The Facts on Varivax, the Chickenpox Vaccine
by Deborah W. Heinrich, PhD

On June 15, 2000, pharmaceutical firm Merck and Co., Inc. (West Point, PA) sponsored a
dinner and lecture at the Yankee Silversmith Inn in Wallingford, CT, titled “Contemporary Vaccine
Issues“. Merck invited area nurses to the dinner and lecture and gave them information about
Varivax, Merck’s chickenpox vaccine.

The lecturer was Peter Hotez, MD, PhD, an Associate Professor of Epidemiology and
Public Health and Pediatrics at Yale University. Dr. Hotez’s research at Yale focuses on the
pathobiology and vaccinology of parasitic infections. Merck presented each of the approximately
35 nurses attending the lecture with a packet of materials about Varivax, including a fact sheet
compiled by Merck\(^1\), an article concerning Varicella Vaccination written by the American
Academy of Pediatrics\(^2\), an excerpt from the Connecticut Department of Public Health regulation
concerning immunization requirements for family day care homes, child day care centers and group
day care homes\(^3\), and a promotional video titled “Chickenpox: A Disease Worth Preventing.” This
article deals with the information presented by Dr. Hotez, as well as that provided in the
complementary packets.

Merck’s materials were presented in a colorful paper bag along with candy; promotional
pens and an eraser; a pin with a hyena, Dalmatian, and a child asking “Who shouldn’t have
spots?”; and a poster of a child’s rubber duck crying about the children who have died from
chickenpox. Also in the bag was a promotional brochure bearing a full-color photograph of a
child grimacing from his chickenpox lesions. The caption read, “Chickenpox infection is one way
to acquire immunity.” Inside the brochure is a picture of a smiling, winking child pointing to a
small bandage on her arm where she has apparently been vaccinated with Varivax. This caption
read, “VARIVAX is another way to help achieve immunity.”

Dr. Hotez spoke about the top ten killers worldwide of children between the ages of 0 and
5 years. This list did not include chickenpox. He reviewed how the smallpox vaccination was
created and then presented a few slides on his research concerning parasitic infections. Next, Dr.
Hotez spoke about chickenpox infection and touched on some secondary complications that may
arise from the illness. Dr. Hotez continued with specifics on Varivax explaining how it was
created as well as giving statistics for its efficacy. Dr. Hotez claimed that Varivax confers
lifelong immunity. He also stated that Merck was performing ongoing studies to establish the
duration of protection afforded by Varivax in order to determine if booster shots would be
necessary to maintain immunity. These statements seem directly contradictory. When asked if the
way the immune system responds to Varivax was comparable to a natural (wild-type) chickenpox
infection, Dr. Hotez was unsure.

Varivax was created from a live, active strain of chickenpox virus obtained from the pock
of an infected person in Japan. This viral strain, called Oka, was acquired by Merck and
attenuated (weakened) to create a viral strain named Oka/Merck. Merck attenuated the Oka strain
by passing it through human embryonic lung cell cultures, embryonic gunea pig cell cultures, and
other human cell cultures. Oka/Merck is the viral strain used in Varivax, which was licensed
exclusively to Merck in 1995.

Most people are familiar with chickenpox, the illness associated with varicella infection.
This highly infectious illness presents with approximately 300-500 itchy lesions and is
accompanied by fever. Chickenpox usually is a relatively mild, self-limiting childhood illness.
Of the nearly 4 million cases per year in the United States, 3.3 million (about 80%) occur in
children under 15 years of age. Approximately 1 in 2,000 of these children per year were
hospitalized due to complications from the infection, including secondary bacterial infections and
respiratory illness including varicella pneumonia. 1 in 100,000 children under 15 years of age
(0.001%) died per year due to secondary complications of chickenpox. A majority of hospitalizations and deaths occurred in children who had risk factors such as immunosuppression or other illnesses.

The American Academy of Pediatrics (AAP) and the Advisory Committee on Immunization Practices (ACIP) advise that “children 12 months of age or older without documentation of varicella immunization or infection who do not have a contraindication should receive a dose of varicella vaccine immediately. In addition, special emphasis should be placed on immunization of susceptible older children and adults, because the likelihood of severe infection increases with increasing age.”

Despite AAP and ACIP recommendations, only 34% of children in the U.S. ages 19-35 months were vaccinated from July 1997 to June 1998. The AAP suggests that the following factors, which are highlighted, are among possible reasons why parents are not seeking varicella vaccination for their children and many physicians are not recommending it:

- “The misconception that varicella is uniformly a mild disease.” The relative risks of secondary complications were mentioned above.
- A concern about vaccine effectiveness and safety. Merck has vaccinated thousands of children over the course of many studies to determine Varivax’s effectiveness. In early clinical trials, 4142 children were injected with a single dose of vaccine. The vaccinated children were followed for up to six years. Merck’s fact sheet states that, “In this group there was considerable variation in chickenpox rates among studies and study sites, and much of the reported data were acquired by passive follow-up.” Thus the results of their preliminary studies lack consistency. Merck reports that between 1 in 50 and 1 in 30 vaccinated children in these preliminary studies still contracted chickenpox (breakthrough infections), though the majority of cases presented with a much milder disease than one would expect from a wild-type varicella infection.

In later trials, Merck reported that the incidence of breakthrough infection was much lower, at 1 in 500 to 1 in 100 children. Again, in most cases, the disease was a milder one than would have been expected from wild-type infection. A closer examination of the studies, however, reveals that the children were vaccinated with doses up to 6.7 times the dosage given in today’s Varivax vaccine. Thus, it seems problematic to draw conclusions about Varivax’s effectiveness from the data in these studies, which is based on administration of much larger doses of the vaccine than any child would actually receive.

Merck also reports that “no placebo-controlled trial was carried out with Varivax using the current vaccine” and “there are insufficient data to assess the rate of protection against the complications of chickenpox (e.g. encephalitis, hepatitis, pneumonia) in children.”

When assessing the effectiveness of Varivax in adults, Merck reports that “although no placebo-controlled trial was carried out in adolescents and adults, efficacy was determined by evaluation of protection when vaccinees received 2 doses of Varivax 4 or 8 weeks apart and were subsequently exposed to chickenpox in a household setting.” Only 64 people were vaccinated for this study, which is an extremely low number of subjects for this kind of study. After 2 years of follow-up, there were 17 cases of breakthrough infection out of the 64 vaccinees. Merck combined these statistics with those from other studies to report 42 breakthrough cases out of 1019 vaccinees. The details of these studies, including vaccine dosage, were not reported in Merck’s fact sheet. It is therefore impossible to evaluate their conclusions from these combined studies. Also Merck reports, “There are insufficient data to assess the rate of protection against the serious complications of chickenpox in adults (e.g. encephalitis, hepatitis, pneumonia) and during pregnancy (congenital varicella syndrome).”

Another method used to measure the effectiveness of a vaccine is to determine its immunogenicity, meaning its ability to cause the vaccinee to produce antibodies against the virus. Immunogenicity is an indirect measurement of vaccine efficiency, because the contribution that
these antibodies make toward actual immunity to wild-type infection is not evaluated. In other words, just because someone has antibodies to a particular virus, it does not automatically mean he or she is immune to future infection from the virus.

Merck found antibodies against varicella in 97% of children vaccinated with one dose of Varivax and in 99% of adults after 2 doses of Varivax. This tells us that Varivax is capable of eliciting antibody reactions in most people when injected into the body. However, Merck warns, “the relative contributions of humoral immunity [antibodies] and cell-mediated immunity [T cells] to protection from chickenpox are unknown.”

Another concern regarding Varivax revolves around the fact that it introduces a live virus into the body. Oka/Merck is an attenuated virus and the process of attenuation renders a virus less able to cause a strong infection. However, it is important to realize that attenuated viruses are still viable. When an attenuated virus such as Oka/Merck is injected into the body, it causes an active infection. Indeed, Varivax’s ability to immunize depends on this active infection. Nevertheless, an active viral infection — whether it results from contracting a wild-type viral infection or from being vaccinated with an attenuated viral strain — comes with risks. These risks include carcinogenesis (cancer), mutagenesis (genetic mutations), and impairment to fertility. According to Merck’s own fact sheet, “Varivax has not been evaluated for its carcinogenic or mutagenic potential, or its potential to impair fertility.”

In a list of adverse reactions to Varivax vaccination, Merck reports that children have experienced fever and injection site complaints such as pain and swelling. In addition, 3% of children experience a localized rash with a median of 2 lesions, and 3% experience a generalized rash with a median of 5 lesions. When lesions are present, it is more likely that the virus will be transmitted to other susceptible individuals. Adults also report fever, injection site complaints, and rash. A few of the many other adverse reactions reported in trials include upper respiratory illness, headache, fatigue, cough, nausea, vomiting, irritability/nervousness, and allergic reactions. Additional adverse reactions reported since the vaccine has been marketed include anaphylaxis, encephalitis, seizures, dizziness, and secondary bacterial infections. “As with any vaccine, there is the possibility that broad use of the vaccine could reveal adverse reactions not observed in clinical trials,” Merck warns in its fact sheet.

• **“A concern about waning immunity.”** In response to the fear that Varivax will not confer lifelong immunity, Merck is performing several ongoing studies following vaccinated children to determine the duration of protection from one dose of Varivax. The AAP reports children have been protected for 11 to 20 years to date. However, it is impossible to determine if this protection was extended by virtue of the children receiving an immunity “booster” from a subsequent exposure to wild-type varicella. So when more and more children are vaccinated and the prevalence of wild-type varicella in the environment is reduced, the duration of protection may wane in the absence of natural boosting. This would lead to protected children becoming susceptible adults.

This concern appears to be valid. If 20% of chickenpox cases occur in adults and adolescents, one would expect to see 20% of the chickenpox-related hospitalizations and deaths in this demographic. However, adults and adolescents account for 67% of the hospitalizations and 50% of the deaths due to chickenpox. This figure clearly indicates that varicella infection has a much higher risk of secondary complications when contracted by adults. Thus, the vaccinated children who became susceptible adults would be at far greater risk from secondary complications than children who contract wild-type virus.

• **“A concern that universal immunization of young children will shift the disease burden to older age groups among whom the disease is more severe.”** According to the AAP, “mathematical models predict that if varicella vaccine coverage in children is more than 90%, a greater proportion of cases will occur at older ages, but the varicella disease burden will decrease
for children and adults.” These models predict that there will be one quarter as much wild-type varicella available for infection, but it will only cut the disease burden in adults in half. So if 90% of children are vaccinated with Varivax, half as many adults will still be infected with wild-type varicella. One must also consider that “although the incidence of disease among adults is low, the risk of complications and death attributable to varicella is 10-20 fold higher than that for children.”

- **A concern regarding the potential transmission of virus from vaccinated people to unvaccinated people.** It would be possible to address this concern, at least theoretically, by assuming a near-100% vaccination rate. But even if everyone wished to be vaccinated with Varivax, there would still be those who should not receive the vaccination because of Varivax’s contraindications. According to Merck, people who should not receive Varivax include those who have a history of hypersensitivity to any component of the vaccine, including gelatin and neomycin; people with certain cancers; people whose immune systems are suppressed or deficient, either due to immunosuppressive therapy or diseases such as AIDS; people who have active untreated tuberculosis; people who have any febrile respiratory illness or other active febrile infection; or women who are pregnant. “The possible effects of the vaccine on fetal development are unknown at this time. However, natural varicella is known to sometimes cause fetal harm. If vaccination of post-pubertal females is undertaken, pregnancy should be avoided for three months following vaccination,” Merck says.

Interestingly, the people who cannot receive the vaccine are exactly those who are at highest risk for secondary complications from wild-type varicella infection. So those at highest risk from varicella infection cannot be vaccinated for it. Also, these people are at serious risk if they contract an infection from a vaccinated individual. Merck found in a placebo-controlled trial that 3 out of 416 susceptible placebo recipients who were exposed to 445 vaccine recipients developed chickenpox and antibodies against varicella. 9 of the 416 contracted a varicella-like rash, but did not develop antibodies against varicella. And 6 had no rash but did develop antibodies against varicella, indicating a potential subclinical infection. Thus, according to this study, possibly 2% of the placebo recipients were infected by the vaccinees.

Given these concerns, further study of Varivax might seem reasonable. However, not only has the FDA approved the sale of Varivax, children seeking admission to a family day care home, child care center, or group day care home in Connecticut are required by state law to receive the varicella (chickenpox) vaccine if they were born after December 31, 1996. In addition, starting this fall 7th graders are also required to receive the varicella vaccine. But Connecticut’s children are also entitled to a religious exemption from receiving Varivax, as they are with any vaccine.

State law requires parents of these children to provide one of the following five forms of documentation:

- a document signed by an appropriate health care provider “indicating that the child is current or in progress with immunizations according to the schedule adopted by the Commissioner”;
- a similar document that indicates the child has an appointment to be vaccinated;
- a similar statement indicating that the child has already had chickenpox;
- a similar statement “indicating that the child has a medical contraindication to immunization” (a medical exemption);
- “a written statement that immunization is contrary to the religious beliefs and practices of the child or the parent of such child. Such statement shall be signed by the child’s parent [and shall include affirmation of church membership by an appropriate church authority].” This documentation constitutes a religious exemption. The requirement for a signature from a church official is denoted here in brackets, indicating that this portion of the law was overturned in
December 1999 and is no longer required. The handouts distributed by Merck failed to reflect this change in the law.

When asked why only children born after December 31, 1996 were required to receive the vaccination, Merck representative, Deborah Schumacher, responded that requiring all children to be vaccinated would be too monumental a task to implement immediately. It is Merck’s hope, however, that all children will eventually be vaccinated with Varivax.

In summary, Varivax is a vaccine recommended for healthy people over 12 months of age to prevent secondary complications due to varicella infection. However, Varivax is contraindicated for the people who are most at risk for those complications. The manufacturer admits that it is unknown whether the vaccine is actually protective against complications of chickenpox illness in both adults and children, yet it is the fear of these complications that the manufacturer is using to justify the campaign for mandated vaccination, not fear of the illness itself. The duration of protection is also unknown, raising concerns that a population of susceptible adults is being created who would be at much greater risk for varicella-related complications and death than children who contract wild-type varicella. The manufacturer’s clinical trials are of questionable value due to variability in both methods and results. As with other active viral infections, vaccination with Varivax carries the risk of carcinogenesis, mutagenesis, and impairment to fertility, but these risks have not been studied. It seems there is still much to be learned about Varivax. Despite this, the government of Connecticut has mandated its administration to our children.

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References