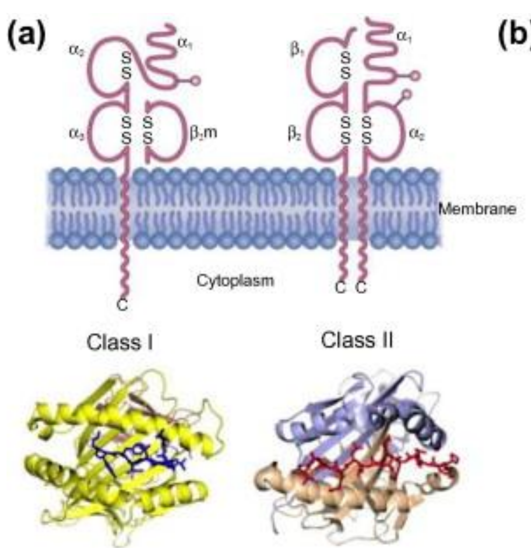
The question becomes, is social grouping evolutionarily favored from an immunological perspective? Is it possible that individuals that live in social groups are genetically related enough that they would have similar immune systems and thus respond (or not respond) to pathogens similarly? The consequence of this could show that there is the risk of a whole group being eliminated by a single pathogen if majority of the group is unable to effectively deal with the resulting illness effectively. Furthermore, since humans are also known to live in social groups, how do these concerns translate in human populations?

Immunology of Social Grouping:

The immune system is designed to remove foreign and potentially harmful proteins (often found on infectious microorganisms) called antigens. It is comprised of two umbrella components: the innate and the adaptive immune responses. Both responses are controlled by genetic codes that result in the production of certain immune related proteins (Shultz and Grieder, 1987).

The innate immune response is the first responder to infections that get into the body. As a result, it needs to have generalized proteins that recognize a large range of antigens. This receptor comes in the form of a Toll-like receptor (TLR), which is specific in that it recognizes particular antigenic structures but non-specific in that those antigenic structures are found on a wide variety of pathogens. Once activated by the presence of a pathogen, molecules with the TLR are capable of inducing a wide variety of responses based on the type activated. This ranges from inciting inflammation to activating and recruiting T cells from the adaptive immune response (Aderem and Ulevitch, 2000). Because the innate immune response is already in effect since birth, it is almost immediate. Thus it is useful in preventing an infection from becoming too developed before the adaptive immune response can get involved and is useful in signaling the adaptive immune response.

The adaptive immune response is a lot more complex because it requires the recruitment and proliferation of many molecules. Once the innate immune response has sent a signal to the lymph tissues that there is an infection, T cells that target the specific antigen are produced. B cells are also produced to help increase the amount of T cells that are activated for proliferation and attack on the infectious agent. However, these T cells can only be recruited by antigen presenting molecules recognized as being part of the host. These molecules will have specific presenting proteins on them called Major Histocompatability Complexes (MHC) which come in two types: Type 1 and Type 2. Each type is capable of presenting different types of antigens and will recruit specific adaptive immune molecules. MHC class I is found on all cells however antigen presenting cells (APCs) typically have MHC class II. A T cell or B cell is presented an antigen by an APC without self-recognized MHC on its surface, no immune response will be generated. This is used as regulatory mechanism to prevent overreaction to various antigens and responses to structures that would normally not be considered an antigen (Janeway et al., 2005). Other molecules would also be produced such as antibodies and the number of different responders to an infection by the adaptive immune response is what makes it so complicated and complex as well as so effective most of the time.



(b)

	MHC class I	MHC class II
Structure	Alpha chain and β2-microglobulin heterodimer	Alpha and beta chain heterodimer
Expression	All nucleated cells	Antigen-presenting cells
Source peptide	Cytosolic (intracellular)	Endosomal (extracellular)
Size-bound peptide	9–11 aa	12–25 aa
Loci	A, B, and C	DR, DQ, and DP
Function	Presentation of antigenic peptides to $CD8^+$ T cell/cells and natural killer cell receptor	Presentation of antigenic peptides to $CD4^+$ T cell/cells

Figure 2: The differences between MHC class I and II from http://ars.els-cdn.com/content/image/3-s2.0-B9780123868824000219-f21-01-9780123868824.jpg?httpAccept=%2A%2F%2A.

Immunology, however, isn't entirely reliant on genetic components or immune-related molecules in the body. Interestingly enough, it is likely that populations living in social groups may not be as closely related as one would assume. One of the ways in which animals seem to avoid inbreeding and increase the amount of diversity in their genetics (which in turn would lead to diversity in immune systems within a group) is through dispersal behaviors. Often times, animals are expected to disperse from their natal group based on social expectations, very often the sex of the individual. This results in distance between closely related individuals which prevents the formation of mating pairs between relatives (Pusey and Wolf, 1996). Therefore new genetic codes are introduced to the groups that accept these new individuals and this in turn would likely develop into new immune system types to combat instances of infection. Currently, there doesn't appear to be any instances of animals living in social groups that don't experience any dispersal at all, meaning none are so isolated as to prevent variation for genetics within the group. However, there are instances of animal species that disperse minimally and those groups would have less variation than other groups (Pusey and Wolf, 1996).

In the case of groups that experience only minimal amounts of dispersal, there are other ways by which individuals avoid inbreeding and thus increase the amount of genetic variation within the group. One such way this is avoided is by breeding with individuals not part of the social group (extra-pair copulations.) Studies have shown that the offspring in some groups (in this study, wrens are mentioned) are not related to the males in the group but to males from nearby groups (Pusey and Wolf, 1996). This, as with dispersal, would also increase the amount of genetic diversity within a group and allow for variety in immune response expression in a group. In a way, it seems like a new genetic combination is implanted into the group through the offspring produced this way.

Mate choice seems to be an important aspect in the overall health of a group and it is likely that some aspects of the choice are driven by the notion of finding a mate with a strong immune system. Not only do females typically avoid males that exhibit signs of illness but they also appear to mate with individuals with MHC classes that are different than their own. Female mice, which often live in some form of social group, use olfactory cues from the urine of potential mates to check for currently existing infection. If infection is noted, the female often will choose a different mate, likely to protect herself and potential offspring from also contracting the infection. Furthermore, they use olfactory cues to sense the MHC class of the potential mate (if they're free from infection upon inspection) likely to avoid mating with closely related individuals (Kavaliers and Choleris, 2011). Since MHC is a major factor in inducing immune responses, a mate expressing a different MHC molecule is likely to have an immune system that is variably different from that of the female's thus meaning that resultant offspring would have portions of the immune systems found in each parent. This increases the variety of immune systems found in a group as each generation produces different combinations of immune system, resulting in increased chances of a group surviving in the event of illness.

Choice of mate based on immune system is related to a hypothesis called the Good Gene Hypothesis. This hypothesis suggests that individuals with stronger immune systems are less likely to be infected with parasites or other diseases. More importantly, it appears that these individuals are more likely to be chosen as a mate (Schad et al., 2012). Schad et al. (2012) tested the parasite level in a group of Lesser Bulldog bats since bats are common vectors for parasites and diseases. Males with less parasites often had fewer parasites and seemed to be chosen more frequently for copulation by the females.

Beyond just ensuring variety in a group's genetics and immune systems, social groups have developed behaviors which increase the survivability of a group in the face of infection and disease. These social behaviors include group size, group isolation, and social avoidance; social avoidance being one of the most interesting and well-studied behavior to reduce rates of infection (Loehle, 1995).

Social avoidance is when the members of the population recognize an infected individual and avoid them (as the term suggests) so as to reduce risk of infection (Loehle, 1995). This concept seems pretty intuitive though its prevalence and effectiveness almost seems surprising. Behringer et al. (2006) looked at social lobsters to test the effectiveness of social avoidance as a method of disease prevention. They infected several members of the group with a lethal virus and then observed how frequently and how long after infection healthy members of the group started to avoid the sick individuals. Their study showed that, even without displaying symptoms, the sick individuals were quickly avoided by the healthy individuals and as a result it took almost six weeks for a healthy individual to catch the virus from a sick individual (Figure 1b). The study also showed that as the sick individuals started to show their illness, the amount of avoidance by healthy individuals also increased (Figure 1c). Social lobsters also refuse to share dens with infected individuals (Figure 1a, Curtis, 2014). The fact that the healthy individuals were, for the most part, successful in preventing the spread of infection via avoidance seemed to support that the behavioral immune system was actually more crucial to the survival of this group than the genetic and molecular immune systems of each individual.

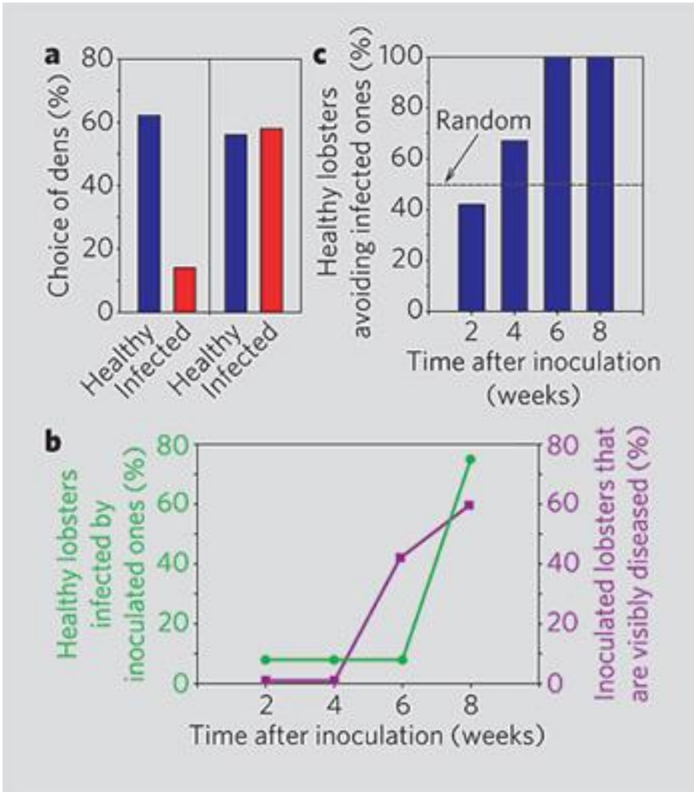


Figure 3 a, Den selection by healthy (left panel) and infected (right panel) lobsters, showing the aversion of healthy lobsters for diseased lobsters. All lobsters were either given a choice of sheltering alone or with a healthy conspecific (blue bars), or given a choice of sheltering alone or with an infected (red bars) conspecific that was tethered in the den. **b,** Increase of infectivity over time for lobsters inoculated with PaV1 virus: green line shows the increasing percentage of healthy lobsters infected by inoculated lobsters, and purple line indicates the increasing percentage of inoculated lobsters that became visibly diseased. **c,** Cohabitation time series indicating that healthy lobsters started to avoid inoculated (but non-infectious) lobsters four weeks after inoculation and completely avoided them after six weeks, which is before they became infectious (Behringer, 2006).

Oxytocin seems to be a very important chemical in social avoidance of infected individuals. Female mice whose normal oxytocin was eliminated from their system were found to be unable to recognize whether or not an individual was infected. Adding oxytocin through the vomeronasal passageway, however, seemed to increase the mouse's ability to recognize and react to every other social cue (though they never regained the ability to tell if another mouse was infected or not). In fact, these females choose infected individuals more often than when they choose non-infected individuals (Kavaliers and Choleris, 2011). This gives a chemical background to the social avoidance method of behavior immunology and suggests that this behavior has been evolutionarily selected for to help reduce the risk of a pathogen wiping out whole populations of a species.

Arginine vasopressin also seems to be involved in social avoidance behavior towards infected individuals. This is likely related to the fact that the two chemicals use the same receptors to send and amplify the same signals (Kavaliers and Choleris, 2011). This is interesting because having two different chemicals that can induce this behavior supports the idea that there is an evolutionary basis to the behavior. Furthermore, it increases the chances of amplification of the behavior by having more than one compound signal for it.

Social avoidance of infected individuals have an effect on group size. Colobus monkeys living in pathogen-heavy environments tend to have smaller group sizes and exhibit less social behavior than groups living in less pathogen-heavy environments. In fact, healthy individuals (male and female) will often leave a larger group that likely has high incidence of parasitism for smaller, hopefully healthier groups and those that don’t leave will prevent new members from joining the infected group (Curtis, 2014). This migration would, just as before, also result in the adding variation in immune systems in the smaller groups as well as help the healthy individuals that left the infected group avoid contracting the parasite or illness afflicting members of the larger group.

Social Grouping Connections and Consequences in Humans:

Humans, like many primates, also live in social groups and in some cases seem to function as relatively isolated populations (ie: small towns, villages, tribes). Therefore, it would be reasonable that the same concerns in terms of pathogens and disease would also apply to people. In truth, this isn't a novel idea; governments create laws and organizations dedicated to the cause of reducing illness and death among populations under their command. However, beyond political control, it also seems likely that humans have evolved some of the same methods to maintaining genetic diversity and behavioral immune responses. These behaviors include dispersal (this is seen by the moving of individuals into new communities), avoiding mating with closely related individuals, and social avoidance of sick individuals.

Humans appear to use odors to detect differences in MHC classes of potential partners and seem to prefer mates that have a different MHC class, much like many animals do (Kavaliers and Choleris, 2011). The MHC molecule is important to the immune system so this shows that the strength and variation of a mate's immune system is as important to humans as it is to mice. Unlike mice though, humans only really have the main olfactory system to detect these differences (Kavaliers, 2011).

Humans also seem to be heavily affected by oxytocin in the same way as monkeys and rodents. Subjects involved in a financial game experiment were more likely to cooperate with other individuals but only if they had been previously acquainted with the other members of their group. If the other members were new and unfamiliar, the oxytocin seemed to actually have the opposite effect in that they cooperated less with the other individuals in the experiment (Kavaliers and Choleris, 2011).

Curtis et al. (2011) showed that the emotion known as disgust maybe heavily involved in the social avoidance. In fact, some studies demonstrate that areas with higher rates of pathogens and disease often report lower cases of behaviors such as extraversion and openness. When humans recognize symptoms of illness such as sneezing or coughing, they often seem repulsed by the action and thus avoid the sick individual as much as possible. Granted, there are exceptions to that, such as a mother taking care of her sick children or a spouse taking care of their sick partner. This could likely be a trade off due to the need of individuals to effectively reproduce and ensure the survival of produced offspring.

While a recent study supports the idea that populations of people living in pathogen heavy environments are more likely to adopt less social behaviors, they don't show an increase in xenophobia or the fear of people from other countries or populations (Cashdan and Steele, 2013). This is interesting because migration of people can increase the incidence of disease as individuals carrying pathogens not normally found in a region can then spread the disease to individuals with unprepared immune systems. This seems to suggest that the need for genetic diversity is still recognized but some precautions against disease are still taken.

The effect of oxytocin also seems to extend into a human's ability and preference to avoided infected individuals. Humans with low levels of oxytocin in their brain experienced increased levels of loneliness and those individuals seemed more likely to interact with sick individuals. At the same time, individuals with normal or high levels of oxytocin seemed to experience higher levels of disgust when dealing with sick individuals which, as mentioned before, perpetuated the social avoidance behavior (Kavaliers and Choleris, 2011).

Conclusion:

Social groupings have effectively found ways to address the risk of infection and annihilation by disease. Genetically, groups experience recombination of individuals via behaviors such as extra-pairing and dispersal which increases the variety of genetics and immune systems found within a group. Since the immune system is dictated heavily by genetics, mate choice also seems to be important in regulating the variety of immune systems and genetics found in a community. Animals and humans alike seem capable of recognizing related individuals who have the same MHC's as themselves and thus are capable of avoiding mating with those individuals. As a result, social groups are effective at keeping their groups diverse enough to withstand selective pressures by disease.

Beyond genetics though, social groups have a set of behaviors that prevent infection of a whole group of individuals. The main one of these being social avoidance in which animals will avoid conspecifics that show signs of infection so as to keep the number of infected individuals to a minimum. While this sounds intuitive, it's actually amazing because it shows that animals have a way of recognizing the threat of infection in other individuals and take precautions against infection.

Humans have the same processes for maintaining variation of genetics in a community as well as avoiding infection which means that, like with animal groups, there actually is limited risk of entire communities being wiped out by a disease. Thus it seems safe to say that a social grouping is still likely evolutionarily favored from the immunological stand point.

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