Handbook of Perinatal Infections

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Preface

Handbook of Perinatal Infections is intended to provide students, residents, and practitioners with a clinically oriented review of perinatal infections in a format compact enough to facilitate quick reference close to patient-care areas. Each chapter has been organized to emphasize in tabular form fundamental aspects of diagnosis, management, and prevention for each infectious process. When feasible, information concerning mother and child has been presented in parallel. Question-and-answer sections have been provided for those topics about which we have received frequent inquiries. As a starting point for more in-depth study, selected readings have been included at the end of each chapter.

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NOTICE

The indications and dosages of all drugs in this book have been recommended in the medical literature and conform to the practices of the general medical community. The medications described do not necessarily have specific approval by the Food and Drug Administration for use in the situations and the dosages for which they are recommended. The package insert for each drug should be consulted for use and dosage as approved by the FDA. Because standards for usage change, it is advisable to keep abreast of revised recommendations, particularly those concerning new drugs.

Contents

I. Viral Infections

1. Rubella

Rubella, three-day measles, was first recognized as a teratogen in 1941 by the ophthalmologist Gregg following an epidemic in Australia. Fetal damage has been associated with maternal infection during the first five months of pregnancy (Fig. 1–1).

FREQUENCY

More than 20,000 cases of congenital rubella occurred during the 1964 epidemic in the United States. Since the widespread use of vaccines in this country late in the 1960s, only 25–90 cases of congenital rubella have been reported each year. Today approximately 10–15 percent of the adult women in the United States have no detectable rubella antibody and are at risk for rubella.

DIAGNOSIS

MOTHER

Clinical

The diagnosis of maternal rubella is usually made on the basis of clinical findings and history of exposure two to three weeks earlier (Table 1–1). The signs include a discrete pink-red maculopapular rash that begins on the face, spreads to the neck, arms, trunk, and legs, and lasts approximately three days. The rash may coalesce into a red blush and an enanthem of red spots may be present. There is usually lymph node enlargement, particularly of the suboccipital, postauricular, and cervical nodes. There may be a slight fever before and during the rash. Clinical findings are evident in approximately two-thirds of women who have rubella. The other third have inapparent infection. Confirmation of the clinical diagnosis requires serologic tests or virus isolation or both.

Serology

Antibody tests are now readily available at most hospitals and at private and state laboratories. Paired blood specimens should be obtained to document a seroconversion. The hemagglutination inhibition (HI) test is generally used.

The first serum specimen should be taken as soon as possible after exposure (within 10 days). If there is detectable antibody, the patient can be considered immune by virtue of previous infection or immunization. However, there is sufficient variation in laboratory results so that in critical cases, titers should be repeated for verification. If there is no detectable antibody, the second specimen then should be taken four weeks later. The paired sera should be run together in the same test to document a seroconversion, because if the two sera

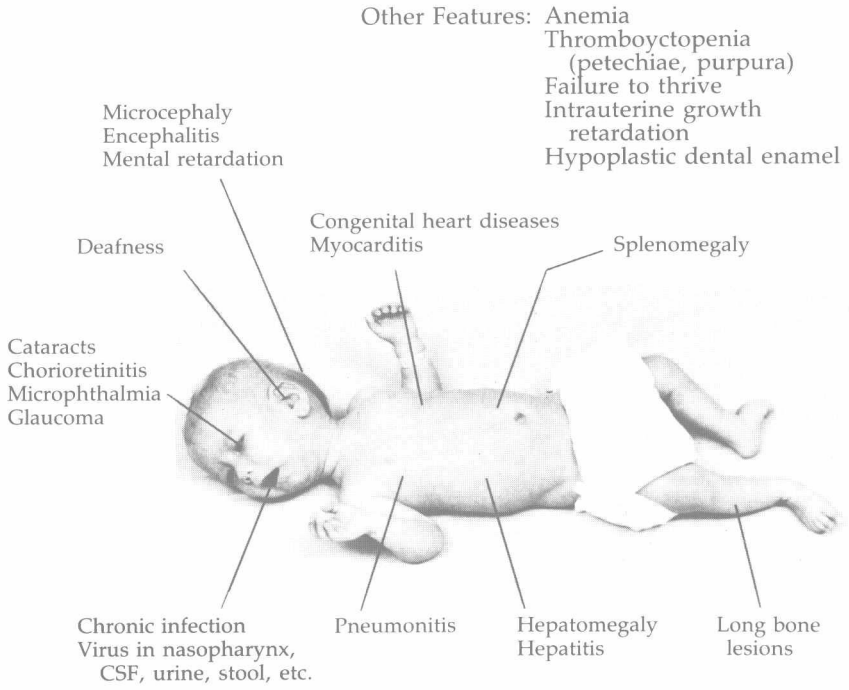

Figure 1–1. Expanded congenital rubella syndrome. Clinical and laboratory findings.

are tested at different times, laboratory variations may give false information. If the first serum specimen is taken at the time of the rash or later, it is often impossible to show a seroconversion, since that specimen may already have elevated levels of rubella antibody. In those cases, it is sometimes possible to establish the diagnosis by the use of the complement fixation (CF) test since CF antibody increases slowly, and this property can be used to demonstrate the seroconversion.

If only a single early convalescent specimen is available, tests for IgM-specific rubella antibody must be used to establish diagnosis. IgM rubella antibody is produced for approximately one month only following clinical rubella, and it is possible to make the diagnosis by appropriate separation of the IgM rubella antibody. At the present time, the Center for Disease Control (CDC) in Atlanta is conducting these tests when requested.

Antibody tests, such as HI, should also be used to identify women who are susceptible to infection. If no detectable HI antibody is found, the women should be considered at risk, and vaccine should be ad-

Table 1–1. Diagnosis of Rubella

Mother	Child (Congenital)
CLINICAL	
History: exposure 2–3 weeks earlier	Eyes: cataracts, glaucoma, salt and pepper retinopathy
3-day rash: pink-red maculopapules. Begins on face and spreads to trunk and extremities. May coalesce to a red blush. Enanthem of small red spots	Heart: peripheral pulmonic stenosis, patent ductus arteriosus, ventricular septal defect, myocarditis
Lymphadenopathy: suboccipital, postauricular, cervical	Head: microcephaly, encephalitis, mental retardation
Mild fever, headache, malaise, anorexia	Deafness, thrombocytopenia with petechiae, hepatosplenomegaly, jaundice, microcephaly, mental retardation, pneumonitis, radiolucency of long bones
Conjunctivitis, cough, arthritis, arthralgia	
LABORATORY	
Antibody seroconversion (HI, CF, ELISA, or RIA test)	HI antibody persistence (more than 3 months)
Specific rubella IgM antibody (CDC test)	Specific rubella IgM antibody (CDC test)
Virus isolation from throat	Virus isolation from throat, urine, or spinal fluid

ministered—provided they are not pregnant and will not become pregnant for three months after the vaccine is given.

Absent or low levels of HI antibody are of concern because test results have been found to be in error in some laboratories. As with all tests, good quality control is essential. If there is reason to question the results, sera should be sent to a reference laboratory and retested, preferably with one of the highly sensitive tests such as the enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay (RIA).

Virus Isolation

A second diagnostic approach is isolation of the virus from the woman at the time of the rash. The virus is present in the nasopharynx for approximately one week before and one week after the appearance of the rash. Throat swab specimens should be obtained and sent to an appropriate virus diagnostic laboratory. Consultation concerning collection, storage, and transportation of the specimen can increase

the yield of positive specimens. The clinician, however, should be aware that rubella isolation usually takes four to six weeks to complete.

Child

Clinical

Classical congenital rubella can be diagnosed on the basis of the presence of cataracts, congenital heart disease (peripheral pulmonic stenosis, patent ductus arteriosus, ventricular septal defect, myocarditis), congenital glaucoma, radiolucent bone lesions, hepatosplenomegaly, petechiae, and thrombocytopenia. Some children have "salt and pepper" retinopathy, hearing loss, interstitial pneumonitis, jaundice, microcephaly, stenosis of various arteries, and rarely, encephalitis. In most cases, however, the child with congenital infection exhibits only a few of these findings. The most frequent abnormalities are deafness and congenital heart disease.

Serology

Laboratory confirmation of congenital rubella can be obtained by detecting rubella IgM antibody in the child during the first months of life. IgM-specific antibody tests for congenital rubella may be obtained on special request through the Center for Disease Control. Elevated rubella antibody (IgG) persisting past the third to sixth month of life is also confirmatory.

Virus Isolation

Children with congenital rubella excrete virus from the nasopharynx for at least six months. Virus is also present in the urine and spinal fluid for a number of months. Thus, specimens for virus isolation may be used to establish the diagnosis if appropriate laboratory facilities are available.

PROGNOSIS

Mother

The mother with rubella experiences only a mild disease that lasts an average of three days. In some cases, there may be mild arthralgia or arthritis of small joints for a short period. Rarely, women have recurrent arthralgia or thrombocytopenia that lasts more than a few days.

Child

Some newborns with severe pneumonitis and myocardial damage may die in the first weeks of life. For most children, however, the prognosis depends on the extent of permanent organ damage. Significant permanent damage is found in approximately 50 percent of

children with maternal rubella in the first month of pregnancy, 22 percent in the second month, 10 percent in the third month, and 6 percent in the fourth and fifth months. Some of the defects may become recognized only after prolonged observation. Thus, approximately one-third of defects in children with congenital rubella are missed in the newborn period because they do not become apparent until the children are several years old. The most frequent of these defects are deafness, mental retardation, and heart and blood vessel defects and diabetes. For this reason, repeated examination of children with congenital rubella should be conducted for six to eight years, to ensure the early detection and treatment of all defects.

Severe late effects of chronic, suppressed rubella infections of the central nervous system have now been recognized as "progressive rubella panencephalitis." In these cases, children with congenital rubella were otherwise healthy until their second decade of life and then developed spasticity, ataxia, mental deterioration, and seizures. They had high serum and spinal fluid antibody titers to rubella and high spinal fluid gamma globulin levels. Rubella virus has been recovered from the brain of at least one child. This late disease must now be recognized as one of the manifestations of congenital rubella. The frequency with which this fatal encephalitis occurs has not been established, but preliminary information indicates that it would seem to be uncommon.

MANAGEMENT

Mother

Women with rubella require no special therapy (Table 1–2). Usually mild analgesics and rest for a few days are sufficient to control the fever, malaise, and arthralgia, if present. The physician's objective must be to document the occurrence of the infection by serology or virus isolation. If infection is established in early pregnancy, the woman may elect to have an abortion because of the increased risk of defects in the fetus. Patients with rubella should be seen at a time and place that minimizes the risk of spreading their infection to other susceptible contacts.

Child

The child with congenital rubella must be recognized as a potential source of rubella infection and should be isolated. Most children excrete the virus in the nasopharynx for about six months, but some children shed virus for over one year. The child should be studied in detail to identify the type and the extent of the damage present. The defects of heart and eyes should be treated by the appropriate subspecialists. Subtle damage, such as mild or moderate hearing loss

Table 1–2. Management of Rubella

Mother	Child (Congenital)
INFECTION	
Mild analgesics Rest Document infection by serology or virus isolation	Isolate. Virus shed for 6–12 months Careful clinical studies for the type and extent of damage Repeated followup: clinical studies for defects and special treatment
VACCINES	
Immunize antibody negative women (10–15% of population have no antibody); make certain woman is not pregnant and will not become pregnant for 3 months Immediate post-partum immunization also useful	Immunize all children at 15 months of age and all unimmunized children before they enter school

and mild mental retardation, may not be established until many years later. For that reason, arrangements must be made for the continued observation of the child, and enrollment in appropriate special education programs should be started as soon as possible. No antiviral chemotherapy is available.

PREVENTION

Vaccines for rubella have been available since 1969 in the United States and appear to be extremely effective. Approximately 95 percent of the people who are immunized develop detectable antibody, which persists for at least a number of years. More recently, immunization programs have not been as enthusiastically supported as in the beginning. Thus, significant groups of some populations have not been immunized and small "epidemics" of rubella have occurred.

The physician should recognize the importance of encouraging immunization against rubella. All children should be immunized. The current recommendations are that immunization be given at 15 months of age on a routine basis and that older children who have not been previously vaccinated be immunized. In addition, women of childbearing age who do not have detectable HI antibody should be immunized, provided they are not pregnant and will not become pregnant for at least three months after immunization is given. This precaution is necessary because the vaccine virus has been shown to transmit to the products of conception and, in rare instances, to the