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Leishmaniosis

The leishmaniosis are a diverse group of diseases caused by intracellular protozoan parasites of the genus Leishmania, which are transmitted by phlebotomine sand flies.

Multiple species of Leishmania are known to cause human disease involving the skin and mucosal surfaces and the visceral reticuloendothelial organs.

. Cutaneous disease is generally mild but may cause cosmetic disfigurement. Mucosal and visceral leishmaniosis is associated with significant morbidity and mortality.

ETIOLOGY

Leishmania organisms are members of the Trypanosomatidae family and include 2 subgenera, Leishmania (Leishmania) and Leishmania (Viannia).

The parasite is dimorphic, existing as a flagellate promastigote in the insect vector and as an a flagellate amastigote that resides and replicates within mononuclear phagocytes of the vertebrate host.

EPIDEMIOLOGY

Localized cutaneous leishmaniasis (LCL) in the Old World is caused by L. (Leishmania) major and L. (L.) tropica in North Africa, (L.) aethiopica is a cause of LCL and diffuse cutaneous leishmaniasis (DCL).

. Visceral leishmaniasis (VL) in the Old World is caused by L. (L.) donovani in Kenya, Sudan, India, Pakistan, and China .

Members of the Viannia subgenus also cause **mucosal leishmaniasis (ML**) in a similar geographic distribution.

PATHOGENESIS

Cellular immune mechanisms determine resistance or susceptibility to infection with Leishmania. within endemic areas, people who have had a subclinical infection can be identified by a positive delayed-type hypersensitivity skin response to leishmanial antigens **(Montenegro skin test),** or by antigeninduced production of interferon-γ in a whole blood assay.

CLINICAL MANIFESTATIONS

The different forms of the disease are distinct in their causes, epidemiologic features, transmission, and geographic distribution.

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Localized Cutaneous Leishmaniasis:

LCL (Oriental sore) can affect individuals of any age, but children are the primary victims in many endemic regions. It may present as 1 or a few papular, nodular, plaque like, or ulcerative lesions that are usually located on exposed skin, such as the face and extremities.

the lesions typically begin as a small papule at the site of the sandfly bite, which enlarges to 1-3 cm in diameter and may ulcerate over the course of several weeks to months

The shallow ulcer is usually nontender and surrounded by a sharp, indurate, erythematous margin. There is no drainage unless a bacterial superinfection develops.

In general, lesions caused by L. (Viannia) species tend to be larger and more chronic.

. Regional lymphadenopathy and palpable subcutaneous nodules or lymphatic cords, the so-called sporotrichoid appearance, are also more common when the patient is infected with organisms of the Viannia subgenus.

Diffuse Cutaneous Leishmaniasis:

DCL is a rare form of leishmaniasis caused by organisms of the L. Mexicana complex in the New World and L. aethiopica in the Old World. DCL manifests as large no ulcerating macules, papules, nodules, or plaques that often involve large areas of skin and may resemble lepromatous leprosy. The face and extremities are most commonly involved. It is thought that an immunologic defect underlies this severe form of cutaneous leishmaniasis.

Mucosal Leishmaniasis:

ML (espundia) is an uncommon but serious manifestation of leishmanial infection resulting from hematogenous metastases to the nasal or oropharyngeal mucosa from a cutaneous infection. It is usually caused by parasites in the L. (Viannia) complex. Approximately half of the patients with mucosal lesions have had active cutaneous lesions within the preceding 2 yr, but ML may not develop until many years after resolution of the primary lesion.

Oropharyngeal and laryngeal involvement is less common but associated with severe morbidity.

Visceral Leishmaniasis;

VL (kala-azar) typically affects children younger than 5 yr of age in the New World and Mediterranean region (L. infantum/chagasi) and older children and young adults in Africa and Asia (L. donovani).

After inoculation of the organism into the skin by the sandfly, the child may have a completely asymptomatic infection or an oligosymptomatic illness that either resolves spontaneously or evolves into **active kalaazar.** Children with asymptomatic infection are transiently seropositive but show no clinical evidence of disease. Children who are

oligosymptomatic have mild constitutional symptoms (malaise, intermittent diarrhea, poor activity tolerance) and intermittent fever; most will have a mildly enlarged liver. In most of these children the illness will resolve without therapy, but in approximately 25% it will evolve to active kalaazar within 2-8 mo. During the first few wk to months of disease evolution the fever is intermittent, there is weakness and loss of energy, and the spleen begins to enlarge. The classic clinical features of high fever, marked splenomegaly, hepatomegaly, and severe cachexia typically develop approximately 6 mo after the onset of the illness, but a rapid clinical course over 1 mo has been noted in up to 20% of patients in some series. At the terminal stages of kala-azar the hepatosplenomegaly is massive, there is gross wasting, the pancytopenia is profound, and jaundice, edema, and ascites may be present. Anemia may be severe enough to precipitate heart failure. Bleeding episodes, especially epistaxis, are frequent. The late stage of the illness is often complicated by secondary bacterial infections, which frequently are a cause of death. A younger age at the time of infection and underlying malnutrition may be risk factors for the development and more rapid evolution of active VL. Death occurs in more than 90% of patients without specific antileishmanial treatment.

LABORATORY FINDINGS ;

Patients with cutaneous leishmaniasis or ML generally do not have abnormal laboratory results unless the lesions are secondarily infected with bacteria. Laboratory findings associated with classic kala-azar include anemia (hemoglobin 5-8 mg/dL), thrombocytopenia, leukopenia (2,000-3,000 cells/µL), elevated hepatic transaminase levels, and hyperglobulinemia (>5 g/dL) that is mostly immunoglobulin G.

DIFFERENTIAL DIAGNOSIS;

Diseases that should be considered in the differential diagnosis of LCL include sporotrichosis, blastomycosis , chromomycosis, lobomycosis, cutaneous tuberculosis, atypical mycobacterial infection, leprosy, ecthyma, syphilis, yaws, and neoplasms. Infections such as syphilis, tertiary yaws, histoplasmosis, paracoccidioidomycosis, as well as sarcoidosis, Wegener granulomatosis, midline granuloma, and carcinoma may have clinical features similar to those of ML.

TREATMENT;

The pentavalent antimony compounds (sodium stibogluconate) , and meglumine antimoniate have been the mainstay of antileishmanial chemotherapy for more than 40 yr.

The recommended regimen is 20 mg/kg/day intravenously or intramuscularly for 20 day, (for LCL and DCL) or 28 days (for ML and VL).

Repeated courses of therapy may be necessary in patients with severe cutaneous lesions, ML, or VL.

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Adverse effects of antimony therapy are dose and duration dependent and commonly include fatigue, arthralgia's and myalgias (50%), abdominal discomfort (30%), elevated hepatic transaminase level (30-80%), elevated amylase and lipase levels (almost 100%), mild hematologic changes (slightly decreased leukocyte count, hemoglobin level, and platelet count) (10-30%), and nonspecific T-wave changes on electrocardiography (30%). Sudden death from cardiac toxicity has rarely been reported with use of very high doses of pentavalent antimony.

Amphotericin B desoxycholate and the amphotericin lipid formulations are very useful in the treatment of VL or ML and in some regions have replaced antimony as first-line therapy.

Amphotericin B desoxycholate at doses of 0.5-1.0 mg/kg every day or every other day for 14-20 doses achieved a cure rate for VL of close to 100%, but the renal toxicity associated with amphotericin B was common. Liposomal amphotericin B is highly effective, with a 90-100% cure rate for VL in immunocompetent children, some of whom were refractory to antimony therapy.

Tuberculosis (Mycobacterium tuberculosis):

Tuberculosis has caused human disease for more than 4,000 yr and is one of the most important infectious diseases worldwide.

ETIOLOGY:

There are 5 closely related mycobacteria in the Mycobacterium tuberculosis complex: M. tuberculosis, Mycobacterium bovis, Mycobacterium africanum, Mycobacterium microti, and Mycobacterium canetti. M. tuberculosis is the most important cause of tuberculosis disease in humans. The tubercle bacilli are non-spore-forming, nonmotile, pleomorphic, weakly Gram-positive curved rods 1-5 µm long, typically slender and slightly bent.

They can appear beaded or clumped under microscopy.

They are obligate aerobes that grow in synthetic media containing glycerol as the carbon source and ammonium salts as the nitrogen source (Löwenstein-Jensen culture media).

: **EXPOSURE, INFECTION, DISEASES :**

There are 3 major clinical stages of tuberculosis: **exposure, infection, and disease.**

Exposure means a child has had significant contact (“shared the air”) with an adult or adolescent with infectious tuberculosis but lacks proof of infection, In this stage, the tuberculin skin test (TST) or interferon-γ release assay (IGRA) result is negative, the chest radiograph is normal, the physical examination is normal, and the child lacks signs or symptoms of disease.

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Infection occurs when the individual inhales droplet nuclei containing M. tuberculosis, which survive intracellularly within the lung and associated lymphoid tissue, The hallmark of tuberculosis infection is a positive TST or IGRA result. In this stage, the child has no signs or symptoms, a normal physical examination is normal, and the chest radiograph is either normal or reveals only granuloma or calcifications in the lung parenchyma.

Disease occurs when signs or symptoms or radiographic manifestations caused by M. tuberculosis become apparent. Not all infected individuals have the same risk of developing disease.

TRANSMISSION :

Transmission of M. tuberculosis is usually by inhalation of airborne mucus droplet nuclei, particles 1-5 µm in diameter that contain M. tuberculosis. Transmission rarely occurs by direct contact with an infected discharge or a contaminated fomite. Environmental factors such as poor air circulation enhance transmission. Most adults no longer transmit the organism within several days to 2 wks after beginning adequate chemotherapy, but some patients remain infectious for many weeks.

PATHOGENESIS:

The primary complex (or Ghon complex) of tuberculosis includes local infection at the portal of entry and the regional lymph nodes that drain the area. The lung is the portal of entry in >98% of cases. The tubercle bacilli multiply initially within alveoli and alveolar ducts. Most of the bacilli are killed, but some survive within nonactivated macrophages, which carry them through lymphatic vessels to the regional lymph nodes. When the primary infection is in the lung, the hilar lymph nodes usually are involved, although an upper lobe focus can drain into Para tracheal nodes.

RISK FACTORS FOR TUBERCULOSIS INFECTION:

1-Children exposed to high-risk adults

2- Foreign-born persons from high-prevalence countries

3- Homeless persons

4- Persons who inject drugs

5- Present and former residents or employees of correctional institutions, homeless shelters, and nursing homes

6-Healthcare workers caring for high-risk patients (if infection control is not adequate)

RISK FACTORS FOR PROGRESSION OF LATENT TUBERCULOSIS INFECTION TO TUBERCULOSIS DISEASE:

1- Infants and children ≤4 yr of age, especially those less than 2 years .

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2-Adolescents and young adults.

3- Persons coinfected with HIV.

4- Persons with skin test conversion in the past 1-2 yr.

5- Persons who are immunocompromised, especially in cases of malignancy and solid organ transplantation, immunosuppressive medical treatments including anti–tumor necrosis factor therapies, diabetes mellitus, chronic renal failure, silicosis, and malnutrition.

RISK FACTORS FOR DRUG-RESISTANT TUBERCULOSIS:

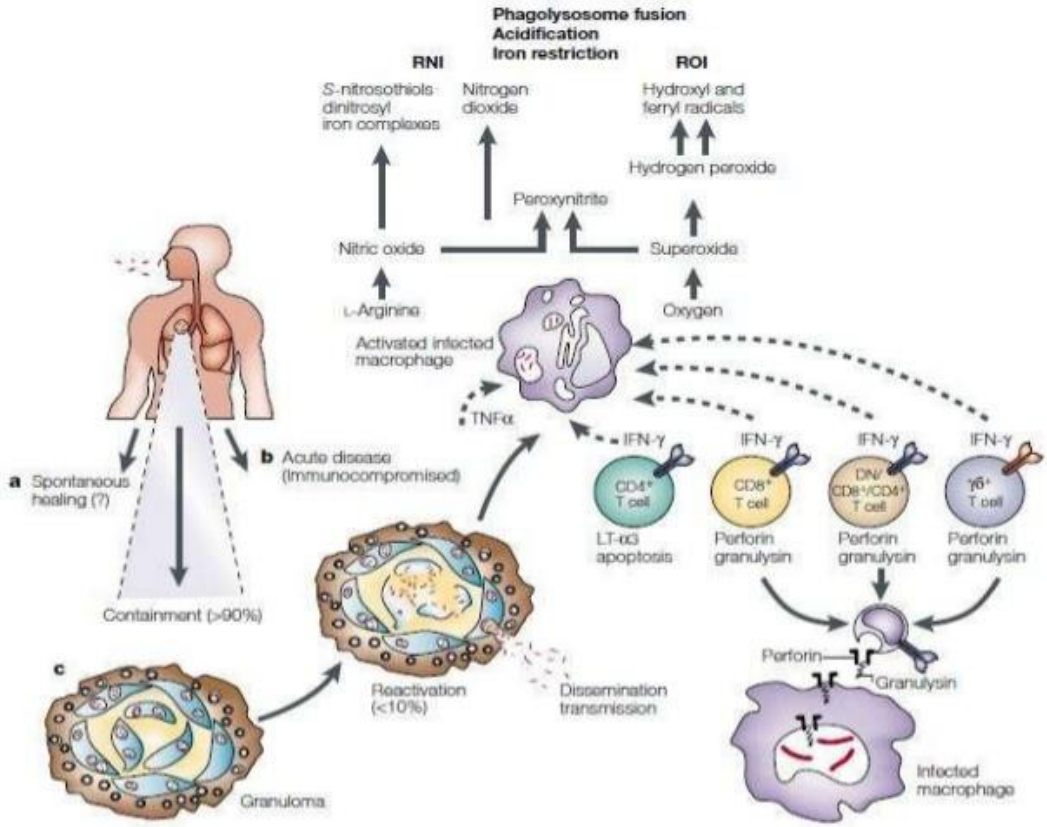
1- Personal or contact history of treatment for tuberculosis

2- Contacts of patients with drug-resistant tuberculosis

3-Birth or residence in a country with a high rate of drug resistance

4- Poor response to standard therapy

5- Positive sputum smears (acid-fast bacilli) or culture ≥2 mo after initiating appropriate therapy.



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Immunity:

Conditions that adversely affect cell-mediated immunity predispose to progression from tuberculosis infection to disease. Rare specific genetic defects associated with deficient cell-mediated immunity in response to mycobacteria include interleukin 12 receptor B1 deficiency and complete and partial interferon-γ (IFN-γ) receptor 1 chain deficiencies. Tuberculosis infection is associated with a humoral antibody response, which plays little known role in host defense. Shortly after infection, tubercle bacilli replicate in both free alveolar spaces and inactivated alveolar macrophages. Cellmediated immunity develops 2-12 wk after infection, along with tissue hypersensitivity, After bacilli enter macrophages, lymphocytes that recognize mycobacterial antigens proliferate and secrete lymphokines and other mediators that attract other lymphocytes and macrophages to the area. Certain lymphokines activate macrophages, causing them to develop high concentrations of lytic enzymes that enhance their mycobactericidal capacity,

CLINICAL MANIFESTATIONS

1-Primary Pulmonary Disease : The primary complex includes the parenchymal pulmonary focus and the regional lymph nodes. Approximately 70% of lung foci are subpleural, and localized pleurisy is common. The hallmark of primary tuberculosis in the lung is the relatively large size of the regional lymphadenitis compared with the relatively small size of the initial lung focus, As delayed-type hypersensitivity develops, the hilar lymph nodes continue to enlarge in some children, especially infants, compressing the regional bronchus and causing obstruction. The usual sequence is hilar lymphadenopathy, focal hyperinflation, and then atelectasis. The resulting radiographic shadows have been called collapse-consolidation or segmental tuberculosis. Erosion of a parenchymal focus of tuberculosis into a blood or lymphatic vessel can result in dissemination of the bacilli and a miliary pattern, with small nodules evenly distributed on the chest radiograph.

2-Reactivation Tuberculosis: Pulmonary tuberculosis in adults usually represents endogenous reactivation of a site of tuberculosis infection established previously in the body. This form of tuberculosis is rare in childhood but can occur in adolescence. Children with a healed tuberculosis infection acquired when they were younger than 2 yr of age rarely develop chronic reactivation pulmonary disease, which is more common in those who acquire the initial infection when they are older than 7 yr of age.

3-Pleural Effusion : Tuberculous pleural effusions, which can be local or general, originate in the discharge of bacilli into the pleural space from a subpleural pulmonary focus or caseated lymph node.

4-Pericardial Disease : The most common form of cardiac tuberculosis is pericarditis. It is rare, occurring in 0.5-4% of tuberculosis cases in children. Pericarditis usually arises from

direct invasion or lymphatic drainage from subcarinal lymph nodes. The presenting symptoms are nonspecific, including low-grade fever, malaise, and weight loss. Chest pain is unusual in children.

5-Lymphohematogenous (Disseminated) Disease: Tubercle bacilli are disseminated to distant sites, including liver, spleen, skin, and lung apices, in all cases of tuberculosis infection. Lymphohematogenous spread is usually asymptomatic. The most clinically significant form of disseminated tuberculosis is **miliary disease**, which occurs when massive numbers of tubercle bacilli are released into the bloodstream, causing disease in 2 or more organs. Rarely, the onset of miliary tuberculosis is explosive, and the patient can become gravely ill in several days. More often, the onset is insidious, with early systemic signs, including anorexia, weight loss, and low-grade fever. At this time, abnormal physical signs are usually absent. Generalized lymphadenopathy and hepatosplenomegaly develop within several weeks in approximately 50% of cases. The fever can then become higher and more sustained, although the chest radiograph usually is normal and respiratory symptoms are minor or absence . Within several more weeks, the lungs can become filled with tubercles, and dyspnea, cough, rales, or wheezing occur. The lesions of miliary tuberculosis are usually smaller than 2-3 mm in diameter when first visible on chest radiograph.

6-Upper Respiratory Tract Disease : Tuberculosis of the upper respiratory tract is rare in developed countries but is still observed in developing countries. Children with laryngeal tuberculosis have a croup-like cough, sore throat, hoarseness, and dysphagia.

7-Lymph Node Disease : Tuberculosis of the superficial lymph nodes, often referred to as scrofula, is the most common form of extrapulmonary tuberculosis in children.

8-Central Nervous System Disease: Tuberculosis of the central nervous system (CNS) is the most serious complication in children and is fatal without prompt and appropriate treatment. Tuberculous meningitis usually arises from the formation of a metastatic caseous lesion in the cerebral cortex or meninges that develops during the lymphohematogenous dissemination of the primary infection.

More commonly, the signs and symptoms progress slowly over weeks and are divided into 3 stages.

The 1st stage typically lasts 1-2 wk and is characterized by nonspecific symptoms such as fever, headache, irritability, drowsiness, and malaise. Focal neurologic signs are absent, but infants can experience a stagnation or loss of developmental milestones.

The 2nd stage usually begins more abruptly. The most common features are lethargy, nuchal rigidity, seizures, positive Kernig and Brudzinski signs, hypertonia, vomiting, cranial nerve palsies, and other focal neurologic signs.

The 3rd stage is marked by coma, hemi- or paraplegia, hypertension, decerebrate posturing, deterioration of vital signs, and eventually death.

DIAGNOSTIC TOOLS

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Tuberculin Skin Testing : The development of delayed-type hypersensitivity in most persons infected with the tubercle bacillus makes the TST a useful diagnostic tool. The Mantoux TST is the intradermal injection of 0.1 mL purified protein derivative stabilized with Tween 80. The amount of induration in response to the test should be measured by a trained person 48-72 hr after administration. In some patients, the onset of induration is longer than 72 hr after placement; this is also a positive result. Immediate hypersensitivity reactions to tuberculin or other constituents of the preparation are short-lived (<24hrs) and not considered a positive result. Tuberculin sensitivity develops 3 wk to 3 mo (most often in 4-8 wk) after inhalation of organisms. Host-related factors, including very young age, malnutrition, immunosuppression by disease or drugs, viral infections (measles, mumps, varicella, influenza), vaccination with live-virus vaccines, and overwhelming tuberculosis, can depress the skin test reaction in a child infected with M. tuberculosis. Corticosteroid therapy can decrease the reaction to tuberculin, but the effect is variable.

Tuberculin Skin Test Recommendations for Infants, Children, and Adolescents:

CHILDREN FOR WHOM IMMEDIATE TST OR IGRA IS INDICATED: :

• Contacts of people with confirmed or suspected contagious tuberculosis (contact investigation)

• Children with radiographic or clinical findings suggesting tuberculosis disease.

• Children immigrating from countries with endemic infection (e.g., Asia, Middle East, Africa, Latin America, countries from the former Soviet Union), including international adoptees.

• Children with travel histories to countries with endemic infection and substantial contact with indigenous people from such countries.

• Children who should have annual TST or IGRA.

• Children infected with HIV.

Definitions of Positive Tuberculin Skin Test Results in Infants, Children, and Adolescent

INDURATION ≥5 MM

Children in close contact with known or suspected contagious people with tuberculosis disease .

Children suspected to have tuberculosis disease:

• Findings on chest radiograph consistent with active or previously tuberculosis disease

• Clinical evidence of tuberculosis disease† Children receiving immunosuppressive therapy‡ or with immunosuppressive conditions, including HIV infection.

INDURATION ≥10 MM

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Children at increased risk of disseminated tuberculosis disease:

• Children younger than 4 yr of age

• Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition .

Children with increased exposure to tuberculosis disease:

• Children born in high-prevalence regions of the world

• Children often exposed to adults who are HIV infected, homeless, users of illicit drugs, residents of nursing homes, incarcerated or institutionalized, or migrant farm workers

• Children who travel to high-prevalence regions of the world

INDURATION ≥15 MM: Children ≥4 yr of age without any risk factors

Recommendations for Use of the Tuberculin Skin Test and an Interferon-γ Release Assay in Children:

TST preferred, IGRA acceptable

- Children 5 yr of age

TST preferred, IGRA acceptable

• Children 5 yr of age who have received the BCG vaccine

• Children >5 yr of age who are unlikely to return for TST reading

TST and IGRA should be considered when:

- The initial and repeat IGRA are indeterminate
- The initial test (TST or IGRA) is negative and:

i. Clinical suspicion for tuberculosis disease is moderate to high†
ii. Risk of progression and poor outcome is high† •

The initial TST is positive and:

a) >5 yr of age and history of BCG vaccination
b) Additional evidence needed to increase compliance
c) Nontuberculous mycobacterial disease is suspected

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TREATMENT :

The basic principles of management of tuberculosis disease in children and adolescents are the same as those in adults. Several drugs are used to affect a relatively rapid cure and prevent the emergence of secondary drug resistance during therapy, The standard therapy of intrathoracic tuberculosis (pulmonary disease and/or hilar lymphadenopathy) in children, as recommended by the CDC and American Academy of Pediatrics, is a 6 mo regimen of isoniazid and rifampin supplemented in the 1st 2 mo of treatment by pyrazinamide and ethambutol.

Extrapulmonary tuberculosis is usually caused by small numbers of mycobacteria. Exceptions are bone and joint, disseminated, and CNS tuberculosis, for which there are inadequate data to recommend 6 mo of therapy. These conditions are treated for 9-12 mo. Surgical debridement in bone and joint disease and ventriculoperitoneal shunting in CNS disease may be necessary adjuncts to medical therapy.

The optimal treatment of *tuberculosis in HIV*-infected children has not been established. HIV-seropositive adults with tuberculosis can be treated successfully with standard regimens that include isoniazid, rifampin, pyrazinamide, and ethambutol. The total duration of therapy should be 6-9 mo, or 6 mo after culture of sputum becomes sterile, whichever is longer.

Corticosteroids:

Corticosteroids are useful in treating some children with tuberculosis disease. They are most beneficial when the host inflammatory reaction contributes significantly to tissue damage or impairment of organ function, Some children with severe miliary tuberculosis have dramatic improvement with corticosteroid therapy if the inflammatory reaction is so severe that alveolocapillary block is present.

Cytomegalovirus:

Human cytomegalovirus (CMV) is ubiquitous in the population, and once infected, individuals remain persistently infected for life with intermittent excretion of infectious virus. Although CMV rarely causes symptoms in normal individuals, it is an important cause of morbidity, and in some cases death, in immunocompromised hosts.

EPIDEMIOLOGY :

CMV infections are acquired through several settings:

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(1) community exposure, (2) nosocomial transmission, and (3) intrauterine infection. Community acquisition occurs throughout life and is linked by exposure to CMV present in saliva and urine.

(2)

Congenital Infection:

Congenital infection with CMV can present with symptomatic infections in approximately 10% of infected newborns, whereas 90% of infected infants will have no clinical manifestations of infection in the newborn period. Severe multiorgan disease is infrequent and occurs in less than 5% of infants with congenital CMV infections. The clinical findings of infants with symptomatic congenital CMV infections can include hepatosplenomegaly, petechial rashes, jaundice, and in some cases microcephaly. Laboratory findings include direct hyperbilirubinemia, elevation of hepatic transaminases, thrombocytopenia, anemia, and abnormal findings on cranial ultrasonography. Finally, because hearing loss is the most common long-term sequela associated with congenital CMV infection, the failure of an infant to pass a newborn hearing screening exam should raise the possibility of congenital CMV infection.

Findings in Infants with Symptomatic Congenital Cytomegalovirus Infection Identified Through Newborn Screening Program:

Prematurity (2 mg/dL) 42% , Petechial 54%, Hepatosplenomegaly 19% , Purpura 3%, Microcephaly 35%, Small gestational age 28%.

LABORATORY FINDINGS :

Elevated alanine aminotransferase (>80 IU/mL) 71%

Thrombocytopenia

Direct hyperbilirubinemia (2 mg/dL) 54%

Head CT abnormalities 42%

DIAGNOSIS:

Serologic reactivity for CMV is lifelong following primary infection; therefore, the presence of immunoglobulin (Ig) G antibody to CMV does not provide evidence of infection.

TREATMENT

Treatment of immunocompromised hosts with invasive CMV disease limits both the morbidity and mortality in the patient with disseminated CMV infections with end-organ

disease . Treatment of congenitally (symptomatic and asymptomatic but at risk for hearing loss) infected infants with ganciclovir has been studied in clinical trials; many infected infants have been treated off-label with this agent because of severe CMV infections.

Herpes Simplex Virus:

The 2 closely related herpes simplex viruses (HSVs), HSV type 1 (HSV-1) and HSV type 2 (HSV-2), cause a variety of illnesses, depending on the anatomic site where the infection is initiated, the immune state of the host, and whether the symptoms reflect primary or recurrent infection. Common infections involve the skin, eye, oral cavity, and genital tract. Infections tend to be mild and self-limiting, except in the immunocompromised patient and newborn infant, in whom they may be severe and life-threatening.

CLINICAL MANIFESTATIONS :

The hallmarks of common HSV infections are skin vesicles and shallow ulcers. Classic infections manifest as small, 2-4 mm vesicles that may be surrounded by an erythematous base. These may persist for a few days before evolving into shallow, minimally erythematous ulcers.

DIAGNOSIS :

The clinical diagnosis of HSV infections, particularly life-threatening infections and genital herpes, should be confirmed by laboratory test, preferably isolation of virus or viral DNA detection by polymerase chain reaction (PCR). Virus culture remains the gold standard for diagnosing HSV infection . Evaluation of the neonate with suspected HSV infection should include cultures of suspicious lesions as well as eye and mouth swabs and PCR of CSF and blood. In neonates testing for elevation of liver enzymes may provide indirect evidence of HSV dissemination to visceral organs. Culture or antigen detection should be used in evaluating lesions associated with suspected acute genital herpes.

LABORATORY FINDINGS:

The electroencephalogram and MRI of the brain may show temporal lobe abnormalities in HSV encephalitis beyond the neonatal period. Encephalitis in the neonatal period tends to be more global and not limited to the temporal lobe (Fig. 252-5). Disseminated infection may cause elevated liver enzymes, thrombocytopenia, and abnormal coagulation.

TREATMENT :

Three antiviral drugs are available in the United States for the management of HSV infections, namely acyclovir, valacyclovir, and famciclovir. All 3 are available in oral form, but only acyclovir is available in a suspension form.

Rubella:

Rubella (German measles or 3 day measles) is a mild, often exanthematous disease of infants and children that is typically more severe and associated with more complications in

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adults. Its major clinical significance is trans placental infection and fetal damage as part of the congenital rubella syndrome (CRS).

CLINICAL MANIFESTATIONS:

Postnatal infection with rubella is a mild disease not easily discernible from other viral infections, especially in children. Following an incubation period of 14-21 days, a prodrome consisting of low-grade fever, sore throat, red eyes with or without eye pain, headache, malaise, anorexia, and lymphadenopathy begins. Suboccipital, postauricular, and anterior cervical lymph nodes are most prominent.

Clinical Manifestations of Congenital Rubella Syndrome in Children Following Maternal Rubella*

Deafness ,
Ocular : Cataracts , Retinopathy .
Heart disease: Patent ductus arteriosus , Right pulmonary artery stenosis , Left pulmonary artery stenosis , Valvular pulmonic stenosis .
Low birthweight .
Psychomotor retardation .
Neonatal purpura .
Death.

LABORATORY FINDINGS :

Leukopenia, neutropenia, and mild thrombocytopenia have been described during postnatal rubella.

DIAGNOSES:

A specific diagnosis of rubella is important for epidemiologic reasons, for diagnosis of infection in pregnant women, and for confirmation of the diagnosis of congenital rubella. The most common diagnostic test is rubella immunoglobulin (Ig) M enzyme immunosorbent assay.

Congenital Rubella Syndrome:

An ophthalmologist first described a syndrome of cataracts and congenital heart disease that he correctly associated with rubella infections in the mothers during early pregnancy. Shortly after the first description, hearing loss was recognized as a common, finding often associated with microcephaly. Most infants have some degree of intrauterine growth restriction. Retinal findings described as salt-and-pepper retinopathy are the most common ocular abnormality but have little early effect on vision. *Cardiac abnormalities* occur in half of the children infected during the 1st 8 wk of gestation. Patent ductus arteriosus is the most frequently reported cardiac defect, followed by lesions of the pulmonary arteries and valvular disease.

TREATMENT :

There is no specific treatment available for either acquired rubella or CRS.

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Congenital Toxoplasmosis :

Transmission to the fetus usually follows acquisition of primary infection by an immunologically normal pregnant woman during gestation. Congenital transmission from mothers infected before pregnancy is extremely rare except for immunocompromised women who are chronically infected.

DIAGNOSIS:

Diagnosis of acute Toxoplasma infection can be established by a number of methods (Table 290-2). For example, isolation of T. gondii from blood or body fluids; identification of tachyzoites in sections or preparations of tissues and body fluids, amniotic fluid, or placenta; identification of cysts in the placenta or tissues of a fetus or newborn; and characteristic lymph node histologic features establish the diagnosis. Serologic tests are very useful for diagnosis. Polymerase chain reaction (PCR) is useful to identify T. gondii DNA in CSF and amniotic fluid, and has been reported to be useful with infant peripheral blood and urine to definitively establish the diagnosis.

Clinical manifestation of CRS :

- **A.** **INFANTS** Chorioretinitis , Abnormal cerebrospinal fluid , Anemia ,) Convulsions , Intracranial calcification , Jaundice , Hydrocephalus , Fever , Splenomegaly , Lymphadenopathy , Hepatomegaly , Vomiting , Microcephalus , Diarrhea , Cataracts , Eosinophilia , Abnormal bleeding , Hypothermia , Glaucoma
- **B.** **CHILDREN** ≥4 YR OF AGE : Mental retardation , Convulsions , Spasticity and palsies , Severely impaired vision , Hydrocephalus or microcephalus , Deafness and may normal.

Treatment

Congenital Toxoplasmosis All fetuses and newborns infected with T. gondii should be treated whether or not they have clinical manifestations of the infection because treatment may be effective in interrupting acute disease that damages vital organs.
The fetus is treated by treating the pregnant woman with pyrimethamine and sulfadiazine (with leucovorin). Infants should be treated for 1 yr with pyrimethamine (2 mg/kg/day divided bid for 2 days, then beginning on the 3rd day, 1 mg/kg/day for 2 or 6 mo, and then 1 mg/kg given on Monday, Wednesday, and Friday, PO), sulfadiazine (100 mg/kg/day divided bid PO), and leucovorin (5-10 mg given on Monday, Wednesday, and Friday, or more often depending on neutrophil count, PO).

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Best wishes