

Contents

Introduction: Celebrating the 50-year Anniversary of Obstetrics and Gynecology Clinics	xiii
William F. Rayburn	
Foreword: Drugs in Pregnancy: Common Use Despite Limited Information	xvii
William F. Rayburn	
Preface: Drugs in Pregnancy: Optimizing Care for our Pregnant Patients	xix
Catherine S. Stika	
Principles of Obstetric Pharmacology: Maternal Physiologic and Hepatic Metabolism Changes	1
Catherine S. Stika	
<p>Since the recognition of pregnancy as a special pharmacokinetic population in the late 1990s, investigations have expanded our understanding of obstetric pharmacology. Many of the basic physiologic changes that occur during pregnancy impact on drug absorption, distribution, or clearance. Activities of hepatic metabolizing enzymes are variably altered by pregnancy, resulting in concentrations sufficiently different for some drugs that efficacy or toxicity may be affected. Understanding these unique pharmacologic changes will better inform our use of medications for our pregnant patients.</p>	
Inclusion of Pregnant and Lactating People in Clinical Research: Lessons Learned and Opportunities	17
Lisa R. Thiele and Catherine Y. Spong	
<p>Pregnant and lactating individuals historically have been excluded from research studies because of the ethical concerns surrounding potential harm to the fetus. Several National Institutes of Health and Food and Drug Administration initiatives have attempted to improve inclusion; however, clinical trials continue to exclude pregnant and lactating people. Drug labeling for safety and efficacy in pregnancy has thus been forced to rely on data from animal studies or limited case reports. Recent changes have sought to improve prescriber understanding of risks, benefits, and limitations of safety information on medications; however, confusion persists.</p>	
Over-The-Counter Drugs and Pregnancy	27
William F. Rayburn	
<p>The obstetric provider should ask about over-the-counter drugs, although most are low dose, used only briefly, and any harm is unlikely and more theoretic than real.</p>	

Antihypertensives in Pregnancy

39

Anna E. Denoble, Sarah A. Goldstein, and Christian M. Pettker

Hypertensive disorders of pregnancy (HDP) can result in significant maternal morbidity and even mortality. Available data suggest that many antihypertensives can be safely used in pregnant patients, albeit with close supervision of parameters like fetal growth and amniotic fluid volume. This article summarizes current guidelines on the diagnosis and treatment of hypertension in pregnancy and provides an in-depth guide to the available safety and efficacy data for antihypertensives during pregnancy and postpartum.

Aspirin and Pravastatin for Preeclampsia Prevention in High-Risk Pregnancy

79

Joe Eid, Kara M. Rood, and Maged M. Costantine

Preeclampsia is a hypertensive disorder of pregnancy affecting up to 8% of pregnancies. It is associated with significant neonatal and maternal morbidities and mortality. Although its pathogenesis is not completely understood, abnormal placentation resulting in imbalance in angiogenic factors, increased inflammation, and endothelial dysfunction are thought to be key pathways in the development of the disease. Administration of low-dose aspirin is recommended by professional societies for the prevention of preeclampsia in high-risk individuals. In this review, we summarize the evidence behind the use of low-dose aspirin and pravastatin in pregnant individuals at high risk of preeclampsia.

Magnesium Sulfate Use in Pregnancy for Preeclampsia Prophylaxis and Fetal Neuroprotection: Regimens in High-Income and Low/Middle-Income Countries

89

Kathleen F. Brookfield and Osinakachukwu Mbata

Magnesium sulfate is one of the most commonly used medications in obstetrics, most notably for the prevention of eclamptic seizures and fetal neuroprotection of the extremely preterm neonate. Pharmacokinetic and pharmacodynamic studies have demonstrated a variety of IV and IM regimens are effective for these indications. Existing models and data can be used to tailor treatment regimens to increase coverage in poor resource areas, maximize efficacy and minimize toxicity for patients of different weights and renal function.

Obstetric Indications for Progesterin Therapy

101

Rupsa C. Boelig

Specifically, meta-analyses of randomized trials demonstrate that vaginal progesterone reduces the risk of preterm birth in selected high-risk singleton pregnancies. 17-OHPC may also reduce the risk of recurrent preterm birth in singletons. Finally, one trial suggests that vaginal progesterone may also be beneficial in improving live birth rates in singletons with prior miscarriages and early pregnancy bleeding.

- Antenatal Steroids and Tocolytics in Pregnancy** 109
Kelsey Pinson and Cynthia Gyamfi-Bannerman
- Preterm birth, typically defined as birth between 20 0/7 weeks and 36 6/7 weeks of gestation, is a major cause of neonatal morbidity, and rates of preterm birth continue to rise. Antenatal corticosteroids have demonstrated benefit for reduction of morbidities and mortality associated with preterm birth, with few observed maternal risks. As such, antenatal corticosteroids have become the standard of care for treating pregnant people at risk of preterm birth. Tocolytics may be beneficial in temporarily slowing uterine contractions to prolong pregnancy long enough for the administration of corticosteroids or stabilization and transfer of a parturient in preterm labor.
- Medications for Managing Preexisting and Gestational Diabetes in Pregnancy** 121
Michaela Rickert, Aaron B. Caughey, and Amy M. Valent
- Persons with gestational and pregestational diabetes during pregnancy may require pharmacologic agents to achieve pregnancy glycemic targets, and the available medications for use in pregnancy are limited. Insulin is the only FDA-approved medication for use in pregnancy and has the greatest evidence for safety and efficacy. Metformin and glyburide are the most commonly used oral agents in pregnancy. Understanding each medication's unique pharmacokinetics, potential side effects, fetal or childhood risks, gestational age of medication initiation and patient's diabetes care barriers are important aspects of shared decision-making and choosing a regimen that will achieve glycemic and pregnancy goals.
- Antibiotics in Labor and Delivery** 137
Joanna M. Izewski, Brandon Z. Bell, and David M. Haas
- Infections are common in obstetric care and often require specific antibiotics, depending on the infection site and prevailing organisms. Summaries of antibiotic recommendations and treatment algorithms are provided for the following conditions: routine labor, group B streptococcus prophylaxis, preterm prelabor rupture of membranes, operative vaginal delivery, cesarean delivery, obstetric anal sphincter lacerations, chorioamnionitis, postpartum endometritis, infections of the urinary tract, and bacterial endocarditis prophylaxis.
- Analgesia in Pregnancy** 151
Leslie Matthews and Grace Lim
- Pain management during labor and delivery is complex and must balance efficacy and toxicity to both the pregnant person and the fetus. There are numerous ways to achieve safe and effective analgesia and anesthesia during labor and delivery, including neuraxial and nonneuraxial techniques. This review describes important anesthetic considerations that should be made when formulating a pain management plan and an overview of common anesthesia-related complications encountered in the obstetric population.

COVID-19 Therapeutics and Considerations for Pregnancy

163

Naima T. Joseph and Ai-Ris Y. Collier

The COVID-19 pandemic has generated an unprecedented amount of novel and repurposed vaccines and therapeutics that have been rapidly developed and implemented into clinical use. Unfortunately, pregnant persons have been excluded from most phase III clinical studies; therefore, our understanding regarding their safety for use in this population stems from understanding of theoretic risks and observational data. In this review, the authors discuss pregnancy-specific considerations for COVID-19 therapeutics.

An Overview of Antiviral Treatments in Pregnancy

183

Naima T. Joseph, Jaspreet Banga, and Martina L. Badell

Viral infections pose unique threats to pregnant persons and their infants. As the frequency of epidemics caused by novel pathogens increases, understanding pregnancy-specific considerations for antiviral treatments is critical for obstetric and nonobstetric providers alike. The use of pharmacologic therapeutics in pregnancy, which include antivirals, pathogen-specific antibodies, and vaccines, is limited due to the lack of purposeful, methodologic, pharmacometrics analyses in this special population. Our current understanding regarding dosing, safety, and efficacy stems from our knowledge of potential maternal or neonatal risks, observational data, and rarely clinical trials. In this review, we provide an overview on the use of antivirals during pregnancy.

Antiretrovirals for Human Immunodeficiency Virus Treatment and Prevention in Pregnancy

205

Kristina M. Brooks, Kimberly K. Scarsi, and Mark Mirochnick

Safe and effective antiretroviral medications are needed during pregnancy to reduce maternal morbidity and mortality associated with untreated human immunodeficiency virus (HIV) infection and to prevent viral transmission to the infant. Pharmacokinetic studies have helped inform the appropriate dosing of antiretroviral medications during pregnancy. However, data from these studies consistently become available years after initial regulatory approvals in nonpregnant adults. In this article, the authors provide an overview of considerations in use of antiretroviral medications in pregnant people with or at risk for HIV, pharmacokinetic studies that helped support recommended options, and therapies either under active investigation or in need of prospective study.

A Clinical Review of the Use of Common Psychiatric Medications in Pregnancy: Guidelines for Obstetrical Providers

219

Shakked Lubotzky-Gete, Lucy C. Barker, and Simone N. Vigod

Psychotropic medications are commonly prescribed in pregnancy, and obstetrical providers should be informed about how and when to use them. The current narrative review addresses the use of some of the most commonly prescribed psychotropic medications—antidepressants, sedatives and hypnotics, and antipsychotic drugs. The aim is neither a complete review of psychiatric disorders in pregnancy nor all possible

psychological and pharmacological treatments for mental illness around the time of pregnancy. Rather, the focus is on therapeutic considerations for general obstetrical providers.

Opioids and Opioid Use Disorder in Pregnancy 229

Aalok R. Sanjanwala, Grace Lim, and Elizabeth E. Krans

Overdose is a leading cause of pregnancy-associated morbidity and mortality in the United States. As such, all obstetric providers have a responsibility to provide evidence-based care for patients with opioid use disorder to mitigate adverse outcomes associated with substance use during pregnancy.

Anticoagulation Regimens in Pregnancy 241

Antonio Saad, Melody Safarzadeh, and Megan Shepherd

This article explores current recommendations for anticoagulation therapy in pregnancy, including antepartum, intrapartum, and postpartum guidelines. The authors review various screening strategies used to assess whether a patient is an appropriate candidate for anticoagulation during pregnancy and the postpartum period. The article includes dosing regimens, optimal surveillance, and medication reversal. The authors also address the challenges of transitioning between low-molecular-weight heparin and unfractionated heparin. Finally, there is a discussion of intrapartum anticoagulation management, especially as it relates to the administration of regional anesthesia, and the indications for and timing of thromboprophylaxis following delivery.

Antiseizure Medications in Pregnancy 251

Alexandra C. Moise and Elizabeth E. Gerard

Globally, epilepsy affects up to 15 million of people assigned female at birth who are of childbearing age. Up to 65% of these people with epilepsy and gestational capacity (PWEGC) have an unplanned pregnancy. Seizure control during pregnancy is important for the safety of both the childbearing and fetus. There are multiple antiseizure medications (ASMs) that can be used to control seizures; however, each medication has its own teratogenic risk profile, which must be considered. The majority of these ASMs will require frequent plasma concentration monitoring during pregnancy with corresponding dosage adjustments. Dosages should be reduced towards pre-pregnancy levels in the first 3 weeks postpartum. Breastfeeding is typically recommended as benefits of breastmilk outweigh risks of seizure medication exposure.