Varicella

Varicella, or chickenpox, is our third acute viral illness of the day. Those of you with inquiring minds may have wondered about the origin of the term chickenpox. What do chickens have to do with a rash illness? As it turns out, nothing. The name chickenpox comes from chick peas. The name refers to the similarity between a varicella skin lesion and a chickpea, or garbanzo bean. The term chickenpox first appeared in the medical literature in 1694, but had probably been in common use long before then. Think about *that* the next time you visit the salad bar.

Zoster has been recognized for hundreds of years, but varicella was not differentiated from smallpox until the end of 19th century. The association between varicella and zoster was deduced in 1888, when it was observed that chickenpox resulted when children were exposed to people with zoster. The virus was not isolated until 1958.

Varicella is a member of the Herpes virus family. Others members include herpes simplex 1 and 2, cytomegalovirus, and Epstein Barr virus. Varicella shares with these viruses the capacity to persist in the body after primary infection, and a tendency to recur. The primary, or initial, infection with varicella zoster virus results in varicella or chickenpox. Recurrent infection results in herpes zoster, or shingles. The virus is fragile, and survives only a short time in the environment.

The incubation period of varicella is usually 14 to 16 days, but may be as long as 21 days. There may be a mild prodrome for 1 to 2 days, followed by several successive crops of pruritic vesicles. Lesions first appear on the head, but are usually most concentrated on the trunk. Almost all primary infections with varicella zoster virus are symptomatic. Subclinical or asymptomatic primary infections are unusual. However, there may be only a few lesions, which may be overlooked by the patient or the parent. But a mild case of varicella results in immunity as well as a severe case with hundreds of lesions.

Herpes zoster, or shingles, represents reactivation of latent varicella zoster virus infection. It is estimated that 15% of the population will experience zoster sometime during their lifetime. While the exact mechanism of reactivation is not clear, factors associated with zoster include aging, immunosuppression, intrauterine exposure, and varicella at less than 18 months of age. Varicella virus may be transmitted from the lesions of patients with zoster. Transmission of varicella virus from a person with zoster to a susceptible person results in chickenpox, not zoster. A person who has already had varicella does not develop shingles if exposed to a person with chickenpox.

Most of you have seen varicella, but here is a short video to illustrate some of the most characteristic features.

THIS CHILD HAS CHICKENPOX, THE PRIMARY INFECTION WITH VARICELLA ZOSTER VIRUS. THIS GIRL HAS TYPICAL VESICULAR LESIONS ON THE FACE. THE LESIONS ARE FAIRLY WIDESPREAD, BUT ARE TYPICALLY MORE CONCENTRATED ON THE TRUNK. THIS IS A FEW DAYS LATER. NOTICE THAT SOME OF THE LESIONS ARE BEGINNING TO CRUST. THIS IS A CLOSE-UP OF THE VESICULAR LESIONS OF VARICELLA. THERE ARE LESIONS IN VARIOUS STAGES OF EVOLUTION, FROM MACULES TO FULLY DEVELOPED VESICLES. UMBILICATED SKIN LESIONS ARE NOT COMMON IN VARICELLA, BUT ARE OFTEN SEEN IN SMALLPOX. THIS CHILD HAS HERPES ZOSTER, OR SHINGLES, INVOLVING HER FIFTH CRANIAL NERVE. ZOSTER INVOLVING THIS NERVE ROOT MAY AFFECT THE EYE. THIS IS MORE TYPICAL HERPES ZOSTER INVOLVING A UNILATERAL THORACIC NERVE ROOT. HERPES ZOSTER IS TYPICALLY VERY PAINFUL. THERE MAY BE PAIN EVEN AFTER THE LESIONS RESOLVE, A CONDITION KNOWN AS POST-HERPETIC NEURALGIA. AN EPISODE OF ZOSTER TYPICALLY LASTS ABOUT 2 WEEKS, BUT THE SKIN MAY NOT RETURN TO NORMAL FOR UP TO A MONTH.

The majority of persons will have a single episode of chickenpox, but second episodes of chickenpox have been reported. The frequency of these repeated episodes is not known with certainty. But one investigation found that as many as 13% of people with chickenpox reported a prior history of chickenpox. Varicella is generally not a serious illness in healthy children but may result in complications.

The most common complications are bacterial infection of lesions. This complication can be very severe or fatal particularly if group A streptococcus is involved. Central nervous system manifestations, such as cerebellar ataxia and encephalitis are not common. Pneumonia may occur after varicella among adults or children. Hospitalization occurs in 3 to 4 per 1,000 cases. However, because of the huge number of cases, this amounted to 11,000 hospitalizations from varicella per year in the prevaccine era. Death occurs in about 1 in 60,000 cases, which meant up to 100 deaths per year in the prevaccine era. About 67% of hospitalizations and 50% of deaths occurred in healthy children.

It seems that one of the biggest obstructions to widespread use of varicella vaccine continues to be the idea that varicella is a trivial disease. While it is true that many cases are relatively mild, 100 deaths a year, and 11,000 hospitalizations in the prevaccine era was not indicative of a trivial disease. The message here is that varicella and its complications can be dangerous. All the more reason to prevent it with vaccine.

Some groups are at increased risk of complications of varicella. For example, healthy adults are 25 times more likely to die from varicella than healthy children. Although adults make up only about 7% of varicella cases, they account for half of all varicella deaths. Of the 11 reported varicella related deaths in 2002, 7 were adults. Adults are often infected by their unvaccinated children. Immunocompromised persons are at high risk of severe varicella disease. These persons may have prolonged illness and an increased risk of complications. One

of the highest risk groups is newborns with maternal rash onset within 5 days before to 48 hours after delivery. This is thought to occur because the fetus receives an intravenous exposure to varicella virus through the umbilical cord, and is then born without the benefit of its mothers' antibody. These children often develop severe varicella, and are one of the most important groups for passive antibody treatment with varicella zoster immune globulin.

Varicella remains an endemic disease in the United States. However, the widespread use of varicella vaccine is beginning to change the epidemiology of this disease.

Varicella is a human disease, and the reservoir is humans with acute and chronic infections. These chronic infections will make eradication very difficult. The disease is transmitted by airborne droplets or by direct contact with the lesions of either chickenpox or zoster. Varicella is communicable from 1 or 2 days before until 4 to 5 days after onset of rash, when all the lesions are crusted. Immunosuppressed people with varicella may transmit longer. Varicella is very contagious, with secondary attack rates of 90% or higher in households. That means that if you had 11 children and one came home with chickenpox, nine of the others would have it within 2 weeks.

In the prevaccination era, 85% of all cases of varicella occurred in children less than 15 years of age. This graph shows the age specific incidence of varicella as the rate per 100,000 population, on the vertical axis, and age groups on the horizontal axis. The highest incidence was among children 1 to 4 years old, who accounted for about 40% of all cases. Children 5 to 9 years of age had the next highest rate of infection. This age group accounted for about 38% of all cases. Adults 20 years of age and older only accounted for about 7% of cases. Although the rates of varicella disease are lower now than in the prevaccination era, the age distribution is probably similar, with the largest proportion of cases among children less than 15 years of age.

In the prevaccination era, an estimated 3 to 4 million cases of varicella occurred every year – basically the entire annual birth cohort. But vaccination coverage in 2002 was 80%, and there is evidence from active surveillance sites that the disease is no longer universal. From 1995 to 1999, the National Immunization Program and state and local health departments conducted active surveillance for varicella in three areas of the country – Antelope Valley in southern California, Travis County, Texas, and West Philadelphia, Pennsylvania. In 2 of these sites – Antelope Valley and West Philadelphia – active surveillance continued from 2000 to the present. Since the active surveillance projects began, they have covered a population of more than half a million individuals annually, and more than a million individuals annually when all 3 sites were conducting surveillance. Vaccination coverage in the sites has risen steadily since 1997, to 89% and 90% in West Philadelphia and Antelope Valley respectively. These are higher than the current coverage for varicella vaccine estimated by the National Immunization Survey for all 19 to 35 month old children in the country, which is 82.5%. This

graph shows the number of varicella cases reported by month in one of the active surveillance sites – Antelope Valley, California, beginning in 1997. Notice the typical seasonal variation. It is not shown on this graph, but the number of cases did not change very much from 1995 through 1998. But since 1999, the number of cases identified through active surveillance has dropped significantly. The seasonal pattern is much less apparent. Data from all of the active surveillance sites have shown an obvious decline in circulation of virus, with a more than 85% decrease in the number of varicella cases. Incidence has declined in all age groups, but particularly among children 1 to 4 years of age. In addition, the number of outbreaks, the number of school days missed due to varicella, and the number and rates of hospitalization have fallen dramatically.

We do not think this reduction in varicella is unique to the active surveillance sites. Several states conducting passive surveillance for varicella have also seen a major decline in cases in the last 3 years. Your efforts to vaccinate children is definitely paying off in ways we can measure. You are seeing the epidemiology of varicella changing right in front of your eyes. You are eliminating varicella as a rite of passage of childhood and you should be proud of this.

Varicella vaccine was developed in 1974 in Japan, and has been licensed in Japan and Korea since the late 1980s. It was licensed in the United States in 1995. The vaccine virus was attenuated in human diploid cells, like rubella, so it does not contain egg protein.

Varicella is a live virus. It contains the Oka-Merck strain of vaccine virus, named for the Japanese child from whom the virus was isolated, and the company that developed the U.S. vaccine. Vaccine efficacy has been estimated at up to 90% against infection, and 95% against severe disease. Vaccine efficacy estimated in clinical trials has been verified in investigations of varicella outbreaks. The duration of immunity is at least 7 to 10 years, because that's how long the cohorts have been followed. Immunity is probably long lasting in the majority of vaccinees. The schedule for children less than 13 years of age is one dose. The vaccine can be given simultaneously with all other childhood vaccines.

One of the most common concerns we hear about varicella vaccine has to do with waning immunity and breakthrough disease. We asked Dr. Aisha Jumaan, team leader of varicella activity for the National Immunization Program, to update us on recent investigations of these issues.

VARICELLA VACCINE WAS APPROVED FOR USE IN THE UNITED STATES IN 1995. PRELICENSURE CLINICAL TRIALS ESTIMATED VACCINE EFFECTIVENESS AT 80% TO 90%. 10% TO 20% OF VACCINE RECIPIENTS WILL DEVELOP VARICELLA DISEASE, ALSO CALLED BREAKTHOUGH VARICELLA. HOWEVER, MOST CASES ARE MILD WITH LESS THAN 50 LESIONS. PRELICENSURE TRIALS ESTIMATED PROTECTION FROM MODERATE OR SEVERE VARICELLA DISEASE AT UP TO 95%.

IN THE YEARS SINCE VARICELLA VACCINE WAS LICENSED, CDC AND STATE AND LOCAL HEALTH DEPARTMENTS HAVE INVESTIGATED VARICELLA OUTBREAKS IN A VARIETY OF SETTINGS, SUCH AS CHILD CARE CENTERS AND SCHOOLS. THE PURPOSE OF THESE

INVESTIGATIONS WAS TO ESTIMATE POSTLICENSURE VACCINE EFFECTIVENESS, AND TO TRY TO IDENTIFY RISK FACTORS FOR VARICELLA VACCINATION FAILURE.

SEVENTEEN OUTBREAK INVESTIGATIONS HAVE ESTIMATED VACCINE EFFECTIVENESS AT 71% TO 100% FOR ALL VARICELLA DISEASE, WITH MOST ESTIMATES AROUND 85%. A LARGE CASE CONTROL STUDY AMONG CHILDREN IN PRIVATE MEDICAL PRACTICES IN CONNECTICUT ALSO ESTIMATED OVERALL EFFECTIVENESS AT 87%.

EFFECTIVENESS AGAINST MODERATE OR SEVERE VARICELLA HAS CONSISTENTLY BEEN FOUND TO BE 90% TO 100%, VERIFYING THAT BREAKTHROUGH VARICELLA IS MUCH LESS SEVERE THAN VARICELLA IN THE ABSENCE OF VACCINATION. TWO OUTBREAK INVESTIGATIONS ESTIMATED VACCINE EFFECTIVENESS OF 44% TO 59%. THE REASON OR REASONS THESE TWO ESTIMATES ARE SO MUCH LOWER THAN ALL THE OTHERS IS NOT CLEAR. HOWEVER, WE GENERALLY INVESTIGATE OUTBREAKS THAT ARE UNUSUAL, AND THESE TWO OUTBREAKS WERE NOT REPRESENTATIVE OF TYPICAL VARICELLA OUTBREAKS.

WHENEVER POSSIBLE DURING STUDIES OF VARICELLA VACCINE EFFECTIVENESS, INVESTIGATORS HAVE ATTEMPTED TO IDENTIFY RISK FACTORS FOR VACCINE FAILURE. ONE OF THE RISK FACTORS FOR BREAKTHROUGH VARICELLA OF GREATEST INTEREST TO INVESTIGATORS IS TIME SINCE VACCINATION. IF BREAKTHROUGH VARICELLA INCREASED WITH INCREASING TIME SINCE VACCINATION, THIS WOULD SUGGEST WANING OF VACCINE INDUCED IMMUNITY OVER TIME. THREE INVESTIGATIONS HAVE FOUND THAT PERSONS VACCINATED 3 TO 5 YEARS EARLIER WERE MORE LIKELY TO DEVELOP BREAKTHROUGH VARICELLA THAN THOSE VACCINATED MORE RECENTLY. HOWEVER, THE MAJORITY OF INVESTIGATIONS THAT WERE OF SUFFICIENT SIZE TO INVESTIGATE THIS ISSUE DID NOT IDENTIFY TIME SINCE VACCINATION AS A RISK FOR VACCINATION FAILURE. THE LARGE CASE CONTROL STUDY OF CONNECTICUT CHILDREN FOUND THAT EFFECTIVENESS DECREASED FROM 97% IN THE FIRST YEAR TO 84% IN YEARS TWO THROUGH 8 FOLLOWING VACCINATION.

AGE OF VACCINATION HAS ALSO BEEN A CONCERN. SOME CHILDREN MAY STILL HAVE CIRCULATING MATERNAL ANTIBODY AFTER THE FIRST BIRTHDAY. IF THIS IS THE CASE, CHILDREN VACCINATED CLOSER TO A YEAR OF AGE MIGHT HAVE A HIGHER RISK OF VACCINE FAILURE BECAUSE OF MATERNAL ANTIBODY INTERFERENCE THAN THOSE VACCINATED A FEW MONTHS LATER. SIX INVESTIGATIONS HAVE FOUND A RELATION BETWEEN AGE OF VACCINATION AND BREAKTHROUGH VARICELLA. MOST HAVE FOUND THE RISK OF BREAKTHROUGH VARICELLA 3 TO 4 TIMES HIGHER AMONG CHILDREN VACCINATED AT 12 TO 14 MONTHS OF AGE COMPARED TO THOSE VACCINATED AT 15 MONTHS OR OLDER. HOWEVER, THIS IS ALSO NOT A CONSISTENT FINDING IN OUTBREAK INVESTIGATIONS. MOST INVESTIGATIONS HAVE NOT IDENTIFIED AGE AT VACCINATION AS A RISK FACTOR FOR BREAKTHROUGH VARICELLA.

ANOTHER RISK FACTOR THAT HAS BEEN IDENTIFIED FOR VARICELLA VACCINE FAILURE IS THE PRESENCE OF ASTHMA. TWO INVESTIGATIONS HAVE FOUND AN INCREASE RISK OF BREAKTHROUGH VARICELLA AMONG CHILDREN WITH ASTHMA. HOWEVER, THESE STUDIES DID NOT INCLUDE INFORMATION ABOUT MEDICATION, SUCH AS STEROIDS, THAT THE CHILD MAY HAVE BEEN TAKING. A RETROSPECTIVE COHORT STUDY EXAMINED THE EFFECT OF BOTH ASTHMA AND SYSTEMIC STEROIDS. THIS STUDY FOUND AN INCREASED RISK FOR CHILDREN TAKING STEROIDS BUT NOT FOR THOSE WITH ASTHMA WHO WERE NOT TAKING STEROIDS.

TAKEN AS A WHOLE, THESE POSTLICENSURE INVESTIGATIONS HAVE CONFIRMED PRELICENSURE ESTIMATES OF VARICELLA VACCINE EFFECTIVENESS AGAINST ALL VARICELLA DISEASE, AND ESPECIALLY AGAINST MODERATE AND SEVERE ILLNESS. ALTHOUGH THE RESULTS OF A FEW STUDIES HAVE SUGGESTED OTHERWISE, MOST INVESTIGATIONS HAVE NOT IDENTIFIED AGE AT VACCINATION OR TIME SINCE VACCINATION AS RISK FACTORS FOR BREAKTHROUGH VARICELLA. IT IS NOT CLEAR

WHETHER ASTHMA OR STEROID USE AT THE TIME OF VACCINATION INCREASES THE RISK OF BREAKTHROUGH DISEASE. UNTIL MORE DEFINITIVE INFORMATION BECOME AVAILABLE, THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES WILL CONTINUE TO RECOMMEND A SINGLE DOSE OF VARICELLA VACCINE FOR ALL CHILDREN AT 12 TO 18 MONTHS OF AGE. HOWEVER, ACIP WILL CONTINUE TO MONITOR RESEARCH IN THIS AREA TO ASCERTAIN THE POSSIBLE BENEFIT OF CHANGES IN THE RECOMMENDED IMMUNIZATION SCHEDULE.

The ACIP recommendations for the use of varicella vaccine were published in July 1996, with an update published in 1999. The ACIP and the American Academies of Pediatrics and Family Physicians agree on how this vaccine should be used.

Both the ACIP and the Academies recommend routine vaccination of all susceptible children at 12 to 18 months of age. This age recommendation is to avoid interference with circulating maternal antibody to varicella. Since almost all women in the U.S. have had varicella, almost all infants are born with antibody. That is why the vaccine should not be given until at least 12 months of age, because of potential interference from circulating maternal antibody. The vaccine is also recommended for all susceptible children by the 13th birthday. It can be given at any time up to that age, with the adolescent visit at 11 or 12 years of age as a good final check point for varicella immunity. So what do we mean by susceptible? A susceptible child is one without a reliable parental history of chickenpox. Routine serologic testing of children is not warranted, because the vast majority of children less than 13 years of age without a clinical history of chickenpox are susceptible.

If varicella vaccine is not given simultaneously with MMR, the two vaccines should be separated by 4 weeks. If varicella and MMR vaccines are **not** given on the same day, but are separated by less than 4 weeks, ACIP now recommends that the vaccine given **second** should be repeated. This is because of the possibility of interference from the vaccine given **first** with the vaccine given second. The repeat dose should be given 4 weeks after the vaccine given second.

Since licensure in 1995, varicella vaccine, like other live virus vaccines, has been contraindicated in persons with significant immunodeficiency from any cause. As a result, most immunocompromised persons should not be vaccinated. But available data indicates that varicella vaccine is both effective and safe in persons with impaired humoral immunity. This includes persons with hypogammaglobulinemia and other selective B cell immune deficiencies. Humoral immunodeficiency alone is no longer considered a contraindication to varicella vaccine. ACIP now recommends that you routinely vaccinate persons with isolated humoral immunodeficiency. Varicella vaccine was previously contraindicated in persons with HIV infection, mainly because of lack of safety or efficacy data in this group. Data from a clinical trial among children with asymptomatic or mildly symptomatic HIV infection showed that two doses of

vaccine was both immunogenic and effective. Because children with HIV infection are at increased risk of morbidity from varicella, and from herpes zoster, ACIP now recommends that providers consider varicella vaccination for asymptomatic or mildly symptomatic HIV infected children. Specifically, this recommendation includes children with age specific CD4 T cell percentage of 25% or higher who are in CDC class A1 or N1. Eligible children should receive 2 doses of varicella vaccine separated by 3 months. The use of varicella vaccine in children with more severe manifestations of HIV infection is currently being investigated. Other contraindications for varicella vaccine have not changed. We will discuss them a little later.

Susceptible adolescents and adults should also be vaccinated. These groups will require 2 doses separated by 4 to 8 weeks. You should recommend the vaccine to all susceptible persons – that is, anyone without a reliable history of varicella. However, special efforts should be made to target two groups of older children and adults. First, you should target susceptible older persons who, if they were to develop varicella, are likely to expose persons at high risk for severe illness. Candidates in this group would include healthcare workers, and household contacts of immunocompromised persons.

The second target population is persons who are themselves at high risk of exposure, such as teachers and college students, and, again, healthcare workers.

In December 1997, ACIP issued a comprehensive set of recommendations for the protection of healthcare workers against vaccine preventable diseases. In this statement, ACIP recommends varicella vaccine for all susceptible healthcare workers. Prevaccination serologic screening for varicella immunity of certain personnel is probably cost effective. Screening could be considered for workers who are uncertain of their varicella history, or who claim not to have had the disease. But postvaccination testing for varicella immunity is not necessary or recommended because 99% of recipients are seropositive after the second dose. Most commercial antibody tests are not sensitive enough to detect antibody in some vaccinated people. So postvaccination testing can make your life more difficult, because it will appear that you have more vaccine failures than you actually do.

Investigations have also shown that varicella vaccine is effective in preventing or modifying the severity of chickenpox if used shortly after exposure. ACIP recommends varicella vaccine for use in susceptible persons after exposure to varicella. The vaccine is 70% to 100% effective if given within 72 hours, and possibly up to 5 days following exposure. The vaccine is not effective if given more than 5 days after exposure, but will produce immunity in the recipient if the person has not been infected with wild varicella virus. If the exposure to varicella results in infection, there is no evidence to indicate that administration of varicella vaccine before onset of illness increases the severity of disease or the risk of vaccine adverse reactions. These recommendations were published in 1999 in a supplemental varicella vaccine ACIP statement. This statement also contains

updates on adverse reactions following vaccination including development of herpes zoster, and transmission of vaccine virus. We will tell you how to get a copy of this and other ACIP recommendations at the end of the program.

Varicella vaccine is usually very well tolerated, and significant adverse reactions are not common. The most common adverse reaction is an injection site complaint, such as pain, swelling and redness. You might not have expected this from a live vaccine, but injection site complaints are reported in about 20% of recipients. 3% to 4% of recipients will develop a varicella-like vesicle at the site of injection. Generalized rash, is reported in 4% to 6% of recipients. The rash may be maculopapular rather than vesicular, and has an average of only 5 lesions. Systemic reactions, like fever, are not common.

Varicella vaccine virus becomes latent, like the wild virus does. So herpes zoster, or shingles, would be expected. And in fact, there have been a few reports of varicella zoster in vaccine recipients. Most cases of zoster after vaccination have been reported in children. This would make sense since most vaccine has been given to children. Vaccine virus has been isolated from only a few of these children. Wild varicella virus has been isolated in some cases. Based on current data, the risk of zoster from vaccine virus appears to be less than the risk of zoster from wild varicella virus. In addition, zoster after vaccine has been mild and without complications, such as post herpetic neuralgia. This issue will continue to be monitored. Can the vaccine prevent shingles in people **already** infected with wild varicella virus, like you and me? It is possible. Studies to examine this are being conducted now. Studies to examine the role of vaccine in prevention of zoster are now being completed, with initial results expected in the next year or so.

The contraindications to varicella vaccine are almost identical to those of the other live virus vaccines. A severe allergic reaction to a vaccine component, or following a prior dose of vaccine is right there at the top of the list. In the case of varicella vaccine, this would include severe allergy to neomycin and gelatin. Varicella vaccine contains no egg protein. Pregnancy and immunosuppression are also contraindications to vaccination. We discussed the use of varicella vaccine in persons with HIV infection and humoral immunodeficiency a little earlier. Varicella vaccine is still contraindicated for children with immunodeficiency from HIV, or with other types of immunodeficiency. HIV testing prior to vaccination with varicella vaccine is not necessary or recommended. Varicella vaccine is also recommended for administration to healthy household contacts of an immunosuppressed person. The rationale is that if the healthy household contact is **not** immune to varicella from vaccination, he or she will eventually develop varicella disease, and expose the immunocompromised household contact to a much greater risk from wild virus. The effect of varicella vaccine on a fetus is unknown, but is probably minimal, since even wild varicella poses only a small risk. ACIP and AAP recommend that women be advised to avoid pregnancy for 1 month after receiving varicella vaccine, even though the package insert suggests 3 months. Also note, a pregnant household contact is **not** a contraindication to vaccination of a child. As with all vaccines, moderate or severe acute illness is a precaution. Vaccination should be deferred until the

acute illness has improved. Finally, a recent blood product could interfere with viral replication. The recommendation is to administer the vaccine at least 3 weeks prior to receiving blood products. Vaccination should be delayed for at least 3 months following administration of blood, immune globulin, or other blood products. The interval depends on the type of blood product. A table listing these intervals is in the General Recommendations on Immunization, and in Appendix A of your text. If the interval between the blood product and vaccine is less than 3 months, you could either test the person for antibody, or just administer another dose of vaccine.

Concerns about vaccinating healthy household contacts of immunosuppressed people or pregnant women are due to fears of transmission of vaccine virus. There have been reports of transmission of vaccine virus, but this appears to be a rare event. Studies of household contacts of vaccinated people have demonstrated that **asymptomatic** transmission of vaccine virus may occur. Household contacts have been observed to develop varicella antibody without having been vaccinated or having chickenpox. It appears that the risk of transmission is increased if the vaccinee develops a rash following vaccination. In fact, transmission may **only** occur when the vaccinee develops a rash. So if a vaccinated child develops a rash, it is recommended that close contact with susceptible persons at high risk of complications of varicella, such as immunocompromised people, be avoided until the rash is gone. This will also be an issue for those of you who work in employee health. You will probably need to develop procedures to prevent transmission between your vaccinated employees and their high risk patients.

We discussed vaccine storage and handling in the first session of this course. Because varicella vaccine is particularly fragile, we would like to remind you of its storage requirements. Varicella vaccine **must** be kept frozen. It must be shipped with dry ice, and must be stored at -15° Celsius, or colder. Varicella vaccine should only be stored in freezers, or combination refrigerator-freezers with separate doors and compartments. If optimal handling conditions for varicella vaccine are not feasible, or the vaccine is to be transported to a distant site, the vaccine may be stored up to 72 hours at refrigerator temperature, which is 35° to 46° Fahrenheit. But any unused vaccine must be discarded after 72 hours at this temperature. Varicella vaccine must be administered within 30 minutes of reconstitution. If not used within 30 minutes, the vaccine should be discarded. No one can know too much about vaccine storage and handling. There is information about vaccine storage and handling in your book, and on our broadcast resources website