Pregnancy and Sexually Transmitted Diseases: An Update

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About the MCH Section

• Mission: The Maternal & Child Health Section of the American Public Health Association was organized in 1921 with the mission of developing innovative and creative approaches to addressing the health needs of mothers, children, adolescents, and families.

Members include professionals from diverse disciplines such as nurses, physicians, midwives, social workers, psychologists, researchers, nutritionists, child care workers, doulas, and many others who are involved at every level of health care delivery and policy development.
Mary Kamb, MD, MPH
Centers for Disease Control and Prevention

• Dr. Kamb is Associate Director for Global Activities at the Division of Sexually Transmitted Diseases (STD) Prevention, Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia where she leads global STD activities. She is a graduate of the University of Washington Medical School and School of Public Health, completed an internal medicine residency at the Brigham and Women’s Hospital, and was a chief medical resident at the Waltham Weston Hospital. A recipient of a National Cancer Institute Training Grant, she completed a Cancer Epidemiology fellowship at Fred Hutchinson Medical Center in Seattle. Since joining CDC as an Epidemic Intelligence Service (EIS) officer in 1989, her work has focused on reproductive and maternal and child health, and evaluation of HIV/STD prevention interventions.
Karen Hoover, MD, MPH
Centers for Disease Control and Prevention

• Dr. Hoover is a health services researcher in the Division of STD Prevention at the Centers for Disease Control and Prevention. She is a graduate of the Boston University School of Medicine and Johns Hopkins Bloomberg School of Public Health, and completed a residency in obstetrics and gynecology at the Johns Hopkins Hospital. Among her research interests are access, utilization, and quality of reproductive healthcare services; development of novel health service models for STD clinical care; adverse outcomes of STDs in women, including pregnant women; elimination of MTCT of syphilis and HIV; STD prevention among MSM; and syphilis diagnostics.
Christine Ross, MD, MPH, & TM
Centers for Disease Control and Prevention

• Dr. Ross joined the Division of STD Prevention at CDC in July 2012 as an Epidemic Intelligence Service Officer (EISO) after practicing family medicine for 10 years. While serving as an EISO, she piloted methods to validate elimination of mother-to-child transmission of HIV and congenital syphilis in the Americas, investigated increasing rates of repeat syphilis and HIV co-infection in men who have sex with men in Baltimore, MD and studied access and utilization of prenatal care services by Medicaid recipients. Dr. Ross received her MD from the Louisiana State University School of Medicine and her MPH & TM from Tulane University School of Public Health and Tropical Medicine and is board certified in Family Practice.
Pregnancy and Sexually Transmitted Diseases: An Update

Karen Hoover, MD, MPH
Christine Ross, MD, MPH & TM
Mary Kamb, MD, MPH

September 18, 2013
Perinatal morbidity and mortality, global perspective

Globally each year

- 2.9 million neonatal deaths (first 28 days of life)
- 2.6 million stillbirths
- 99% of infant (and maternal) deaths occur in developing countries
- With more effective child health interventions, neonatal deaths account for an increasing proportion of child < 5 mortality

Levels and Trends in Child Mortality, Report 2013: UN Inter-agency Group for Child Mortality Estimation
Neonatal mortality: Risk of death, by day during the first month of life

Changes in late fetal, neonatal and post-neonatal mortality rates, 1983 to 1999

WHO presentation at “Neonatal Survival Intervention Research Workshop,” Kathmandu, Nepal, and in: The Unheard Cry for Newborn Health, CARE/USA
Global burden of sexually transmitted diseases (STDs)

- STDs are among most common of all infections
- Although > 30 pathogens, most burden due to 8 infections:
  - Curable STDs: syphilis, gonorrhea, chlamydia, trichomonas
  - Chronic STDs: HIV, genital herpes (HSV), human papillomavirus (HPV), hepatitis B virus (HBV)

- WHO estimates 499 million new cases of curable STDs each year
- STDs rank in the top 5 disease categories for which adults seek health care services

STDs disproportionately affect women and infants

- Reproductive health (ectopic pregnancy, pelvic inflammatory disease, infertility)
- Perinatal mortality and morbidity (syphilis, herpes, chlamydia, gonorrhea)
- Preterm birth/low birth weight (syphilis, trichomonas, gonorrhea, chlamydia)
Global burden of mother-to-child transmission of syphilis (congenital syphilis)

• WHO estimates each year
  – 1.4 million pregnant women have active syphilis globally, of whom most (80%) attend antenatal care services
  – Untreated infections results in 521,000 adverse pregnancy outcomes, of which 305,000 are perinatal deaths
  – 2/3 of these are among women who were either not tested or not treated for syphilis

• Preventable with syphilis screening and treatment (IM penicillin) during pregnancy
  – Highly cost-effective public health intervention

Major causes of death in children under 5 years, global 2008

Deaths among children < 5 years

- HIV/AIDS: 2%
- Neonatal: > 40%
- Diarrhea diseases (post neonatal): 14%
- Measles: 1%
- Malaria: 8%
- Pneumonia: 19%
- Others: 10%
- Injuries: 3%

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Neonatal deaths

- Other: 12%
- Diarrheal diseases: 3%
- Neonatal tetanus: 2%
- Neonatal infections: 25%
- Birth asphyxia and birth trauma: 23%
- Congenital: 7%
- Prematurity and low birth weight: 29%

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Preventing adverse outcomes of STDs in pregnancy

- Mother-to-child transmission (MTCT) of syphilis
- Neonatal herpes
- MTCT of HIV
- Chlamydia and gonorrhea
- MTCT of hepatitis B
- How often are pregnant women tested for STDs?
Primary & secondary syphilis is usually catastrophic for fetus.

About half (52%) of untreated latent infections result in adverse pregnancy outcomes:

- Fetal loss and stillbirth: 21%
- Neonatal death: 9.3%
- Prematurity or low birth weight: 5.8%
- Congenital syphilis: 15%

Gomez et al. 2013
Syphilis in pregnancy

- Increased risk of adverse outcome
  - Older compared to younger fetus
  - Primary & secondary syphilis compared to latent syphilis
Signs of congenital syphilis
Sequelae of congenital syphilis
Rates of congenital syphilis and primary and secondary syphilis in women aged 15-44 years — United States, 1995–2011

MMWR 2010; STDNet 2013
Preventing adverse outcomes from syphilis in pregnancy

- MTCT of syphilis is prevented by testing and treatment of pregnant women
  - Initial prenatal visit
  - 28 weeks gestation
  - Delivery

- Timely and appropriate treatment is critical
  - At least 30 days prior to birth for effective treatment of the fetus
  - Benzathine penicillin

- Partner testing and treatment
Testing women for syphilis in prenatal care

401 cases

125 cases (31%)
No prenatal care

276 cases (69%)
Prenatal care

4 cases
Not tested

170 cases
Tested >30 days of delivery

75 cases
Tested ≤30 days of delivery

27 cases
Other

67 cases
Untreated

33 cases
Inadequate treatment

70 cases
Inadequate response

MMWR 2010
Syphilis serologic screening algorithms

**Traditional**

- **Manual**
  - Quantitative RPR
    - RPR+
      - TP-PA+ or other trep. test
        - TP-PA+ Syphilis (past or present)
    - RPR−
      - TP-PA− Syphilis unlikely

RPR – Rapid plasma reagin
TP-PA – *Treponema pallidum* particle agglutination

MMWR 2011
Syphilis serologic screening algorithms

Traditional

Manual

Quantitative RPR

RPR+

RPR-

TP-PA or other trep. test

TP-PA+ Syphilis (past or present)

TP-PA- Syphilis unlikely

Reverse sequence

Automated

EIA

EIA+

EIA-

Quantitative RPR

RPR+

RPR-

TP-PA

TP-PA+

Syphilis (past or present)

TP-PA- Syphilis unlikely

Manual

RPR – Rapid plasma reagin
TP-PA – Treponema pallidum particle agglutination
EIA – Enzyme immunoassay

MMWR 2011
False positive immunoassay results (EIA+/RPR-/TPPA-) among discordant sera (EIA+/RPR-)

- Low Syphilis prevalence: 100% True positive, 40% False positive
- High Syphilis prevalence: 100% True positive, 40% False positive

MMWR 2011
Recommendations for testing pregnant women for syphilis with a reverse sequence

- CDC recommends the use of the traditional algorithm for testing of pregnant women.

- If reverse sequence testing is used, confirmatory testing with RPR and TP-PA testing must be performed as recommended by CDC.

- An infant should be treated only if their mother has syphilis.
HSV in pregnancy

- HSV-1 and HSV-2 both cause neonatal herpes
  - 33-50% of cases caused by HSV-1

- Infants acquire infection during labor and delivery from exposure to virus in mother’s genital tract

- Risk is greatest in infants who are exposed during delivery and do not have protection from maternal antibodies
  - Primary infection near delivery: 30-50% transmission
  - Primary infection in first half of pregnancy or recurrent infection: < 1% transmission
Clinical manifestations of neonatal herpes

- Skin, eyes, mouth: 45%
- Central nervous system: 30%
- Disseminated: 25%
Clinical manifestations of neonatal herpes

- Disseminated:
  - Mortality: 30%
  - 25 cases

- Skin, eyes, mouth:
  - 45 cases

- Central nervous system:
  - 30 cases
Clinical manifestations of neonatal herpes

- Skin, eyes, mouth: 45
  - Mortality: 30%
- Central nervous system: 30
  - Mortality: 4-6%
- Disseminated: 25
  - Mortality: 30%

Neurologic impairment: 20%-50%
Infant with neonatal herpes
Seroprevalence of HSV-1 and HSV-2 in men and women — United States, 2005–2010

Bradley et al. 2013
Seroprevalence of HSV-1 and HSV-2 among pregnant women by race and ethnicity — United States, 1999–2002

Xu et al. 2006
Incidence of neonatal herpes by race and ethnicity — United States, 2006

Flagg et al. 2010
Prevention of neonatal herpes

- Preventing acquisition of new infections late in pregnancy
  - Serologic testing of women with infected partners
  - Suppression of infected partner not studied
  - Avoidance of intercourse and oral sex in third trimester

- Preventing transmission in women with recurrent genital herpes
  - Suppressive therapy starting at 36 weeks
    - Diminishes frequency of recurrences
    - Lower cesarean section rates
Prevention of neonatal herpes

- Preventing exposure of infant during delivery
  - Cesarean section if mother has lesions or prodromal symptoms

- Routine serologic testing of pregnant women is not recommended
Preventing MTCT of HIV in pregnancy

- HIV screening of all pregnant women
  - Initial prenatal visit
  - 36 weeks if at increased risk

- In 2006, CDC recommended opt-out testing
  - In some states, counseling and informed consent required to test pregnant women

- Antiretroviral therapy for infected women

- Cesarean section for women with an HIV viral load > 1,000
Chlamydial and gonococcal infections during pregnancy

- STDs caused by *Chlamydia trachomatis* and *Neisseria gonorrhoea*

- Vast majority asymptomatic
  - Screening is important

- Lower genital tract infection

- Facilitates HIV transmission
Adverse pregnancy outcomes associated with chlamydial and gonococcal infections

- **Pregnancy**
  - Miscarriage
  - Preterm labor
  - Premature rupture of membranes
  - Postpartum endometritis

- **Infant**
  - Low birth weight
  - Neonatal infections
    - Conjunctivitis
    - Pneumonia
    - Disseminated infection
Perinatal transmission of gonococcal infection

Gonococcal ophthalmia neonatorum

The Public Health Image Library, CDC, photo by Dr. J Pledger
Burden of chlamydial and gonococcal infections in the United States

- Chlamydia is the most commonly reported infectious disease
  - 1.4 million cases reported to the CDC in 2011

- Gonorrhea is the second most commonly reported infectious disease
  - >300,000 cases reported to the CDC in 2011
Case rates of chlamydia and gonorrhea in women in the United States, 2011

STD NET Data
Chlamydia and gonorrhea prevalence in pregnant women by age

Blatt et al. 2012
Case rates of gonorrhea in U.S. women aged 15–24, by race and ethnicity, 2011

STD NET Data
Prevention of adverse outcomes associated with chlamydial and gonococcal infections during pregnancy

- Screening
- Appropriate treatment
- Vigilance for treatment failure
- Partner management
Screening:
Chlamydial infection during pregnancy

- CDC recommends routine screening of all women at first prenatal visit
- Test-of-cure 3 weeks after completion of therapy
- Retest women found to have an infection in the first trimester (3 months later)
- Repeat screening of women at high risk of infection in the third trimester

STD Treatment Guidelines, 2010
Screening: Gonococcal infection during pregnancy

- Screen women *at risk* for gonorrhea infection at first prenatal visit
  - Under 25 years old
  - Infected with other STD’s
  - New or multiple partners, inconsistent condom use
  - Commercial sex work, drug use
  - Communities with a high prevalence of disease

- Retest women found to have infection in first trimester (3-6 months later)

- Repeat screening of women at risk in third trimester
Screening:
Updated diagnostic recommendations

- Nucleic acid amplification tests (NAATs) are the preferred test
  - Sensitivity ~ 96% and specificity >98%
  - Specimens: urine, vaginal and endocervical

- Vaginal specimen preferred
  - Provider or patient-collected
  - Test sensitivity higher with patient-collected specimen
Treatment: Chlamydial/gonococcal infection during pregnancy

- Treatment prevents newborn infections
- Test of cure recommended for chlamydia

http://www.cdc.gov/std/treatment/2010/
Treatment:
Update on treatment of gonococcal infections

- Complicated by emerging antimicrobial resistance
- Vigilance for treatment failure

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w
Partner management

- Notification, evaluation and treatment of sex partners

- Reduce reinfection rates and transmission in the community

- Expedited partner therapy (EPT)
  - Delivery of medications by persons infected with STD to their sex partners
Legality of expedited partner therapy in the United States

http://www.cdc.gov/std/ept/legal
Hepatitis B infection in pregnancy

- Vaccine preventable STD caused by the hepatitis B virus (HBV)
- Effective vaccines available since 1981
- Perinatal transmission important cause of chronic liver disease and liver cancer
Prevention of perinatal transmission of Hepatitis B infection

- Universal screening of pregnant women with hepatitis B surface antigen (HBsAg)
- Provision of hepatitis B immunoprophylaxis to infants born to infected women or those who status is unknown at time of delivery
- Universal vaccination of newborns
Prenatal STD screening rates in the United States

- Medicaid administrative claims data
- Study population >110,000 pregnant women
- Determined screening rates for the CDC universally recommended tests plus gonorrhea
Prenatal STD screening rates in United States, 2010–2011

- Rh/ABO: 100%
- Syphilis: 98%
- HBV: 96%
- HIV: 84%
- Chlamydia: 88%
- Gonorrhea: 79%

Ross, et al. (work in progress)

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Thank you

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.