May 10, 2019

Reneé Coleman-Mitchell, MPH
Commissioner
State of Connecticut Department of Public Health
410 Capitol Avenue, P.O. Box 340308
Hartford, CT 06134

Dear Commissioner Coleman-Mitchell:

We are troubled by your decision to release vaccination rates for Connecticut school children and its use by legislators to overturn the religious exemption. Democratic leadership is convinced we are in a public health crisis which necessitates the removal of the exemption despite no case of measles among Connecticut children and only three (3) cases of measles in adults. The argument is that we are on the cusp of losing herd immunity and therefore have to take immediate action. There are many flaws to this argument which we would like to discuss.

Herd immunity is the reassuring theory that high vaccination rates within a population as a whole will protect the small number of individuals who are vulnerable to contracting an infection due to a variety of factors such as being unvaccinated, being immunocompromised, or vaccine failure. This theory was first described by observing natural disease outbreaks prior to the existence of vaccines. When these diseases are contracted naturally, lifetime immunity typically results and plays an important part in the concept of herd immunity. In order for herd immunity to hold true there must be a homogenous population, well-mixing of the population must occur, unvaccinated status must be random, vaccines must have perfect efficacy, and the age distribution of the population must be uniform. Those criteria are not currently in place.

Vaccinated populations do not share the same characteristics as naturally immune populations, which renders the theory of herd immunity to be quite erroneous. The first flawed assumption is that perfect vaccine efficacy occurs. In actuality, *primary vaccine failure* can occur in up to 2-10% of vaccinated individuals.[1] These individuals do not respond with sufficient antibody production to provide protection and some will fail to do so even with additional boosters.

In addition, *secondary vaccine failure* can occur. This is when vaccine-induced antibodies wane over time and render an individual unknowingly unprotected later in life.[2,3] A serious consequence of this is shifting disease burden to more vulnerable populations. As a result, illnesses that were typically benign and self-limiting in children are now occurring in

adults where the risk of serious complications are much greater. One study suggests that lapsed vaccine immunity has led to negative outcomes that are 4.5 times worse for measles, 2.2 times worse for chickenpox and 5.8 times worse for rubella, compared to the pre-vaccine era.[4] The waning immunity that occurs with secondary vaccine failure will never result in a population with true herd immunity with 90-95% being protected. Even if every single child in Connecticut was fully vaccinated, herd immunity will not be achieved because so many adults have lost their vaccine-induced antibodies.

Both primary and secondary vaccine failure account for the occurrence of vaccine-preventable illnesses in highly and even fully vaccinated populations. This has been described extensively in published literature. One example cited by NYU School of Law Professor Mary Holland, Esq. and Chase Zachary, J.D., Ph.D Chemistry,[5] was a 1985 measles outbreak in a Texas high school where 99% of the students had been vaccinated, and 96% had detectable measles antibodies. The authors of the outbreak report acknowledged that "such an outbreak should have been virtually impossible[6]." More recent studies around the world describe mumps[7] and pertussis[8] outbreaks in highly or fully vaccinated middle and high school populations, including in Belgium[9] (2004), Korea[10] (2006), the U.S.[11] (2007) and Ontario[12] (2015). The Ontario researchers perplexedly stated, "In light of the high efficacy of the MMR [measles-mumps-rubella] vaccine against mumps, the reason for these outbreaks is unclear."

The failure of the current MMR vaccine and its inability to prevent measles outbreaks in highly vaccinated populations is specifically addressed by Gregory Poland, MD, MACP, and Robert Jacobson, MD, FAAP, in the January 2012 issue of *Vaccine* (article attached):

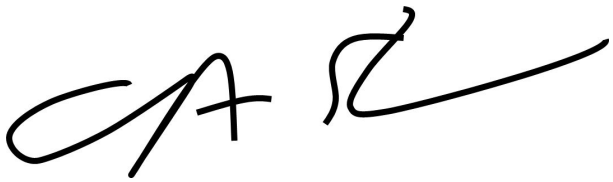
> Receiving less attention, however, is the issue of vaccine failure. While the current vaccine is acknowledged as a good vaccine, we and others have demonstrated that the immune response to measles vaccine varies substantially in actual field use. Multiple studies demonstrate that 2–10% of those immunized with two doses of measles vaccine fail to develop protective antibody levels, and that immunity can wane over time and result in infection (so-called secondary vaccine failure) when the individual is exposed to measles. For example, during the 1989–1991 U.S. measles outbreaks 20–40% of the individuals affected had been previously immunized with one to two doses of vaccine. In an October 2011 outbreak in Canada, over 50% of the 98 individuals had received two doses of measles vaccine. Thus, measles outbreaks also occur even among highly vaccinated populations because of primary and secondary vaccine failure, which results in gradually larger pools of susceptible persons and outbreaks once measles is introduced. This leads to a paradoxical situation whereby measles in highly immunized societies occurs primarily among those previously immunized[13]."

Despite these caveats, most public health officials continue to push even higher rates of compulsory vaccination and continued boosters throughout the lifespan without any convincing

evidence of efficacy. As Holland and Zachary painstakingly show, illogical mandates and "imperfect vaccine technology" mean that "herd immunity does not exist and is not attainable." Even one hundred percent vaccination "cannot reliably induce herd immunity." Thus, herd immunity is a "weak rationale" to compel all vaccines for all children.[5]

Despite higher than average cases of measles in 2019, Connecticut does not have a public health emergency warranting the repeal of the religious exemption. The data published by DPH is littered with inaccuracies and does not provide strong evidence to justify removing the religious exemption for a small minority of schoolchildren. The idea of herd immunity is flawed and will never be achievable due to primary and secondary vaccine failure, unvaccinated adults, and importation of disease from travelers. The herd immunity theory is not strong enough to justify withholding a child's constitutionally protected right to public education.

Sincerely,



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Published in final edited form as:
Vaccine. 2012 January 5; 30(2): 103–104. doi:10.1016/j.vaccine.2011.11.085.

The Re-Emergence of Measles in Developed Countries: Time to Develop the Next-Generation Measles Vaccines?

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Measles is the most transmissible infectious disease known in humans, and remains one of the top causes of death in children worldwide. Even in highly developed countries, measles kills approximately 3 of every 1,000 persons infected. While no treatment exists for measles, prevention in the form of vaccination has been available since the 1960's. Despite the significant global morbidity and mortality of measles, considerable progress is evident. Just a decade ago, in 2000, measles killed an estimated 777,000 people a year worldwide. In 2010, measles killed only 160,000 worldwide – a testament to widespread use of vaccine.

But concerns lurk, unnoticed for the most part. Despite the above gains measles is reemerging as a serious public health threat, and outbreaks are occurring even in highly developed countries where vaccine access, public health infrastructure, and health literacy are not significant issues. This is unexpected and a worrisome harbinger - measles outbreaks are occurring where they are least expected. As illustrated in the Table, since 2005 these outbreaks have also occurred in the U.S.—with surprising numbers of cases occurring in persons who previously received one or even two documented doses of measles-containing vaccine. In fact, as of September 2011, the U.S. has had 15 measles outbreaks with 211 confirmed cases—the highest number of cases since 1996 [1;2].

Large measles outbreaks are also occurring in many other developed countries [3–6]. Thirty-three European countries have reported outbreaks of measles this year [5] with more than 30,000 known cases [4]. The UK has declared measles once again endemic [3]. In the first seven months of 2011, France alone suffered 14,025 cases of measles, and Spain has reported 1,777 cases [7]. In none of these countries are vaccine access, nor health care infrastructure, serious issues. Where data exist such outbreaks result from both failure to vaccinate, and vaccine failure.

Failure to vaccinate is a serious socio-cultural issue, and significantly hampers public health goals. Measles immunization rates, particularly in certain areas of the US and western Europe, have plateaued or decreased and experts suspect this is a result of the now-debunked notion that measles vaccine caused autism – a false claim that adversely influenced MMR vaccination choices among a generation of parents. In addition, few current parents have any direct experience with measles and are uninformed about its infectivity, morbidity, and mortality. Because measles outbreaks have occurred in scattered areas of the country, the

Disclosures: Dr. Poland chairs data monitoring committees for non-measles vaccines being developed by Merck & Co. Dr. Jacobson also serves on a data monitoring committee as well as a safety review committee concerning non-measles vaccines produced by Merck & Co.

average parent is unaware of the danger, and feels no urgency to respond by immunizing their children – thus further enlarging the pool of susceptibles.

Receiving less attention, however, is the issue of vaccine failure. While the current vaccine is acknowledged as a good vaccine, we and others have demonstrated that the immune response to measles vaccine varies substantially in actual field use. Multiple studies demonstrate that 2–10% of those immunized with two doses of measles vaccine fail to develop protective antibody levels, and that immunity can wane over time and result in infection (so-called secondary vaccine failure) when the individual is exposed to measles. For example, during the 1989–1991 U.S. measles outbreaks 20–40% of the individuals affected had been previously immunized with one to two doses of vaccine. In an October 2011 outbreak in Canada, over 50% of the 98 individuals had received two doses of measles vaccine. The Table shows that this phenomenon continues to play a role in measles outbreaks. Thus, measles outbreaks also occur even among highly vaccinated populations because of primary and secondary vaccine failure, which results in gradually larger pools of susceptible persons and outbreaks once measles is introduced [8]. This leads to a paradoxical situation whereby measles in highly immunized societies occurs primarily among those previously immunized [8].

The WHO and others have called for both country or region-specific elimination and global eradication of measles [9]. However, eradication (complete elimination of the global spread and transmission) of measles is unlikely as modeling studies suggest that herd immunity of approximately 95% or greater is required to eliminate persisting measles endemicity [10]. Because field studies demonstrated evidence of primary vaccine failure and population-levels of immunity below this threshold, the United States, like many other countries, adopted a two-dose measles vaccination policy in the early 1990's. However, even with two documented doses of measles vaccine, our laboratory demonstrated that 8.9% of 763 healthy children immunized a mean of 7.4 years earlier, lacked protective levels of circulating measles-specific neutralizing antibodies [11], suggesting that even two doses of the current vaccine may be insufficient at the population level.

Thus, while an excellent vaccine, a dilemma remains. As previously mentioned, measles is extraordinarily transmissible. At the same time, measles vaccine has a failure rate measured in a variety of studies at 2–10%, and modeling studies suggest that herd immunity to measles requires approximately 95% or better of the population to be immune [12]. It remains then an open question as to whether the current vaccine is sufficiently immunogenic and efficacious to allow eradication – even though measles can be controlled, and even eliminated in some regions for defined periods of time. Whether elimination can, in fact, be sustained is unknown, as it has not been evident over sufficiently long periods of time (decades) across geographic regions.

Other limitations of the vaccine should also be acknowledged and raise concern in terms of the current vaccine's utility in eradication efforts [13–16]. Practical limitations of the vaccine are that it cannot be administered to those who are immunocompromised, who have allergies to vaccine components, or who are pregnant. Additional limitations are the need for a cold-chain, the need for trained health care personnel to administer vaccine, and the need to delay immunization until 12 months of age due to passively transferred maternal immunity. Socio-cultural limitations are also extremely important, and often either overlooked by the architects of elimination and eradication efforts, or unexpectedly arise due to temporal trends. Primary among these are that surprising numbers of otherwise well-educated people reject the vaccine due to safety fears—effectively diminishing its worth as a public health tool. Thus, current measles vaccines can only be used to protect individuals without contraindications, and those willing to accept the vaccine, conditions that leave a

large enough segment of the population susceptible and unprotected from measles such that cases will continue to occur.

The practical answer to the dilemma of measles re-emergence is the development of better, next-generation vaccines. Given recent public opinion and large numbers of parents rejecting the current vaccine, combined with practical and immunologic limitations, new vaccines appear to be necessary. The ideal vaccine would require only one dose to be given at or soon after birth; it would lack contraindications and permit administration without highly trained health care personnel; it would be inexpensive, and heat stable. Next-generation vaccines such as peptide-based subunit vaccines, perhaps with adjuvants, DNA vaccines, aerosol vaccines, and other approaches are possible, and active research is ongoing. Such next-generation vaccines could achieve the goal of measles eradication if such vaccines are more immunogenic than current vaccines, result in extremely high rates of protective immunity stable over a lifetime, and are widely accepted by the populace.

To date, despite multiple efforts, the reality is that for the practical, socio-cultural, and immunologic reasons outlined above, we have not eradicated measles. As a result, measles is re-emerging as a public health threat, and our current tool for prevention has limitations that increasingly look to be significant enough that sustained elimination, much less eradication, are unlikely. Perhaps it is time to consider, in earnest, the development of the next generation of measles vaccines.

Acknowledgments

Acknowledgment

This work is supported in part by funding from the National Insitutes of Health, AI-033144.

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Table 1

Recent Measles Cases in US as of September 15, 2011

Year	Total Infected	Unknown Vaccine Status	No Doses of Measles Vaccine	Received Only 1 Dose	Having Received 2 Doses	Any Dose where Known
2005	66	8	50	7	1	13.8%
2006	55	15	25	12	3	37.5%
2007	43	10	25	4	4	24.2%
2008	140	21	108	6	5	9.2%
2009	71	15	49	6	1	12.5%
2010	63	20	37	2	4	14.0%
2011	211	48	134	16	13	17.8%

Source: Div Viral Diseases, Epi Branch, Natl Ctr Immunization & Resp Dis, CDC, Sep. 21, 2011

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