CE **2.0 ANCC Contact Hours**

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SAFETY OF Over-the-Counter MEDICATIONS IN PREGNANCY

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Abstract

Approximately 90% of pregnant women use medications while they are pregnant including both over-the-counter (OTC) and prescription medications. Some medications can pose a threat to the pregnant woman and fetus with 10% of all birth defects directly linked to medications taken during pregnancy. Many medications have documented safety for use during pregnancy, but research is limited due to ethical concerns of exposing the fetus to potential risks. Much of the information gleaned about safety in pregnancy is collected from registries, case studies and reports, animal studies, and outcomes management of pregnant women. Common OTC categories of readily accessible medications include antipyretics, analgesics, nonsteroidal anti-inflammatory drugs, nasal topicals, antihistamines, decongestants, expectorants, antacids, antidiarrheal, and topical dermatological medications. We review the safety categories for medications related to pregnancy and provide an overview of OTC medications a pregnant woman may consider for management of common conditions.

Key words: Pharmacology; Pregnancy; Safety; Self-medication.

The increased prevalence of pregnant women taking medications, including over-the-counter (OTC) medications presents a challenge to nurses providing care to women of childbearing age. Approximately 90% of women take at least one medication and 50% take at least four medications during some point in pregnancy (Schonfeld, Schmid, Brown, Amoura, & Gordon, 2013). Whether a healthcare provider prescribes a medication, or it is OTC, medications can pose a threat not only to the pregnant woman, but also to the fetus due to potential teratogenicity. At least 10% of birth defects were noted to be a result of maternal drug exposure and thus a catalyst for establishing pregnancy risk categories (Black & Hill, 2003; Wilson, 1977). More than 50% of pregnancies are unplanned and inadvertent administration of certain medications can jeopardize the outcome of an unborn child before a woman realizes that she is pregnant (Parisi, Spong, Zajicek, & Guttmacher, 2011).

Although some medications are well documented to be safe for the pregnant woman, more studies need to be conducted to generate a robust list of safe and effective medications for the woman and fetus. The lack of safety data to inform appropriate prescribing of medications during pregnancy is related to safety, financial incentives, and ethics (Sheffield et al., 2014). Safety is the primary concern addressed by researchers and pharmaceutical companies for conducting pharmacokinetic and pharmacodynamic studies in pregnant women (Sheffield et al.). These concerns are shared by institutional review boards and are the basis for ethical arguments (Sheffield et al.). The lack of a federal mandate does not impose a financial incentive (Sheffield et al.). Most information gleaned about the effects of medications on pregnant mothers and the fetus has been obtained from pregnancy registries, case studies, case reports, animal studies, extensive discussions with mothers during and after pregnancies, and children and infants with birth defects (Addis, Sharabi, & Bonati, 2000; Schaefer, Peters, & Miller, 2007; Schonfeld et al., 2013).

Informed nurses who understand the maternal-fetal risk with medications, classification and safety of OTC drugs, and limitation in research can help to decrease risk and improve patient education. We outline the safety categories for medications related to pregnancy, review common OTC medications that a pregnant woman may consider, and address therapeutic guidance for the nurses who assist in the care of the pregnant population.

Background

In 1979, the United States Food and Drug Administration (US FDA, 1979) developed a classification system for pregnant women to categorize the level of safety associated with medications and their effects on fetal development and outcomes. There are five categories that were created and still used in most healthcare settings. The categories are A, B, C, D, and X (US FDA, 1979).

Category A shows no risk to the fetus based on the result of human studies. Category B indicates no evidence of fetal risk in humans. There are no human studies to confirm identified risks in animal-reproduction studies or completed animal studies show no harm. The assignment of Category C has two indications; (1) limited or no research has been conducted about use in pregnancy, and (2) animal studies identified adverse fetal risks (Brucker & King, 2017). The dual indications have resulted in the majority (60–70%) of US FDA-approved drugs being assigned to this category (Brucker & King). Category D indicates fetal risks are evident in human studies. Use of these medications may be necessary for the pregnant woman despite the risk to the fetus. Category X indicates there is evidence based on human experience showing fetal harm or animal and human studies demonstrated fetal abnormalities. The risk of use clearly outweighs any medicinal benefits and therefore, the drug is contraindicated (Wilmer, Chai, & Kroumpouzos, 2016).

Although these categories were the standard over the past 30-plus years, concerns still exist with the ambiguity of some of the categories. In response to concerns identified by the Teratology Society Public Affairs Committee, the US FDA made major changes in the way healthcare should manage medication administration in the pregnant population (Public Affairs Committee of the Teratology Society, 2007). The challenge has always been how healthcare providers interpret the pregnancy categories when counseling pregnant women on benefits versus specific risks. In December 2014, the US FDA developed the Pregnancy and Lactation Labeling Rule that replaces the letter categories with a narrative-based labeling requirement (US FDA, 2016). The new label consists of three subsections—pregnancy (including labor and delivery), lactation (including nursing mothers), and females and males of reproductive potential (US FDA, 2014b). The pregnancy subsection includes a risk summary, clinical considerations, and available safety-related information obtained from pregnancy exposure registries (US FDA, 2014b). The lactation subsection includes details about the amount of drug transferred into breastmilk and the potential for adverse effects on the breastfeeding infant (US FDA, 2014b). The newest category, females and males of reproductive potential, includes "relevant information when pregnancy testing or contraception is required or recommended before, during, or after drug therapy or when there are human or animal data that suggest drug-associated fertility effects" (US FDA, 2014b, p. 3).

The Pregnancy and Lactation Labeling Rule ensures that prescription drugs include the following subcategories: the pregnancy exposure registry, risk summary, clinical considerations, and data (US FDA, 2016). All four sections of the Pregnancy and Lactation Labeling Rule allow healthcare providers and patients to obtain a global view of medications. The new labeling format was effective June 30, 2015 (US FDA, 2014a). A phased approach will be used for drugs approved on or after June 30, 2001 (US FDA, 2014a). Drugs approved prior to June 30, 2001 are not required to use the Pregnancy and Lactation Labeling Rule; however, must remove the "old" pregnancy category by June 29, 2018 (US FDA, 2017). The Pregnancy and Lactation Labeling Rule does not apply to OTC medication; only prescription medications (US FDA, 2014a).

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Informed nurses who understand the increased fetal risk associated with how the physiologic changes of pregnancy affects the pharmacokinetics of over-the-counter medications can help to decrease risk and improve patient education.

Medication safety in pregnancy has a few unique challenges. "The physiology of pregnancy affects the pharmacokinetics of medications used and certain medications can reach the fetus and cause harm" (Sachdeva, Patel, & Patel, 2009, p. 1). Preexisting medical conditions prompt a thorough evaluation to determine the most appropriate medical management during pregnancy. In many instances, the management plan may remain the same. However, the associated fetal risk may prompt a management plan change or closer surveillance of fetal growth. The "safety profile of some medications may change according to the gestational age of the fetus" (Black & Hill, 2003, p. 2517).

Use of OTC medications is a common concern among pregnant women; therefore, it is important for nurses to recognize their role in patient counseling and medication safety. Accessibility, affordability, and convenience of OTC medications warrant discussion of common categories queried and used by pregnant women—antipyretics and analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), nasal topicals and antihistamines, decongestants and expectorants, antacids and antidiarrheals, and topicals (dermatological).

Antipyretics & Analgesics

Acetaminophen

Over-the-counter use of acetaminophen (Tylenol), whether taken alone or in readily available combination drugs, is common during pregnancy (Servey & Chang, 2014). The National Births Defects Prevention Study found no increased risk of birth defects with in-utero exposure to acetaminophen during the first trimester and it may be protective against birth defects if taken by the mother for febrile illness (Feldkamp, Meyer, Krikov, & Botto, 2010). When taken for febrile management, a protective factor has been demonstrated, as untreated febrile illness can lead to various cranial and facial defects (Servey & Chang). See Table 1. The timing of taking acetaminophen, whether during the first or second trimester, has limited evidence to possible defects, little is known about the impact of consumption on the fetus during the third trimester (Servey & Chang). Ongoing studies evaluating the potential impact of frequent maternal use of acetaminophen and risk of subsequent wheezing and asthma in the infant have demonstrated a potential relationship (Perzanowski et al., 2010). Recent cohort studies evaluating the relationship between consumption of acetaminophen and risk of attention-deficit hyperactivity and other kinetic disorders seem to demonstrate some risk. Stergiakouli, Thapar, and Davey Smith (2016) reviewed data from a prospective birth cohort of 7,796 mothers and found an association of prenatal exposure of acetaminophen to an increased risk of multiple behavioral difficulties. Parker et al. (2017) suggest a possible relationship between oxidative stress, inflammation, and acetaminophen exposure after birth to the development of autism. They recommend an "acetaminophen withdrawal study" as a viable option to explore (Parker et al.). Therefore, recommend use of acetaminophen with caution and when medically necessary such as with fever (Andrade, 2016; Servey & Chang).

Nonsteroidal Anti-Inflammatory Drugs

The risks of NSAIDs (Aspirin, Motrin, Advil) are dependent upon the medication, dosage, gestational age, and duration of treatment. Currently, the US FDA (2016) recommends a risk–benefit analysis using prescribed NSAIDs due to the increased risk of miscarriage in the first half of pregnancy. Antonucci et al. (2012) associated NSAID use in early pregnancy to increased risks of miscarriage and birth defects, but they did not define the term "early pregnancy" by gestational age. However, "exposure to NSAIDs after 30 weeks' gestation is associated with an increased risk of premature closure of the fetal ductus arteriosus and oligohydramnios" (Antonucci et al., p. 474).

TABLE 1. Antipyretics & Analgesics in Pregnancy

Drug/Drug Category	Old FDA Category[a] Current Pregnancy and Lactation Labeling Rule Labeling[b]	Risks/Side Effects
Acetaminophen	B/B/B Acetaminophen (Paracetamol; Tylenol; FeverAll, etc.) Crosses the placenta No increased risk for teratogenic effects observed Not associated with increased risk of miscarriage or spontaneous abortion Frequent use during pregnancy may be related to wheezing or asthma in early childhood	• Skin rash, anaphylaxis
Nonsteroidal anti-inflammatory drugs	B/B/D Crosses the placenta; Class impact: dependent on dose, gestational age, duration Diclofenac (Voltaren): avoid use starting at 30-weeks' gestation Birth defects have been noted after exposure to some NSAIDs; however, data conflicting Premature closure of ductus arteriosus in the fetus Nonteratogenic effects: review pregnancy considerations for data Mild rheumatoid arthritis: may be ok for early flairs; avoid late usage Avoid third trimester: premature closure patent arteriosus in the fetus Migraine: other treatments preferred Naproxen (Aleve, Naprosyn): avoid use starting at 30-weeks' gestation Data conflicting on teratogenic effects Nonteratogenic effects: review pregnancy considerations for data Ibuprofen (Advil, Motrin): Ibuprofen: may be associated with low birthweight and increased asthma risk of fetus Diclofenac/Naproxen: crosses placenta; may increase risk of early spontaneous abortion	• Elevated blood pressure, headache, dizziness, medication allergy, gastrointestinal distress, renal insufficiency • Increased risk of acute kidney injury, HELLP syndrome, anemia, etc. • Edema, elevated blood pressure, dizziness, drowsiness, allergic reaction, gastrointestinal distress, renal insufficiency, elevated liver enzymes • Edema, dizziness, headache, rash, allergic reaction, fluid retention, gastrointestinal distress

[a]X/X/X indicates pregnancy trimester as per FDA drug classifications

[b]Pregnancy and Lactation Labeling Rule available recommendations

Source: Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online (2018).

Several sources, including the US FDA (2015), advise use with caution in the first and second trimester, and to avoid in the third trimester (Antonucci et al., 2012; Bloor & Paech, 2013). Bloor and Paech estimate prevalence of use from preconception through the first trimester, as 2.9% to 18%. The ability of medications, such as diclofenac and naproxen, to cross the placenta in the first trimester highlights the potential for increased risk of spontaneous abortion. Case-control and cohort studies have demonstrated an increased risk of spontaneous abortion associated with NSAID use during early pregnancy (Bloor & Paech).

Nezvalová-Henriksen, Spigset, and Nordeng (2013) were unable to associate NSAID use with infant survival, congenital malformation, or structural heart defects among a study population of 6,500 pregnant women. However, there was an association of ibuprofen use in the second trimester with low birthweight and an association of ibuprofen use in the second and third trimester with asthma in 18-month-old children (Nezvalová-Henriksen et al.). Maternal use of diclofenac in the second trimester was associated with low birthweight. Use of diclofenac (Cambia) in the third trimester was significantly associated with maternal vaginal bleeding (Nezvalová-Henriksen et al.).

Nonsteroidal inflammatory drugs were identified as a causative factor for acute kidney injury in pregnancy (Wiles & Banerjee, 2016). The development of acute kidney injury in pregnancy is a serious complication and requires early identification and timely intervention to minimize perinatal complications. The best safety profile has been associated with ibuprofen [Motrin, Advil] (Wiles & Banerjee). However, management of medical

complaints that warrant ibuprofen use at the lowest effective dose and discontinuation at the earliest opportunity are recommended (Wiles & Banerjee). In the presence of preeclampsia, volume depletion, acute kidney injury, and chronic kidney disease, NSAIDs are not recommended (Wiles & Banerjee).

Nasal Topicals and Antihistamines

Hormonal changes cause vascular engorgement and increased mucous production in the nose; especially, in the third trimester when plasma volume and fluid shifts cause more nasal discharge and nasal blockage (Shiny Sherlie & Varghese, 2014). The complaint of nasal congestion often interferes with sleep and appetite. Patients may be advised to raise the head of the bed at least 30 degrees and participate in light physical activity to increase nostril patency (Pray & Pray, 2014). Saline lavage using an isotonic saline product (Simply Saline Nasal Relief Spray) and external nasal dilators (Breathe Right Nasal Strips) are additional treatment options to facilitate air movement (Pray & Pray).

Pharmacologic options may include topical intranasal decongestants (Afrin, NasalCrom), intranasal corticosteroids (Nasacort Allergy 24HR), and intranasal anticholinergics [Atrovent] (Namazy & Schatz, 2014). See Table 2. Topical intranasal decongestants containing oxymetazoline (Afrin) are strongly discouraged due to the potential complication of rhinitis medicamentosa (Namazy & Schatz). Oxymetazoline and xylometazoline are well absorbed from the nasal mucosa to produce systemic effects; however, there is no knowledge regarding fetal effects. Yau, Mitchell, Lin, Werler, and Hernández-Díaz (2013) conducted the first study exploring the risks associated with first-trimester intranasal decongestants. The risk of pyloric stenosis and tracheoesophageal fistula was associated with first-trimester intranasal decongestants; oxymetazoline or xylometazoline (Yau et al.). There was an association between second-trimester exposure to oxymetazoline and renal collecting system anomalies (Yau et al.).

The only OTC option for an intranasal corticosteroid is Nasacort Allergy 24HR. There have been no studies on its use among pregnant women; thus, a risk–benefit analysis should be conducted by the individual healthcare provider. Likewise, there are no adequate or well-controlled studies regarding intranasal anticholinergics (Atrovent) among pregnant women; and, healthcare providers should decide the treatment plan on an individualized basis.

Use of antihistamines for the management of allergic rhinitis and nausea is common in pregnant women and readily available as OTC preparations (Servey & Chang, 2014). Oral or systemic absorption of antihistamines is generally considered safe with both first- and second-generation antihistamines and are readily available and inexpensive. Oral ingestion may be less effective than topical in addressing the nasal symptoms and women should be educated to start with second-generation options due to side effect profile (Servey & Chang). Side effects of first-generation antihistamines include sedation, performance impairment, and anticholinergic effects and is generally the reason behind adoption of second-generation antihistamines as a reasonable choice (Kar, Krishnan, Preetha, & Mohankar, 2012). According to recent studies, there is, however, no significant risk to fetal malformations with first-generation antihistamines and they are considered safe in pregnancy. For example, chlorpheniramine (Chlor-Tabs) is recommended as the antihistamine of choice for pregnant women (American College of Obstetricians and Gynecologists [ACOG] & American College of Allergy, Asthma and Immunology [ACAAI], 2000).

Second-generation antihistamines such as loratadine (Claritin) and cetirizine (Zyrtec) are considered the second-generation drugs of choice OTC. Extensive studies have not identified any teratogenic effects to date (ACOG & ACAAI, 2000). Kar et al. (2012) recommend avoidance of second-generation drugs in early pregnancy during organogenesis. Fexofenadine (Allegra), a second-generation antihistamine has been associated with early pregnancy loss in animal studies, but this has not been found in humans (Servey & Chang, 2014). Fexofenadine is a metabolite of terfenadine that was removed from the market in 1998 due to cardiotoxicity; however, there was no evidence of congenital malformations on safety of terfenadine in human pregnancy (Servey & Chang).

Oral Decongestants and Expectorants

"Nearly one in four pregnant women seek relief of nasal congestion caused by upper respiratory infection, allergic rhinitis, or pregnancy rhinitis" (Servey & Chang, 2014, p. 549). Pseudoephedrine (Sudafed) and phenylephrine (Sudafed PE) are the most common oral decongestants in OTC medications. The overall safety of oral and intranasal decongestants has not been established. Decongestant use in the first trimester has been associated with gastroschisis, small intestinal atresia, and hemifacial macrosomia.

Pseudoephedrine, guaifenesin (Mucinex), and dextromethorphan (Robitussin, Delsym) are the most commonly used cold medications taken during pregnancy (Black & Hill, 2003). "Among the cold, allergy, and cough medications, pseudoephedrine and guaifenesin use increased from pre-pregnancy to the second trimester, then decreased in the third trimester" (Werler, Mitchell, Hernandez-Diaz, Honein, & the National Birth Defects Prevention Study, 2005). Decongestants have not been shown to improve nasal itching, sneezing, or rhinorrhea. Yawn and Knudtson, (2007, p. 296) reported short-term benefits using intranasal decongestants "for nasal congestion that interferes with sleep, but pregnant women should reserve their use until after the first trimester and avoid them during labor." Inhaled decongestants, such as xylometazoline (Otrivin) and oxymetazoline (Afrin, Zicam), are available OTC. The extent of systematic absorption is unknown, and the nurse should be prepared to discuss the limitations in research and recommendations on these drugs in efficacy and safety.

There is little research on use of expectorants during pregnancy. Guaifenesin was weakly associated with neural tube defects and inguinal hernias. Dextromethorphan, a cough suppressant, is associated with teratogenic effects

TABLE 2. Nasal Topicals & Antihistamines

Drug Category	Old FDA Category[a] Current Pregnancy and Lactation Labeling Rule Labeling[b]	Class Risks/Side Effects
Nasal topicals	B/B/B Cromolyn (NasalCrom) Topicals generally considered safe, first-line Cromolyn (NasalCrom): considered safe for topical use C/C/C Glucocorticoid Nasal Topical Fluticasone propionate (Flonase OTC): adverse events seen in animal studies (limited data on intranasal use) Intranasal Decongestant: Oxymetazoline (Claritin Allergic Decongestant, Dristan Nasal, Drixoral Nasal): adverse events noted in first trimester with high doses; not preferred for treatment of rhinitis in pregnancy	• Topical skin irritation most frequent reported side effect • Short-term use only; dependence and rebound congestion with prolonged use
Antihistamines	B/B/B First-Generation Antihistamines: generally considered safe—see class risks and side effects. Chlorpheniramine (Aller-Chlor, Allergy Relief OTC, Chlor-Trimeton) B/B/B Second-Generation Antihistamines Loratadine (Claritin, Alavert): no associated risk of fetal malformations. Generally considered safe. Cetirizine (Zyrtec): no associated risk of fetal malformations. Generally considered safe. C/C/C Fexofenadine (Allegra): limited information available, animal studies indicate early pregnancy loss. Fexofenadine: metabolite of terbinafine, removed from the market due to cardiotoxicity. Providers may want to discourage use in pregnant women.	• First-generation antihistamines are generally avoided due to side effects of class; sedation, performance impairment, dizziness, excitability, urinary retention, headache, for example • Sedation, headache, drowsiness, and fatigue potential side effects for both Loratadine and Cetirizine • Headache, drowsiness, fatigue, diarrhea, dyspepsia

[a]X/X/X indicates pregnancy trimester as per FDA drug classifications

[b]Pregnancy and Lactation Labeling Rule available recommendations

Source: Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online (2018).

in chicken embryos; however, a human epidemiological study did not demonstrate an increased risk of congenital malformation again further highlighting the need to recommend with caution and use for the shortest necessary timeframe (Servey & Chang, 2014).

Antacids and Antidiarrheals

In pregnant women, almost 80% experienced some symptoms of gastrointestinal distress by the end of the third trimester (Kahrilas, 2018; Servey & Chang, 2014). First-line management of reflux type symptoms includes avoidance and prevention. Nurses should encourage pregnant women to avoid food and drinks most likely to trigger symptoms such as high acid foods, fried and spicy foods, avoid lying flat after eating, and elevation of the head of the bed and dietary management (Kahrilas). If first-line management fails to resolve symptoms, then OTC management with antacids containing calcium and magnesium (Tums, Mylanta) may be considered first-line and safe in pregnancy. Antacids with aluminum taken at high dose can lead to neurotoxicity and recommendations for nurses include education to read labels and daily dosages (Mahadevan & Kane, 2006; Servey & Chang).

Second-line management may include sucralfate, available OTC as sucralfate (Carafate). This is not readily absorbed and does not appear to have any adverse effects in utero during the first trimester (Kahrilas, 2018; Mahadevan & Kane, 2006). It is important for nurses to know this medication works by protecting the gastric mucosa. If first-line options of avoidance fail in conjunction with sucralfate, then women may opt to try other options for acid-reducing therapy and symptom management, such as histamine receptor antagonist (H2RAs), ranitidine [Zantac] (Kahrilas; Mahadevan & Kane). Histamine receptor antagonist

blockers have been used safely in all trimesters of pregnancy and there are no known teratogenic effects (Kahrilas; Servey & Chang, 2014). Proton pump inhibitors (PPIs) such as omeprazole (Prilosec), lansoprazole (Prevacid), or pantoprazole (Protonix) are also considered a safe second-line option, have been widely used in pregnancy, and have generally good short-term use safety profiles (Katz, Gerson, & Vela, 2013; Kahrilas; Servey & Chang). However, the majority of studies determining safety of PPI therapy for the management of reflux symptoms in pregnant women involve the first available PPI; omeprazole.

Loperamide (Imodium) is a readily available OTC drug that is commonly used for noninfectious diarrhea. The goal of managing diarrheal episodes in a pregnant woman is to identify the etiology, restore or maintain hydration status, and avoid a food-based response from a nursing perspective (Mahadevan & Kane, 2006). A medical condition of infectious diarrhea during pregnancy should be managed by a healthcare provider. The nurse may provide education on strategies to maintain adequate hydration. Although loperamide is an OTC medication, the decision to use is based upon the presence of debilitating symptoms and with provider recommendation (Kallen, Nilsson, & Otterblad Olausson, 2008; Mahadevan & Kane).

For pregnant women with constipation, it is recommended to avoid OTC medications that contain bismuth, mineral oil, and castor oil (Servey & Chang, 2014). Polyethylene glycol 3350, commonly marketed as Miralax®, is considered a safe and readily available alterative for the management of constipation (Mahadevan & Kane, 2006). This medication is minimally absorbed, and there is little research on this drug related to in-utero effects (Mahadevan & Kane; Servey & Chang). The nurse can assist with preventive management of constipation in educating on hydration needs, dietary sources of fiber, and preventative measures.

Antifungals and Topicals

Common skin conditions during pregnancy can be preexisting, hormone-related, and pregnancy-specific. Preexisting (i.e., atopic dermatitis, psoriasis, and fungal infections) and pregnancy-specific conditions (i.e., pruritic urticarial papules and plaques of pregnancy, prurigo of pregnancy, and intrahepatic cholestasis of pregnancy) require a medical evaluation for diagnosis and appropriate treatment and the nurse can assist with ensuring appropriate evaluation, diagnosis, and management.

Melasma, also known as "the mask of pregnancy" occurs in up to 50% of pregnant women (Ogbechie-Godec & Elbuluk, 2017). Exposure to sunlight and other ultraviolet radiation causes the condition to worsen; therefore, recommendations to prevent development or exacerbation include high-potency broad-spectrum sunscreens and avoiding excessive exposure to sunlight is an appropriate nursing intervention (Tunzi & Gray, 2007).

Topical steroids are the most common medication used to treat skin conditions; however, little clarity exists about safety or potential harm they may pose during pregnancy. A systematic review of 14 observational studies to examine the safety of topical steroids in pregnancy concluded no association between maternal use of topical steroids of any potency and birth mode with congenital malformations, preterm births, or low Apgar scores (Chi, Wang, & Kirtschig, 2016). Nurses should provide adequate education and ensure appropriate diagnosis and management for skin conditions that may require this treatment.

Antifungal agents, such as clotrimazole (Desenex), miconazole (Monistat 3), and tioconazole (Vagistat-1), are the most common medications available OTC. One of the largest population-based, case-control studies exploring the teratogenicity of clotrimazole did not conclude an association with congenital malformations (Black & Hill, 2003). The authors recommend clotrimazole as "probably" safe in the first trimester and safe in the second and third trimesters (Black & Hill). "Several small trials have indicated butoconazole and miconazole are likely to be safe during the second and third trimesters" (Black & Hill, p. 2522). There are no sufficient data on the safety of tioconazole in pregnancy. Based on this limited data, the nurse should educate the woman to ensure appropriate diagnosis, risk and benefit of treatment, and appropriate referrals as needed.

Insect Repellents

The Zika Virus and other mosquito-borne diseases sparked concern and raised questions about the safe and effective use of insect repellents during pregnancy and lactation. The Centers for Disease Control and Prevention (CDC, 2018b) recommends several Environmental Protection Agency (EPA)-registered insect repellents to prevent mosquito bites, including diethyltoluamide (DEET [Off!]), picaridin (Repel), and IR3535 (Avon Skin-So-Soft Bug Guard Plus Towelettes). Since 1950, DEET has been marketed worldwide as an insect repellent (Wylie, Hauptman, Woolf, & Goldman, 2016). There are limited data on the effects of DEET in pregnant women. To date, no studies have been conducted among women in the first trimester when most birth defects occur. Safe use of DEET is recommended at concentrations of 30% or less, during pregnancy or lactation (Wylie et al.). Newer products, Picaridin and IR3535, have been deemed safe for use among pregnant women. Efficacy studies have demonstrated no significant difference when picaridin or IR3535 was compared with DEET (Environmental Working Group, 2018). Oil of lemon eucalyptus, or para-menthane-diol, is the only plant-based repellent recommended by the CDC with comparable effectiveness to DEET. Para-menthane-diol is a synthesized version of oil of lemon eucalyptus. It is important to note "pure" oil of lemon eucalyptus has not been evaluated for safety and efficacy, and is not an EPA-registered insect repellent. Pregnant women should be cautioned that no repellent is 100% effective; therefore, additional precautions

TABLE 3. Recommendations for Repellent Use for Pregnant Women

Indication	Product	Percent Concentration
Zika virus	DEET	20–30%
	Picaridin	20%
Lyme disease	DEET	20–30%
	Picaridin	20%
	IR3535	20%
West Nile virus	DEET	7–30%
	Picaridin	10–20%
	IR3535	20%
Outdoor activities (Short time)	DEET	7–10%
	Picaridin	5–10%
All-day bug protection	DEET	7–10%
	Picaridin	5–10%
Sensitive skin or allergies	Picaridin	5–10%

Source: Environmental Working Group (2018).

Note. Products should always be used as directed.

are recommended. Table 3 lists product recommendations for use of insect repellents among pregnant women (Environmental Working Group).

Natural Supplements

Herbal and dietary supplements in the United States are not regulated by the US FDA; therefore, do not have the same safety and efficacy standards as pharmaceutical products. Despite the lack of data on safety of use during pregnancy, natural supplements are used by a significant portion of the US population for common primary care complaints or to simply maintain a healthy state (Gray & Rutledge, 2013). Studies have found that up to 6% of mothers use natural products during pregnancy (Louik, Gardiner, Kelley, & Mitchell, 2010). Use appears to increase with age and is also affected by geographic regions, most likely reflecting cultural acceptance of natural medicine use among particular populations (Louik et al.).

In a multinational, cross-sectional study, the largest group of contraindicated herbal supplement users were from the United States (Kennedy, Lupattelli, Koren, & Nordeng, 2016). Researchers were able to associate the following maternal factors with the use of contraindicated herbal supplements during pregnancy; housewife, university education, not using folic acid, and alcohol consumption (Kennedy et al.). Study participants indicated use of an herbal supplement was classified as safe for use in pregnancy; and, in many instances, the supplement was recommended by a healthcare provider (Kennedy et al.). "The paucity of human studies on herbal medicines safety in pregnancy stands in stark contrast to the widespread use of these products among pregnant women" (Kennedy et al., p. 8). Nurses and other healthcare professionals are encouraged to use reliable resources, such as the National Institutes of Health's Dietary Supplement Label Database (www.dsld.nlm.nih.gov) and the Natural Medicines Comprehensive Database (www.naturaldatabase.com) to obtain current safety-related information when natural supplements are used in pregnant or lactating women.

Sunscreens

Hormonal changes during pregnancy may increase the skin's sensitivity to ultraviolet (UV) rays. The effects of increased sun exposure are well known—skin cancer, premature aging, and hyperpigmentation (US FDA, 2018). Sunscreens are an effective OTC skin care product to prevent and minimize the damaging effects of UV rays (US FDA). During pregnancy, sunscreens with zinc oxide and titanium dioxide block damaging UV rays; they have been deemed safe and are the preferred agents (Krause et al., 2012; Ruszkiewicz et al., 2017). Advise pregnant women to avoid OTC products with oxybenzone and retinyl palmitate. Oxybenzone has been linked to allergies, disruption of hormones, and cell damage; and, retinyl palmitate is a vitamin A derivative (Krause et al.). Oral versions of vitamin A derivatives (Isotretinoin) have been demonstrated to be teratogenic (Krause et al.). It is less clear whether retinol topical products can have negative effects; and therefore, should be avoided as well (Krause et al.).

Clinical Implications

The decision to prescribe or recommend a medication for a pregnant woman is an everyday challenge for many healthcare providers and it is important for nurses to be aware of risks, benefits, and limitations of current literature. "Numerous medications have been used safely and effectively in pregnancy with minimal risk to the fetus and mother, although the decision to use them is not without apprehension" (Pernia & DeMaagd, 2016, p. 713). The purpose or intent of the Pregnancy and Lactation Labeling Rule is to provide the healthcare provider, whether physician, pharmacist, or nurse, with relevant data for critical decision-making when treating pregnant or lactating women, recommending medications, and offering accurate information. The new labeling allows for a more complete statement of the known risks based upon available data, including considerations of medical/disease factors, animal data put into context of human exposure, human data (upon availability), and explicitly states if no data are available. High use of OTC medications and the transition to the new prescription drug labeling highlight the critical need for nurses to be familiar with indications, risks, and benefits of all OTC and other medications administered during pregnancy. Limited data on OTC medications present challenges in providing accurate and timely advice to pregnant women and those of childbearing age about medication safety and potential risks. ✣

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Clinical Implications Table

Over-the-counter (OTC) medications are widely used during pregnancy; approximately 9 out 10 pregnant women take at least one OTC medication.
Nurses caring for pregnant women will likely be asked about safety of these types of drugs during pregnancy and should be able to provide current information and direct them to additional resources.
The information we offer here can be used as a source to seek more data on specific medications.
The CDC provides information about OTC medications during pregnancy and breastfeeding. Women can be referred to these CDC resources at this site: https://www.cdc.gov/pregnancy/meds/treatingfortwo/index.html

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The authors declare no conflicts of interest.

DOI:10.1097/NMC.0000000000000537

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