THE NORTHERN HOSPITAL

MEASLES

"Cortes entering America", from a series of 16th century panels by Miguel Gonzales in the Museo de America, Madrid.

In 1518 Hernan Cortes and his 600 "Conquistadors" in one of the most startling military feats in history, defeated the Aztec nation then numbering in the millions.

He landed on the gulf coast to find himself in a world of pyramids and human sacrifice, of stone tools and flint knives. There could be no compromise between Catholic Spain and this fantastic Neolithic structure. The Aztecs hurled themselves forward to be slaughtered by the arquebuses, swords and pikes of Cortes' tiny army. And also and by disease. For even more deadly than the invader's weapons and technology were the new microbes bought with them from the "Old World". Disease annihilated whole villages and in time millions would succumb to these new diseases for which they had never previously been exposed".

Colin McEvedy

Deadliest among these diseases were smallpox, influenza and above all measles. Ultimately only the 20th century technology of vaccination could have saved the Aztec civilization.

MEASLES

Introduction

Measles (also occasionally known as rubeola - and not to be confused with rubella) is a **highly infectious**, acute viral illness spread by respiratory secretions, via aerosol transmission.

It is a disease that is often misunderstood by the public and even some health care professionals as a "mild" disease. Often enough however it is **not mild at all** and may have immediate or delayed lethal complications.

Measles should be suspected in patients (adults as well as children) who present with typical features, particularly:

- During outbreaks
- If they are not *fully* vaccinated (two measles vaccines)
- There is uncertainty of vaccination status.

There is no specific treatment once measles is contracted, it is therefore entirely supportive.

For a suspected case in the ED, these patients should:

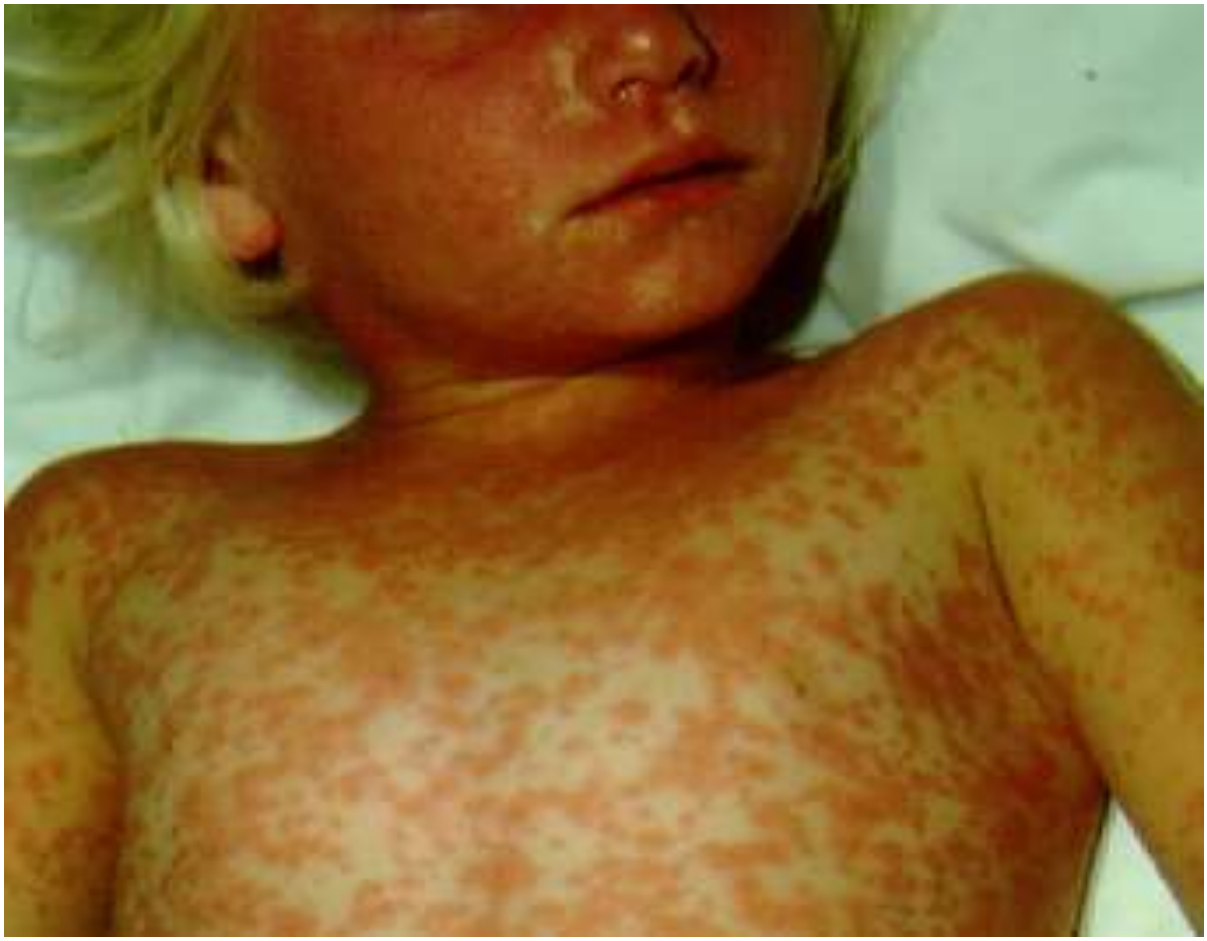
- **Not be kept in the general waiting area.**
- **Given an N95 face mask**

- **Be assessed in an isolation (negative pressure) room.**

- **Be admitted until such time as measles has been excluded, IgM serology and/ or PCR testing.**

Additionally:

- Leave vacant all consultation rooms used in the assessment of patients with suspected measles for at least 30 minutes after the consultation.



Typical measles rash

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History

Measles has been one of humanity's greatest scourges.

Estimates based on modern molecular biology place the emergence of the measles virus as a human disease sometime after 500 AD. This information therefore discounts

previous speculation that the great Antonine Plague during the reign of Marcus Aurelius, and which killed his co-Emperor, Lucius Verus, was caused by measles.

The first scientific description of measles, and its distinction from smallpox and chickenpox, is credited to the Persian physician **Rhazes** (860 - 932 A.D).

Some work indicates that the measles virus emerged from rinderpest (Cattle Plague) as a zoonotic disease between 1100 and 1200 AD. Before this period limited outbreaks possibly involved a virus not yet fully acclimated to humans.

In populations not having endemic measles, exposure can be devastating, as demonstrated by its into the new world by Europeans in the Fifteenth and Sixteenth centuries.

In 1954, the virus causing the disease was isolated from a 13 year old boy from the United States, **David Edmonston**, and adapted and propagated on chick embryo tissue culture. From this the brilliant American microbiologist **Maurice Hilleman** developed the first successful measles vaccine.

In Australia, live attenuated measles vaccine was licensed in **1968** and it was included in routine childhood vaccination schedules in **1971**.

Epidemiology

Measles is now rare in Australia and no longer has endemic spread due to the success of vaccination programs, however sporadic cases still occur, especially when the child (or adult) is unvaccinated, or partially vaccinated.

Measles may also be seen in unimmunized immigrants.

Before measles vaccination began in the **United States** in 1963, many children contracted this highly contagious disease and simply suffered through a miserable illness. Almost 500 people died each year from measles, with 1000 cases of encephalitis and 48,000 hospitalizations - in a population one third the current size. (Andrew T. Pavia, Medscape, May 02, 2019).

Although measles was declared “eliminated” from the United States in 2000, 704 cases have been reported from 22 states as of April 26, 2019.

On a global scale, measles is still a major cause of death among children under 5 years of age. In 2008, there were **164,000** measles deaths globally.

Pathology

Organism

- Measles virus is a single stranded RNA virus of the paramyxovirus family and the morbillivirus genus.

It is a genetically stable virus.

It has a short survival time in air, (< 2 hours) and is rapidly inactivated by heat light and acidic pH. [1]

Reservoir

- Humans

Transmission

- Measles is **highly contagious**, even without close direct contact.

  It is spread by airborne respiratory droplets or direct contact with infected nasal or throat secretions.

  Aerosols that can remain suspended in the air and infectious for up to 2 hours.

Incubation Period

- Approximately 10 days (range 7-18 days) from exposure to the onset of fever.
- The rash usually appears at day 14.

Period of communicability

- Measles is highly infectious from the **beginning of the prodromal period (3-5 days before the rash appears)** for **up to 4 days after the appearance of the rash.**

Susceptibility & resistance

- **Natural infection provides lifelong immunity.**

  A patient history of prior measles infection should be **confirmed serologically** before vaccination is deferred, as most reports of "clinical measles" infection are subsequently tested as **negative**.

- Note that the presence of measles antibodies will not necessarily confer protection to **immunocompromised** individuals and whilst antibody testing may be done to make a diagnosis it is not appropriate for the evaluation of "immune status" in these patients.

- Vaccination at 12 months of age produces a protective antibody in approximately 95 % of recipients.

The second and third doses of vaccine, recommended at 18 months and 4 years, increases protection to approximately 99 % of recipients.

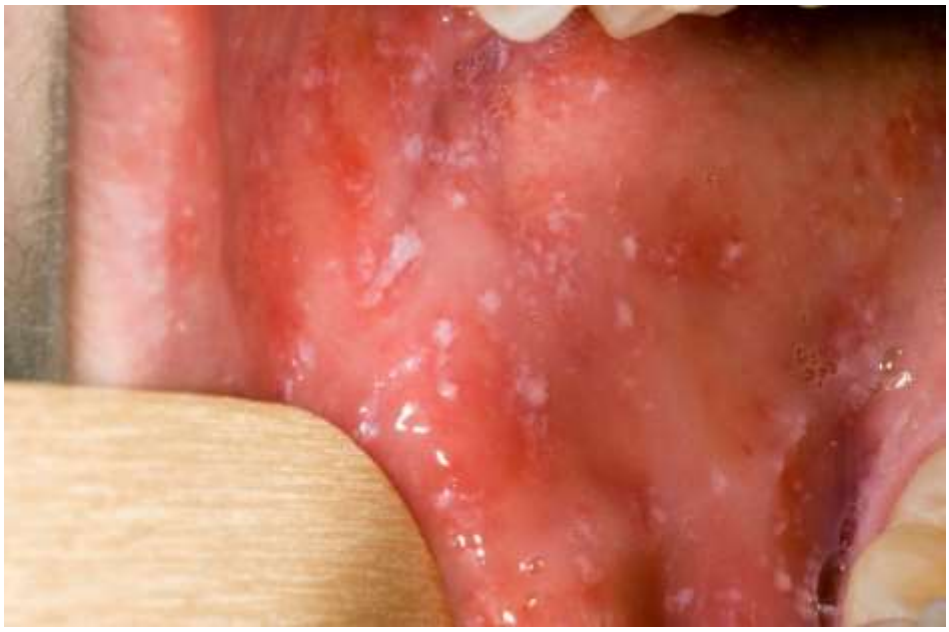
Clinical Features

1. Following the incubation period is a prodromal period of about 3 days.

   This consists of:

   - Fever
   - The 3 "C"s:
     - ♥ Cough
     - ♥ Coryza
     - ♥ Conjunctivitis.
   - Koplick's spots may be seen on the buccal mucosa, in about 60% of cases.

     Classically described as "grains of salt on a red background"



Kolpick's spots on the buccal mucosa of a nineteen year old woman, (Science photo library).

2. The characteristic rash then appears ("examthemous" stage) at about day **3-7** of the clinical illness.

- It typically begins on the **face** and **neck**, *before* becoming **generalized**.
- It has a characteristic maculopapular appearance that blanches on pressure.

  Typical lesions are **large** and **blotchy** often with confluent areas. (Rubella lesions tend to stay small and discrete).
- It is non-vesiculating and non-itchy.
- It generally lasts 4-7 days, fading in the sequence in which it appeared and sometimes ending as a "brawny desquamation" or "staining", which may persist for as long as several months.

3. Generalized lymphadenopathy and splenomegaly may be seen.
4. GIT symptoms, including diarrhea, can occur.
5. **Patients can be significantly unwell with measles.**

Note that a small number of those vaccinated may still contract measles, however the disease will be much attenuated and will not show the "classical" clinical features.

Serious complications are possible, and are listed below.

Complications:

Complications of measles are more common and more severe in:

- The chronically ill
- Immunocompromised
- Very young children

These may include:

1. Otitis media, (secondary bacterial infection)
2. Pneumonia:
   - This can be a primary measles infection or a secondary bacterial infection.

     This is the main cause of death in measles.
3. Meningitis / Encephalitis:

- Measles encephalitis has a high mortality rate (up to 15%) and up to 15 - 40% of survivors of this complication will have some irreversible brain damage.

4. Subacute sclerosing panencephalitis, (SSPE):

   - This may develop very rarely as a late sequelae several years after measles.

     There is progressive brain damage and is always fatal

Investigations

When measles was common the diagnosis was traditionally made on clinical and epidemiological grounds, however **laboratory confirmation is now recommended, as it is now a rare disease.**

Testing is also recommended as a public health measure well as well as a medical measure. [3]

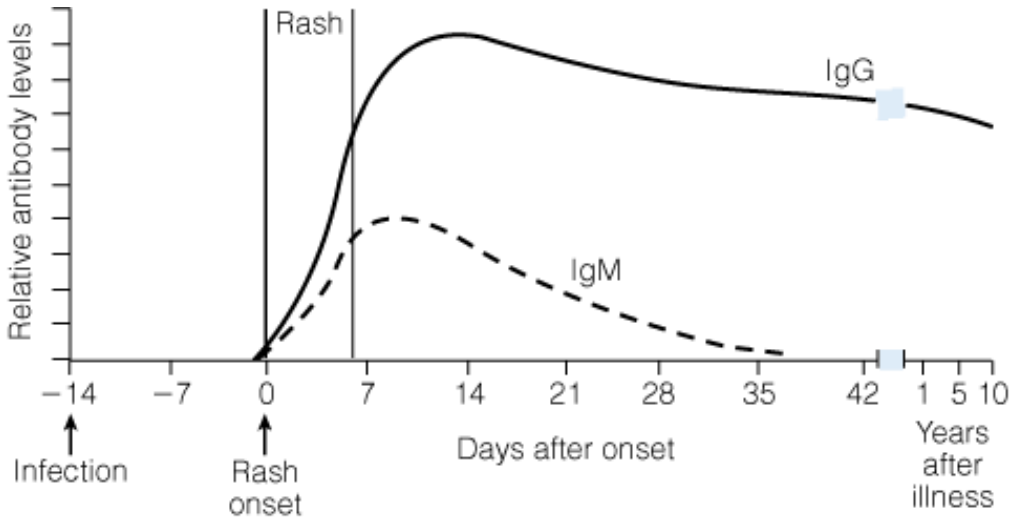
1 FBE:

- Leukopenia is common.

2. U&Es/ glucose

3. LFTs

4. **Serology:**



Serology markers for measles, (from MJA) [3]

- **Demonstration of measles specific IgM antibody.**

  If a patient has measles, IgM is generally positive if the rash has been present for 3 or more days.

  If the result is equivocal the test can be repeated in 10 days.

- If IgM is negative and IgG levels are elevated this could indicate previous infection or previous vaccination and the patient will be protected from measles.

- A **fourfold** or greater increase in measles IgG antibody titre between acute and convalescent phase sera, obtained at least 2 weeks apart, with the tests preferably conducted at the same laboratory.

- **Rubella** and **parvovirus** testing should also be considered in the differential diagnosis. These can also be tested for serologically.

- Timing of IgM testing:

  - ♥ The detection of anti-measles IgM increases to 100 % for samples taken 4 - 14 days after rash onset.

    If testing is negative for anti-measles IgM on a sample collected ≤ 3 days after rash onset, it should be *repeated* 4 - 14 days after rash onset.

5. PCR testing:

   - If there is **a high clinical suspicion** of measles and the patient is presenting within 3 days of rash, then a throat or nose swab for PCR may be advised by the health department in order to implement early public health measures at the time of confirmation.

     This should be discussed at the time of notification.

   - Swabs for PCR testing can be taken from throat / nasopharynx swabs.

   - Lumbar puncture:

     PCR testing for measles virus can also be done on CSF if meningitis or encephalitis is suspected.

     This test may be positive, even before serology tests become positive.

6. Viral culture is particularly useful for epidemiological purposes.

7. CXR:

- If there are significant respiratory symptoms.

Management

Prevention:

Vaccination:

Measles is **vaccine-preventable** disease

As of 2016 in the state of Victoria, vaccination is achieved by 2 doses at:

- 12 months, given as a part of the **MMR** (measles - mumps - rubella) vaccine.
- 18 months, given as a part of the **MMRV** (measles, mumps, rubella, varicella (i.e. chickenpox) vaccine.

Measles vaccine is a **live attenuated** preparation.

Measles immunity induced by 1 dose vaccination provides long-term immunity in most recipients. However, approximately 5% of recipients fail to develop immunity to measles after 1 dose. Following a 2nd vaccine dose, approximately 99% of subjects overall will be immune to measles. [1]

The MMR vaccine viruses are not transmissible, hence there is no risk of infection from vaccinees. [1]

Note that pregnant women and immunocompromised persons should not receive MMR live vaccines. If given to women of child bearing age pregnancy should be avoided for 2 months, as for the rubella vaccine.

For a full description of adverse reactions and contraindications to the MMR vaccine, see latest edition of "The Australian Immunization Handbook".

Post exposure prophylaxis:

1. As vaccine induced measles antibody develops more rapidly than that following natural infection, MMR vaccine can be used to protect **susceptible contacts**, provided it is administered within **72 hours** of exposure. [1]

    - It should be noted that antibody responses to the rubella and mumps components of MMR vaccine are too slow for effective use of vaccine as prophylaxis after exposure to these infections.

2 Normal human immunoglobulin can prevent or modify measles if administered within **7 days** of exposure. [1]

It may be considered for:

- Susceptible persons who **did not receive a MMR vaccination within 72 hours of contact and is within 7 days from contact.**

- Those who have a contra-indication to MMR, such as the immunocompromised.

For full information on post exposure prophylaxis – see latest edition of Australian Immunization Handbook

Contacts include (*in priority order for prophylaxis*):

1. All household members

2. All people sleeping overnight in the same room as the case (for example, in a hospital, boarding school or military barracks)

3. All children and adults in family day care, childcare, preschool, school or other educational settings who share a classroom with the case

4. People who stayed in a waiting area at the same time as the case (for example, patients in a healthcare facility's waiting room and any people accompanying those patients) and people who waited in the waiting area or who were seen in the same consultation room up to 30 minutes after the case left

5. All work colleagues of the case who share the same work area

6. Others who attend or work in the same educational institution as the case, and may have spent time in the vicinity of the case, but do not share a classroom (for example, in a high school, college or lecture theatre block)

7. Passengers on an aeroplane who were seated in the same row or two rows in front of or behind a case.

Treatment

There is no specific treatment once measles is contracted, it is therefore entirely supportive.

For a suspected case in the ED, these patients should:

- **Not be kept in the general waiting area.**

- **Given an N95 face mask**

- **Be assessed in an isolation (negative pressure) room.**

- **Be admitted until such time as measles has been excluded, with IgM serology and/ or PCR testing.**

Additionally:

- Leave vacant all consultation rooms used in the assessment of patients with suspected measles for at least **30 minutes** after the consultation.

The Role of Vitamin A

Vitamin A deficiency can predispose to severe and complicated measles.

Vitamin A may be given as:

- Two oral doses (given over two consecutive days) of 200,000 IU

  (100,000 IU if aged 6 - 11 months, 50 000 IU if aged < 6 months).

- A third dose is given 2 - 4 weeks later.

(Clay Smith - JournalFeed 7 May 2019)

Notification:

Measles is a Group A disease

It is an urgent notifiable condition and must be notified by medical practitioners and pathology services immediately by telephone upon initial diagnosis (presumptive or confirmed).

Pathology services must follow up with written notification within 5 days.
This is a Victorian statutory requirement.

School exclusion:

Exclusion for cases and contacts is as follows:

- Cases should be excluded for at least 4 days after rash onset.

- Immunized contacts do not need exclusion.

- Unimmunised contacts should be excluded until 14 days after the first day of appearance of rash in the last case.

  If unimmunized contacts are vaccinated within 72 hours (3 days) of their first contact with the first case, or if they receive immunoglobulin within 6 days of the contact, they may return to school.

References:

1. The Australian Immunization Handbook, 10th ed.

2. The Blue Book, Website, Accessed May 2019.

3. Durrheim DN, et al. Remaining measles challenges in Australia, MJA vol 187 no. (3) 6 August 2007

Dr J. Hayes.
Reviewed May 2019.