Taking a Shot for the Team:
Using a Simulation to Explore How Immunization Programs Help Protect Communities from Infectious Diseases

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ABSTRACT

Centuries of practice clearly demonstrate that immunization by means of vaccination reduces the disease burden in human and nonhuman animal species. While the emphasis on individual health and fitness is important, the role of immunization in maintaining the health of entire populations or communities is also important. I developed a simulation that allows participants to actively explore the value of herd immunity in controlling the spread of infectious disease, first by considering how quickly an entire population may become ill if no one has immunity, and then after immunization of 80% of the population. Pretest, posttest, and four-week follow-up questionnaire data collected from nonmajor introductory biology students suggest that active engagement in an activity such as the one described may contribute to longer-term retention of the principles and concepts than presentation by lecture alone.

Key Words: immunization; simulation; vaccination; epidemiology; health; math integration.

○ Introduction

In 1796, Edward Jenner sparked a revolution in medicine (Stern & Markel, 2005). Using the common knowledge that milkmaids infected with cowpox were immune to the human disease of smallpox, he vaccinated the eight-year-old James Phipps with pus collected from a milkmaid’s cowpox lesion. Jenner allowed six weeks for the boy’s body to process the assault on his immune system, and challenged him with a variation (or inoculation) of smallpox. The boy was not affected by the usually devastating disease. This famous episode was reportedly the first in a series of experiments that opened the door to a new era of medicine in which humans would become proactive in reducing suffering by introducing pathogens under controlled conditions to stimulate the immune system to be able to fight the infectious agents they might encounter in everyday activities.

Vaccines work by stimulating the immune system (CDC, 2018b). When challenged with an infectious agent, the body enlists macrophages and other phagocytic cells to engulf the invader, leaving residues such as cellular components and proteins that function as antigens. These in turn stimulate B-lymphocytes to produce antibodies to neutralize and participate in the clearance of the antigens. T-lymphocytes attack cells infected with the pathogen. Introducing a vaccine that contains a dead pathogen (e.g., a heat-killed virus) or one that has little ability to cause a full-blown illness (e.g., an attenuated virus) causes the body to respond by producing antibodies and “memory” T-lymphocytes, but usually will only cause a brief discomfort rather than a fully expressed illness.

The effectiveness of immunization has been demonstrated against many of the diseases that have plagued humans and many nonhuman animal species. However, protests have occurred throughout the history of vaccination programs (Stern & Markel, 2005), including a strong popular backlash as early as the 1830s, when some common citizens suggested that compulsory smallpox vaccination laws established in 1821 were little more than a ruling-class attack on their communities and personal rights. Perhaps the loudest of such protests in modern times erupted after the release of a now discredited study by Wakefield et al. (1998) in The Lancet, which erroneously linked application of the MMR (measles, mumps, rubella) vaccine to the development of autism. The very limited study was later shown to be flawed, and numerous large-scale studies since that time have found no connections between the use of vaccines and autism spectrum disorders. The editors of that prestigious British medical journal took the rare action of retracting the study in 2010. The controversy linking vaccines with autism still rages, resulting in numerous groups of parents refusing to vaccinate their children. This has had direct consequences: while measles had been declared to have been effectively eradicated in the United States in 2000 (CDC, 2018a), with increasing numbers of unvaccinated children, a measles outbreak in early 2019 reached levels not seen in more than a quarter century (CDC, 2019).

While the emphasis has often been on protecting the individual from illness, immunization programs are extremely effective in protecting entire communities, reducing suffering and death as well as maintaining economic productivity by reducing time and resources...
lost to illness. This is based on the principle of herd (or community) immunity, a concept that suggests that by immunizing a large enough proportion of a population, the likelihood of the disease spreading is sharply reduced, since it reduces the likelihood that a nonimmunized person will come into contact with the pathogen (Barratt & Kirwan, 2009). In other words, the chain of transmission can be broken. This means that not every member of a population needs to be immunized, although in many cases the more that are immunized, the better.

The proportion of a population that needs to be immunized for effective herd immunity varies depending on the basic reproduction number, \( R_0 \), of the disease in question. \( R_0 \) is a dimensionless measure (not a true “rate” dependent on a time factor) of the number of new cases likely to be caused by exposure to an active case (Jones, 2007). For example, a conservative (low) estimate of the \( R_0 \) for measles is 12 (Smith, 2017). The influenza pandemic of 1918 had an estimated \( R_0 \) of only 2 (Smith, 2017). The herd immunity threshold (HIT) is the target proportion of a population to be immunized in order to achieve herd immunity. This is estimated by \( \text{HIT} = 1 - (1/R_0) \) (Barratt & Kirwan, 2009). For measles, the HIT is \( \approx 92\% \) or higher. For a disease like the 1918 pandemic, the HIT would have been 50%. But remember, these are minimal threshold values. Higher proportions give reasonable assurance of even better protection.

○ Development of an Immunization Simulation Exercise

I became interested in actively illustrating the topic of immunization for community protection as I was teaching the epidemiology unit of a course in environmental health. To do this, I developed an exercise that can be used in a number of different settings with participants of different ages and levels of science literacy. For example, I have presented versions of this to a summer enrichment program primarily targeted at elementary age children, as well as middle school groups during the annual science-career-day program at the University of Tennessee at Martin. I have also presented this to several college-level introductory classes.

In a session, I begin with background on the nature of immunity and some simple principles of epidemiology, then engage the group in a simulation using readily available materials like different-colored poker chips to act as tokens to designate those with a disease, those who may be susceptible, and those who have been immunized. For younger groups, the process is most direct, focusing on the idea that with immunization, a disease can be controlled since it cannot easily spread through a population because we are breaking the chain of transmission. In some cases, the disease may even be stopped as soon as it is introduced. For groups with older participants, I integrate some simple epidemiological calculations (cumulative incidence and prevalence) to give some quantitative evidence of the effectiveness.

○ Supplemental Calculations

The prevalence of a disease in a population is calculated as the frequency of active cases in the overall population at a given point in time (point prevalence) or time interval (period prevalence) (Merrell, 2008). The cumulative incidence, or risk, is calculated as the number of new cases in a population during a time interval among those at risk at the beginning of the interval (Merrell, 2008). Those who have been immunized, are already sick, or have recovered are not counted as being at risk. Thus, the population at risk would usually be a smaller number than the overall population, with the direct implication that the denominator of this fraction would usually be smaller than the total population used in the prevalence calculation. The scale on which these values are reported may vary depending on the population in question. For example, values in very large populations may be reported as cases per 100,000 population. Values for smaller populations may be reported as cases per 10,000, cases per 1,000, or even cases per 100 population (or simply as a percentage). Obviously, increasing the scale may make small fractions easier to read.

○ The Simulation

In the simulation, students explore two scenarios: one in which a new disease against which no one has immunity is introduced to a population, and then a second scenario in which 80% of the population has been immunized against the disease. The present description is set for a class with 25 students, but it can be scaled up or down to meet demands. However, it works well if there are enough students to simulate at least three rounds of the game.

In the first scenario, I act as a person who has been infected with some new, unknown, emerging pathogen against which no one has any natural immunity. I visit a town and come into contact with a number of people. The disease has an \( R_0 \) value of 3, causes high morbidity (referring to the disease condition) but no mortality (i.e., death associated with the disease), and has a duration of several weeks. This is to make calculations easier, since death and recovery are not concerns in this basic simulation.

In the group of 25 students, I randomly “contact” people by handing them four white poker chips. These first three subjects are the first incident cases in the population. Each incident case keeps one of the chips and passes out the other three, resulting in complete exposure of the population of 25 in three rounds of the game. Figure 1 shows a diagram of how the disease as described spreads through a population in three rounds.

For calculations, three people become ill in a population where all are at risk in round 1 of the first scenario. The cumulative incidence would be calculated as 3 new cases / 25 population at risk = 0.12, or 12%. The prevalence for round 1 would be the same: 3 active cases / 25 population = 0.12, or 12%. In round 2, there are nine new cases, but the cumulative incidence denominator changes, since there are now only 22 at risk in the population. Thus, the cumulative incidence for round 2 is 9 new cases / 22 at risk = 0.4091, or 40.91%. The prevalence for round 2 would be 12 active cases / 25 population = 0.48, or 48%. In round 3, the cumulative incidence would be 13 new cases / 13 population at risk = 1.00, or 100%. The prevalence would also be 25 active cases / 25 population = 1.00, or 100%.

In the second scenario, 80% immunization is simulated by having students blindly draw either a red or a blue poker chip from a small drawstring stuff sack or bag containing 20 blue and five red chips. Blue chips signify that the subject has been immunized, while red means the subject is susceptible to infection. As they draw their chips, participants are instructed not to let me or anyone else see
their chips to avoid bias in the transmission rounds. Again, I approach members of the population with four white chips. When I contact individuals, they must show their chips. If they hold a blue chip, they are immune, so they cannot become sick or make anyone else sick. If they hold a red chip, they can become sick and can then try to transmit the pathogen to others. I continue the simulation until there are three unsuccessful attempts at transmission. At 80% immunity, this often happens in the first contact round as illustrated in Figure 2.

Figure 2 represents one possible outcome of the immunity simulation: for this example, I generated a table populated randomly with either dark gray or light gray squares. I then randomly generated three cell addresses to represent individuals for contact with the pathogen, designated by the white circles. None of the three attempts at transmission were successful, in that they all landed on the light gray squares of immunized community members, suggesting that we can effectively stop the spread of disease by having a large enough proportion of the population immunized.

For this simulation (illustrated in Figure 2), the cumulative incidence in the first round would be zero, since there are no new cases out of a population at risk of only five (20% of the total population), since 20 members (80%) of the population were immunized. The prevalence would also be zero.

**Evaluation of the Simulation**

In order to test the effectiveness of this simulation in helping students attain the concepts, I developed a 10-question true-false questionnaire to which they responded immediately before and after the presentation (and simulation activity for one group), and then a follow-up after four weeks. Members of my nonmajors introductory biology (Biology 110) classes in the fall semester of 2018 and the spring semester of 2019 were compensated with bonus quiz points for their participation in this project. The classes were quite evenly matched in terms of composition. Students in the fall semester (n = 28) had the full simulation activity, while students in the spring semester (n = 33) were given only an introductory lecture with no simulation activity. In each class, more students participated in the first session, but some failed to complete the follow-up. Only students who completed both the initial activity and the follow-up were included in the analysis.
Mean scores from the pretest, posttest, and follow-up questionnaires for each treatment are presented in Figure 3. The data were analyzed via a repeated-measures ANOVA followed by a Tukey’s honestly significant difference (HSD) test. In each treatment, there was a significant increase in score from pretest to posttest (fall + activity, $P = 2.4465 \times 10^{-7}$; spring + lecture only, $P = 5.4286 \times 10^{-6}$). After four weeks, however, the fall semester group with the full simulation had experienced a nonsignificant decline of <2% ($P = 0.825924458$), while the spring group had significantly decreased in retention by ~9% ($P = 0.04146588$). These results suggest that modeling the effects of immunization in a community is effective in helping participants retain the take-home message. More broadly, this reflects what teachers have known for a very long time: that active participation increases learning and retention.

**Considerations for Expansion**

The simulation as presently described is a simple iteration, but it can be easily modified to explore how other factors would affect the progression of the disease through the population. For example, you could set shorter morbidity durations to allow for recovery, which would change active case numbers but not total population sizes and therefore would change prevalence values. This would also alter the denominator for cumulative incidence calculations. You could add in a mortality component, which would change not only the cumulative numbers of active cases but also the total population size, affecting the denominator for subsequent prevalence measures. Changing the $R_0$ value to reflect well-known pathogens along with the proportion of a population immunized against the pathogen would also allow you to simulate the spread of real-world pathogens in different populations around the world.

**Conclusion**

Immunization programs benefit individuals by reducing the likelihood of becoming ill with communicable diseases. However, through the principle of herd immunity, the more people in a population who are immunized against a specific disease, the likelihood that an unvaccinated person will get sick also diminishes, resulting in better community health, and better overall economic productivity as less time and resources are lost to illness. The safety of vaccines has been demonstrated repeatedly for decades despite claims to the contrary.

The cellular and physiological bases of immunization are well known and can easily be communicated through traditional means of delivery. However, the larger significance of how immunization protects populations may be more difficult to instill without experiencing it, even if the experience is a simulation. The present exercise seems to be effective in helping students understand these larger-scale principles and may help them retain the concepts longer.

**Acknowledgments**

I thank the dozens of students who participated in the development of this activity, especially those enrolled in BIOL 110 sections in fall 2018 and spring 2019. Dr. Linda Husmann provided valuable suggestions on the description of vaccine action and immune system function.
References

Barratt, H. & Kirwan, M. (2009). Epidemic theory (effective and basic reproduction numbers, epidemic thresholds) and techniques for infectious disease data (construction and use of epidemic curves, generation numbers, exceptional reporting and identification of significant clusters). https://www.healthknowledge.org.uk/public-health-textbook/research-methods/1a-epidemiology/epidemic-theory.

CDC (2018a). Measles history. Centers for Disease Control and Prevention. https://www.cdc.gov/measles/about/history.html.

CDC (2018b). Understanding how vaccines work. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/hcp/conversations/downloads/vaccine-understand-color-office.pdf.

CDC (2019). Measles cases and outbreaks. Centers for Disease Control and Prevention. https://www.cdc.gov/measles/cases-outbreaks.html.

Editors of The Lancet (2010). Retraction—Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet, 375, 445.

Jones, J.H. (2007). Notes on R0. https://web.stanford.edu/~jhj1/teachingdocs/Jones-on-R0.pdf.

Merrell, R.M. (2008). Environmental Epidemiology: Principles and Methods. Boston, MA: Jones and Bartlett.

Smith, T.C. (2017). The unforgiving math that stops epidemics. Quanta Magazine, October 26. https://www.quantamagazine.org/the-unforgiving-math-that-stops-epidemics-20171026/.

Stern, A.M. & Markel, H. (2005). The history of vaccines and immunization: familiar patterns, new challenges. Health Affairs, 24, 611–621.

Wakefield, A.J., Murch, S.H., Anthony, A., Linnell, J., Casson, D.M., Malik, M., et al. (1998). Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet, 351, 637–641.

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