J. PERINATAL AND GYNECOLOGIC INFECTIONS

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INTRODUCTION

Information regarding perinatal, obstetric, and gynecologic infections will be presented in considerable detail, reflecting the editors' judgment that such infections are major causes of morbidity and mortality for Native American women and their babies. Even so, it is recognized that the topics covered are not all-inclusive, but that they are intended to serve as guidelines for management of common clinical problems. It cannot be over-emphasized that judicious use of antibiotics requires knowledge of both the prevalence patterns and the antibiotic sensitivities of specific infectious organisms isolated at a given Service Unit. The first portion of this chapter is devoted to a discussion about Perinatal and Newborn Infections. This will be followed by a discussion of Obstetric and Gynecologic Infections and the general principles of their diagnosis and treatment.

I. PERINATAL AND NEWBORN INFECTIONS

Definition and Scope of the Problem

Perinatal infections involve infectious diseases occurring in pregnancy that affect the fetus, and those occurring in the immediate newborn period caused by viruses, bacteria, protozoa (e.g., toxoplasma, treponema), fungi, mycoplasma, and chlamydia. Although each infecting organism has its own epidemiology, pathologic effect, clinical presentation and diagnostic tests, it is convenient to group perinatal infections together because of their occurrence in this well-defined period of life and because of their often rather similar clinical presentation. As many as 2 percent of fetuses are infected in utero, and up to 10 percent of infants are infected during delivery or in the first weeks of life.

Perinatal infections remain a constant source of morbidity and mortality for the mother, fetus, and newborn infant, potentially leading to one or more of the following adverse outcomes:

- Maternal illness or death
- Resorption of the embryo
- Abortion
- Stillbirth
- Congenital malformations of the fetus and newborn
- Intrauterine growth restriction of the fetus, and failure to thrive of the newborn infant
- Premature delivery
- Acute neonatal illness or death
- Long-term sequelae (even life-long damage) in the surviving infant, with resultant impairment of the potential of many individuals in all societies

Anticipation of the Problem

Mothers at particular risk for perinatal infection include the following groups:

- Women who have had no previous exposure to the infectious agents, either in the wild form or through vaccination.
- Women who have limited immune response of their own due to hereditary immune deficiency, poor nutritional status, or disease states (e.g., diabetes, cancer, HIV infection).
- Women of lower socioeconomic status or who live in less hygienic environments.
- Women with certain behavioral habits or lifestyles that lead to substance abuse, inadequate or excessive weight gain, or lack of prenatal medical surveillance and care.

There are also well-defined groups of newborn infants at high-risk for acquiring perinatal infections and in particular bacterial sepsis as a result of either increased exposure to infectious organisms or reduced response on the part of the newborn to infection.

Increased exposure:

- Infants born of mothers with peripartum infections, such as urinary tract infections within the last 2 weeks prior to delivery, recent sore throat or fever, or vaginal discharge
- Premature rupture of membranes greater than 24 hours prior to delivery, most particularly if numerous vaginal exams were performed during labor
- Prolonged 2nd stage of labor
- Invasive procedures performed on the fetus
- Maternal sepsis
- Meconium aspiration at birth
- Maternal carriage of Group B Beta hemolytic Streptococcus

Reduced resistance:

- All newborns, but especially the premature (see below)
- Fetal distress or perinatal asphyxia
- Traumatic delivery
- Illness requiring neonatal intensive care
- Male infants, who have a higher incidence of bacterial sepsis but not of intrauterine, viral or protozoan infections

Pathogenesis of Perinatal Infections

Pregnancy tends to increase maternal susceptibility for certain infections because of various hormonal and anatomic changes in the body. Previously latent or asymptomatic infections may be reactivated during pregnancy. Also, the course of some infections may be prolonged or the severity of others may be increased during pregnancy due to these same hormonal and physiologic changes.

For the fetus it is generally true that the earlier in pregnancy an infection is acquired the more serious the consequences are likely to be in terms of development of congenital malformations or adverse outcome. Also, primary infections in the mother are more serious for the fetus and newborn than reinfection or reactivation of a latent infection in the pregnant woman, due to the lack of protective antibodies transferred through the placenta.

The newborn infant, and especially the prematurely born infant, has a number of cell-mediated immune system deficiencies that predispose him or her to certain types of infection. Phagocytosis (or the intracellular destruction of invading organisms) is deficient in terms of chemotaxis, opsonization, and digestion:

- Chemotaxis—This deficiency partially explains the newborn's inability to respond to pneumococcal or Hemophilus influenzal antigen.
- Opsonization—This deficiency partially explains the newborn's susceptibility to gram-negative organisms and certain viruses.
- Digestion—This deficiency partially explains the newborn's low resistance to staphylococcal infections.

The newborn infant also has certain limitations of the humoral immune system, which is responsible for production of specific antibodies. Considerable protection is provided by the mother by means of passive transplacental transfer of primarily IgG antibody. Table 1 lists the specific types of antibody exhibiting good, poor, or no passive transfer across the placenta. Large-molecular IgM antibody isn't able to cross the placenta and leaves the newborn especially prone to contract salmonella, shigella, and gram-negative infections such as E. coli. The fetus can produce IgM antibody beginning at about 20 weeks gestation given the necessary "antigenic stimuli" (i.e., intrauterine infection), but production capability is limited. Normally, the IgM level at term is about 20 percent of normal adult levels (or 20 mg/dl) and doesn't reach full adult levels until about one year of age. Because it doesn't cross the placenta, the presence of specific IgM antibody in cord or newborn blood suggests prior infection of the fetus with the specific infectious agent, and constitutes the means of making the definitive diagnosis in a number of congenital infections to be discussed below.

TABLE 1 NEONATAL PASSIVE IMMUNITY: PLACENTAL PASSAGE OF MATERNAL ANTIBODIES

GOOD PASSIVE TRANSFER (IgG)	POOR PASSIVE TRANSFER	NO PASSIVE TRANSFER[A]
Tetanus antitoxin	*B. pertussis* Ab	*Salmonella* somatic (O) Ab
Diphtheria antitoxin	*Shigella flexneri* Ab	*Escherichia coli* H and O Ab
Bordetella pertussis agglutinin	*Streptococcus* Mg Ab	Heterophile Ab
Antistreptolysin Ab[b]		Wassermann Ab
Antistaphylolysin Ab		Natural (anti-A, anti-B) isoagglutinins
Poliomyelitis Ab		
Measles, mumps, rubella Ab		Rh saline (complete) agglutinins
Herpes simplex Ab		Reaginic Ab (IgE)
Hemophilus influenza Ab (see text)		
Group B streptococcal Ab		
Salmonella flagellar (H) Ab		
Rh incomplete (Coombs') Ab		
Immune (anti-A, anti-B) isoagglutinins		
VDRL Ab		
Long-acting thyroid stimulator		
Antinuclear Ab (ANA)		

[a]Mostly IgM.

[b]Ab = antibodies

Adapted from Miller ME, Stiehm ER. Immunology and resistance to infection. In: Remington JS, Klein JO. Infectious Diseases of the Fetus and Newborn Infant, 2nd ed. Philadelphia(PA), WB Saunders; 1983 with permission. (Level III)

Fetal Infections

The embryo or fetus may become infected or be affected by invading organisms in several ways. Infectious spread may come from adjacent maternal tissues (a) by way of ascension through defects in the membranes overlying the cervical os, (b) by descending through the fallopian tubes in cases of peritonitis or salpingitis, or (c) by direct extension from an infection in the uterus. Infection of the fetus may also occur after invasion of the maternal bloodstream with resultant bacteremia or viruses in circulating lymphocytes, neutrophils, or erythrocytes. Microbial invasion of the maternal bloodstream may result in placental infection only, infection of both placenta and fetus, or toxic effects on both mother and fetus, such as fever, anoxia, hypoxia, cardiovascular collapse, coagulopathy, or metabolic disturbances. All of these latter pathologic effects can likewise lead to abortion, stillbirth, or premature delivery. Table 2 lists major adverse effects on the fetus produced by various organisms.

Table 2 EFFECTS OF TRANSPLACENTAL FETAL INFECTION

Effect of Infection on the Fetus and Newborn Infant

Organism or Disease	Intrauterine Prematurity	Growth Restriction And Low Birth Weight	Developmental Anomalies	Congenital Disease	Persistent Postnatal Infection
Viruses					
Rubella	-	+	+	+	+
Cytomegalovirus	+	+	+	+	+
Herpes simplex	+	-	-	+	+
Varicella-zoster	-	(+)	+	+	+
Mumps	-	-	-	(+)	-
Rubeola	+	-	-	+	-
Vaccinia	-	-	-	+	-
Smallpox	+	-	-	+	-
Coxsackieviruses B	-	-	(+)	+	-
Echoviruses	-	-	-	-	-
Polioviruses	-	-	-	+	-
Influenza	-	-	-	-	-
Hepatitis B	+	-	-	+	+
Human Immunodeficiency virus	(+)	(+)	(+)	+	+
Lymphocytic choriomeningitis virus	-	-	-	+	-
Parvovirus	-	-	-	+	-
Bacteria					
Treponema pallidum	+	-	-	+	+
Mycobacterium tuberculosis	+	-	-	+	+
Listeria monocytogenes	+	-	-	+	-
Campylobacter fetus	+	-	-	+	-
Salmonella typhosa	+	-	-	+	-
Borrelia burgdorferi	-	-	-	+	-
Protozoa					
Toxoplasma gondii	+	+	-	+	+
Plasmodium	(+)	+	-	+	+
Trypanosoma cruzi	+	+	-	+	-

+ = evidence for effect; (-) = no evidence for effect; (+) = association of effect with infection has been suggested and is under consideration

From Remington JS, Klein JO. Infectious diseases of the fetus and newborn infant. 5th ed. Philadelphia(PA): W.B. Saunders Company; 2001 with permission. (Level III)

Intrapartum and Early Postpartum Infections

Both antiviral and antimicrobial factors are contained in the amniotic fluid. With rupture of the membranes, not only are these protective factors lost but also vaginal flora now have an unobstructed path to ascend into the amniotic cavity, potentially infecting the fetal membranes (chorioamnionitis), the placenta, the cord (umbilical vasculitis), and the fetus. Amnionitis occurs in approximately 11 percent of all cases of premature rupture of membranes (i.e., membrane rupture prior to onset of labor), increasing the incidence of neonatal sepsis and death 3 to 6 times. The longer the duration of ruptured membranes prior to delivery, the greater the potential risk for sepsis (or generalized infection) in the neonate; if less than 24 hours the risk is between 4 and 5 percent and it increases if there have been any digital examinations of the cervix.

Passage through a contaminated birth canal at the time of vaginal delivery can likewise lead to serious neonatal infection. There are variable degrees of association between neonatal disease and the specific microorganisms present in the maternal birth canal, as illustrated in Table 3. That is to say, the risk of colonization and subsequent infection depends on the contaminating pathogen: In the case of acute Herpes simplex, the rate of infection is between 20 and 50 percent; for CMV it is approximately 10 percent; for *E. coli* with K-1 antigen it is 60 percent; and for chlamydia it is estimated to be 50 percent or more.

TABLE 3 ASSOCIATION OF NEONATAL DISEASE WITH MICROORGANISMS PRESENT IN THE MATERNAL BIRTH CANAL

Microorganism	Significant	Uncommon	Rare or None
Bacteria			
Lactobacillus			+
Staphylococcus epidermidis			+
Staphylococcus aureus		+	
Alpha-hemolytic *Streptococcus*	+		
Group A *Streptococcus*	+		
Group B *Streptococcus*	+		
Group D *Streptococcus*	+		
Escherichia coli	+		
Proteus species		+	
Klebsiella species		+	
Pseudomonas species		+	
Salmonella species		+	
Shigella species		+	
Alkaligenes faecalis		+	
Neisseria meningitidis		+	
Neisseria gonorrhoeae	+		
Haemophilus influenzae		+	
Haemophilus parainfluenzae		+	
Haemophilus vaginalis		+	
Listeria monocytogenes	+		
Vibrio fetus		+	
Corynebacterium			+
Bacillus subtilis			+
Anaerobic bacteria[100]			
Bacteroides		+	
Peptostreptococcus			+
Veillonella			+
Clostridium species		+	
Bifidobacterium			+
Eubacterium			+
Mycobacterium tuberculosis			+
Viruses			
Cytomeglovirus	+		
Herpes simplex (type 2)	+		
Rubella			+
Hepatitis B	+		
Human papilomavirus			+
Lymphocytic choriomeningitis virus			+
Human immunodeficiency virus		+	
Fungi			
Candida albicans	+		
Torulopsis glabrata			+
Coccidioides immitis		+	
Saccharomyces			+
Chlamydiaceae			
Chlamydia trachomatis	+		
Mycoplasmataceae			
Mycoplasma hominis		+	
Ureaplasma urealyticum		+	
Protozoa			
Toxoplasma gondi		+	
Trichomonas vaginalis		+	

Modified from Remington JS, Klein JO. Infectious diseases of the fetus and newborn infant. 5th ed. Philadelphia(PA): W.B. Saunders Company; 2001 with permission. (Level III)

Aspiration of amniotic fluid during the birth process brings with it special problems if the material aspirated is contaminated with infectious organisms. Not only are the mucosal membranes of the eyes (conjunctiva), nasal and oral passages, and upper GI tract contaminated, but also the lower respiratory tract and lungs. From resultant pneumonia to generalized sepsis is a very short step in cases involving compromised hosts (e.g. premature infants) or virulent organisms (e.g. Group B streptococci).

Nosocomial and Late Neonatal Infections

After birth the neonate is quickly colonized and is subject to infectious agents from human carriers and the hospital (nosocomial = hospital or infirmary) environment. Important sources of nosocomial and late neonatal infections include:

- Contaminated instruments or non-sterile technique while performing internal fetal monitoring.
- Non-sterile technique while performing invasive procedures on the newborn infant, such as intubation, umbilical vessel catheterization, chest tube placement, or bladder catheterization.
- Contaminated respiratory therapy equipment carrying so-called “water bugs,” such as *Serratia*, *Pseudomonas*, and *Flavobacterium*.
- Contaminated bathing solutions (most frequently containing *Candida* or *Staphylococci*).
- Hands of nursery personnel that serve as a reservoir or passing source of organisms such as *Staphylococcus aureus*, Group B streptococcus, or Herpes simplex.
- Droplets from adult caretakers with upper or lower respiratory tract infections involving viruses such as respiratory syncytial virus (RSV) or bacteria such as *Pneumococci* or *H. influenza*.
- Transfused blood products containing cytomegalovirus (CMV) or Hepatitis B virus.
- Breast milk from mothers who are carriers of viruses such as CMV or Hepatitis B, or who have *Staphylococcus mastitis*.

Nosocomial infections in newborn intensive care units have been shown to carry a 3-fold increase in neonatal mortality for those infected over what would otherwise be expected given their basic condition. Nursery epidemics may necessitate temporary closure of the neonatal unit.

Factors Determining Outcome of Perinatal Infection

Factors that determine the outcome of viral, bacterial, and protozoan infections in the perinatal period include:

- Species and virulence of the infective organism
- Quantity of the inoculum
- Host resistance of the mother and fetus or newborn
- Speed and appropriateness of countermeasures taken

Diagnostic Considerations

Although some cases of perinatal infection are quite obvious and exhibit the classical signs and symptoms of infection, a large percentage of perinatal infections are subclinical and run an asymptomatic course in the mother and initially in the newborn infant as well.

Clinical signs of perinatal infection generally lack specificity, with the same signs found in many of the more common infections (see Table 4). Furthermore, symptoms of bacterial infection in the newborn tend to be subtler than in the adult. Such vague complaints as poor feeding, irregular breathing, apnea, or lethargy may constitute the initial presentation. Since early diagnosis and intervention can be so critical in achieving satisfactory outcome, the thought “rule out possible sepsis” must be constantly on the mind of the primary care physician or practitioner.

Table 4 CLINICAL MANIFESTATIONS OF NEONATAL INFECTION ACQUIRED IN UTERO OR AT DELIVERY

	Microorganism						
Clinical Sign	Rubella Virus	Cytomegalo-virus	Toxoplasma Gondii	Herpes simplex Virus	Treponema pallidum	Enteroviruses	Group B *Steptococcus* or E. coli
General							
Hepatosplenomegaly	+	+	+	+	+	+	+
Jaundice	+	+	+	+	+	+	+
Adenopathy	+	-	+	-	+	+	-
Pneumonitis	+	+	+	+	+	+	+
Lesions of skin or mucous membranes							
Petechiae or purpura	+	+	+	+	+	+	+
Vesicles	-	+	-	++	+	-	-
Maculopapular exanthems	-	-	+	+	++	+	-
Lesions of nervous system							
Meningoencephalitis	+	+	+	+	+	+	+
Microcephaly	-	++	+	+	-	-	-
Hydrocephalus	+	+	++	+	-	-	-
Intracranial calcifications	-	++	++	-	-	-	-
Paralysis	-	-	-	-	-	++	-
Hearing deficits	+	+	-	-	+	-	-
Lesions of the Heart							
Myocarditis	+	-	+	+	-	++	-
Congenital defects	++	-	-	-	-	-	-
Bone lesions	++	-	+	-	++	-	-
Eye lesions							
Glaucoma	++	-	-	-	+	-	-
Chlorioretinitis or retinopathy	++	+	++	+	+	-	-
Cataracts	++	-	+	+	-	-	-
Optic atrophy	-	+	+	-	-	-	-
Microphthalmia	+	-	+	-	-	-	-
Uveitis	-	-	+	-	+	-	-
Conjunctivitis or keratoconjunctivitis	-	-	-	++	-	+	-

- = either not present or rare in infected infants;
+ = occurs in infants with infection;
++ = has special diagnostic significance for this infection.
Modified from Remington JS, Klein JO. Infectious diseases of the fetus and newborn infant. 5th ed. Philadelphia(PA): W.B. Saunders Company; 2001 with permission. (Level III)

Of the various clinical signs and symptoms in the pregnant woman that might signify infection potentially damaging to the fetus, the following are perhaps the most important and should be looked for routinely:

- Skin rash or lesions
- Recurrent fever or chills
- Lymphadenopathy, especially in the post-auricular and inguinal regions
- Flu-like syndrome with myalgia or malaise
- Pain in the vulvar, vaginal, or flank regions

Chorioamnionitis, or bacterial infection of the placental membranes and amniotic fluid, is found in about 1 percent of all pregnancies and is a major cause of perinatal mortality including maternal death when fulminant. Although chorioamnionitis can occasionally occur with intact membranes, it most commonly develops after rupture of the membranes. Diagnosis of chorioamnionitis can be difficult when the infection is confined within the amniotic cavity and maternal symptoms are minimal. With penetration of both the

amnion and chorion, toxins are usually released by maternal lymphocytes and PMN's to cause maternal fever and fetal tachycardia. Later a whole series of signs and symptoms may appear:

- Uterine tenderness
- Foul smelling amniotic fluid if an anaerobic organism is involved, whereas a fulminant aerobic infection may be present without odor
- Maternal chills
- Sharp further rise in maternal temperature
- Maternal leukocytosis with shift to the left
- Leukocytes and/or bacteria demonstrated on amniotic fluid aspirated from an IUPC (intrauterine pressure catheter) or by amniocentesis
- Fetal tachycardia or unexpected fetal distress or low Apgar scores

The major clinical signs of neonatal infection acquired in utero or during delivery have been listed in Table 4. Diagnostic clues and confirmatory tests to diagnose the individual infections making up the TORCH[4] complex are included in the sections that follow later in this Chapter. General clinical symptoms alerting one to possible neonatal infection or sepsis can be related to major organ system dysfunction as follows:

CNS: Hypothermia or hyperthermia indicating temperature instability, reduced muscle tone and lethargy, or hyperreflexia and irritability indicating disturbed neuromuscular control.

Cardiovascular: Tachycardia, bradycardia, or other cardiac arrhythmias; mottling or pallor of the skin, delayed capillary filling, and cold distal extremities indicating loss of vasomotor control; hypotensive shock.

Pulmonary: Early or unexpected respiratory distress or failure, especially if accompanied by apnea, shallow or irregular breathing, metabolic acidosis, or shock.

Gastrointestinal: Poor feeding or loss of appetite; delayed gastric emptying leading to gastric residuals, regurgitation, or bilious vomiting (initially without signs of complete ileus, such as air-fluid levels); reduced or increased gut motility, leading to abdominal distention or diarrhea.

Laboratory testing is crucial for the early and specific diagnosis of every form of perinatal infection because of the frequent overlap of clinical signs and symptoms of the various infections as mentioned above.[5,6] Also, there is need to always assess the infant's status or response to infection, as well as to sort out (if possible) the degree of passive protection or response provided by the mother. The most useful screening tests used to support the clinical impression of neonatal sepsis or systemic infection are listed in Table 6, along with the type of specimen to be sent to the laboratory, normal values for these tests, and some pertinent comments.[7] Other screening tests suggestive of infection include the following:

- Reduced platelet count (i.e., $<$125,000)
- Elevated IgM (i.e., $>$20 mg/dl)
- Presence of "toxic granulations" and "Dohle bodies" in neutrophil leukocytes
- Evidence of disseminated intravascular coagulation (DIC) with prolonged PT and PTT, low fibrinogen (i.e., $<$100 mg/dl), thrombocytopenia (see above), and presence of fibrin split products
- Microscopic examination of frozen sections of umbilical cord or amniotic membrane looking for infiltration with macrophages or PMN's as signs of vasculitis or chorioamnionitis

Isolation and identification of the specific organism is the ultimate goal of laboratory testing in cases of suspected perinatal infection. This means recovery of specific bacteria from blood, urine, CSF or other culture sites for the diagnosis of bacterial sepsis, meningitis or localized infection. In cases of viral infection it usually means positive tissue culture or specific IgM fluorescent antibody tests. For the

protozoan infections it is a matter of either identifying specific IgM antibodies using the immunofluorescent technique (as for Toxoplasma and Treponema) or actual visualization of the organism under dark field microscopy or electron microscopy (as for Treponema).

Blood cultures from the neonate for bacteria should be obtained from a peripheral vein rather than from an umbilical vessel catheter. The skin over the puncture site should be cleaned with Betadine solution and allowed first to dry. (It should not be wiped off with an alcohol sponge since alcohol deactivates the iodine-containing antiseptic solution.) At least 5 to 10 percent of the total culture medium volume should be blood, which represents 0.5 to 1 ml of blood sample in the 10 ml trypticase broth pediatric blood culture set.

Figures 1 and Figure 2, below, illustrate the changes in normal values over the first 60 hours after birth for Absolute Neutrophil Count (ANC) and for Absolute Band Count respectively. The natural rise and fall of the outer limits of normalcy for these two parameters reflect the effects of “stress” on the fetus and newborn produced by even “normal” labor and delivery.

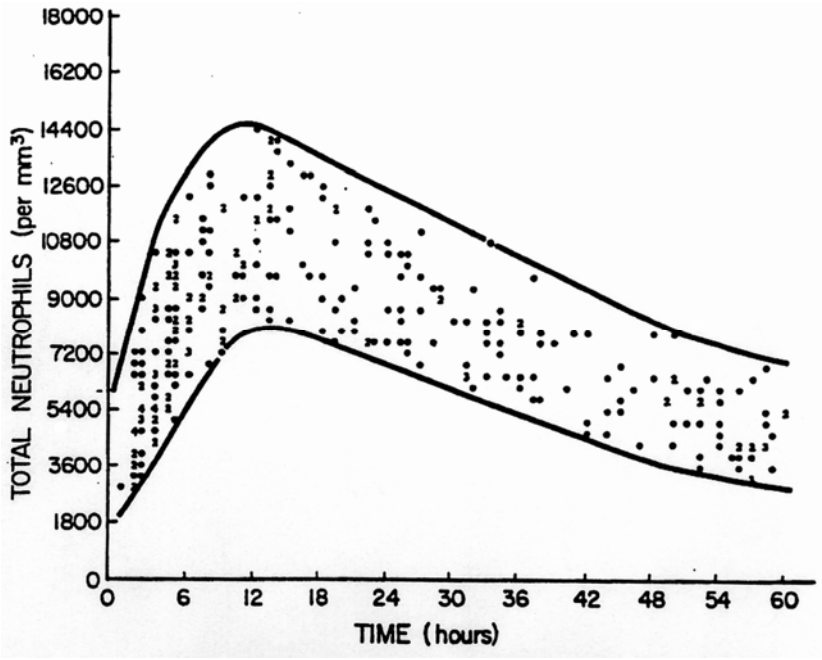

Figure 1. Normal range variations in Absolute Neutrophil Count with time in hours after birth. From Manroe et al., *J Pediatr* 1979; 95:89-98.

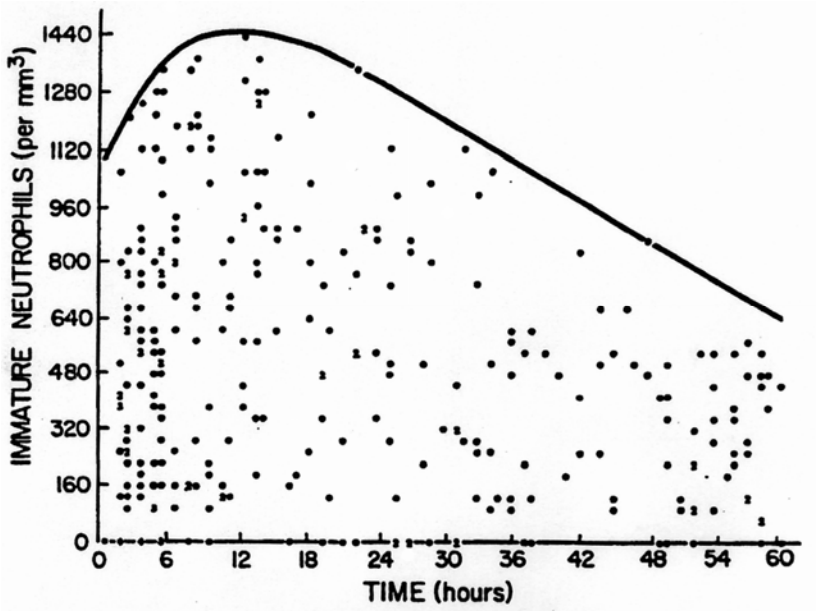

Figure 2. Normal range variations in Absolute Band Count with time in hours after birth. From Manroe et al., *J Pediatr* 1979; 95:89-98.

* THERAPEUTIC CONSIDERATIONS

Suspected or confirmed bacterial sepsis or meningitis in the newborn period is a medical emergency and treated immediately. In premature infants especially, this means institution of IV or IM antibiotic therapy almost as soon as one "even thinks of sepsis." The use of a "scoring system" involving various lab procedures as proposed by Spector and co-workers[6] and by Philip (J Pediatr 98: 795-799, 1981) to diagnose neonatal bacterial infections and to decide when to use or not use antibiotics has no role to play when dealing with the "sick" neonate. That is to say, broad-spectrum antibiotic coverage should be started after appropriate culture specimens are collected in any and all premature or sick newborns with respiratory or CNS symptomatology irrespective of how many points they score on the Spector or Philip infection scoring system. These systems are only useful in babies who are at high risk for infection (see above) because of some maternal or perinatal historical risk factor being present but who are still completely asymptomatic. Once signs and symptoms of specific or generalized infection develop, antibiotic therapy should never be withheld until the culture results are back.

Initial choice of antibiotics should be on the basis of the most likely organisms involved and on known local resistance patterns based on local epidemiological surveillance data. We all must face the problem of the changing profile of microorganisms responsible for severe infections, and the changing resistance patterns of these microorganisms to our standard antibiotics. On the other hand, the use of new, less well-understood antimicrobials is not encouraged unless proven by local sensitivity patterns to be needed, since aspects of maternal and fetal pharmacology for these new drugs are not yet likely to have been worked out.

In every case of neonatal sepsis as well as intrauterine infection due to viruses or protozoa, supportive therapy of breathing, CNS regulatory functions, the cardiovascular system and nourishment is crucial for improved survival with minimal lasting damage. Generally speaking, such full supportive therapy can only be provided in a secondary or tertiary neonatal special care unit.

TABLE 5: DOSAGE SCHEDULE FOR COMMONLY PRESCRIBED ANTIBIOTICS IN NEWBORN INFANTS

Antibiotic	Gestational Age (weeks)	Dose (mg/kg/dose)	Interval (hours)
Amikacin[†]	<28*	18	48
	28-30	18	36
	31-33	16	36
	>33	15	24
Gentamicin[†]	<30*	5	48
	30-33	4.5	48
	34-37	4	36
	>37	4	24
Tobramycin[†]	<30*	5	48
	30-33	4.5	48
	34-37	4	36
	>37	4	24
	Postmenstrual Age (weeks)	Postnatal Age (days)	Interval (hours)
Ampicillin Dose:			
***For Septicemia*:**	<30*	0-28	12
25-50 mg/kg/dose		>28	8
By slow IV push	30 to 36	0 to 14	12
***For meningitis* or GBS**		>14	8
100 mg/kg/dose	37 to 44	0 to 7	12
by slow IV push		>7	8
	>45	ALL	6
Cefotaxime[†] **Dose:**			
50 mg/kg/dose	<30	0 to 28	12
For Gonococcal infections:		>28	8
25 mg/kg/dose	30 to 36	0 to 14	12
		>14	8
	37 to 44	0 to 7	12
		>7	8
	>45	All	6
Methicillin Dose:			
25 to 50 mg/kg/dose	<30	0 to 28	12
by slow IV push		>28	8
	30 to 36	0 to 14	12
		>14	8
	37 to 44	0 to 7	12
		>7	8
	>45	All	6
Vancomycin Dose:			
For bacteremia:	<30	0 to 14	18
10 mg/kg/dose		>14	12
Over 60 min IV pump	30 to 36	0 to 14	12
For meningitis:		>14	8
15 mg/kg/dose	37 to 44	0 to 7	12
Over 60 min IV pump		>7	8
	>45	All	6
Penicillin G Dose:			
For bacteremia:	<30	0 to 28	12
25,000 to 50,000 IU		>28	8
Per kg per dose	30 to 36	0 to 14	12
Slow IV push or IM		>14	8
For meningitis:	37 to 44	0 to 7	12
75,000 to 100,000 IU		>7	8
Per kg per dose	>45	ALL	6
Slow IV push or IM			

Table 5 (cont.)

For GBS infections, some use 200,000 IU/kg/day for bacteremia, and 400,000 IU/kg/day for meningitis in divided doses at shorter intervals as those listed above; for synergistic effect, an aminoglycoside is almost always used in combination.

For Congenital Syphilis, give 50,000 IU/kg/dose of Aqueous Crystalline Penicillin G by slow IV push Q12 hours for the first 7 days, and then Q8 hours for the rest of the 10-day course. Procaine Penicillin G given IM once daily at a dosage of 50,000 IU/kg for 10 to 14 days is also acceptable.

(**Please note:** Use only Aqueous Crystalline Penicillin G for IV administration; Procaine and Benzathine Penicillin G are for IM use only)

***** Dosage schedule for infants less than 28 week gestation, and for other infants, irrespective of their gestational age, whose course is complicated by prior severe asphyxia, significant PDA, renal insufficiency or need for indomethacin treatment

ǂ IV infusion by syringe pump over 30 minutes

THREE MAJOR CONGENITAL INFECTIONS

CYTOMEGALOVIRUS (CMV)

ETIOLOGY/ EPIDEMIOLOGY

- Human CMV is a DNA virus and member of the herpes virus group, and represents the most frequently recognized cause of congenital infection.
- CMV is ubiquitous, and is transmitted horizontally by direct person-to-person contact with virus-containing secretions (urine, blood, semen, and cervical fluids), and vertically from mother to infant before, during, or after birth (breastmilk being a primary vector).
- CMV persists in latent form (in leukocytes and tissues) after primary infection, with "reactivation" possible years later, especially under conditions of immunocompromise.
- Approximately 1% of all live-born infants are infected in utero and excrete CMV at birth.
- Although in utero fetal infection can occur both after maternal primary infection or after reactivation of CMV infection during pregnancy, sequelae are far more common in infants after maternal primary infection:
  - 10-20 % mental retardation and/or sensorineural deafness
  - Profound CNS involvement may be evident at birth (see below) and may include symmetrical IUGR with microcephaly, intracranial calcifications, chorioretinitis, and diffuse encephalopathy with leukomalacia and cortical atrophy.
- Primary infection of the mother at the time of impregnation or early in the pregnancy is more likely to lead to interference with organ development and thus more pronounced clinical findings at or shortly after birth; such cases obviously have a poorer prognosis.

CLINICAL PRESENTATION

Congenital CMV is usually asymptomatic. However, approximately 5% of infants with congenital CMV infection will have major signs, symptoms, and problems at or shortly after birth:

- Symmetrical IUGR with or without microcephaly
- Hepatosplenomegaly due to subacute hepatic and splenic inflammation
  - With or without moderately abnormal LFT's
  - Usually with jaundice, largely due to an elevated conjugated Bilirubin
-

Cutaneous lesions may include:

- Petechiae and purpura secondary to thrombocytopenia
- "Blueberry muffin" spots of extramedullary hematopoiesis (and not due to viral replication in the skin as is the case in congenital Rubella syndrome)

- Interstitial pneumonia (more frequently seen in premature or otherwise debilitated, immunosuppressed infants)
- Encephalitis or aseptic meningitis with elevation of CSF protein and/or lymphocyte cell count
- Chorioretinitis

CRANIAL ULTRASOUND FINDINGS

- Periventricular calcifications
- Ventriculomegaly (or hydrocephalus ex vacuo) due to generalized white matter and cortical (gray matter) atrophy
- Periventricular leukomalacia

LABORATORY DIAGNOSIS

- Culture of the virus is the "gold standard!" Virus can be isolated in cell culture from urine, pharynx by NP swab, peripheral blood leukocytes, human milk, cervical secretions, semen, and other tissues & body fluids.
  - Amniocentesis and culture or PCR-testing of the amniotic fluid has been used successfully to establish the presence of intrauterine CMV infection.
  - Examination of cells shed in urine for intranuclear inclusions is an insensitive test.
  - Proof of congenital infection requires obtaining specimens from the baby within three weeks of birth!
- Shell vial technique is being used in some centers to detect the presence of CMV viral DNA, with results available within 48-72 hours.
- PCR detects viral DNA, and may be used on amniotic fluid, CSF or plasma samples.

TREATMENT/PREVENTION

- A live attenuated vaccine using the Towne 125 strain of CMV has been developed but is only "somewhat protective." Concerns remain regarding the vaccine virus being shed from the cervix and present in breast milk, and for its possible oncogenic potential.
- The antiviral agent Ganciclovir, a nucleoside analogue, is available in both IV and oral formulations, but is associated with significant bone marrow toxicity and is thus not recommended routinely for use in congenitally infected infants until more "efficacy" data can be collected.
- CMV hyperimmune gamma globulin used in conjunction with Ganciclovir in the treatment of symptomatic newborns with congenital CMV has shown some promise in a Phase II collaborative study, but long-term effectiveness remains unknown at this time.
- Hand washing when caring for newborn infants or young children or when around immunocompromised individuals is particularly important for pregnant medical & nursing personnel.

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HERPES SIMPLEX VIRUS (HSV)

PATHOPHYSIOLOGY/EPIDEMIOLOGY

- Herpes simplex virus (HSV) type 1(HSV-1) and 2 (HSV-2) are large, double-stranded DNA viruses. In the United States, about 75% of neonatal infections are caused by HSV-2, and 25% by HSV-1.
- By integrating itself into host DNA primarily within sensory ganglia, it can establish latency and periodically be reactivated, depending on poorly understood host and environmental *factors.* Thus, "active infection" in a mother can be either primary or recurrent, both of which pose a threat to her fetus or newborn.
- Vertical transmission may occur during gestation (in utero; ~ 4%), at the time of labor & delivery (perinatal or intrapartum; ~ 80-90%), or following the delivery (postnatal; ~ 10%).
- It is presumed that the majority of infected neonates are born to mothers acquiring their primary infection during pregnancy. The risk of HSV infection at delivery in an infant born vaginally to a mother with primary genital infection is estimated between 33-50%. Although primary infection during pregnancy usually leads to symptomatic disease in the mother, a significant number of such woman give no "history" of a problem nor complain of local or systemic signs or symptoms at the time of delivery. Thus, over 75% of cases of neonatal herpes are in effect "unsuspected."

CLINICAL PRESENTATION

The spectrum of clinical disease in neonatal herpes depends on the time of exposure (in utero vs. intrapartum vs. postnatal), the route of exposure (transplacental, or ascending through apparently intact membranes or during prolonged rupture of membranes), or direct contact during delivery through the birth canal); also depends on the presence or absence of maternal immunity (primary vs. recurrent maternal infection).

Intrauterine HSV infection with severe problems already present at birth is due to maternal primary HSV-2 genital infection during the first month or two of pregnancy.

- Skin changes seen at delivery are the result of residua from primary fetal infection plus latent virus reactivation at previous skin sites of fetal infection.
  - 70% will have vesicular lesions
  - 30% will have evidence of scar formation on the face, trunk, and extremities
  - Generalized lesions characteristic of epidermolysis bullosa may also occur
- Extracutaneous findings are almost invariably associated with CNS tissue damage of longstanding, and include microcephaly (in 50% of cases), chorioretinitis (in 60% of cases), and intractable seizures (but not showing signs of systemic toxicity or overwhelming sepsis as occurs with primary perinatal or postnatal infection (see below).

Neonatal HSV infection acquired intrapartum or postpartum manifests itself as one (or more) of the following:

- Disseminated disease, involving multiple organs, most prominently liver and lungs in approximately 25% of cases:
  - Produces a "sepsis-like" clinical picture, but bacterial cultures are negative
  - Severe liver dysfunction often ending in hepatic failure
  - Respiratory distress leading to respiratory failure
- Localized central nervous system (CNS) disease in approx. 35% of cases:
  - Fever, irritability, and seizures
  - Abnormal CSF findings

- Disease localized to the skin, eyes, and mouth, in approx 40% of cases:
  - This starts as clear vesicles or bullae mainly at mucocutaneous junctions or where there was prior local trauma to the skin.
  - The vesicles turn hemorrhagic and then show central necrosis, and new adjoining or adjacent skin necrosis appears. (The word HERPES from the Greek means "to creep.")

LABORATORY DIAGNOSIS

- Herpes simplex virus grows readily in cell culture, and special transport media are available for specimens that cannot be inoculated immediately.
  - Specimens for culture should be obtained from skin vesicles, nasopharynx, urine, blood, stool or rectum, and CSF.
  - Cytopathogenic effects typical of HSV can be observed within 1 to 3 days of inoculation.
  - Positive cultures obtained from any of the sites listed above more than 48 hours after birth indicate new viral replication in an infected infant, rather than simple colonization after delivery through a contaminated birth canal.
- The usual **serologic tests** included in the so-called TORCH work-up generally are not helpful in making the diagnosis of acute HSV infections. Extensive cross-reaction between anti-HSV-1 and anti-HSV-2 antibodies precludes differentiation between the two using serologic tests. However, some have proved useful for rapid diagnosis, including the following:
  - Direct fluorescent antibody staining of vesicle scrapings
  - Enzyme immunoassay detection of HSV antigens
  - Shell vial technique (results usually available within 48-72 hours)

  Histologic examination of epithelial cells from the bottom of a vesicle scraping looking for multinucleated giant cells and eosinophilic intranuclear inclusions typical of HSV (i.e., Tzanck preparation) has low sensitivity, and is thus not recommended for use as a rapid diagnostic test.
- PCR testing for Herpes simplex virus DNA in CSF is of particular value in evaluating for suspected herpes encephalitis.

TREATMENT

Parenteral Acyclovir is the treatment of choice for all neonatal HSV infections, irrespective of presenting clinical findings:

- *Dosage*: 60 mg/kg IV per day in 3 divided doses (or 20 mg/kg q.8 hours).
- *Duration*: 14 days if disease limited to the skin, eyes, and mouth, and 21 days if disease is disseminated or involves the CNS.

Infants with ocular involvement should also receive a topical ophthalmic anti-viral drug such as 1-2% trifluridine, or 1% iododeoxyuridine, or 3% vidarabine along with the parenteral Acyclovir therapy.

OUTCOME

- Approximately 50% of neonates with disseminated disease die despite antiviral therapy.
- Although most infants treated for HSV encephalitis survive, the majority suffer major neurologic sequelae.
- Babies with disease limited to the skin, eyes, and mouth have the best outcomes in terms of morbidity and mortality, but it remains unpredictable. Thus, these infants also require long-term follow-up.

PREVENTION OF PERINATAL TRANSMISSION

- Neonates with HSV infection should be hospitalized in a private room (preferably rooming in with the mother) and managed with contact precautions for the duration of the illness. Infants born to women with active HSV lesions should be managed with contact precautions during the incubation period (2 days to 2 weeks). This may not be necessary if born by C-section, provided the membranes were not ruptured for more than 4 – 6 hours. (It should be noted that the risk of HSV infection in possibly exposed infants born to a mother with a history of recurrent genital herpes is low.)
- Women with active HSV lesions should be managed with contact precautions during labor, delivery and the postpartum period.
  - These mothers need instruction about careful hand washing before and after caring for their infant(s).
  - A clean covering gown is helpful in avoiding contact of the infant with the lesions or infectious secretions.
  - If the mother has herpes labialis (cold sores) or herpes stomatitis, she should wear a disposable mask until the lesions have crusted and dried; she also should avoid kissing or nuzzling her baby until the lesions have cleared.
- During prenatal evaluations and during labor, all pregnant women should be asked about past or current signs and symptoms consistent with genital herpes infection in themselves and their sexual partner(s). When first presenting in labor, they should be examined carefully for active Herpes lesions.
- If active lesions are found, C-section delivery is indicated, even if membranes have been ruptured greater than 6 hours. Fetal scalp monitors should be avoided.
- The prophylactic use of *acyclovir* in mothers presenting with ruptured membranes and active genital lesions, or in babies born to mothers with primary genital infection (where the risk of transmission is as high as 50%) or unknown primary vs. recurrent Herpes status, remains a most controversial area. An alternative approach in these situations is to await HIV culture results before instituting *acyclovir* therapy.

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CONGENITAL SYPHILIS

PATHOPHYSIOLOGY

- The spirochete T. pallidum is transported in leukocytes within the blood stream, and thus immediately infects the placenta and crosses easily over into the fetus.
- T. pallidum preferentially adheres to endothelial cells, and consequentially induces a vasculitis, especially in the liver & spleen, long bones, cartilage, kidneys and skin.

EPIDEMIOLOGY

- Between 1983 and 1991, the rate of CDC-reported cases of congenital syphilis rose from 4.3 to 107 cases per 100,000 live births.
- In Maricopa County, Arizona, alone (including Phoenix and surrounding cities), the number of reported cases rose from 0 in 1989 to 31 in 1990, 11 of which ended in fetal demise.

- The incidence of acquired and congenital syphilis remains disproportionately high in large urban areas like Phoenix, and in the rural South of the United States.
- Almost 50% of the newborns that acquire congenital syphilis are born to mothers receiving no prenatal care!
- Nearly all infants born to mothers with *primary* or *secondary* syphilis during pregnancy are infected, but more than half are asymptomatic at birth.
- Vertical transmission may occur at any time during pregnancy, labor or delivery, but a number of factors play a determinant role:
  - **Kassowitz's law**: The longer the interval between the mother's infection and pregnancy, the more benign the outcome for the fetus and newborn.
  - Treponemes can cross the placenta at any stage in a pregnancy, but passage in the first 20 weeks usually results in only mild inflammatory changes. First trimester spontaneous abortions are not associated with syphilis.
  - The later in a pregnancy a woman becomes primarily infected, the more devastating the results for the fetus.
  - In untreated newly-acquired syphilis, 40% of pregnancies end in spontaneous second-trimester abortion, stillbirth or perinatal death.

CLINICAL PRESENTATION

Although most infected infants are asymptomatic at birth, some will present with "early" signs & symptoms (i.e., at birth or within the first 3 months of life) which include the following:

- Hydrops fetalis due to severe hemolytic anemia and resultant CHF
  - May be misdiagnosed as erythroblastosis fetalis or congenital toxoplasmosis or CMV or even congenital leukemia
  - Coombs' test is Negative
  - High NRBC (up to 500 per 100 leukocytes)
- Thrombocytopenia due to decreased platelet survival time
- Lymphocytosis on WBC/differential
- Jaundice resulting from hepatitis and/or hemolysis, with elevated conjugated and unconjugated Bilirubin
- Hepatomegaly (in 50 to 90% of cases; with or without splenomegaly) due to extramedullary hematopoiesis and subacute hepatic and splenic inflammation
  - With abnormal LFT's
  - With or without jaundice
  - May mimic other infectious causes of acute liver failure by presenting with hypoglycemia, metabolic acidosis, encephalopathy, DIC, and shock!
- Cutaneous lesions in 38% of affected newborns:
  - Erythematous macular, papulosquamous, annular eruptions skin over the entire body, including palms and foot soles
  - Occasionally one sees "pemphigus syphiliticus," or vesicles and bullae that can become hemorrhagic and often rupture *(Caution: These are loaded with spirochetes)*
  - Condyloma lata or flat-topped plaques at mucocutaneous junctions
- Generalized lymphadenopathy
- Syphilitic rhinitis or "snuffles" that starts clear but soon becomes purulent & hemorrhagic; *Caution: Loaded with spirochetes*
- Renal abnormalities (nephrotic syndrome, hematuria, proteinuria)
- Aseptic meningitis (CSF protein elevation)
- Ocular changes (uveitis, glaucoma, chorioretinitis, interstitial keratitis, optic atrophy)
- Pseudoparalysis due to osteolytic bone lesions (see below)

X-RAY DIAGNOSIS

- Osteochondritis in metaphyseal regions of the long bones:
  - Radiopaque bands
  - Punctate lucencies or mottled appearance
- Periostitis and new bone formation in diaphyseal (midshaft) region of long bones, especially Tibia

SEROLOGIC DIAGNOSIS

Non-Treponemal Tests:		Comments:
VDRL	Advantages:	Quick results, inexpensive
RPR	Disadvantage:	False positives from diseases like Lupus False negative ("Prozone effect" where antibody titer is so high it hinders flocculation; sample must be diluted)
ART	Advantages:	Fully automated

Anti-Treponemal Tests: (specific Treponemal tests that result from presence of passively acquired antibody)

FTA-ABS	Advantages:	Specific, definitive
MHA-TP	Disadvantage:	Expensive, time consuming

DEFINITIVE DIAGNOSIS

- Direct identification of spirochetes by dark field microscopy
- Spirochetes visualized by fluorescent antibody stains of placenta, umbilical cord or body tissues

PRESUMPTIVE DIAGNOSIS (important for treatment):

- Serology: Non-Treponemal:
  - VDRL (venereal disease research laboratories; a flocculation test using the nonspecific antigen *cardiolipin*)
  - RPR (rapid plasma regain)
- Serology: Treponemal
  - FTA-ABS (fluorescent treponemal antibody absorption)
  - MHA-TP (microhemagglutination test for *T pallidum)*

The usual sequence in performing serologic testing is to start with "non-Treponemal" testing, followed by the more expensive and specific "Treponemal" tests.

CDC TREATMENT RECOMMENDATIONS

1. **Symptomatic infants**

   10 days of IV Aqueous Crystalline Penicillin G;
   50,000 – 75,000 Units/Kg q 12 hours during the first 7 days of life, and q 8 hours thereafter for a total of 10 days

2. **Asymptomatic infant, specific test positive**
   Same as above

3. **Asymptomatic, previously treated mother or mother treated with erythromycin:**
   Single dose of Benzathine Penicillin G, 50,000 Units/Kg, IM

4. Neurosyphilis (positive CSF)

Aqueous Crystalline Penicillin G for 14 days:

- When Identified between birth and 1 week: 50,000 units/Kg IV q 12 hours
- Between 1- 4 weeks: 50,000 units/Kg IV q 8 hours
- After 4 weeks: 50,000 units/Kg IV q 6 hours

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II. INFECTIONS IN OBSTETRICS AND GYNECOLOGY

The discussion and tables that follow are designed to provide the clinician with an overview of the principles involved in the diagnosis and management of commonly encountered infections in obstetrics and gynecology. Our understanding of these infections has been rapidly improving and new infections or significant variants of older infections are being discovered. Thus, the information that follows should be considered as general guidelines.

The TORCH Complex

The TORCH acronym was first suggested by Dr. Andre Nahmias and incorporates the major infections acquired in utero:

- **T** is for toxoplasmosis.
- **O** is for "others," most importantly the enterovirus infections due to Coxsackie viruses, echoviruses, and (rarely) poliovirus.
- **R** is for rubella.
- **C** is for cytomegalovirus infection or CMV.
- **H** is for herpes simplex (usually type II) virus infections.
- **S** is for congenital syphilis, which is often added to complete this group.

These infections often present with similar clinical manifestations, or conversely, they may be clinically unapparent in the infected mother and the newborn Infant. Nevertheless, they still may be the cause of serious long-term ill effects like deafness and mental retardation. Using CMV infection as an example:

- CMV infection is the most common intrauterine infection, occurring in 1 to 2 percent of all infants.
- Clinically obvious affected infants represent less than 5 percent of all CMV-infected infants; 50 to 75 percent of those 5 percent die in utero or within the first few months of life.
- For every infant born with symptoms of CMV infection, there are at least 10 more infected infants without suggestive symptoms in the immediate newborn period.
- Among those initially asymptomatic CMV-infected infants, between 10 and 20 percent will later develop major handicaps such as sensorineural hearing loss, mental retardation and minimal cerebral dysfunction. Perinatal CMV infection is now recognized as the leading cause of hearing impairment in children in the U.S.A.

Note that it makes no sense to draw a single serum sample from an infant for a serologic "TORCH screen" in hopes of ruling out all of these infections in the case of a baby born SGA and becoming jaundiced. Not only would such a procedure not be helpful in enterovirus and herpes simplex infections, but also serology is no longer the preferred initial test for possible CMV infection. What one needs to do is consult with the local laboratory people and find out what their capabilities and preferences are when confirming the diagnosis of one of these intrauterine infections.

Table 6 gives detailed information about prevention and possible therapy for each of the TORCH infections plus congenital syphilis. Although specific therapy is not available for most of these infections, specific as well as general preventative measures are known in most cases. For these preventive measures to have an impact, considerable education of expectant mothers is required. Surely such patient education must be incorporated into any sound prenatal care regimen, similar

to providing the potential or expectant mother with information on the ill effects of smoking and alcohol consumption during pregnancy (see sections on Maternal Smoking and the Fetal Alcohol Syndrome).

TABLE 6 Measures to be taken to Prevent and/or Treat TORCH Infections and Congenital Syphilis. (Data obtained in large part from chapters 3-9 in Infectious Diseases of the Fetus and Newborn Infant.) From Remington JS, Klein JO. Infectious diseases of the fetus and newborn infant. 5th ed. Philadelphia(PA): W.B. Saunders Company; 2001 with permission. (Level III)

	PREVENTION	**THERAPY**
TOXOPLASMOSIS	Decrease risk of exposure in susceptible pregnant women (i.e., without specific antibody titers). Screen for protective antibody titers early in pregnancy and advise accordingly: • Avoid eating or handling of raw meat or meat products • Avoid contact with cats who have been allowed to hunt or eat raw meat products • Avoid providing litter pan care for any cats, and encourage other persons to clean pan daily so that oocysts have no chance to sporulate to an infectious state.	Spiramycin used in Europe to treat maternal infection but it doesn't cross the placenta and it is not approved in this country. Sulfadiazed and pyrimethamine in combination are used in this country to treat infants with congenital Toxoplasmosis at doses of 100-150mg/kg/day and 2mg/kg/day respectively per os for a total of 30 days.
(Others) ENTEROVIRUSES (I.E. COXSACKIE AND ECHO VIRUSES)	Since man is the only natural host of enteroviruses and spread is from person to person by fecal-oral or possibly oral-oral (respritory spread) route avoidance by pregnant women of persons (particularly children) with diarrhea or URI-like illnesses is advised. Avoidance of contact with human fecal material and good handwashing techniques are particularly important. Passive protection with human immune globulin may be useful in preventing disease in exposed individuals late in pregnancy.	There is no specific therapy for any of the enterovirus infections. In generalized catastrophic neonatal infection administration of immune globulin is recommended but may not be helpful. Corticosteroids should not be given even in cases of coxsackie myocarditis. Rather, supportive therapy with Digitalis diuretics and careful fluid and electrolyte balance are indicated. Antibiotic coverage of possible bacterial sepsis is usually provided. Phenobarb for seizures.
RUBELLA	Routine childhood immunization provided "herd immunity" by severely curtailing circulation of virus in the community and thereby limiting spread to pregnant women. Since vaccine virus may infect the fetus and cause damage, one must avoid pregnancy for at least two months postvaccination.	Supportive, symptomatic therapy is all that can be recommended. There are no effective chemotherapeutic agents presently available to treat Rubella.
CYTOMEGALO-VIRUS OR CMV	Active prevention of fetal CMV infection is currently not possible. Termination of pregnancy when primary maternal infection is diagnosed early in pregnancy may be an option. Transmission to a susceptible pregnant woman or newborn infant by way of needed blood transfusion can be minimized by using citrated blood stored for at least 72 hours or using only donors who are seronegative for CMV.	No specific therapy for CMV infection is presently available. Three antiviral chemotherapeutic agents have been tried on research protocols: Cystosine arabinocide (ara-C) 5-iodo-2-deozyuridine (IDU) Adenine arabinocide (ara-A) However, none of these agents are presently recommended for routine clinical use.
HERPES SIMPLEX	Cesarean delivery when active genital herpes lesions are confirmed at the time of labor will significantly reduce the risk for neonatal infection	Since CNS involvement occurs in 50% of disseminated cases and the prognosis for survivors is bleak, administration of Ara-A can be justified under these circumstances. Otherwise, supportive therapy is all that one can offer.

GROUP B BETA HEMOLYTIC STREPTOCOCCAL INFECTIONS

Starting in the early 1970's, Group B beta streptococcus (GBS) disease became the single most common cause of death from neonatal infection or sepsis, and it still accounts for 1 to 2 deaths per 1,000 births. Because of its high degree of lethality and the special problems of differential diagnosis it presents, GBS disease is discussed in some detail.

There is a wide spectrum of infections caused by GBS, but most frequently the neonatal presentation takes one of two distinct forms: The first is an **early-onset form** starting within 48 hours of birth with signs of respiratory distress and progressing rapidly to respiratory failure, shock, neutropenia, and often death. The second is a **late-onset form** starting insidiously at 2 to 4 weeks of age with poor feeding and fever and progressing to meningitis. Other less common presentations involve mostly localized infection such as septic arthritis, osteomyelitis, otitis media, or cellulitis. In the **early-onset form** of GBS infection, the isolated organisms are the same as found in the maternal genital tract. Between 5 and 25 percent of all pregnant women will grow GBS from cervical cultures, and the same organism (with identical serotype) can often be cultured from the urethra of the mother's sexual partner. Neonatal colonization occurs in approximately 50 to 70 percent of mother-infant pairs, yet only 1 to 2 percent of cases result in stillbirth or a symptomatic, infected newborn. The primary focus of infection is usually in the lungs, producing a rapidly progressing pneumonia as well as systemic septicemia. Only rarely is there spread to the brain (i.e., meningitis) in this early-onset form of the disease. Early diagnosis and treatment is crucial since the course is so fulminating.

Obstetrical complications predisposing to GBS sepsis in the newborn include:

- Premature delivery (occurring in 50 to 80 percent of cases).
- Rupture of membranes for more than 12 hours before delivery (found in 60 percent or more of cases).
- Chorioamnionitis (present in about 50 percent of cases).

Differentiation from commonly occurring hyaline membrane disease or respiratory distress syndrome (RDS) can be difficult since prematurity is so frequently involved and the chest x-ray pictures can be nearly identical. Differentiating features suggesting early-onset GBS infection rather than RDS (or just RDS) include the following:

- Apnea occurring in the first 8 to 16 hours after birth.
- Early onset of shock, evidenced by weak pulses, mottled skin, peripheral pallor or cyanosis, hypotension (i.e., systolic BP 40 mm Hg), and worsening metabolic acidosis.
- Gram-positive cocci found in the gastric or tracheal aspirate, with concomitant paucity of PMN's (considering the number of bacteria present).
- Low initial peak inspiratory pressures needed to adequately ventilate the infant.
- Evidence of pleural effusions along with the diffuse granularity and air bronchograms of RDS.
- Elevated I:T ratio seen in the white cell differential. (8) A normal I:T ratio is less than 0.4.

Respiratory failure develops acutely in these babies because of the apneic episodes and rapidly progressing pneumonia. The shock may respond poorly to volume expansion and require vasopressors (usually Dopamine starting at 5 ug/kg/min) by continuous drip. A particularly ominous sign is leukopenia or subnormal total neutrophil count. (See Figures 1 and 2 for establishing lower limits of norm for the first 60 hours of life). At this point an exchange transfusion with very fresh whole blood or a neutrophil transfusion should be considered. Obviously, these infants belong in a neonatal intensive care center, and even there, their chances of surviving are often less than 50 percent.

Many cases of early-onset neonatal GBS disease can be prevented by **selective intrapartum chemoprophylaxis.** Since infection attack rates are increased substantially in infants born to

mothers with prenatal group B strep colonization or in cases where certain perinatal risk factors exist (see below), intrapartum prophylaxis with intravenous Ampicillin (initial does of 1-2 gram IV followed by 1 gram every four hours IV until delivery) can substantially reduce both the rate of neonatal colonization with GBS and the rate of neonatal GBS bacteremia.

Perinatal risk factors include:

- Premature labor (less than 37 weeks of gestation)
- Prolonged rupture of amniotic membranes (greater than 12 hours)
- Intrapartum maternal fever (temperature greater than 37.5+C)

Thus, any mother in premature labor or who ruptures her membranes prematurely should have cervical cultures taken for GBS and started on IV Ampicillin if found to be colonized or doesn't deliver within 12 hours. Likewise, gastric aspirates from the baby should be collected within 30 minutes of birth in all premature infants and those with the risk factors listed above or any signs suggestive to chorioamnionitis. If gram-positive cocci are found, a blood culture specimen should be drawn and the infant started on IV or IM Penicillin or Ampicillin. Appropriate dosage schedules for these and other commonly used antibiotics in the newborn period are given in Table 5.

In the **late-onset form** of GBS infection, the organisms isolated are rarely identical with those found colonizing the mother. Since time of onset is at least a week beyond delivery, it must be assumed that infection did not occur at the time of delivery. Presenting symptoms are most frequently poor feeding and fever. Meningitis is almost always present. Antibiotic treatment in this form of GBS infection must be continued for no less than 21 days, yet outcome is generally better with a mortality rate rarely exceeding 10 percent.

GROUP B STREPTOCOCCAL INFECTIONS DURING PREGNANCY – OBSTETRIC MANAGEMENT STRATEGIES [14]

Intrapartum administration of antibiotics to the mother has been demonstrated to reduce early-onset neonatal GBS disease. The CDC has issued the following Obstetric Prevention Strategies for early-onset GBS disease:

A) **Universal Screening (Culture) -** of **ALL** women at 35-37 weeks gestation. All women with a positive culture (or identified risk factors, listed below) should be offered intrapartum chemoprophylaxis.

OR

B) **Risk Factors** – Women with one or more of the following risk factors should be offered intrapartum chemoprophylaxis:

1) **Previous infant with invasive GBS disease**
2) **GBS Bacteriuria this pregnancy**
3) **Delivery < 37 weeks of gestation**
4) **Duration of ruptured membranes > 18 hrs (any gestational age)**
5) **Temperature >38.0 C (100.4 F) in labor**

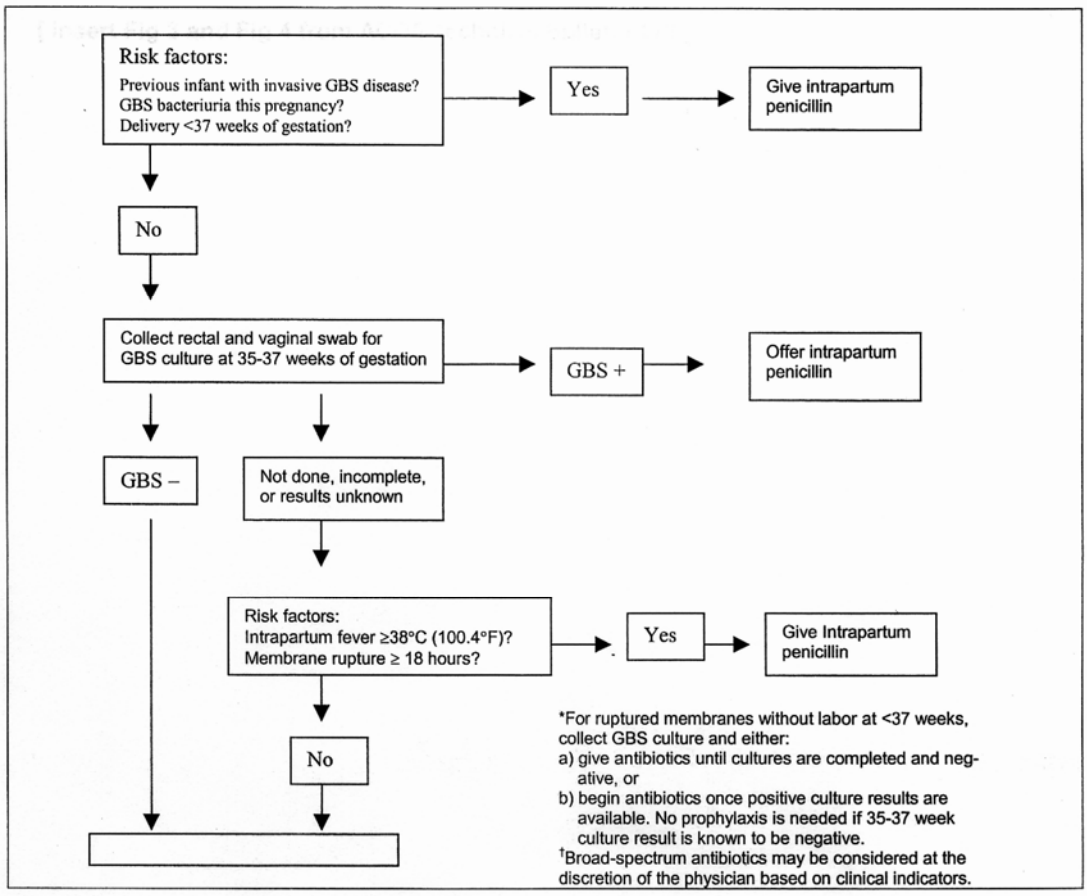


Fig. 3. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep 2002;51(RR-11):1-22. (Level III)

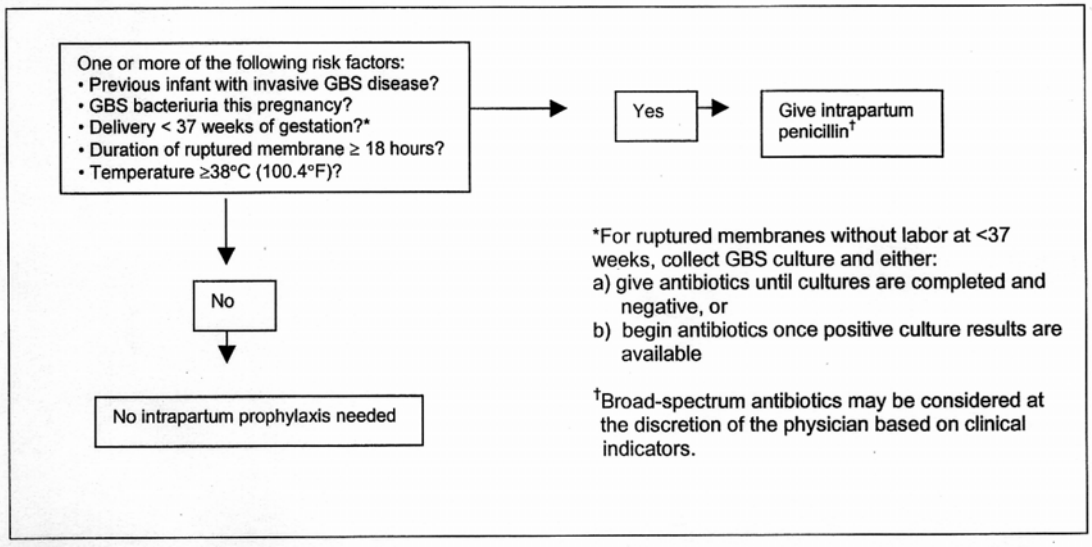


Fig. 4. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep 2002;51(RR-11):1-22. (Level III)

Intrapartum Prophylaxis

Regimen A

Penicillin G 5 million units IV initially and then 2.5 million units every 4 hours, in labor, until delivery.

Regimen B

Ampicillin 2 g IV initially and then 1 g every 4 hours, in labor, until delivery

If the patient is afebrile and without symptoms of active infection, antibiotics are discontinued at the time of delivery.

Regardless of the prevention strategy used, women should be managed as follows:

- Treat women found to have **symptomatic or asymptomatic GBS BACTERIURIA** during pregnancy **at the time of diagnosis**. Because such women are usually heavily colonized with GBS, they should also receive intrapartum chemoprophylaxis.
- Give intrapartum chemoprophylaxis to women with a history of previously giving birth to an infant with GBS disease; prenatal screening is **NOT** necessary in this situation.
- Women who are identified as **asymptomatic** carriers of **VAGINAL** GBS should **NOT** receive treatment during the pregnancy – but **MUST** be offered chemoprophylaxis during labor.

Implementation of **EITHER** of the above strategies is expected to **reduce** the incidence of early-onset GBS disease significantly. Neither will prevent early-onset GBS disease entirely.

RUBELLA (GERMAN MEASLES)

General Principles

- Transmission to the fetus is transplacental.
- The effects of rubella virus on the fetus depend to a large extent on the gestational age at the time of infection. Risk of fetal infection during the first 8 weeks of gestation is 40 to 60 percent; from 8 to 12 weeks, 30 to 35 percent; and from 12 to 16 weeks, 10 percent.
- Delayed manifestations of rubella have been observed as late as school age. Careful follow-up and examination of the child should extend over several years.
- Susceptible women may be vaccinated in the immediate postpartum period. Pregnancy should be avoided for three months after vaccination.
- If vaccine is inadvertently administered to a pregnant woman, pregnancy termination may be discussed. To date however, **NO** infant with congenital rubella syndrome has been born to a woman vaccinated while pregnant. A potential risk remains, however, since virus has been isolated from aborted tissue.

Maternal Clinical Manifestations

The incubation period is 14-21 days. A non-confluent maculopapular rash begins on the face and moves down the trunk to finally affect the extremities. The rash is generally present for three to five days.

Prodromal symptoms include malaise, fever, and anorexia. Lymphadenopathy is generally

present, involving the posterior auricular, posterior cervical, and suboccipital chains. Complications include conjunctivitis and arthritis involving the fingers, wrists, and knees.

Diagnosis

- Serologic testing using hemagglutination inhibition is the most commonly used technique. A fourfold or greater increase in titer indicates infection.
- A specific rubella IgM antibody identification is available in reference laboratories.
- Viral isolation may be obtained through throat culture or amniotic fluid culture.

Treatment of Maternal Symptoms

There is no specific therapy. Immune serum globulin is **NOT** recommended. However, symptomatic relief may be obtained with bed rest, analgesics, and antipyretics.

Fetal/Neonatal Clinical Manifestations

- Head: microcephaly, mental retardation, seizure disorders, degenerative brain disease.
- Eyes: glaucoma, cataracts, microphthalmia, retinopathy, cloudy cornea, myopia.
- Thorax: patent ductus arteriosis, pulmonic stenosis, myocarditis, cardiac malformations (atrial or ventricular septal defects).
- Miscellaneous: deafness, pneumonitis, low birth weight, thrombocytopenic purpura, hepatitis, interstitial nephritis, diabetes, dysgammaglobulinemia.
- Neonatal diagnosis is based on clinical suspicion or persistent rise of serum antibody titer beyond three months of age, specific rubella IgM antibody identification, and virus isolation.
- Neonatal treatment: **No** specific treatment is available. Infected infants can shed virus from the nasopharynx up to one year of age.

TOXOPLASMOSIS

General Principles

- Maternal infection may be acquired by ingestion of raw meat or by close contact with infected cats. Direct person-to-person transmission does **not** occur.
- Transmission to the fetus is primarily transplacental.
- The incidence of congenital infection depends on the trimester during which maternal infection occurred. Incidence of fetal infection: First trimester, 15 percent; second trimester, 25 percent; third trimester, 60 percent. Overall, one-third of infants born to mothers who acquired toxoplasmosis during pregnancy will be infected.
- Spontaneous abortion, stillbirth, or premature delivery may occur.
- Pathologic examination of the placenta may identify *Toxoplasma gondii* cysts.
- Most infected infants are asymptomatic at birth.

Maternal Clinical Manifestations

The mother may be completely asymptomatic, or a mononucleosis-like illness may develop.

Diagnosis

- Serologic testing, with an **eight-fold** increase in titer by the Sabin-Feldman dye test; a

fourfold increase in titer by indirect immunofluorescence, complement fixation, or hemagglutination.

- Histological identification of cysts in the placenta.

Maternal Treatment

- **Pyrimethamine**, 25 mg/day orally for 28 days,
  and
- **Sulfadiazine**, 1 gm orally four times a day for 28 days.

Pyrimethamine should not be used during the first trimester and sulfadiazine should not be used during the third trimester. In addition, potential drug toxicity should be monitored with a complete blood count and platelet count every other week.

Neonatal Clinical Manifestations

These may be extremely variable and include: chorioretinitis, seizures, microcephaly, intracranial calcification, abnormal CSF, hepatosplenomegaly, jaundice, fever, thrombocytopenia, interstitial pneumonitis, nephritis, focal adrenal necrosis.

- Neonatal diagnosis is based upon identification of specific IgM antibodies and by recovery of the organism.
- Neonatal treatment: Pyrimethamine and sulfadiazine.

RUBEOLA (MEASLES)

General Principles

- The virus is acquired by inhalation of contaminated aerosols/respiratory droplets that infect the upper respiratory tract initially.
- In utero infection may occur by transplacental passage of the virus. Case-controlled studies have failed to demonstrate any increase in congenital anomalies.
- The incidence of spontaneous abortion and premature labor has been reported to be increased.

Maternal Clinical Manifestations

- Incubation period: 10-14 days. Illness typically begins with a prodrome of fever and malaise. A maculopapular rash begins on the face and moves down the trunk to affect the extremities.
- The patient is contagious from 1-4 days BEFORE the coryza to 7 days AFTER the appearance of the rash.
- Koplik spots may be present on the oral mucosa.
- Additional symptoms include fever, malaise, cough and keratoconjunctivitis.
- Encephalitis and myocarditis are rare complications.
- A secondary bacterial pneumonia may occur.

Diagnosis

- Clinical suspicion based on exposure to a documented case.
- Identification of virus by immunofluorescence or by culture.

- Serologic testing using either hemagglutination inhibition or complement fixation will reveal a greater than fourfold increase in titer.

Treatment

- Maternal treatment of rubeola is supportive, with the use of analgesics and antipyretics as needed. The development of bacterial pneumonia, however, requires specific antibiotic treatment.
- Immune globulin – if given during the incubation period – will modify the severity of maternal symptoms. It is unknown whether this will modify disease in the fetus. The dose is 0.25 mL/kg body weight.

Neonatal Clinical Manifestations

The neonate may develop typical exanthematous lesions. An increased incidence of congenital malformations is disputed.

NEONATAL DIAGNOSIS is based on viral identification and serologic testing.

NEONATAL TREATMENT: No specific treatment is available.

CYTOMEGALOVIRUS (CMV)

General Principles

Infection may occur in utero by transplacental transmission or during passage through an infected birth canal. Infants have also acquired CMV via transfusion with infected blood. Primary maternal infection is associated with a high intrauterine infection rate.

Virus may be shed from the urine, cervix, or nasopharynx for months to years after primary infection.

Maternal Clinical Manifestations

- May be completely asymptomatic.
- A mononucleosis-like illness may develop.

Diagnosis

- Viral isolation from the urine or cervix.
- Serologic testing: a greater than **fourfold** increase in titer with paired sera (IHA, ELISA, FA, CF).

MATERNAL TREATMENT: No specific treatment is available.

Neonatal Clinical Manifestations

- May be asymptomatic.
- Jaundice, hepatosplenomegaly, petechial rash, microcephaly, motor disability, chorioretinitis, periventricular calcification, mental retardation.

NEONATAL DIAGNOSIS: Established by virus isolation and demonstration of IgM specific antibody.

NEONATAL TREATMENT: No specific treatment is available

VARICELLA (CHICKEN POX)

General Principles

- In utero infection may occur by transplacental passage of the virus.
- Maternal infection that occurs within 7 to 10 days of delivery is associated with severe fetal infection that may result in neonatal death in one-third of cases.
- Infection transmitted via respiratory droplets.
- Period of highest contagion/infectivity is 2-3 days PRIOR to the onset of the rash.

Maternal Clinical Manifestations

- Incubation period: 10-21 days. A vesiculopapular rash occurs shortly after prodromal symptoms of fever and malaise.
- Pneumonia is a common complication.

Diagnosis

- Typical intranuclear inclusion bodies may be demonstrated in scrapings of the base of the vesicles.
- Antibodies are detectable two to four weeks after infection.

Maternal Treatment

- Treatment is generally supportive with the use of antihistamines to control pruritus and local cleansing to prevent secondary infection of open lesions. VZIG is only effective within 72 hours of exposure and it does NOT prevent fetal infection.
- Pneumonia may lead to significant alveolar-capillary block, hypoxia, and death. Hospitalization and aggressive support are indicated when pulmonary symptoms are present.
- Acyclovir is recommended **ONLY** in complicated cases or in immunocompromised patients (e.g., HIV infected).

Neonatal Clinical Manifestations

- Maternal infection early in pregnancy has been associated with numerous fetal anomalies including limb atrophy, cortical atrophy, and scarring of the skin.
- Convulsive disorders and paralysis in the neonate have been reported.
- Infants born within 7 to 10 days of maternal infection will generally develop severe infection with significant mortality.

NEONATAL TREATMENT: No generally satisfactory treatment is available, although the use of Zoster immune globulin (VZIG) may be of some benefit.

MUMPS

An increased incidence of spontaneous abortion has been reported with first-trimester infection. No association with congenital anomalies has been reported. Maternal treatment is supportive.

POLIOMYELITIS

This disease is rare in the United States due to widespread vaccination. The fetus may become infected, leading to paralysis and restricted growth. Maternal treatment is supportive, with ventilatory assistance often necessary.

LISTERIA MONOCYTOGENES

General Principles

- *L. monocytogenes* is a microaerophilic, motile, gram-positive bacillus ubiquitous in nature.
- Infection in humans is generally a sporadic event.
- Occasional epidemics associated with contaminated foods (especially milk products) are reported. Person-to-person transmission other than venereal has not been recognized.
- Transmission to a fetus may be either transplacental at the time of maternal viremia or ascending from cervical infection. (The latter may occur even across intact membranes.)

Maternal Clinical Manifestations

- Many pregnant women infected with *L. monocytogenes* are asymptomatic.
- Flu-like symptoms characterized by fever, chills, malaise, myalgias, nausea, vomiting, diarrhea, or headache may occur.
- A small percentage of patients will present with sepsis or signs of meningitis.
- Patient may present with an intrauterine fetal demise or signs of premature labor and/or chorioamnionitis.

Diagnosis

- Bacterial isolation from blood, cervix/vagina, rectum, or amniotic fluid.
- Serologic testing is possible though not usually readily available.

Maternal Treatment

- Bacterial isolation, but no symptoms: Ampicillin 500 mg po qid for 14 days.
- Patient symptomatic with a positive culture: Parenteral Ampicillin plus Gentamicin for 2-3 weeks.

Neonatal Clinical Manifestations

Perinatal listeriosis is usually classified as early-onset and late-onset disease of the newborn. Early onset disease usually presents within the first five (5) days of life as congenital sepsis. It is especially common in premature infants. The infant may present with severe respiratory distress, cyanosis, or hypothermia. It may have a papular skin rash and/or purulent conjunctivitis. The neonatal mortality rate is high (greater than 50%).

Late onset disease occurs usually in the second week of life (range 1-4 weeks). The infection is acquired from delivery through an infected birth canal. Characteristic symptoms are that of meningitis. Survival is better than for early-onset disease, but the survivors have a high incidence of long-term sequelae.

NEONATAL DIAGNOSIS: Established by bacterial isolation from blood, CSF, or other body sites.

Neonatal Treatment

- Ampicillin 200-300 mg/kg/day in 4-6 divided doses for 3 weeks.
- Some authors advocate a combination regimen of Ampicillin plus an aminoglycoside.

III. HEPATITIS

General Principles

- Hepatitis A, Hepatitis B, and Non-A Non-B (Hepatitis C) are major viral agents causing hepatitis.
- Hepatitis A (infectious hepatitis) is caused by an RNA virus. Incubation period is 15-50 days. Transmission is generally fecal/oral. No carrier state is recognized.
- Hepatitis B (serum hepatitis) is caused by a DNA virus. Incubation period is 30-180 days. Transmission is parenteral or via body fluids. Chronic forms of the disease occur in 5-10 percent of infected individuals.
- Certain groups of women have been identified who are at high risk for Hepatitis B infection (see Table 11). Serologic screening of individuals with these risk factors is strongly recommended.

Maternal Clinical Manifestations

During the prodromal phase of the disease, anorexia, nausea, vomiting, fever, lassitude, myalgia, arthralgia, headache, and abdominal pain may be seen. As symptoms abate jaundice is first observed. With the onset of jaundice the liver tends to enlarge and become tender. As a rule the peak changes in liver enzyme elevations occur within 1 or 2 days before or after the onset of jaundice.

Diagnosis

Diagnosis depends on antigen and antibody determinations:

- Hepatitis A—demonstration of hepatitis A antibody.
- Hepatitis B—demonstration of hepatitis B surface antigen, HBs antibody or HBe antigen.
- Hepatitis C—demonstration of hepatitis C antibody by EIA.

Maternal Treatment

No specific therapy is available, however, general management principles include:

- Institute appropriate isolation precautions.
- Determine the need for prophylaxis with serum globulin preparations for close contacts of the patient.
- Activity determined by patient tolerance. Diet as tolerated. Antiemetics are occasionally needed.

Neonatal Clinical Manifestations

- Vertical transmission in greater than 70% of mothers who are HBe Ag positive or HBs Ag positive around the time of delivery.
- The majority of infants infected in utero remain anicteric and show no sign of an acute clinical hepatitis.
- The risk of perinatal transmission of HCV is uncertain but appears to be rare.

Neonatal Diagnosis

The same antigen and antibody markers should be evaluated in the newborn as in the adult.

Neonatal Treatment

- Hepatitis B immune globulin (HBIG) and vaccine are recommended for all infants born to HBsAg-positive mothers—see table below for schedule and dosage.
- Clinical illness is treated with supportive measures only.

Table 7 Forms of Viral Hepatitis

Characteristics	Hepatitis A	Hepatitis B	Hepatitis C
Older name	Infectious hepatitis	Serum hepatitis	Non-A, Non-B Hepatitis
Virus type	RNA	DNA	Unknown
Virus size	27 nm	42nm	Unknown
Incubation period	15-50 days	30-180 days	30-160 days
Transmission	Fecal-oral	Parenteral or body fluids	Parenteral, Water-bone
Vertical transmission to fetus	Not observed	Common	Probably occurs
Immunologic diagnosis	HA antibody IgM and IgG types	HB_s AG; Hb_cAb HB_sAb; Hb_eAg, Ab	By exclusion
Maximum infectivity	Prodrome	Prodrome or Hb_eAg positive, Hb_sAg carriers	Probably prodrome and carriers
Carrier State	None	5-10 per cent	10-40 per cent
Acute clinical forms	Asymptomatic to fulminant	Asymptomatic to fulminant	Asymptomatic to fulminant
Chronic clinical forms	None	Cronic persistent hepatitis; Chronic active hepatitis	Cronic persistent hepatitis; Chronic active hepatitis

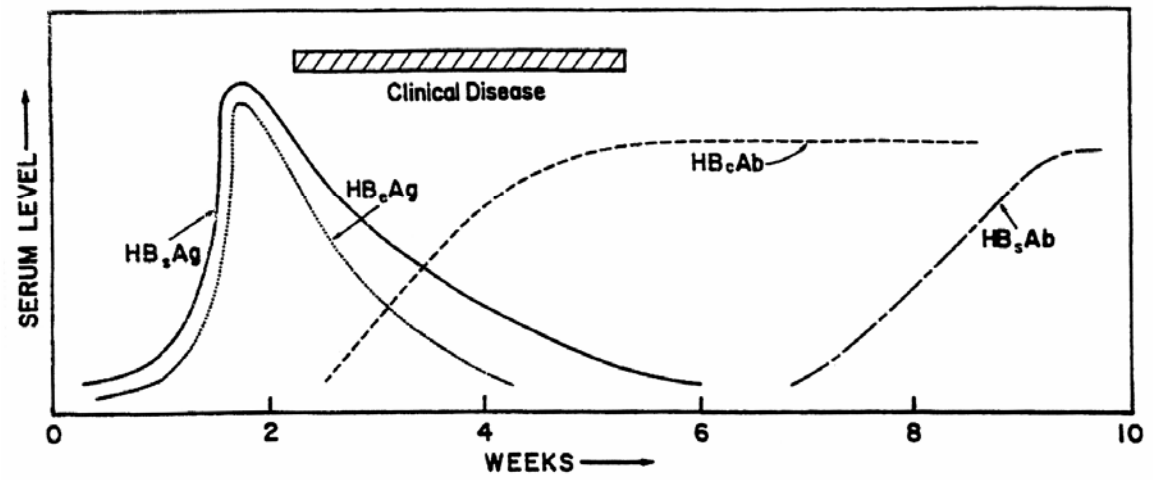
Burrow GN, Duffy TP. Medical complications during pregnancy. 5th ed. Philadelphia(PA): WB Saunders;1999. (Level III)

Table 8 Hepatitis B Terminology

Hepatitis B virus	Dane particle
Hepatitis B core antigen	HB_cAg
Hepatitis B core antibody	HB_cAb
Hepatitis B surface antigen	HB_cAg
Hepatitis B surface antibody	HB_cAb
Hepatitis “e” antigen	HB_cAg
Hepatitis “e” antibody	HB_cAb
Hyperimmune serum globulin	HBIG
Hepatitis B vaccine	HB-Vac

Burrow GN, Duffy TP. Medical complications during pregnancy. 5th ed. Philadelphia(PA): WB Saunders;1999. (Level III)

Figure 5 **Immunologic Changes in Hepatitis B**



Burrow GN, Duffy TP. Medical complications during pregnancy. 5th ed. Philadelphia(PA): WB Saunders;1999. (Level III)

Table 9 **VERTICAL TRANSMISSION OF HEPATITIS**

	Hepatitis A	Hepatitis B		Hepatitis C
Maternal Infection	**Acute Infection**	**Acute Infection**	**Carrier State**	**Acute & Chronic**
Transmission risk to infant	Rare	1st and 2nd trimesters: <10% 3rd trimester ≅65%	He$_e$g-positive: 85-95% He$_e$Ab-positive <5% Hb$_e$Ag, HbeAb-Negative ≅50%	Reported
Infant disease	Rare clinical hepatitis (at 30-120 days of age) Commonly become carriers	Usually mild hepatitis, rarely severe hepatitis (at 30-120 days of age) Commonly become carriers	May have severe or fatal hepatitis (at 30-120 days of age) Commonly become carriers Cirrhosis or hepatoma late complications (10-20 years later)	Acute hepatitis, also Probable chronic hepatitis or carrier state
Recommended prophylaxis for infants	ISG—optional, for infant of mother with acute infection at birth	ISG—no HBIG--<24 hr, 0.5 ml (repeat at 3,6 mo if no vaccine given) HB-VAC<24 hr, 1mo, 6 mo (20 mg ea)	ISG—no HBIG--<24 hr, 0.5 ml (repeat at 3,6 mo if no vaccine given) HB-VAC<24 hr, 1mo, 6 mo (20 mg ea)	Effectiveness of ISG Unknown

Combined HBIG and HB-Vac is 85-95% effective in preventing HB infection in infant (H-4). The HB-Vac may be given at birth or as late as 3 months after HBIG

Burrow GN, Duffy TP. Medical complications during pregnancy. 5th ed. Philadelphia(PA): WB Saunders;1999. (Level III)

Table 10 Management of Typical Viral Hepatitis In Pregnancy

Establish type by immunological test
Institute approporiate isolation and precautions
Determine need for contact prophylaxis with serum globulin preparations
Activity—determined by tolerance
Diet—patient preference, parenteral if necessary
Antiemetics—phenothiazines may be used
Corticosteroids—not indicated

Burrow GN, Duffy TP. Medical complications during pregnancy. 5th ed. Philadelphia(PA): WB Saunders;1999. (Level III)

Table 11 The High-Risk Groups for Hepatitis B

Women who are at high risk for hepatitis B infection should be screened prenatally for the Hepatitis B surface antigen, HB_sAg according to the Centers for Disease Control. Identified high-risk groups include women who:

- Are of Asian, Pacific Island, or Alaskan Eskimo descent whether they are immigrants or US natives
- Were born in Haiti or sub-Saharan Africa
- Have histories of acute or chronic liver disease
- Work or get treatment in a hemodialysis unit
- Work or live in an institution for the mentally retarded
- Have previously been rejected as blood donors
- Have hereditary or acquired disorders (e.g. hemophilia, thalassemia) requiring repeated blood transfusions
- Work in health professions and are frequently exposed to blood
- Have household contact with HBV carriers or hemodialysis patients
- Have had multiple episodes of veneral diseases
- Are or have been users of illicit injectable drugs

Adapted from Post-exposure prophylaxis of hepatitis B. MMWR Morb Mortal Wkly Rep 1984;33(21): 285-90. (Level III)

Table 12 Hepatitis B Virus Postexposure Recommendations

		HBIG		
Exposure	Dose	Recommended timing	Dose	Recommended timing
Perinatal	0.5 ml IM	Within 12 hours of birth	0.5 ml IM*	Within 12 hours of birth†
Sexual	0.06ml/kg IM	Single dose within 14 days of last sexual contact	1.0ml IM*`	First dose at time of HBIG treatment†

*For appropriate age-specific doses of each vaccine, see Table 3

†The first dose can be given the same time as the HBIG dose but in a different site; subsequent doses should be given as recommended for specific vaccine.

Anda RF, Waller, MN, Wooten KG, Mast EE, Escobedo LG, Sanderson LM. Behavioral Risk Factor Surviellance, 1988. MMWR CDC Surveill Summ 1990;39(SS-2):1-21. (Level III)

Table 13 Recommendations for Hepatitis B Prophylaxis Following Percutaneous or Permucosal Exposure

	Treatment when source is found to be:		
Exposed person	HB_sAg-positive	Initiate HB vaccine†	Initiate HB vaccine†
Unvaccinated	HBIG x 1* and initiate HB vaccine†	Initiate HB vaccine†	Initiate HB vaccine†
Previously vaccinated Known responder	Test exposure for anti-HBs 1. if adequate,§ no treatment 2. if inadequate, HB vaccine booster dose	No treatment	No treatment
Known nonresponder	HBIG x 2 or HBIG x 1 plus 1 dose HB vaccine	No treatment	If known high-risk source, *may treat as if source were HB_sAg-positive*
Response unknown	Test exposure for anti-HBs 1. if adequate,§ HBIG x 1 plus HB vaccine booster dose 2. if inadequate,no treatment	No treatment	Test exposure for anti-HBs 1. if inadequate§, HB vaccine booster dose 2. if adequate, no treatment

* HBIG dose 0.06 ml/kg IM.

† HB vaccine dose –see Table 3.

§ Adequate anti-HBs is ≥10 SRU by RIA or positive by EIA

Hepatitis B virus: a comphrensive strategy for eliminating transmission in the United States through universal childhood vaccination. Recommendations of the Immunization Practices Advisory Committee(ACIP). MMWR Recomm Rep 1991;40(RR-13):1-25. (Level III)

Table 14 Routine Pediatric Vaccination Schedule and HBV Prophylaxis for Infants of HBs-Ag-Positive Mothers

Age (months)	Hepatitis B prevention schedule	HBV marker screening	Routine pediatric schedule
Birth	HBIG* HB Vaccine† HB Vaccine		
1			
2			DPT§, Polio
4			DPT§, Polio
6	HB Vaccine	HbsAg test ¶¨	DPT
12-15		HbsAg test ¨ & anti-HBs†† test	
15			MMR§§
18			DPT§, Polio

- Hepatitis B immune globulin 0.5 ml IM within 12 hours of birth.

† HB Vaccine 0.5 ml IM within 7 days of birth.

§ Diptheria-tetanus-pertussis.

¶ Optional. If positive, indicates infection, and a third HB vaccine dose need not be given

¨ HBsAG-positive indicates therapeutic failure

†† Anti-HBs-positive indicates therapeutic success

§§ Measles-mumps-rubella.

Hepatitis B virus: a comphrensive strategy for eliminating transmission in the United States through universal childhood vaccination. Recommendations of the Immunization Practices Advisory Committee(ACIP). MMWR Recomm Rep 1991;40(RR-13):1-25. (Level III)

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