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Committee on Obstetric Practice

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Sulfonamides, Nitrofurantoin, and Risk of Birth Defects

ABSTRACT: The evidence regarding an association between the nitrofuran and sulfonamide classes of antibiotics and birth defects is mixed. As with all patients, antibiotics should be prescribed for pregnant women only for appropriate indications and for the shortest effective duration. During the second and third trimesters, sulfonamides and nitrofurantoins may continue to be used as first-line agents for the treatment and prevention of urinary tract infections and other infections caused by susceptible organisms. Prescribing sulfonamides or nitrofurantoin in the first trimester is still considered appropriate when no other suitable alternative antibiotics are available. Pregnant women should not be denied appropriate treatment for infections because untreated infections can commonly lead to serious maternal and fetal complications.

Because antibiotics are commonly prescribed in pregnancy, there is a considerable body of pharmacoepidemiologic data addressing the relationship of antibiotic exposure and birth defects. The debate surrounding this relationship was heightened in November 2009, with a new publication by Crider and colleagues (1). The goal of this Committee Opinion is to assess the current evidence regarding the use of certain specific antibiotics in pregnancy and their association with birth defects (1).

In 2009, Crider and colleagues published a population-based case–control study of the relationship between antibiotics and birth defects that used data from the National Birth Defects Prevention Study. In this study, two classes of antibiotics commonly used to treat urinary tract infections—1) nitrofuran derivatives and 2) sulfonamides—were found to be significantly associated with multiple birth defect categories. Although this was a large study, it has several significant limitations. First, it is subject to recall bias because women were asked about antibiotic use after pregnancy. Second, the prescription of antibiotics was not confirmed by the medical record; approximately 35% of patients could not recall the specific product name. Third, because this was an observational study, it is not possible to determine whether the birth defect was due to the antibiotic itself, the infection for which the antibiotic was prescribed, or some other confounding factor. Other studies examining the relationship between prenatal exposure to these antibiotics and birth defects have reported potential fetal risks, whereas other studies have not found such risks among other populations or when using different epidemiologic methods (2–8).

It is reassuring that commonly used antibiotics, namely, penicillins, erythromycin, cephalosporins, and a less commonly used group, the quinolones, were not associated with an increased risk of birth defects in the 2009 study (1). These findings are in agreement with many other studies also reporting no increased risk of birth defects associated with prenatal exposure to penicillin (9), ampicillin (10), augmentin (6), pivampicillin (11), cephalosporins (12–13), gentamicin (14), oxacillin (15), erythromycin (16), metronidazole (17), and quinolones (18–19).

Conclusion and Recommendations

Commonly used antibiotics, such as penicillins, erythromycin, and cephalosporins, have not been found to be associated with an increased risk of birth defects. However, the evidence regarding an association between the nitrofuran and sulfonamide classes of antibiotics and birth defects is mixed. As with all patients, antibiotics should be prescribed for pregnant women only for appropriate indications and for the shortest effective duration. In pregnancy, many urine cultures show bacterial contaminants that do not represent true infection. Thus, cultures showing mixed gram-positive bacteria, lactobacilli, and Staphylococcus species (other than *S saprophyticus*), may be presumed to be contaminants and not

treated. When selecting an antibiotic for a true infection during the first trimester of pregnancy (that is, during organogenesis), health care providers should consider and discuss with patients the benefits as well as the potential unknown risks of teratogenesis and maternal adverse reactions. Prescribing sulfonamides or nitrofurantoin in the first trimester is still considered appropriate when no other suitable alternative antibiotics are available. During the second and third trimesters, sulfonamides and nitrofurantoins may continue to be used as first-line agents for the treatment and prevention of urinary tract infections and other infections caused by susceptible organisms (8). Pregnant women should not be denied appropriate treatment for infections because untreated infections can commonly lead to serious maternal and fetal complications.

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