THE NORTHERN HOSPITAL

CHICKEN POX (VARICELLA ZOSTER)

"The Milkmaid", c1658, Johannes Vermeer, oil on canvas,
Rijksmuseum, Amsterdam, Netherlands.

Where are you going to, my pretty maid?
I'm going a milking, sir, she said
May I go with you, my pretty maid?
You're kindly welcome, sir, she said
What is your father, my pretty maid?
My father's a farmer, sir, she said
What is your fortune, my petty maid?
My face is my fortune, sir, she said.

18th Century Anonymous

"In 1736, I lost one of my sons, Francis, a fine boy of 4 years old by the smallpox. I long regretted bitterly and still regret that I had not given it to him by inoculation. This I mention for the sake of parents, who omit the operation on the supposition that they should never forgive themselves if the child died under it: my example shows the regret may be the same either way, and that therefore, the safer should be chosen."

Benjamin Franklin, Autobiography 1791

So wrote Benjamin Franklin towards the end of his life reflecting back on the death of his small son over half a century after the event. In his old age he makes an impassioned plea to all parents to vaccinate their children with "variolation", should they suffer the same loss as himself. However in the context of the early Eighteenth century one can well understand the hesitation that any parent would have had in submitting their children to "variolation". Smallpox had been one of the scourges of mankind since recorded history. If a person survived it they would often be horribly disfigured thereafter. The 19th century British historian, Thomas Macaulay described it's ravages thus, "Tormenting with constant fears all whom it had not yet stricken, leaving on those whose life it spared the hideous traces of it's power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of the betrothed maiden objects of horror to the lover."

The only known defense against it was the practice of variolation a primitive form of vaccination involving scratching the skin with a needle infected with the smallpox virus. However this practice was very controversial even among the medical profession. It was a rather desperate undertaking as the fatality rate of the procedure was estimated at two percent, but this had to be compared with a fatality rate of thirty percent in those who contracted the disease naturally. In 1716 Lady Mary Wortely Montagu, the wife of the British ambassador to Constantinople, and a notable beauty of the time had contracted smallpox and survived, however her face was left severely pock marked by the disease. Against the advice of the embassy Chaplin who regarded the practice as "unchristian", she had her son variolated, and he was protected against smallpox thereafter. She took the news and evidence back to London and in due course the practice spread within England and thence to the Americas.

At the end of the Eighteenth century, just a few years after Franklin's death Edward Jenner made one of the greatest medical advances in history. It was known throughout rural England of the time that the fairest skinned women in the land appeared to be the

milkmaids. One theory was that they were protected from the ravages of smallpox through having contracted cowpox, a disease similar to smallpox, though without its lethality. In 1796 Jenner decided to carry out the definitive experiment. He inoculated a small boy of eight years of age by the name of James Phipps, with the cowpox virus. Then with supreme courage and nerve (on the part of both himself and the boy,) he deliberately infected the boy with smallpox. The boy was completely protected. Dr Jenner's fame and the practice of cowpox vaccination then spread rapidly throughout England and Europe. A safe way of protection against smallpox had been found and the modern method of vaccination was born. Napoleon Bonaparte was so impressed by the safeness and effectiveness of the new vaccination that he declared he would not refuse Doctor Jenner any request.

Since Dr Jenner's time vaccination of smallpox has been so successful that it has been eliminated from the world. In the 21st century another similar, though far less deadly pox is still with us, in the form of chickenpox. Although less deadly than smallpox it nonetheless can have serious complications and can still be fatal in the immunocompromised. We would do well to remember the sad words of Benjamin Franklin in his autobiography and strongly consider vaccination against this pox, for our children. We should be grateful that this is a far easier choice than was variolation for Benjamin Franklin.

The Milkmaid, oil on canvas, William Edward Milner, (1849-1895)

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Introduction

Chickenpox (Varicella) is a highly contagious disease caused by the **varicella zoster virus.**

Although people of all ages are affected, most cases occur in children under the age of five years.

More than 90 % of people have been infected by the age of 15 years.

Varicella-zoster virus (VZV) infection causes two clinically distinct forms of disease:

Varicella (chickenpox):

- Primary VZV infection results in the diffuse vesicular rash of varicella, or chickenpox.

And

Herpes zoster (shingles):

- Endogenous reactivation of latent VZV typically results in a localized skin infection known as herpes zoster, or shingles.

Chickenpox tends to be a more severe disease adults than in children.

Infants, the immunosuppressed, and **pregnant women** are at highest risk of **severe disease.**

Anti-herpes agents are not routinely required, in children > 1 year and < 12 years) but should be given to the **immunosuppressed, very unwell, or those with significant complications**, and should be considered in adults.

Post exposure protection of the non-immune can be archived with the live-attenuated vaccine if given with **5 days.**

If live-vaccine is contraindicated the varicella-zoster immunoglobulin can be given in the non-immune within **96 hours (i.e. 4 days).**

Chickenpox is a vaccine preventable disease

See also separate documents on:

- **Herpes Zoster (Shingles) (in Infectious Diseases folder)**
- **Acyclovir (in Drugs folder).**

History

It is unknown for how long the Old World disease, chickenpox, has been a human affliction, but possibly for thousands of years

In the Middle Ages, various infectious "poxes" where defined, amoung these were included the **Great Pox (syphilis), the Smallpox, the Cowpox,** and **the Chickenpox**.

Some accounts credit the Italian physician, **Giovanni Filippo** (1510 - 1580) of Palermo, student of the great anatomist, Andreas Vesalius of Brussels, with the first medical description of varicella (chickenpox). Being of somewhat delicate constitution, however, that is as far as Giovanni's contribution to the field of Infectious Diseases went, preferring to refer on his cases to those "base physicians who attend to... poor, sickly looking people full to overwhelming with the coarsest and filthiest of humours".

The English physician **Richard Morton** (1637 - 1698) considered chickenpox to be a mild form of smallpox, but it wasn't until 1767 when the English physician **William Heberden**, (1710 - 1801) demonstrated for the first time that chickenpox was in fact a different disease to smallpox.

The origin of the term "chickenpox" is lost in the obscurity of distant centuries, but speculations have included:

- **Samuel Johnson** suggesting that the disease was "no very great danger" thus a "chicken" version of the small pox
- That the vesicles looked like the skin of plucked chickens.
- That it was named after chick peas, due to a supposed similarity in size of the seed and the lesions
- That the term reflected a corruption of the Old English word "giccin" meaning "itchy"
- That a "pox" in the Middle Ages was a black magic curse placed onto children, (*…a pox be upon ye, and all ye descendants, being an example of a particularly powerful incantation against one's enemies*).

Epidemiology

Varicella-zoster virus (VZV) is one of 8 herpes viruses known to cause human infection and is distributed **worldwide.**

Chickenpox is endemic in Australia

It becomes *epidemic* among *susceptible* individuals.

More than 90 % of cases are children aged one to 14 years.

More than 90% of people have been infected by the age of 15 years.

The epidemiology of varicella changed dramatically in the US since the introduction of the varicella vaccine in 1995. Prior to 1995 the Centers for Disease Control and Prevention (CDC) estimated the yearly incidence of chickenpox in the United States at approximately four million cases with nearly 11,000 admissions and 100 deaths.

Although children were most commonly affected by varicella, **adults** and **infants less than one year of age** were overrepresented among those who developed complicated disease with high rates of mortality. [2]

One decade after the introduction of the varicella vaccine, overall varicella incidence in active surveillance sites had declined by 90 %.

The rate of complications from varicella infection have also declined dramatically after the introduction of the vaccine.

Pathology

Organism

- The causative agent is the **varicella zoster virus** (VZV)

  It is also known as human herpesvirus 3 (HHV-3)

- It is a member of the herpes virus family and is a DNA virus.

Reservoir

- Humans

Transmission

Chicken pox is **highly** contagious, (second only to measles)

In general terms infectiousness compared to other vaccine preventable illnesses is as follows: [4]

Measles > Varicella > mumps and rubella.

Shingles (zoster) has a *much lower* rate of transmission, (the non-immune contact develops chicken pox).

Those who are infected from others will develop chickenpox (not shingles)

Chickenpox can be transmitted from person to person by:

- Direct contact of vesicle fluid (from patients with either chickenpox or shingles).
- Droplet or airborne spread of secretions from the respiratory tract
- Indirect contact through articles freshly soiled by discharges from vesicles of infected persons, (however the virus does not long survive in the environment).

Scabbed lesions are *not* infective.

Incubation Period

The incubation period ranges from 10 - 21 days

Most commonly it is around 14 - 16 days.

This period may be prolonged:

- In immunosuppressed persons
- Following immunoglobulin administration as passive immunization against varicella.

Period of communicability

- Chickenpox is usually communicable for up to 48 hours before the onset of the rash, until crusting of *all* lesions has occurred.
- Communicability may be prolonged in patients with altered immunity.
- Those with zoster may be also infectious until the lesions have crusted (at around one week).

Susceptibility & resistance

- Chickenpox is a highly contagious disease, infection is universal among those not previously infected

  Shingles (i.e. *as a cause of chickenpox in others*) is not as contagious as chickenpox.
- Neonates whose mothers are not immune and immunosuppressed patients may suffer severe, prolonged or fatal chickenpox.
- Recovery from primary varicella infection usually provides immunity for life.
- In otherwise healthy people, a second occurrence of varicella is uncommon and usually occurs in people who are immunocompromised.

- As with other viral infections, re-exposure to natural (wild-type) varicella may lead to re-infection that boosts antibody titers without causing illness or detectable viremia

- Chickenpox may still occur in up to 2 % of those vaccinated, however the disease is usually only mild.

Clinical Features

Varicella is usually a mild disease in healthy children, however a number of *rare but serious complications* may occur.

The severity of symptoms can range from asymptomatic, to mild disease with very few vesicular lesions to florid disease with extensive rash.

The disease tends to be more severe in adults.

Cases of varicella in vaccinated persons (that is, "breakthrough cases") are generally much milder, with a lower fever and more rapid recovery.

Severe, even fatal illness can occur in **high risk** groups, which include:

- **The immunocompromised, including:**
    - ♥ **Patients with Hematological malignancies**
    - ♥ **Patients on chemotherapy or high-dose steroids**
    - ♥ **Patients with HIV**
- **Newborns (< 1 month)**
- **Pregnant women**

It is important to ascertain the following:

1. Has there been any recent contact with a case of chickenpox or shingles?
2. Has the patient been vaccinated?
3. Does the patient have any immunocompromise?
4. Is the patient (or could the patient be) pregnant?

Typical cases show:

1. Following the incubation period there is abrupt onset of 1-2 days of a non specific "prodrome", before the rash appears.

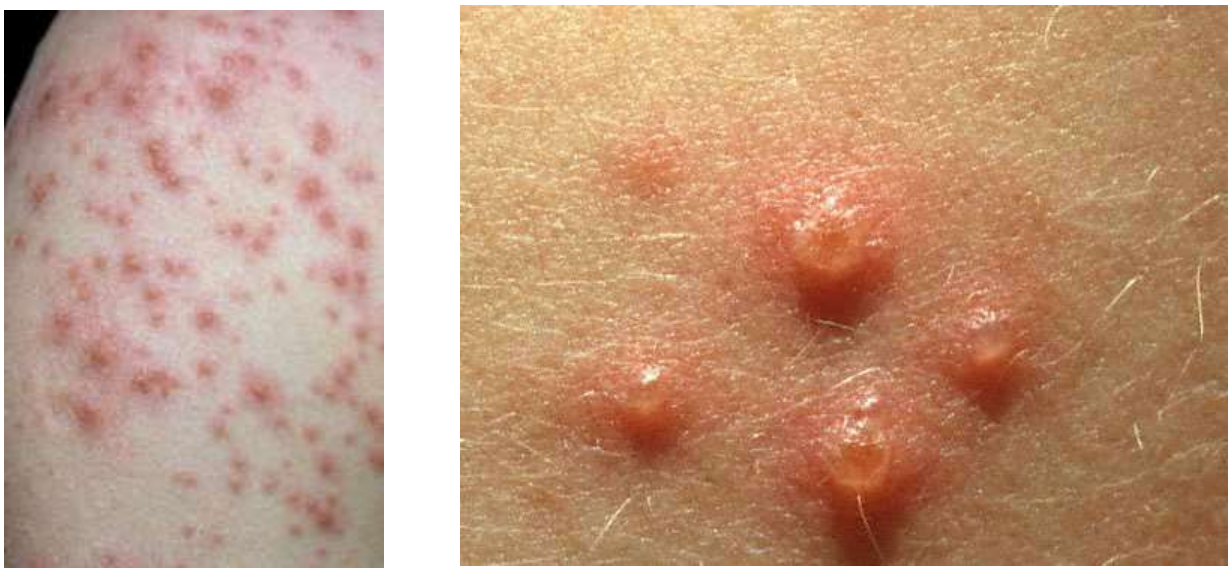
   In some cases, however, the rash may be the initial manifestation of the disease, (particularly in children).

   - Fever
   - Non specific "constitutional" symptoms:
     - ♥ Lethargy/ malaise
     - ♥ Myalgias
     - ♥ Anorexia/ nausea/ vomiting
     - ♥ Headache

2. Rash:
   The evolution of the rash generally occurs over **4-5** days as follows:

   Macules → papules → vesicles → pustular type lesions → crusting lesions

   Crusting scabs can then last **1-2 weeks.**



Typical appearance of the vesicular eruption of chickenpox.

The vesicular rash typically occurs as successive crops in various stages of evolution.

Lesions are most numerous on the trunk (chest and back) and less so on the face, scalp, limbs

An enanthem may also occur, i.e lesions within the mouth and throat.

Lesions can be pruritic.

Complications

1. Viral Pneumonia:

    - This can be a severe complication in adults, it may be fatal in the immunocompromised.

2. Pregnancy [1]

    - Varicella infection during the first trimester of pregnancy confers a small risk of miscarriage.

    - Maternal infection before 20 weeks rarely may result in the fetal varicella zoster syndrome, with the highest risk (2 per cent) occurring at 13 - 20 weeks. Clinical manifestations include growth retardation, cutaneous scarring, limb hypoplasia and cortical atrophy of the brain.

    - Intrauterine infection can also result in herpes zoster in infancy. This occurs in less than 2 per cent of infants.

    - The highest risk is associated with infection in late pregnancy. In the third trimester, maternal varicella may precipitate the onset of premature labour.

    - Severe maternal varicella and pneumonia at any stage of pregnancy can cause fetal death.

3. Infection in the newborn: [1]

    - Where newborns develop varicella before 10 days of age, or when maternal chickenpox develops within 7 days of delivery and up to 48-hours postpartum, the neonatal fatality rate is up to 30 per cent without treatment.

    - Treatment of mothers and newborns is vital

4. Secondary bacterial infection of skin lesions.

5. Reye's syndrome:

    - An acute encephalopathy with fatty infiltration and dysfunction of the liver.

6. Encephalitis/meningitis.

7. Rare neurological sequelae:
    - Gillian Barre syndrome.
    - Transverse myelitis
    - Acute cerebellar ataxia, (usually seen in children)
8. Hepatitis
9. "Shingles", (i.e. **herpes zoster**):
    - This occurs as a result of reactivation of latent virus within the dorsal root ganglia, in a period of waning immunity.
    - It is most commonly seen in the elderly.

Investigations

Blood tests:

1. FBE:
    - Thrombocytopenia may occur
2. CRP
3. U&Es / glucose
4. LFTs
5. Serology:
    - IgM antibody:
        - ♥ A positive IgM result indicates recent infection.
    - IgG antibody:
        - ♥ A positive IgG result coupled with a negative IgM result indicates previous vaccination to or infection with VZV.

          These individuals are considered to have protective immunity to reinfection.

PCR testing for VZ virus.

This can be done on:

- **Skin lesion, vesicular fluid**
- CSF
- Urine
- Blood
- Saliva

Viral culture:

Virus isolation by culture is sometimes available but is insensitive and associated with low yield (approximately 60 - 75 %) when compared with PCR testing .

Specific VZV culture isolation from a swab of vesicular skin lesion or sterile body fluid, such as CSF, typically requires prolonged incubation with a turnaround time of one to two weeks.

Sensitivity of culture also declines when lesions progress beyond the vesicular stage.

CXR:

Features typical of a viral pneumonia may be seen with bilateral diffuse reticular or alveolar type infiltrates and peri-bronchial thickening.

Pulmonary lesions usually resolve within 10 days, but may persist for months.

Occasionally lesions may calcify and become permanent.

Management

Most cases can be managed symptomatically.

For more unwell patients:

1. Attend to any immediate ABC issues as required
    - Monitoring of oxygenation and oxygen therapy as required is important in cases of viral pneumonia.

      Give oxygen as required to the hypoxic patient
2. IV fluids as required

3. Analgesia as required:

   - Simple oral analgesia is usually sufficient:
   - Paracetamol
   - Aspirin should be **avoided** in **children** and **adolescents** because of the association with Reye's syndrome. Paracetamol is a better option for "constitutional" symptoms in children.

4. Pruritus:

   - Non-sedating antihistamines
   - Sedating antihistamines may be suitable at night

5. Anti-herpes virus agents:

   Children (> 1 year and < 12 years):

   Anti-herpes virus agents are not normally necessary in most children > 1 year and < 12 years who are not significantly unwell, and have normal immune systems and uncompleted disease.

   Adults: [2]

   For adults who are not unwell, nor immunocompromised, with uncomplicated disease some would give oral acyclovir.

   Although most adults who develop varicella have an uncomplicated course, they are at increased risk of developing pneumonia, which often leads to hospitalization and carries an increased risk of mortality.

   Antiviral therapy is given even if they were previously vaccinated.

   Antiviral therapy can reduce the duration and severity of symptoms in adults, and there is a theoretical benefit of antiviral therapy in reducing complications.

   Severe, Complicated and High Risk Patients:

   Anti-herpes virus agents should be given (irrespective of rash duration) for:

   - Immunocompromised patients:
     - ♥ Including patients with chronic pulmonary disorders.
   - If the disease is severe

- Neonates
- Pregnant women
- Patients with pre-existing skin disease (e.g. eczema)
- If the disease is complicated, including:
    - ♥ Pneumonia
    - ♥ Neurological complications such as encephalitis

For immunosuppressed patients or those with significant complications intravenous acyclovir rather than oral therapy is preferred.

Relatively higher doses of acyclovir are used to treat VZV compared with herpes simplex virus (HSV). VZV is less usually less susceptible to acyclovir than herpes simplex virus.

The typical duration of treatment is **7 - 10 days.** Intravenous therapy is continued until no new lesions are occurring. Patients can then be transitioned to oral therapy until **all** of the lesions have **crusted.**

See latest therapeutic guidelines for exact dosing regimens.

Isolation:

Cases of chickenpox (or suspected chicken pox) should be nursed in a specialized isolation room, using airborne spread precautions.

Pregnant non-immune and **non-immune staff** in general should avoid tending these patients.

Immunization:

Routine immunization against varicella zoster virus (VZV) reduces:

- Varicella (chickenpox):
    - ♥ Routine immunization with two doses of varicella vaccine is at least 90% effective in preventing primary varicella infection and is 99% effective in preventing severe varicella disease. [2]
- Disease severity in breakthrough cases
- The risk of transmission to others

"Herd" immunity extends protection to infants too young to be vaccinated and unvaccinated adults

Routine immunization is recommended at:

- **18 months**

And

- **12-13 years**

Chickenpox may still occur in up to 2% of those vaccinated, however disease is usually mild. [2]

Note that the VZV is a *live attenuated* virus, and as such should not be given in pregnancy or to the immunosuppressed. In addition vaccinees should not become pregnant for 1 month after vaccination.

For full vaccination information see, latest edition of The Australian Immunization Handbook.

Post-exposure Prophylaxis:

Essential factors to consider prior to providing post-exposure prophylaxis include:

- An assessment of the exposure itself.
- The risk of severe infection
- The patient's vaccination status

Post Exposure Prophylaxis can be achieved with *either* **vaccination** or with **herpes zoster immune globulin** (in those with contraindications to live-vaccination) in high-risk groups who have had a significant exposure.

Significant exposure is defined as living in the same household as a person with active varicella or herpes zoster, or direct face-to-face contact with a person with varicella or zoster for at least 5 minutes, or being in the same room for at least one hour. [2]

Note that immunoglobulins can interfere with the response to live attenuated virus vaccines by preventing vaccine strain viral replication after vaccine administration.

Therefore, administration of live attenuated vaccine viruses such as varicella zoster and measles should be deferred for at least 3 months after the IM administration of immunoglobulin.

For the same reason immunoglobulin products should not be administered until at least 2 weeks after a vaccine has been given.

Note that inactivated vaccines such as tetanus, hepatitis B and rabies may be administered concurrently with "passive antibody" immunoglobulin, providing separate syringes and separate injection sites are used, (The Australian Immunization Handbook, 8th ed 2003, p.160)

VZ vaccination is usually successful if given to the non-immune within **5 days after exposure**. The earlier it is given, however the more effective it will be.

If exposure has occurred in a **high risk patient** (or a in a patient who cannot have the live vaccine), varicella **zoster immune globulin (VZIG)** should be given.

VZIG is effective in modifying or preventing the disease if administered within **96 hours of exposure.**

Exposed patients should be tested for varicella-zoster antibodies to assess their immune status before VZIG is given. The sample should be marked urgent and the laboratory notified by phone. Results can be available the same day.

High risk patients who should especially receive post exposure VZIG prophylaxis include:

1. Neonates, including:
    - Those with post natal exposure.
    - Newborns of mothers who develop chickenpox within five days prior to, or within 48 hours after, delivery.
2. Pregnant women
3. Patients with significant immunocompromise, including leukaemias.
4. Those with severe generalized eczema, (to prevent an eczema herpeticum type syndrome. This is normally due to herpes simplex)

For full Post-exposure Prophylaxis information see, latest edition of The Australian Immunization Handbook.

Notification:

Varicella (Group B disease) must be notified in writing within 5 days of diagnosis.

This is a Victorian statutory requirement

School exclusion:

Cases should be excluded until all blisters have dried.

This is usually at least **5 days after the rash appears** in **unimmunized children**, but may be less in previously immunized children.

Any child with an immune deficiency or receiving chemotherapy should be excluded for their own protection. Otherwise, immune contacts are not excluded.

Dr Edward Jenner performs the first vaccination on 8 year old James Phipps on 14 May 1796, oil on canvas, c. 1910, Ernest Board.

References

1. The Blue Book Website, Accessed November 2016.

2. Mary A Albrecht et al. Chickenpox in Up to Date Website, 8 February 2016.

3. The Australian Immunization Handbook, 10th ed

4. Chickenpox in CDC Website, Accessed November 2016.

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Reviewed November 2016.