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The rash with maculopapules and fever in adults

Sonal Muzumdar, MD, Marti Jill Rothe, MD, Jane M. Grant-Kels, MD*

Dermatology Department, University of CT Health Center, Farmington, Connecticut, USA

Abstract There is a broad differential diagnosis for the presentation of fever and maculopapular rash in an adult. Although some causative conditions are benign, others are medical emergencies that require prompt diagnosis. We describe various conditions that result in a fever and maculopapular rash in adults. These include infectious processes (meningococcemia, infectious mononucleosis, West Nile virus, zika virus, rubella, primary human immunodeficiency virus, parvovirus B19, ebolavirus), tick-borne illnesses (Rocky Mountain spotted fever, ehrlichiosis), and hypersensitivity reactions (exanthematous drug reactions). We also provide an algorithm to aid in the diagnosis of the patient with fever and maculopapular rash. Such conditions that can occur in adults but are seen predominantly in children are discussed in the article "Rash with maculopapules and fever in children" of this issue.

Introduction

The differential diagnosis for adults presenting with fever and maculopapular rash is broad. It includes bacterial and viral infections as well as such hypersensitivity reactions as those due to drugs (Table 1). Although some of these eruptions are benign, others are medical emergencies. Prompt diagnosis is, therefore, crucial. We describe some of the more common causes of maculopapular rashes and fever in adults and how to identify and treat them.

Diagnostic algorithm

Because a number of conditions can cause fever and maculopapular rash in adults, eliciting a thorough history is crucial for diagnosis. Questions that should be asked of all patients include the following[1]:

1. Did you notice any clinical manifestations before the rash started?
2. Are there any clinical manifestations associated with the rash?
3. Have you started any new medications recently?
4. Is anyone around you sick with similar clinical manifestations?
5. Have you traveled anywhere recently?
6. Describe the distribution of the rash. Where did the rash start? Has it changed over time?

A diagnostic algorithm for evaluating patients with fever and maculopapular rash is provided in Figure 1.

Drug reactions

Etiology

Exanthematous (maculopapular) drug eruptions are delayed (type IV) hypersensitivity reactions, which are mediated

* Corresponding author. Tel.: 860-519-7008.
E-mail address: grant@uchc.edu (J.M. Grant-Kels).

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by T cells. Classically, drugs bind proteins or peptides within the body to form haptens. These haptens are presented to T cells by antigen-presenting cells, eliciting a hypersensitivity reaction.[2]

Epidemiology

More than 4 billion medications are prescribed annually in the United States.[3] Cutaneous reactions are one of the most common adverse events secondary to medications, with an average incidence of 10 cases for every 1000 new medication users.[2] Exanthematous drug eruptions are the most common type of cutaneous drug reaction.[4] Drugs that are commonly implicated in cutaneous drug reactions include antiepileptics, such as carbamazepine, phenytoin, and lamotrigine (100 cases/1000 new users), and antibiotics, such as penicillins, cephalosporins, and sulfonamides (50 cases/1000 new users).[2] In addition, most patients with infectious

Table 1 Selected causes of fever and maculopapular rash in adults

Disease	Epidemiology in adults	Characteristic clinical presentation
Rubeola (measles)	Unvaccinated populations	Cough, coryza, and conjunctivitis. Punctate white or gray lesions on erythematous base on buccal mucosa (Koplik spots). High fever and a blanching maculopapular rash originates on forehead and upper neck; descends to the trunk and lower extremities.
Rubella (German measles)	Unvaccinated populations	Tender adenopathy in the posterior auricular, posterior cervical, and suboccipital lymph nodes. Pink maculopapular rash that starts on the face and spreads to the trunk and extremities. May be associated with petechiae on the soft palate (Forchheimer's sign).
Zika virus	Travelers from endemic regions (Africa, Southeast Asia, South and Central America, Pacific Islands and Caribbean)	Maculopapular rash that starts on trunk and descends to lower extremities. Associated with numerous birth defects in fetuses of infected pregnant women, including microcephaly.
Parvovirus B19	Adults who work with children (teachers, daycare workers, etc.)	High fever followed by rash that originates on trunk and spreads to extremities. Rash starts as discrete pale, pink macules and may become confluent. Arthralgias and arthritis common in adults and may be the only sign of infection.
Rocky Mountain spotted fever	Throughout United States; especially North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri	Fever, nausea, abdominal pain, and headache. Pink macular rash that starts on the ankles and wrists and spreads to the trunk.
Meningococcemia	Young adults aged 16-23	Fever, nuchal rigidity, photophobia, and altered mental status. Rash is found on the trunk and extremities and may be maculopapular, petechial, or purpuric.
Hand foot mouth disease (Coxsackie virus)	Less common in adults; highest incidence in infants and children aged <5 y	Maculopapular or vesicular rash on the hands, feet, buttocks, legs, and arms.
Ehrlichiosis	Increased incidence in the Southeast and South Central United States. Males and people aged >50 y were most frequently infected.	Widespread, erythematous maculopapular rash with fever, headache, and malaise.
Exanthematous drug eruption	Typically 4-21 days after initiation of a new drug. Increased risk with antiepileptics (carbamazepine, lamotrigine, and phenytoin) and antibiotics (penicillins, cephalosporins, and sulfonamides)	Rapidly evolving, symmetric, diffuse erythematous maculopapular rash with a low-grade fever.
Infectious mononucleosis	Adolescents and young adults	Fever, cervical lymphadenopathy, and pharyngeal inflammation. Maculopapular rash on trunk and arms.
West Nile virus	Africa, Europe, Middle East, North America, and West Asia. Increased frequency in elderly.	Fever, headache, myalgias, and a maculopapular rash on the trunk. Complications include severe central nervous system disease and death.
Primary HIV infection	Prominent in the United States, with increased incidence in gay men and heterosexual African American women.	Maculopapular rash on the face, upper extremities, and trunk associated with fever and myalgias. Clinical manifestations typically manifest 2-6 weeks after exposure and last for 1 week.

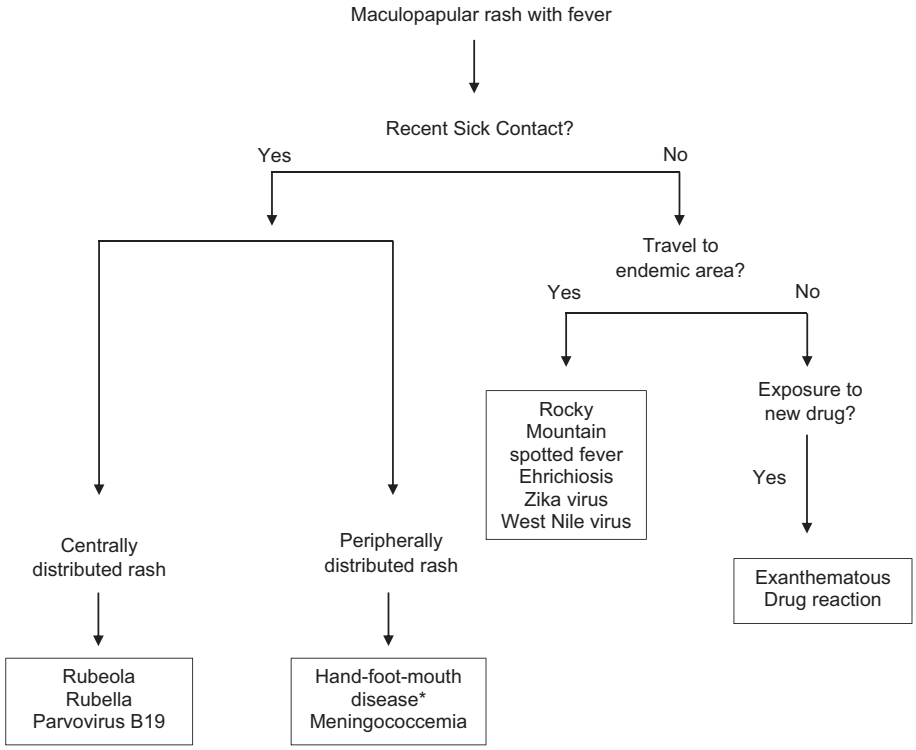

Fig. 1 Diagnostic algorithm for fever and maculopapular rash in adults. *Hand foot mouth disease is much more common in children under the age of 5 years, but can rarely occur in adults.

mononucleosis, who are treated with aminopenicillins, develop a maculopapular eruption.[2]

Clinical manifestations

Exanthematous drug eruptions typically present 4 to 21 days after the initiation of a new medication and evolve rapidly.[2] They consist of symmetric erythematous macules and papules (Figures 2A and B) that start on the trunk and intertriginous areas.[5] The lesions may be pruritic and are commonly associated with a low-grade fever (<38.5°C). Mucous membranes are not characteristically involved. Most drug eruptions fade within a week of discontinuation of the offending drug.[2] A high-grade fever (>38.5°C), mucous membrane involvement, or lymphadenopathy may be indicative of a more serious evolving reaction, including Stevens-Johnson syndrome, toxic epidermal necrolysis,[2] or drug reaction with eosinophilia and systemic clinical manifestations, which is often associated with inflammation of various internal organs (such as the liver and less commonly the kidney, lung, and heart, and rarely pancreas) and a 10% incidence of mortality.

Diagnosis and treatment

An exanthematous drug reaction should be considered in any patient presenting with a symmetric, widespread maculopapular rash and low-grade fever. Maculopapular drug reactions can mimic viral exanthems, such as measles, rubella, erythrovirus (parvovirus B19), chikungunya (alphavirus), zika, and even varicella (when vaccinated persons exhibit clinical manifestations), and so it is critical for clinicians to take a thorough history and identify any new drugs that the patient may be taking. Cutaneous reactions typically appear 4 to 21 days after the initiation of a new drug.[2] Resolution of the rash after cessation of the suspected drug may also help identify the causative medication.[2] The reaction will typically resolve within 2 weeks of withdrawal of the causative drug but has been reported to resolve slower over the course of many weeks.[4]

Treatment of exanthematous drug eruptions primarily involves discontinuing the causative drug and managing the patient's clinical manifestations. Pruritus may be controlled with topical or oral antihistamines. Glucocorticoids (topically or systemically) may also be used to control clinical manifestations. If it appears that a serious drug reaction is evolving (ie, Stevens-Johnson syndrome or toxic epidermal necrolysis), the patient may need to be hospitalized for monitoring and supportive therapy.[2]

Meningococcemia

Microbiology

Neisseria meningitidis, an encapsulated, gram-negative diplococcus, causes meningococcemia.[6] Disease is most commonly caused by serogroups B, C, and Y.[7]

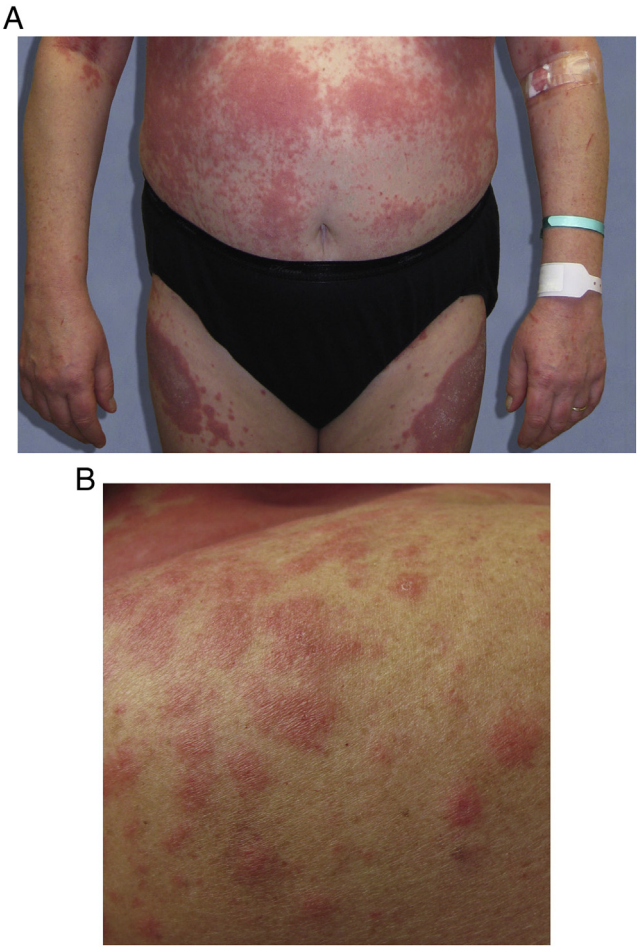

Fig. 2 A, Papular drug eruption (courtesy Justin Finch, MD, and the UCONN Department of Dermatology). B, Close-up of lesions of a papular drug eruption (courtesy Justin Finch, MD, and the UCONN Department of Dermatology).

Epidemiology and incidence

The incidence of meningococcemia has been declining in the United States, with only 370 cases reported in 2016.[7] Meningococcemia occurs in all age groups, but infection is most common in infants and young adults aged 16 to 23.[7] Risk of infection is also increased in patients with human immunodeficiency virus (HIV), complement deficiencies, and functional or anatomic asplenia.[7] Patients taking eculizumab (Soliris), a monoclonal antibody that is a terminal complement inhibitor used to treat paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome, are also at increased risk for meningococcemia.[7]

Clinical findings

Meningococcemia presents with fever, nuchal rigidity, photophobia, and altered mental status. On clinical examination, Kernig and Brudzinski signs may be positive. Patients have a diffuse, erythematous maculopapular rash that evolves into petechiae and purpura that are most commonly found on the trunk and extremities.[8] Large, hemorrhagic lesions may be found in some patients and are associated with a poor prognosis.[6]

There are a number of complications, which may result from meningococcal infection. Acutely, vasodilation and capillary leak may result in decreased intravascular volume with subsequent cardiovascular collapse. Patients may also experience pulmonary edema, acute respiratory distress syndrome, disseminated intravascular coagulation, or bilateral hemorrhage into the adrenal glands (Waterhouse-Friderichson syndrome). Of the patients, 10% to 15% will die of meningococcemia,[9] and 10% to 20% of survivors will suffer from long-term neurologic complications, including deafness, mental retardation, and seizures.[9]

Diagnosis and treatment

Meningococcal disease can be diagnosed in a variety of ways, including culture, gram stain, bacterial polymerase chain reaction (PCR), and antigen detection using latex agglutination.[9] Meningococcemia should be considered in all patients presenting with fever, headache, nausea, vomiting, and a maculopapular or petechial rash. Because of the high complication rate secondary to this infection, all patients with suspected disease should be treated promptly.

Ceftriaxone is the first-line antibiotic for treating meningococcemia due to its effective penetrance into the cerebrospinal fluid.[9] If possible, blood cultures should be drawn before antibiotic administration to confirm the diagnosis; however, antimicrobial therapy should not be delayed if a culture report is not readily available. Close contacts of the patient (defined as individuals with >8 hours of contact in proximity <3 feet to the patient or those with direct contact with oral secretions from 1 week before the onset of clinical manifestations to 24 hours after patient antibiotic initiation) should be given antibiotic prophylaxis.[9] Rifampin is the first-line prophylactic agent for meningococcal meningitis.[9]

Infectious mononucleosis

Virology

Infectious mononucleosis is caused by the Epstein-Barr virus (EBV), also known as human herpes virus-4, an enveloped DNA virus, which is part of the herpes virus family.[10]

Epidemiology and incidence

Infection with EBV is prominent globally, with 90% to 95% of adults testing seropositive.[11] When EBV is acquired in childhood, it is typically mild or asymptomatic. In contrast, approximately 75% of adolescents who are infected present

with symptomatic infectious mononucleosis. In developing countries, infection with EBV occurs earlier in childhood and clinical infectious mononucleosis is rare. The disease is more common in developed countries, where infection tends to occur later in adolescence or early adulthood.[12] The peak incidence of infectious mononucleosis occurs between 15 and 24 years of age.[11] The disease is most commonly spread by saliva but can also be transmitted via semen and blood.

Clinical findings

Clinical manifestations of infectious mononucleosis typically present 4 to 6 weeks after infection with EBV.[13] The prodrome consists of usually severe persistent fatigue and myalgias and typically lasts 1 to 2 weeks.[12] After the prodrome, patients present with cervical lymphadenopathy, fever, severe sore throat due to pharyngeal inflammation, hepatomegaly, and spenomegaly.[14] A generalized maculopapular, urticarial, or petechial rash may also be seen in some patients.[11] The characteristic exanthem is a maculopapular rash that involves the trunk and arms. It appears shortly after the onset of clinical manifestations, lasts for 1 to 6 days, and is identified in 3% to 15% of patients.[14] Complications from infectious mononucleosis are rare but may include splenic rupture, hepatitis, myocarditis, and central nervous system dysfunction secondary to meningitis or encephalitis.[15] Ten percent of patients will develop persistent fatigue that lasts for more than 6 months.[12]

Diagnosis and treatment

Infectious mononucleosis is typically diagnosed clinically. Serology may be used to confirm infection with EBV.[10] In cases with inconclusive serologic results, real-time PCR and measurement of EBV viral load may be used. Patients typically have lymphocytosis with greater than 10% atypical lymphocytes.[12]

Treatment for infectious mononucleosis is symptomatic. Patients should receive adequate rest. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used to manage pain. Patients should be instructed to avoid vigorous physical activity in the first month, as this may increase the risk for splenic rupture.[12] Most patients with infectious mononucleosis, who are treated with amoxicillin or ampicillin, will develop a maculopapular rash.[2]

West Nile virus

Virology

West Nile virus (WNV) is a positive-sense RNA virus, which is part of the *Flavivirus* genus. WNV is primarily transmitted by the *Culex* mosquito.[16]

Epidemiology and incidence

WNV is most frequently found in North America, Africa, Europe, the Middle East, and West Asia.[17] WNV is the leading cause of arboviral encephalitis in the United States.[18] In 2016, there were 2149 reported cases of WNV in the United States with 106 deaths. Incidence of infection is highest in older adults. Infections peak between August and October.[19]

Clinical findings

Eighty percent of patients who are infected with WNV are asymptomatic.[19] Those who are symptomatic typically present 3 to 14 days after infection with fever, headache, myalgias, diarrhea, nausea, and vomiting.[18] Patients may also develop a maculopapular rash, which is concentrated on the trunk.[18] Complications from WNV may include encephalitis, central nervous system damage, and death.[18] These occur more frequently in the elderly and in patients with hypertension or diabetes. One in 150 patients will develop severe central nervous system infection, and out of those, 1 in 10 will die.[19] For those patients who are pregnant, it is possible for the virus to cross the placenta and infect the fetus[19]; however, transplacental infection appears to be rare.[20]

Diagnosis and treatment

WNV infection may be diagnosed using serology. Anti-WNV IgM may be detected 3 to 8 days after infection. PCR or viral culture may also be used for diagnosis.[19] Treatment for WNV is primarily supportive. Patients should receive adequate hydration. NSAIDs may be used to control pain and fever. Patients with severe disease may need to be hospitalized for supportive care.[19]

Rocky Mountain Spotted Fever

Virology

Rocky Mountain spotted fever (RMSF) is caused by *Rickettsia rickettsii,* an obligatory intracellular gram-negative bacillus that is part of the Rickettsiacae family. It is transmitted through tick bites, with *Dermacentor variabilis* (American dog tick) being the most common source of RMSF infection in the United States.[6] Other ticks in the United States that can transmit the RMSF bacteria include the Rocky Mountain wood tick (*Dermacentor andersoni*), the lone star tick (*Amblyomma americanum*), and the brown dog tick (*Rhipicephalus sanguineus*).[6]

Epidemiology and incidence

RMSF occurs in all age groups, with the highest incidence of infection in people aged above 40 years. Men are more

commonly infected than women.[21] Native Americans often have higher rates of RMSF than other ethnic groups.[21] RMSF occurs throughout the year, with the highest incidence during the summer months.[21] Although RMSF infections have been reported throughout the contiguous United States, more than 60% of cases have been reported in 5 states (North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri).[21] In 2012, in total 4470 cases of RMSF were reported to the Centers for Disease Control and Prevention (CDC).[21]

Clinical findings

RMSF has an incubation period of 3 to 12 days.[21] Patients may present with a fever, headache, nausea, vomiting, and abdominal pain. Two to 4 days after the onset of fever, patients usually develop rash. The rash is highly variable but classically presents with small, pink macules (Figure 3) that originate on the wrists and ankles and spread to the trunk. The palms and soles may be involved. Petechiae might develop 5 to 6 days after the onset of illness and are indicative of progression to severe disease.[21] Additional clinical manifestations, which can present in children, are altered mental status and edema around the eyes and/or on the dorsum of the hands. Untreated RMSF may result in severe complications, including encephalitis, shock, seizures, acute respiratory failure, and renal failure. The majority of deaths from RMSF occur within the first 8 days.[21]

Diagnosis and treatment

RMSF is primarily diagnosed clinically. Sera may appear negative for the first 7 to 10 days after infection and cannot be relied upon for diagnosis. Doxycycline is the first-line treatment for all patients with suspected RMSF, including children (adults: 100 mg every 12 hours; children under 45 kg: 2.2 mg/kg body weight every 12 hours). Despite the fact that doxycycline, being a tetracycline, is usually not given to children under age 8 years due to the risk of permanent teeth staining, treating RMSF adequately outweighs this risk. Pregnant women should be counseled on the risks and benefits of treatment. Treatment should continue until 3 days after fever subsides and clinical improvement. A child, who has had RMSF, cannot be re-infected. Protective clothing and insect repellants are recommended in high-risk areas.[21]

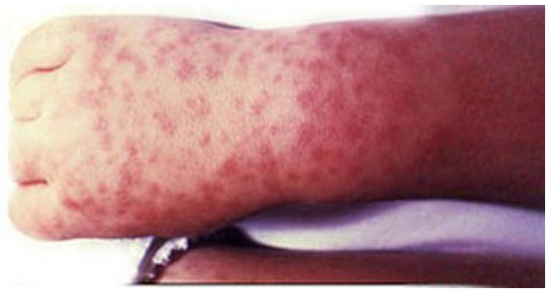

Fig. 3 Spotted eruption of Rocky Mountain spotted fever on the wrist and hand of a child. (Image courtesy of the Centers for Disease Control and Prevention).

Ehrlichiosis

Virology

In the United States, ehrlichiosis is caused by *Ehrlichia chaffeensis, Ehrlichia ewingii,* and *Ehrlichia muris–like.*[22] Ehrlichia are obligate intracellular, gram-negative bacteria that are part of the Anaplasmataceae family. Ehrlichiosis is transmitted by the lone-star tick, *A americanum*, found in wooded areas.[23] It generally requires a tick carrying the bacterium that causes ehrlichiosis to feed for at least 24 hours to transmit the bacterium. The lone-star tick can also transmit Lyme disease, anaplasmosis, and babesiosis; RMSF coinfections have been reported.[22]

Epidemiology and incidence

Ehrlichiosis occurs most frequently in the Southeast and South Central United States. Disease is primarily reported during the summer months, with peak incidence in June and July. In 2016, in total 1377 cases of ehrlichiosis caused by *E chaffeensis* were reported in the United States, with the highest frequency of cases in males and people aged above 50 years. Severe infection may be more common in immunocompromised patients.[22]

Clinical findings

The incubation period for ehrlichiosis is typically 7 to 14 days. Most patients will present with fever, headache, myalgias, and malaise. Less common clinical manifestations include gastrointestinal upset and respiratory clinical manifestations, including cough and dyspnea. The rash is identified in approximately 30% of patients, with a higher frequency in children. The eruption associated with ehrlichiosis typically presents 5 days after the onset of clinical manifestations. It may be maculopapular, petechial, or even widespread erythema. The rash is typically diffuse and may involve the face, trunk, extremities, palms, and soles.[23]

Diagnosis and treatment

Ehrlichiosis should be considered in patients presenting with fever, headache, and rash in an endemic region. Serology can be used to make a diagnosis. Antibody levels typically rise after clinical manifestations present and therefore may not be elevated within the first few days after infection. Additionally, during this time, a Wright- or Giemsa-stained peripheral blood

smear can be used to visualize morulae within monocytes (*E chaffeensis*) or granulocytes (*E ewingii*).[23]

Doxycycline is the antibiotic of choice for treatment of ehrlichiosis in adults and children of all ages (100 mg twice a day for adults; 2.2 mg/kg twice a day for children under age of 8 years). In pregnant patients or those with a life-threatening tetracycline allergy, rifampin may be used.[22]

Zika virus

Virology

Zika virus is a single-stranded RNA virus, a member of the *Flaviviridae* family. It is an arbovirus, which is primarily transmitted by mosquitoes of the Culicudae family and the *Aedes* genus.[24]

Epidemiology and incidence

Before 2007, zika infections were rare and occurred mainly in Asia and Africa. Since 2007, multiple zika outbreaks have been reported in Southeast Asia and the Western Pacific. In 2015, zika was first documented in the Western Hemisphere, with multiple large outbreaks reported in Brazil. Subsequent to 2015, zika has spread throughout most of the Americas.[25] In 2016, the incidence of zika reached an all-time high in the United States with 5168 symptomatic cases reported of which 4897 occurred in travelers from endemic areas and 224 resulting from presumed mosquito-borne transmission in Florida and Texas. In 2017 the incidence of symptomatic zika in the United States fell to 433 cases. Travelers to zika-affected regions are most at risk of contracting the infection. High-risk zika regions include Africa, Southeast Asia, the Caribbean, the Pacific islands, and South and Central America.[25]

Clinical findings

The majority of zika infections are asymptomatic. Those that are symptomatic are typically mild.[25] Common clinical manifestations include fever, arthralgias, headache, and a maculopapular rash that typically originates on the trunk and then progresses to involve the lower extremities.[26,27] The most serious consequence of zika infection is the increased incidence of birth defects in infants born to zika-infected pregnant women. These include central nervous system defects such as microcephaly, brain abnormalities, eye abnormalities, and neural tube defects. The incidence of birth defects in fetuses of women with laboratory evidence of zika infection reported to the CDC's US Zika Pregnancy Registry was 5% between January 15 to December 26, 2016. For women with confirmed zika infection in their first trimester of pregnancy, this number rose to 15%.[28]

Rubella (German Measles)

Virology

Rubella virus is an enveloped, single-stranded RNA virus in the togavirus family.[29]

Epidemiology and incidence

With increased vaccination efforts, the incidence of rubella has fallen significantly. Between 2005 and 2011, a median of 11 cases of rubella were reported annually in the United States.[30] Although rubella is no longer endemic in the United States, approximately 10% of U.S.-born persons remain susceptible to infection. Risk of infection is highest in those who are less likely to be vaccinated, such as people born outside of the United States and social groups who reject vaccination.[29] Since 2004, 60% of rubella infections have occurred in patients aged 20 to 49 years. The median age of infection is 32 years.[30] Rubella's peak incidence is during the late winter and early spring.[29]

Clinical findings

The prodrome for rubella presents with malaise and adenopathy in the posterior auricular, posterior cervical, and suboccipital lymph nodes. The exanthem for rubella consists of pink macules and papules 1 to 4 mm in diameter (Figure 4) and

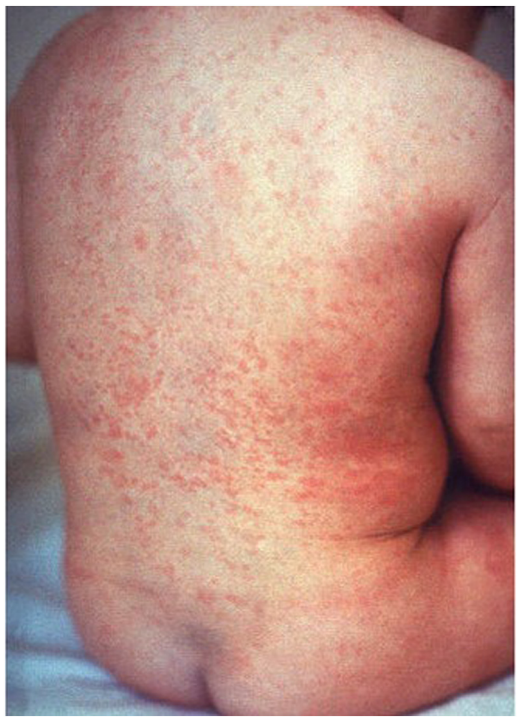

Fig. 4 Exanthem of rubella. (Image courtesy of the Centers for Disease Control and Prevention.)

originates on the face, neck, and scalp with subsequent extension to the trunk and extremities. It may occur with fever, myalgias, and arthralgias. Forchheimer's sign, the enanthem for rubella, occurs in 20% of patients and consists of petechiae on the soft palate. It may occur during the prodrome or with the onset of the rash.[29]

Complications of rubella are not common. They include arthritis, which occurs primarily in women and increases in incidence with age, and rarely thrombocytopenia and encephalitis. An infected pregnant woman may infect the fetus who can develop congenital rubella syndrome. Although congenital rubella syndrome is classically characterized by a fetal triad of congenital cataracts, deafness, and patent ductus arteriosus, multiple fetal organs may be involved. The incidence of congenital rubella syndrome depends on the time when the mother contracts rubella. Congenital rubella syndrome affects 50% of women infected in the first 12 weeks of pregnancy. This falls to 25% for women infected between weeks 13 and 24 of pregnancy. Infection after 24 weeks of pregnancy rarely causes congenital rubella syndrome.[29]

Diagnosis and treatment

Rubella is typically mild and treatment is primarily supportive in nature. NSAIDs may be used to treat severe arthralgias. Pregnant women who are infected with rubella in early pregnancy should consider treatment with intramuscular immunoglobulin.[29]

HIV: primary infection

Virology

HIV is a member of the Retroviridae family. Its genome is made up of two pieces of single-stranded RNA. There are two types of HIV that can cause infection, HIV-1 and HIV-2. HIV-1 is found globally and is the subtype that is responsible for most HIV infections in the United States. HIV-2 is primarily found in Western Africa and has a lower infectivity than HIV-1.[31]

Epidemiology and incidence

Since the height of the HIV epidemic in the 1980s, the incidence of HIV in the United States has decreased, with 37,600 new infections reported in 2014 compared with 130,000 in 1985.[32] Advances in HIV therapy have led to increased survival with a resultant increase in the prevalence of HIV. In 2015 the CDC estimated that 1.1 million people were living with HIV in the United States. All populations may be affected by HIV. Incidence is highest in men who have sex with men, followed by heterosexual African American women.[32] HIV is transmitted through contact with infected bodily fluids, including semen, preseminal fluids, blood, rectal fluids, vaginal fluids, and breast milk. In the United States, HIV is primarily transmitted through sexual intercourse and sharing of infected needles.[33]

Clinical findings

Primary HIV infection typically presents with fever, malaise, myalgias, and lymphadenopathy 2 to 6 weeks after exposure,[34] and 30% to 50% of patients will develop a rash. The exanthem for primary HIV is maculopapular and occurs on the face, upper extremities, and trunk. The rash may also include the palms and soles. Patients may have oral lesions with resultant dysphagia. Clinical manifestations of primary HIV typically resolve within 1 to 3 weeks.[35]

Diagnosis and treatment

Initial diagnosis of primary HIV may be made by nucleic acid testing or testing for p24 antigen or HIV viral load.[36] Most patients will test positive 7 to 28 days after infection. Antibody testing for HIV will not be positive until 3 to 12 weeks after initial infection.[32] Antiretroviral therapy should be started in all patients who test positive for HIV as soon as possible.[36]

Parvovirus B19

Parvovirus B19 is described in "The Rash with Fevers and Maculopapules in Children." Although parvovirus B19 is predominantly an infection of childhood, adults who work closely with children, such as daycare workers and teachers, are also at risk for infection. In adults, parvovirus B19 is more likely to cause arthralgias than it is in children, with up to 60% of adults who are affected developing arthralgias. The arthropathy is characteristically symmetrical and involves multiple joints. The metacarpophalangeal and proximal interphalangeal joints are typically affected. Arthralgias typically resolve within a few weeks; however, in women, they can last for months to years.[37] In adults, infection with parvovirus B19 may rarely manifest as papular-purpuric gloves and socks syndrome. This syndrome typically presents with erythema, pruritus, and symmetrical edema of the hands and feet. It is generally self-limiting, with spontaneous resolution typically occurring 7 to 14 days after onset.[38]

Ebolavirus

Virology

Ebolavirus is an enveloped, single-stranded RNA virus, which is part of the Filoviridae family.[39] Three species of ebolavirus have been responsible for the majority of recent outbreaks in Africa: *Zaire, Bundibugyo,* and *Sudan ebolavirus.*[40]

Epidemiology and incidence

Ebolavirus is found primarily in Western Africa. It was first discovered in 1976. Since then, it has periodically caused outbreaks. The largest outbreak to date occurred from 2014 to 2016 and was centered in Guinea, Sierra Leone, and Liberia. It spread to several other countries, including Italy, Spain, the United Kingdom, and the United States. In total, 28,616 suspected infections occurred, with 11,310 deaths.[40] There were 4 cases of ebola in the United States during the outbreak. People affected were travelers to West Africa and health care workers who cared for patients with ebola. Since the 2014 to 2016 outbreak, the incidence for ebola has dropped substantially. In 2017 there were only 8 known cases of ebolavirus, found in the Democratic Republic of Congo.[40] In 2018, there has been one outbreak of ebola in the Democratic Republic of Congo, resulting in 59 cases and 27 deaths as of June 7, 2018.[41] People at risk for ebolavirus include travelers to endemic regions in West Africa and health care workers who may be exposed to ebolavirus.

Clinical findings

The incubation period for ebolavirus is 8 to 12 days. Patients present with an abrupt onset of fever, chills, and malaise. After 5 days, patients develop gastrointestinal clinical manifestations. They may also have chest pain, shortness of breath, headache, and possibly conjunctival injection. Bleeding may occur, with patients developing petechiae, ecchymosis, or oozing from venipuncture sites. Between days 5 and 7, patients may develop a diffuse maculopapular rash on their neck, trunk, and arms, with subsequent desquamation.[40]

There may be multiorgan failure and septic shock, leading to death. There is a high case fatality rate for ebolavirus, ranging from 18.5% in the United States and Europe to 74% in parts of Western Africa. In nonfatal cases of ebola, patients usually start to improve on day 6. They typically have a long recovery period.[40]

Diagnosis and treatment

Treatment of ebolavirus infection is primarily supportive. Volume should be maintained, along with blood pressure using vasopressors if needed and oxygenation. Pain control and nutritional support are usually required. The use of broad-spectrum antimicrobials, especially in the setting of septic shock, may be required.[40]

Conclusions

There is a broad differential diagnosis for maculopapular rash with fever in adult patients. Because some conditions are medical emergencies and highly contagious, prompt identification is critical. A thorough history can help to differentiate a benign condition from the more severe. Important factors to consider are the distribution of the rash, presence of sick contacts, travel to possible endemic areas, and the initiation of new medications.

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