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Increasing communication through improved nursing education

Abstract
Increasing nursing education of vaccines is incredibly important when nurses are attempting to educate families on the risks and benefits of many childhood vaccines. Through learning about the history of major vaccines, vaccine policies and the vaccine manufacturing process, nurses may better understand how to communicate with families.

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INCREASING COMMUNICATION THROUGH IMPROVED NURSING EDUCATION: THE HISTORIES, POLICIES, AND MANUFACTURING PROCESS OF VACCINES

By

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INCREASING COMMUNICATION THROUGH IMPROVED NURSING EDUCATION

Increasing communication through improved nursing education: The histories, policies and manufacturing process of vaccines

From birth to age 18, a child can receive up to 42 doses of scheduled vaccines, not including annual influenza vaccinations. Vaccines are an important part of a child’s life, aiming to prevent the child from contracting serious and potentially deadly diseases that in the past have killed several million children collectively throughout the world. While many vaccines today contain antigens for diseases that have been considered eradicated, it is important to continue vaccination to prevent wild type versions of eradicated diseases from working its way back into the population. Should an event like this happen, immunocompromised and young children could contract diseases like polio and diphtheria, serious diseases that killed thousands of children over the last 100 years.

This paper will outline the history of many vaccines that are recommended by the World Health Organization (WHO), the severity of illness those diseases cause, the vaccine manufacturing process, and vaccine policies. These topics will highlight the rationale of why children should continue to be vaccinated against said diseases.

The nurse’s role in enhancing communication between parents and providers is one of the most important aspects of the paper, as alarmingly increasing numbers of parents have decided to withhold from vaccinating their children. It is through providers’ increased communication that successful vaccination rates will improve, thereby decreasing incidences of preventable disease and death.

History of Disease and Vaccine Production

Parents today do not seem to recognize the severity of the diseases modern children are vaccinated against, as many state they do not believe their children need
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vaccines for the diseases the CDC recommends. Parents believe this due to the sparse incidences of preventable disease that remain in the United States (London et al. 2017).

The history of how vaccines became as important for human health as they are today began with the smallpox vaccine. Research on the smallpox vaccine opened the door for many other vaccines to be produced and perfected.

Smallpox

Smallpox is a progressive disease with several stages, each with different symptoms. During the initial stage, an individual may be contagious with a high fever, head and body aches, and vomiting. In the early rash stage, the individual is most contagious with a rash that manifest as small red spots on the tongue and in the mouth. The spots break open and turn into sores that ooze the virus into the mouth and throat. A skin rash begins on the face and spreads down to the arms and legs. After 10-14 days, the pustular rash scabs over and fall off. After approximately four weeks, all scabs will have fallen off and the individual is no longer contagious (Center for Disease Control and Prevention, 2016c).

History of disease.

Smallpox can be traced back to approximately 10,000 BC in northeastern Africa (Riedel, 2005). Mummies from 1570-1085 BC were the first to be noted with smallpox pustules on their faces. In the 18th century, approximately 400,000 Europeans died annually from the disease (Riedel, 2005). Those who survived were left with significant scarring.
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History of vaccination.

One of the first recorded incidences of vaccination occurred in China around 900-1000 A.D, when physicians noted that people who were exposed to the scabs of those with smallpox developed either a milder version of the disease or no symptoms at all. Physicians crushed the scabs into a powder and directed those at risk to inhale the powder through the nose. For hundreds of years after, thousands of people were protected from smallpox with this method in Asia, Africa, and the Middle East (Feemster, 2018, p. 17).

The first record of inoculation in the United States was in 1721 during the Boston smallpox epidemic. Cotton Mather was first introduced to inoculation by slaves from Africa who were inoculated in their home country. While Mather was adamant in treating the ill, there were not any physicians who gave their support. Dr. Zabdiel Boylston agreed to inoculate as many patients as he could with the help of Mather. Dr. Boylston introduced fluid from an infected individual’s pustule to a healthy individual through a small cut made in the skin. The individual would still develop smallpox, but a generally milder case. Those who were inoculated this way were also protected from additional smallpox infections through antibody protection. At the end of the epidemic, Boylston had inoculated approximately 248 patients (Feemster, 2018, p. 18).

Through additional smallpox epidemics through the years, more and more people began to believe that the practice of inoculation was beneficial. Since smallpox was incredibly contagious, those who received the inoculation were quarantined afterwards to prevent the spread of infection. This was difficult for healthy individuals who felt that it was unnecessary to make themselves willfully ill for the sake of not contracting the full-blown smallpox disease. As successful inoculations began to rise, the medical community
slowly embraced the practice, though it was still considered illegal in many colonies for
years to come (Feemster, 2018).

In 1796, Dr. Edward Jenner treated a milkmaid who stated she had never contracted smallpox because she had been exposed to cowpox. Cowpox was a rarer and
less severe disease that mostly infected farmworkers through contact with cow udders. Jenner extracted pus from a milkmaid's cowpox lesion and injected an eight-year-old boy, James, with it. Six weeks later he injected James with smallpox. The boy never developed any symptoms of smallpox at that time, nor did he contract any subsequent smallpox infections (Stern & Markel, 2005, p. 612). By this experiment, Jenner was able to prove that cowpox protected individuals from smallpox infections. Five years later, in 1801, nearly 100,000 people had been vaccinated with the first cowpox-based vaccine throughout Europe (Feemster, 2018, p. 20).

By 1801, smallpox was still ravaging its way through America, though curiously, American cows did not suffer from cowpox. This made it difficult to create a vaccine like Jenner's. Thomas Jefferson, the American president at the time, was the first to establish the import of cowpox fluid to use in vaccines against smallpox from Europe. The vaccine was pushed in more urban areas, where smallpox outbreaks were more likely due to living in closer quarters (Stern & Markel, 2005).

Eradication.

With increased mass vaccination efforts, the last case of naturally acquired smallpox occurred in Somalia in 1977 (Center for Disease Control and Prevention, 2016b). The patient made a full recovery after a period of isolation. On May 8th, 1980,
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smallpox was declared eradicated throughout the world (Center for Disease Control and Prevention, 2016b). Diseases that have been eradicated or are approaching near eradication by the WHO will be mentioned throughout the paper, though not all diseases listed have published eradicated efforts.

Polio

Poliovirus is an enterovirus causing the poliomyelitis disease. Poliomyelitis is an acute paralytic disease stemming from lower motor neuron damage that results in unilateral or bilateral lower extremity weakness (Baicus, 2012). The upper extremities, throat, chest and facial muscles may also be affected.

History of disease.

Poliomyelitis has been traced back to ancient times of Egyptians, approximately 1580-1350 BCE, where steles showed an adult with a smaller, flaccid looking leg and a crutch; similar to what victims of poliomyelitis looked like in the 1900s (Nathanson & Kew, 2010). While poliomyelitis was observed in European countries prior to the United States, the first documented cases of polio in the United States were seen in 1894 in Rutland County, Vermont by Dr. Charles Caverly (The College of Physicians of Philadelphia, 2018b). There were 18 deaths and 132 cases of permanent paralysis. While Caverly was one of the first physicians to recognize that polio could occur with or without permanent paralysis, he did not believe that the disease was contagious and could be spread. It would not be discovered that poliomyelitis was indeed contagious until 1905 by Swedish physician Ivar Wickman (The College of Physicians of Philadelphia, 2018b). Polio was found to be passed from person to person via pharyngeal secretions and
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contaminated feces, as polio entered through the oral route and traveled through the digestive tract (Nathanson & Kew, 2010).

In 1916, the United States faced its first of many summertime polio epidemics that claimed the lives of 2,000 people in New York City alone, and approximately 6,000 total across the country, leaving thousands more paralyzed in its wake (The College of Physicians of Philadelphia, 2018b). In 1929, the use of the iron lung, an artificial respirator, was used for patients with paralytic polio who could no longer breathe on their own due to the diaphragm and intercostal muscles becoming paralyzed (The College of Physicians of Philadelphia, 2018b).

Vaccine history.

The first polio vaccine trials began in 1935, four years after Australian researchers Frank Burney and Jean McNamara found that there was more than one type of poliovirus. Maurice Brodie and John Kollmer both set to work producing the world’s first polio vaccines. However, there was no extensive testing prior to vaccinating thousands of subjects. Brodie’s vaccine was made with a killed virus that did not leave the subject with a sufficient level of antibodies to fight off the virus and produced severe allergic reactions in some recipients. Kollmer’s vaccine was made with the live polio virus was not attenuated correctly, producing polio in some of the recipients (Baicus, 2012). Because there were no regulations on human experimentation, many test subjects died of either poliomyelitis, severe allergic reactions, were left paralyzed, or were made ill (The College of Physicians of Philadelphia, 2018b).
In 1948, Dr. Hilary Koprowski, a researcher from Lederle Laboratories, ingested his Type II poliovirus vaccine after testing it successfully on chimpanzees. He did not suffer any ill effects. This discovery came one year before David Bodian, MD, PhD and Isabel Morgan, PhD published their work that identified three types of polioviruses. This research was monumental in the development of vaccines for poliovirus, as the vaccine would need to prove immunity to all three types of the virus (The College of Physicians of Philadelphia, 2018b). Dr. Koprowski began his human trials of his vaccine in 1950, beginning with 20 disabled children at a New York State facility. It was proven a success as not one child developed polio, and all developed the Type II poliovirus antibodies (The College of Physicians of Philadelphia, 2018b).

Another surge of the polio epidemic shook the United States in 1952, infecting approximately 57,628 people and paralyzing more than 21,000 of them. Jonas Salk and his team of researchers began their first human subject testing in 1952 using their killed-virus vaccine (inactivated poliovirus (IPV)). The subjects were institutionalized children that were physically or mentally disabled. It was found that the subjects developed antibodies to the type of poliovirus they were vaccinated with, which gave way to larger scale trials. The Vaccine Advisory Committee approved a large-scale human trial that included a double-blind study of over 1.3 million American children in 1954 (The College of Physicians of Philadelphia, 2018b). Only the researchers knew which child had been vaccinated with either the polio vaccine or placebo fluid. It was found a year later that Salk’s poliovirus vaccine proved to be 80-90% effective, and the United States government licensed the vaccine the same day (The College of Physicians of Philadelphia, 2018b).
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A few months after the vaccine was licensed, reports from local health authorities began to show new cases of paralytic polio in newly vaccinated children. Paralysis appeared to begin in the vaccinated arm compared to the more common lower extremities (The College of Physicians of Philadelphia, 2018b). An investigation traced the issue back to Cutter Laboratories based in California, which gave way to public health officials making drastic changes to the production of the poliovirus vaccine and later all other vaccines. Changes included testing larger samples of each vaccine lot, lengthen the treatment time with formaldehyde, and use special filters that could filter accumulations of the virus that would be resistant to the chemical inactivation of formaldehyde (The College of Physicians of Philadelphia, 2018b).

By 1957, Koprowski had begun trials of a new oral poliovirus (OPV) vaccine that only provided immunity against Type I poliovirus in the Democratic Republic of Congo. While the vaccine did not provide protection against all three types of poliovirus, Type I was most widely found in the Congo (The College of Physicians of Philadelphia, 2018b).

Albert Sabin worked with Soviet health officials to produce an OPV that included all three polioviruses. Sabin’s live vaccine was cheaper to produce than Salk’s IPV vaccine. It also was proved to have many advantages over the IPV. The OPV produced an immune response faster than the IPV and traveled through the entire digestive system unlike the IPV. The OPV was given on a sugar cube and was preferred by children compared to a vaccine. One issue that was found with the OPV was that the virus could revert to virulent forms, whereas the IPV could not (The College of Physicians of Philadelphia, 2018b). With these advantages in mind, the Soviet Union vaccinated over
10 million Soviet children using the OPV vaccine and did not include a control group (The College of Physicians of Philadelphia, 2018b).

In 1960, the United States' Surgeon General recommended that Sabin's OPV vaccine be licensed for use in the US. At first, the vaccine only provided protection against Type 1 poliovirus, but all three types were included in the vaccine by 1963 (The College of Physicians of Philadelphia, 2018b).

Salk's IPV vaccine was slowly phased out in 1968, as the OPV vaccine was greatly preferred by the public and the American government. It would be used again in 1997 when authorities found that an average of 8-10 polio cases per year were caused by the OPV vaccine (The College of Physicians of Philadelphia, 2018b). By 2000, the OPV vaccine would no longer be used in the United States, completely switching to a new and improved version of Salk's IPV vaccine. However, the rest of the world, specifically underdeveloped countries, would continue to use the OPV vaccine (The College of Physicians of Philadelphia, 2018b).

The World Health Organization (WHO) set a goal in 1985 for polio to be completely eradicated from the Americas by 1990, however, polio was not declared eradicated from the Americas until 1994. In 2000, it was found that there had been a reduction of wild polio cases by 99%, a decrease from 350,000 cases in 1988 to only 719 worldwide in 2000 (The College of Physicians of Philadelphia, 2018b). Wild polio cases were considered polio diagnoses that did not stem from recent polio vaccinations or contact with a recently vaccinated individual (The College of Physicians of Philadelphia, 2018b).
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In April of 2016, the elimination of Type II poliovirus vaccines began to stop vaccine-derived Type II polio in high risk countries. Approximately 150 countries still using the OPV vaccine were directed to switch from the three-strain OPV to the two-strain vaccine. Because there has not been a case of wild Type II poliovirus since 1999, the WHO hopes that Type II poliovirus should eventually die out, leaving only Types I and III to be eliminated (The College of Physicians of Philadelphia, 2018b).

Today, polio has still not been declared eliminated worldwide. The number of wild poliovirus cases are still decreasing, most recently reported as 22 cases worldwide in 2017 compared to 37 reported cases in 2016. All cases in 2017 were in Afghanistan, Nigeria, and Pakistan, where political unrest appears to make continuing to vaccinate the population difficult. The WHO’s focus is to fully eradicate poliovirus, as even with today’s medical and scientific advancements, there is no cure for polio. Pain relievers, ventilators, and physical therapy are the only available treatments for individuals affected by the disease (The College of Physicians of Philadelphia, 2018b).

Measles, Mumps, and Rubella (MMR)

Measles.

Measles is an infectious viral disease that induces systemic infection in an individual via respiratory secretions. The incubation period lasts 10-12 days, followed by a prodromal phase lasting 2-4 days. During this time, the individual will experience high fever, cough, and runny nose. After the prodromal phase, Kolpik spots form on the buccal mucosa. The spots are characteristic to the disease and normally can be used for a differential diagnosis. A fully body measles rash appears shortly after, lasting 5-6 days. It
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begins on the head and moves laterally and inferiorly to the hands and feet and fades in order of appearance several days later (Hamborsky, Kroger, & Wolfe, 2015). Complications are more likely in children younger than five and adults older than 20 and include anorexia, diarrhea, otitis media, pneumonia, and acute encephalitis. Deaths that occur from the disease are usually complicated with secondary disease, such as pneumonia (Hamborsky, Kroger, & Wolfe, 2015).

History of disease.

In 1676, English physician Thomas Sydenham published his paper successfully distinguishing smallpox from measles, but it wasn't until 1757 that measles was identified to be an infectious virus (Oldstone, 2010).

During the American Civil War, particularly in 1861, there were 21,676 cases of measles with 551 deaths due to respiratory or cerebral complications (Oldstone, 2010). People all over the world continued to contract measles, some dying from secondary complications. There were not any advances in finding a cure nor a vaccine combination to stop the spread of infection until 1916, when the measles-specific antibodies were identified. Patients that had been previously infected by measles had a protective antibody in their blood. Drs Charles Nicolle and Ernest Conseil believed that the serum from measles patients' blood could be used to provide immunity to those who had not yet contracted the disease (Oldstone, 2010). Meanwhile, the disease killed over 12,000 Americans in the same year. The highly infectious disease continued to spread, leading to a massive outbreak in southern Greenland that affected 99.9% of the population, many of them dying (Oldstone, 2010).
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Vaccine history.

Dr. Thomas Peebles was the first to isolate the measles virus in 1954, doing so from the blood of a 13-year-old boy who had been infected with measles. The isolated virus would then be used to create the first of a series of vaccines. Dr. Peebles employed Dr. Sam Katz, who in 1958 tested the first measles vaccine on mentally and physically disabled children. All children developed the antibodies, but most also developed a rash from the vaccine. For the vaccine to be considered effective, the virus would need to be weakened more (Oldstone, 2010).

The first successful measles vaccine was created by John Enders and was licensed in 1963. Over the next 12 years, 19 million vaccines would be administered, however one downfall of the vaccine was that an injection of gamma globulin would also need to be administered to reduce complications and adverse effects (Oldstone, 2010). Merck pharmaceutical company used Enders’ vaccine to create a more attenuated version of the vaccine. To weaken the virus further, it was passed through chick embryo cells 40 times. By weakening the vaccine, it eliminated the need of gamma globulin injections and showed less adverse effects. Since its licensure in 1968, it has been the only measles vaccine used in the U.S (Oldstone, 2010).

Measles was declared eliminated from the United States in 2000, however in 2014, there was an outbreak of 111 cases of measles at Disneyland in Anaheim, California. Most of the infected individuals were children who had not reached the minimum age threshold to be vaccinated for measles, or individuals who were never
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vaccinated for the disease. Infected individuals spread the disease to five different states and Mexico by the end of 2015 (Broniatowski, Hilyard, & Dredze, 2016).

Mumps.

Mumps is an acute viral illness caused by the paramyxovirus Rubulavirus. The virus, like measles, is spread through respiratory droplets or by touching surfaces previously contaminated with respiratory droplets from an infected individual. During the prodromal phase which lasts for approximately two days, symptoms usually consist of headache, malaise, muscle pain, and fever (World Health Organization, 2007). This period is when an individual is most contagious, as well as for approximately nine days after the onset of swelling of the parotid glands, the most characteristic symptom of mumps. Other complications may include asymptomatic pleocytosis, found in 50-60% of patients, and symptomatic meningitis, found in approximately 15% of patients (World Health Organization, 2007).

While mumps is not considered a deadly disease, secondary complications may occur. Paralysis, seizures, cranial nerve palsies, aqueductal stenosis, hydrocephalus, and deafness are the most reported serious secondary complications. Approximately 25% of women who contract mumps during the first 12 weeks of pregnancy experience spontaneous abortion (Center for Disease Control and Prevention, 2015a).

History of disease.

Mumps has been found throughout history as early as 5th century BC. Hippocrates described the disease as swelling near the ears, with some males having testicular swelling of one or both testicles (Choi, 2010). Johnson and Goodpasture studied the
etiology of mumps by showing that the virus could be transmitted from infected humans to monkeys in 1934 (Center for Disease Control and Prevention, 2015a). The virus was not isolated and cultured until 1945, and the first vaccine for mumps, a killed virus vaccine, was licensed and used throughout the United States from 1950 to 1978. It induced short term immunity but showed low efficacy (World Health Organization, 2007).

Vaccine history.

Maurice Hilleman created the first live attenuated mumps vaccine in 1967 by isolating the virus from the saliva of his five-year-old daughter, who had been infected with mumps. The vaccine was named after his daughter, Jeryl-Lynn. Merck bought the vaccine from Hilleman in 1967, renaming it MumpsVax. While other countries have developed their own vaccines against mumps, the United States has continued to use Hilleman’s vaccine since it was licensed. It was combined with the measles and rubella vaccine in 1971 to create today’s MMR vaccine (World Health Organization, 2007).

Rubella.

Rubella is considered a rather mild disease, caused by a togavirus virus, named Rubivirus (Center for Disease Control and Prevention, 2015b). Symptoms of acquired rubella include with low grade fever, headache, conjunctivitis, muscle aches, lymphadenopathy, cough, and rhinorrhea. Some patients develop a mild red rash that begins on the face and moves inferiorly. It usually dissipates in the same sequences three to four days after onset. Approximately 25-50% of individuals with rubella will not show any symptoms of disease (Center for Disease Control and Prevention, 2016a). There is no
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cure or treatment, other than acetaminophen or NSAIDs to reduce fever and muscle aches.

History of disease.

First previously described as a variant of measles, rubella was not considered a separate entity until 1814 by George Maton in Germany, who named it the German measles. In 1914, Alfred Fabian Hess described Rubella to be a virus after working with the infection on monkeys (Center for Disease Control and Prevention, 2015b). Hess’ beliefs were confirmed in 1938 when Hiro and Tosaka were able to replicate the virus by using clean and filtered nasal washings from children to induce infection in healthy schoolchildren who had not been previously exposed (Center for Disease Control and Prevention, 2015b). In 1966, rubella became a nationally recognized infectious disease, with 57,686 cases reported in the United States in 1969 alone (Center for Disease Control and Prevention, 2015b).

Vaccine history.

Three rubella vaccines were licensed in 1969, RA 27/3, or Meruvax, attenuated through duck embryo, Rubelogen, attenuated through dog kidney, and Cendevax, attenuated through rabbit kidney. Rubelogen was removed from the market shortly after licensing after reports of severe joint pain following vaccination (Plotkin, 2005). In 1971, the rubella vaccine was added to the mumps and measles vaccines, effectively created the MMR combination vaccine. In 1979, the Meruvax and Cendevax vaccines used in the MMR were discontinued to make way for the Meruvax II vaccine to be included in the MMR vaccine (Center for Disease Control and Prevention, 2015b).
Meruvax II is a live attenuated virus vaccine first isolated in 1965 from a rubella-infected fetus that was spontaneously aborted (Center for Disease Control and Prevention, 2015b). The virus was passed through the fetus's tissue 25-30 times using human diploid fibroblasts. Meruvax was replaced by the Meruvax II vaccine due to its high efficacy percentage, over 95%, inducing lifelong immunity with only one dose (Center for Disease Control and Prevention, 2015b).

Combination MMR vaccine history.

The combination MMR vaccine was developed in 1971 by Merck and was incredibly effective. Further testing that began several years prior to licensure showed that the adverse effects of the MMR vaccine did not outweigh the adverse effects of any single measles, mumps, or rubella vaccine (Center for Disease Control and Prevention, 2015b).

In 1998, Andrew Wakefield published a popular article in the Lancet, claiming that the MMR vaccine had impacted the digestive systems of children, inducing autism (Wakefield, 1998). Vaccination rates subsequently plummeted, increasing outbreaks of measles around the world. Among controversy, the paper was retracted by the Lancet, after it was found that there was no link between the vaccine and autism. Wakefield later was barred from practicing medicine in Britain. While many studies have not been able to find a link between the MMR vaccine and autism like Wakefield claimed to do, many parents are still convinced that the MMR vaccine was responsible for their child's development of autism.
Diphtheria, Tetanus, and Pertussis (DTaP or TDaP)

Diphtheria.

Diphtheria is a bacterial infection of Corynebacterium diphtheriae that is spread from individual to individual through respiratory droplets and secretions that are inhaled. The bacteria infect the upper airways and throat and damages other organs by producing a toxin that could cause myocarditis and peripheral neuropathy. The bacteria colonize in the throat before excreting a toxin that destroys the surrounding cells, forming a thick gray membrane over the pharynx that can obstruct the airway (The College of Physicians of Philadelphia, 2018a).

Presently, treatment for diphtheria is aggressive. Physicians inject the infected with the diphtheria antitoxin to neutralize it. Penicillins and erythromycin are used to combat the bacteria (Mayo Clinic, 2018). In most cases, the patient needs to be hospitalized for observation and to prevent the patient from spreading the highly contagious disease to others (Mayo Clinic, 2018).

History of disease.

The first record of diphtheria-like symptoms appeared in 1613 during a Spanish epidemic. It was known as the year of strangulations, “El Año de los Garotillos” (The College of Physicians of Philadelphia, 2018a). Halfway through the fifteenth century, diphtheria epidemics swept their way through New England, killing entire families of children. In 1735, diphtheria was known as the “plague of children”, as the disease targeted mostly children under 10 years of age. It is believed that anywhere between 32-
40% of the children under 10 were killed by the disease in New England (The College of Physicians of Philadelphia, 2018a).

In 1836, French physician Pierre Bretonneau gave diphtheria its name, diphtérite. He also was the first to successfully use a tracheostomy to remove throat secretions and allow patients to breathe with more ease. This was the only effective treatment for the disease at the time, and only approximately 25% of patients survived the tracheostomy. Tracheostomies continued to be used until 1885, when American physicians Joseph P. O’Dwyer introduced intubation. O’Dwyer created the tools and methods needed for the procedure, which quickly replaced the use of the tracheostomy, as it was less invasive with higher patient outcomes (The College of Physicians of Philadelphia, 2018a).

Vaccine history.

In 1890, Shibasaburo Kitasato and Emil von Behring isolated the S. diphtheriae anti-toxin in guinea pigs. The scientists injected heat-treated bacteria into guinea pigs and found that animals’ blood contained a substance, antitoxin, that prevented the guinea pigs from being reinfected when injected with the bacteria again (The College of Physicians of Philadelphia, 2018a). Kitasato and von Behring also found that by injecting an infected animal with the blood serum from an immunized animal, it would cure the animal of diphtheria. This practice was named serum therapy. By 1894, the antitoxin had made its way to production in the United States. G.J Hermann, MD and Charles Reynolds, MD used antitoxin to treat the youngest of four children who had all contracted diphtheria. The treated youngest child and another untreated child survived, while the other two children did not (The College of Physicians of Philadelphia, 2018a). A year later, the
antitoxin began to be tested and produced, first by Mulford Company of Philadelphia, then the New York City Health Department (The College of Physicians of Philadelphia, 2018a).

Emil von Behring published a study in 1907 that showed that by mixing the diphtheria toxin and the antitoxin in a precise way, it produced lasting immunity in humans. The balance between the toxin and antitoxin needed to be just right to elicit an immune response yet prevent the toxin from causing disease (The College of Physicians of Philadelphia, 2018a).

The Schick test was an important development in the diagnosis of diphtheria. Bela Schick created the test in 1913 by injecting a small amount of diphtheria toxin under the skin that would either produce reddening and swelling at the inject site, or no change. If there was no change after the injection, this was a negative reaction—a sign that the patient had been previously exposed to the diphtheria toxin and was immune to the bacteria (The College of Physicians of Philadelphia, 2018a). The Schick test was used throughout Europe before Schick immigrated to New York City and implemented the use of his test throughout the city (The College of Physicians of Philadelphia, 2018a).

In 1926, Alexander Thomas Glenny added aluminum salts to the vaccine to increase the effectiveness, and therefore immunity of the diphtheria vaccine (The College of Physicians of Philadelphia, 2018a). The salts increased the level of antibody response, increasing the length of immunity. Today, substances like aluminum salts are called adjuvants, and they are still used in many modern vaccines.
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In the 1970s, it was estimated that there were approximately one million cases of diphtheria that killed 50,000-60,000 people each year in undeveloped countries (World Health Organization, 2017).

Tetanus.

Tetanus is a serious disease caused by an exotoxin released by Clostridium tetani. It is often fatal if left untreated or vaccinated for. The bacteria are found in an individual’s environment and are not contagious. C. tetani can be found in soil and the intestines and feces of many animals. There have also been cases of C. tetani found in contaminated heroin (The College of Physicians of Philadelphia, 2018e). Since tetanus enters the body through a wound on the skin, wound care and management are most important in at risk individuals. Use of the tetanus immune globulin (TIG) is important to remove tetanus that has not traveled to nerve endings (Center for Disease Control and Prevention, 2015e). Once the exotoxin binds to the nervous system, TIG will not remove it. There is no cure for tetanus, only medication and antibiotics to relieve symptoms, along with wound care can help manage the disease until complete recovery (Center for Disease Control and Prevention, 2015c).

There are three different forms of tetanus. The most common, generalized tetanus, presents with a descending pattern starting with the jaw (lockjaw), neck stiffness, difficulty swallowing, and stiffened abdominal muscles. Other presenting symptoms may include pyrexia, diaphoresis, hypertension, and tachycardia (Center for Disease Control and Prevention, 2015c). Complete recovery of tetanus may take months. In some cases, intubation and use of a ventilator are needed when the muscles needed for respiration are
affected. If contractions of the muscles are strong enough, bone fractures may also occur (The College of Physicians of Philadelphia, 2018e). Local tetanus is uncommon, where patients have sustained local muscle contraction where the bacteria entered the body. The contractions can last for several weeks and may precede the onset of a milder form of generalized tetanus (The College of Physicians of Philadelphia, 2018e). Cephalic tetanus is the rarest and are usually contracted by \textit{C. tetani} entering the ear canal, causing otitis media, or wounds to the head. There is usually involvement of the cranial nerves (The College of Physicians of Philadelphia, 2018e).

History of disease.

While there are records of tetanus-like symptoms from 500 BCE, it was not until 1884 that the first tetanus infection was produced in animals. Antonio Carle and Giorgio Rattone discovered the etiology of tetanus by taking pus from a deceased human with tetanus and injecting it into animals (Center for Disease Control and Prevention, 2015c). Arthur Nicolaier, a German-Jewish internist, produced tetanus in animals by injecting them with soil the same year (Center for Disease Control and Prevention, 2015c).

In 1889 Baron Kitasato Shibasaburō, a Japanese bacteriologist, isolated \textit{C. tetani} from a human and injected it into animals to produce disease. He also reported that antibodies could neutralize the spread of the exotoxin (Center for Disease Control and Prevention, 2015c).

Vaccine history.

French bacteriologist and veterinarian, Edmond Nocard, published research of a tetanus antitoxin that induced immunity in humans in 1897 (Center for Disease Control
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and Prevention, 2015c). He stated the antitoxin could be used for prophylaxis and treatment of tetanus.

Gaston Ramon found that by using formaldehyde to inactivate the tetanus toxoid, it would induce immunity in its receiver without inducing infection. This finding led to the development of the first tetanus toxoid vaccine in 1924 by P. Descombey (Center for Disease Control and Prevention, 2015c).

The single vaccine for tetanus is still available and is recommended that individuals receive a booster shot every ten years, or six vaccines total to ensure that the body remains immune to the exotoxin, especially because there is no way to test for tetanus. It is only diagnosed by clinical symptoms (Center for Disease Control and Prevention, 2015c).

Pertussis.

Pertussis is an incredibly contagious disease that is spread through respiratory secretions of an infected individual. The disease causes uncontrollable violent coughing that impedes breathing and can cause apneic episodes. Vomiting after paroxysms are also common. The disease mostly affects children under the age of one, and approximately 50% of babies who contract pertussis need to be hospitalized for treatment (Center for Disease Control and Prevention, 2017).

In patients with pertussis, early detection and treatment is important. Currently, use of antimicrobials such as azithromycin, clarithromycin, and erythromycin are common. Trimethoprim-sulfamethoxazole may also be used. The CDC recommends that anyone who may have been exposed to pertussis be treated with a prophylactic regime,
especially those who are high risk or are in contact with high risk patients, such as children under the age of one (Center for Disease Control and Prevention, 2017).

History of disease.

One of the first epidemics of pertussis, or whooping cough, was described in Paris, France in 1578 by Guillaume De Baillou, who believed the name came from the distinctive cough that individuals with the disease had (The College of Physicians of Philadelphia, 2018d). For the next two hundred years, pertussis made its way through the U.S population, but there were no advances until 1906 when Bordet and Gengou isolated the bacterium, *Bordetella pertussis* (Cherry, 1996). In 1912, Bordet and Gengou attempted and failed to create a pertussis vaccine from killed whole cell *B. pertussis* (The College of Physicians of Philadelphia, 2018d).

Vaccine history.

In 1939, American bacteriologist Pearl Kendrick and Grace Elderding publishing their findings of an effective pertussis vaccine they had created and tested. The vaccine was used until it was combined with diphtheria and tetanus (DTP) in 1948. The DTP was discontinued in the mid-1990s due to concerns of adverse reactions. The killed whole cell pertussis vaccine was replaced with an acellular vaccine, creating the DTaP vaccine that is used presently (The College of Physicians of Philadelphia, 2018d).

Combination diphtheria, tetanus, and pertussis vaccine.

The diphtheria, tetanus, and pertussis vaccines were combined in 1948 to create the DTP vaccine. The World Health Organization (WHO) recommended the combination diphtheria, tetanus, and pertussis vaccine in 1974 for its Expanded Program on
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Immunization (EPI) in developing countries. While these diseases had nearly disappeared in developed countries in Europe and the United States, polio, diphtheria, pertussis, and tetanus continued to ravage developing countries, killing thousands of children. It is estimated that fewer than 5% of all children throughout the world had been vaccinated by their first birthday (The College of Physicians of Philadelphia, 2018a). The whole-cell pertussis antigen was replaced with the acellular pertussis antigen, renaming in the combination vaccine DTaP in the early 1990s (Skibinski, Baudner, Singh, & O’Hagan, 2011).

Several categories of vaccines were produced throughout the last century to provide the best protection from a disease while avoiding many secondary side effects due to inadequately weakened bacteria or viruses. The composition of a vaccine determines the type of immune response created by the body. It is important to note each category to understand why certain diseases must be vaccinated against in a specific way due to the natural volatile nature of the bacteria or viruses.

**Categories of Vaccines**

A vaccine is a manufactured and biological mixture that when injected, provides protection against a number of diseases in humans. The composition of a vaccine determines the type of immune response created by the body. There are six categories of vaccines: live attenuated, inactivated, protein subunit, polysaccharide, polysaccharide conjugate, and recombinant, that each elicit a different immune response.
Live Attenuated

Live attenuated vaccines have been available since the 1950s and are derived from viruses or bacteria that generally cause disease (World Health Organization, 2018c). With this type of vaccine, the virus enters human cells in a weakened state, replicating and infecting just enough cells to create an immune response within the body, but not enough to cause illness of the disease (Feemster, 2018). In live attenuated vaccines, the immune response created by the body is nearly as good as if the body were to encounter the disease itself and provides adequate time for the body to produce memory cells. In extremely rare cases, ranging anywhere from 0.0002%-0.0004% of recipients, the virus may revert to its pathogenic state, causing severe illness in the recipient. Examples of this have been seen with vaccine-associated paralytic poliomyelitis, and vaccine-derived poliovirus related to the oral polio vaccine (World Health Organization, 2018c). While this type of vaccine generally creates the closest immune response to natural disease, it is less safe compared to other categories. Vaccines in this category include the MMR combined vaccine, smallpox, varicella, rotavirus, and yellow fever (U.S Department of Health and Human Services, 2018b).

Inactivated

Inactivated vaccines are made from whole cell viruses or bacteria that have been killed through chemical or physical processes (World Health Organization, 2018b). Chemical processes usually use a small amount of formaldehyde to kill yet retain the composition of the virus or bacteria (Feemster, 2018). Because the cell is dead, there is no risk of disease in recipients. However, an immune response may not be induced with a
single dose potentially requiring several doses throughout the patient’s lifespan to maintain immunity. Vaccines in this category include Hepatitis A, influenza, rabies and inactivated polio vaccine (IPV) (U.S Department of Health and Human Services, 2018b).

Toxoid

Toxoid vaccines are created with the toxin produced by a certain bacterium that invades the bloodstream, eliciting an immune response and causing symptoms of disease. To create the vaccine, the pure toxin is treated with either heat or chemical to attenuate it (London et al., 2017, p. 1046). To increase the immune response, the toxoid is adsorbed to calcium or aluminum salts (adjuvants) (World Health Organization, 2018e). One downfall of the toxoid vaccine is that the vaccine is not as immunogenic as other vaccine categories, therefore several doses may be needed throughout an individual’s lifetime. However, a toxoid vaccine cannot cause the disease it prevents and is usually long lasting and more stable than other vaccine categories (World Health Organization, 2018e). Examples of toxoid vaccines include tetanus and diphtheria (London et al., 2017, p. 1046).

Subunit

Polysaccharide and polysaccharide conjugate.

Polysaccharide and polysaccharide conjugate vaccines are used to target bacteria that are encapsulated by polysaccharides, primarily sugars. The body targets the capsule first because it is the first material to encounter, so the vaccine does not include the actual bacteria the body should protect itself from, but the capsule protecting the bacteria inside. A downside of this technique is that capsule vaccines do not adequately create immune
memory cells, therefore multiple vaccines but be given over a period. Several bacteria that can cause severe disease in children are protected against using this technique, such as *Haemophilus influenzae* (Hib), pneumococcus, and meningococcus (Feemster, 2018).

**Protein-based.**

Protein-based vaccines isolate the antigens of the bacteria that are important to inducing a protective immune response in the body. The vaccine does not consist of a whole bacteria or viral cell, therefore to isolate the antigens responsible for inducing disease, the bacteria must be studied before a vaccine can be created. Because the bacteria or virus in the vaccine is not live, there is no risk of disease and are much more stable than live attenuated virus vaccines (World Health Organization, 2018d). Though an immune response can be triggered by the vaccine, there is no real guarantee that the body's memory cells will form correctly. Examples of protein-based vaccines include acellular pertussis and Hepatitis B (World Health Organization, 2018d).

As new types of vaccines began to be introduced into the healthcare market, there was an increased need of knowledge of how communicable and infectious diseases were spread throughout a population. The fathers of immunology, several men who developed aseptic techniques—who influenced how vaccines are manufactured today.

**Manufacturing A Vaccine**

To understand how vaccines can prevent the spread of human disease throughout a population, it is crucial to also understand how the study of immunology and bacteriology began. Louis Pasteur first introduced the concept that vaccination could
theoretically be applied to any microbial disease, including prophylactically post-exposure. He also was one of the first scientists to discover that microbes were responsible for decay of tissues, dairy, beer, wine, and vinegar when introduced to bacteria (Smith, 2012).

Later in Pasteur’s career, he shifted from microbiology to the study of immunology using live attenuated vaccines. He produced a post-exposure prophylactic rabies vaccine using the live attenuated method, which paved the way for other scientists to create vaccines using similar methods, such as the live attenuated yellow fever vaccine in the 1930s (Smith, 2012).

Today, the manufacturing process of vaccines includes many steps to prevent bacteria and other organisms from growing in the vaccine, as well as keep the vaccine viable prior to administration. However, when vaccines were first introduced to the public, there was not as large of a concern. Edward Jenner began by inoculating humans with bovine cowpox pustules, he did not attempt to attenuate the vaccine, but simply extracted the fluid from pustules and injected it into humans. While those vaccinated did not contract smallpox, some had reactions to the vaccine. Many more developed infections in the injection site and surrounding tissue from lack of proper processing to remove bacteria from the vaccine (Stern & Markel, 2005). As more vaccines were developed over the next 100 years, creating safer vaccines was one of the main concerns.

Creating a new vaccine can range from 5 to 18 years including the research phase of development (Plotkin et al., 2017, p. 4066). With each type of vaccine, the manufacturing process differs in specificity. The antigens of bacteria or viruses are what
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stimulate a human’s immune system to create an immune response. Once an antigen is identified and isolated, it is extracted and concentrated. Attenuation, the process of weakening the virus or bacteria enough so that the cells may still reproduce to elicit an immune response, but not elicit the disease in those vaccinated is an important step for a safe vaccine. Different types of vaccines are manufactured differently, however all must be attenuated. Once attenuated, preservation and adjuvant ingredients are combined with the antigenic substance. Once a vaccine is produced, exploratory and pre-clinical trials begin, followed by human clinical trials with multiple phases. If the results of the clinical trials show significant efficacy, the vaccine may then be approved and license for widespread production and use (Plotkin et al., 2017, p. 4069). The completed vaccine is then put into a vial and packaged or freeze-dried into a powder form for better stability for transport (Sanofi Pasteur, 2018).

Sanofi Pasteur (2018), a large vaccine production company owned by the Sanofi pharmaceutical company, outlines their manufacturing process as follows:

1. Bacteria, virus or cell culture: the antigens are developed using raw material.
2. Harvesting: The antigens produced from microorganisms are extracted.
3. Purification: Impurities are removed and concentrated through physical and chemical processes.
4. Inactivation: Pathogenicity is suppressed while retaining immunological properties.
5. Valence assembly: The active antigenic substances are combined in a single component.
6. Formulation: All the ingredients are melted together.
7. Filling: the vaccine is filled into a vial or syringe.

8. Freeze drying: this step makes it possible to remove the water in a product by transforming it into powder, which ensures a better stability and therefore a better conservation.

9. Packaging: The vaccine is labeled in accordance with regulatory requirements and packed, ready for shipping.

10. Batch release: Quality assurance confirms the product has been manufactured and tested in accordance with the correct procedures. The national regulatory authority gives the final authorization to release the product for distribution.

11. Transport: Our vaccines are distributed all around the world, respecting the cold chain and a temperature between 2-8°C.

Quality control (QC) tests are completed during each stage of the manufacturing process. For a batch to be released and distributed, it must pass all stages of QC testing. Assays include pH and osmolality, antigen stability analyses, excipients and adjuvants, sterility testing, and concentration and potency tests (Smith, Lipsitch, & Almond, 2011, p. 2-3). Depending on the vaccine, additional QC may be warranted. This process may take weeks, not including additional QC, before batch release for transport (Smith, Lipsitch, & Almond, 2011).

Once a batch of vaccines are released, they are transported using the cold chain, a series of facilities from manufacturer to end-user to ensure that the batch remains at a temperature of 2-8°C to maintain product quality (Smith, Lipsitch, & Almond, 2011, p. 4).
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Costs of Vaccines

At each stage of vaccine development, specialized equipment performs certain tasks in the development process. The more complicated the vaccine is to reproduce, the more expensive it is. For example, the live attenuated oral polio vaccine is much less expensive than the pneumococcal conjugate vaccine in terms of lower Cost of Goods Sold (COGS), or the direct costs related to the production of vaccines sold (Plotkin, Robinson, Cunningham, Iqbal, & Larsen, 2017, p. 4066). The cost includes both the materials used and cost of labor to produce the vaccine. One of the main issues plaguing the vaccine industry over the last 70 years is how to reduce vaccine costs.

A few of the vaccines used today in childhood schedules were developed in the mid-20th century. The vaccines' life cycle are maximized by using raw materials and other supplies that would be available for decades at relatively low cost to developers, though competition with other industries using the same materials can drive up vaccine cost (Plotkin et al., 2017, p. 4065).

According to Gerson and Mukherjee (2005), there are three major ways to minimize vaccine cost: manufacturing at the largest scale practical, use a well understood and reputable production process, and use the most efficient facilities, equipment, and machinery to minimize the use of raw energy, personnel, and uncontrolled effects. Major costs can be attributed to product development (research and development laboratories and employees), direct labor (employee wages and benefits), and management or IT systems. Recurring costs such as maintenance and repairs, as well as utilities can make up between $50-700 million USD depending on facility size (Plotkin et al., 2017, p. 4067).
Product development remains high, usually greater than $500 million USD (Plotkin et al., 2017, p. 4067). The United States Department of Defense has estimated that a vaccine with a 25-year life cycle will ultimately cost 1.56 billion dollars and seven years of time from start to finish (Plotkin et al., 2017, p. 4069).

Controversial Vaccine Ingredients

When physicians and vaccine developers realized that patients were getting more ill from bacteria that had grown in the vaccine prior to injection, new ingredients were added to vaccines to preserve the ingredients and sterilize the vaccine to prevent bacterial growth. Within the last 20 years, several preservatives and adjuvants used in certain vaccines, such as the influenza and MMR vaccines, have gained the attention of parents and caused controversy. Additionally, London et al. (2017) stated that while vaccines are tested rigorously to ensure safety, serious vaccine reactions may still occur in children. In 1988, The Vaccine Adverse Event Reporting System (VAERS) was created to track serious vaccine reactions. Should a serious vaccine reaction occur, the National Vaccine Injury Compensation Program provides compensation for the family (London et al., 2017).

Since Andrew Wakefield’s publication (Wakefield et al., 1998), stating that the MMR vaccine may expose children to behavioral regression and pervasive development disorder, and eventually the diagnosis of Autism, parents have become more vocal about not vaccinating their children due to multiple concerns regarding the safety and efficacy of vaccines. While the sample size of the study only consisted of 12 children and only
included speculated conclusions, it was deemed a success and received plenty of publicity.

These ingredients, such as aluminum salts and thimerosal, are believed by parents to cause heavy metal toxicity in the brain and digestive system, inducing a disorder on the autism spectrum in the child.

**Aluminum salts.**

In the United States, several vaccines use aluminum salts as an adjuvant to increase the immune response in an individual after injection, as well as reduce the number of vaccines needed per antigen for immunity, as well as decrease the amount of antigen needed in a vaccine reducing possible side effects from the antigen (Fernandez, 2016, p. e231). According to the Food and Drug Administration in the United States, aluminum hydroxide, aluminum phosphate, and potassium aluminum sulfate are licensed for use in vaccines (U.S Food and Drug Administration, 2018a). Aluminum salts are used in DTaP, pneumococcal conjugate, tetanus, and hepatitis A and B vaccines. It is known after over 60 years of research that the levels of aluminum that the body is exposed to after an aluminum containing vaccine is must less than an individual's normal exposure to aluminum in food and water supplies, approximately 0.125 to 0.85 mg per dose (U.S Food and Drug Administration, 2018a; Fernandez, 2016 p. e231). The FDA limits the amount of aluminum compounds in a vaccine to 0.85-1.25 mg per dose (Fernandez, 2016, p. e232). Another study by Principi and Esposito (2018) stated that there is no data available that show an association between the use of aluminum in vaccines and
neurotoxicity, though the possible correlation of aluminum adjuvants and macrophagic myofaciitis should be investigated in the future (Principi & Esposito, 2018, p. 5835).

However, an article was found that compared the data of Autism Spectrum Disorder (ASD) prevalence from 1991-2008 in the United States and the amount of aluminum in each vaccine that an infant receives during the first few months of life (Tomljenovic & Shaw, 2011). The study found a casual correlation between increased aluminum levels in the body and number of ASD cases related to higher aluminum adjuvant exposure, however the study did state that correlation does not mean causation, and that further studies would need to be conducted to confirm the correlation.

**Thimerosal.**

Thimerosal is an ethylmercury, an organic compound that is 49.55% mercury (Hg) by weight. First introduced to the medical field in the 1920s, it was a crystalline powder that quickly replaced the use of Joseph Lister’s carbolic acid as antiseptic in operating rooms. After being patented in 1928 as merthiolate, researchers found that the patented Hg compound was 40-50 times as effective compared to carbolic acid when combating *Staphylococcus aureus* (Baker, 2008, p. 245). In 1929, physicians gave their patients merthiolate to treat an epidemic of meningococcal meningitis. While merthiolate did not get rid of the meningitis, there were no ill effects in the patients from the drug (Baker, 2008, p. 245).

One of the largest issues facing the growing vaccine industry in the 20th century was bacterial contamination of multi-use vaccine vials. In 1916, a batch of typhoid vaccine became tainted after being stored at room temperature. In all, there were 68
severe reactions, 26 abscesses, and 4 total deaths (Baker, 2008, p. 245). In 1928, an incident in Australia occurred with a contaminated batch of diphtheria toxoid, resulting in 12 deaths of the 21 children who received the vaccine due to staphylococcus infections and toxemia (Baker, 2008, p. 245).

After two cases of bacteria infected vaccines causing disease or death, vaccine researchers decided that some sort of antibacterial would need to be added to the vaccine in order to eliminate bacteria that could grow in multidose vials. However, the use of phenol and cresol in vaccines decreased the effectiveness by reducing the potency of the products the antiseptics were used to protect against (Baker, 2008, p. 245). When the use of thimerosal was introduced, it was found to possess the protective properties of phenol and cresol without reducing the potency (Baker, 2008).

As thimerosal became one of the main antiseptics used in childhood vaccines into the 1930s and 1940s, the question arose from parents regarding the concern of mercury poisoning. It was important to educate parents in that organic mercury is a methylmercury, usually found in fish and air pollution, and was different than thimerosal, an ethylmercury. Thimerosal dissociates into ethyl-mercury chloride, ethyl-mercury hydroxide, and sodium thiosalicylate in saline, therefore it is believed it reacts similar in the human body (Gier et al., 2015).

In the late 1990s and early 2000s, further concerns from parents arose with the popularity of Andrew Wakefield's study regarding the possible correlation with autism and other neurotoxicity disorders. Though the FDA and other researchers conducted several studies, each study concluded that there was little to no risk of neurotoxic
disorders or generalized toxicity concerns. However, the FDA decided to remove the use of thimerosal from all common childhood vaccines by 2001 to remove the possibility of reactions or side effects in children (U.S (Center for Disease Control and Prevention, 2015e). Today, common vaccines that still contain thimerosal include multidose influenza trivalent and quadrivalent vaccines, single strain influenza, and tetanus-diphtheria (not to be confused with Tdap) (U.S Food and Drug Administration, 2018b).

**An Overview of Vaccination Policies**

Regulations regarding vaccinations throughout the world help shape policies for each country and state to best protect their citizens from communicable diseases. Due to the dangerous and potentially deadly nature of the diseases mentioned previously, several government organizations have set guidelines and policies for childhood vaccines that work to decrease the incidences of preventable disease and death in children.

**Global Vaccination Policies**

Global vaccination policies are outlined by the World Health Organization (WHO) and the WHO Strategic Advisory Group of Experts (SAGE). The SAGE committee meets biannually to review the currently vaccination recommendations. The committee also regularly updates position papers on vaccinations of communicable diseases that pose an international public health impact and are used in large scale vaccination programs. These papers are updated when new information and scientific evidence emerges regarding the disease and potential vaccination changes (Duclos & Okwo-Bele, 2007). In the position papers, SAGE outlines the major clinical manifestations of the disease and at-risk groups. Vaccinations that are available to the
public for each specific disease are also mentioned, including the type of vaccination (often there is more than one option for each disease), which age group it is available to, when during the lifespan the vaccination should be administered, and contraindications.

It is important to recognize that developing countries also must work to devote more funding into healthcare and increased vaccination percentages to reduce the risk of infectious disease outbreaks that could turn into an epidemic. Funding appears to be the main setback in developing countries being unable to increase vaccination rates among their general population, with isolated communities being the second. If citizens are difficult to reach due to geography, the chance of those citizens being vaccinated, even for the five vaccinations that are available due to mass funding from the WHO and other government agencies are slim (Duclos & Okwo-Bele, 2007).

In 1974, the WHO launched the Expanded Program on Vaccination (EPI). The program helped namely developing countries by providing guidelines on how to implement and access essential vaccinations. Focusing on infants and pregnant women, the initial phase attempted to vaccinate these populations with bacilli Clamette-Guerin (BCG) for tuberculosis (which is no longer mandated for administration due to issues with vaccine efficacy), measles, pertussis, diphtheria, tetanus, and poliomyelitis (Duclos & Okwo-Bele, 2007). Because of this initiative, by the 1990s, over 70% of the global population was considered effectively vaccinated (Duclos & Okwo-Bele, 2007). As an example, since the implementation of the EPI the mortality rate of measles has fallen by 60% worldwide since 1999, which exceeded the goal of 50% between 1999 and 2005 set by the United Nations (Duclos & Okwo-Bele, 2007).
As of 2011, many of the vaccinations that are regularly administered in developed countries, examples including Influenza, \textit{Haemophilus influenzae} type b, Rubella, and Hepatitis, are underused in developing countries. Developing countries do not have clear disease surveillance and reporting systems, making it difficult for government agencies to understand the potential impact of certain communicable diseases, as well as risk versus benefit when investing in additional vaccinations for citizens. (Duclos & Okwo-Bele, 2007). Therefore, most developing countries continue to only vaccinate for the original five vaccinations that were launched in 1974.

**United States of America Vaccination Policies**

The United States has a strict schedule for vaccination administration that is carefully chosen by the CDC with recommendations from the WHO. Within the CDC, there is the Advisory Committee on Vaccination Practices (ACIP) that chooses the recommended vaccination schedules for children, adolescents, and older adults based on scientific evidence from internal studies and from the WHO. The ACIP shares their vaccination schedule recommendations with the CDC, who then mandates the schedule for the general population of the United States.

**Birth to age 18 requirements.**

From birth to age 2, children are given up to 30 vaccinations. School-age and daycare requirements are namely used as “safety nets” for the children that are either not old enough to receive the vaccination (MMR or MMRV, for example), or are behind on their vaccination schedule (National Conference of Legislatures, 2015). While the ACIP
and CDC mandate and recommend a safe vaccination schedule, it is ultimately up to each state’s legislation to decide which vaccinations should be mandated for administration.

The recommended vaccination schedule for children and adolescents aged 18 or younger is updated each year. It is approved by the Advisory Committee on Vaccination Practices, the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists (U.S Department of Health and Human Services, 2018a). The current schedule recommends 30 vaccinations, not including yearly influenza vaccinations (Appendix A). For some vaccinations, additional doses may be administered if the child is considered high risk for contracting the disease.

**Federal Programming**

**Funding.**

Childhood vaccinations are costly to the country. Recommended vaccinations until the age of 18 costs $1,105 for male populations, and $1,407 for females as of 2008 for one child. In contrast, the recommended vaccinations in 1985 cost $45 per child. It is believed that inflation and the introduction of new vaccinations have boosted vaccination costs (National Conference of Legislatures, 2015).

In the United States, there are two main sources of federal funding for vaccination programs. The Vaccines for Children Program (VFC) provides free vaccinations for children who are without insurance, are underinsured, eligible for Medicaid, Native American, or an Alaska Native. According to the National Conference of State Legislators (2015), the National Vaccination Program within the CDC donated
approximately $2.5 billion in funds to state and local public health centers for vaccination purchases, all in the VFC’s name. Section 317 of the Public Health Services act is a program that provides grants to states and cities for vaccination purchase, as well as public health programs including disease surveillance. Under the Affordable Care Act (ACA), the program can now also purchase recommended vaccinations for adults as well as children. These two programs account for approximately 95% of all publicly funded vaccinations (National Conference of Legislatures, 2015).

State of Michigan Vaccination Policies

School requirement laws are stated based, chosen by recommendation of ACIP. However, there are several vaccinations that are required to be administered by the time a child reaches certain ages to attend daycare or school in the state. The child must meet the criteria by the time they enter kindergarten, and again once the child begins seventh grade or are 7-18 years old (Appendix B).

The state of Michigan does not mandate any other vaccinations to allow children to attend school, but still follows the recommendation of the United States’ policy regarding vaccinations. Should the child attend child care or preschools before the age of 5, there are additional mandated vaccinations that the child must have to attend before certain age milestones. The state of Michigan also has a PDF file that clearly outlines the specifics of when each vaccination should be administered. In addition to the vaccinations the child must have to attend kindergarten and seventh grade if the child also attends child care or preschools they must also show immunity to pneumococcal conjugate (PCV13) and H. influenzae type b (Hib). Four total doses of PCV13 must be
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administered before the child is four years old, and three doses of Hib must be administered at or 15 months (Michigan Department of Health and Human Services, 2017a).

Should the child attend school, they must either be vaccinated, or the family must submit documentation of vaccine exemption, which allows the child to remain unvaccinated yet still attend school.

**Provider and Parent Communication**

With many families recently becoming more adamant on not allowing their children to be vaccinated, an increase in preventable diseases have been recognized. The single most important factor when interacting with parents who do not wish to vaccinate their children is to ask the parents what specifically is keeping their children from getting vaccinated. It is now up to the provider to provide proper and effective education to parents regarding their concerns and possible misconceptions of vaccine injury, safety, and effectiveness.

Adequate communication between patients, parents, and providers ensures that everyone understands the risks and benefits involved when approaching vaccination and disease. One of the first and most famous incidences of miscommunication regarding the spread of disease and later vaccination, was that of Mary Mallon, also known as Typhoid Mary.
Mary Mallon

Mary was an Irish-American immigrant who worked for wealthy families as a cook beginning in 1906. She was one considered a “healthy carrier”, a subject who contracted the disease but did not show symptoms. While working as a cook, Mary unknowingly infected upwards of three thousand people in Manhattan, New York. George Sober, a sanitary engineer, began to investigate the new typhoid outbreak in Manhattan and traced it back to Mary Mallon. He followed her for many months to obtain blood and stool samples from Mary, who refused each time. Mary continued to work in kitchens around New York City for months, even though she knew she would infect countless other citizens (Marineli, Tsoucalas, Karamanou, & Androutsos, 2013).

Mary did not seem to understand the severity of the disease she was spreading to thousands of people, and no doctor ever attempted to describe how serious typhoid fever was to her. Symptoms of typhoid fever included fever, headache, nausea, constipation or diarrhea, loss of appetite, and rash. If left untreated, the disease could progress to intestinal bleeding and perforation, causing severe abdominal pain, nausea, vomiting, and sepsis. Other complications included myocarditis, endocarditis, pneumonia, hepatosplenomegaly, meningitis, and delirium (The College of Physicians of Philadelphia, 2018f). The progressed symptoms of disease are what killed thousands prior to the discovery of the typhoid vaccine.

A vaccine for typhoid fever would not be developed until 1911, nor any antibiotic treatment made available until 1948. Therefore, it was crucial for Mary to be removed from the public to prevent her from continuing the spread of disease. Sober enlisted the
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help of Dr. Biggs, who worked for the New York Department of Health, and the local police department to bring in Mary for testing. She attempted to run from the police for over five hours, but in the end was captured and forced to give a stool sample, which returned positive for typhoid. She was then taken to Riverside Hospital on North Brother Island for quarantine (Marineli et al, 2013).

Mary was held on North Brother Island for nearly two years. In that time, not one doctor attempted to explain the importance of Mary’s carrier diagnosis or how to properly avoid the spread of the disease. Instead, they offered multiple times to remove her gallbladder, and treated her multiple times with laxatives and yeast (Marineli et al, 2013).

Mary was freed from captivity after vowing to never work with food or as a cook again, though she never kept the promise. She continued work under a new name, Mary Brown, and infected a minimum of 25 people before she was placed back on North Brother Island until her death in 1938. An autopsy revealed the Mary shed the disease from gallstones in her gallbladder, which rose the question of whether Mary would have continued to infect individuals had she accepted the operation when first proposed so many years ago (Marineli et al, 2013).

By officials and physicians electing to punish Mary for the outbreaks she caused, they left out the most important facet to patient care, communication. Had Mary been properly educated on the spread of disease and how to prevent it, perhaps she could have stopped the infection of several thousand people, as well as the death of hundreds. Since the Typhoid Mary incident, and many other situations like it, healthcare providers have realized that patient education is important in maintaining high rates of vaccination.
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However, there are still many shortcomings when attempting to educate parents on vaccinating their children.

**Continued Shortcomings of Vaccine Education**

With many parents electing to not vaccinate their children under the pretenses of nonmedical or religious exemption, in December of 2014 the Michigan Department of Health and Human Services, along with the Joint Committee on Administrative Rules, approved a new educational requirement for parents who decide to opt their children out of vaccinations before starting kindergarten (Michigan Department of Health and Human Services, 2018). The education is through each county’s health department and includes outlining the benefits of vaccination and the risk of disease for children who are not vaccinated. A health educator with the local health department must also be present to answer any questions or concerns parents may have about vaccines (Michigan Department of Health and Human Services, 2018).

One weakness that the 2014 program faces, as well as nearly every health care setting in the United States, is the lack of appropriate literacy levels for parents. A study by Davis et al. (2004) stated that on average, most American adults read at or below a sixth-grade reading level, though vaccine information statement (VIS) pamphlets made available for parents by the CDC at vaccination appointments or through the health department’s education classes are typically written at around a ninth-grade reading level. This means that adults reading at a lower level are only comprehending less than half of each VIS provided for vaccine education. When parents attend vaccine exemption education classes, they are given information that they cannot process. Therefore, it is
almost impossible for parents to ask questions to soothe their concerns regarding childhood vaccinations if they do not understand what they are reading.

In the healthcare setting, provider education is another shortcoming. Nurses reported spending much more time discussing vaccines and addressing parents’ questions compared to pediatricians or physicians (Davis et al., 2001). Public health nurses reported that they believed they were doing a good job communicating with families regarding how the child handled their previous vaccinations, educating parents on the vaccinations their children would receive during their visit, discussing potential side effects and treatment options, and stressing the importance of returning for subsequent vaccinations. However, the nurses stated they avoided discussing risks of vaccinations with families, as they felt unskilled and undereducated in the topic and were unsure of how to facilitate the conversation with families (Davis et al., 2004). Instead, the topic was avoided, and parents left with their concerns and questions unanswered, and potentially left without vaccinating their children (Davis et al., 2004).

**Parental Concerns**

When vaccine preventable diseases were still prevalent in the general American population, the decision for parents to vaccinate their children was almost automatic. With vaccination and herd immunity rates beginning to drop, today’s vaccine hesitant parents may not remember or know how severe vaccine preventable diseases may be (Glanz, Kraus, & Daley, 2015). According to London et al. (2017) some parents today believe that vaccine-preventable diseases are no longer a danger to children because they occur in the popular so infrequently.
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High vaccination rates are needed to protect vulnerable populations via herd immunity, such as those who cannot receive vaccinations due to medical complications, children who have vaccine failure and whose body does not respond to vaccinations, and those who are simply too young to be vaccinated (Glanz et al., 2015).

Advocates for vaccines have typically used information from “pro-vaccine” sources, such as government agencies, local health departments, and pharmaceutical companies. However, vaccine hesitant parents have been shown in recent studies to be untrusting of such evidence due to potential sponsorships or incentives given for disseminating the information to the public, for example, “kick-backs” the sponsoring companies may receive (Glanz et al., 2015). In another recent study, the use of evidence-based information from agencies such as the CDC to educate vaccine hesitant parents decreased parents’ intention to vaccinate (Nyhan, Reifler, Richey, & Freed, 2014).

A survey of parents found that they preferred one-on-one conversations about information regarding their child’s vaccinations. Topics parents wanted to be educated about included vaccine side effects, treatment of side effects, and the date of their child’s next vaccines (Davis et al., 2004). Focus groups held for parents reported that many parents were never educated on potential severe side effects from vaccines and believed that they should have been informed as a matter of respect from the physician or nurse (Davis et al., 2004). However, parents may have felt that they could not ask the questions they wanted to be educated on due to appointment time constraints. Davis et al., (2004) stated that as of 2004, immunization visits lasted for an average of 20 minutes from start to finish. Communication between parents and providers regarding the risks and benefits
of the vaccines the child would receive that day lasted for an average of 16 seconds.

Between written materials for parents created at too high of a literary level and allowing an average of 16 seconds for concerns to be discussed (Davis et al., 2004), it is no wonder that parents have increasingly decided to not vaccinate their children and continue to have unresolved concerns regarding vaccination.

In a 2010 survey that was completed by 4,198 families, only 23% (964) of parents stated that they had no concerns regarding their child's vaccinations (Kennedy, Basket, & Sheedy, 2011). Another study revealed that parents' greatest concerns regarding vaccines include the increasing number of vaccines administered at each visit, ingredients in vaccines, and the increasing media attention of controversies including vaccines, namely that vaccines may cause autism (Kennedy, LaVail, Nowak, Basket, & Landry, 2011).

Research by Glanz et al., (2014) shows that vaccine hesitant parents have a high regard for their providers but are skeptical of their provider's education of vaccines. Parents report that physicians and nurses are more likely to discuss the positive effects vaccinations have rather than a more balanced view, also highlighting the possible negative side effects or severe side effects vaccines may have on their children. It appears that parents want providers to explicitly and frankly state the rare but real several adverse effects that can occur when vaccinating a child. Parents believe that a provider acknowledging the risks parents are concerned about can facilitate a sense of trust on a higher level (Glanz et al., 2014). They are looking for unbiased trustworthy sources of information regarding the safety and potential risks of vaccines, and their providers
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simply handing then a leaflet from the CDC is not going to cut it anymore (Glanz et al., 2014).

Current Education Practices

A systematic review completed by Connors, Slotwinski, and Hodges (2017) outlined nine studies regarding current communication practices by healthcare providers throughout the world regarding vaccination. In the United States, it was reported that a fear-based education regarding vaccinating against preventable communicable disease was used most often. Another study mentioned in Connors et al., (2017), stated that 44% of family practice physicians and 53% of pediatricians attempted to soothe parental concerns by advising the parents it was more painful for the child to receive their vaccinations throughout multiple office visits as opposed to receiving all at once. Fewer physicians also reported feeling confident about answering the more difficult questions of adverse reactions (Connors et al., 2017).

In a Canadian study by Busse, Walji, and Wilson (2011), physicians were considered biased by clients due to only providing positive or incomplete vaccine information when parents expressed concern. Parents requested unbiased resources regarding vaccine safety, and 17.3% of parents reported that discussing vaccine choices and concerns created a conflict between the provider and parent. A study by Connors et al., (2017) reported that the literature referenced above supported involving vaccine hesitant families in their child’s care; most often through participation and using a more individualized plan of care to ease parental concerns and answer potential questions.
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Providers reported many barriers to vaccine discussion with parents, such as the length of time discussions took, the precedence of other health issues, providers believing that the discussion would not be likely to change parents' minds of vaccinating their child on schedule, providers reporting they did not know enough regarding the evidence of vaccine safety, or believing that parents would not understand the information given to them regarding risks and benefits (Kempe et al., 2011). Many providers also reported not knowing how to communicate with parents the risks of vaccines (Kempe et al., 2011).

Pediatric or public health nurses are often responsible for facilitating difficult conversations with parents regarding vaccination, as they are usually the provider administering vaccines to children. Davis et al. (2004) stated that nurses may be less apt to give detailed education regarding vaccines because there is a lack of national policy regarding vaccine communication that specifically outline vaccine risks and benefits. While many risks are in the vaccine information statements (VIS) given to parents at vaccination office visits, nurses should not rely on the VIS alone to provide such sensitive information to parents. Because of the lack of policy, nurses are often left wondering how they can help to increase vaccination rates to prevent outbreaks of preventable disease.

Nursing and Improving Vaccination Rates

As nurses, it is our job to be the patient's advocate. In terms of vaccination, the nurse's goal should be to provide unbiased evidence-based information to the family to make an educated decision on vaccinating their child, as well as ensuring children are fully vaccinated. Improving communication between parents and providers should also
be a priority, with the concerns of parents mentioned previously in the forefront of the mind. Parents want to protect their children and do what they believe will be best for them. Without proper education, parents may unknowingly harm their child by preventing them from being vaccinated. There are many ways that nurses can facilitate and improve communication with parents without passing judgement or blame onto the parents.

Prior to any education with parents, nurses must self-evaluate their own position on vaccination. Regardless of whether a nurse may be for or against vaccines, they must be educated in all aspects, including administration, side effects, safety, efficacy, and education. Taking the time to self-educate will make having conversations with parents who have difficult questions much easier, as the nurse will be educated appropriately using evidence-based practice.

Increasing the time for education opportunity is an important improvement that should be made in the healthcare setting. Such a small amount of time spent, especially with vaccine hesitant parents, is not long enough to fully vaccinate a child while ensuring parents are properly educated on all aspects of vaccination. It is a nurse’s position to facilitate a conversation with parents, particularly with parents who do not seem to have any questions about vaccination, as parents tend to only ask questions about vaccines 27% of the time at their child’s vaccine appointments (Davis et al., 2004). Using the teach-back method for parents such as these may prove to be helpful, especially to gauge how much of the discussion was retained (Fredrickson, Davis, & Bocchini, 2001).
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Mentioned previously, nurses spent an average of 16 seconds educating parents on the potential for risks and severe reactions, amounting to less than 3% of total visit time (Davis et al., 2004). Davis et al.'s (2004) study followed nurses at several different physician's offices and found that in more than 90% of the observed visits, nurses did discuss common side effects of vaccines and how to treat them at home. Benefits of vaccination were discussed 48% of the time, whereas only 28% of the time were severe risks and how to take care of a child discussed. In approximately 13% of visits, severe reactions such as a fever over 105°F or seizures were mentioned.

In addition to increasing conversation time and encouraging parents to ask questions, providers and nurses reported a few strategies that could be more helpful in educating vaccine resistant parents. Ideas included adjusting information to concerns voiced by the parent or the parent’s background, providing information for the vaccine their child would receive at their next visit prior to the appointment, and providing a screening tool for a parent to fill out prior to the appointment to help identify specific parental concerns if they are evident (McRee, Gilkey, & Dempsey, 2014). Another study stated that parents who received education information regarding their child’s vaccinations at the time of the visit did not give them enough time to process the information and ask questions (Glanz et al., 2015). By providing information and screening tools prior to a vaccination visit, providers could better individualize a plan of care for the family and address parental concerns more adequately (McRee, Gilkey, & Dempsey, 2014).
London et al. (2017) lists several additional ways that nurses can ensure that children are fully vaccinated and reduce the number of missed opportunities for vaccination:

1. Place a reminder in the child's health record to alert health professionals about the child's need for immunizations. Establish a system to send parents a reminder when the child's immunizations are due or overdue.

2. Give vaccines when the child has a minor illness, even with a low-grade fever and antibiotic treatment, or has a recent exposure to an infectious disease.

3. Use combination vaccines (e.g., DTaP-HepB-IBV) to reduce the number of injections from 20 to 13 in the first 2 years of life.

4. Give multiple vaccines at the same time using separate syringes and injecting in separate sites. If using the same extremity, separate injection sites by an inch.

5. Give medically stable low-birth-weight infants all vaccines appropriate for chronologic age as full-term infants. Use the full dose.

6. Give the vaccine even when a prior dose caused a local reaction or a family member had an adverse response.

It is the nurse's position to prevent increased morbidity and mortality of individuals in relation to preventable disease via vaccination. If nurses and physicians are willing to take the time to sit down with parents and attempt to truly understand parents' concerns regarding vaccination, parents will leave feeling more trusting of their providers, and feel that the nurse or physician's best interest is in the wellbeing of the child. With increase trust and education, parents are more likely to vaccinate their
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children on time, increasing herd immunity and protecting children who are unable to be vaccinated from preventable disease.

Educating parents on the history of now preventable disease and why vaccinating is so important is the first step in increased communication. Concerns regarding the safety of vaccines can be educated on by sharing the manufacturing process and rigorous quality control testing that each dose of vaccine must go through, as well as mentioning controversial ingredients and explaining why the ingredients may not be harmful for children after all. Vaccine policy may also be mentioned, particularly when and why children get the vaccines they are scheduled for at specific intervals. To communicate these topics with parents effectively and without bias, strategies mentioned above should be used to ease parental concerns. Through increased communication with families, vaccination rates should increase, protecting children from preventable disease and potential lifelong disability or death.
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References


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Appendix A

Recommended Vaccine Schedule for Children Aged 0 to 18 Years in The United States, 2017

For those who fall behind or start late, see the Catch-Up Schedule (Figure 21).

These recommendations must be read along with the footnotes that follow. For those who fall behind or start late, proceed with catch-up vaccination at the earliest opportunity to determine minimum intervals between doses. See the catch-up schedule (Figure 21) for school entry and adolescent vaccine age groups. Shaded in gray,

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19-33 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B (HepB)</td>
<td>1 dose</td>
<td></td>
<td>2 dose</td>
<td>3 dose</td>
<td></td>
<td>3 dose</td>
<td>4 dose</td>
<td>5 dose</td>
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<td></td>
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<tr>
<td>Rotavirus (RV) (Int 2 dose series, RV1-3 dose series)</td>
<td>1 dose</td>
<td>2 dose</td>
<td>2 dose</td>
<td>3 dose</td>
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<td>3 dose</td>
<td>4 dose</td>
<td>5 dose</td>
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<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis (DTaP)</td>
<td>1 dose</td>
<td>2 dose</td>
<td>3 dose</td>
<td>4 dose</td>
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<td>5 dose</td>
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<tr>
<td>Haemophilus influenzae type b (Hib)</td>
<td>1 dose</td>
<td>2 dose</td>
<td>3 dose</td>
<td>4 dose</td>
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<td>5 dose</td>
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<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>1 dose</td>
<td>2 dose</td>
<td>3 dose</td>
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<tr>
<td>Inactivated poliovirus (IPV)</td>
<td>1 dose</td>
<td>2 dose</td>
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<td>4 dose</td>
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<td>Influenza (IV)</td>
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<td>Annual vaccination (PD1 or 2 doses)</td>
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<tr>
<td>Measles, mumps, rubella (MMR)</td>
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<td>Varicella (VAC)</td>
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<td>Hepatitis A (HepA)</td>
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<tr>
<td>Meningococcal A (MCV)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis (Tdap)</td>
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<tr>
<td>Human papillomavirus (HPV)</td>
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<tr>
<td>Meningococcal B (Meningococcal B conjugate)</td>
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<tr>
<td>Pneumococcal/pneumocystis jirovecii (PPSV23)</td>
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</tbody>
</table>

Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages for groups that may receive vaccine

Individual clinical decision makes

NOTE: The above recommendations must be read along with the footnotes of this schedule.

For further information on the recommended vaccine schedule and a catch-up schedule, see https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
## Appendix B

### Vaccines Required for School Entry (2017)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Kindergarteners 4-6 years old</th>
<th>7th graders or children 7-18 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTP, DTaP, Tdap</td>
<td>4 doses DTP or DTaP, 1 dose at or after 4 years old</td>
<td>1 dose Tdap at 11 years old prior to entry into 7th grade</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>4 doses or 3 total doses if dose 3 was given after 4 years old</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>2 doses after 12 months of age (or documented immunity)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3 doses (or documented immunity)</td>
<td></td>
</tr>
<tr>
<td>Meningococcal conjugate</td>
<td>N/A</td>
<td>1 dose at 11 years old prior to entry into 7th grade</td>
</tr>
<tr>
<td>Varicella</td>
<td>2 doses after 12 months of age, lab immunity, or history of disease</td>
<td></td>
</tr>
</tbody>
</table>

Number of vaccine doses per child needed to attend schools in Michigan for full immunity.