PERINATAL INFECTIONS

TRANSMITTED BY
THE MOTHER TO HER INFANT

EDUCATIONAL MATERIAL FOR HEALTH PERSONNEL

Pan American Health Organization
Regional Office of the
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Latin American Center for Perinatology
Woman and Reproductive Health - CLAP/WR

PERINATAL INFECTIONS
Transmitted by the mother to her infant

EDUCATIONAL MATERIAL FOR HEALTH PERSONNEL

THIS MANUAL CONTAINS UPDATED BASIC INFORMATION ON:

- THE PATHOGEN AND THE DISEASE

- BURDEN OF PROBLEM AND BURDEN OF DISEASE IN THE COUNTRIES OF LATIN-AMERICAN AND CARIBBEAN REGION

- DIAGNOSIS

  - o CLINICAL FEATURES IN THE MOTHER AND NEONATE

  - o LABORATORY AND SYSTEMATIC SCREENING

- PREVENTION AND TREATMENT INTERVENTIONS DURING

  - o PRECONCEPTIONAL,

  - o ANTENATAL,

  - o PERINATAL AND

  - o POSTPARTUM/POSTNATAL CARE PERIODS

INTRODUCTION:

Mother to baby transmission of infection can occur in utero (congenital), at and around the time of delivery (perinatal) or subsequently (postnatal) as illustrated by transmission of organisms by breastfeeding.

Maternal infections spread to the embryo and fetus by:

- Ascending infection from the upper vagina via the uterine cervix to the amniotic fluid or by
- Hematogenous spread as a result of maternal viremia, bacteremia or parasitemia.

When infections are acquired by ascending route, microorganisms, more commonly can cause funisitis and inflammatory changes in the amnion and chorion (chorioamnionitis) and may lead to premature rupture of the membranes and preterm delivery.
Often, fetal pneumonia will occur as a result of the entrance of the infected amniotic fluid into the lungs.

In infections spread hematogenously, more commonly viral infections, the placenta is often infected resulting in deciduitis and villitis.

Infections during pregnancy are one of the major causes of fetal and neonatal morbidity and mortality.

Although congenital anomalies are rare, in utero infections may lead to embryonic or fetal death.

Asymptomatic infections at birth may have late clinical manifestations that become evident only later in life, but mostly in the first years of childhood..

The fetus may be affected not only by the direct transmission of the agent, but also indirectly by the consequences of maternal infection, such as preterm birth or intrauterine growth restriction (IUGR). In utero transmission occurs variably depending on the infectious agent, gestational age at the time of transmission, and the immune status of the mother.   In general, primary infections during pregnancy are substantially more damaging than re-infections or reactivations of infection. Likewise, infections acquired at an earlier gestational age tend to lead to more serious infections.

Prevention

Systematic Screening

Maternal infections that could affect the fetus can be diagnosed when resources are available. Because in many circumstances, even when first acquired, infections are asymptomatic, diagnosis depends on effective screening methods. For some infections, the cost benefit value of routine screening during pregnancy is lacking. In many areas, the most specific and sensitive tests are not readily available. If maternal infection is confirmed, transmission in utero is often difficult to confirm.

When available, preconceptional and antenatal screenings of the mother, and neonatal screening of the infant, play a major role in early diagnosis and timely treatment.

Education

Prevention of maternal primary infection by modifying habits that may increase contact with agents of communicable diseases is a relevant medical intervention. (See table of General Preventive Measures that women should follow to avoid infection during pregnancy).
Additionally, educating mothers about preconceptional and antenatal screenings and prevention strategies in the case of maternal infection is critical to ensuring that missed opportunities for prevention do not occur.

Immunization

Maternal immunity is transmitted passively to the fetus for those agents for whom she has developed antibodies. Vaccines should be administered in the preconceptional period. If vaccines are administered during childhood, protection is conferred through the childbearing years against:

Poliomyelitis	Mumps
Hepatitis B	Rubella
Measles	Varicella zoster (not yet confirmed)
Tetanus	

During pregnancy women should receive a vaccine only when:

- It is unlikely to cause harm,
- The risk of exposure is high, and
- The infection would pose a significant risk to the mother or fetus/neonate or both, such as:
  - Influenza,
  - Diphtheria,
  - Tetanus and
  - Hepatitis B

THE MANUAL

This manual will review the updated information on the most common infectious diseases that the mother may transmit to her infant during pregnancy, at birth or by breast feeding the infant. Summary of this information will emphasize the basic knowledge of the pathogen, the disease, the burden of problems caused by the disease in the mother and her offspring, epidemiological aspects, and how to manage the disease. Most of the emphasis is directed to preventive measures, screening when interventions are available, and the detailed analysis of interventions during the preconceptional period, antenatal care, perinatal care and maternal and neonatal care after birth.

Two tables are presented that integrate all the principal components of management for diseases that are vertically transmissible.

Table I:
VERTICAL INFECTIONS TRANSMITTED FROM THE MOTHERS TO THEIR INFANTS; SYSTEMATIC SCREENING AND INTERVENTIONS

This table summarizes for each infectious agent the route of transmission, the systematic maternal screening, the preconceptional and perinatal interventions, the systematic screening of neonates and the post natal interventions.

Table II.
UNIVERSAL MEASURES TO PREVENT INFECTIONS DURING PREGNANCY

This table summarizes the preventive measures that every woman should follow in order to avoid an acute infection that may put her at risk of transmitting the infection to her infant during pregnancy or breastfeeding. The table includes specific recommendations regarding contact with adults, including sexual contact, contact with blood products, contact with children, precautions with food and environmental risks, and work related risks.

TABLE I: VERTICAL INFECTIONS TRANSMITTED FROM THE MOTHERS TO THEIR INFANTS. SYSTEMATIC SCREENING AND INTERVENTIONS

| Pathogen (Disease) | USUAL ROUTE OF TRANSMISSION | | | SYSTEMATIC MATERNAL SCREENING | | INTERVENTIONS TO REDUCE ADVERSE OUTCOMES | | | | SYSTEMATIC OR SELECTIVE NEONATAL SCREENING | | INTERVENTIONS TO REDUCE ADVERSE OUTCOMES | | |
| | | | | | | PRECONCEPTIONAL OR ANTENATAL | | PERINATAL | | | | POSTNATAL | | |
	Intra uterine	Peri natal	Post natal	CLINICAL	LABORA-TORY	IMMUNI-ZATION	PREVENTION	TREATMENT	PREVENCION/TRATAMIENTO	CLINICAL	LABORATORY	IMMUNI-ZATION	PREVENTION	TREATMENT
Treponema pallidum (Syphilis)	+ + (H)	—	—	Genital ulcer. Rash flu like illness, may have no symptoms	VDRL/RPR	NO	Safe sex/condoms	Penicillin G prior to 4 weeks before delivery	VDRL/RPR	Congenital syndrome	VDRL/RPR Test rápidos	NO	NO	Penicillin G
Human immunodeficiency virus (HIV)	±	+ + (H)	+	Flu like	HIV Antibody	NO	Safe sex/condoms no i/v drugs ZDV, Nevirapine, or other drugs regimens	Highly-active antiretroviral therapy (HAART)	Scheduled C/section if maternal viral load >1000 near delivery. ZDV, Nevirapine, or other regimens	NO	Antibody follow up Antigen. Nucleic acid testing for infant. NOTE: Positive antibody test in infant indicates maternal infection (not infanti infection)	NO	ZDV. Nevirapina	ZDV + other RV
Rubella virus	+ +	—	+	Rash arthritis	IgG	MMR	Avoid contacts	NO	Vacunación triple viral posparto. Sin trátamiento	Síndrome congénito	IgM/ cultivo de virus	NO	NO	Symptomatic treatment for s/s
Plasmodium falciparum (Malaria)	+ +	—	—	Fever in endemic areas	Microscopy in blood	NO	Insecticide treated bed nets	Quinine	NO	IUGR	NO	NO	NO	NO
Hepatitis B virus	±	+ + (H)	+ / —	NO	HBsAg	YES	Hepatitis B vaccination of persons at risk	NO	Hepatitis B vaccine for newborns within 12 hours of birth. In addition, where resources permit and maternal HBsAg testing occurs, administration of HBIG to infants.	NO	HBsAg and anti/HBs testing of infants born to HBsAg positive women	HIBG + VACCINE	Vaccine	Interferon alfa-2b, peginterferon alfa-2b, lamivudine, adefovir, dipivoxil, entecavir, and telvibudine
Trypanosoma Cruzi (Chagas disease)	+ +	—	—	NO	IgG	NO	NO	NO	NO	Congenital syndrome	Microscopy by blood	NO	NO	Nifurtimox Bensnidazole
E. Coli (Asymptomatic bacteriuria)	+ +	—	—	NO	Urine culture	NO	NO	Antibiotics	NO	NO	NO	NO	NO	NO
Group B streptococci	+ / —	+ + (G,H)	+ / —	Risk factors	Vaginal/ Rectal swab	NO	NO	NO	Penicillin or Ampicillin i/v > 4 hs. before birth	Sepsis signs	PCR/CBC blood culture, lumbar puncture	NO	NO	Ampicillin
Varicella zoster virus (Chickenpox)	+	+ + (H)	—	Typical rash	NO	YES	Avoid contacts/ IgG G if contact	Acyclovir if severe	Post partum vaccine NO treatment	Congenital syndrome	NO	Inmuno-globulin if recent at birth	Isolate mother and neonate	Acyclovir
Herpes simplex virus I or II	±	+ + (G,H)	—	Genital or oral typical lesions	NO	NO	Safe sex/condoms	Acyclovir if severe	Schedule C-section if active lesions	Neonatal Herpes	NO	NO	NO	Acyclovir
Neisseria gonorrhoeae	+	+ + (G)	—	Cervicitis Vaginal discharge	Culture	NO	Safe sex/condoms	Penicillin, Cifixime, Ceftriaxzone	NO	Ophtalmia/Pre term delivery	Culture	Credé/Topical ATB	NO	Penicillin Ceftriaxzone
Chlamydia trachomatis	+	+ + (G)	—	Cervicitis	NAAT	NO	Safe sex/condoms	Erythromycin Azithromicin	NO	Ophtalmia Pneumonia	NAAT	Topical ATB	NO	Erythromycin Azithromycin
Toxoplasma gondii	+ +	—	—	Flu like	Ig G / IgG avidity	NO	Avoid cat litter Soil	Controversial but tretatment usually given	NO	Síndrome congénito	IgG, IgM, IgA	NO	NO	Pyrimethamine + Sulfadiazine
Cytomegalovirus	+ +	+ + (G,H)	+	Flu like	NO	NO	Avoid infant saliva and urine	Ampicillin	NO	Congenital syndrome	Antigen PCR	NO	NO	Controversial
Parvovirus	+ +	—	—	Flu like, arthritis	NO	NO	NO	Fetal transfusion	NO	Fetal Hydrops	Antigen PCR	NO	NO	Blood transfusion
Hepatitis C virus	±	+ + (H)	—	NO	NO	NO	No i/v drugs	NO	NO	NO	NO	NO	NO	NO
Listeria monocytogenes	+ +	+ (G,H)	—	Diarrhea, fever	NO	NO	Avoid cold cuts/soft Cheeses	Penicillin	NO	Sepsis	Culture	NO	NO	Penicillin

++ = main route of transmission. + = recognized, but less common, route. ± = uncommon or possible, but uncertain, route (G) = genital. (H) = haematogenou

TABLE II : UNIVERSAL MEASURES TO PREVENT INFECTIONS DURING PREGNANCY		

CONTACT WITH ADULTS	RESPIRATORY OR FLU LIKE SYMPTOMS	• Avoid close or intimate contact with adults with communicable diseases, acute or recent fever or flu like symptoms
		  o Kissing
		  o Sharing food utensils, drinking from the same container
		• Wash hands frequently and if available use alcohol gel rub after shaking hands and before eating

	SEXUAL CONTACT	• Abstain from sex (oral, vaginal, or anal) unless you are in a long-term, mutually monogamous relationship with an uninfected partner.
		• Vaginal spermicides containing nonoxynol-9 (N-9) are not effective in preventing infectious diseases.
		• Use male latex condoms consistently and correctly.
		  o Carefully handle the condom to avoid damaging.
		  o Put the condom on after the penis is erect and before any genital, oral, or anal contact with the partner
		  o To prevent the condom from slipping off, hold the condom firmly against the base of the penis during withdrawal, and withdraw while the penis is still erect.
		  o Do not use the condom more than once
		• Avoid receptive oral sex with a partner with oral herpes or intercourse during the third trimester with men who have genital herpes.

	BLOOD CONTACT	• Consider the risks if you are thinking about getting a tattoo or body piercing. You might get infected if the tools have someone else's blood on them.
		• Do not shoot drugs
		  o if you shoot drugs, stop and get into a treatment program;
		  o if you can't stop, never share needles, syringes, water, or "works",
		• Do not share personal care items that might have blood on them (razors, toothbrushes).

CONTACT WITH CHILDREN	RESPIRATORY, FLU LIKE SYMPTOMS OR SKIN RASH OR ANYTIME IF CHILD IS UNDER 3 YEARS OLD	• Careful hand washing with soap and running water for 15 to 20 seconds; if available at home use alcohol gel rub after
		  o exposure to a child's bodily fluids and diaper changes,
		  o bathing the child in the tub
		  o handling dirty laundry,
		  o touching the child's toys and other objects
		• Protective gloves may be additional protection during diaper changes, bathing or when handling the child's dirty laundry
		• Avoid close or intimate contact with child such as
		  o kissing on the mouth or cheek (kiss them on the head or give them a hug)
		  o sleeping together,
		  o sharing towels and washcloths,
		• Avoid contact with babies' saliva while feeding them
		  o sharing or tasting foods with the same utensils (spoons, forks)
		  o drinking from the same container

FOOD and Water	CONSUMPTION HANDLING, AND PROCESSING	• Avoid consumption of raw or undercooked lamb, pork, beef or poultry.. Reheat until steaming: hot dogs, luncheon meats or deli meats • Check for hygienic warranties and freshness in refrigerated perishable and ready-to-eat food (e.g., cold meats, hotdogs, deli meat, pâté and salads) • Do not eat unpasteurized dairy products (including all soft cheeses), • Pates, meat spreads and smoked sea food may only be eaten if they are canned or shelf-stable • Peel or wash raw fruit and vegetables thoroughly to remove contaminated soil. • Wash hands, knives, and cutting boards after handling uncooked foods or fluids from their packages. • Wash hands thoroughly after handling raw meat. • Cook all meat (lamb, pork and beef) until it is no longer pink and the juices run clear • Avoid untreated (unfiltered) water.
ENVIRONMENTAL RISKS	HANDLING SOIL AND ANIMAL LITTER	• Wear gloves when gardening or working in soil. • Avoid handling cat litter but if you must do it, use gloves and wash hands immediately after. • If possible, keep cats indoors throughout pregnancy and do not feed cats uncooked meat. • Cover children's sandboxes when not in use (cats like to use them as litter boxes) • Change cat litter daily
	PROTECTION FROM INSECTS	• Always use Insecticide-treated bed nets if you live in an endemic malaria area.
LABOR RELATED RISKS	INFANT DAY CARE o HEALTH CARE	• Avoid working with children younger than 3 years of age. • If you are a health care or public safety worker, always follow routine barrier precautions and safely handle blood, needles and other sharps.

This manual discusses each of the most common infections transmitted vertically from the mother to her offspring. It contains information on asymptomatic bacteriuria because, although it is not a vertically transmitted disease, its screening and treatment contributes to a decrease in the risk of premature birth.

Each chapter is independent of the others. Infections that are included in all national public health initiatives have been presented first. Presentation of each infectious agent follows the order in Table I.

Treponema pallidum
(Syphilis)
Human immunodeficiency virus
(AIDS)
Rubella virus
Plasmodium falciparum
(Malaria)
Hepatitis B virus

Trypanosoma cruzi
(Chagas disease)
E.Coli
(Asymptomatic bacteriuria)
Group B streptococci
Varicella zoster virus
(Chickenpox)
Herpes simplex virus

Neisseria gonorrhoeae
(Gonorrhea)
Chlamydia trachomatis
Toxoplasma gondii
Cytomegalovirus
Parvovirus
Hepatitis C virus
Listeria monocytogenes

The final chapter of this manual is a brief reference to the Perinatal Information System, currently used in all the countries of the LA&C region, distributed free by the Pan American Health Organization. The Perinatal Clinical Record and Maternal Antenatal Card register useful information on many of these infections and help to assess several indicators related to the burden of the problem and its management in health services.

Syphilis

Syphilis is a disease caused by the bacterium *Treponema pallidum,* which is transmitted sexually during vaginal, anal or oral sex. Syphilis is easy to treat with antibiotics in the early stages of the disease.
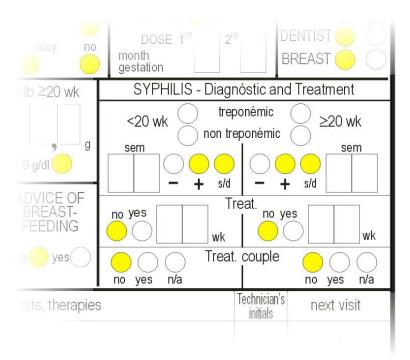
Its clinical stages are:

- primary stage (one or more painless indurated ulcer or chancre at the infection site)
- secondary stage (manifestations include but are not limited to: skin rash, mucocutaneous lesions, and lymphadenopathy)
- tertiary stage (cardiac, neurological or ophthalmic manifestations, auditory abnormalities, or gummatous lesions)

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Latent Syphilis – period after infection. Patients are seroreactive but have no clinical manifestations of disease:

- Early latent syphilis is acquired within the preceding year
- Late latent syphilis include all other cases

Congenital syphilis can be acquired from an infected mother via transplacental transmission of T. pallidum at any time during pregnancy or at delivery. Transmission to the fetus can occur at any stage of disease. The rate is highest (60% to 100%) during primary and secondary syphilis decreasing to approximately 40% during early latent infection and 8% during late latent infection.

MATERNAL SYPHILIS

Maternal infection is like that in any non pregnant women, and may be acquired at any stage of pregnancy.

Epidemiological Definition: (Pan American Health Organization)

Any pregnant woman, regardless of **the stage** of gestation or **having recently suffered abortion, with** clinical evidence (genital ulcer or signs compatible with secondary syphilis) or who has reactive treponemal (including rapid treponemal tests) or nontreponemal tests, and who has not received adequate treatment (carried out before the 20th week of pregnancy and at the very least 30 days before delivery) for syphilis during the current pregnancy.

CONGENITAL SYPHILIS

Epidemiological Definition (Pan American Health Organization)

• Any live born infant, stillborn infant, or pregnancy outcome (e.g., spontaneous or other abortion) whose mother has clinical evidence (genital ulcer or lesions compatible with secondary syphilis) or a positive or reactive treponemal test (including rapid treponemal tests) or nontreponemal test during pregnancy, delivery, or puerperium, and who has not been treated or has been treated inadequately.
Or
• any infant with RPR/VDRL titers fourfold or greater than the mother's titer. This would be equivalent to a change in two dilutions or more from the mother's titers (for example, of 1:4 in the mother to 1:16 in the child).
Or
• any child with one or more clinical manifestations suggestive of congenital syphilis on either physical or radiographic examination or with a reactive result of a treponemal or nontreponemal test.
Or
• any birth product in which the *T. pallidum* is evidenced by Dark field, immunofluorescence, or similar procedures.

BURDEN OF DISEASE

The Pan American Health Organization estimates that in Latin America and the Caribbean countries, 330,000 pregnant women who test positive for syphilis do not receive treatment during their antenatal care visits. Although the stage of the disease is a determining factor, it is estimated that two thirds of the cases of maternal syphilis during pregnancy result in congenital syphilis or miscarriage. Annually, 110,000 children are born with congenital syphilis, and a similar number of pregnancies result in fetal loss. Preterm birth occurs in 20% of cases of maternal syphilis.
In those LAC countries reporting national data in 2003, maternal syphilis ranged from 0.5 to 6 cases per 1,000 live births. The highest incidence of congenital syphilis was 4.0 cases per 1,000 live births.

DIAGNOSIS: Maternal Syphilis

CLINICAL FEATURES

The first clinical manifestation of syphilis is usually a local lesion at the site of entry of the agent.
It typically first appears after 2 to 6 weeks as a single, firm round and painless red sore called a chancre and enlarged local lymph nodes (swollen glands) on the area where there has been sexual contact with the infected person.

Many primary infections are asymptomatic and the signs of infection are missed because the chancre may be hidden in the vagina, cervix, or oropharynx. This highly infective chancre heals after 4 to 6 weeks.

Secondary stage begins 1 to 2 months later. In untreated cases, the clinical manifestations include skin rash, mucocutaneous lesions, and lymphodenopathy.

The rash is maculopapular, polymorphic and generalized, and typically includes the palms and the soles. The rash is not itchy or painful. In areas around the vulva and anus, hypertrophic papular lesions (condyloma lata) can occur and can be confused with the lesions (condyloma acuminata) caused by papillomavirus infection. Other clinical manifestations include generalized lymphadenopathies, malaise, fever, splenomegaly, arthralgia, sore throat, and headache. Secondary Syphilis manifestations will disappear spontaneously with time. In the first years of its latency, the infectious lesions of the skin and mucous membranes can recur.

Approximately a third of untreated secondary syphilis cases will remain latent for weeks or even years. If not treated, the clinical manifestations of the tertiary stage of the infection can reappear, even after many years, affecting the brain, nerves, eyes, large blood vessels, heart, the skin, joints and bones, persisting throughout life. Neurosyphilis is defined as infection extending to the central nervous system. Clinical manifestations of neurosyphilis can occur at any stage of the infection. People infected with HIV are at increased risk.

LABORATORY TESTS

Definitive diagnosis is made by demonstrating spirochetes by darkfield microscopy or direct fluorescent antibody tests of the exudate of lesions or in tissues such as placenta, umbilical cord or lymph node aspirates.

Presumptive diagnosis is possible using nontreponemal and treponemal tests. The use of only one type of test is insufficient for diagnosis due to false positive nontreponemal tests results. This can occur with a variety of medical conditions unrelated to syphilis. False positive treponemal test results can occur with other spirochetal diseases.

1. Nontreponemal Tests (e.g.). Venereal Disease Research Laboratory [VDRL] and Rapid Plasma Reagin [RPR] Nontreponemal test antibody titers usually correlate with disease activity and become nonreactive with time after effective treatment. No further treatment is required in patients with two consecutive non-reactive nontreponemal test results

2. Treponemal Tests (e.g.). Microhaemagglutination assay for antibodies to *T. pallidum* (MHA-TP), *T. pallidum* haemagglutination assay (TPHA), *T. pallidum* particle agglutination (TP-PA) and the rapid test (diagnostic technique that uses whole blood on strips and is based on the utilization of treponemal proteins as antigens with a reading time of several minutes). Treponemal tests will remain reactive regardless of treatment or disease activity, and cannot be used to assess treatment response.

PRE-PREGNANCY OR ANTENATAL SCREENINGS

All women should be screened serologically by treponemal or nontreponemal antibody testing and, if syphilis is confirmed, they must receive treatment during the first prenatal visit.

For communities and populations in which the prevalence of syphilis is high, serologic testing should be repeated during the third trimester, at 28 to 32 weeks gestation, and at delivery.

Any woman who delivers a stillborn infant after 20 weeks gestation should be tested for syphilis.

No infant should leave the hospital without the maternal serologic status having been determined at least once during pregnancy.

TREATMENT: Maternal Syphilis

Based on 50 years of clinical experience, penicillin G, administered parenterally is the preferred drug for treatment.

Treatment during pregnancy should be the penicillin regimen appropriate for the stage of syphilis diagnosed.
Parenteral penicillin G is the only therapy with documented efficacy for syphilis during pregnancy.

Those who have a history of penicillin allergy should be desensitized and then treated with penicillin. Up to 10% of persons may experience allergic response to penicillin such as urticaria, angioedema, upper airway obstruction, bronchospasm, or hypotension. Re-administration of penicillin to these patients can cause severe, immediate reactions. Tests for allergy to penicillin and desensitation should be available. Acute desensitization with Penicillin V suspension to eliminate anaphylactic sensitivity takes 4 hours.

Tetracycline and doxycycline usually should not be administered during pregnancy
Erythromycin is not effective.

All patients who have syphilis should be tested for HIV infection.

Follow-Up of Maternal Treatment

Serologic titers should be repeated at 28–32 weeks gestation, at delivery, and following the recommendations for the stage of disease.

Regarding neonatal health, maternal treatment should be considered inadequate if
- delivery occurs within 30 days of therapy, or
- clinical signs of neonatal infection are present at delivery, or
- Maternal antibody titer is fourfold higher than the pretreatment titer, or
- The mother's penicillin dose is unknown, undocumented or inadequate, or
- The mother received any non-penicillin treatment during pregnancy.

Intrauterine infection can occur at any gestational age. However, the pathological changes in fetal tissues are not evident before the 18th week of gestation. This phenomenon is most likely the result of a lack of fetal immune/inflammatory response.

The risk of transmission in utero as well as the severity of fetal infection, as assessed by stillbirth and symptomatology at birth, are inversely related to the time elapsed since the mother acquired syphilis (see table).

Outcome	Maternal Syphilis	
	Acquired During Last Year	Acquired Earlier than Last Year
Healthy newborn	20-60%	70%
Stillborn	16%	10%
Neonatal death	4%	1%
Preterm delivery	20%	9%
Congenital syphilis	40%	10%

DIAGNOSIS: Congenital Syphilis

The diagnosis of early congenital syphilis requires a high index of suspicion. It should even be entertained in any infant born at less than 37 weeks of gestation with no other apparent explanation or if a large placenta is encountered at birth.

Maternal epidemiological factors that must be ascertained include:
- Maternal untreated syphilis or sexual contact during pregnancy with a known syphilitic.
- Maternal syphilis treatment with drugs other than penicillin.
- Maternal treated during pregnancy but without follow-up at delivery.

Neonatal physical findings (in order of specificity)

- Radiological signs of dactylitis and other signs of osteochondritis and periostitis
- Snuffles, hemorrhagic rhinorrhea
- Condylomata lata
- Bullous skin lesions involving palms and soles
- Mucous patches
- Hepatosplenomegaly
- Jaundice
- Non-immune hydrops fetalis
- Generalized lymphadenopathy
- Pneumonitis
- Large placenta
- Intrauterine growth restriction.

Late Congenital Syphilis

In the first years of life, the late clinical manifestations represent scars induced by the initial lesions and the persistent and ongoing inflammation. These may include defects in dentition (Hutchinson's teeth); eye lesions (chorioretinits, uveitis, corneal scarring, and interstitial keratitis); sensorineural hearing loss; facial defects (saddle nose, protuberant mandible, rhagades); bone abnormalities (saber shins, Clutton's joints); and, central nervous system abnormalities (optic nerve atrophy, seizures, hydrocephalus, cranial nerve palsies).

SYSTEMATIC SCREENING AT BIRTH

In populations in which the risk for congenital syphilis is high, no infant or mother should leave the hospital unless the maternal serologic status has been documented at least once during pregnancy and at delivery.

Serologic testing of the mother's serum is preferred to testing of the infant's serum, because the serologic tests performed on infant serum can be nonreactive if the mother's serologic test result is of low titer, or infection occurred late in pregnancy.

The diagnosis of congenital syphilis is complicated by the transplacental transfer of maternal nontreponemal and treponemal IgG antibodies to the fetus.

All infants born to mothers who have reactive nontreponemal and treponemal test results should be evaluated by:

1. Quantitative nontreponemal serologic test (RPR or VDRL). The most specific and sensitive assays are serum IgM immunoblot and serum PCR.

2. Clinical examination for nonimmune hydrops, jaundice, hepatosplenomegaly, rhinitis, skin rash, and/or osteochondritis or periostitis (long bones) with or without pseudoparalysis of an extremity.

3. Pathologic examination of the placenta and umbilical cord (use of specific fluorescent antitreponemal antibody staining if possible).

4. The diagnosis of neurosyphilis is very challenging. Patients with reactive CSF on VDRL testing, or patients with CSF leukocytosis ($\geq$ 25 WBC per mm^3) and elevated protein content ($\geq$ 150 mg/dl in full term and $\geq$ than 170 mg/dl in preterm infants), should receive treatment for presumptive neurosyphilis. The most sensitive and specific tests available are T. pallidum isolation by inoculation into rabbits and PCR. Unfortunately, their availability is very limited. When comparing infants with recognizable congenital syphilis (clinical and serological evidence) with infants who lacked this evidence, the specificity and sensitivity finding a reactive CSF VDRL test, and CSF leukocytosis and elevated protein were 71% and 92%, 43% and 92%, and 43% and 92%. The use of FTA techniques applied to CSF testing in not recommended due to conflicting results.

TREATMENT: Neonatal

Neonatal treatment decisions based on maternal syphilis, must be made on the basis of
- Diagnosis of maternal syphilis;
- Adequacy of maternal treatment;
- Evidence of clinical, laboratory, or radiographic evidence of syphilis in the infant; and
- Comparison of maternal (at delivery) and infant nontreponemal serologic titers by using the same test.

The following scenarios summarize the main criteria for the management of congenital syphilis in the most common clinical situations.

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1. Infants who have clinical and laboratory evidence of congenital syphilis must be treated with Aqueous Crystaline Penicillin G 100,000 – 150,000 units/kg/day, **administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days** of life and every 8 hours thereafter for a total of 10 days.

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2. Infants who have a normal physical examination and a serum quantitative nontreponemal serologic titer the same or less than fourfold the maternal titer and the

- mother was not treated, inadequately treated, or has no documentation of having received treatment;
- mother was treated with Erythromycin or other nonpenicillin regimen; or
- Mother received treatment less than 4 weeks before delivery.

Recommended Evaluation
- CSF analysis for VDRL, cell count, and protein
- CBC and differential and platelet count
- Long-bone radiographs

A complete evaluation is not necessary if 10 days of parenteral therapy is administered. However, such evaluations might be useful; a lumbar puncture might document CSF abnormalities that would prompt close follow-up.

If a single dose of Penicillin G is used, then the infant must be fully evaluated (i.e., through CSF examination, long-bone radiographs, and CBC with platelets), the full evaluation must be normal, and follow-up must be certain.

If any part of the infant's evaluation is
- abnormal or
- not performed, or if
- the CSF analysis is rendered uninterpretable because of contamination with blood, a 10-day course of penicillin is required.

Recommended Regimens
Aqueous crystalline Penicillin G 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hoursthereafter for a total of 10 days
Or
Procaine Penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days

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3. Infants who have a normal physical examination and a serum quantitative nontreponemal serologic titer the same or less than fourfold the maternal titer and the
   - mother was not treated during pregnancy, treatment was appropriate for the stage of infection, and treatment was administred >4 weeks before delivery; and
   - mother has no evidence of reinfection or replace.

Recommended Evaluation
No evaluation is required

Recommended Regimen
Benzathine Penicillin G 50,000 units/kg/dose IM in a single dose

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4. Infants who have a normal physical examination and a serum quantitative nontreponemal serologic titer the same or less than fourfold the maternal titer and the
   - maternal treatment was adequate before pregnancy, and
   - maternal nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (VDRL <1:2; RPR <1:4)

Recommended Evaluation
No evaluation is required

Recommended Regimen
No treatment is required

FOLLOW-UP

All seroreactive infants should receive careful follow-up examinations and a nontreponemal test every 2–3 months until the test becomes nonreactive or the titer has decreased significantly.
Nontreponemal antibody titers should decline by age 3 months, and should be nonreactive by age 6 months.

Infants whose initial CSF evaluations are abnormal should undergo a repeat lumbar puncture approximately every 6 months until the results are normal. A reactive CSF VDRL test, or abnormal CSF indices that cannot be attributed to other ongoing illness, requires re-treatment for possible neurosyphilis.

HIV-AIDS

HIV MATERNAL AND PERINATAL INFECTION

Human Immunodeficiency virus (HIV) is a retrovirus that infects helper T cells of the immune system, causing a progressive reduction in their number, and eventually **Acquired Immunodeficiency Syndrome (AIDS)**.

HIV infection is a pandemic disease that affects more than 2.5 million children worldwide. Most children are infected during the peripartum period.

It is estimated that, in the absence of intervention in non-breast feeding settings, up to 50% of HIV transmission from mother to child occurs late in the third trimester (from 36 weeks), during labor, or at delivery.

Two factors have led to an increase in the prevalence of pregnant women who are HIV positive and expose their infants to this infection:
- A steady increase in the incidence of heterosexually acquired HIV infection in woman
- Increased life expectancy of infected individuals, as a result of treatment

There are several factors associated with the risk of vertical transmission. These factors can be divided into those associated with maternal, obstetric or postnatal transmission.

- Maternal
  - advanced maternal HIV disease,
  - Maternal antenatal CD4 counts less than 200 cells/mm3 and
  - high maternal plasma viral loads

- Obstetric risk
  - vaginal delivery
  - duration of membrane rupture
  - chorioamnionitis and
  - Preterm delivery.

- Postnatal
  - Breastfeeding is associated with a two-fold increase in the rate of HIV transmission

Without treatment, 15%–25% of infants born to HIV-infected mothers, independent of breastfeeding, will become infected with HIV. An additional 12%–14% of infants will become infected during breastfeeding if HIV-infected women breastfeed their infants into the second year of life

The risk of perinatal HIV transmission can be reduced substantially by:
- universal antenatal HIV screening
- access to anti-retroviral therapy
- elective caesarean section at 38 weeks of pregnancy (when maternal viral load is over 1000) and
- exclusive artificial formula feeding (eliminate breast feeding), *when an acceptable, feasible, affordable, sustainable and safe supply of formula is available (there is evidence that inappropriate formula feeding increases mortality even in cases in which the child does not become infected with HIV)*.

BURDEN OF DISEASE

In Latin America, some 140,000 people are newly infected with HIV each year with an estimated 1.6 million people living with the virus. The estimated death toll of HIV among children under 15 years in the LA&C in 2001 was more than 8000 per year.

Brazil is home to more than one-third of the people living with HIV in Latin America The most intense epidemics, however, are underway in the smaller countries of Belize, Haiti and Honduras. In each of these countries, as of 2005 more than 2 % of adults were living with HIV.

While notable gains in access to HIV treatment have been made in some countries such as Argentina, Brazil, Chile, Costa Rica, Mexico, Panama, Uruguay and Venezuela, the poorest countries of Central America and those in the Andean region of South America are struggling to expand treatment access in the face of affordability and other barriers.

DIAGNOSIS: Maternal

CLINICAL FEATURES

Fever, malaise, lymphadenopathy, and skin rash occur in 40%–90% of cases during the first few weeks following infection with HIV, and before antibody test results become positive. However, acute HIV infection often is not recognized by primary care clinicians because the symptoms resemble those of influenza, infectious mononucleosis, and other viral illnesses.

Following the acute phase, infected individuals may be free of clinical signs or symptoms for many months or years. Only after this period will other clinical manifestations appear. These include opportunistic infections and certain cancers, which develop as the immune system is progressively weakened by the HIV infection. It has been estimated that, in the absence of treatment, over 90% of HIV infected individuals will go on to develop AIDS.

LABORATORY: Antenatal Screening

Standard Antibody Test

HIV antibody is detectable in at least 95% of patients within 3 months after acquiring the infection. Negative results cannot exclude a possible recent infection.

All pregnant women should be tested for HIV infection as part of the routine panel of prenatal tests at the first visit, unless the patient declines the test (i.e., opt-out screening).

A second HIV test near term and before 36 weeks is recommended for the subpopulations of persons at higher risk, typically defined on the basis of behavioral, clinical, or demographic characteristics.

For high risk women (women with sexually transmitted infections or who are users of illegal drugs by injection), consider a repeat test near term. Reactive screening tests must be confirmed by a supplemental test.

Rapid Tests:

Women who have not received antenatal care and were not offered HIV counseling and testing are one of the groups at high risk for transmitting HIV to their infants. Rapid testing should be done during labor for all women with unknown HIV status.

Immediate initiation of appropriate antiretroviral prophylaxis should be recommended to women on the basis of a reactive rapid test result, without waiting for the result of a confirmatory test.

The benefits of neonatal antiretroviral prophylaxis are best realized when it is initiated <12 hours after birth. Rapid testing must be done as soon as possible in labor and delivery or postpartum in order to initiate neonatal antiretroviral (ARV) prophylaxis in a timely manner.

Evaluation of an Infected Pregnant Woman:

If the mother is infected with HIV, initial and repeated evaluation every trimester should include:
- an assessment of HIV 1 disease status
  - CD4+ count (degree of immunodeficiency)

- level of plasma RNA (risk for disease progression)
- and decisions on
  - antiretroviral treatment, ZDV chemoprophylaxis regimen and,
  - whether prophylaxis against *Pneumocystis carinii* pneumonia should be initiated.

(An HIV specialist should be involved in the follow-up and treatment decisions).

LABORATORY: Neonatal Tests

Because maternal HIV antibody passes through the placenta, antibody tests for HIV are expected to be positive in the sera of both infected and uninfected infants for a period between 6 and 18 months after birth. Therefore, a positive HIV antibody test in an infant does not necessarily indicate the existence of HIV infection.

The preferred diagnostic test is HIV DNA polymerase chain reaction (PCR) assay, which detects HIV DNA within the peripheral blood mononuclear cells.
The blood specimen must be a neonatal, not a cord blood sample. If the HIV DNA PCR assay results (obtained at birth, at 4–7 weeks of age, and at 8–16 weeks of age) are negative, then HIV infection has been reasonably excluded. In the near future, new methods will allow us to detect the infection at earlier ages. If the infection is confirmed, an HIV specialist should be consulted for advice regarding antiretroviral therapy.

PREVENTION AND TREATMENT: Maternal HIV Management and Perinatal Prevention of Vertical Transmission

ANTIRETROVIRAL TREATMENT

Treatment with antiretroviral therapy can be expected to reduce viral replication in the mother, leading to a decrease in viral load in the infant and/or prophylaxis during and after exposure to the virus. Efavirenz is contraindicated during pregnancy due to concerns about teratogenicity. The following table summarizes four possible clinical scenarios considering prior antiretroviral therapy at the time of first maternal assessment.

For women diagnosed with HIV during pregnancy and eligible for treatment with antiretroviral drugs, such treatment should be initiated as soon as possible. The initiation of treatment may be delayed until after the first trimester. However, when the woman is severely ill, the benefits of treatment outweigh any potential risk to the fetus.

TREATMENT SCENARIOS AT FIRST CONTACT WITH A PREGNANT WOMEN OR INFANT IN CONSIDERATION OF PRIOR ANTIRETROVIRAL THERAPY			
Prior Antiretroviral Therapy			Treatment recommendations
Mother	At first antenatal visit	No prior therapy.	o Consider delaying initiation of therapy until after 10-12 weeks gestation. o Initiate three-part ZDV chemoprophylaxis regimen after the **first trimester** o Add other antiretroviral if HIV RNA is over 1,000 copies/mL
		Receiving therapy	o Continue therapy o If possible, ZDV should be a **component after the first trimester.**
	In labor	No prior therapy	o Intrapartum intravenous ZDV followed by six weeks of ZDV for the newborn (Standard recommendation) o Maternal post partum assessment with CD4+ count and HIV RNA copy number and appropriate therapy
Neonate	At birth	No antenatal or intrapartum therapy	o ZDV should be initiated as soon as possible after delivery - preferably within 6-12 hours of birth and continued for six weeks o Maternal post partum assessment with CD4+ count and HIV RNA copy number and appropriate therapy

Zidovudine Perinatal Prophylaxis:

According to the Pediatric AIDS Clinical Trials Group (PACTG) a three-part regimen of Zidovudine (ZDV) is recommended unless the woman is intolerant of ZDV. (See the following table)

PEDIATRIC AIDS CLINICAL TRIALS GROUP (PACTG) PROTOCOL 076 THREE-PART REGIMEN OF ZIDOVUDINE (ZDV)	
Maternal antepartum	Oral ZDV Initiated at 14-34 weeks gestation and continued throughout the pregnancy. • 100 mg five times or 300 mg twice daily
Maternal intrapartum	Intravenous ZDV • Initial dose, 2 mg/kg body weight in 1 hour. • Followed by a continuous infusion of 1 mg/kg /hour until delivery.
Neonatal at birth	Oral ZDV Beginning at 8-12 hours after birth and continuing for six weeks • More than 35 weeks: 2 mg/kg /dose, every 6 hours • 30 to 35 weeks 2mg/kg/dose, every 12 hours advancing to every 8 hours at 2 weeks • Less than 30 weeks 2mg/kg/dose, every 12 hours advancing to every 8 hours at 4 weeks (If oral route is not tolerated, give intravenous dose 1.5 mg/Kg at same time intervals) (Monitor hemoglobin before and after treatment, anemia has been the primary adverse effect)

Route of delivery:

Scheduled cesarean delivery:
- Perinatal HIV transmission is significantly reduced by scheduled cesarean delivery in:
  - women who did not receive antenatal antiretroviral therapy
  - women receiving only ZDV for prophylaxis of perinatal transmission
  - when plasma HIV RNA levels determined during pregnancy are higher than 1,000 copies/mL.

Not scheduled cesarean delivery:
- It is not clear that cesarean delivery after rupture or onset of labor provides a benefit in reducing transmission.

PERINATAL OBSTETRIC SCENARIOS AT TERM IN HIV INFECTED WOMEN	
Conditions deciding perinatal care.	Treatment recommendation
· Diagnosed at 36 weeks of gestation · Not receiving antiretroviral therapy	Mother: · Start on antiretroviral therapy · Schedule cesarean section at 38 weeks of gestation · ZDV infusion beginning three hours before surgery Infant: · Six weeks of ZDV therapy after birth.
· Receiving highly active combination antiretroviral therapy, · High HIV RNA levels (over 1,000 copies/ mL at 36 weeks of gestation).	Mother: · Current antiretroviral regimen should be continued. (Efavirenz is contraindicated) · Scheduled cesarean at 38 weeks' gestation · ZDV infusion beginning three hours before surgery Infant: · Six weeks of ZDV therapy after birth.
· Receiving highly active combination antiretroviral therapy · Undetectable HIV RNA level at 36 weeks of gestation.	Mother: · Current antiretroviral regimen should be continued (Efavirenz is contraindicated) · The woman should be informed that her risk of perinatal transmission of HIV is low, probably 2% or less, even with vaginal delivery. Infant: · Six weeks of ZDV therapy after birth.
· Scheduled for elective cesarean section · Seen in early labor or shortly after rupture of membranes	Mother: · Intravenous ZDV should be started immediately. · Vaginal delivery is an option if it is not delayed. Infant: · Six weeks of ZDV therapy after birth.

Rubella

Rubella virus is the first virus documented to be a teratogen, causing severe congenital anomalies.

It is a contagious disease transmitted via the respiratory system secretions from the nose or throat. Viremia occurs 5-7 days after the contact period during which the virus may be transmitted from the mother to the fetus by hematogenous transplacental spread.

BURDEN OF DISEASE

In the pre-vaccine era, rubella epidemics usually occurred approximately every 6-9 years. With the successful introduction of rubella vaccine in many countries, the incidence of rubella and congenital rubella syndrome (CRS) decreased significantly. In some countries (e.g. Finland, United States, Cuba), rubella and CRS have been eliminated.

With the success of vaccination programs in some industrial countries, the proportion of women of childbearing age susceptible to rubella has been reduced to between 2-3%.

However, in developing countries that have not introduced rubella vaccine into their national programmes, the proportion of susceptible women may vary from < 10% to >25%. For countries that only vaccinate females, males may remain susceptible and are a potential source of infection for rubella-susceptible pregnant women.

Rubella is preventable by vaccination. Vaccine induced immunity is presumed to be lifelong. Available data on duration of immunity documents protection lasting for more than 16 years.

Rubella continues to be endemic in many parts of the world. Susceptible pregnant women may be exposed and become infected with rubella. When rubella infection occurs during pregnancy, especially during the first trimester, serious consequences can result such as miscarriages, fetal deaths/stillbirths, and an infant born with constellation of severe birth defects known as (CRS).

Rarely a woman who is immune to rubella is re-infected. If the woman is reinfected the risk of congenital rubella defects is rare, considerably less than the risk of primary rubella during the same period of pregnancy.

In women who were vaccinated and did not know that they were pregnant, there have been no cases of CRS identified among their infants. Therefore, termination of pregnancy is not indicated in such cases.

DIAGNOSIS: Maternal

CLINICAL FEATURES

Adults may experience a 1-5 day prodrome of low grade fever, malaise, mild coryza, and conjunctivitis. Swollen, tender lymph nodes, usually in the back of the neck and behind the ears, are characteristic and precedes the rush by 5-10 days. Arthralgia or arthritis may occur in up to 70% of adult women with rubella. The rash is a maculopapular and usually starts on the face and then spreads down the body, lasting about 3 days and is occasionally itchy.
Children usually develop few or no constitutional symptoms.

LABORATORY

Acute rubella infection can be confirmed by the presence of serum rubella IgM, a significant rise in IgG antibody titer in acute and convalescent serum specimens, positive rubella virus culture, or detection of the rubella virus by RT-PCR. ELISA is a commonly used test.
Pregnant women with a rubella-like illness or exposed to a person with rubella-like illness should be tested for both IgG and IgM. Recent infection may be confirmed by either rising IgG antibody titer or rubella specific IgM. If the initial Rubella specific IgM is negative and drawn before 5 days after rash onset, a repeat serology is needed.
Rubella specific IgM may persist 6 weeks after onset of rash.

DIAGNOSIS: Neonatal

CONGENITAL RUBELLA SYNDROME (CRS)

CRS is characterized by:

Cardiac defects
Cataracts
Hearing impairment
Developmental delay
Hepatosplenomegaly
"blueberry muffin" skin lesions
Pneumonitis
Myocarditis
Disturbances of bone growth
Microcephaly
IUGR and Thrombocytopenic purpura

The incidence of these congenital anomalies depends on the gestational age at which infection occurred:
- 90% during the first 8 weeks,
- 50% from 9-12 weeks and
- 15% between 13 and 16 weeks.

Risk of fetal damage falls steeply after the first trimester and is negligible after 16 weeks.

CONGENITAL DEFECTS ACCORDING TO THE TIME OF INFECTION		
Gestational period	Congenital anomaly	Risk (%)
First trimester	Ocular , Cardiovascular, CNS, Hearing Impairment, IUGR	38- 100
Second trimester	Hearing impairment, retinopathy, microcephaly, mental retardation	4- 60
Third trimester	IUGR	0-18

The affected infants continue shedding virus for 6-12 months after birth.

PREVENTION

Since 1969, rubella vaccine has been available. A single dose of rubella-containing vaccine (e.g: MMR vaccine), is 95% effective, in producing life-long immunity. Studies have documented that seropositivity rates remain high at least 16 years following vaccination.

Susceptible women should be aware of the risk of contact during pregnancy with children or adults with rubella-like or any flu like illness.

Screening for rubella susceptibility by history of vaccination or by serology is recommended for all women of childbearing age at their first preconception encounter to reduce incidence of Congenital Rubella Syndrome.

All susceptible non pregnant women of childbearing age should be offered vaccination.

Pregnant women who remain seronegative to rubella should receive rubella vaccine post partum, as part of MR or MMR, unless two previous attempts at immunization have failed. There are no known adverse consequences to vaccination postpartum while breastfeeding.

Malaria

Plasmodia species are the parasites responsible for Malaria.

The parasite is transmitted by *Anopheles* mosquitoes. Warm climates with high humidity and abundant rain create favorable conditions for the growth and development of mosquitoes.

Only 4 of the over 100 species of plasmodia are infectious to humans. The majority of cases and almost all deaths are caused by *Plasmodium falciparum*. In contrast, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae* cause less severe disease.

Over 90% of all malaria cases occur in Africa, and most of these are caused by *P. falciparum*. *P. falciparum* also predominates in Haiti and the Dominican Republic. In Mexico, and in Central and South America, both *P. falciparum* and *P. vivax* are endemic.

Malaria infection during pregnancy results in a wide range of adverse consequences for the pregnant woman, the developing fetus and the newborn infant. HIV infection can further reduce immunity to malaria during pregnancy.

BURDEN OF DISEASE

Malaria is a preventable infection that carries with it an enormous global burden. The global estimate is that there are up to 500 million people affected.

Malaria continues to be endemic with low transmission rates in 21 countries of the Latin American and the Caribbean (LAC) region. Malaria can be found in all age groups and epidemics also occur. The Pan American Health Organization is calling for an increase in activities to eradicate malaria from the continent.

In 2004 there was a reported incidence of more than 800,000 infected persons and 150 deaths caused by malaria in the LAC region. These figures represent a 23% reduction in the incidence and 55% decrease in mortality. Efforts to develop a malaria vaccine have not yet been successful.

Areas of low (unstable) transmission

Low or unstable malaria transmission predominates in the LAC countries. Women of reproductive age have relatively little acquired immunity to malaria, and therefore all pregnant women are at similar risk for malaria infection. Consequences of infection include life threatening maternal illness, central nervous system complications and severe anemia.

Sequestration of the parasites in the placenta increases the rate of adverse reproductive outcomes, including stillbirths, spontaneous abortions and low birth weight (LBW). Symptomatic malaria infection during the third trimester contributes to premature delivery, (hence LBW), or congenital infection, resulting in an increased risk of neonatal death. Other consequences during pregnancy commonly associated with *P. falciparum* infection include hypoglycaemia, hyperpyrexia, severe hemolytic anemia and pulmonary edema. Severe malaria may also present immediately following delivery. Postpartum bacterial infection is a common complication in these cases. Maternal mortality is approximately 50%, which is higher than in non-pregnant adults.

In contrast to the LAC region, stable transmission predominates in Africa south of the Sahara. This region is the focus of significant efforts to reduce the burden of malaria. The 4 main components of the global Roll Back Malaria program include:
- improving access to effective treatment,
- preventing malaria during pregnancy,
- reducing mosquito–human contact by widespread use of insecticide-treated bed nets and
- ensuring timely and appropriate action during malaria epidemics.

DIAGNOSIS

A high degree of epidemiological and clinical suspicion and rapid diagnosis are essential to optimize outcome.

LABORATORY

Thick and thin peripheral blood smears, stained with Giemsa stain, remain the "gold standard" for routine clinical diagnosis.
Malaria smears permit both species identification and quantification of parasites.

Malaria should not be excluded until at least 3 negative blood smears have been obtained within 48 hours from the patient.

Parasitological diagnosis should be promoted in pregnant women in endemic areas in order to improve the differential diagnosis of fever and to reduce unnecessary use of antimalarials in pregnancy.

Rapid malaria tests, which require minimal skill to perform and interpret, have been developed to overcome the problems of malaria smears. The rapid antigen detection tests (RDTs) detect parasite proteins in finger-prick blood samples, but sensitivity falls dramatically with low level parasitemia.

Serologic tests have no role in the diagnosis of acute malaria.

TREATMENT: Maternal

Immunity is reduced in pregnancy. Pregnant women with symptomatic acute malaria are a high-risk group and must receive effective antimalarials. In the treatment of severe malaria in pregnancy, saving the life of the mother is the primary objective.

There is insufficient information on the safety and efficacy of most antimalarials in pregnancy, particularly for exposure in the first trimester. For this reason, treatment recommendations for pregnant women differ from those for non-pregnant adults.

Quinine is the most effective, and can be used in all trimesters of pregnancy, including the first trimester. Hypoglycemia/hyperglycemia should be expected. Blood glucose should be checked frequently.

Recommendations on the treatment during the first trimester of uncomplicated falciparum malaria in pregnancy:

Quinine + Clindamycin (if available and affordable) to be given for 7 days.

There is increasing experience with artesunate derivatives in the second and third trimesters, though data on safety are still insufficient.

Recent evidence shows that in non-pregnant adults with severe malaria in areas of low transmission, artesunate was superior to quinine, reducing mortality by 35% compared to treatment with quinine. Artesunate may be the preferred option in the second and third trimesters, however, as noted above, data on safety during pregnancy are still insufficient. Given the disadvantages of quinine, (i.e. the long course of treatment, and the increased risk of hypoglycemia in the second and third trimesters), it is considered a suitable alternative for these trimesters.

In the first trimester, the risk of hypoglycemia/hyperglycemia associated with quinine is lower, and the uncertainties over the safety of the artemisinin/artesunate derivatives are greater.

Recommendations on the treatment during 2nd and 3rd trimesters of uncomplicated falciparum malaria in pregnancy:

Artemisinin-based Combination Therapy (ACT) is known to be effective where it has been used.

PREVENTION

Insecticide-Treated Nets:
Insecticide-treated bed nets (ITNs) offer effective protection against malaria. The benefits are not limited to individual users but may be conferred to communities as a whole. The use of ITNs in malaria-endemic regions significantly reduces the incidence of malaria and childhood mortality, as well as the incidence of malaria and associated anemia during pregnancy.

<u>Effective Case Management of Malaria Illness and Anemia</u>:

Effective case management of malaria illness for all pregnant women in malarious areas must be assured. All pregnant women should also be screened for anemia. Iron supplementation should be given to pregnant women as part of routine antenatal care. Anemia should be suspected in all pregnant women diagnosed with malaria.

<u>Intermittent Preventive Treatment (IPT) </u>(Only in areas of stable perennial or seasonal transmission)

All pregnant women living in areas of stable malaria transmission should receive at least two doses of IPT. The doses of IPT can be given during each scheduled visit after the 20th week of pregnancy. This will insure that a high proportion of women receive at least two doses.

Currently, the most effective drug for IPT is sulfadoxine-pyrimethamine (SP) because of its safety for use during the 2nd and 3rd trimesters of pregnancy, efficacy in reproductive-age women and feasibility for use in programs, as it can be delivered as a single-dose treatment under observation by the health worker.
In areas of low or unstable malaria transmission, the role of IPT, in addition to prompt and effective case management and ITNs, remains to be established.

Hepatitis B

Hepatitis B virus (HBV) is a blood borne virus that is transmitted by percutaneous or mucosal exposure to blood or body fluids. For infants and children, the primary source of HBV infection is transmission from infected mothers. After birth the risk of infection continues by transmission from infected household contacts. The major sources of transmission among adults are sexual contacts and percutaneous exposures to blood.

Transmission from mother to the neonate most often occurs at the time of delivery. In utero infection occurs rarely. Breast milk is known to contain the virus, but breastfeeding has not been shown to increase an infant's risk of acquiring HBV. Children who are not infected at birth remain at risk from long-term interpersonal contact with their infected mothers. Up to 40% of infants who are born to HBsAg-positive mothers and are not infected during delivery may become infected by age 4 years.

Hepatitis B vaccination is the most effective measure to prevent HBV infection and its consequences. Before universal infant immunization, up to 2/3 of the chronic HBV infections occurred in children born to (HBsAg)-negative mothers. A substantial proportion of these chronic infections would not have been prevented by a selective program of identification and immunization of only infants born to HBsAg-positive mothers. All babies should be protected.

BURDEN OF DISEASE

Infections in infants and young children are typically asymptomatic, and only half of newly acquired HBV infections among older children and adults are symptomatic. Approximately 1% of reported cases result in acute liver failure and immediate death. Risk for chronic infection is inversely related to age at infection. Approximately 90% of newly infected infants develop chronic infection, compared with 2%-6% of newly infected adults. The majority of infants who become positive after maternal exposure are clinically healthy, remain anicteric, show no signs of acute clinical hepatitis and remain HBsAg positive for an extended period They may have persistently elevated values on liver function tests and 5% have histopathologic changes on liver biopsy.

Globally, approximately 70% of persons with chronic infection are believed to have acquired the infection as a result of perinatal or early childhood transmission. Death from cirrhosis or hepatocellular carcinoma (HCC) occurs in about 25% of persons who acquire chronic HBV infection during childhood and 15% of persons who acquire infections at older ages.

In Latin America, the Amazonian region has the highest prevalence of chronic HBV infection (over 8% HBsAg-positive). Brazil, Venezuela, Surinam, Ecuador, Guatemala and Nicaragua have intermediate HBsAg prevalence (2 - 8 %) and the Southern Cone and Andean countries have low HBsAg prevalence (less than 2%).

DIAGNOSIS

SEROLOGIC SCREENING

Diagnosis of acute or chronic HBV infection requires serologic testing.

The antigens and antibodies associated with HBV infection include HBsAg and antibody to HBsAg (anti-HBs), Hepatitis B core antigen (HBcAg) and antibody to HBcAg (anti-HBc). At least one serologic marker is present during the different phases of HBV infection. (See Table)

HBsAg is present in both acute and chronic infection. The presence of a confirmed HBsAg result is indicative of ongoing HBV infection. All HBsAg-positive persons should be considered infectious.

All pregnant women should be tested for HBsAg, when laboratory resources are available.
In situations where pregnant women are screened for HBsAg, infants born to HBsAg positive women should be prophylaxed with Hepatitis B immunoglobulin (HBIG) and immunized with hepatitis B vaccine per recommended schedule.
Six months following the completion of the prophylaxis and the immunization series, a negative anti hepatitis B core antibody test indicates that the prophylaxis was effective.

TABLE: Serologic markers in different stages of Hepatitis B virus (HBV) infection:

Stages of HBV infection	HBsAg*	Anti-HBs+	Anti-HBc§	Total¶IgM
Late incubation period	+	-	-	+/-
Acute	+	-	+	+
Chronic	+	- (+ rarely)	+	-
Recent (<6 months) window period	-	+/-	+	+
Distant (>6 months); resolved.	-	+	+	-
Immunized	-	+	-	-

*Hepatitis B surface antigen. †Antibodies to hepatitis B surface antigen. §Antibodies to hepatitis B core antigen ¶The total anti-HBc assay detects both IgM and IgG antibody.

TREATMENT

No specific therapy is available for persons with acute Hepatitis B.

Treatment of chronic Hepatitis B with antiviral drugs can achieve sustained suppression of HBV replication and remission of liver disease in some people.

Therapy for HBV infection has not been systematically studied in children. The decision to treat a child who is usually asymptomatic is still evolving and requires expert management.

PREVENTION

The primary strategy to prevent HBV infection is universal vaccination of infants beginning at birth with subsequent hepatitis B vaccine doses integrated into the routine childhood immunization schedule.

➤ Universal Vaccination of Infants.
  o Birth dose of hepatitis B vaccine. In resource-poor areas, ensuring the universal administration of a birth dose of hepatitis B vaccine may be the single most important intervention
  o Subsequent Hepatitis B vaccine doses integrated into the routine childhood immunization schedule.
  o Birth dose administration without maternal screening is a WHO-recommended approach.

Other hepatitis B immunization strat
egies that can be considered depending on the epidemiology of HBV infection and the availability of resources include:
  ➤ Routine screening of all pregnant women for Hepatitis B surface antigen (HBsAg)
  ➤ Post exposure immunoprophylaxis of infants born to HBsAg-positive women (HBIG plus vaccine)
  ➤ Vaccination of children and adolescents who were not previously vaccinated
  ➤ Vaccination of unvaccinated and seronegative adults, including pregnant women, if they are at increased risk of infection.

PRE-PREGNANCY AND ANTENATAL PROPHYLAXIS

Avoidance of high-risk behavior (unprotected intercourse with multiple partners, use of unclean injection needles).
  • Avoidance of blood contact in occupations that involve contact with human blood.
  • Vaccination of pregnant women who are identified as being at risk for HBV infection during pregnancy (e.g., having more than one sex partner during the previous 6 months, been evaluated or treated for an STD, recent or current injection-drug use, or having had an HBsAg-positive sex partner)
  • If the woman's HBsAg test result is positive, she should receive appropriate medical management, and any household, sexual, or needle-sharing contacts should be identified and vaccinated.

PREVENTION OF PERINATAL TRANSMISSION

Passive-active post exposure (post partum) prophylaxis (PEP) with hepatitis B vaccine and HBIG administered 12--24 hours after birth, followed by completion of a 3-dose vaccine series, has been demonstrated to be over 70% effective in

preventing acute and chronic HBV infection in infants born to women who are HBsAg-positive   .

<u>Hepatitis B immune globulin (HBIG)</u>

HBIG administration as late as 1 week after birth provides passively acquired anti-HBs and temporary protection, 3--6 months, to infants born to HBsAg-positive mothers and infants born to mothers with unknown HBsAg status.

The recommended dose of HBIG is 0.5 mL at birth. Before the use of simultaneous administration of the vaccine, HBIG alone decreased infection rates from over 90% to less than 25%.

Neonatal Birth Dose: in the first 12 hours

- <u>Infants born to mothers who are HBsAg positive</u>

Hepatitis B vaccine and HBIG should be administered to the neonate, at different sites, 12–24 hours after birth. Completion of a 3-dose vaccine series (2nd month, and 6th month) is 85%–95% effective in preventing acute and chronic HBV infection in infants born to women who are positive for both HBsAg and HBeAg.

A birth dose of Hepatitis (B)N1 vaccine, even without HBIG, serves as a "safety net" to prevent perinatal infection.

Infants born to HBsAg-positive mothers should be followed and tested for anti-HBsAg at 9 to 15 months of age. A negative anti-HBc antibody test confirms effective prophylaxis.

- <u>Infants born to mothers whose HBsAg status is unknown</u>

Hepatitis B vaccine should be given to the neonate in the first 12 hours of birth.

The maternal HBsAg status should be tested, and if she is HBsAg positive, the infant should receive HBIG as soon as possible, no later than 7 days. Both interventions prevent 70%–95% of perinatal HBV infections.
Infants of HBsAg-positive mothers who receive adequate prophylaxis should be allowed to breastfeed immediately after birth.

Neonatal Discharge Dose should be administered to:

- Infants born from HBs Ag-negative mothers:
- Full-term infants over 2,000 g should receive Hepatitis B vaccine at hospital discharge.
- Preterm infants weighing under 2,000 g have a decreased response to Hepatitis B vaccine administered before age 1 month.
  They should receive Hepatitis B vaccine 1 month after birth or at hospital discharge. If they received the birth dose, this should not count for the complete immunization scheme.

Vaccination is recommended for all adults who fulfill any of the following conditions:
- o If they have been exposed to HBsAg-positive blood through needle stick injury, wounds, mucous membrane or damaged skin.
- o Users of intravenous illegal drugs
- o Sexual partners of patients with a acute or chronic HBV infections
- o If moving to work in hyperendemic areas
- o If they are family members of patients with a acute or chronic HBV infections
- o If they have high-risk sexual behavior (e.g. have had more than one sex partner in the previous 6 months)
- o If they are health care workers with the potential for exposure to infected blood

Administration of the vaccine to adults:
- o <u>Hepatitis B vaccine</u>: 1.0 ml i.m. The dose is repeated at 1 and 6 months. No boosters are necessary after the initial series of successful vaccinations.
- o About 10% of the vaccinated persons do not obtain sufficient immunity. If the risk of exposure to the virus is high and long-lasting, (e.g. health care workers with ongoing exposures to blood, sex partners of HBsAg – positive persons), the presence of immunity should be confirmed serologically about 2 months after the third dose. If there is no antibody response, counseling should be offered to decrease exposure risk.

Chagas Disease
(South American Trypanosomiasis)

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi*. It is a zoonotic disease that can be transmitted to humans when infected feces from blood-sucking triatomine insects are inoculated into the bite wound or into mucous membranes such as the conjunctivae.

Chagas is also transmitted through blood transfusions, organ transplantation, by transplacental transmission from an infected mother to her infant, or in laboratory accidents. It may also be acquired by ingestion of contaminated foods or liquids. Transmission of *T. cruzi* has been documented in cases in which the small triatomine insects, hidden in sugarcane or some fruits such as "açai", are accidentally mixed into juices.   Infection is chronic with parasitemia lasting many years.

BURDEN OF DISEASE

Chronic Chagas disease is a major health problem in 18 Latin American countries, mostly in poor, rural areas of Central and South America, where approximately 10-11 million persons are affected and 90 million others are at risk of being infected by the parasite.

Congenital transmission occurs in many countries where Chagas disease is endemic, affecting 1% to 15% of babies born to infected mothers. Reduction of the infection in blood donors and pregnant women has contributed to, and is a consequence of, vector control.

Measures to control the vector and prevent transfusion transmission are adequate in many regions, however, in some areas, measures remain inadequate. To be effective, all blood donors must be screened by serologic tests and if found positive should be excluded from the donor pool. Regions such as the Amazon and Central American rainforests, are new potential areas for endemic disease.

DIAGNOSIS

CLINICAL FEATURES

Chagas disease has an acute phase and a chronic phase. The acute phase is usually asymptomatic or causes only non-specific symptoms, but can present with manifestations that include fever, anorexia, lymphadenopathy, mild hepatosplenomegaly, and myocarditis. When transmitted by the triatomine bug, a local lesion (chagoma, palpebral edema) can appear at the site of inoculation. The acute phase resolves over a period of 2 to 3 months into an asymptomatic chronic phase. During the acute phase, *T. cruzi* can be detected by direct examination of fresh blood or blood-culture.

Infection is lifelong, but most chronic patients will remain asymptomatic for decades or for the rest of their lives. However, 20% to 30% of infected individuals will develop cardiomyopathy, (the most serious manifestation), or pathologies of the digestive tract such as megaesophagus and megacolon.

Congenital infection occurs in up to 15% of pregnancies in infected women. Congenital infection may be asymptomatic or symptomatic in the newborn; when symptomatic it can cause fever, petechiae, enlarged liver, enlarged spleen and/or anemia, and microcephaly.

LABORATORY
Maternal Screening

A serologic test should be done at the first antenatal visit or at delivery.

In the chronic phase, parasites are difficult or impossible to detect in peripheral blood. The diagnosis depends on detecting IgG antibodies by at least 2 distinct assays, such as ELISA and indirect fluorescent antibody (IFA) or indirect hemagglutination assay.

Neonatal Diagnosis

In endemic areas neonatal systematic screening should be considered for all newborns. Neonatal selective screening should be done for all children of chagasic mothers (detected before or during pregnancy), and for neonates born to women with no antenatal screening.

Detection of *T. cruzi* is the diagnostic procedure in congenital Chagas disease.

- Microscopic examination: a) of fresh anticoagulated blood, or its buffy coat, for motile parasites; and b) of thin and thick blood smears stained with Giemsa, for visualization of parasites.

- Isolation of the agent by: a) inoculation into mice; and b) culture in specialized media (e.g. NNN, LIT).

The standard method for diagnosis of congenital Chagas disease in Latin America is the microhematocrit examination of fresh heparinized blood. If conducted by an experienced laboratory, the sensitivity for microhematocrit examination of several capillary tubes from one cord blood or peripheral blood specimen is approximately 60%. Therefore, for optimal sensitivity, repeated specimens should be examined over the first 2-3 months of life.

All infants of chagasic mothers, not previously diagnosed with *T.cruzi* infection, should be serologically screened at 9-12 months of age using two conventional IgG assays such as ELISA and IFA.

TREATMENT

Treatment with Nifurtimox or Benznidazol has very high efficacy during the acute phase of the infection but appears to have lower efficacy in the chronic phase. Treatment should be started in the acute phase, congenital infection, or early chronic disease.

Infant dose: Benznidazol 5 mg/Kg/daily for 2 months.
                Nifurtimox 10mg/Kg/daily for 2 months.
The simplest and most pragmatic approach for congenital Chagas disease is early antenatal or neonatal diagnosis. Treatment of infected newborn infants in the acute phase has optimal results.

PREVENTION

- Vector control (most triatomine bugs are vulnerable to control with residual household insecticide application). This is the basic and most successful strategy for preventing endemic Chagas disease.
- Control of transmission through blood transfusions.
- Maternal screening during pregnancy, allowing early detection and treatment of congenital infection in the acute phase, achieving infant cure rates close to 100%.

Group B Streptococcus

Group B *Streptococcus* (GBS), also known as *S agalactiae,* is an encapsulated gram-positive bacterium that is a common inhabitant of the human gastrointestinal and genitourinary tracts.

Although most women infected with GBS have no symptoms associated with genital tract colonization, GBS can cause urinary tract infection as well as serious maternal and fetal complications. During pregnancy or the postpartum period, women can contract amnionitis, endometritis or sepsis caused by GBS.

Intrauterine infection of the fetus results from ascending spread of GBS from the vagina or during passage through the birth canal, of a colonized woman who is typically asymptomatic. However, transmission of GBS from mother to child primarily occurs after the onset of labor or membrane rupture. Infants can become ill after passage through a colonized birth canal, via aspiration of contaminated amniotic fluid, via ascending infection through ruptured membranes, or very rarely when GBS is transmitted via the maternal bloodstream.

GBS disease in infants is usually divided into early onset (within the first 7 days after birth) and late onset (between 7 – 89 days after birth). Early-onset disease results from vertical transmission. In contrast, the mode of transmission of late-onset disease is not well understood, and effective prevention measures have not been identified. Both early and late-onset GBS can leave survivors with permanent impairments such as seizure disorders or difficulties with speech, hearing, or vision. Case-fatality rate is likely to vary from country to country, depending partly on the availability of neonatal intensive care.

BURDEN OF DISEASE

Approximately 10% to 30% of pregnant women are colonized (transient, chronic, or intermittently) with GBS in the vagina or rectum. Virtually 100% of women will be colonized at some point in their lifetime. Urinary tract infections caused by GBS complicate 2%–4% of pregnancies. During pregnancy or the postpartum period, women can contract amnionitis, endometritis or sepsis caused by GBS. Maternal intrapartum GBS colonization is a common (up to 30% of women) and major risk factor for early-onset disease in infants.

In the absence of prevention, approximately 50% of infants born to colonized mothers become colonized with GBS during delivery, and about 2% of those go on to develop invasive GBS disease. In the United States, pre-prevention incidence of early-onset GBS disease was approximately 2 cases /1000 live births. Globally, incidence has been reported from 0.6-2.5 cases / 1000 live births, in the absence of widespread prevention efforts.

Prophylaxis has reduced the number of affected infants. Intrapartum antimicrobial chemoprophylaxis with Penicillin G or Ampicilin reduces infant colonization and early-onset disease, if administered more than 4 hours prior to delivery.

GBS late-onset disease occurs at an incidence of 0.3 to 0.5 cases / 1000 live births. Maternal vertical transmission may be responsible for only 50% of this late onset disease.

DIAGNOSIS - neonatal

Early-onset disease causes severe invasive neonatal sepsis within the first 7 days after birth, presenting as respiratory distress, apnea, poor perfusion and shock. Late-onset disease presents primarily with sepsis, meningitis or pneumonia, and more rarely with arthritis or cellulitis.

TREATMENT

MANAGEMENT OF MATERNAL COLONIZATION AND RISK OF VERTICAL TRANSMISSION

The most desirable approach to eliminate neonatal GBS infection would be the use of GBS vaccines before, or early in pregnancy. However, until effective GBS vaccines become available, intrapartum antibiotic prophylaxis (IAP) is the mainstay for prevention of GBS infection in neonates. There are two methods of determining when IAP is indicated, a clinical risk-based approach and a maternal screening-based approach.

Identification of Candidates for Intrapartum Chemo Prophylaxis

Maternal Clinical Risk-based approach:

The following are indications of administration of intrapartum antibiotics:
- gestational age <37 completed weeks,
- duration of membrane rupture > 18 hours,
- intrapartum temperature >38ºC
- Previous delivery of an infant with invasive GBS disease
- GBS bacteriuria during current pregnancy

Antenatal Maternal Screening

GBS colonization early in pregnancy is not predictive of neonatal sepsis, but colonization late in gestation is associated with early onset neonatal disease. Therefore, culture-based screening of both lower vagina and rectum for GBS between weeks 35 and 37 of gestation is recommended. Screening should be preformed regardless of whether a Caesarian section is planned, in case early labor occurs. The vaginal and rectal swabs should be cultured in a single selective enrichment broth to maximize the isolation of GBS and avoid overgrowth of other organisms.

Intrapartum antibiotic prophylaxis is indicated for mothers who screen positive. Under this approach, intrapartum antibiotics are also recommended for women with GBS bacteruria at any time during the current pregnancy and/or a previous infant with GBS disease. GBS identified in clean-catch urine specimens is also associated with a higher risk for early-onset GBS disease and is included among indications for intrapartum antibiotic prophylaxis.

Screening may be more effective than the risk-based approach because near 20% of all deliveries of mothers colonized with GBS have no obstetric risk factors. Also, women with a known GBS positive status are more likely to receive intrapartum antibiotics than women with obstetric risk factors that have not been screened.

If laboratory screening is not available, procedures should account for clinical criteria.

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS

Penicillin G (5 million units IV followed by 2.5 million units every 4 hours until delivery) is the recommended first-line agent for intrapartum antibiotic prophylaxis. Optimal timing of prophylaxis is at least 4 hours prior to delivery. Ampicilin is also an acceptable first-line therapy.

For women who are allergic to penicillin but not at high risk for anaphylaxis, Cefazolin (2 g IV initially, then 1 g IV every 8 hours until delivery) is an alternative. For women at high risk for anaphylaxis, options include Clindamycin (900 mg IV every 8 hours until delivery), Erythromycin (500 mg IV every 6 hours until delivery), or, for GBS resistant to Clindamycin or erythromycin, Vancomycin (1 g IV every 12 hours until delivery.)

Intrapartum antibiotic prophylaxis is not routinely recommended for women undergoing planned cesarean deliveries in the absence of labor or amniotic membrane rupture, regardless of whether the woman is colonized with GBS.

Management of Infants Exposed to Intrapartum Antibiotics:

Neonates who have been exposed to intrapartum antibiotic prophylaxis for GBS should be managed according to the risk of GBS sepsis. Early empiric treatment with Ampicilin and Gentamicin is recommended when there is high clinical presumption of disease. Maternal GBS screening results, antenatal risk factors, degree of suspicion of chorioamnionitis, preterm birth and the infant's clinical status

should be considered. In addition to close clinical observation, laboratory testing such as complete blood count, C - reactive protein, cerebrospinal fluid analysis and blood culture may help to determine whether therapy is indicated.

In low risk cases in asymptomatic neonates, blood culture may be postponed until symptoms appear. Blood culture should be obtained at this moment because the greatest organism yield occurs when the infant is symptomatic rather than when the infant appears well. The high negative predictive value of normal serial CBC and C-reactive protein helps to reduce the excessive use of blood cultures in asymptomatic neonates.

The following table provides guidelines to select management according to risk of sepsis.

NEONATAL RISK	NEONATAL AND MATERNAL CONDITIONS	ASSESSMENT AND TREATMENT
HIGH	• Symptomatic neonates (respiratory distress, apnea, poor perfusion and shock)	• Full diagnostic evaluation (Complete blood count (CBC), lumbar puncture and blood culture) • and treatment with intravenous ampicillin and gentamicin
	• Infants born to mothers who have suspected or proven choriomanionitis at any gestational age, • regardless of whether the mother received antibiotics (penicillin, or ampicillin) 4 or more hours prior to delivery	• Full diagnostic evaluation (Complete blood count (CBC), lumbar puncture and blood culture) and • treatment with intravenous ampicillin and gentamicin
MEDIUM	• Preterm infants less than 35 weeks	• Complete blood count (CBC) and blood culture and • clinical observation for 48 hours
LOW	• Healthy near term or term infants (at least 35 weeks) gestation whose mothers were • colonized with GBS or had • fever, or • premature rupture of membranes of at least 18 hours, or • history of a previous infant who had GBS disease • and did not receive appropriate antibiotics (penicillin, ampicillin,) 4 or more hours prior to delivery.	• Complete blood count (CBC), blood culture and clinical and • clinical observation for 48 hours Or • Clinical observation for 48 hours and • two serial CBC and C-reactive protein in the first 24hs. • If becomes symptomatic: blood culture and empiric intravenous antibiotics
MINIMUN	• Healthy near-term or term (at least 35 weeks) asymptomatic infants whose mothers received adequate IAP	• Clinical observation for at least 24 to 48 hours.

Varicela-Zoster virus (VZV)

Varicella (also known as Chickenpox), is a highly contagious disease of childhood caused by Varicella Zoster Virus (VZV). After an average incubation period of 14 to 16 days (range 10-20 days) following primary infection, lesions develop in three or more successive waves for 3 to 7 days. Lesions progress through macular, papular, vesicular, and pustular stages. Eventually scabs form, which usually heal without scarring unless secondary bacterial infection occurs. Skin lesions appear on trunk, face, scalp and extremities, with greatest concentration on trunk. Virus is spread by the airborne route from the skin lesions and oropharynx of infected individuals.

After primary infection, VZV can establish latent infection in dorsal-root ganglia and subsequent reactivations manifested as (herpes) zoster may occur. Zoster presents as a painful cutaneous eruption affecting one or more dermatomes.

When primary infection with VZV occurs during pregnancy, the consequences for both the mother and the fetus must be considered. Chickenpox in pregnancy may be associated with severe maternal disease, fetal death and rarely, (during the first two trimesters), with congenital varicella syndrome. Maternal infection around term carries the risk of serious neonatal disease.

BURDEN OF DISEASE

In temperate climates, near 90% of child-bearing age women are immune to VZV, with a history of infection or vaccine administration providing reliable evidence of immunity. This proportion may be somewhat lower in tropical countries or in countries without a long term established varicella vaccination program.

Varicella may be more severe in pregnant women than in other adults, in particular the risk of varicella pneumonia, which usually develops within one week of the rash onset. The risk to the mother may be greatest towards term (i.e., third trimester).

| Clinical manifestation of congenital varicella infection following chickenpox in pregnancy ||
Stage of maternal infection	Sequelae
First and second trimester	Congenital varicella syndrome
Second and third trimester	Zoster in infancy or childhood
Perinatal	Disseminated neonatal varicella

Varicella occurrence within the first 20 weeks gestation may lead to fetal loss (2.6%); and after 20th week to intrauterine death (0.7%). Varicella in pregnant women may also lead to asymptomatic fetal infection. The proportion of infants with asymptomatic intrauterine infection may rise from 5-10% in the first and second trimester, to 25% near 36 weeks gestation.

CONGENITAL VARICELLA SYNDROME

Congenital varicella syndrome can occur among infants born to mothers infected during the first half of pregnancy (i.e., within the first 20 weeks of gestation); and may be manifested by:

Low birthweight	Cortical atrophy
Cutaneous scarring	Chorioretinitis
Limb hypoplasia	Cerebral ventriculomegaly
Microcephaly	Cataracts and other eye anomalies

The risk of congenital varicella syndrome is highest (2%) when maternal infection occurs during 13-20 weeks gestation. Zoster develops during infancy or early childhood in 0.8% of those who were exposed to VZV during 13-24 weeks gestation and 1.7% of infants who were exposed during 25-36 weeks gestation.

NEONATAL VARICELLA

The onset of varicella in pregnant women in the period from 5 days before birth to 2 days after birth can result in severe neonatal varicella in 17-30% of the newborn infants. These infants are exposed to VZV without sufficient maternal antibodies which lessen the severity of disease. The risk of death among neonates has been estimated to be 31% among those whose mothers had rash onset 0-4 days before delivery. The interval between the mother's rash and the infant's rash is usually 12-13 days, but may be as brief as 2 days, suggesting transplacental infection.

DIAGNOSIS

MATERNAL VARICELLA

Clinical diagnosis of varicella in pregnancy can be confirmed by rapid tests such as PCR or Direct Fluorescent Assay with monoclonal antibody on vesicle scraping or swab of lesion base. Viral culture is cumbersome due to rapid inactivation of virus. Seroconversion or a significant increase in serum varicella IgG antibody from acute and convalescent samples by any standard serologic assay can confirm the diagnosis retrospectively. IgM tests are not reliable for routine confirmation of acute infection. Positive result indicates recent/current infection.

INFANT VARICELLA

The criteria for the diagnosis of congenital varicella syndrome include: a history of maternal symptomatic varicella infection during pregnancy, presence of cicatricial skin lesions, or immunological evidence of in utero VZV infection. The latter should include either the demonstration of specific IgM antibody after birth, and persisting IgG antibodies after 7 months of age, in the absence of postnatal varicella. Common late clinical manifestations of congenital varicella infection include herpes zoster in the first year of life.

TREATMENT

Oral acyclovir treatment should be used if varicella infection occurs during pregnancy due to the risk of severe outcomes and should be initiated within 24 hours of rash onset. If varicella pneumonia occurs, or other signs of dissemination, hospitalization and early treatment with intravenous acyclovir is essential and life-saving at any stage of pregnancy.

Newborn infants with stigmata of congenital varicella do not require treatment. Newborn infants with severe or rapidly progressing varicella should be treated with intravenous acyclovir at a dose of 1500 mg/m^2 in three divided daily doses.

PREVENTION

MATERNAL VACCINATION

Varicella vaccination offered to susceptible women of child-bearing age can reduce the incidence of congenital and neonatal varicella and should be administered before conception.

Varicella vaccine should not be administered during pregnancy.

MATERNAL EXPOSURE

Pregnant women should avoid exposure to persons with varicella and / or Zoster infection.

IgG antibody to VZV should be tested if the mother had close contact with VZV and no previous history of the disease. If seronegative, they should be offered Zoster Immunoglobin (ZIG), preferably administered within 48 hours of contact (maximum, 96 hours).

INFANT EXPOSURE

Passive immunization of the neonate with ZIG is recommended if the mother develops infection from 5 days before to 2 days after birth. Zoster immune globulin (ZIG) should be administered as soon as possible after birth as there will have been no passive transfer of maternal antibodies to the fetus.

ZIG should be given to hospitalized, exposed premature infants born at ≥28 weeks of gestation who are exposed during the neonatal period and whose mother lacks a reliable history of chickenpox or serologic evidence of protection. ZIG should also be given to preterm infants (<28 wks of gestation or <1,000 g birth weight) regardless of maternal history of varicella or antibody status.

Infants may develop late clinical manifestations of congenital varicella infection, including rashes of herpes zoster, which are usually benign.

Genital herpes is a chronic, life-long, viral disease that can have recurrent genital or oral lesions or can be entirely asymptomatic. It is caused by herpes simplex virus types 1 or 2 (HSV-1 or HSV-2).

Genital Herpes Simplex Virus (HSV)

The two types of HSV have different disease characteristics:

HSV-2

The majority of cases of genital herpes are caused by HSV-2 and nearly all are sexually acquired. Recurrent lesions are common.
Most infections are asymptomatic. When symptoms occur, the classical finding is painful vesiculo-ulcerative lesions.
Symptoms during primary infection, if they occur, typically begin with pain, tenderness, or itching in the genital area and also include fever and headache. Vesicles often appear on the area around the vagina and on the cervix in women and on the penis in men, and may also appear on the thighs and buttocks. Vesicles soon erupt to form painful sores that typically last 1 to 3 weeks. Other symptoms may include: pain or a burning sensation during urination; a clear mucus-like discharge from the vagina or urethra; and tender, swollen glands in the groin area.

The virus remains dormant in nearby nerves and can be reactivated later in life. The symptoms of recurrent genital herpes are similar to those of first outbreak, but are generally less severe and of shorter duration. Most HSV-2 infected persons, even those with mild or unrecognized infections, shed virus intermittently in the genital tract during asymptomatic periods. Both clinical and subclinical reactivations can occur for many years, but usually decrease with time.

HSV-1

Herpes simplex virus type 1 is very common, in fact it is more common than HSV-2 infection

The majority of persons with HSV-1 antibody have oral HSV infection (cold sores around the mouth) acquired during childhood, which might also be asymptomatic.
This form of the virus is usually transmitted from person to person by saliva or direct contact, such as kissing or sharing eating utensils. The virus can lie dormant without causing any symptoms for some time, but can reactivate at a later time, leading to a tingling and numbness around the mouth, then a blister that breaks and forms a crust.

However, sexual transmission of HSV-1 is becoming increasingly common, especially through oral-genital contact.

In some populations, up to 50% of first-episode cases of genital herpes may be caused by HSV-1 Recurrences and subclinical viral shedding are much less frequent for HSV-1 than HSV-2, therefore HSV-2 is a much more common cause of recurrent genital herpes.

BURDEN OF DISEASE

Primary HSV infection in the first trimester is associated with an increased risk of early miscarriage, but there is no recognized pattern of fetal abnormality in pregnancies that continue.

The risk for transmission to the neonate from an infected mother is high (30%–50%) among women who acquire genital herpes near the time of delivery. The risk is low (<1%) among women who acquire genital HSV during the first half of pregnancy or who have histories of recurrent genital herpes lesions at term.

Among mothers of infants who acquire neonatal herpes, the majority lack histories of clinically evident genital herpes.

The vast majority of neonatal herpes cases occur as a result of contact with HSV in the maternal birth canal during delivery. Much less commonly, neonatal herpes results from transplacental or ascending infection, or from postnatal acquisition of HSV-1 from close contact with persons with oral herpes.
Although rare, neonatal HSV infection may lead to severe disseminated neonatal HSV syndrome and/or encephalitis, which are often either fatal or produces long term sequelae.

DIAGNOSIS

CLINICAL

Neonatal herpes can be classified as:
1) Disseminated disease: involving multiple organs including lung, liver, adrenal glands, skin, eye, and/or brain
2) Central nervous system (CNS) disease, with or without skin involvement
3) Skin, eyes, and/or mouth (SEM) disease

Newborns with disseminated disease commonly present around day 10-12 of life with viral sepsis, including hepatic failure, respiratory collapse, and disseminated intravascular coagulation (DIC). CNS involvement, hepatitis, and pneumonitis are common. About 20% will not have the characteristic vesicular rash.

Newborns with CNS disease commonly present around day 16-19 of life with seizures, lethargy, irritability, tremors, poor feeding, and temperature instability. Only 60-70% will have skin vesicles, making the initial presentation often indistinguishable from other bacterial and viral infections in neonates.

Newborns with SEM disease commonly present around day 7-12 of life with more limited infection, mostly with vesicular lesions apparent on physical examination.

LABORATORY

Indirect Serologic Tests:

Serologic test for HSV-1 and HSV-2, including IgM tests, have limited value in the diagnosis of neonatal herpes.

Type-specific serologic tests might be useful in certain circumstances for diagnosing genital herpes in a pregnant woman or her sexual partner to guide antenatal counseling and management.

Direct Viral Tests:

Viral isolation using culture remains the definitive diagnostic method for detecting HSV, especially from skin and mucous membrane sites. Direct immunofluorescent staining of scraped cells from vesicular lesions with monoclonal antibodies provide a rapid and inexpensive diagnostic alternative.

PCR assays for HSV DNA are more sensitive than viral culture and are the preferred method for detecting HSV in the cerebrospinal fluid (CSF).

TREATMENT

MATERNAL GENITAL HERPES

Suppressive antiviral therapy is effective in preventing symptomatic recurrent episodes and subclinical shedding, and episodic therapy may shorten the duration of recurrent episodes. Suppressive acyclovir treatment late in pregnancy has been shown to reduce the frequency of cesarean sections among women who have recurrent genital herpes by diminishing the frequency of recurrences at term.

Antiviral therapy is recommended for women with a symptomatic first episode of genital herpes during pregnancy. Acyclovir may be administered orally to pregnant women with first episode or recurrent genital herpes, but should be administered IV to pregnant women with severe HSV infection.

NEONATAL HERPES

The recommended regimen for infants with known or suspected neonatal herpes is systemic Acyclovir 20 mg/kg body weight IV every 8 hours for 21 days for disseminated and CNS disease, or for 14 days for disease limited to skin, eye, and mucous membranes.

PREVENTION

MATERNAL COUNSELING

Pregnant women and women of childbearing age who have genital herpes should inform their pregnancy care provider, as well as the health care provider caring for their newborn infant.

Women should be aware of:

- potential for recurrent episodes
- asymptomatic viral shedding
- sexual transmission when lesions are present
- risk of receptive oral sex with a partner with oral herpes or intercourse during the third trimester with men who have genital herpes

NEONATAL PREVENTION

- Maternal antenatal management is the best prevention for vertical transmission.

- Type of delivery
  C- section is not routinely recommended in women with recurrent genital herpes, as the risk of vertical transmission is small.
  C- section should be considered only if active genital lesions that cannot be covered are present at the onset of labor.
  C- section does not completely eliminate the risk for HSV transmission to the infant

- Scalp electrodes to monitor fetal distress must not be used in women with active lesions or a history of recent recurrent infection.

Gonococcal infection

Neisseria gonorrhoeae is a bacterium that infects humans only, and is transmitted by intimate sexual contact.

Newborns infants can also acquire gonococcal infections in their eyes if they are delivered vaginally while their mothers have a cervical gonococcal infection.

BURDEN OF DISEASE

Gonococcal infections are common, particularly among younger sexually active adults. Improved diagnosis and treatment has reduced the burden in regions with adequate health care services. Therefore, the burden of disease is generally higher in populations with poor access to health care.

DIAGNOSIS

GONOCOCCAL GENITAL INFECTION

Frequently, there are no overt signs of gonococcal genital infection. Such infections can "silently" damage woman's reproductive organs, causing pelvic inflammatory disease and infertility.

Gonococcal cervicitis is frequently asymptomatic, but some women complain of an abnormal vaginal discharge or report previous inter-menstrual vaginal bleeding.

Two major diagnostic signs are:

1. Purulent or mucopurulent endocervical exudate visible in the endocervical canal, and

2. Sustained endocervical bleeding easily induced by gentle passage of a cotton swab through the cervical os.

Microscopic examination of Gram-stained smears of exudates from eyes, vagina, cervical secretions, male urethra and skin lesions may be useful in the initial evaluation. Specimens for *N. gonorrhea* culture from cervix, vagina, urethra and rectum must be inoculated immediately because the bacteria is extremely sensitive to drying and temperature changes.

Bacterial culture in the laboratory with selected media is better than a Gram stain of endocervical fluid, which allows identification of only 50% of women with gonococcal cervical infection.

The most sensitive and specific test available for *N. gonorrhoeae* is nucleic acid amplification tests (NAAT) performed on either urethral (males), endocervical swab, or urine samples.

The majority of persistent cases of cervicitis after repeated courses of antibiotic treatment are not caused by relapse or reinfection with *N. gonorrhoeae*.

TREATMENT: Maternal

Gonococcal infections are usually cured within 1 to 2 weeks after appropriate antibiotic treatment begins.

Recommended Regime:

Ceftriaxone 125 mg IM in a single dose.

Pregnant women should not be treated with Quinolones or Tetracyclines.

Dual therapy for gonococcal and chlamydial infections is indicated if the prevalence of this infection is high (>5%) in the patient population.

PREVENTION: Maternal

Is based on two main behaviors:

- Having a sexual partner that has been tested and is known to be uninfected, or
- Correct use of latex male condoms.

DIAGNOSIS: Neonatal – Gonococcal Ophtalmia Neonatorium

The most severe manifestations of *N. gonorrhoeae* infection in newborns are ophthalmia neonatorum and sepsis, which include arthritis and meningitis. Less severe manifestations include rhinitis, vaginitis, and urethritis.

CLINICAL FEATURES

Gonococcal eye infections usually begin 2 to 5 days after birth causing severe conjunctival purulent secretions and palpebral edema. It may also result in perforation of the globe of the eye and blindness.

LABORATORY

Gonococcal ophthalmia is strongly suspected when intracellular gram-negative diplococci are identified in conjunctival exudate, justifying presumptive treatment.

Appropriate cultures for *N. gonorrhoeae* should be obtained and tested for antibiotic susceptibility before a definitive diagnosis is made. It can also be diagnosed with the use of rapid antigen or DNA tests.

TREATMENT

Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 125 mg
Infants who have gonococcal ophthalmia should be hospitalized and evaluated for signs of disseminated infection (e.g., sepsis, arthritis, and meningitis).

PREVENTION

Antenatal diagnosis and treatment of gonococcal and chlamydial infections in pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease.

PROPHYLAXIS

Ocular prophylaxis is warranted because it can prevent sight-threatening gonococcal ophthalmia and because it is safe, easy to administer, and inexpensive.

Silver Nitrate 1% solution recently prepared
(Credé Method)
Or
Erythromycin (0.5%) ophthalmic ointment in a single application
Or
Tetracycline ophthalmic ointment (1%) in a single application

Instill into both eyes of every neonate as soon as possible after delivery regardless of whether they are delivered vaginally or by cesarean section.
Bacitracin is not effective

Chlamydia Trachomatis

Chlamydia trachomatis, is a bacterium that can live and reproduce inside human cells without actually damaging them, and can cause prolonged infections with minimal or no symptoms. 90% of infected women and about 80% of infected men have no symptoms.

Of all children born to mothers with genital chlamydial infections, almost 50% develop conjunctivitis within 1 to 2 weeks after birth and close to 20% develop pneumonia between 1 and 3 months of age.

Chlamydial genital infection is transmitted sexually during oral, vaginal, or anal sex, *C. trachomatis* can "silently" damage woman's reproductive organs causing pelvic inflammatory disease, ectopic pregnancy, chronic pelvic pain and infertility.

BURDEN OF DISEASE

Chlamydial genital infections are common worldwide. Recognition and treatment has improved over the past two decades, particularly in areas with adequate health care infrastructure. Chlamydiae are becoming increasingly recognized as the etiologic agents of a number of sexually transmitted infections, and responsible also for eye and lung infections in neonates whose mothers are infected.

DIAGNOSIS

CLINICAL FEATURES

Chlamydial cervicitis frequently is asymptomatic, but some women complain of an abnormal vaginal discharge and may report previous intermenstrual vaginal bleeding

In the majority of cases of cervicitis, no organism is isolated. When an etiologic organism is isolated in the setting of cervicitis, it is typically C. trachomatis or N. Gonorrhea. However, trichomoniasis and genital herpes (especially primary HSV-2 infection) can also cause cervicitis. The majority of persistent cases of cervicitis after repeated courses of antibiotics are not caused by relapse or reinfection with C. trachomatis.

Lymphogranuloma venereum:

A common clinical manifestation of chlamydial infection in pregnant women is a tender inguinal and/or femoral lymphadenopathy that is typically unilateral. A self-limited genital ulcer or papule sometimes occurs at the site of inoculation.

LABORATORY

C. trachomatis urogenital infection in women can be diagnosed by testing urine or swab specimens collected from the endocervix or vagina. Identification of *C. trachomatis* can be achieved by tissue culture, direct immunofluorescence, enzyme immuno assay (EIA), nucleic acid hybridization tests, and nucleic acid amplification tests (NAATs) on endocervical secretions, urine or conjunctival swab specimens. The most sensitive and specific test available for *C. trachomatis* is nucleic acid amplification tests (NAAT)

In some countries with high prevalence of *C. trachomatis*, (>5%), annual screening of all sexually active women aged <26 years may be recommended. Routine antenatal screening may be cost-effective only in those population groups with relatively high incidence and provided effective treatment is prescribed before delivery.

TREATMENT

Presumptive treatment of cervicitis or lymphogranuloma venereum with antibiotics for *C. trachomatis* should be done if

- age <26 years,
- new or multiple sex partners,
- unprotected sex
- NAAT unavailable

Treating pregnant women cures infection, relieves symptoms and usually prevents transmission of *C. trachomatis* to infants during birth. If untreated, the infection can last for weeks or months.

Recommended Regimens for treatment of genital *C. trachomatis*

Azithromycin
1 g orally in a single dose
Or
Amoxicillin
500 mg orally three times a day for 7 days

Alternative Regimens

Erythromycin base 500 mg orally four times a day for 7 days
Or
Erythromycin base 250 mg orally four times a day for 14 days
Or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days
Or
Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days

The frequent gastrointestinal side effects associated with erythromycin might discourage patient compliance with the alternative regimens

- Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity.
- Doxycycline, ofloxacin, and levofloxacin are also contraindicated in pregnant women

Dual therapy for gonococcal and chlamydial infections is indicated if the prevalence of this infection is high (>5%) in the patient population
Pregnant women should not be treated with quinolones or tetracyclines
Management of Sex Partners
Simultaneous treatment of sex partners is essential for decreasing the risk of reinfection

PREVENTION

Prevention Is based on any of two behaviors:
- having a sexual partner that has been tested and is known to be uninfected or
- correct use of latex male condoms

DIAGNOSIS: Neonatal chlamydial infections

C. trachomatis infection of the neonate results from perinatal exposure to the mother's infected cervix.

Neonatal ocular prophylaxis with silver nitrate solution or antibiotic ointments does not prevent perinatal transmission of *C. trachomatis* from mother to infant. However, ocular prophylaxis with those agents does prevent chlamydial ophthalmia and, therefore, should be continued.

CLINICAL FEATURES: Ophthalmic

Conjunctivitis, single or bilateral, 5–12 days after birth

LABORATORY

Sensitive and specific methods used to diagnose chlamydial ophthalmia in the neonate include both tissue culture and non culture tests (e.g., DFA tests, EIA, and NAAT)

Ocular exudate from infants being evaluated for chlamydial conjunctivitis also should be tested for *N. gonorrhoeae*.

A specific diagnosis of *C. trachomatis* infection confirms the need for treatment not only for the neonate but also for the mother and her sex partner.

Recommended Regimen
Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days
A short course of azithromycin, 20 mg/kg/day orally, 1 dose daily for 3 days, may be effective.

<u>CLINICAL FEATURES: Pneumonia</u>

- o at ages 1–3 months
- o afebrile
- o subacute
- o a repetitive staccato cough with tachypnea,
- o **hyperinflation and**
- o **bilateral diffuse infiltrates on a chest radiograph.**
- o Peripheral eosinophilia (>400 cells/mm3) occurs frequent

<u>LABORATORY</u>

Tissue culture of nasopharyngeal secretions is the definitive standard for chlamydial pneumonia.

The results of tests for chlamydial infection assist in the management of an infant's illness and determine the need for treating the mother and her sex partner(s).

Because of the delay in obtaining test results for chlamydia, the decision to provide treatment for *C. trachomatis* pneumonia must frequently be based on clinical and **radiological findings**

Recommended Regimen

Erythromycin base or **ethylsuccinate**; 50 mg/kg/day orally divided into 4 doses daily for 14 days

PREVENTION

Antenatal diagnosis and treatment of gonococcal and chlamydial infections in pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease.

Ocular prophylaxis is warranted because it can also prevent sight-threatening gonococcal ophthalmia and because it is safe, easy to administer, and inexpensive.

Recommended Prophylactic Regimens

Erythromycin (0.5%) ophthalmic ointment in a single application
Or
Tetracycline (1%) ophthalmic ointment in a single application
Instill into both eyes of every neonate as soon as possible after delivery regardless of whether they are delivered vaginally or by cesarean section.

Bacitracin is not effective.

Toxoplasmosis

TOXOPLASMOSIS

Toxoplasma gondii is an intracellular protozoan parasite that infects up to a third of the world's population.

Infection is acquired primarily by ingestion or handling of undercooked or raw meat (especially pork, lamb and wild game meat) containing tissue cysts or by ingestion of food or water contaminated with oocysts excreted in the faeces of infected cats.

Primary infection is usually asymptomatic or has mild, non-specific, symptoms. Some individuals develop cervical lymphadenopathy or ocular disease.

BURDEN OF DISEASE

Seroprevalence of *T gondii* infection rises with age and does not vary greatly between sexes. In general, incidence of the infection varies with the population group and geographic location. In countries such as El Salvador, up to 75% of the population may be seropositive by the fourth decade of life. In various countries, however, the prevalence of *T gondii* antibodies has been steadily falling over the past few decades.

The prevalence of congenital toxoplasmosis ranges in the region from 1 to 20 per 10,000 live births.

Frequency of transmission to the fetus, and the severity of disease in the fetus **and subsequently in the infant are inversely related.** Early maternal infection (first or second trimester) carries a low likelihood of fetal infection (9% to 27%), but if it occurs, may result in severe congenital toxoplasmosis, and can result in death of the fetus in utero and spontaneous abortion.
By contrast, late maternal infection (third trimester) is more likely to lead to infection of the fetus (up to 60% in the third trimester), but fetal damage is less likely and, if it occurs, less severe.

Frequency of subclinical congenital toxoplasmosis is as high as 85%, and infants can later develop chorioretinitis, especially if untreated. 10% of infected children have retinochoroiditis during infancy, rising to 16-18% by 4 years old. Bilateral visual impairment is rare, affecting up to 4% of children with retinochoroiditis. However, in many countries more cases of ocular disease occur in children that acquired toxoplasmosis after birth than in those who were infected congenitally. In adulthood, a majority of ocular toxoplasmosis would be due to postnatally acquired infection.

	Infection acquired during		
Outcome in offspring	First trimester	Second trimester	Third trimester
Congenital toxoplasmosis	9·0%	27·0%	59·0%
Subclinical (at birth)	22·2%	74·4%	89·8%
Clinically apparent	77·8%	15·6%	10·2%
Perinatal death or stillbirth	5·0%	2·0%	0%

DIAGNOSIS: Congenital Toxoplasmosis

CLINICAL FEATURES

Neonatal clinical manifestations of congenital toxoplasmosis vary widely and include:

Hydrocephalus	Blindness
Microcephaly	Epilepsy
Diffuse intracranial calcifications	Psychomotor or mental retardation
Chorioretinitis	Petechiae due to thrombocytopenia
Strabismus	Anemia.

The classic triad of chorioretinitis, hydrocephalus, and cerebral calcifications is rare.

LABORATORY

Diagnosis of toxoplasmosis can be established by a direct test such as PCR or by indirect means such as serological tests.

IgG and IgG avidity tests.

The IgG test is recommended for pre-pregnancy and antenatal screening but not for neonatal screening.

If the IgG test is negative, there is a risk of acquiring infection with *T. gondii* Therefore, women should follow strict preventive measures. A negative test result indicates the need for an antenatal IgG follow up test.

If IgG is positive in a pre-pregnancy screening the woman is protected.

If IgG is positive in a first antenatal visit, an IgG avidity test should be done. Recent (less than 4 months) infection is ruled out by a positive test result.

Definitive diagnosis of acute maternal infection requires demonstration of a rise in titers in serial specimens (either conversion from a negative to a positive titer or a significant rise from a low to a higher titer). However, this change is rarely seen in countries where systematic screening during pregnancy is not available.

Toxoplasma IgM and IgA for Neonates

IgM may be used for neonatal screening. In some studies, screening sensitivity was increased when used with IgA measurement.

IgM for Women

Screening women by measuring IgM is not recommended for asymptomatic women during pre-pregnancy and antenatal visits because it is an unreliable marker of recent infection. False positive toxoplasma IgM results are not uncommon and low levels of IgM may persist for many months or years after primary infection.

Direct detection

PCR examination of the amniotic fluid enables early prenatal diagnosis of congenital toxoplasmosis while avoiding more invasive procedures on the fetus.
In any neonate suspected by either clinical signs or positive IgM to have congenital disease, PCR examination of peripheral blood, cerebrospinal fluid, and urine should be considered.

	Antibody class	Screening test	Pregnancy	Newborns
Indirect detection/ serology	IgG	+	+ (identification of women at risk and those protected) - (women at risk of acquiring infection)	+ (maternal antibodies may persist until 12 months of age)
	IgG avidity	-	+ (high avidity results rule out infection in recent 3–4 months)	-
	IgM	May be used in neonatal screening	+ (IgM antibodies persist for prolonged times, negative IgM rules out infection in pregnant women during the first two trimesters)	+ (ISAGA more sensitive than EIA; differentiation of maternal and fetal IgG by western blot)
	IgA	May be used in neonatal screening	+ (IgA antibodies may persist for prolonged times)	+ (more sensitive compared to IgM tests)
Direct detection	PCR	-	+ (amniotic fluid)	+ (blood, urine)

TREATMENT

There is no solid evidence that antenatal or neonatal screening and treatment effect fetal infection rates and long-term outcomes.

Although there are no established definitive treatments, clinical recommendations include treatment with Spiramycin (for the first and early second trimester) or Pyrimethamine/ sulfadiazine (for late second and third trimester) for women with suspected or confirmed acute *T gondii* infection. Treatment is based on the plausibility of its reducing sequelae of the disease in the newborn.

In acute maternal infection, if amniotic fluid PCR is negative, pregnant women should receive Spiramycin prophylaxis until the 17th week, then undergo amniocentesis for diagnosis of fetal infection with PCR.

In case of a positive PCR result or very highly probable infection of the fetus (i.e., acquisition of maternal infection in late second or third trimesters), the recommended treatment is with Pyrimethamine/ sulfadiazine, which may be alternated with Spiramycin.

Folinic acid is added to pyrimethamine treatment to reduce bone-marrow suppression; careful monitoring for haematotoxicity is mandatory.
In most countries, treatment of the fetus is followed by treatment of the newborn throughout the first year of life. The following table summarizes the standard treatments.

	Drug	Dosage	Duration
Acute toxoplasmosis in pregnant women	Spiramycin	3 g qd in three doses	Until term or until fetal infection is documented
Documented fetal infection (after 18 weeks of gestation).	Pyrimethamine	Loading dose: 100 mg qd in two doses for 2 days, then 50 mg qd	Until term
	plus Sulfadiazine	Loading dose: 75 mg/kg qd in two doses (max 4 g qd) for 2 days, then 100 mg/kg qd in two doses (max 4 g qd)	Until term
	plus Leucovorin (folinic acid)	5–20 mg qd	During and for 1 week after Pyrimethamine treatment
Congenital toxoplasma infection in the infant	Pyrimethamine	Loading dose 2 mg/kg qd for 2 days, then 1 mg/kg qd for 2–6 months, continue same dose three times a week	1 year
	plus Sulfadiazine	100 mg/kg qd in two doses	1 year
	plus Leucovorin	10 mg three times a week	During and for 1 week after Pyrimethamine treatment
	Corticosteroids (prednisone)	1 mg/kg qd in two doses and symptoms	Until resolution of signs and symptoms

PREVENTION

There is no effective vaccine against human *T gondii* infection.

A lack of reliable data on the incidence of congenital infection, difficulties with sensitivity and specificity of serological tests, and findings that suggest Spiramycin may have limited effectiveness, are all factors that make it difficult to assess the cost-effectiveness of antenatal screening in public health programs.

Several countries have opted for neonatal screening.

Primary prevention of toxoplasmosis for children and adults including pregnant women is based on education. Pregnant women need to be made aware of the risk congenital toxoplasmosis associated with consumption of undercooked meat and contact with soil contaminated with oocysts.

Recommendations are:

- Avoid consumption of undercooked meat.
- Cook all meat until it is no longer pink and the juices run clear.
- Wash hands thoroughly after handling raw meat.
- Thoroughly wash all utensils that are in contact with undercooked meat.
- Wash all uncooked vegetables thoroughly.
- Wear gloves when gardening or working in soil.
- Wash your hands thoroughly before you eat and after handling raw meat, soil, or sand.
- If possible, keep cats indoors throughout pregnancy and do not feed cats uncooked meat.
- Avoid handling cat litter, or use gloves while handling litter and wash hands immediately after.
- Change cat litter daily
- Cover children's sandboxes when not in use (cats like to use them as litter boxes)
- Avoid untreated (unfiltered) water.

Cytomegalovirus

Human CMV is a DNA virus of the herpes virus group that infects cells and causes them to become enlarged. CMV spreads through human contact, by the infected person's saliva, blood, urine, semen, cervical/vaginal secretions or breast milk. CMV survives on fomites, including diapers, toys, and the hands.

Prenatal infection is by transplacental route. Perinatal infection may occur intrapartum by exposure to CMV in the genital tract. Postnatally, the infant can become infected with CMV by contact with infected body fluids such as human milk or saliva or by receipt of blood transfusions. Of the many possible CMV transmission routes, the most common are via breast milk, exposure to young children, or through sexual contact. Transmission is especially frequent in day care settings. Among infants of CMV-positive breastfeeding women, CMV seroconversion is relatively common, with transmission risk increasing as months of breastfeeding increases.

Following primary (i.e., first-time) infection, children usually shed CMV much longer than adults, excreting CMV in urine and saliva for 6 to 42 months (mean, 18 months). In urban settings, approximately 15% to 70% of seronegative children in group day care acquire CMV infection over the course of a year.

Seronegative women with children who are shedding CMV in saliva or urine acquire CMV infections at rates 5 to 25 times higher than other women, and at least half of these women will become infected within 1 year after their child becomes infected. Women particularly at risk of seroconversion in pregnancy include those who cared for preschool children in the year before delivery and those who became sexually active within the 2 years prior to delivery.

BURDEN OF DISEASE

As a rule, prevalence of CMV antibody in the general population ranges from 40% to 60% in developed countries and 70% to 100% in developing countries, although there are exceptions.

In persons with healthy immune systems, CMV seldom causes symptoms and usually has no long term consequences. In individuals with impaired immunity, such as HIV-positive persons, organ transplant recipients, infants born prematurely, or fetuses, CMV can cause severe disease. Most people infected with CMV have not been clinically diagnosed.

CMV seroconversion (primary infection) during pregnancy occurs in 1-4% of women and reactivation or reinfection during pregnancy leads to transmission to the fetus in <1% of cases. There is approximately a one in three chance of transmitting the CMV to the fetus.

CMV is the most common congenital viral infection, it may affect up to 1% of all live births. Most congenitally infected newborns appear normal, but approximately 10% will be symptomatic at birth. Infection in symptomatic infants ranges from mild, to severe disseminated life-threatening disease, resulting in up to 20% perinatal mortality. More than 80% of symptomatic newborns will eventually exhibit sequelae such as mental retardation, cerebral palsy, seizures, visual defects, and sensorineural hearing loss. Of the approximately 90% of infants who are asymptomatic at birth, 8% to 15% will later develop complications, principally hearing loss.

Although disabilities and other severe symptoms were originally thought to occur exclusively among the children of women who experience primary CMV maternal infection during pregnancy, subsequent studies have shown that serious outcomes occasionally occur as the result of maternal reactivation or reinfection.
CMV is the most common cause of congenital infection and non-hereditary deafness, and the second most common cause of motor retardation after Down's syndrome. No single cause of birth defects and developmental disabilities currently provides greater opportunity for improved outcomes in more children than congenital CMV.

DIAGNOSIS

CLINICAL FEATURES

Pregnant Women

CMV infection may be asymptomatic or may cause mild hepatitis, atypical lymphocytosis and non-specific symptoms during the self-limited primary infection. The virus then becomes latent, but is reactivated periodically without clinical signs or symptoms during episodes of mild immunosuppression caused by intercurrent infection, pregnancy or stress. It is often difficult to establish the timing of an infection during pregnancy because it is usually subclinical. It is also well known that seropositive individuals can be reinfected with different strains of CMV.

Infants:

Clinical symptoms in the infant can be non-specific and may include:
> Intrauterine growth retardation (IUGR)
> Jaundice
> Hepatosplenomegaly
> Petechiae or Purpura
> Chorioretinitis
> Sensorineural hearing loss
> Periventricular calcifications
> Encephalitis
> Microcephaly

LABORATORY

Maternal and Prenatal Diagnosis

Maternal serum IgM may indicate a recent primary infection, viral reactivation, persistent low level IgM after past primary infection, or recent reinfection with a different CMV strain. However, serum IgM is not always sensitive as a test for primary CMV infection (IgM may be absent despite IgG seroconversion). Likewise, IgM is not highly specific, since the mother may have false positive results because of cross-reactions.

IgG avidity tests can help establish the occurrence of a primary CMV infection, since low avidity is suggestive of recent infection. However, intermediate avidity values are difficult to interpret.

Among women with proven primary infection, amniocentesis is the best way to diagnose fetal infection. Detection of CMV DNA by PCR after 22 weeks gestation is highly indicative of fetal infection. Testing prior to 22 weeks is much less reliable.

Ultrasound screening searching for IUGR, intracranial calcification, ventriculomegaly or hydrops, has low sensitivity and specificity for fetal disease.

Screening during pregnancy is not currently recommended because IgM is an unreliable marker of recent infection, IgG avidity assays are not always commercially available, and amniocentesis carries some risk. In addition even if fetal infections were confirmed, the majority of fetuses would not be affected in the long-term. Furthermore, treatments remain controversial and of questionable safety and efficacy. However, there is some preliminary evidence that CMV hyperimmune globulin may prevent some mother-to-fetus transmission or fetal disease.

Newborn Diagnosis

Congenital CMV infection is diagnosed best via the shell-vial culture assay, a technique in which a monoclonal antibody is used to detect early CMV antigen to identify the virus in urine or saliva before 3 weeks of age.

PCR detection of CMV DNA in urine or saliva has been shown to reliably diagnose congenital CMV. Most evidence to date suggests that newborn dried blood spots may also be used for the diagnosis of congenital CMV.

Congenital CMV cannot be diagnosed in specimens collected after 3 weeks of age because the newborn could have acquired CMV postnatally.

TREATMENT

Patients with proven symptomatic congenital CMV infection can be treated with intravenous ganciclovir at a dose of 6 mg/kg every 12 hours for a total of 42 days. The most significant toxicity is neutropenia. Treatment is likely to preserve normal hearing or in some cases even improve hearing loss. Ganciclovir toxicity is common and can be severe such as neutropenia requiring discontinuation of treatment or dose reduction. The focus of care for healthy adults is on education to prevent transmission of the infection. For immunocompromised individuals who develop CMV retinitis, treatment with Ganciclovir, IV and PO, and foscarnet IV are approved for use. Combined with anti-CMV immune globulin, these drugs may also be helpful in treating immunocompromised individuals who develop pneumonitis.

PREVENTION

Because vaccines against CMV are not yet available, it is important to modify maternal behaviors to significantly reduce the risk that CMV-seronegative pregnant women will acquire CMV from their young children.

- Careful hand washing with soap and running water for 15 to 20 seconds after

  - o   exposure to a child's bodily fluids and diaper changes
  - o   handling dirty laundry
  - o   touching the child's toys and other objects
  - o   bathing the child

- Wearing protective gloves

  - o   during diaper changes
  - o   when handling the child's dirty laundry

- Avoiding intimate contact with the child such as

  - o   kissing on the mouth or cheek (kiss them on the head or give them a hug)
  - o   sleeping together
  - o   sharing towels and washcloths
  - o   sharing or tasting foods or drinks with the same utensils (spoons, forks glasses)

- For pregnant women working in a day care center,

  - o   avoid working with children younger than 2 ½ years of age.

Mothers who have CMV infection should not stop breastfeeding.

Parvovirus B19

Parvovirus B19, (also known as erythrovirus B19), is a small virus that causes **erythema infectiosum (fifth diseases) among children, arthropathy in normal adults** and transient aplastic anemias in patients with increased erythropoiesis, such as a child with sickle cell anemia.

Parvovirus B19 can cause hydrops fetalis and congenital anemia. The P antigen on the red cell is a cellular receptor for erythrovirus B19. The virus is a potent inhibitor of the erythroid cell differentiation, cytotoxic for erythroid precursor cells, and can cause erythroid aplasia.

The virus is spread by respiratory droplets and transplacentally during pregnancy. Parvovirus B19 only infects humans. There are no animal reservoirs.

BURDEN OF DISEASE

Most people are exposed to Parvovirus B19 and will seroconvert during their life time. Once a person has developed immunity to the virus they can not be reinfected.

Between 25 % and 80% of women are already immune to the virus before pregnancy.

The annual proportion of women of childbearing age who seroconvert is 1.5%.

Transplacental Parvovirus B19 infection occurs in 30-50% of acute maternal Parvovirus B19 infection. However, most neonates are born normal.

DIAGNOSIS

CLINICAL FEATURES

In children the disease consists of a mild rash (fifth disease).. The ill child typically has a "slapped-cheek" rash on the face and a lacy red rash on the trunk and limbs. Occasionally, the rash may itch. An ill child may have a low-grade fever, malaise, or a "cold" a few days before the rash breaks out. The child is usually not very ill, and the rash resolves in 7 to 10 days.

Most adults with acute infection have no symptoms. Few adults develop the typical **rash of fifth disease, but joint pain and/or swelling is common. Usually, more than** one joint is affected. The joints most frequently affected are the hands, wrists, and knees. Joint pain and swelling usually resolve in a week or two, but can persist for several months.

A person infected with parvovirus B19 is contagious from 4 to 7 days before the onset of rash and for up to 2 weeks after.

The interval between acute maternal infection and the diagnosis of fetal disease ranges between 2 and 6 weeks.

The risk of adverse fetal outcome is very low, but higher if infection occurs during the 1st and 2nd trimesters, especially between 9 and 16 weeks gestation. Fetal disease may be expressed as severe fetal anemia, non immune hydrops fetalis, or fetal death.

Other fetal abnormalities associated with this virus are extremely rare. No neurodevelopmental sequelae have been reported

LABORATORY

Acute maternal Parvovirus B19 infection is diagnosed by the presence of anti-parvovirus B19 IgM antibodies. Anti-parvovirus B19 IgG antibodies indicate previous infection. To diagnose fetal infection, anti-parvovirus B19 IgM can be detected in fetal cord blood or polymerase chain reaction assays can detect the **presence of the virus in maternal blood, amniotic fluid and cord blood.**

TREATMENT

There is no specific treatment against Parvovirus B19. Some specialists recommend ultrasound after acute maternal Parvovirus B19 infection has been documented to detect early signs of hydrops fetalis. Intrauterine transfusions of packed red blood cells have been used to treat hydrops fetalis. However, no randomized controlled trials have evaluated the effectiveness of this therapy.

PREVENTION

Pregnant women should practice good handwashing practices, especially when working with young children. Community outbreaks of Parvovirus B19 are common and a child is infectious before symptoms are obvious.

A vaccine for human Parvovirus B 19 is under investigation.

Hepatitis C

The hepatitis C virus (HCV) is an RNA virus with at least six different genotypes. HCV is primarily parenterally transmitted; in health care settings via needle-sticks, among intravenous drug users through the sharing of needles, or via blood transfusion where blood is not adequately screened. . Chronic infections may persist for up to 20 years before the onset of sequellae, including cirrohosis or hepatocellular carcinoma.

Approximately 5% of infants born to HCV-infected mothers become infected perinatally. The risk is significantly higher (19%) for mothers co-infected with HIV. No vaccine or treatment is available to prevent transmission. Persons newly infected with HCV typically are either asymptomatic or have a mild clinical illness. Chronic HCV infection develops in 60%–85% of HCV infected persons. 60%–70% of chronically infected persons have evidence of active liver disease and 1%-5% of infected persons may die from cirrhosis or liver cancer.

BURDEN OF DISEASE

HCV has a worldwide distribution, with a prevalence of between 0.5% and 2.0% in Europe and North America, and over 4% in parts of Africa. Infection rates vary greatly among populations. HCV infection is a common chronic blood borne infection in well-defined high-risk groups (e.g. intravenous drug users).

DIAGNOSIS

Measurements of antibodies to HCV or nucleic acid testing by PCR are the serologic tests used to determine if someone is infected with HCV.

Routine testing for HCV infection is not recommended for all high-risk groups (i.e., ever injected illegal drugs, ever was transfused blood that was not tested for HCV, ever was transplanted with an organ from a person not previously tested for HCV, ever been on long-term kidney dialysis, ever had evidence of liver disease).

PREVENTION

- No vaccine is available to prevent transmission, and prophylaxis with immune globulin is not effective.
- During delivery, percutaneous procedures on the infant should be avoided.
- Do not shoot drugs
  - if you shoot drugs, stop and get into a treatment program;
  - if you can't stop, never share needles, syringes, water, or "works", and
  - get vaccinated against hepatitis B.
- Do not share personal care items that might have blood on them (razors, toothbrushes).
- If you are a health care or public safety worker, always follow routine barrier precautions and safely handle needles and other sharps.
- Consider the risks if you are thinking about getting a tattoo or body piercing. You might get infected if the tools have someone else's blood on them or if the artist or piercer does not follow good health practices.
- HCV can be spread by sexual activity, but this is rare. If you are having sex with more than one steady partner, use latex condoms, correctly and every time to prevent the spread of sexually transmitted diseases. You should also get vaccinated against hepatitis B.
- If you are HCV positive, do not donate blood, organs, or tissue.
- Mothers should be advised that approximately five of every 100 infants born to HCV-infected woman become infected. If coinfected with HIV the risk for perinatal infection is about 19%

TREATMENT

No treatment or delivery method is known to decrease this risk of transmission from mother to infant.

Breastfeeding does not appear to transmit HCV, although HCV-positive mothers should consider abstaining from breastfeeding if their nipples are cracked or bleeding.

Infants born to HCV-positive mothers should be tested at 12 to 18 months for HCV infection and, if positive, evaluated for the presence.

Listeriosis

Listeriosis is caused by ingesting food contaminated with the gram-positive motile bacterium *Listeria monocytogenes*.

This bacterium is unusual in that it grows between 4ºC and 37ºC. Because of this property, it can grow on foods that are stored in refrigerators, and unless these foods have been thoroughly cooked, the consumer may be exposed to a large dose of the bacterium.

Listeria monocytogenes has been found in foods such as uncooked meats, prepared meat products (deli meats, pate, hot dogs, seafood), and vegetables. Unpasteurized milk or foods made from unpasteurized milk (soft cheeses) may contain the bacterium. In the United States, large outbreaks caused by contaminated dairy products have been reported since the 1950s. The much higher incidence of Listeriosis in the Latin American population is believed to be related to the consumption of "queso fresco" (fresh cheese).

The disease affects primarily pregnant women, newborn infants, and adults with weakened immune systems. Adults above age 65 may be at risk relative to young persons.

The predilection of Listeria for the fetoplacental unit and intrauterine infection is well documented. Fetal infection results from transplacental transmission following maternal bacteriemia or by ascending infection from vaginal colonization.

BURDEN OF DISEASE

The incidence of neonatal listeriosis in the U.S. is estimated at 13 per 100,000 births. Pregnant women are more likely to contract the infection than are other healthy adults. During pregnancy, vertical transmission can cause abortion or stillbirth, premature delivery, or severe SNC infection of the newborn. In immunocompromised persons, the infection may result in sepsis and meningitis with a high mortality.

DIAGNOSIS

CLINICAL FEATURES

Infected pregnant women may experience only a mild, flu-like illness with fever, muscle aches, nausea or diarrhea. In severe cases it may cause meningoencephalitis with risk of death.

Neonatal early onset
Clinical signs develop during the first week of life. Signs and symptoms include respiratory distress, fever, and neurologic abnormalities. In severe sepsis, an infant may present with granulomatous rash (infantspeticum) and neutropenia.

Neonatal late onset
Late-onset neonatal disease may express from 7 days to several weeks after birth. Neonates with late-onset disease present most frequently with meningitis.

LABORATORY
There is no routine serologic screening test for listeriosis infection during pregnancy, however diagnosis may be made via a blood culture of a febrile pregnant woman.

TREATMENT: Pregnant women
When infection occurs during pregnancy, antibiotics given promptly to the pregnant woman can often prevent infection of the fetus or newborn. Ampicilin 4-6 g / day divided in 4 equal doses intravenously during 14 days.

TREATMENT: Neonatal
Ampicilin: 200 mg/Kg/day divided in four to six equal doses, however dose should be adjusted for age and weight: 50-200 mg/Kg/24hrs every 6-12 hours) intravenously during 14 days. And

Gentamicin 5 mg/Kg/day divided in three equal doses increasing to 7.5 mg/Kg/ day after the 7th day (dose varies with age and weight: 2.5-3 mg/kg/dose every 8-12 hours).

Cerebrospinal fluid should sterilize in less than 3 days of treatment, if not review treatment.

PREVENTION

- Thoroughly cook beef, pork, or poultry.

- Wash raw vegetables before eating.

- Avoid unpasteurized milk or foods made from unpasteurized milk, including cheeses such as "queso fresco".

- Wash hands, knives, and cutting boards after handling uncooked foods or fluids from their packages.

- Consume perishable and ready-to-eat foods while fresh.

- Reheat until steaming hot dogs, luncheon meats, or deli meats..

- Do not eat any soft cheeses unless you are sure that were made from pasteurized milk.

- Pâtés, meat spreads and smoked sea food may only be eaten if they are canned or shelf-stable.

The Perinatal Information System

Since 1985 the Latin American Centre for Perinatology, the technical centre of the Pan American Health Organization has been developing and implementing an information system to increase the quality of perinatal care in more than 25 countries the region of Latin America and the Caribbean.

Standards of care of the pregnant woman and neonate supported by the best evidence available are updated as guidelines for health care personnel. After a consensus process, health systems agree to follow a body of procedures that have strong evidence to lead to better health outcomes.

The health record includes at least the minimal information required to achieve these standards and make its evaluation feasible.

The Perinatal Information System has a Basic Health Record that includes the minimal data set necessary to care for all mothers. The information is registered from the first antenatal visit until discharge of the mother and neonate after birth. The same information is copied to the Perinatal Card that is always carried by the mother.

By filling in the form the care provider is guided through a predetermined set of procedures (history, clinical and lab exams, assessments and interventions). The form includes the expected data and highlights the unexpected by checking a yellow box.

Training health personnel for basic perinatal care uses the Perinatal Record as a route map for the main components and there are manuals and tools (like the Gestational Wheel or Disk, the Fundal Height measuring tape and others) that provide additional information for improving assessment and care.

The use of these technologies and the Perinatal Information System in all levels of care in the LA&C region has also allowed to file and analyze the perinatal data at the local level with a free domain software distributed by PAHO.

Find more information at www.clap.ops-oms.org

This manual has been designed as a tool to increase knowledge of the main components of care to decrease vertical transmission of infectious diseases from the mother to her offspring, many of which are recorded in the Perinatal Clinical Record.

The following page shows both sides of the current regional version of the Perinatal Clinical Record.

PERINATAL CLINICAL RECORD - CLAP/WR - PAHO/WHO

CODE LISTING

Perinatal Electronic System

Number at left correspond to codes as used in this form. Codes at right are the International Code of Diseases. Rev. 10 (ICD - 10) PAHO/WHO 1992

CONDITIONS OF PREGNANCY, CHILDBIRTH & PUERPERIUM (PCP)

50	MULTIPLE GESTATION	O30
51	PRE-EXISTING HYPERTENSION	O10
01	Essential pre-existing hypertension complicating pregnancy childbirth and the puerperium	O10.0
02	Secondary pre-existing hypertension complicating pregnancy childbirth and the puerperium	O10.4
52	PREECLAMPSIA	O13 and O14
04	Transient gestational (pregnancy-induced) hypertension	O16
05	Mild pre-eclampsia	O13
06	Severe and moderate pre-eclampsia	O14
53	Pre-existing hypertension with superimposed proteinuria	O11
54	ECLAMPSIA	O15
55	CARDIOPATHY	Z86.7
56	DIABETES	O24
57	Pre-existing insulin-dependent diabetes mellitus	O24.0
58	Pre-existing non-insulin-dependent diabetes mellitus	O24.1
59	Diabetes mellitus of gestational onset	O24.4
07	Abnormal glucose tolerance test	R73.0
60	URINARY TRACT INFECTION	O23.0-23.4
08	Asymptomatic gestational bacteriuria	R82.7
61	OTHER INFECTIONS	O98, B50-B54,A60
62	Infections of the genital tract in pregnancy	O23.5
09	Syphilis complicating PDP	O98.1
10	Gonorrhea complicating PDP	O98.2
11	Malaria	B50-B54
12	Ano-genital Herpes Infection (herpes simplex)	A60
63	Viral hepatitis	O98.4
64	TBC complicating PDP	O98.0
80	Rubella complicating PCP	B06.O, B06.8 y B06.9
65	PARASITIC INFECTION complicating PDP	O98.8
77	Chagas	O98.6
78	Toxoplasmosis	O98.6
66	INTRAUTERINE GROWTH RETARDATION	P05
67	PREMATURE CHILDBIRTH THREAT (PREMATURE DELIVERY)	O60
13	Cervical incompetence	O34.4
68	CEPHALOPELVIC INCONSISTENCY	O64, O65, O69
14	Obstructed labour due to malposition and mal presentation of fetus	O64
15	Obstructed labour due to maternal pelvic abnormality	O65
16	Other obstructed labour due to the fetal cause	O66
69	HEMORRHAGETHE FIRST TRIMESTER	O20
17	Hydatiform mole	O01
18	Spontaneous abortion and retained	P021.1, O03
19	Ectopic pregnancy	O00
20	Induced or medical abortion	O06,O04
21	Threatened abortion	O20.0
70	HEMORRHAGE THE 2nd & 3rd TRIMESTER	
22	Placenta previa with hemorrhage	O44.1
23	Premature separation of placenta (abruptio placentae)	O45
24	Antepartum hemorrhage with coagulation defect	O46
25	Uterine rupture before or during delivery	O71.0, O71.1
26	Obstetric laceration of cervix	O71.3
71	ANEMIA	O99.0
27	Iron deficiency anemia	D50
79	Sickle cell anemia	D57.0-D57.2 y D57.8
72	PREMATURE RUPTURE OF MEMBRANES	O42
28	Infection of amniotic sac and membranes	O41.1
73	PUERPERAL INFECTION	O85, O86
29	Puerperal sepsis	O85
30	Infections of breast associated with childbirth	O91
74	Postpartum hemorrhage	O72
31	Retained placenta	O72.0, O72.2
32	Atonic uterus	O72.1
33	1° & 2° degree perineal lacerations	O70.0, O70.1
34	3° & 4° degree perineal lacerations	O70.2, O70.3
75	OTHER MATERNAL CONDITIONS	(Min O00-O99)
35	Placenta praevia without hemorrhage	O44.0
36	Pregnancy-related excessive vomiting	O21
37	Unspecified renal disease in pregnancy, without mentioning of hypertension	O26.8, O99.8 (conditions in N00-N39)
38	Drug dependency	F10-F19
39	Fetal distress	O68
40	Polyhidramnios	O40
41	Oligoahydramnios (without mention of rupture of membranes)	O41.0
42	Labor and delivery complicated with umbilical cord complications	O69
43	Complication of anesthesia during childbirth and puerperium	O74
44	Obstetric embolism	O88
45	Failed closure of cesarian section wound	O90.0
46	Failed of episiotomy closure	O90.1
47	AIDS	B20-B24
76	HIV Positive	R75
48	Malignant neoplasia of ce°vix	C53
49	Malignant neoplasia of breast	C50

MAIN INDICATION OF SURGICAL DELIVERY OR INDUCTION

01	Previous cesarean section
02	Fetal distress
03	Cephalo pelvic disproportion
04	Contractility disorders
05	Prolonged delivery
06	Failed of induction
07	Arrested descent of presentation
08	Multiple pregnancy
09	Retarded intrauterine growth
10	Preterm childbirth
11	Pos term childbirth
12	Breech presentation
13	Posterior position
14	Transverse position
15	Premature rupture of membranes
16	Eggs infection (suspected or confirmed)
17	Placenta praevia
18	Abruptio placentae
19	Uterine rupture
20	Preeclampsia and eclampsia
21	Anogenital herpes
22	Condylomatosis of the genitalia
23	Other maternal conditions
24	Fetal death
25	Exhausted mother
26	Others
76	HIV

MEDICATION DURING LABOUR

01	Lidocaine or the like
02	Sympathomimetic amines
03	Anesthetic gases (pentrane-fluorane-nitrous oxide)
04	Barbiturates
05	Muscle relaxants
06	Diazepoxides
07	Meperidine
08	Spasmolytics
09	Oxytocin
10	Prostaglandins
11	Betalactamics (Penicillins-cephalosporins)
12	Aminoglycosides (gentamicin-amykacin)
13	Erithromycin
14	Metronidazole
15	Beta mimetics
16	Prostaglandin inhibitors
17	Calcium antagonists
18	Magnesium sulphate
19	Hycralazin
20	Beta blockers
21	Other antihypertensives
22	Blood and derivatives
23	Heparine
24	Corticosteroida
25	Cardiotonics
26	Diuretics
27	Aminophyllin
28	Insulin
29	Diphenylhydantoine
30	Others
31	Antiretrovirals
32	Sulphadoxin-Pirimetamine
33	Chloroquines

NEONATAL CONDITIONS

50	HIALINE MEMBRANE DISEASE	P22.0
51	ASPIRATION SYNDROME	P24
52	PREMATURITY-INDUCED APNEAS	P28.3-P28.4
53	OTHER RDSs	Q25.0, P29.3, P23, P25, P22, P27
01	Patent ductus arteriosus	Q25.0
02	Persistence of fetal circulation	P29.3
03	Congenital pneumonia	P23
04	Pneumothorax and intestinal emphysema	P25
05	Transient tachypnea	P22.1
06	Chronic respiratory disease originated in the perinatal period	P27
	HEMORRHAGES	
07	Hemorrhagic disease of the newborn	P53
55	Pulmonary hemorrhage originated in the perinatal period	P26
08	Umbilical hemorrage (not including omphalitis with hemorrhage)	P51
	HYPERBILIRUBINEMIA	
08	Hemolytic disease due to Rh immunization	P55.0
09	Hemolytic disease due to ABO immunization	P55.1
10	Preterm-associated neonatal jaundice	P59.0
58	HEMATOLOGICAL (Excluding P50-P59)	P60-P61
11	Neonatal polycythemia	P61.1
12	Congenital anemia	P61.3
79	Sickle cell anemia	D57.0-D57.2 y D57.8
13	Other hematological conditions	(rest of P60-P61)
	INFECTIONS	
14	Diarrhea	G00
15	Meningitis	P38
16	Onphalitis	P39.1, A54.3
17	Conjunctivitis	P39.4,L00
59	Newborn's skin infections	P36
18	Septicemia	(rest of P35-P39)
61	Viral congenital diseases	P77
49	Neonatal tetanus	A33
60	Congenital syphilis	A50
61	Viral congenital diseases	P35
68	Congenital rubella syndrome (SRC)	P35.5
69	Cytomegalovirus (CMV)	P35.1
70	Congenital Toxoplasmosis	P37.1
39	HIV positive	R75
19	Other perinatal period infections	(rest of P60-P61)
	NEUROLOGICAL (EXCLUDING MALFORMATIONS)	
		G91
33	Acquired hydrocephalus	P91.1,P91.2
34	Periventricular and brain leukomalacia	P10,P11,P14
35	Obstetric trauma with intracranea injury of the CNS and the PNS	P52
36	Intracranial hemorrhage unrelated to trauma	P90
37	Seizures	P21
71	Hypoxic-Ischemic encephalopathy	P91
38	Other conditions of the brain	
	METABOLIC-NUTRITIONAL	P70.0, P70.1
43	Child born to diabetic mother	P70.3, P70.4, E16.2
45	Hypoglycemia	P75-PT8
46	Other metabolic and nutritional conditions	
66	OTHER NEONATAL CONDITIONS	
40	Prematurity retinopathy	H35
41	Inguinal hernia	K40
65	Cold injuty syndrome	P80.0 (excludes mild hypothermia P80.8)

CONGENITAL ABNORMALITIES

120	Anencephaly	Q00.0
121	Spina bifida/Myelomeningocele	Q05,Q07.0
122	Hydrancephaly	Q04.3
123	Hidrocephalus	Q03
124	Microcephaly	Q02
125	Holoprosencephaly	Q04.2
127	Other congenital malformations of the Central Nervous System	Q04,Q06
128	Troncus arteriosus	Q20.0
129	Transpositions of the large vessels	Q20.3
130	Tetralogy of Fallot	Q21.3
131	Single ventricle	Q20.4
132	Double autlet right ventricle	Q20.1
133	Complete atrio-ventricular canal	Q21.2
134	Pulmonary atresia	Q22.0
135	Tricuspid atresia	Q22.4
136	Left heart hypoplasia syndrome	Q23.4
137	Coarctation of the aorta	Q25.1
138	Total anomalous pulmonary venous connection	Q26.2
139	Other circulatory/respiratory abnormalities	Q24,28,34
140	Cleft palate	Q35
141	Tracheo-oesophageal fistula	Q39.1
142	Oesophageal atresia	Q39.0,Q39.1
143	Colon or rectal atresia	Q42.0,Q42.1,Q42.8,42.9
144	Imperforate anus	Q42.3
145	Omphalocele	Q79.2
146	Gastroschisis	Q79.3
147	Duodenal atresia	Q41.0
148	Jejunal atresia	Q41.1
149	Ileal atresia	Q41.2
150	Other GI malformations	Q40.43,45
151	Malformation of the genitalia	Q50-56
152	Bilateral renal agenesia	Q60.1
153	Poly or multicystics or dysplastic kidneys	Q61.1-61.9
154	Congenital hydronephrosis	Q62.0
155	Bladder extrophy	Q64
156	Other nephrourinary abnormalities	Q63,64
157	Trisomy 13	Q91.4, Q91.5,Q91.6
158	Trisomy 18	Q91.0, Q91.1,Q91.2
159	Down syndrome	Q90
160	Other chromosomal abnormalities	Q92,97-99
126	Cleft lip	Q36
161	Polydactily	Q69
162	Syndactily	Q70
163	Skeletal displasia	Q77-78
164	Talipes equinovarus - Talipes calcaneo varus/valgus (club foot)	Q66.8
165	Diaphragmatic hernia	Q79.0
166	Hydrops fetalis	P56,P83.2
167	Severe oligoamnios	P01.2
168	Other musculo skeletal abnormalities	Q68,74,75,79
169	Tegumentary abnormalities	Q82,84

PERINATAL INFECTIONS

TRANSMITTED BY THE MOTHER TO HER INFANT

EDUCATIONAL MATERIAL FOR HEALTH PERSONNEL

Pan American Health Organization

Regional Office of the World Health Organization

march of dimes

Latin American Center for Perinatology Woman and Reproductive Health - CLAP/WR