

Diseases, Complications, and Drug Therapy in Obstetrics



*A Guide
for
Clinicians*

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Foreword

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This book is the result of many years of collaboration between pharmacists, physicians, and nurses in the care of obstetric patients and drugs affecting the fetus and newborn. Pharmacists in the clinical care of pregnant obstetric patients started at a few medical centers in the late 1960s and early 1970s. Today, with the possible exception of pharmacist services in labor/delivery, the pharmacy profession still has little involvement with pregnant patients, especially in the pharmacotherapeutic care of pregnant women with chronic disease and infections. There is an unmet demand for pharmacy services in the care of these patients. Moreover, there are numerous opportunities to work with maternal-fetal medicine physicians (a subspecialty of obstetrics that cares for high-risk pregnancies) in clinical research involving the drug therapy of pregnant or breastfeeding women.

The text provides an organized compilation of subject matter that can be used in the teaching of obstetric pharmacotherapy to pharmacy students and pharmacists. Knowledge of the physiology and diseases/complications unique to pregnancy is a prerequisite to understanding why drug therapy for the pregnant patient is markedly different from that of the nonpregnant patient. The arrangement of the book provides a good first step toward that knowledge and understanding. It also raises an important question to pharmacy educators and practitioners: What services are needed to increase the protection of the pregnant patient and fetus in acute, ambulatory, and community-based pharmacy services? Hopefully, the answer to the question will catalyze the teaching of medication use in pregnant patients and newborns in the curricula of pharmacy schools and will spur the interest of pharmacist practitioners. If this occurs, significant changes in the types and quantity of pharmacist clinical services for pregnant patients and newborns in acute and ambulatory care settings can occur.

An important feature of this text is the interprofessional relationship that has developed over the years between the editors. Gerald Briggs has been consistent and persistent in his pursuit over three decades to improve the quality of drug use in the pregnant patient to protect the fetus and newborn. He has provided clinical care to these patients, developed drug therapy guidelines, conducted research, published, and freely given his time to teach physicians, nurses, pharmacists, residents, and students.

Dr. Michael Nageotte, a superb maternal-fetal medicine physician, has assembled a highly proficient group of maternal fetal medicine physicians, labor and delivery nurses, clinical pharmacists, and other health professionals. Under his leadership, the combined efforts of this group consistently achieve extraordinary outcomes in complicated pregnancies. Their well-earned reputation has made the MemorialCare Center for Women at Long Beach Memorial Medical Center a major referral hospital for high-risk pregnancies.

The book also reflects the relationships that have developed over the years between the editors and contributors. Many of the contributors are recognized leaders in their fields. From their knowledge and clinical experience, the quality and safety of patient care have increased significantly. Their efforts to prepare and publish this textbook will benefit the care received by many more obstetric patients and newborns in the future.

Foreword

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Those who participate in the obstetric care of a pregnant patient are challenged with making sure that their actions are beneficial to the mother and fetus-newborn. The use of drugs in the pregnant patient may be directed at the mother, fetus, or both. Only in pregnancy and lactation can a drug administered to one patient have a direct beneficial or detrimental effect on another being. It is for this reason that practitioners involved with pregnant and/or lactating patients must be constantly vigilant when using drugs.

Certainly there are instances in which a drug may be beneficial to both mother and fetus either directly or indirectly (eg, anti-infectives, anticonvulsants). In other circumstances a drug administered to the mother may have untoward effects on the fetus (eg, cancer chemotherapy), and drugs administered for the benefit of the fetus may have detrimental effects on the mother (eg, digoxin for treatment of fetal supraventricular tachycardia). These strategies must be undertaken with consideration for the risks. However, there are inevitably going to be instances in which there are currently unknown effects that may be detrimental to mother or fetus when treatment is directed at one or the other.

This text is aimed at educating obstetric caregivers, including physicians, pharmacists, and nurses, in the use of drugs in pregnancy. However, an equally important goal is to increase awareness of over-the-counter drugs to which patients have access. The use of such drugs is frequently unknown by the practitioner, which increases the need for obstetric caregivers to inquire about a patient's self-administered substances, both legal and illegal.

In recent years, clinical pharmacists have become increasingly pro-active in counseling patients about the drugs prescribed for them, as well as inquiring about other drugs a patient may be taking. At our hospital, clinical pharmacists are always present

on maternal-fetal medicine patient care rounds, and they have become much more involved in monitoring and managing the drug therapy of pregnant women with complicated conditions. This responsibility includes both hospitalized patients and ambulatory care. It is because of this increased involvement that this text is focused on pharmacists, as well as physicians and nurses who comprise the team that maximizes both safety and efficacy when drugs are used in pregnancy.

Preface

The concept for this book emerged in 2005. In our collective memories, there has always been a close working relationship between physicians and nurses and pharmacists in the MemorialCare Center for Women at Long Beach Memorial Medical Center. This professional relationship has played a major role in helping to make Women's a premier center for the care of both routine and high-risk pregnancies. Thus, it is in our best interest to assist in the training of these health care professionals for the care of obstetric patients. All nurses receive some training in obstetrics during their academic years. This has made the transition of new nurses into obstetrics an easier task.

However, such is not the case with pharmacists. For pharmacists, the absence of any training in obstetrics during their 4 years of formal postgraduate education makes such a transition a daunting journey, which can take many months to years before an acceptable level of competence is reached. It is encouraging that a number of pharmacy students come to Women's every year for an introduction to obstetrics. Their time with us is brief, but the students' feelings of accomplishment are universal in that they leave with an initial understanding and appreciation of this discipline. It is rewarding to observe these students progress from just "learning the language of Obstetrics" to becoming fledgling clinicians. Provided with the right opportunity, many of these students will become clinical pharmacists who have the ability to make outstanding contributions in the care of pregnant and lactating women. This book is one step of assistance toward making that opportunity a reality.

We are grateful for the 32 contributors who captured the essence of their topics. They covered complex subjects in a way that is easily understood, in spite of the restrictions of space and time. Each of the chapters could be expanded to many times their current size if all of the available information was included. Their ability to condense and select pertinent information and to present it in a meaningful way that promotes understanding is, in our opinion, a major accomplishment. We sincerely appreciate what they have done and thank them for their efforts.

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Introduction

Gerald G. Briggs and Michael P. Nageotte

In 2006, approximately 4,300,000 babies were born in the United States and slightly over 350,000 in Canada. Although the majority of the births resulted in full-term, normal, healthy newborns, a significant number were premature or involved infants with structural birth defects. Additionally, a significant number of pregnancies had major complications or ended in abortions, either spontaneous or elective. Thus, although it is easy to overlook, pregnancy is a condition that can result in both good and poor outcomes.

Regardless of the eventual outcome, drug therapy is very common in pregnancy. There are many complications that are unique to pregnancy, and nearly all are treated with drugs. Furthermore, there are many chronic diseases that predate pregnancy and require continued drug treatment during gestation. Appropriate drug therapy is usually beneficial for the mother and the developing infant, but it can adversely affect the pregnancy and the newborn, as well as the nursing infant if continued after delivery. In order to obtain optimal pregnancy outcomes, the treatment of unique complications and chronic diseases requires clinicians with specific knowledge of obstetrics. Because drugs are used so commonly during pregnancy and lactation, pharmacists providing services to women of reproductive potential also require knowledge of obstetrics. Ideally, an introduction to obstetrics should be included in the pharmacy curriculum. The purpose of this book is to help meet that goal.

This book is primarily about drug therapy in pregnancy and, to a lesser extent, during lactation. It is critical to understand that treatment of the mother in either of these conditions potentially involves exposure of at least one other unintended patient: the embryo, fetus, or nursing infant. Clinicians must have access to references to estimate the risk of the therapy to these other "patients." The various chapters in this book will assist them in meeting this obligation. However, because the pharmacologic therapy of pregnant women is undergoing continuous change, no single source, including this book, will have all of the published reports or even cover all of the drugs. Thus, in addition to this book, we recommend a reference library that contains several other sources, such as those listed below (arranged alphabetically):

Books

- Briggs GG, Freeman RK, Yaffe SJ. *Drugs in Pregnancy and Lactation. A Reference Guide to Fetal and Neonatal Risk*. 8th ed. Philadelphia: Lippincott, Williams & Wilkins, 2008.

- Hale T. *Medications and Mothers' Milk*. 13th ed. Amarillo, TX: Pharmasoft Medical Publishing, 2008.
- Koren G. *Medication Safety in Pregnancy and Breastfeeding*. New York: McGraw-Hill, 2007.
- Schaefer C, Peters P, Miller RK. *Drugs during Pregnancy and Lactation*. 2nd ed. London, UK: Academic Press, 2007.
- Schardein JL. *Chemically Induced Birth Defects*. 3rd ed. New York: Marcel Dekker, 2000.
- Shepard TH, Lemire RJ. *Catalog of Teratogenic Agents*. 12th ed. Baltimore: The Johns Hopkins University Press, 2007.

Online or Telephone

- LactMed, an online service of the National Library of Medicine. Available at: <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>.
- Organization of Teratology Information Specialists (OTIS). Available at: <http://otispregnancy.org> (free counseling on exposures during pregnancy and lactation for patients and healthcare professionals; toll free 866-626-OTIS).
- REPRORISK system: A commercially-available CD-ROM that contains electronic versions of REPROTEXT, REPROTOX, Shepard's Catalog, and TERIS. The system is available from <http://www.micromedex.com/products/reprorisk>.

There are three sections in this book: General Considerations in Pregnancy and Lactation, Complications Unique to Pregnancy, and Treatment of Chronic Diseases in Pregnancy.

The first section covers the physiological changes that occur in every pregnancy, as well as drug-induced developmental toxicity, drug exposure during breastfeeding, pregnancy-induced changes in pharmacokinetics, over-the-counter drugs in pregnancy, and risk communication. The focus of the latter chapter is on methods of communicating risks to patients so that it is done with current information and an understanding of counseling aspects. If risk communication is done properly, it can provide a significant measure of protection from medical liability for pharmacists working with pregnant patients.

Complications unique to pregnancy are covered in the second section. Preterm labor and delivery, fetal lung immaturity, gestational hypertension, preeclampsia and eclampsia, preterm rupture of the membranes, fetal cardiac arrhythmias, labor induction, fetal cardiac arrhythmias, and complications of the placenta are examples of complications that only occur in pregnancy. Also included is a chapter on how safe and effective pain control during child birth can be achieved. This is important because for many women child birth will be the most painful experience in their life. Additionally, there is a critical need to correctly recognize and treat postpartum hemorrhage. This condition has a high potential for maternal morbidity and mortality and is a leading cause of maternal death in the period immediately after delivery.

Section III addresses the treatment of chronic diseases and other disorders in pregnancy. The diseases and disorders covered are diabetes mellitus, infections, nausea and vomiting of pregnancy, chronic hypertension, depression, asthma, epilepsy, two

autoimmune disorders, thromboembolic disorders, and thyroid disease. Obviously, there are many more diseases that could have been discussed, but these are the most common in pregnancy. In each case, their treatment is complicated by the fact that at least one, and sometimes more, unintended patients are always present, the embryo(s) and/or fetus(es). Furthermore, the effects of a disease on the embryo-fetus are often much more severe than on the mother; diabetes mellitus is an excellent example. In other cases, there may be no proven benefit for the mother or the fetus from treatment, such as in mild chronic hypertension. In these situations, treatment may result only in risk. An understanding of the pregnant state, in addition to the disease pathology, is critical to achieving optimal pregnancy outcomes.

In addition to the editors, there are 32 contributors to the book. We have been very fortunate to obtain their assistance. We believe that their quick acceptance of our invitations to contribute was due to their recognition of the need for this book. All are clinicians and have special knowledge involving the treatment of pregnant women. Many are considered to be leading authorities on their subjects. In spite of their busy schedules, they have done very well in capturing the essence of their topics.

In our dual roles as editors and contributors, we hope this book will fulfill its purpose. If it does, we believe that pregnancy will be safer with improved outcomes for women everywhere.

