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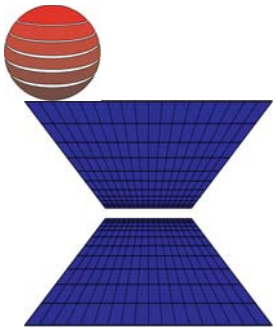
February 2012 "Drug Effects during Pregnancy & Lactation"



THIS MONTH "Drug Effects in Pregnancy & Lactation"

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Use of drugs during pregnancy & lactation is common, and must be taken cautiously. The goal of this lesson is to discuss common drugs & side effects that may arise during these times
This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-12-002-H01-P. Pharmacists completing this lesson by February 28, 2015 may receive full credit.**

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. List the routes through which drugs and nutrients cross the placenta.
2. Discuss the rate at which drugs penetrate the placental barriers.
3. Differentiate between the five categories of drugs as established by FDA based on the potential benefits & risks during pregnancy.
4. List the factors that affect drug transport into human milk.
5. Describe the risk from drugs taken while breastfeeding.

DRUG EFFECTS DURING PREGNANCY

The use of drugs during pregnancy is a common occurrence even though absolute safety has not been established. Many women become pregnant while suffering from chronic illnesses, while others may develop an acute condition during pregnancy. It has been estimated that half of all pregnancies in the U.S. may be unplanned; thus, exposure of fetus to medications, including OTCs, may occur before realization. The adverse effects of drugs depend to a large extent on the stage of pregnancy. The risk of causing harm to the fetus is highest in early pregnancy when major organs of the body are being formed. The physiology of the body of a pregnant woman undergoes gradual changes that may influence drug absorption, distribution, metabolism and excretion. Additionally, weight gain of approximately 25 to 30 pounds. may occur due to increased blood volume, accumulation of interstitial fluid, increase in uterine and breast size, placental growth, and increased fat deposition. Furthermore, pregnancy is accompanied by an increase in the requirements for nutrients, energy and protein. The nutritional needs should be assessed early in prenatal care. A balanced diet that provides the needed vitamins and minerals should be attained.

During its various stages, pregnancy produces symptoms that if treated with medications are capable of crossing the placental barrier and may produce teratogenic effects. The tragic effects of thalidomide and diethylstilbestrol are vivid examples. Drugs and nutrients cross the placenta via:

1. **Simple diffusion**
2. **Facilitated diffusion**
3. **Active transport, and**
4. **Pinocytosis**—-(A process of taking in fluid together with its contents into the cell by forming narrow channels through its membrane that pinch off into vesicles, and fuse with lysosomes that hydrolyze or break down contents).

The rate at which drugs penetrate the placenta depends on:

1. The **molecular weight of the drug**. Drugs having low molecular weight tend to diffuse into the placenta at a rate faster than those with higher molecular weight. Thus, many drugs can cross the placenta and reach the fetus, but usually in small concentration.
2. **Lipid solubility**. Lipid soluble drugs are capable of crossing the placenta faster than water soluble drugs.
3. **Ionization**. Likewise, non-ionized molecules are transferred rapidly into the mother's circulation, as well as that of the fetus. Ionized molecules at physiologic pH have poor ability to diffuse. However, weak acids and bases with pKa between 4.3 and 8.5 reach the fetus very quickly.
4. **Protein binding**. Only free molecules in circulation can cross the placenta. Protein bound drugs are incapable of reaching the placenta.
5. **Placental and uterine blood flow**. The increase in placental and uterine blood flow tends to increase the transfer of medication from blood into the placenta.

TERATOGENICITY

Teratogenicity is the ability to cause fetal malformation, birth defects or developmental anomalies in the fetus. Things such as viruses, chemicals, and radiation, that cause teratogenicity are known as teratogens. The mechanism of teratogenicity is usually unknown. The study of teratogenicity is difficult to pursue due to ethical issues that prevent exposing a pregnant woman to a substance that potentially can be dangerous. Animal tests do not give a true picture of the extent of teratogenicity in humans, and the reverse is also true. A number of drugs that cause fetal malformations in animals fail to give similar results in humans. For example, corticosteroid compounds are teratogens in animals but not necessarily in humans. Drug manufacturers are reluctant to engage in efficacy and safety studies during pregnancy due to the current ethical, regulatory and legal issues. Even though animal studies have provided a vast wealth of information concerning teratogenicity of drugs, the conclusion of these studies cannot always be extrapolated from one species to another as from animals to humans. Thalidomide was safely tested in some animals but proved to be a teratogen in humans and rabbits. The following are examples of drugs with proven teratogenic effect: **methotrexate, ACE inhibitors, antineoplastics, antithyroids, barbiturates, carbamazepine, cocaine, diethylstilbestrol, ethanol in excessive quantities, lithium, phenytoin, retinoids, tetracycline and thalidomide**.

In 1975 the FDA established the following five categories of drugs based on the potential benefits and risks for a pregnant woman and fetus.

Category A: Indicates drugs for which well-controlled studies in pregnant women have failed to show a risk to the fetus. Even though one cannot entirely rule out a risk, it is assured that when a drug is placed in this category, its use during pregnancy is relatively safe.

Category B: Indicates drugs that show no evidence of risk to humans. Either animal studies failed to demonstrate a fetal risk in these animals, and there are no adequate studies in women; or animal studies have shown some fetal risk that has not been demonstrated in humans.

Category C: This category indicates that risk cannot be ruled out as no adequate animal or human studies have been conducted, or adverse fetal effects have been demonstrated in animals, but studies in humans are lacking.

Category D: It refers to drugs that show evidence of risk to the human fetus, but the benefits may justify the risks in certain cases as in life-threatening disorders or in diseases for which safer drugs cannot be used or are ineffective.

Category X: It refers to drugs in which studies in human and animals have shown fetal risk that clearly outweighs any possible benefits.

Drug manufacturers in the US use a disclaimer statement in the drug package inserts indicating that the safe use of this drug in pregnancy has not been established and should be used only if the anticipated benefits outweigh the potential risks to the fetus.

The following are examples of drugs with proven teratogenicity:

Androgens: Masculinization of female fetus.

Buslfan, chlorambucil, cyclophosphamide, mechlorethamine: Growth retardation, cleft palate, cardiac and other defects.

Carbamazepine: Developmental delay.

Cocaine: Microcephaly and neurobehavioral abnormalities.

Coumarine derivatives: Fetal warfarin syndrome.

Diethylstilbestrol: Vaginal adenosis and clear cell carcinoma in female offspring. In male offspring, hypogo-

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Total	2700	2700
Percent Paid and/or Requested Circulation	100%	100%

nadism and diminished spermatogenesis may occur.

Isotretinoin: Spontaneous abortion, micro/hydrocephaly, deformation of ear, face, heart and limbs.

Lithium: Increased risk of Ebstein anomaly (congenital condition of the heart—- symptoms of which are fatigue, palpitation, and dyspnea).

Misoprostol: Limb reduction defects.

Penicillamine: Hyperflexibility of joints.

Phenytoin: Fetal hydantoin syndrome.

Progestins: masculinization of female fetus.

Smoking: Placental lesions, increased neonatal morbidity and mortality.

Streptomycin: Hearing impairment.

Tetracycline: Discoloration of deciduous teeth. Effects may be seen from four months of gestation on.

Thalidomide: Limb malformation, congenital heart defects and renal malformation.

Valproate: CNS and cardiac defects, facial changes.

Vitamin D: Large doses of Vitamin D may cause supervalvular aortic stenosis and elfin faces.

COMMON DISORDERS IN PREGNANCY—-DRUGS USED IN TREATMENT

1. Anemia

The majority of women develop some degree of iron deficiency during pregnancy. Additionally, folic acid deficiency could contribute to anemia. Well-balanced diet is important for nourishment of mother and fetus. Meat, fish, dairy products, beans and peas are good sources of protein. Eggs, liver, enriched bread or cereal and green vegetables are good sources for iron. The intake of vitamins, iron and folic acid is helpful in preventing anemia.

2. Nausea and Vomiting

The majority of pregnant women experience nausea and vomiting. It usually begins after 4 to 8 weeks of gestation and typically disappears by the sixteenth week. These symptoms are mild, unpleasant, and usually not harmful. Hyperemesis gravidarum occurs in 10% of women and could lead to dehydration, electrolyte imbalance and metabolic acidosis. The exact mechanism that triggers nausea and vomiting is not clearly understood. It is believed that the increased plasma concentration of chorionic gonadotropin hormone and progesterone play a role in causing these symptoms. Non-pharmacologic measures such as eating a few crackers upon awakening as well as small frequent meals high in carbohydrates or protein may reduce the intensity of nausea and vomiting. Keeping the stomach empty may aggravate the problem. Avoidance of spicy food, noxious odors, and fatty food is recommended. If such measures fail to provide relief, then the use of drugs may be warranted. Antiemetics such as meclizine, dimenhydrinate, cyclizine and certain phenothiazines have been used. Meclizine has been shown to be teratogenic in animals, but apparently not in humans. Dimenhydrinate appears not to cause fetal malformation. Prochlorperazine has been linked to increased risk of cardiovascular abnormalities. Even though meclizine and promethazine appear to have no fetal effects in humans, their use during the last weeks of pregnancy should be avoided.

3. Gastrointestinal Reflux Disease (GERD)

GERD often occurs in the third trimester and affects about 25% of pregnant women. It is due to relaxation of the esophageal sphincter allowing gastrointestinal fluid to re-enter the lower portion of the esophagus. Antacids that are available as OTC drugs may provide symptomatic relief. The use of aluminum, magnesium and calcium salts is believed to be safe during the last two trimesters. Sodium bicarbonate should not be used.

4. Constipation

Constipation during pregnancy may occur due to decreased GI motility, elevation of estrogen and progesterone levels, decreased activity and the intake of iron. Bulk forming laxatives and stool softeners are recommended because of their safety and efficacy. Irritant laxatives should be avoided.

5. Backache

Backaches which range from mild to severe may occur due to relaxation of ligaments of joints and pelvis to allow expansion during delivery. Furthermore, the change in center of balance that results from growth of the uterus and fetus can alter posture. Acetaminophen and ibuprofen are often used.

6. Acne

A large number of pregnant women may experience an outbreak of acne which may be due to hormone imbal-

ance. It usually disappears after delivery. Topical treatment using erythromycin, clindamycin, tretinoin and benzoyl peroxide are used. The systemic use of isotretinoin is contraindicated due to its teratogenic potential.

7. Hemorrhoids

Hemorrhoids appear during pregnancy due to pressure that the enlarged uterus exerts on the middle and inferior hemorrhoidal vessels. The increased blood volume results in venous dilation and congestion. Hemorrhoids trigger itching, burning, pain and occasional rectal bleeding. Hemorrhoids may enlarge and protrude during infant delivery. Avoidance of constipation may alleviate this condition and its symptoms. Locally applied preparations containing anesthetics or anti-inflammatory agents, as well as practicing proper hygiene are helpful.

8. Urinary Tract Infections

Urinary tract infections among pregnant women are common due to the reduced flow of urine from the pressure on the ureter by the uterus and the fetus. Microorganisms may accumulate, resulting in infection.

9. Common Cold

Like the rest of the population, pregnant women are susceptible to common colds. Oral cold preparations usually contain a combination of two or more drugs such as analgesics, antihistamines and decongestants. The antihistamine brompheniramine should be avoided in the first trimester due to the risk of birth defects. Likewise, the use of sympathomimetic amines such as decongestants during the first trimester may cause malformation (examples are-club foot and inguinal hernia. Phenylpropanalamine may cause physical deformaties of the eye and ear when used in the first trimester, and thus use should be avoided. Nasal administration of decongestants will minimize systemic exposure of the fetus to these drugs. No potential risk has been reported following the use of the antitussive dextromethorphan and the expectorant guaifenesin. The use of iodides as expectorants should be avoided, since they may cause goiter in the fetus.

POTENTIALLY HARMFUL CHEMICALS TO FETUS

Tobacco: It has been shown that smoking may result in increased fetal, neonatal and infant mortality, low birth weight as well as complications of pregnancy. The harmful effect of smoking appears to be quantity-related. Smoking less than one pack a day resulted in 20% increase in risk of fetal mortality; whereas, smoking more than one pack a day caused an increase of 35%.

Alcohol: Consumption of alcohol during pregnancy can produce a group of fetal abnormalities known collectively as fetal alcohol syndrome (FAS). This is characterized by intrauterine and postnatal growth retardation, characteristic patterns of facial features such as short palpebral fissures, flattened maxilla, and cleft palate. Furthermore, CNS abnormalities such as microcephaly, behavioral abnormalities and mental retardation may be encountered. These anomalies usually appear in infants of women who, during pregnancy, consumed the equivalent of 2-3 ounces of absolute alcohol or 4-6 drinks of hard alcoholic beverages per day throughout the pregnancy, or with frequent binge drinking (6 or more drinks on one occasion per month). Moderate consumption (more than one ounce of absolute alcohol per week) may result in low birth weight, spontaneous abortion, and impaired motor and mental development. Consumption of one to two drinks daily may be associated with growth-retarded babies.

Opioids: It has been estimated that 0.2% of pregnant women are heroine or methadone users. Infants exposed to opioids encounter growth retardation as well as neonatal withdrawal syndrome characterized by irritability, GI disturbances, respiratory distress and seizures.

Cocaine: About 1% of pregnant women in the U.S. use cocaine. The most commonly encountered complications are placental abruption (separation of the placenta from its attachment to the uterus wall before the baby is delivered), premature delivery, and uterine rupture. Effects on the fetus include cerebral infarction, seizures and intrauterine growth retardation.

Caffeine: Coffee is one of the most commonly used drinks worldwide. Depending on the way it is brewed, 6 ounces of coffee may contain from 30 to 180 mg. of caffeine. In addition to coffee, caffeine is found in tea and chocolate. Conflicting results of studies concerning the effect of caffeine consumption on pregnant women have been reported. The relationship between low to moderate consumption of coffee and fetal abnormalities has not been firmly established. However, it has been postulated that low birth weight of infants and spontaneous abortion may be associated with caffeine intake. The FDA recommended that pregnant women refrain from ingestion of caffeine during pregnancy.

DRUG EFFECT ON LACTATION

Lactation is the process in which milk is produced by the mammary glands for a specific period of time needed

for a mother to feed her offspring. Its main purpose is to deliver nutrition and immunity to the newly born. In humans this process is also known as breastfeeding and nursing. Milk is the major source of the nourishment of infants before they are able to digest other foods. In late pregnancy and early lactation, milk is produced as colostrum which is a form of milk rich in immunoglobulin antibodies such as IgA, IgG, and IgM to defend the body of the newborn against infections and other diseases such as lowering the risk of Sudden Infant Death Syndrome (SIDS), decreased likelihood of contracting middle ear infections, common cold, flu, lower risk of childhood diabetes, decreased risk of asthma, dental problems, and obesity later in life. Health benefits to be gained by the breastfeeding mother include allowing the uterus to return to the size prior to pregnancy, minimizing post-partum bleeding, assisting the mother in retaining her pre-pregnancy weight and it may reduce the risk of breast cancer later on as the mother gets older.

Colostrum contains higher concentrations of protein and lower fat contents than milk. The nutrient contents of raw milk (not pasteurized and homogenized) from cattle vary from one species to another, but it contains abundant amounts of saturated fat (triglycerides containing only fatty acids), protein, calcium, and vitamin C. Cattle milk is usually slightly acidic. Starting from the second and third trimester, the body of the pregnant woman begins to produce hormones (progesterone, estrogens, prolactin, growth hormones, ACTH, TSH, and oxytocin) that stimulate the development of milk duct systems in the breast. The breast consists mainly of connective and fatty tissues to protect the milk producing apparatus. The nipple and the areola are the dark part of the breast located in the center. Milk is produced by the alveoli and from there it passes through the ducts to the nipple. The bumps on the areola and nipple are tubercles that produce sweat and sebum for lubrication of the nipple. The suckling effect of the infant stimulates the flow of milk through a process known as letdown. The sensation on the nipple produced by the sucking of the infant induces the pituitary gland to release oxytocin which upon reaching the breast causes the muscular tissue around the milk-producing alveoli to contract, thereby squeezing the milk to flow to the ducts and to the infant’s mouth. Breasts increase in size during lactation and pregnancy.

The composition of human milk is consistent and depends mainly on the mother’s food supply. However, the exact composition may change from day to day depending on food intake and the environment. Following baby delivery, breasts produce thin yellowish colostrum which often leaks from the breasts of pregnant women. Within 3 to 4 days, production of milk begins. Human milk consists of 7.1% carbohydrate (mainly lactose); 0.8 to 0.9% protein (casein, alpha-lactoalbumin, lactoferrin, IgA, lysozyme, and serum albumin); 4.5% fat (triglycerides of palmitic and oleic acids and trans fats such as faccenic acid and conjugated linoleic acid); and 0.2% minerals, such as calcium, phosphorus, sodium, potassium and chlorine. The World Health Organization (WHO) recommends breast feeding for the first six months following delivery. Occasional breastfeeding is recommended until the age of two. Breastfeeding and human breast milk are speculated to be healthiest for babies. However, this is not the case if the mother is taking certain drugs or is infected with diseases that may be transmitted to the infant.

All drugs taken by breastfeeding mothers are excreted into the milk and ultimately into the infant’s system. Normally, drugs taken during lactation enter the infant’s circulation in lesser amounts than during pregnancy. Studies indicate that the vast majority of drugs taken by breastfeeding mothers do not cause any significant damage to the infant. Thus, breastfeeding should not be discontinued when a mother is taking medications that do not pose a real harm to the infant. Some drugs may be contraindicated while others may be used with caution or upon the physician’s advice. The main objective is to minimize the amount of drugs ingested by the infant from breast milk. The safety of administering a drug should be evaluated in each patient’s case. All factors affecting drug excretion into milk such as dosage, duration of therapy, age of infant, amount of ingested milk, rate of absorption of drug by infant, possible interference with breastfeeding are potential for adverse effects.

Factors that play a role in determining the amount of drugs excreted in the mother’s milk include:

1. Characteristics of the Drug

Most drugs cross mammary alveolar membranes to some degree and reach milk by passive diffusion; others may pass through the aqueous-filled pores or by carrier mediated transport. The factors that determine the extent of diffusion of the drug into the breast milk include plasma protein binding, molecular weight of the drugs, ionization, and lipophilic nature of the drug.

In order for a drug to cross any biological membrane, it must be present in the free form. Thus, drugs that are highly protein bound may be excreted in breast milk in low quantities. Highly protein bound drugs such as warfarin are incapable of crossing the mammary membrane in appreciable amounts. Drugs whose molecular weight is large such as insulin and heparin will not be excreted into breast milk.

The pH of breast milk, which is about 7.00, is somewhat more acidic than plasma. Consequently, acidic drugs will occur as ionized molecules in the plasma and will fail to diffuse into breast milk. In contrast, basic drugs will be available as un-ionized molecules in the plasma and will be able to cross the membrane and reach the milk compartment. Since the milk of nursing mothers is rich in fat, lipophilic drugs may bind to milk causing accumulation of the drug in the milk.

2. Age of the Infant

Age of an infant is an important consideration. The younger the infant, the more potential for a stronger response to drugs, especially when the kidneys and liver are not functioning effectively.

3. Frequency of Feeding Infants

Frequency of breastfeeding an infant has an effect on the amount of drugs reaching the milk. Younger infants are usually breast fed frequently and for extended periods of time. They will be more exposed to drugs than infants who are breast fed less frequently as is the case with older infants or those who receive solid food supplement.

4. Gastric Emptying Rate

Infants who are breast fed have a considerably shorter gastric emptying rate than infants who are bottle-fed. This results in reduction of exposure time of the drug.

5. Drug Regimen of Nursing Mothers

The drug regimen of nursing mothers may contribute to the amount of drug reaching milk. Feeding the infant one hour after drug intake, when it is at peak level in the mother's plasma and milk compartment, will result in exposing the infant to larger quantities of the drug.

6. Long-or Short-Acting Medications

Long-or short-acting drugs taken by a nursing mother may affect the breast fed infant. Long-acting drugs pose more risk to the newly born than short-acting ones.

7. Nature of the Drug

Nature of the drug taken can play a role in drug effect. If the drug taken by the nursing mother can be given to infants, then it is unlikely that the amount of the drug reaching milk will exceed the pediatric therapeutic dose. Such drugs are safe to use during lactation. However, if the drug taken by the mother is not recommended to infants, then there is a risk potential for harmful effects to breastfeeding the baby.

RISK OF ADVERSE EFFECTS FROM DRUGS TAKEN DURING BREASTFEEDING

The following is information regarding the risk for adverse effects that may be caused by certain drugs to infants as a result of exposure in breast milk.

1. **Aspirin**: Metabolic acidosis, bleeding as a result of the effect on platelet function, and Reye Syndrome.
2. **Phenobarbital**: Sedation and possible spasm after cessation of breastfeeding.
3. **Acebutolol**: Hypertension and bradycardia.
4. **Primidone**: Sedation.
5. **Sulfasalazine**: Bleeding diarrhea.
6. **Ethanol**: Large doses may cause a decreased milk ejection reflex in mothers, drowsiness and decreased growth and weight in infants.
7. **Caffeine**: High caffeine consumption may cause irritability and irregular sleep.
8. **Methotrexate**: Immunosuppression and neutropenia.
9. **Fluoxetine**: Colic.
10. **Doxepin**: Sedation.
11. **Tetracycline**: Even though tetracycline induced teeth discoloration of breast fed infants has not been reported, the potential risk needs to be taken into consideration.
12. **Diazepam**: Poor weight gain.
13. **Alprazolam**: Withdrawal symptoms after discontinuation of breast feeding.

14. **Bromocriptine**: Suppression of milk production.
15. **Theophylline**: Irritability.
16. **Androgens**: Suppression of milk production.
17. **Ergot Derivatives**: Suppression of milk production.
18. **Thiazide Diuretics**: Suppression of milk production.
19. **Nicotine**: Diarrhea, vomiting and restlessness.
20. **Amphetamine, cocaine, marijuana and heroin**: Intoxication and can reduce milk supply.

Examples of Drugs that are Safe to be taken in Usual Dose

Acetaminophen, Antacids, Cephalosporins, Clotrimazole, Progestin, Fexofenadine, Ibuprofen, Bulk Forming and Stool Softeners Laxatives, Metoprolol, Miconazole, and Penicillins.

Examples of Drugs that are Probably Safe in Usual Dose

ACE Inhibitors, Depakote, Dilantin, First Generation Antihistamines such as Benadryl, INH, Sudafed, Fluconazole, Cimetidine, Zantac, and Sertraline.

Examples of Potentially Hazardous Drugs in Usual Doses

Atenolol, Long-acting Benzodiazepines (such as Librium, Valium, Dalmane, Chlorthalidone), Contraceptives containing estrogens which may reduce milk supply, and Metronidazole.

Examples of Drugs Not Safe to Take

It is recommended that these drugs and others, including OTCs, should be taken at the advice of a physician only: Amantadine, Amiodarone, Lipitor, Zocor (and other antillipidemic drugs), and Lithium.

SUMMARY

The intake of medications during pregnancy and lactation is common and such practice may risk the health of the fetus as well as infants. Prior to taking a medication, including OTCs, a mother should consult a physician. Many drugs are capable to cross the placental barrier and may produce teratogenic effects. The FDA established five categories based on the potential benefits and risks for a pregnant woman and fetus.

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ANTICIPATED TOPICS FOR BALANCE OF 2012

New drugs 2011-2012	Cholesterol management
DHD	*C diff.*
Update: nuclear pharmacy	Prevalence of skin cancers
Nosocomial infections	Healthcare impact on pharmacy

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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

List the routes through which drugs and nutrients cross the placenta	Yes	No
Discuss the rate at which drugs penetrate the placental barriers	Yes	No
Differentiate between the 5 categories of drugs based on risk during pregnancy	Yes	No
List factors that affect drug transport into human milk	Yes	No
Describe risks from drugs taken while breast feeding	Yes	No

2. Was the program independent & non-commercial Yes No

	Poor			Average		Excellent	
3. Relevance of topic	1	2	3	4	5	6	7

4. What did you like most about this lesson?_____

5. What did you like least about this lesson?_____

Please Select the Most Correct Answer(s)

1. Which of these has no effect on the rate that drugs cross the placental barriers?
   A. Lipid solubility of drug
   B. Protein binding
   C. Ionization of the drug
   D. Age of the pregnant mother
2. A drug in which studies in humans & animals have shown fetal risk that clearly outweigh any possible benefits is:
   A. Category B
   B. Category X
   C. Category C
   D. Category A
3. Alcohol consumption during pregnancy affects women who are older than 35.
   A. True
   B. False
4. Colostrum contains higher concentrations of protein & lower fat content than cow's milk.
   A. True F. False
5. Which of these is contraindicated during pregnancy?
   A. Clindamycin
   B. Benzoyl peroxide
   C. Erythromycin
   D. Oral isotretinoin
6. Which of these when taken during pregnancy may cause vaginal adenosis & clear cell carcinoma in female offspring?
   A. Diethylstilbestrol
   B. Lithium
   C. Cocaine
   D. Tetracycline
7. Which of these should be avoided during the last weeks of pregnancy?
   A. Dimenhydrinate
   B. Meclizine
   C. Vitamin B6
   D. Prochlorperazine
8. Drug excretion into mother's milk is not affected by the age of the infant.
   A. True
   B. False
9. Which of these can cause metabolic acidosis in breast fed infants?
   A. Aspirin
   B. Primidone
   C. Caffeine
   D. Sulfasalazine
10. Frequency of breast feeding an infant may affect drug excretion in milk.
    A. True
    B. False

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