

## **HERD IMMUNITY: CAN MASS VACCINATION ACHIEVE IT?**

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Even though endemic outbreaks of common childhood diseases, such as measles, have been eliminated in some regions after prolonged mass vaccination efforts, we are still being constantly reminded that reducing vaccination coverage of children in a community poses the risk of a reimported disease outbreak with potentially dire consequences to infants and immuno-compromised individuals. We are also being persuaded that implementing strict vaccination compliance will prevent an outbreak and protect vaccine-ineligible infants via the *herd immunity* effect.

There is no question that a disease outbreak can happen in a non-immune community, if a virus gets there. The real question is, how well can high vaccination compliance ensure herd immunity and protect a community from an outbreak?

### **Herd Immunity, in Theory and in Reality**

Herd immunity is not an immunologic idea, but rather an epidemiologic construct, which theoretically predicts successful disease control or viral eradication when a certain pre-calculated percentage of people in the population become immune. A scholarly article on herd immunity states:

*“Along with the growth of interest in herd immunity, there has been a proliferation of views of what it means or even of whether it exists at all. Several authors have written of data on measles, which “challenge” the principle of herd immunity and others cite widely divergent estimates (from 70 to 95 percent) of the magnitude of the herd immunity threshold required for measles eradication.”<sup>i</sup>*

Early research performed by A.W. Hedrich has been deemed instrumental to the idea that herd immunity is readily attainable. Hedrich analyzed measles outbreaks occurring in Baltimore, MD every 2-3 years between 1900 and 1931. He found that just prior to a major outbreak in that city, the proportion of susceptible children under the age of 15 was about 45-50%. At the end of any outbreak, the proportion of still susceptible children never fell below 32%.<sup>ii</sup> Nevertheless, 95-97% of children experienced measles before they reached the age of 15.<sup>iii</sup> For this reason adults were immune from measles.

The finding that a rather large number of susceptible children routinely escaped measles during any particular outbreak gave optimism to the United States Public Health Service that herd immunity works at a threshold, which is considerably less than 100%. An official prediction was made that measles would be swiftly eradicated in the USA as early as 1967 by establishing and maintaining this readily attainable threshold via mass vaccination,<sup>iv</sup> which already started in 1963. This prediction failed to

materialize and measles epidemics in the U.S. did not stop in 1967. The concept that vaccine-based herd immunity is readily attainable for the purposes of rapid disease eradication appeared to be invalid.

The concept of herd immunity then evolved to justify the idea of vaccinating children against a very mild childhood disease, not for their own health benefit, but to protect a vulnerable but vaccine-ineligible segment of the population. For example, rubella is not dangerous for children. However, for pregnant women who have not become immune from rubella prior to pregnancy, a rubella virus poses a danger during the first trimester by increasing the risk of fetal developmental abnormalities (congenital rubella).

Perhaps with a good intention to immediately put an end to any risk of congenital rubella in their community, elementary school children were vaccinated *en mass* against rubella in 1970 in Casper, Wyoming. Ironically, nine months after this local vaccination campaign took place, an outbreak of rubella hit Casper, Wyoming. The herd immunity effect did not materialize and the outbreak involved over one thousand cases and reached several pregnant women, whereas recently vaccinated children were spared from rubella. The perplexed authors of the study describing this outbreak wrote:

*“The concept that a highly immune group of pre-pubertal children will prevent the spread of rubella in the rest of the community was shown by this epidemic not always to be valid.”<sup>v</sup>*

Disregarding these realities of failed disease control via attempted herd immunity effects, the unsubstantiated belief in herd immunity continues to influence vaccine-related legislation in many U.S. states and other countries. The notion of herd immunity is used as a trump card to justify any measures, often at odds with personal freedom of choice, aiming to increase vaccination compliance. An implicit assumption is that vaccine exemption policies would somehow compromise this precious herd immunity, which the public health authorities strive to establish and maintain via mass vaccination.

Although the evidence for vaccination-based herd immunity is yet to materialize, there is plenty of evidence to the contrary. Just a single publication by Poland & Jacobson (1994)<sup>vi</sup> reports on 18 different measles outbreaks throughout North America, occurring in school populations with very high vaccination coverage for measles (71% to 99.8%). In these outbreaks, vaccinated children constituted 30% to 100% of measles cases. Many more similar outbreaks occurring after 1994 are described in epidemiologic publications.

### **What to Blame?**

The medical establishment was quick to blame Mother Nature on frequent

occurrence of measles outbreaks in highly vaccinated communities. It has been noticed that if vaccinated too early, an infant might fail to respond to the measles vaccine due to the inhibitory (and at the same time protective) effect of maternal antibodies transferred via the placenta. Before the 1990s, a single dose of the measles vaccine was on the childhood schedule in North America. To compensate for the potential “interference” of maternal immunity transfer with the first round of measles vaccination in some children, a double MMR (measles-mumps-rubella) vaccination strategy was introduced in the United States and Canada in the early 1990s.

Endemic measles got subsequently eliminated in North America, but in 2011 an imported measles outbreak – the largest so far in the post-elimination era – hit a community in Quebec, Canada with 95-97% measles vaccination compliance in the era of double vaccination against measles. If double vaccination is not enough to patch those early-age vaccination failures and ensure the elusive herd immunity, should we then look forward to triple (or, might as well, quadruple) MMR vaccination strategy to see how that might work out with respect to herd immunity? Or, should we instead re-examine the herd immunity concept itself?

### **Faulty Assumption**

The herd immunity theory is based on a faulty assumption that vaccination elicits in an individual a state equivalent to *bona fide* immunity (life-long resistance to viral re-infection). As with any *garbage in-garbage out* type of theory, the expectations of the herd immunity theory are bound to fail in the real world.

Some relevant information about anti-viral immunity can be gleaned from experiments in research animals. Ochsenein *et al.* (2000)<sup>vii</sup> conducted an experiment in mice, in which they compared the effect of injecting mice with two preparations of the vesicular stomatitis virus (VSV). They immunized mice with either unmodified VSV (live virus) or ultraviolet light-inactivated VSV incapable of replication (dead virus). Then they tested the capacity of the serum from the two groups of immunized animals to neutralize VSV (i.e., render VSV incapable of infecting cells) over the 300-day span following immunization.

The injection of the live-virus preparation induced long-lasting capacity of the serum to neutralize the virus, which persisted for the whole duration of the study without any noticeable decline. In contrast, the injection of the dead-virus preparation induced much lower levels of virus-neutralizing serum antibody titers to start with. Virus-neutralizing serum titers reached a peak at 20 days post-immunization and then started to wane rapidly. They went below the level detectable by the neutralization test by the end of the study.

*The conclusion of this experiment was that a procedure that attenuates or inactivates the virus also diminishes its ability to induce long-lasting virus-neutralizing serum titers upon immunization of animals.*

It should be noted that vaccines against viral childhood diseases are similarly prepared by first isolating a wild virus from a sick person, then rendering it artificially attenuated or inactivated to make a vaccine-strain virus. The attenuation or inactivation of a wild virus to become a vaccine-strain virus is done to reduce the likelihood of it inducing viral disease symptoms, although this happens anyway in some cases. The process of attenuation, while making a vaccine-strain virus “safer” than the original wild virus, as far as the induction of viral disease symptoms are concerned, also impacts the durability of vaccine-based protection.

The protective threshold for measles-virus neutralizing serum titers in humans has been determined by the Boston University Measles Study by Chen *et al.*<sup>viii</sup> A subsequent study by LeBaron *et al.*<sup>ix</sup> further estimates how long it takes, after the receipt of the second MMR shot, for measles-virus neutralizing serum titers to drop below the protective threshold level. Let us examine these two relevant studies side-by-side.

### **The Boston University Measles Outbreak Study**

In 1990, a blood drive was conducted among students of Boston University a month before the campus happened to be hit with a measles outbreak. Due to these natural circumstances, researchers happened to have access to blood samples of many students who either got measles or were spared from the disease during the outbreak. The measles virus-neutralizing serum titers were measured a month prior to and two months after the exposure. Pre-exposure titers could then be correlated with the degree of their current protection from measles: (1) no detectable infection or disease; (2) a serologically confirmed measles virus infection with a modified clinical course of disease; or (3) full-blown clinical measles. By the way, seven out of eight students who ended up getting full-blown measles, had been vaccinated against measles in their childhood, some twice-vaccinated.

The outcome of the Boston University measles outbreak study was the following:

- (a) In all previously vaccinated students who experienced full-blown measles, pre-exposure measles-neutralizing titers were below 120;
- (b) Seventy percent of students whose pre-exposure titers were between 120 and 1052, ended up having a serologically confirmed measles infection, but since their altered disease symptoms did not conform to the clinical measles case definition, they were categorized as non-cases during the outbreak;
- (c) Students with pre-exposure titers in excess of 1052 were for the most part protected both from the typical clinical disease as well as the measles virus infection.

### **Subsequent Measles Vaccine Observations**

The other study, by LeBaron *et al.* (2007), sought to determine the duration of

measles virus-neutralization serum titers after the receipt of the second MMR booster. The study enrolled several hundred healthy Caucasian children from rural U.S. areas free of measles outbreaks for the duration of the study.

The study revealed that about a quarter of these children generated relatively high serum titers in response to the MMR vaccination. The rest responded modestly to the booster, but some did very poorly. Although this particular study could not compare measles-neutralizing titers between vaccinated and naturally immune, the study by Itoh *et al.* (2002) has previously demonstrated that measles-neutralizing titers induced by vaccination are about nine times lower than those induced by natural infection.<sup>x</sup> Therefore even those individuals, who respond relatively well to the measles vaccine, do not reach the levels of measles-neutralizing titers achieved after natural infection.

Serum titers in all vaccinated children, regardless of being relatively high, moderate, or low, reached a peak in a month after the MMR booster, then came down in six months to the pre-booster levels and continued to decline gradually over the next 5-10 years of observation. Only about a top quarter of children (called high-responders) were able to maintain serum titers in excess of 1000 units 10 years following their second MMR booster, received at the age of five. This fraction of children is likely to be still protected from the measles virus infection by the time they are adolescents. No assurances about their vaccine protection can be made once they reach older age.

The least efficient vaccine responders (bottom 5%) had their serum titers fall below 120 units within 5-10 years after the second MMR shot. This percentage of vaccinated children is expected to have full-blown, clinically identifiable measles upon exposure when they get a bit older. This is the reason why vaccinated (and even twice-vaccinated) people show up as disease cases in numbers equal to or even exceeding the unvaccinated cases in communities with very high (>95%) vaccination coverage.

*Rapid loss of vaccine protection in low-responders is the reason for the paradox of a "vaccine-preventable" disease becoming the disease of the vaccinated. Such disease cases are not early-age vaccine failures due to maternal antibody interference, they are anticipated vaccine failures due to waning vaccine protection.*

For the majority of MMR-vaccinated children, measles-neutralizing titers fall between 120 and 1000 by the time they reach adolescence. These children can acquire the measles virus upon exposure and be potentially contagious during an outbreak, although they might experience a modified course of disease and not be labeled as measles cases for the purposes of reporting. In fact, during the Boston University measles outbreak, many students with pre-exposure titers between 120 and 1052, who were officially categorized as non-cases, had some of the viral disease (flu-like) symptoms, including runny nose, cough, photophobia, headache, fever, and diarrhea. These sick "non-cases" ended up with high post-exposure serum titers for measles, just as the typical disease cases did, which is indicative of viral replication and, hence,

transmission.

## **High Vaccination Compliance Does Not Result in Herd Immunity**

Cases of the measles virus re-importation into North America after the eradication of the endemic virus had typically resulted in small or no sustained outbreaks in the last decade, in part due to the vigilance of the public health authorities in quarantine implementation. However, the 2011 imported outbreak of measles in Quebec, Canada characterized by de Serres *et al.*<sup>xi</sup> appeared to be ominously different. Strict quarantine measures were not implemented, possibly because of the assumption that the region was well under the herd immunity effect due to an exceptionally high and uniform vaccination compliance for measles (95-97%). The consequences of relying on non-existent herd immunity as opposed to quarantine in curbing an imported disease outbreak were very telling.

Imported by a high-school teacher during the spring break trip abroad (himself vaccinated against measles in his childhood), the outbreak happened to spread swiftly from this index case, involved more than 600 individuals, including 21 infants, and lasted for half a year. Nearly half of the measles cases in this outbreak were twice-vaccinated individuals. This high contribution of twice-vaccinated individuals to disease cases was revealed only by active case finding, performed by de Serres *et al.* On the other hand, passive surveillance has resulted in significant underreporting of measles among twice-vaccinated, thus skewing the official statistics.

Indicative of the gradually waning nature of vaccine-based protection, the contribution of twice-vaccinated children to disease cases increased with age. Twice-vaccinated cases constituted only 4.1% of the 5-9 age group, but 18% of the 10-14 age group, and 22% of the 15-19 age group. The study did not assess how many previously vaccinated individuals ended up getting the measles virus infection with a modified clinical course of disease and thus were not counted as disease cases for the purposes of reporting, yet were spreading the virus around in the community.

## **Can the Vaccinated Transmit the Measles Virus?**

The medical establishment assumes that vaccinated children, if they themselves get virally infected or even develop full-blown (called breakthrough) disease, cannot transmit it to others. Some cite a paper published in the *Journal of American Medical Association (JAMA)* in 1973 as providing evidence for this assumption. Indeed, the title of the article reads "Failure of Vaccinated Children to Transmit Measles."<sup>xii</sup> However, careful examination of the study design reveals that the study did not properly address the question it should have addressed: whether vaccinated children who got infected during an outbreak transmitted the virus to susceptible contacts.

The results of the *JAMA* study show that during an outbreak of measles in an Iowa community in the 1970s, which involved both vaccinated and unvaccinated

children, non-sick children were unlikely to transmit measles to their younger pre-school siblings, many of whom could have been recently vaccinated themselves and therefore not susceptible to measles anyway during that particular outbreak. The vaccination status of those younger siblings was not determined (or disclosed) by the study. Curiously, the study data show that non-sick *unvaccinated* children also “fail” to transmit measles (which they obviously did not contract during that particular outbreak) to their younger pre-school siblings with undisclosed vaccination status. This makes it clear that vaccination status is not a predictor of viral transmission.

A recent study, based on the 2011 outbreak of measles in New York City, has clearly documented that a twice-vaccinated person (an adult) can transmit measles to and sicken other twice-vaccinated adults.<sup>xiii</sup>

## **Doing the Math**

Let us now remind ourselves that the touted purpose of establishing herd immunity via a high degree of vaccination compliance is to be able to promptly cease any outbreak of a benign childhood disease so that a vulnerable but vaccine-ineligible population (i.e., infants or individuals taking immuno-suppressive medications) could avoid contracting the disease that is dangerous *only* at their age or given their state of the immune system. To prevent an outbreak, 70-95% of the population, according to very broad theoretical estimates, has to be truly immune – that is, *resistant to viral infection*, not just protected from developing the full range of symptoms that conform to the accepted clinical definition of the disease. However, 100% vaccination compliance can at best make only a quarter of the population become resistant to viral infection for a decade. This makes it apparent that stable herd immunity cannot be achieved via childhood vaccination in the long term regardless of the degree of vaccination compliance.

## **Is Revaccination a Solution to Waning Vaccine Protection Against Measles?**

Typical variations in the gene pool (i.e., personal immuno-genetic profile) affect how efficiently vaccines get processed and presented to the immune system for the purposes of antibody production. This might be one of the reasons why only a fraction of healthy children respond well to vaccination (i.e., can generate and maintain relatively high measles-neutralizing titers for many years), whereas other healthy children respond poorly to vaccination. Would re-vaccinating those whose personal immuno-genetic profile does not favor high antibody production in response to the measles vaccine, correct their inherently low degree of vaccine-responsiveness? The research that attests to the futility of such an endeavor is gleaned from observations summed up by Dr. Gregory Poland:

*“In studies of measles, post-immunization measles antibody in the ‘low positive’ range did not protect against clinical measles when subjects were exposed to the wild measles virus, whereas high levels were protective. Furthermore, non-responders to a single dose*

*of measles vaccine, who demonstrated an antibody response only after a second immunization, were still six times more likely than were responders to a single dose of measles vaccine to develop measles on exposure to wild virus. Others examined 'poor responders,' who were re-immunized and developed poor or low-level antibody responses only to lose detectable antibody and develop measles on exposure 2–5 years later.*"<sup>xiv</sup>

The answer is clear: poor responders to the measles vaccine remain poor responders to further vaccination and cannot rescue herd immunity. Having these data, why does the medical establishment insist that *vaccine-based* herd immunity is even possible, if only stricter or more frequent vaccination measures could be implemented? Why, for the sake of an unattainable idea, do mainstream pediatricians and public health officials pester those families who choose to shield their children from potential vaccine injuries or ensure their children's health via natural vaccine-independent strategies?

### **Self-Defeating Public Health Venture**

The biomedical belief that a vaccine-exempt child endangers the society by not contributing to herd immunity is preposterous, because vaccinating every single child by the required schedule cannot maintain the desired herd immunity anyway. It is time to let go of the bigotry against those seeking vaccination exemptions for their children. Instead, we should turn our attention to the outcome of mass vaccination campaigns that lies ahead.

Mass vaccination of children initially achieves rapid results in disease reduction through attempted viral eradication only because it hitch hikes on top of the permanently immune majority of adults who acquired their immunity naturally in the pre-vaccination era. The problem is, however, that the proportion of vaccinated but non-immune young adults is now growing, while the proportion of the older immune population is diminishing due to age. Thus, over time mass vaccination makes us lose rather than gain cumulative immunity in the adult population. At this stage the struggle to control imported outbreaks is going to become an uphill battle regardless of vaccination compliance, with the Quebec measles experience of 2011 being a harbinger for more of such out-of-control outbreaks to come.

Mass vaccination eventually ceases endemic disease outbreaks by removing viral circulation in the community, instead of inducing permanent immunity in the vaccinated. However, viral diseases, although reduced in incidence in many countries, are not fully eradicated from all parts of the world. A region-specific elimination of viral exposure at the time when the virus is present globally is hardly good news. Prolonged mass childhood vaccination is a measure of disease control that with time makes our entire adult population more and more defenseless against the incompletely eradicated virus, which can be easily re-imported.

*Why do public health authorities choose to put so much effort into a self-*



## *defeating venture of non-uniform viral eradication?*

Perhaps a bit belated, comes a theoretical recognition of the epidemiologic disaster we are heading towards:

*“For infectious diseases where immunization can offer lifelong protection, a variety of simple models can be used to explain the utility of vaccination as a control method. However, for many diseases, immunity wanes over time.... Here we show how vaccination can have a range of unexpected consequences. We predict that, after a long disease-free period, the introduction of infection will lead to far larger epidemics than that predicted by standard models. These results have clear implications for the long-term success of any vaccination campaign and highlight the need for a sound understanding of the immunological mechanisms of immunity and vaccination.”<sup>xv</sup>*

The medical establishment got it all in reverse. It is not a vaccine-exempt child who endangers vulnerable infants and immuno-compromised individuals. It is the long-term effects of mass vaccination campaigns that have accomplished that already. It is time to wake up to the reality of our public health vaccination policies and their long-term implications.

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<sup>iv</sup> Sencer DJ, Dull HB, Langmuir AD. “Epidemiologic basis for eradication of measles in 1967.” *Public Health Rep* **82**, 253-256 (1967).

<sup>v</sup> Klock LE, Rachelefsky GS. “Failure of rubella herd immunity during an epidemic.” *N Engl J Med* **288**, 69-72 (1973).

<sup>vi</sup> Poland GA & Jacobson RM. “Failure to reach the goal of measles elimination. Apparent paradox of measles infections in immunized persons.” *Arch Intern Med* **154**, 1815-1820 (1994).

<sup>vii</sup> Ochsnein AF *et al.* “Protective long-term antibody memory by antigen-driven and T help-dependent differentiation of long-lived memory B cells to short-lived plasma cells independent of secondary lymphoid organs.” *Proc Natl Acad Sci USA* **97**, 13263-13268 (2000).

<sup>viii</sup> Chen RT *et al.* “Measles antibody: reevaluation of protective titers.” *J Infect Dis* **162**, 1036-1042 (1990).

<sup>ix</sup> LeBaron CW *et al.* “Persistence of measles antibodies after 2 doses of measles vaccine in a post-elimination environment.” *Arch Pediatr Adolesc Med* **161**, 294-301 (2007).

<sup>x</sup> Itoh M, Okuno Y, Hotta H. “Comparative analysis of titers of antibody against measles virus in sera of vaccinated and naturally infected Japanese individuals of different age groups.” *J Clin Microbiol* **40**, 1733-1738 (2002).

<sup>xi</sup> De Serres G *et al.* “The largest measles epidemic in North America in a decade—Quebec, Canada, 2011:

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<sup>xii</sup> Brandling-Bennet AD, Landrigan PJ, Baker EL. "Failure of vaccinated children to transmit measles." *JAMA* **224**, 616-618 (1973).

<sup>xiii</sup> Rosen JB *et al.* "Outbreak of measles among persons with prior evidence of immunity, New York City, 2011." *Clin Infect Dis* (2014).

<sup>xiv</sup> Poland GA. "Variability in immune response to pathogens: using measles vaccine to probe immunogenetic determinants of response." *Am J Hum Genet* **62**, 215-220 (1998).

<sup>xv</sup> Heffernan JM, Keeling MJ. "Implication of vaccination and waning immunity." *Proc R. Soc. B* **276**, 2071-2080 (2009).