IJTMGH International Journal of Travel Medicine and Global Health

Int J Travel Med Glob Health. 2023 Jun;11(2):269-279
http://ijtmgh.com

doi 10.30491/IJTMGH.2023.391295.1357

Mini Review Open Access

A Comprehensive Review Global Impact of *Varicella Zoster Virus* and its Vaccination Programs

Paniz Ghasempour Kalkhoran[1], Mohadese Jafari[2], Fatemeh Aminian[3], Ghazal Vakilzadeh[1*]

[1] Department of Cellular and Molecular Biology-Microbiology, faculty of advanced science and Technology, Tehran Medical science Islamic Azad University, Tehran, Iran.
[2] Department of Microbial Biotechnology, faculty of advanced science and Technology, Tehran Medical science Islamic Azad University, Tehran, Iran.
[3] Department of Molecular Cell Biology and Genetics, Bushehr Islamic Azad University, Bushehr, Iran.
[4] Department of Microbiology, faculty of advanced science and Technology, Tehran Medical science Islamic Azad University, Tehran, Iran.

***Corresponding Author:** Ghazal Vakilzadeh, Department of Microbiology, faculty of advanced science and Technology, Tehran Medical science Islamic Azad University, Tehran, Iran. Email: ghazalvakilzadeh@yahoo.com.

Received 2023-03-29; **Accepted** 2023-05-24; **Online Published** 2023-06-01

Abstract

Varicella Zoster Virus (VZV) is an alpha herpes virus that can conceal itself and produce shingles in addition to generating chicken pox. Varicella is a highly contagious illness brought on by vesicular skin sores, contamination, and maybe to a lesser extent, the propagation of the aerosolized virus. In comparison to children, adults with varicella had a much higher rate of primary VZV infection death. Different nations produce the varicella vaccines known as (Varivax; ProQuad; Merck & Co.), (Varilrix; Priorix-tetra; GSK), (Okavax; Biken, by Sanofi Pasteur), and (SuduVax; Green Cross). The amount of HDC passes, specific antibiotics included to assure sterility, stabilizers, and other minor components vary between different vaccines. The spread of the virus can be decreased dramatically by the widespread use of the varicella vaccine, particularly in a worldwide vaccination program. The World Health Organization suggested varicella vaccination in 1998 for nations where the illness poses a serious threat to public health. Nevertheless, many nations delayed the introduction of the universal varicella vaccine due to worries about the disease spreading to older populations, an increase in elderly herpes zoster, and cost-effectiveness. The purpose of the current research is to review varicella vaccination programs and their global effect.

Keywords: Varicella zoster virus, Vaccination programs, Global Health

Citation: Ghasempour Kalkhoran P, Jafari M, Aminian F, Vakilzadeh Gh. A Comprehensive Review Global Impact of *Varicella Zoster Virus* and its Vaccination Programs . Int J Travel Med Glob Health, 2023;11(2):269-279. doi: 10.30491/IJTMGH.2023.391295.1357.

Introduction

Herpes zoster and varicella are diseases brought on by the varicella-zoster virus (shingles). By the fourth decade of life, 100 people will be infected with (varicella) in a mild climate without vaccination. As some people may only experience a soft case of varicella.[1] According to epidemiological studies, primary infections can cause significant disease and even occasionally death in otherwise healthy individuals. To prevent infection in children, adolescents, and healthy adults, monovalent varicella vaccines are authorized and accessible worldwide.[2] The first licensed combination vaccine against Measles, Mumps, Rubella, and varicella occurred in the USA in 2005. Clinical trial participation has been put to the test as some progress has been made in understanding the etiology of herpes zoster (HZ). Except for the varicella vaccine, which is legal in South Korea, all vaccinations currently marketed worldwide are based on the strain. In a live vaccine used to prevent HZ, there are at least 14 times as many live attenuated varicella vaccine viruses as in the original vaccine.[3]

Historical aspect

In the past, people frequently confused smallpox with varicella in numerous investigations that varicella is an infectious disease by infecting volunteers with vesicular fluid or by exposing them to patients or volunteers who had the condition. These two illnesses have a typical agent and are brought on by the reactivation of a virus contracted early in life. In cell culture, the virus was initially found in the sac fluid of varicella patients by Stoddard and Weller in 1952.[4] The virus was named when tests revealed that the viruses isolated from varicella were morphologically and serologically identical. With secondary attack rates of between 61 and 100 percent

after contact with those who are varicella-sensitive families, varicella is highly contagious and spreads through the air.[5] VZV can also affect HZ patients, who are more likely to be transferred. The HZ, in effect, reactivates latent VZV-caused VZV also can from patients with HZ; the people are prone to be shared, although studies show that the risk of transmission of the virus from HZ is considerably less than is. Molecular analyses revealed patterns of limiting genome, viral of a person with HZ, the subsequent, and also recipients of the vaccine with HZ, the consequent is the same.[6]

Pregnancy and children

Those with immune systems can acquire later bouts of varicella, though it is unknown how frequently this occurs. Clinically referred to as congenital varicella syndrome, these issues affect infants whose mothers contracted varicella during pregnancy. After an infection in the third trimester (346 pregnancies with women between the ages of 25) and 36 weeks of follow-up, there were rare birth abnormalities compatible with congenital varicella syndrome, with the worst cases being documented at 28 weeks of pregnancy.[7] Immunocompromised people may experience instances of isolated varicella defects, which can be quite dangerous. Pediatric leukemia is less likely to occur than severe varicella, although it has affected children who have been infected.[8] The dorsal root ganglion, cranial nerves, brain, and gut neurology acquire sensory nerves once the virus infects the sensory ganglia during primary infection via viremia. When activated later in life or while receiving immunosuppression, the cell-induced immune loss can cause a unilateral, unpleasant vesicular rash. Immunocompromised individuals are likelier to have severe and widespread illnesses than healthy individuals.[9]

Varicella-zoster virus

An alpha herpes virus is VZV. Only humans and certain higher mammals are subject to it. Viruses have a double-stranded DNA core that is either rounded or polygonal. Around 100 nm in size, the nucleocapsid has 162 hexagonal capsomeres organized in an icosahedron (20 sides). A fabric and an envelope comprising a portion of the cell membrane encircle the capsid. The size of a VZV particle ranges from 180 to 200 nm. At least 30 polypeptides, at least 9 of which are glycosylated, have been found in VZV. In virions and on the outside of infected cells, glycoproteins are expressed.[10] They deactivate antibodies and make it easier for other cells to become infected. The primary glycoprotein of the VZV is gE, which is also the most prevalent and immunogenic glycoprotein. On infected cells, gE and gI are linked via an Fc receptor. Together with other viral glycoproteins, which are essential for VZV infection, it binds to mannose 6-phosphate receptors. VZV glycoproteins bind to mannose 6-phosphate receptors, and interactions between these receptors and VZV are crucial for the virus to enter and leave cells.[11] VZV can only incubate in nerve cells. Patients with cellular immunodeficiency had a higher incidence of herpes zoster, which aligns with the theory that VZV reactivation is under immunological control. Cellular immunity is essential for host defence since VZV spreads almost exclusively from cell to cell in an infected person. To creat cell-free VZV in vitro, the infectious viruses must be intentionally released by breaking cells using methods such as sonication. VZV is a cell-associated virus, which has hindered research and slowed the development of a vaccine.[12]

Immune response

React (respond) Immunoglobulin G antibodies in serum following natural infection, IgG antibodies for VZV, etc., as by testing antibodies fluorescent antigen membrane (FAMA) measured with antibodies neutralizing VZV is associated, in most patients within four days after the rash can be identified. According to clinical observations, people with isolated gammaglobulinemia have typical varicella episodes and continue to be immune to the illness. In contrast, people with cell-induced immunodeficiency are susceptible to spreading infections that can be fatal.[13] The historical history of high activity, casual, and symptom-free VZV infection in healthy individuals revealed the presence of response antibodies, which indicated exposure to the virus with greater safety. Because it is possible in the case of recurrent HSV in person, safe to increase heterogeneous in the headline antibodies to VZV occur, it is demonstrated in experiments for the diagnosis of HZ of the value of the Limited is entitled, etc., reactivate under clinical VZV by PCR in healthy subjects and exposed to the immune deficiency. When comparing the amounts of neutral wind antibodies and gp-ELISA titers, there was a linear association, and this method demonstrated repeatability when several vaccine batches were utilized for immunization.[14]

Vaccination

A study revealed that children of parents who vaccinate have rejected, etc., nine times more frequently than children whose parents vaccine for their children, have accepted the need to visit a doctor for and in a comparative study, the prevalence of serum pre-vaccination, VZV with the use of serum in 11 European countries from 1995 to 2003, etc., revealed that while the vast majority of children are exposed to VZV during their childhood, the rates at which the virus spreads

significantly vary between the various countries. The prevalence of serum VZV at age 5 was 97% in the Netherlands, nearly 70% in Spain and Germany, and 38% in Italy.[15] According to the most recent serum tests performed in the United States, childhood exposure, vaccination schedules, and other factors caused the prevalence of serum in children aged 6 to 11 years to rise from 86% during the outbreak to 98% in 2009, while other estimates for the age group were, respectively, comparable to pre-vaccination forecast. Although population-based epidemiology data for tropical nations are less extensive than for temperate countries, serum prevalence suggests a more significant average age of infection and higher susceptibility in adults.[16]

Varicella-zoster virus strain identification and viral vaccination characteristics

Various Oka vaccine strains are present in every varicella vaccine. This strain is suited to grow at 34°C and has been proven more immunogenic in guinea pigs. 42 SNPs, 30% of which result in amino acid changes, have been found throughout the 125,000-pair length of this strain's sequenced genome. The ORF62 and ORF71 areas, which are not known to weaken the vaccine, were the main sites of the polymorphisms discovered during vaccine sequencing.[17] After enzymatic digestion with restriction endonucleases and PCR, the first practical experiment to distinguish between the wild strain and the Oka strain revealed that all Oka strains lack the restriction site for PstI but have the restriction site for BglI. Conducted on the same premise in other nations, all of which produced comparable outcomes. As a result, it may be helpful to identify adverse effects of the varicella vaccination by using the PstI marker alone as a signal of the vaccine-type strain. Identifying the strain is important for determining if neurological episodes or other HZ issues in a patient are brought on by prior vaccines linked to the Oka strain or by WT.[18]

Molecular evidence

The Oka vaccine virus was distinguished from the parental virus and other clinical isolations using restriction enzyme length polymorphism analysis using the restriction enzymes NaeI, SmaI, and BssHII. These cut sites in gene 62 are absent in the parental virus Oka and 200 other clinical isolations. A mutation in Oka gene 62 may affect virus replication and, as a result, weaken VZV since this gene is crucial in viral replication.[19]

Clinical evidence

Those who received the vaccination experience rash significantly less frequently than those who catch the infection spontaneously. Also, the disease will manifest itself in a very modest manner if the immunized person unintentionally spreads this virus to another healthy and sensitive individual. A susceptible person is exposed to the virus five times less frequently than a sick person with the wild strain than they are from a person who has had the vaccination. In contrast, viremia may develop following immunization, though it does so less frequently than WT varicella.[20]

Preparation of vaccine

The Oka vaccine was made from virus seeds that had been passed through 11 times in human fetal lung fibroblast cells, 12 times in guinea pig fibroblast cells, and five times in HDC. VZV-infected cells cultured in a vaccine culture medium are extracted for the vaccine and sonicated or killed to obtain virus free of cells. This vaccine is offered in the lyophilized form to increase stability. The liquid required for the reconstruction is supplied by the producers, along with the technique and the vaccine.[21]

Vaccine effectiveness

In 1974, Takahashi began clinical studies with the Oka vaccine on 70 healthy children in Japan. The results demonstrated that the Oka virus was immunogenic at doses of more than 200 PFU and that the vaccinated children did not contract the virus following exposure. While the unvaccinated kids all had the disease, they did not. Hyde Yeager then conducted clinical trials across Canada, the United States, Europe, and Asia. Although research has also been done on alternate delivery methods, such as inhalers, and their immunogenicity and safety have been shown, the studies have not been sufficient to allow the use of this vaccine.[22] Although the intramuscular approach appears to be equally secure and efficient, this vaccination is given subcutaneously. Be released Even though it is now apparent that a vaccine's immune response increases with dose, the dose currently employed in production by various companies ranges from 1000 to 50000 PFU. It is simple to detect the blood IgG antibody response one month after immunization, and it can be detected for months or years after that. Depending on the amount of the vaccine virus, the number of doses administered, and the patient's age at the time of vaccination, IgG antibody titers may be 10- to 30-fold lower than in naturally infected persons.[23] In immunizations administered by inhalation, serum IgA antibody is only seldom and weakly detectable, while secretory IgA antibody has not been seen. It indicates that vaccination-induced B and T cell activity cooperates to protect the body. In clinical investigations carried out in the United States between 1982 and 1991, associations between the dose of the immunization administered and

the antibody levels assessed by gp-ELISA were observed. Studies were also conducted to assess the impact of administering the second dose of the vaccine at various time intervals.[24] The findings showed that after receiving the first dose of the varicella vaccine, 85 to 89% of children reached a high level of antibodies, and after receiving the second dose, more than 99% of children had reached the same level. A considerable improvement in humoral and cellular immunity results with the second dose, given three months or between three and five years later. On the other hand, Serological findings demonstrated that vaccination in young children has more remarkable results than vaccination in adolescents aged 13 to 17 years.[25] Studies conducted over 10 and 20 years in Japan also demonstrated that the vaccine's immunogenic effects persisted beyond this time. The researchers wanted to know if a person who has had vaccinations would still have a high level of immunity if they were not exposed to or reminded of any naturally occurring infections in the population. To determine the answer to this question, hospitalized disabled children who were not exposed to any natural VZV infections were studied for five years.[26] The findings revealed that these children's antibody titers remained high, which may suggest that even without the vaccine's effect being strengthened. This vaccination can be sufficiently effective through spontaneous infection. Studies on the vaccine's efficacy conducted after the vaccine was licensed are critical, particularly in nations where the vaccination program has been in place for more than 20 years. These investigations, which took place in the US in 2008, showed that a single varicella immunization dose was 100% effective in preventing severe varicella and 84.5% successful in preventing mild varicella. Similar findings were also found in some other investigations.[27] Only one study explicitly evaluated the single-dose effects of Varivax and Varilrix to compare the efficacy of vaccines from various manufacturers. That study discovered a lower effect for Varilrix than for Varivax. To compare monovalent vaccines against the MMRV vaccine, further trials have been carried out. The currently available data support the monovalent varicella vaccines' similar effectiveness in preventing varicella, and additional research, particularly on the efficacy of the MMRV vaccine, may show that giving children a second dose regularly is a better way to boost efficacy and boost herd immunity.[28] According to research on what can go wrong with vaccinations, conditions like asthma, eczema, immunization at a young age, the timing of immunization, receiving varicella vaccine within 28 days of MMR vaccine, and taking oral steroids close to the time of disease onset can all be factored in vaccination failure. These were unrelated to the lack of success with vaccinations. Children who received the vaccine within three days after coming into contact with the household illness were 100% successful in preventing moderate or severe disease, according to a study on the vaccine's effectiveness during household exposure. It worked well. This investigation yielded 90% of the outcomes in another study.[29]

Varicella's progress and success

A breakout occurs when varicella (or a variant thereof) appears more than 42 days after vaccination. Most published studies that followed up on healthy children who had had a single dose of vaccination over an extended period found that, despite the substantial serological change, we still observe 1% to 3% annual progression of chicken pox. Most successful varicella cases exhibit a skin rash and fever of less than 50. Vesicular lesions are possible however, they are often infrequent and feature papules that do not develop into vesicles.[30] The clinical and epidemiological characteristics of 1671 cases with a single dose of the varicella vaccine and 5609 cases with no vaccination in children aged 1 to 14 years were compared. The vaccinated cases had fewer lesions, a lower risk of high and prolonged fever, moderate or severe disease, and fewer complications. Rarely hospitalization or death has been reported among vaccinated cases with a single dose; if it does, it typically affects patients unknowingly immunosuppressed by medical conditions or medications at the time of vaccination.[31] Pneumonia, sepsis, secondary infections brought on by bacteremia, encephalitis, and aseptic meningitis, which varicella WT confirms to have occurred, are serious consequences in cases of vaccination. Successful varicella vaccine instances may disseminate the WT virus to susceptible people, in contrast to the Oka strain's rarity. Only one-third of those who had received vaccinations and had less than 50 skin lesions were contagious. The incidence of varicella and the occurrence of HZ caused by WT VZV are expected to decline in populations where two doses are frequently advised.[32]

Safety duration

Investigations of American individuals who had received vaccinations as part of a collaborative NIAID study revealed that 60% to 90% had a positive FAMA test or latex agglutination antibodies up to 13 years after receiving the vaccination. Four years after receiving two doses of the varicella vaccine, a recent study using a sensitive gp-ELISA test discovered that 12% of 101 healthcare workers were serologically negative.

Following up on 100 medical professionals who received two doses of the GlaxoSmithKline varicella vaccine, it was shown that 3 out of 81 participants had lost measurable antibodies in their serum 12 months following the second dosage.[33, 34]

Efficiency and proficiency

A joint NIAID investigation found that 26% of 57 persons who had household exposure to varicella had an attack. The probability of an attack would be 80% if they were completely susceptible. According to the study, this 26% attack rate seems to be higher than what is observed in children who receive the same dose of vaccination.[35]

Adverse effects of the vaccine

In a post-licensure clinical study, 900 youngsters between the ages of 12 months and 12 years were given two doses rather than one dose. The incidence of problems at the injection site following the second dosage was somewhat greater than following the first dose three days or less after vaccination. With the second dose, the frequency of systemic clinical problems decreased. Fever incidence was 7% after the first dose and 4% after the second dose between 7 and 12 days after vaccination. After the first treatment, there was a 3% incidence of varicella rash compared to 1% after the second dose. An early post-licensure examination found the vaccination to be safe and devoid of unusual side effects.[36] It's also unusual for varicella immunization to cause serious negative effects. Skin rashes, fever, and adverse responses at the injection site have consistently been the most reported side effects, making up 67% of all reports. There have been reports of the serious side effects of the varicella vaccine, including death, urticaria, ataxia, thrombocytopenia, pneumonia, allergy, encephalitis, brain stroke, and multi-model arrhythmia.The vaccination virus did not cause the majority of these occurrences.[37] Stroke is an uncommon complication of untreated varicella, and there is no evidence that the vaccine increases the risk of a subsequent brain stroke. An institute of systematic medical evaluation of the epidemiologic, clinical, and biological evidence for adverse events connected to the varicella vaccination through 2010 found that the evidence supports causality in 5 adverse events: [(I)]A virus from the vaccine strain that has propagated throughout the body without affecting organs (for instance, a rash resembling varicella that has spread to dermatomes past the injection site). [(II)]A widely disseminated vaccination strain virus that can cause organ involvement (Pneumonia, meningitis) in people who have blatant immunodeficiency. [(III)]Organ-independent reactivation of the vaccination strain (HZ). [(IV)]Organ involvement and reactivation of the vaccination strain (HZ). [(V)]Anaphylaxis. These occurrences are rare or unusual. Antiviral therapy is frequently linked to recovery from VZV complications.[38]

Vaccine virus transmission

The transmission probability was inversely correlated with the number of skin lesions in the immunizations in leukemia-vaccinated people. The seropositivity rate was 23% in 93 nonimmune susceptible siblings exposed to vaccine-exposed individuals with leukemia who had a positive vaccine-associated rash. Twenty-four percent of these exposed kids never got a skin rash. In comparison, WT varicella often had a preclinical attack rate of around 5%. The average number of skin lesions among infected siblings who experienced skin rashes was 12 (from 1 to 200).[39] The amount of skin lesions in people who have received vaccines increases the risk that they may spread the Oka strain. The fact that there was just one report of a third incident further implies that the vaccination virus is not very contagious. Siblings of leukemia patients who had had vaccination exposure but had no rashes from the immunization were not affected by any outbreaks, making a total of 121 siblings. In contrast to data from immunized persons with leukemia in research trials, the transmission of Oka has been extremely rare in healthy vaccine recipients.[40] WT virus, in contrast, is extremely contagious from unvaccinated individuals to susceptible individuals under comparable settings, including family contacts, with a subsequent attack rate of up to 87%. Vaccinated people can also contract it from naturally occurring varicella cases (secondary attack rate: about 37%). The Oka strain in the vaccination causes a rash in every instance of vaccine-type VZV transmission that has been positively identified. The low transmission rate of the Oka strain is crucial due to the possibility of VZV vaccination spreading from healthy vaccine recipients to other vulnerable persons. There is no possibility of the virus spreading among healthy vaccine recipients who do not have a rash.[41]

Herpes zoster in vaccinated individuals

Laboratory testing has shown that HZ is a wild-type and vaccine-derived VZV strain in the post-licensing period. Hospitalization may be necessary for some vaccine_ strain HZ infections. HZ typically manifested 362 days after immunization, according to an analysis of data on the occurrence of the disease in passively immunized people submitted to the vaccine manufacturer. WT VZV was the root cause of 30–40% of these instances. These data, however, lack a population basis and are prone to reporting bias. Long-term monitoring of immunized and healthy children is necessary to precisely estimate the lifetime risks and severity of vaccine-strain-induced HZ.[42]

Indications for vaccination

MMRV vaccines are no longer the only available vaccines; single antigen (monovalent) varicella vaccines are now widely available throughout the world. Varicella vaccines are only permitted for use in healthy children 12 months of age and older, the except for the GlaxoSmithKline varicella vaccine, which may be administered to infants as young as nine months in several nations. The indications for utilizing the varicella vaccine vary from one country to the next depending on the goals of the varicella immunization program. To prevent the development of a susceptible population that has neither received a vaccine nor has been exposed to wild VZV, possible measures include universal vaccination of children after 9 or 12 months of age, especially in conjunction with immunization of older children or adolescents.[43] Additional techniques include immunizing teenagers and adults, including women of childbearing age, or specifically immunizing high-risk groups, such as children with HIV infection and organ transplant candidates, medical professionals, and close relatives of people with immune system compromises. Because of the decreased VZV transmission in nations with universal vaccination, children with leukemia, and other malignancies or otherwise immunocompromised shouldn't receive the vaccine. As a result, they are now less likely than ever to contract varicella. For post-exposure prophylaxis, VARIZIG is advised if they have been exposed to varicella or HZ. Acyclovir treatment should begin as soon as varicella symptoms appear.[44]

A popular two-dose recommendation for children changed as a result of the following causes

The spread of varicella outbreaks, the cost of investigating and containing outbreaks, the increase in humoral and cellular immunity following the second dose of the vaccine, and the vaccine's greater effectiveness with two doses are all predicted. This is true even though vaccination rates for varicella are high.[45] In the absence of a second dose, it was anticipated that there would be a pool of adolescents who had received the vaccination who either had not seroconverted or had developed a fully protective antibody response after only one dose and were thus at risk of becoming varicella-vulnerable young adults. Although it was not anticipated that the typical two doses of varicella vaccine would completely protect against the disease, it is expected that as the virus's propagation declines, the number of outbreaks will dramatically decline.[46]

Common vaccination schedule

A standard two-dose varicella vaccine was recommended in the US in 2007. All young children under the age of 13 who are healthy should receive two subcutaneous doses of the varicella vaccination totalling 0.5 ml each. Immunization is crucial for those over 13 since varicella infection is more severe in this age group (The MMRV vaccine is not approved for use in this age group). Two doses of the monovalent varicella vaccine should be given to those at risk and those without any signs of immunity four to eight weeks apart. VZV transmission through nosocomial contact is a well-known medical and public health issue.[47] Due to the increased risk of exposure to varicella or HZ and close contact with those who are at risk, healthcare professionals should consistently obtain two doses of the varicella vaccination unless they have other confirmation of immunity. While about 80% of staff members are immune to varicella, serological testing before vaccination of those with a negative or questionable history is likely to be cost-effective in healthcare settings. The varicella vaccine is safe to give to nursing mothers.[48] A small study including 12 seronegative mothers who received the postpartum varicella vaccine and breastfed their children found no evidence that the VZV vaccine virus is secreted in breast milk. VZV was not found by PCR in any of the 217 breast milk samples. Six newborn serum samples tested negative for VZV DNA by PCR, and none of the infants tested positive. In small clinical studies, monovalent varicella vaccine was administered twice, three months apart, to HIV-infected children between the ages of one and eight. After one year after vaccination, more than 80 of the children developed detectable immune responses (antibody and, or CMI) to VZV, and the CD4+ T lymphocyte level was higher than 25 in 41 children and 15 or higher in 44 children.[49] Compared to healthy kids, children with HIV are more likely to get varicella and HZ. Eligible children should receive two doses of the monovalent varicella vaccine, spaced three months apart. There is no information on administering the varicella vaccination to adults and adolescents who are HIV-positive. The univalent varicella vaccine is quite effective at preventing both varicella and HZ in kids who are HIV-positive.[50]

Contraindications and precautions

It is important to thoroughly read the instructions on the packaging before giving the varicella-containing vaccination. Although no infants have been documented with congenital varicella syndrome brought on by a virus of this type, immunization is not advised during pregnancy.[51]

Vaccination goals and Cost-effectiveness

Programs to prevent varicella include a variety of objectives. These objectives may include preventing

varicella and its complications, severe sickness and mortality, or disease prevention and control in certain target populations like adults, adolescents, or healthcare professionals. In nations where varicella has a large public health impact, the World Health Organization has advised that routine varicella vaccination of children be considered.[52] The WHO recommends both one dosage and two dosages if the goal is to reduce the number of varicella cases and its prevalence (Health workers form a special group that should receive two doses, especially if they come into contact with immunocompromised patients). The costs and public health impacts of varicella disease in hospital settings have been well documented for factors such as sick leave, serological testing, patient isolation, administration of passive immunization, remuneration paid to substitute health care workers, and infection control costs.[53]

Post-vaccine epidemiology

Varicella incidence and mortality have significantly decreased in the **United States** since the single-dose varicella vaccination program was implemented. In the context of the decreased prevalence of varicella in all age groups, the peak age of varicella infection increased from 3 to 6 years in 1995 to 9 to 11 years in 2005, but the proportion of those who were inoculated increased from less than 1% to 60% over the same period. Varicella mortality decreased from an average of 145 deaths per year in the five years (1990 to 1994) before the immunization program to 66 deaths per year from 1999 to 2001, accounting for all ages and the major and contributing causes of death. From 2002 and 2007, there were no racial differences in death rates.[54] Varicella outbreaks have happened in highly immunized schoolchildren, albeit in minor cases and over a brief time, despite the amazing results in the United States in suppressing the disease and its serious sequelae. Adopting a two-dose regimen became customary in the United States for children in 2007. Due to this a single dose of the vaccine for children may not produce enough long-term protective memory, which may result in groups of partially vaccinated or fully susceptible children in adulthood. The CDC received reports of varicella outbreaks in six states.[55] A study of those outbreaks revealed that the typical two-dose regimen dramatically decreased the incidence, size, and duration of outbreaks. More knowledge about the efficacy of single-dose varicella vaccination programs for kids has become accessible as other nations have introduced them. Varicella and its consequences decreased in **Germany** in 2004 following the implementation of a countrywide single-dose immunization program. In a surveillance effort in and around **Munich**, hospitalizations for varicella were found to have decreased by 43% in children under 17 between 2005 and 2009 and by 78% in children under the age of 5.[56] The prevalence of varicella dramatically decreased in the **Veneto** area of Italy 2.5 years after the universal vaccination program was put into place and reached more than 70% vaccine coverage. Varicella hospital cases decreased by 81% to 88% in **Canada**, where a varicella immunization program was suggested in 1999, and from 2000 to 2008. Reports on the effectiveness of a single-dose immunization program against varicella and related repercussions have also been published, with examples coming from Uruguay, Taiwan, Sicily, and Australia.[57] Studies in Australia have shown a significant decline in both congenital varicella syndrome (100%) and neonatal varicella (85%) as a result of the statewide immunization effort that began in 2005. A two-dose regular childhood program was implemented in the **Navarre** region of **Spain** and high coverage was attained early on, resulting in a 98.5% decrease in children and an 89% decrease in hospitalizations in just five years.[58]

Varicella and zoster vaccine

Understanding how the varicella vaccine influences the epidemiology of HZ is crucial since the Oka varicella virus may reactivate and cause HZ. Hope Simpson was the first to suggest that external immunity may be increased by exposure to varicella, HZ, or both, while internal immunity could be sustained through periodic reactivation of VZV. A large amount of pre-licensure study was conducted on the effect of the varicella vaccine on the risk of HZ due to the severity of HZ in immunocompromised groups.[59] Since patients with spontaneous chicken pox acquire HZ at a considerably higher rate than healthy children, it was able to examine the rate of HZ in these people in a relatively short period of time. In a study of French children who received kidney transplants, the 10-year rate of HZ was 7% in those who had received vaccinations, 13% in those who had varicella before transplantation, and 38% in those who had varicella after transplantation. Long-term incidences of HZ in healthy, immunized children and adults have been documented in some pre-licensure investigations.[60] Few studies have examined the risk of HZ in healthy, immunized persons. It is now possible to determine the risk of HZ in healthy, immunized children, although there are still difficulties related to the rarity of HZ in children and the availability of data in a cohort of kids with a history of varicella. Post-vaccination HZ may be less frequent than spontaneous infection for several reasons. One is that, compared to the WT virus, the virus is weaker and less likely to reactivate.[61] Another factor is

that the vaccine strain may have less access to sense neurons to cause incubation since the prevalence of skin infection following vaccination is lower than that of natural infection. Finally, compared to a natural infection, virus latency may be decreased following vaccination. The VZV, which has entered neurons with asymptomatic viremia, is the most common cause of WT HZ in vaccine recipients without clinical varicella. As a result, children who have gotten two doses of the varicella vaccine are less likely to have HZ.[62]

External enhancement of immunity through varicella exposure and HZ risk

Many studies have looked at how varicella exposure affects the risk of HZ in both immunocompetent and healthy populations. In their temporal study of weekly reported data, Garnett and Grenfell found no correlation between the temporal occurrence of varicella and HZ. Varicella exposure boosts VZV-specific immunity, but it's unclear if lifetime exposure is necessary to sustain immunity to VZV through external reinforcement, especially as the population ages. Many studies have found a correlation between living with or being near children (as a proxy for varicella exposure) and a lower risk of HZ.[63] The authors hypothesized that only a tiny portion of the population might be affected by chickenpox exposure as a way to preserve cellular immunity against HZ. Among the difficulties nations face observing how varicella immunization affects HZ is the following: The baseline data may not be accessible to infer trends because (I) changes over time for HZ have not yet been thoroughly characterized; interpreted HZ. (II) It has been challenging to compare research due to the use of various methodologies. (III) HZ is diagnosed clinically and infrequently tested-laboratory verified. (IV) Because the age distribution of the research population can fluctuate, age-adjusted rates must be calculated to compare studies and assess long-term trends within studies. And (V) only a small number of research have looked at the epidemiology of HZ, immunodeficiency illnesses, drugs, and other particular situations (e.g., diabetes, stress).[64]

the population's prevalence of herpes zoster

In the US and other nations, HZ is becoming more commonplace. The United States, where a pediatric immunization program has existed for two decades, has the most experience observing the impact of the varicella vaccination program on HZ. There are statistics from different countries that can be used to analyze trends in HZ after immunization. These countries either lack immunization programs or have just begun to implement them.[65]

The potential to stop disease transmission and eradicate it

When a person has varicella, the varicella-zoster virus can also spread, and because it can conceal itself and produce herpes simplex, there is a chance that it could also spread in the general population. Even with a two-dose policy, endemic transmission may still exist, and HZ patients will continue to expose people to VZV.[66] However, widespread vaccination against varicella, especially as part of a national vaccination program, has significantly reduced the spread of the virus and improved the health of many children, teenagers, and adults who are no longer required to deal with varicella and its serious side effects and will experience less HZ. Although it appears doubtful that VZV will ever be eradicated, creating a highly efficient zoster subunit vaccine that stops incubation may play a critical role in further lowering VZV transmission. There may be more chances to lower VZV transmission if inactivated or subunit vaccinations, which prevent latent varicella and HZ, are made available.[67]

Conclusion

Even though varicella is typically a minor, self-limiting condition, problems can still happen. Most studies have not verified concerns about an increase in the incidence of herpes zoster in older people, though some of them have indicated a trend in that direction. Longer observations may be required in this respect. Additionally, even though precise burden statistics may be challenging to find, the universal varicella vaccine appears to be cost-effective by lowering the rate of complications. The majority of data are only accessible from high- and middle-income nations, so the impact in low-income nations might not be exactly as reported. Additionally, some nations are still struggling with the severe mortality and impact of other diseases like measles, rotavirus, pneumococcal, and meningococcal disease. Finally, the introduction of universal vaccination should be taken into consideration if it is economically viable as the varicella vaccine is a crucial step in public health strategies.

Review Highlights

What Is Already Known?

Varicella Zoster Virus (VZV) is an alpha herpes virus that can conceal itself and produce shingles in addition to generating chicken pox. Varicella is a highly contagious illness brought on by vesicular skin sores, contamination, and maybe to a lesser extent, the propagation of the aerosolized virus. In comparison to children, adults with varicella had a much higher rate of primary VZV infection death. Different nations produce the varicella vaccines known as (Varivax; ProQuad; Merck & Co.), (Varilrix; Priorixtetra; GSK), (Okavax; Biken, by Sanofi Pasteur), and (SuduVax; Green Cross). The amount of HDC passes, specific antibiotics included to assure sterility, stabilizers, and other minor components vary between different vaccines.

What Does This Study Add?

The spread of the virus can be decreased dramatically by the widespread use of the varicella vaccine, particularly in a worldwide vaccination program. The World Health Organization suggested varicella vaccination in 1998 for nations where the illness poses a serious threat to public health. Nevertheless, many nations delayed the introduction of the universal varicella vaccine due to worries about the disease spreading to older populations, an increase in elderly herpes zoster, and cost-effectiveness.

Conflict of Interest Disclosures

The author has no conflict of interest to declare.

Ethical Approval

No ethical approval was indicated, as the present was a review study.

Funding/Support

The research did not receive any specific grant from funding agencies.

Reference:

1. Gershon AA, Breuer J, Cohen JI, Cohrs RJ, Gershon MD, Gilden D, Grose C, Hambleton S, Kennedy PG, Oxman MN, Seward JF, Yamanishi K. Varicella zoster virus infection. Nat Rev Dis Primers. 2015 Jul 2;1:15016. doi: 10.1038/nrdp.2015.16.
2. Mourad M, Gershon M, Mehta SK, Crucian BE, Hubbard N, Zhang J, Gershon A. Silent reactivation of varicella zoster virus in pregnancy: implications for maintenance of immunity to varicella. Viruses. 2022 Jun 30;14(7):1438. doi: 10.3390/v14071438.
3. Di Pietrantonj C, Rivetti A, Marchione P, Debalini MG, Demicheli V. Vaccines for measles, mumps, rubella, and varicella in children. Cochrane Database Syst Rev. 2020 Apr 20;4(4):CD004407. doi: 10.1002/14651858.CD004407.pub4.
4. Galetta KM, Gilden D. Zeroing in on zoster: A tale of many disorders produced by one virus. J Neurol Sci. 2015 Nov 15;358(1-2):38-45. doi: 10.1016/j.jns.2015.10.004.
5. De Paschale M, Clerici P. Microbiology laboratory and the management of mother-child varicella-zoster virus infection. World J Virol. 2016 Aug 12;5(3):97-124. doi: 10.5501/wjv.v5.i3.97.
6. Schmid DS, Jumaan AO. Impact of varicella vaccine on varicella-zoster virus dynamics. Clin Microbiol Rev. 2010 Jan;23(1):202-17. doi: 10.1128/CMR.00031-09.
7. Lamont RF, Sobel JD, Carrington D, Mazaki-Tovi S, Kusanovic JP, Vaisbuch E, Romero R. Varicella-zoster virus (chickenpox) infection in pregnancy. BJOG. 2011 Sep;118(10):1155-62. doi: 10.1111/j.1471-0528.2011.02983.x.
8. Gershon AA, Gershon MD. Pathogenesis and current approaches to control of varicella-zoster virus infections. Clin Microbiol Rev. 2013 Oct;26(4):728-43. doi: 10.1128/CMR.00052-13.
9. Gilden D, Mahalingam R, Nagel MA, Pugazhenthi S, Cohrs RJ. Review: The neurobiology of varicella zoster virus infection. Neuropathol Appl Neurobiol. 2011 Aug;37(5):441-63. doi: 10.1111/j.1365-2990.2011.01167.x.
10. Wachtman L, Mansfield K. Viral Diseases of Nonhuman Primates. Nonhuman Primates in Biomedical Research. 2012:1–104. doi: 10.1016/B978-0-12-381366-4.00001-8.
11. Oliver SL, Yang E, Arvin AM. Varicella-Zoster Virus Glycoproteins: Entry, Replication, and Pathogenesis. Curr Clin Microbiol Rep. 2016 Dec;3(4):204-215. doi: 10.1007/s40588-016-0044-4.
12. Laing KJ, Ouwendijk WJD, Koelle DM, Verjans GMGM. Immunobiology of Varicella-Zoster Virus Infection. J Infect Dis. 2018 Sep 22;218(suppl_2):S68-S74. doi: 10.1093/infdis/jiy403.
13. Pan D, Wang W, Cheng T. Current Methods for the Detection of Antibodies of Varicella-Zoster Virus: A Review. Microorganisms. 2023 Feb 17;11(2):519. doi: 10.3390/microorganisms11020519.
14. Kinchington PR, Leger AJ, Guedon JM, Hendricks RL. Herpes simplex virus and varicella zoster virus, the house guests who never leave. Herpesviridae. 2012 Jun 12;3(1):5. doi: 10.1186/2042-4280-3-5.
15. Chen F, He Y, Shi Y. Parents' and Guardians' Willingness to Vaccinate Their Children against COVID-19: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2022 Jan 24;10(2):179. doi: 10.3390/vaccines10020179.
16. Chen Z, He Q. Immune persistence after pertussis vaccination. Hum Vaccin Immunother. 2017 Apr 3;13(4):744-756. doi: 10.1080/21645515.2016.
17. Tillieux SL, Halsey WS, Thomas ES, Voycik JJ, Sathe GM, Vassilev V. Complete DNA sequences of two oka strain varicella-zoster virus genomes. J Virol. 2008 Nov;82(22):11023-44. doi: 10.1128/JVI.00777-08.
18. Ross AH, Lenchner E, Reitman G. Modification of chicken pox in family contacts by administration of gamma globulin. New England Journal of Medicine. 1962 Aug 23;267(8):369-76. doi: 10.1056/NEJM19620823267080
19. Jenkins GJ, Williams GL, Beynon J, Ye Z, Baxter JN, Parry JM. Restriction enzymes in the analysis of genetic alterations responsible for cancer progression. Br J Surg. 2002 Jan;89(1):8-20. doi: 10.1046/j.0007-1323.2001.01968.x.
20. Gambichler T, Boms S, Susok L, Dickel H, Finis C, Abu Rached N, Barras M, Stücker M, Kasakovski D. Cutaneous

findings following COVID-19 vaccination: review of world literature and own experience. J Eur Acad Dermatol Venereol. 2022 Feb;36(2):172-180. doi: 10.1111/jdv.17744.

21. Chen P, Zhang KH, Na T, Wang L, Yin WD, Yuan BZ, Wang JZ. The hUC-MSCs cell line CCRC-1 represents a novel, safe and high-yielding HDCs for the production of human viral vaccines. Sci Rep. 2017 Oct 2;7(1):12484. doi: 10.1038/s41598-017-11997-1.

22. Matsumoto K, Ohfuji S, Inohara K, Akechi M, Kumashiro H, Ishibashi M, Irie S, Hirota Y. Effectiveness of Live Attenuated Varicella-Zoster Vaccine in Adults Older than 50 Years in Japan: A Retrospective Cohort Study. Vaccines. 2023 Jan 25;11(2):259. doi: 10.3390/vaccines11020259.

23. Zhang L, Wang W, Wang S. Effect of vaccine administration modality on immunogenicity and efficacy. Expert Rev Vaccines. 2015;14(11):1509-23. doi: 10.1586/14760584.2015.1081067. Epub 2015 Aug 27.

24. Sheikh-Mohamed S, Sanders EC, Gommerman JL, Tal MC. Guardians of the oral and nasopharyngeal galaxy: IgA and protection against SARS-CoV-2 infection. Immunological Reviews. 2022 Aug;309(1):75-85. doi:10.1111/imr.13118.

25. Schmid DS, Jumaan AO. Impact of varicella vaccine on varicella-zoster virus dynamics. Clin Microbiol Rev. 2010 Jan;23(1):202-17. doi: 10.1128/CMR.00031-09.

26. Hegde NR, Gore MM. Japanese encephalitis vaccines: Immunogenicity, protective efficacy, effectiveness, and impact on the burden of disease. Hum Vaccin Immunother. 2017 Jun 3;13(6):1-18. doi: 10.1080/21645515.2017.1285472.

27. Chi, WY., Li, YD., Huang, HC. *et al.* COVID-19 vaccine update: vaccine effectiveness, SARS-CoV-2 variants, boosters, adverse effects, and immune correlates of protection. *J Biomed Sci* **29**, 82 (2022). https://doi.org/10.1186/s12929-022-00853-8

28. Pillsbury M, Carias C, Samant S, Greenberg D, Pawaskar M. Comparison of performance of varicella vaccines via infectious disease modeling. Vaccine. 2022 Jun 23;40(29):3954-3962. doi: 10.1016/j.vaccine.2022.05.003.

29. Papaloukas O, Giannouli G, Papaevangelou V. Successes and challenges in varicella vaccine. Ther Adv Vaccines. 2014 Mar;2(2):39-55. doi: 10.1177/2051013613515621.

30. Schmid DS, Jumaan AO. Impact of varicella vaccine on varicella-zoster virus dynamics. Clin Microbiol Rev. 2010 Jan;23(1):202-17. doi: 10.1128/CMR.00031-09.

31. Chaves SS, Zhang J, Civen R, Watson BM, Carbajal T, Perella D, Seward JF. Varicella disease among vaccinated persons: clinical and epidemiological characteristics, 1997-2005. J Infect Dis. 2008 Mar 1;197 Suppl 2:S127-31. doi: 10.1086/522150.

32. Manohar P, Loh B, Nachimuthu R, Hua X, Welburn SC, Leptihn S. Secondary bacterial infections in patients with viral pneumonia. Frontiers in medicine. 2020 Aug 5;7:420.

33. Michalik DE, Steinberg SP, Larussa PS, Edwards KM, Wright PF, Arvin AM, Gans HA, Gershon AA. Primary vaccine failure after 1 dose of varicella vaccine in healthy children. J Infect Dis. 2008 Apr 1;197(7):944-9. doi: 10.1086/529043.

34. Ceyhan M, Tezer H, Yildirim I. Secondary attack rate of hepatitis A, varicella and mumps in household settings and reliability of family history to detect seronegative children for necessity of vaccination. Scand J Infect Dis. 2009;41(6-7):501-6. doi: 10.1080/00365540902968027.

35. Dbaibo G, Tatochenko V, Wutzler P. Issues in pediatric vaccine-preventable diseases in low- to middle-income countries. Hum Vaccin Immunother. 2016 Sep;12(9):2365-77. doi: 10.1080/21645515.2016.1181243.

36. Sherman SM, Lingley-Heath N, Lai J, Sim J, Bedford H. Parental acceptance of and preferences for administration of routine varicella vaccination in the UK: a study to inform policy. Vaccine. 2023 Feb 17;41(8):1438-46.

37. Amlie-Lefond C, Gilden D. Varicella Zoster Virus: A Common Cause of Stroke in Children and Adults. J Stroke Cerebrovasc Dis. 2016 Jul;25(7):1561-1569. doi: 10.1016/j.jstrokecerebrovasdis.2016.03.052.

38. Marin M, Leung J, Gershon AA. Transmission of Vaccine-Strain Varicella-Zoster Virus: A Systematic Review. Pediatrics. 2019 Sep;144(3):e20191305. doi: 10.1542/peds.2019-1305.

39. Proal AD, VanElzakker MB. Long COVID or post-acute sequelae of COVID-19 (PASC): an overview of biological factors that may contribute to persistent symptoms. Frontiers in microbiology. 2021 Jun 23;12:1494. doi: 10.3389/fmicb.2021.698169

40. Marin M, Leung J, Gershon AA. Transmission of vaccine-strain varicella-zoster virus: a systematic review. Pediatrics. 2019 Sep 1;144(3). doi: 10.1542/peds.2019-1305.

41. Seward JF, Zhang JX, Maupin TJ, Mascola L, Jumaan AO. Contagiousness of varicella in vaccinated cases: a household contact study. JAMA. 2004 Aug 11;292(6):704-8. doi: 10.1001/jama.292.6.704.

42. Campsall PA, Au NH, Prendiville JS, Speert DP, Tan R, Thomas EE. Detection and genotyping of varicella-zoster virus by TaqMan allelic discrimination real-time PCR. J Clin Microbiol. 2004 Apr;42(4):1409-13. doi: 10.1128/JCM.42.4.1409-1413.2004.

43. Fleurant-Ceelen A, Tunis M, House A. Adult immunization: What is new in the Canadian Immunization Guide: November 2016 to November 2018. Canada Communicable Disease Report. 2018 Dec 12;44(12):351. doi: 10.14745/ccdr.v44i12a06

44. Duchini A, Goss JA, Karpen S, Pockros PJ. Vaccinations for adult solid-organ transplant recipients: current recommendations and protocols. Clinical microbiology reviews. 2003 Jul;16(3):357-64. doi: 10.1128/cmr.16.3.357-364.2003

45. Gershon AA, Gershon MD, Shapiro ED. Live attenuated varicella vaccine: prevention of varicella and of zoster. The Journal of Infectious Diseases. 2021 Oct 1;224(Supplement_4):S387-97. doi: 10.1093/infdis/jiaa573

46. Hambleton S, Gershon AA. Preventing varicella-zoster disease. Clin Microbiol Rev. 2005 Jan;18(1):70-80. doi: 10.1128/CMR.18.1.70-80.2005.

47. Wutzler P, Knuf M, Liese J. Varicella: efficacy of two-dose vaccination in childhood. Dtsch Arztebl Int. 2008 Aug;105(33):567-72. doi: 10.3238/arztebl.2008.0567.

48. Lachiewicz AM, Srinivas ML. Varicella-zoster virus post-exposure management and prophylaxis: A review. Prev Med Rep. 2019 Nov 6;16:101016. doi: 10.1016/j.pmedr.2019.101016.

49. Singh S, Sharma A, Rahman MM, Kasniya G, Maheshwari A, Boppana SB. Congenital and Perinatal Varicella Infections. Newborn (Clarksville). 2022 Jul-Sep;1(3):278-286. doi: 10.5005/jp-journals-11002-0040.

50. Gershon AA, Levin MJ, Weinberg A, Song LY, LaRussa PS, Steinberg SP, Bartlett P; Pediatric AIDS Clinical Trials Group 391 Team. A phase I-II study of live attenuated varicella-zoster virus vaccine to boost immunity in human immunodeficiency virus-infected children with previous varicella. Pediatr Infect Dis J. 2009 Jul;28(7):653-5. doi: 10.1097/INF.0b013e3181998f06.

51. Sauerbrei A. Preventing congenital varicella syndrome with immunization. CMAJ. 2011 Feb 22;183(3):E169-70. doi: 10.1503/cmaj.110055.

52. Pawaskar, M., Méroc, E., Samant, S. et al. Economic burden of varicella in Europe in the absence of universal varicella vaccination. BMC Public Health 21, 2312 (2021). https://doi.org/10.1186/s12889-021-12343-x

53. Gabutti G, Bolognesi N, Sandri F, Florescu C, Stefanati A. Varicella zoster virus vaccines: an update. Immunotargets Ther. 2019 Aug 6;8:15-28. doi: 10.2147/ITT.S176383.

54. Goldman GS, King PG. Review of the United States universal varicella vaccination program: Herpes zoster incidence rates, cost-effectiveness, and vaccine efficacy based primarily on the Antelope Valley Varicella Active Surveillance Project data. Vaccine. 2013 Mar 25;31(13):1680-94. doi: 10.1016/j.vaccine.2012.05.050. Epub 2012 Jun 1. PMID: 22659447; PMCID: PMC3759842.

55. Zhong JM, Zhang M, Huang ZY, Qiu GP, Rao F, Lu ZH, Chen T, Zhang QL. A persistent outbreak of varicella in a primary school in Dongguan City, Guangdong Province, China. J Int Med Res. 2020 Mar;48(3):300060519887847. doi: 10.1177/0300060519887847. Epub 2019 Nov 27. PMID: 31771379; PMCID: PMC7607272.

56. Shu M, Zhang D, Ma R, Yang T, Pan X. Long-term vaccine efficacy of a 2-dose varicella vaccine in China from 2011 to 2021: A retrospective observational study. Front Public Health. 2022 Nov 8;10:1039537. doi: 10.3389/fpubh.2022.1039537. PMID: 36424959; PMCID: PMC9679788.

57. Bechini A, Boccalini S, Baldo V, Cocchio S, Castiglia P, Gallo T, Giuffrida S, Locuratolo F, Tafuri S, Martinelli D, Prato R, Amodio E, Vitale F, Bonanni P. Impact of universal vaccination against varicella in Italy. Hum Vaccin Immunother. 2015;11(1):63-71. doi: 10.4161/hv.34311. Epub 2014 Nov 1. PMID: 25483517; PMCID: PMC4514224.

58. Khandaker G, Marshall H, Peadon E, Zurynski Y, Burgner D, Buttery J, Gold M, Nissen M, Elliott EJ, Burgess M, Booy R. Congenital and neonatal varicella: impact of the national varicella vaccination programme in Australia. Arch Dis Child. 2011 May;96(5):453-6. doi: 10.1136/adc.2010.206037. Epub 2011 Feb 24. PMID: 21349886.

59. Guzzetta G, Poletti P, Merler S, Manfredi P. The Epidemiology of Herpes Zoster After Varicella Immunization Under Different Biological Hypotheses: Perspectives From Mathematical Modeling. Am J Epidemiol. 2016 Apr 15;183(8):765-73. doi: 10.1093/aje/kwv240. Epub 2016 Mar 18. PMID: 26994062; PMCID: PMC4832050.

60. Wutzler P, Casabona G, Cnops J, Akpo EI, Safadi MA. Herpes zoster in the context of varicella vaccination–An equation with several variables. Vaccine. 2018 Nov 12;36(46):7072-82. doi: 10.1016/j.vaccine.2018.09.013

61. Rafferty E, Reifferscheid L, Russell ML, Booth S, Svenson LW, MacDonald SE. The impact of varicella vaccination on paediatric herpes zoster epidemiology: a Canadian population-based retrospective cohort study. Eur J Clin Microbiol Infect Dis. 2021 Nov;40(11):2363-2370. doi: 10.1007/s10096-021-04298-z. Epub 2021 Jun 26. PMID: 34175998; PMCID: PMC8520524.

62. Wang W, Pan D, Fu W, Ye X, Han J, Yang L, Jia J, Liu J, Zhu R, Zhang Y, Liu C, Ye J, Selariu A, Que Y, Zhao Q, Wu T, Li Y, Zhang J, Cheng T, Zhu H, Xia N. Development of a skin- and neuro-attenuated live vaccine for varicella. Nat Commun. 2022 Feb 11;13(1):824. doi: 10.1038/s41467-022-28329-1. PMID: 35149692; PMCID: PMC8837607.

63. Ogunjimi B, Van Damme P, Beutels P. Herpes Zoster Risk Reduction through Exposure to Chickenpox Patients: A Systematic Multidisciplinary Review. PLoS One. 2013 Jun 21;8(6):e66485. doi: 10.1371/journal.pone.0066485. PMID: 23805224; PMCID: PMC3689818.

64. Ogunjimi B, Van Damme P, Beutels P. Herpes zoster risk reduction through exposure to chickenpox patients: a systematic multidisciplinary review. PloS one. 2013 Jun 21;8(6):e66485. doi:10.1371/journal.pone.0066485

65. Bakker, K.M., Eisenberg, M.C., Woods, R.J. et al. Identifying optimal vaccination scenarios to reduce varicella zoster virus transmission and reactivation. BMC Med 20, 387 (2022). https://doi.org/10.1186/s12916-022-02534-7

66. Kennedy PGE, Gershon AA. Clinical Features of Varicella-Zoster Virus Infection. Viruses. 2018 Nov 2;10(11):609. doi: 10.3390/v10110609. PMID: 30400213; PMCID: PMC6266119.

67. Sauboin, C., Holl, K., Bonanni, P. et al. The impact of childhood varicella vaccination on the incidence of herpes zoster in the general population: modelling the effect of exogenous and endogenous varicella-zoster virus immunity boosting. BMC Infect Dis 19, 126 (2019). https://doi.org/10.1186/s12879-019-3759-z.