

## CONTENTS

### **Preface**

Barbara J. Stoll and Leonard E. Weisman

xiii

### **The Global Impact of Neonatal Infection**

Barbara J. Stoll

1

This article concerns the impact of neonatal infections on the less-developed countries of the world, reviewing the burden of disease, the proportion of neonatal mortality attributed to infection, medical and scientific aspects of infection, and strategies to reduce both the incidence of neonatal infection and morbidity and mortality in those who do become infected. The 1996 World Health Report highlights the global importance of infectious diseases, especially among young children, and stresses the impact of new or emerging diseases. Neonatal infections are old diseases. What is needed is a new recognition that they are important causes of morbidity and mortality and that simple interventions are available that can make a significant impact on reducing both the incidence of infection and death related to infection.

### **Sexually Transmitted Diseases and Adverse Outcomes of Pregnancy**

Robert L. Goldenberg, William W. Andrews, Amy C. Yuan, H. Trent MacKay, and Michael E. St. Louis

23

The effect of sexually transmitted diseases on various adverse outcomes of pregnancy owing to direct fetal and infant infection and increased preterm birth is estimated for the entire population of the United States. The large potential impact of bacterial vaginosis on adverse outcomes through an increased risk of preterm birth is emphasized. This type of analysis may be useful for priority determinations in research and intervention programs.

---

## CLINICS IN PERINATOLOGY

---

## **Intra-Amniotic Infection and Premature Rupture of the Membranes**

43

Petra H. Belady, Lisa J. Farkouh, and Ronald S. Gibbs

The outcome of the fetus and newborn often is linked to maternal complications. Intra-amniotic infection (IAI) and premature rupture of the membranes (PROM) are key risk factors for neonatal sepsis. This article describes the etiologies, diagnoses, treatments, and outcomes of IAI and PROM and addresses recent controversies in management.

## **Group B Streptococcal Infections**

59

Carol J. Baker

Group B streptococcal disease remains a prominent cause of infectious morbidity in pregnant women and their infants. This article highlights recent developments that are relevant for obstetricians, perinatologists, and neonatologists caring for patients with group B streptococcal disease. The morbidity of group B streptococcal infections in pregnancy and the proposed association of colonization with adverse pregnancy outcome is discussed, as is the emergence of serotype V and the impact of late, late-onset disease for infants. Finally, the recently proposed guidelines for intrapartum chemoprophylaxis are summarized. Implementation of the guidelines should have substantial impact on reduction of early-onset group B streptococcal infections in infancy.

## **Syphilis in Pregnancy**

71

Pablo J. Sánchez and George D. Wendel

Syphilis in pregnancy remains a problem despite the availability of adequate diagnostic tests and years of penicillin therapy. During pregnancy, syphilis is compounded by its occurrence among populations that under-use the health care system and by its association with cocaine use and infection with HIV. The potentially devastating effect of syphilis on the fetus and attendant adverse outcomes on the pregnancy continue to make syphilis a global problem of major medical and public health consequences.

## ***Ureaplasma Urealyticum* Infections in the Perinatal Period**

91

Elaine E. L. Wang, Anne G. Matlow, Arne Ohlsson, and Susan C. Nelson

*Ureaplasma urealyticum* is a micro-organism that frequently is recovered from the female lower genital tract. *U. urealyticum* recently has been linked to peripartum infections in both mothers and neonates. A critical appraisal of the evidence linking this organism with various infectious syndromes is provided. Details

of specimen type and handling and culture methods for identifying the organism also are included.

## **Tuberculosis: An Old Disease but a New Threat to the Mother, Fetus, and Neonate**

107

Jeffrey R. Starke

Tuberculosis is the leading infectious disease in the world. In developing countries and certain areas of industrialized countries, rates of tuberculosis are highest among women and men of childbearing age. True congenital tuberculosis is rare; the greatest threat to the neonate is the acquisition of tuberculosis infection shortly after birth, which tends to progress rapidly to serious tuberculosis disease in a large proportion of untreated infants. Effective methods for prevention and treatment of the disease are available and inexpensive but still are not used appropriately in most parts of the developing world. The clinician caring for pregnant women should be aware of the risk factors for tuberculosis infection and disease and should test women and families according to risk.

## **Neonatal Herpes Simplex Virus Infection**

129

Steve Kohl

The incidence of genital herpes simplex virus (HSV) and neonatal HSV infection is increasing in the United States. The risk to the neonate of a woman with genital recurrences (1%–3%) versus first-episode infection (30%–50%), even when asymptomatic, has been defined. Appreciation of the subtle clinical signs, as well as more obvious cutaneous signs of neonatal infection, will lead to appropriate diagnostic evaluation (including, at times, polymerase chain-reaction assay) and therapy. Understanding the immune defects predisposing the neonate to severe HSV infection will enhance efforts to reconstitute the neonate's immune function. Maternal vaccination, chemoprophylaxis, and appropriate use of cesarean-section delivery may prevent cases of neonatal herpes now and in the future.

## **Cytomegalovirus Infection in the Pregnant Mother, Fetus, and Newborn Infant**

151

Christopher T. Nelson and Gail J. Demmler

Cytomegalovirus (CMV) is a common virus that infects persons of all ages, races, and backgrounds. Originally described as a rare cause of "cytomegalic inclusion disease," CMV is now known to cause a broad spectrum of illness in the fetus and newborn, with most infections being asymptomatic at birth. This article discusses the epidemiology and diagnosis of CMV infection in pregnant women, the fetus, and the newborn, including recent advances in antenatal diagnosis. In addition, the challenges of treatment and prevention of congenital CMV are explored.

## **Human Immunodeficiency Virus Infection in Pregnant Women and Their Newborns**

161

Michael K. Lindsay and Steven R. Nesheim

Along with increasing knowledge of factors that put infants at risk for mother-to-infant HIV transmission (e.g., maternal-viral load, HIV-disease state, prematurity, and prolonged membrane rupture), there are new approaches to reducing the likelihood of such transmission (e.g., zidovudine treatment). Additional means of reducing transmission may become available in years to come. In this context, prenatal voluntary identification of HIV-infected women is vital. Finally, appropriate use of early diagnostic tests in HIV-exposed infants will allow effective use of prophylactic and therapeutic means.

## **Hepatitis Viruses and the Neonate**

181

Mark A. Kane

The study of viral hepatitis has expanded rapidly over the past decade with the discovery of several new viruses, some of them of great importance to medicine, and the availability of new vaccines and therapies and new strategies for their use. There now are five well-described hepatitis viruses (A through E) and a sixth virus, hepatitis G, which may join the group if it proves to be an important hepatotropic pathogen. This article discusses a number of ways that viral hepatitis infections interface with areas of interest to neonatologists and pediatricians and presents some newer concepts on the epidemiology, natural history, treatment, and control of hepatitis infections.

## **Other Viral Agents of Perinatal Importance: Varicella, Parvovirus, Respiratory Syncytial Virus, and Enterovirus**

193

Harry L. Keyserling

This article summarizes new information on the natural history of maternal varicella and maternal parvovirus B19. Controversies in the therapy of respiratory syncytial virus are presented. Prophylactic and therapeutic immunotherapy of neonatal enteroviral disease are reviewed.

## **Novel Approaches to the Prevention and Therapy of Neonatal Bacterial Sepsis**

213

Eduardo M. Perez and Leonard E. Weisman

A variety of adjunctive treatments have been shown to offer potential benefits for neonates with sepsis. Most are not available clinically, and those that are available should be considered experimental or limited in their use; however, these efforts are far from complete and should continue to evolve in the coming years. Efforts toward the rapid diagnosis of bacterial infections are a necessary component in the eventual implementation of these potential novel strategies. As a better understanding of the intricate mechanisms of neonatal sepsis is developed, it will be

possible to provide patients with an increasingly effective array of treatment and prevention strategies.

## **Prospects for Vaccines During Pregnancy and in the Newborn Period**

231

Gerald W. Fischer, Martin G. Ottolini, and James J. Mond

Infection continues to cause significant morbidity and mortality during the first few months of life. Immunization of mothers or newborn babies may provide an effective method to further reduce infections in young infants. The current status of maternal and neonatal immunizations are reviewed, and new vaccine strategies for immunization of newborns are discussed. Increased use of vaccines in mothers or newborn babies will, however, require a concerted effort from several groups, including the pharmaceutical companies, public health organizations, and medical communities.

## **Antibacterial Therapy in Pregnancy and Neonates**

251

Morven S. Edwards

This article reviews the effects of the physiologic changes accompanying pregnancy on the pharmacokinetics of antimicrobials commonly employed during pregnancy. The possible adverse effects on the fetus from maternal use of antibacterials and their excretion into breast milk are reviewed. Principles of antibiotic pharmacology in newborn infants are summarized. The indications for use, dosages, and potential for adverse effects are reviewed for antibiotics currently in use and for several agents for which approval is pending for use in the newborn.

## **Treatment of Viral Infections During Pregnancy and the Neonatal Period**

267

Richard J. Whitley and David W. Kimberlin

Over the past 15 years, successful antiviral therapy of herpes simplex virus (HSV) infection has emerged with safe therapeutics. Despite the major impact of acyclovir on the severity of HSV infection, morbidity and mortality from neonatal herpes exist. The development of therapeutics that impact on the natural history of HIV and AIDS just now are being realized, nearly a decade after the first beneficial effects of therapy were reported. Early investigations of antiviral agents in pregnant women and children must occur more promptly as the field of antiviral therapy advances. Improved therapeutics are likely to emerge over the next decade for both pregnant women and their offspring.

**Index**

285

**Subscription Information**

**Inside back cover**