Clinical Manifestations of Measles and Rubella

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Abstract: Currently, the incidence of measles and rubella has decreased and the diseases have been eliminated in some countries with high vaccination coverages. Awareness of the clinical manifestations of the two diseases is essential, as there is always the possibility of new cases, which should be suspected on the basis of the medical history and physical examination. The diagnosis is based on clinical features and epidemiology, but should always be confirmed by determination of IgM or IgG.

The clinical manifestations of measles are quite uniform and those of rubella less so. However, in both diseases, four periods of evolution are recognized: incubation; prodromal, (catarrhal, enanthem or pre-exanthem); exanthem (rash) period; and, convalescent period (recovery or desquamation).

This work describes the clinical manifestations, presentation and complications of measles and rubella.

Keywords: Measles, Rubella, Maculopapular rash, Immunization, Congenital rubella syndrome, Complications of measles, Complications of rubella.

INTRODUCTION

Exanthematic diseases are characteristic of children, although they may occur in adults, and their main etiology is infectious. The most frequent rashes are maculopapular and are caused by viruses. The first six erythematosus rashes of childhood described historically and their corresponding diseases were named chronologically; all, except scarlet fever, which is of bacterial origin, were viral. In 1627, measles and scarlet fever were differentiated and named first and second disease, respectively. In 1881, a third disease was recognised as a separate entity and named rubella (German measles). Filatow in 1885 and Dukes in 1891 described a fourth disease, also known as Dukes's disease, which has disappeared as an independent clinical disease over time [1]. In 1905, a fifth disease, erythema infectiosum (slapped cheek disease) was defined and was later discovered to be caused by parvovirus B19. Finally, in 1910, exanthema subitum (roseola infantum) or sixth disease was discovered to be caused by human herpes virus type 6, although in later years the term exanthema subitum also began to be applied to rashes caused by other viruses, including human herpes virus type 7.

Measles (first disease) headed a long list of maculopapular rashes and later gave the name "exanthem morbilliform" (as it is a member of the genus *Morbillivirus* of the family Paramyxoviridae) to cutaneous eruptions with morphological characteristics similar to measles. Rubella, the third disease identified, although the second of viral etiology, is also known as German measles. Currently, the incidence of measles and rubella has decreased and the diseases have been eliminated in some countries with high vaccination coverages. Awareness of the clinical manifestations of these two diseases is essential, as there is always the possibility of new cases which should be suspected on the basis of the medical history and physical examination. This is especially true for physicians who did not have the opportunity to observe measles or rubella during their medical training.

The diagnosis is based on clinical features and epidemiology, but should always be confirmed by determination of IgM or IgG in two samples separated by a 2-3 week interval, even though this diagnosis is late. Early confirmation is important to enable preventive measures to be adopted in contacts and the patient's surroundings (home, day-care centres, school, waiting rooms and emergency departments of primary heath care centres and hospitals, etc.).

Clinical Presentation

Measles [2-8]

The clinical manifestations of measles are quite uniform and four periods of evolution are recognized (Table **1**): incubation; prodromal period, (catarrhal, enanthem or pre-exanthem); exanthem period (rash or eruptive); and, convalescent period (recovery or desquamation).

Table 1. Clinical Periods of Measles and Rubella

1. Incubation period
2. Prodromal period (catarrhal, enanthem or pre-exanthem)
3. Exanthem period
4. Convalescent period (recovery or desquamation)

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The period of communicability is from 1-2 days before the beginning of the prodromal period (3-5 days before rash onset) to 4 days after appearance of the rash. Children should not attend day-care centres or schools until 5 days after rash onset, and then only if their general health permits it. In immunosuppressed patients, viral excretion may be prolonged and they may remain contagious for several weeks after rash onset.

- Incubation period. The incubation period may be 5-21 days, with a mean of 10 days, although this may be prolonged by administration of polyvalent immunoglobulin as post-exposure prophylaxis or in substitutive treatment of patients with hypogammaglobulinemia, due to the persistence of transplacental maternal antibodies in infants, and also in immunodepressed patients. This period may be shortened in exceptional cases because contagion is produced by direct contact with infected secretions from a skin lesion or by contagion by the parenteral route. The incubation period extends from the time of exposure and penetration of the virus in the body to the beginning of the prodromal period, which coincides with the second viremia and involvement of the respiratory mucosa. It is an asymptomatic period except for some fleeting changes in temperature, slight malaise or mild respiratory symptoms, which are almost always difficult to detect.
- Prodromal period. The prodromal period lasts a mean of 4 days, although not infrequently is prolonged to 10 days. As in the exanthem period, the symptoms may be modified or attenuated by administration of immunoglobulin or vaccination. The prodrome is manifested by sustained high fever that may sometimes give rise to febrile convulsions, accompanied by headache, somnolence, general malaise and catarrhal symptoms due to involvement of the conjunctival, nasal, oropharyngeal and upper respiratory tract (larynx and trachea) mucosae (Table **2**). Ocular, nasal and oral alterations, together with swelling, produce what is known as the "measles face".

Koplik's spots were described in 1860 by Flindt and in 1896 Koplik demonstrated that they were pathognomonic for measles, an observation reported in 1905 by Rembold and Flindt. Koplik's spots are white punctiform micropapules ("like salt splashes"), surrounded by a reddish halo or with an erythematosus base, that appear in the jugal mucosa (internal face of the cheeks) near the molars, in 70-90% of cases. They appear at the end of the prodromal period, immediately before rash onset (1-2 days), and disappear 24-48 hours after the rash appears. Koplik's spots, a manifestation of measles enanthem, allow measles to be diagnosed before the rash appears. Similar spots may appear in the labial, palpebral, conjunctival, nasal and vaginal mucosae, and in the posterior wall of the pharynx, although these sites are infrequent.

- Exanthem period. At the onset of rash, the temperature rises and the catarrhal symptoms and general malaise reach their greatest intensity. The rash usually lasts from 3 to 5 days and regresses progressively. The rash is initially non-confluent and normally non-itchy, red-violet, and composed of many maculopapules; it appears first in the retroauricular region and, during the following 3 days, descends craniocaudally to the rest of the face and neck, the trunk and the limbs, respecting the palms and soles, and becoming confluent. If the fever increases or reappears, the complications of measles should be suspected (Table **3**).

Table 2. Clinical Manifestations of the Prodromal Period of Measles

Fever
Conjunctivitis: mucopurulent secretions, tearing, photophobia and palpebral edema
Rhinitis: sneezing and mucopurulent rhinorrhea
Buccal enanthem:
- Pharynx, tonsils and palatine
- Oral mucositis: congested lips and tongue
- Koplik's spots
Laryngitis: irritative dry cough, aphonia and hoarseness
Tracheobronchitis: cough
Otalgia
Abdominal pain and vomiting
Malaise and anorexia

Table 3. Clinical Manifestations of the Exanthem Period of Measles

Fever: rises and then declines
Catarrhal and general manifestations: maximum intensity and attenuation
Disappearance of Koplik's spots
Maculopapular rash
Manifestations secondary to possible complications

- Convalescent period. This begins on the third or fourth day of the exanthem period with the lessening and disappearance of fever and catarrhal symptoms, except cough, which may persist for days or even weeks. The rash disappears in the same order that it appeared and the general health improves notably. Furfuraceous desquamation (with small bran-like flakes) leaves the skin violet or brown, which allows a retrospective diagnosis and is characteristic of this period. The cough and bronchial manifestations are the last symptoms to disappear.

Rubella [3, 9-14]

The clinical manifestations of acquired rubella are not as uniform as those of measles. Four periods of the infection can be distinguished although they are not so marked and there are subclinical or asymptomatic forms (Table **1**). Rubella is not as contagious as measles. The period of communicability is from about one week before to at least 4 to 7 days after the appearance of the rash, when it is at its maximum. Some breast-feeding babies with congenital rubella eliminate the virus in nasopharyngeal secretions and urine

for more than a year and may therefore transmit the infection to susceptible contacts.

- Incubation period. The incubation period is normally 16-18 days but may be between 14 and 23 days. This period lasts from the time of exposure and penetration of the virus in the nasopharynx to the beginning of the prodromal symptoms, which coincides with the second viremia. It is an asymptomatic period.
- Prodromal period. The prodromal period lasts between 1 and 5 days, with a mean of 2 days. It is manifested, especially in adolescents and adults, by low-grade fever, malaise, lymphadenopathy (retroauricular, posterior cervical and suboccipital) and catarrhal symptoms of the upper respiratory tract (Table **4**). There may be a fleeting enanthema in the soft palate, with small red spots or petechiae (Forschheimer spots).

Table 4. Clinical Manifestations of Acquired Rubella

1. Prodromal period:
Often unnoticed
Discrete fever
Mild catarrh of airways
Inconstant palatine enanthem
Adenitis
2. Exanthem period:
Mild, brief fever
Maculopapular rash
Swollen and tender glands

- Exanthem period. This period is characterized by the triad of fever, rash and swollen tender lymph nodes (Theodor's sign) (Table **4**). The fever is mild and short-lasting. The rash is pink (more tenuous than that of measles), maculopapular, with small, less-prominent, non-confluent spots; it begins in the face and extends rapidly, predominantly to the trunk. The rash usually lasts 3 days and the symptoms regress progressively. The adenopathy may be generalized and last between 5 and 8 days and, in some cases, several weeks. In adults arthralgia and arthritis are frequent and the rash may sometimes be itchy.
- Convalescent period. This begins on the third day of the exanthem period and there is usually no desquamation.

CONGENITAL RUBELLA SYNDROME

In 1941, Gregg, an Australian ophthalmologist, observed cataracts and cardiac alterations in a series of newborns. Medical records showed their mothers had suffered rubella in the first weeks of pregnancy. The association of cataracts or other ocular abnormalities (microphthalmia, glaucoma, strabismus, retinitis), congenital heart disease (patent ductus arteriosus, septal defects, pulmonary valve stenosis), deafness, microcephaly, central nervous system involvement and abnormal intra-uterine growth, were defined as Gregg's syndrome. The rubella virus, which was isolated later, was established as the cause. The incidence and type of congenital abnormalities vary according to the time of maternal infection. The neonatal manifestations (expanded rubella syndrome) are thrombocytopenic purpura, hepatosplenomegaly, jaundice, anemia, bone alterations, pneumonitis, etc. These abnormalities occur in up to 85% of neonates when maternal infection occurs in the 12 first weeks of gestation, in 54% when the infection is between weeks 13 and 16, and in 25% when infection occurs at the end of the second trimester (Table **5**).

Table 5. Most-Frequent Clinical Manifestations of Congenital Rubella

1. Permanent lesions:
Deafness
Cataracts and other ocular defects
Heart disease
Microcephaly
Psychomotor delay
Type 1 diabetes mellitus (late manifestation)
2. Transient lesions or neonatal manifestations:
Delayed fetal growth
Thrombocytopenic purpura
Hepatosplenomegaly
Radiolucent bone disease
Interstitial pneumonitis
Meningoencephalitis

Clinical Presentations

Measles [2-8]

The clinical profile of measles may be modified and present characteristics other than those already explained. Comorbidity (influenza, pertussis, diphtheria, tuberculosis, mumps, scarlet fever, varicella and aphthous stomatitis) is comparatively frequent . The clinical presentations are:

- Modified (mild) measles syndrome occurs primarily in patients with a degree of passive immunity against the virus. The rash is mild and the symptoms are mild and may be subclinical. The incubation period is longer. This form of measles is due to the previous administration of polyvalent immunoglobulin in the incubation period or first half of the prodromal period, or to the monovalent, bivalent (measles and rubella) or MMR vaccines. It may also occur in breast-feeding babies due to the persistence of maternal antibodies; in these cases, a second clinical infection may occur after one year if immunity is incomplete.
- Modified measles as an adverse vaccine reaction.
- Measles without rash or without fever. These are two very rare forms of measles that may be observed in a

family member during a measles outbreak. The retrospective diagnosis is made by determination of measles-specific IgG, since the medical history shows the patient has not suffered the disease.

- Purpuric and hemorrhagic measles. The morbilliform exanthem become hemorrhagic due to rupture of the papular capillaries (purpuric form). This clinical presentation is not indicative of greater severity, as long as it is not a hemorrhagic diathesis with mucocutaneous haemorrhages in other sites due to thrombocytopenia or disseminated intravascular coagulation (hemorrhagic form), which is more severe.
- Vesicular (blister) measles. This may occur in children with severe hyperhydrosis and in warm, moist environments.
- Confluent scarlatiniform measles. The catarrhal symptoms aid the differential diagnosis with scarlet fever.
- Measles with pseudo appendicular syndrome. Abdominal pains are frequent in the prodromal and exanthem periods. They may become severe in the iliac fossa, which may require an appendectomy to discard mesenteric lymphadenitis or, more rarely, true appendicitis.
- Atypical measles. This occurs in people immunized with the inactivated vaccine during the 1960s who are exposed to the wild virus. The rash begins in the distal parts, affects the palms and soles, and may be vesicular and purpuric. There are usually two phases, initially it appears as measles modified by immunization and at two weeks the rash of atypical measles appears. Pulmonary complications are frequent, with hilar adenopathies and diffuse nodular infiltrates.
- Adult measles. Measles is more severe in adults than in children and may be accompanied by a wider range of complications (pneumonia, bacterial respiratory secondary infections, bronchospasm, hepatitis and otitis media).
- Severe measles in patients with disorders of cellular immunity, in which there may be no rash and frequent complications: acute progressive encephalitis with measles inclusion bodies and giant cell pneumonia.
- Measles in pregnant women. The most important effect of measles on pregnant women is the increased risk of complications, especially respiratory (pneumonitis), and the risk of miscarriage or premature birth. Measles has not been shown to have teratogenic effects.

Rubella [3, 9-14]

The clinical presentation of rubella, in contrast to measles, is fairly uniform and usually appears with the characteristics described above. There are scarlatiniform (smaller and more abundant spots) and hemorrhagic types, and more cases present without rash than was formerly believed. Comorbidity is exceptional.

Complications

Measles [2-8]

The most important and most frequent complications of measles are respiratory and neurological and almost always occur during or after the exanthem period. They should be suspected if the fever persists or reappears. The most-frequent complications are acute otitis media, mastoiditis, sinusitis, cervical lymphadenitis, stenosing laryngitis, laryngotracheobronchitis (croup), pneumothorax, pneumomediastinum and subcutaneous emphysema, pneumonia or bronchopneumonia (viral, bacterial or mixed), enteritis, thrombocytopenic purpura, pyodermitis, febrile convulsions, hepatitis, appendicitis, myocarditis and post-infectious acute encephalitis with permanent cerebral lesions (1 per 1000 cases of measles). The most-frequent microorganisms involved in secondary bacterial infections are *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus*.

Subacute sclerosing panencephalitis (SSPE) is a chronic degenerative disease of the central nervous system caused by chronic activation of the measles virus. The clinical manifestations begin after a mean latent period of 12 years after measles infection. The risk of SSPE is 4-8.5 per million cases of measles and 0.14- 0.7 per million doses of vaccine. In a case of SSPE secondary to vaccination, there is always the doubt of whether it is in reality SSPE due to undiagnosed measles.

Deaths due to measles are caused by respiratory and neurological complications. Case-fatality rates are higher in children <5 years of age, in adults and in immunosuppressed people, including children with leukemia, people infected by the human immunodeficiency virus (HIV) and those with severe malnutrition.

Rubella [3, 9-14]

The severe complications of rubella occur in cases of congenital rubella (Table **5**). Acquired rubella is normally benign and the few complications that occur are mostly in adults and adolescents, especially women. In children, there may be post-infection purpura, usually thrombocytopenic although there may be a vascular component; most patients recover in weeks or months. It may be accompanied by digestive, cerebral or intrarenal haemorrhage.

The most-frequent complications are transient polyarthralgia and polyarthritis, which occur in 33-70% of young women with rubella. The joints of the fingers, wrist and knees are often affected. The clinical manifestations appear during or shortly after the exanthem period and may last for a month; chronic arthritis is rare.

Other infrequent complications are encephalitis, orchitis, neuritis, hepatitis and a late form of progressive panencephalitis.

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