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Pregnancy and lactation

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Pregnancy results in physiologic changes in almost all organ systems in the body mediated mainly by female sex hormones. Physiologic changes of pregnancy influence the dental management of women during pregnancy. Understanding these normal changes is essential for providing quality care for pregnant women. This review article briefly discusses the cardiovascular, respiratory, gastrointestinal, urogenital, endocrine, and oral physiologic changes that occur during normal gestation. A summary of current scientific knowledge of ionizing radiation is presented. Information about the compatibility, complications, and excretion of the common drugs during pregnancy is provided. Drugs and their usage during breast-feeding are also discussed. Guidelines for the management of a pregnant patient in the dental office are summarized. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;97:672-82)**

Pregnancy involves complex hormonal interactions, which cause profound physiologic changes. Some changes are more evident than others. The changes that occur are the result of increasing maternal and fetal requirements for the growth of the fetus and the preparation of the mother for delivery. An increase in the secretion of female sex hormones, estrogen by 10-fold and progesterone by 30-fold, is important for the normal progression of pregnancy.[1]

Increased hormonal secretion and fetal growth induce several systemic, as well as local physiologic and physical changes in a pregnant woman. The main systemic changes occur in the cardiovascular, hematologic, respiratory, renal, gastrointestinal, endocrine, and genitourinary systems. Local physical changes occur in different parts of the body, including the oral cavity. These collective changes may pose various challenges in providing dental care for the pregnant patient. Therefore, understanding the physiologic changes of the body and the effects of dental radiation and medications used in dentistry on the pregnant and lactating mother and the fetus is essential for management of the pregnant and nursing mother.

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SYSTEMIC CHANGES IN PREGNANCY

Cardiovascular change

The cardiovascular system undergoes profound changes during pregnancy. The main cardiovascular changes are an increase in the total blood volume and cardiac output, a decrease in blood pressure, and the potential occurrence of the supine hypotensive syndrome.

The total blood volume increases by 40% to 50% by the 32nd week of gestation, caused primarily by a 40% to 50% increase in plasma volume.[2,3] In addition to an increase in the plasma volume there is also a 30% increase in the red cell volume contributing to the increase of the total blood volume.[3]

An increase in cardiac output by 30% to 50% occurs between the 25th and the 33rd week of pregnancy secondary to an increase in stroke volume.[4-7] These changes produce a functional heart murmur and tachycardia in 90% of women, which disappears shortly after delivery. [5] The increase in cardiac output also increases the heart rate by 10-20 beats/minute in response to the increased metabolic demands of the mother and the fetus[8,9] (Table I). The blood pressure decreases early, and reaches its nadir at approximately the 16th to 24th week of pregnancy. After the 16th week, blood pressure increases to the baseline level. [10] There is also a drop in

systemic vascular resistance due to the relaxation of the smooth muscles of the veins, mediated by progesterone (Table I).[11,12]

Supine hypotensive syndrome is a condition that affects up to 8% of pregnant women and occurs mainly after the late part of second trimester.[13] When the pregnant woman is in the supine position, there is impaired venous return to the heart due to compression of the inferior vena cava by the fetus. The resulting decrease in the stroke volume stimulates the baroreceptors as a normal compensatory mechanism to maintain cardiac output. This leads to hypotension, nausea, dizziness, and fainting. To prevent supine hypotensive syndrome in the dental chair, the pregnant woman should have the right hip elevated 10 to 12 cm or rolled to the left side to lift the uterus off the inferior vena cava.[14]

Respiratory changes

The respiratory changes occurring during pregnancy accommodate the increasing size of the developing fetus and the maternal-fetal oxygen requirements. The main changes in the respiratory system are dyspnea, hyperventilation, alterations in the oxygen intake and reserve, and an increase in both the tidal volume and minute ventilation rate. Dyspnea occurs in 60% to 70% of normal pregnant women.[15] The mechanism causing dyspnea is not fully understood. Maternal oxygen intake increases by 20% and oxygen reserve decreases, which exposes the fetus and the mother to the potential risk of hypoxia.[5,16] The increase in the tidal volume (amount of air inspired and expired with normal breath) and the minute ventilation rate (tidal volume × respiratory rate/minute) are a result of the displaced diaphragm.[16-18] The enlarged fetus pushes the diaphragm up by 3 to 4 cm causing an increase in intrathoracic pressure. This leads to an increase in chest circumference that results in outflaring of the ribs.[19] The respiratory rate remains unchanged.[19]

The effect of an increase in circulating estrogen causes engorgement of the nasal capillaries and rhinitis in 30% of pregnant women. This may lead to frequent nosebleeds and a predisposition to upper respiratory infections.[20]

Hematological change

Significant hematological changes include an increase in red blood cells, white blood cells, erythrocyte sedimentation rate, and all coagulation factors, except factors XI and XIII, and a decrease in the hemoglobin content of blood (Table I).

The increase in plasma volume is disproportionately greater than the increase in the red cell volume resulting in hemodilution and, hence, a physiological anemia.[21] Increased circulatory catecholamines and cortisol lead to leukocytosis[22] (Table I). Clotting factors VII-X are increased and anticlotting factors XI and XIII are decreased.[23] Therefore, pregnancy is considered to be a hypercoagulable state, increasing the risk for thromboembolism.[24] Pregnant women who have antiphospholipid syndrome are at significant risk for thromboembolism and are placed on subcutaneous low molecular weight heparin (LMWH) for the prevention of embolic events. These patients must be hospitalized for dental care. Measuring plasma heparin level best assesses the blood coagulation levels of these patients. Activated partial thromboplastin time (aPTT), which is normally used for monitoring LMWH in nonpregnant patients, is not useful for assessment of blood coagulation level in pregnant women. The precise mechanisms by which antiphospholipid antibodies alter hemostasis remains unknown.[24]

Table I. Systemic physiologic alterations of pregnancy in comparison with nonpregnant women

Systemic functional changes	*Nonpregnant*	*Pregnant*
Cardiovascular[2,3,7,9,10,18]		
Blood volume (L)	4.5-5	6.2-6.7
Cardiac output (L/min)	4.3 ± 0.9	6.2 ± 1.0
Heart rate (beat/min)	70 ± 10	80 ± 10
Systemic vascular resistance (dyne/cm/sec^{-5})	1530 ± 520	1210 ± 266
Systolic blood pressure (mm/Hg)	120	110 (early)
Diastolic blood pressure (mm/Hg)	80	50-60 (early)
Respiratory[15-19]		
Tidal volume (mL)	500	700
Minute ventilation volume (L)	7	10
Blood[5,22,32]		
RBC (10^5/mm^3)	4-5	Increased by 25%-30%
Hgb (g/100 mL)	12-16	11.5-12.3
WBC (10^3/mm^3)	5-9	5-12
ESR (mm/hour)	0-20	0-20
Liver[7,8,35]		
Total proteins (g/dL)	6.5-7.5	5.7-6.5
Albumin	3.2-3.8	2.4-3.1
Alkaline phosphatase (IU/L)	30-115	100-210
Cholesterol (mg/dL)	120-190	190-330
Triglycerides (mg/dL)	76-92	205-247
AST (IU/L)	0-42	>72
ALT (IU/L)	0-48	>48
Kidney[3,40,41]		
Renal plasma flow	420	695
GFR (mL/min)	100 ± 18	150 ± 30
Serum creatinine (mg/dL)	0.8-1.2	1.2-1.8
BUN (mg/dL)	8-25	<15
Endocrine[43]		
Thyroid binding globulin (ng/dL)	19-30	40-60
T_4 (ng/dL)	5-10	8-16
T_3 (ng/dL)	65-140	140-180

Antiphospholipid syndrome (APLS) in pregnancy is characterized by the presence of autoantibodies in association with recurrent fetal loss and severe complications such as preeclampsia, fetal growth retardation, or placental insufficiency. The most clinically important serologic markers are lupus anticoagulant, anticardiolipin antibodies, and recently anti-beta-2-glycoprotein 1 antibodies.[25]At present, standardization does not exist and a definitive association between specific clinical manifestation and antibody level is not yet known. Experimental data gave evidence that passive transfer of antiphospholipid antibodies result in clinical manifestation of APLS, that is, fetal loss and thrombocytopenia.[25] Treatment with heparin, aspirin, or intravenous immunoglobulins decreased the fetal loss rate.[25]

Gastrointestinal and liver changes

Mechanical changes resulting from an enlarging fetus, in combination with hormonal changes, are responsible for alterations in the GI system. The main GI changes are nausea, vomiting, and heartburn. Other changes include hepatic dysfunction and iron deficiency.

Nausea and vomiting occur in about 66% of pregnant women beginning approximately 5 weeks after the last menstrual period and peaking between 8 and 12 weeks. Thereafter, the symptoms decline gradually.[26] Hyperemesis gravidarium (excessive and an uncontrolled vomiting), occurs in less than 1% of all pregnancies.[26] The pathophysiology of nausea and vomiting during pregnancy is poorly understood, but is thought to be due to the hormonal effects of estrogen and progesterone.[27] For pregnant women with hyperemesis gravidarium requiring dental treatment, morning appointments should be avoided. Also, they should be advised to avoid citrus drinks or fatty foods as they may cause gastric upset or delay gastric emptying.[28] To prevent dehydration due to recurrent vomiting, pregnant women should be advised to sip small volumes of salty liquids such as sports beverages.[28] During dental procedures, pregnant patients should be seated in a semisupine or comfortable position. In case of vomiting, the procedure should be stopped immediately and the patient should be repositioned upright. When the vomiting is over, rinsing the mouth with cold water or a mouthwash is recommended.

Pyrosis (heartburn) occurs in approximately 30% to 50% of pregnant women.[29] Reflux occurs as a result of an increased intragastric pressure due to the enlarging fetus, slow gastric emptying rate, and decreased resting pressure of the lower gastroesophageal sphincter.[30,31] Increased circulating levels of progesterone and estrogen are responsible for abnormally decreased lower gastroesophageal sphincter resting pressure.[30]

During pregnancy there is an increased demand for energy to enable the fetus and placenta to grow. This demand affects the metabolism of all the nutrients. The most important nutrient deficiencies affecting the fetus profoundly are iron and folic acid. Iron is required for fetal erythropoesis and folic acid for amino acid and nucleic acid synthesis. Therefore, additional supplements are required.[32-34]

Abnormal liver function tests (bilirubin, AST, ALT) are occasionally reported during pregnancy. Bilirubin, serum aspartate aminotransferase (AST), and serum alanine aminotransferase (ALT) are slightly elevated. In a study of 4377 deliveries during a period of 15 months in the UK, 142 patients (3%) had abnormal liver tests that were related to the pregnancy.[35]

There is a decrease in serum albumin level secondary to the increased plasma volume.[36-37] Alkaline phosphatase level rises from the fifth month of pregnancy till parturition. This increase is due to the leakage of placental alkaline phosphatase into the maternal blood.[37] There is also an increase in cholesterol and triglyceride levels.[37] The biochemical changes reflecting the dysfunction of the liver are summarized in Table I.

Liver dysfunction may lead to preeclampsia (a placental-induced triad of hypertension, proteinuria, and edema), HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), obstructive cholestasis, and acute fatty liver of pregnancy.[35,37] Preeclampsia occurs in approximately 5% of all pregnancies.[38] The exact cause of preeclampsia has not been identified. Numerous theories of potential causes exist, including genetic, dietary, vascular (blood vessel), and autoimmune factors. None of the theories have yet been proven.[38]

Hypertension in pregnancy can be classified into 2 groups: women who have hypertension before they become pregnant and women who become hypertensive for the first time in the second half of pregnancy. Blood pressure generally falls during the first and second trimesters. Therefore, women with high blood pressure before the 20th week of gestation are assumed to have preexisting hypertension.[39] Regardless of the type of the hypertension, pregnant women with elevated blood pressure should be referred to the primary physician or obstetrician to be evaluated for possible developing preeclampsia.

Renal and genitourinary changes

The principal renal and genitourinary changes are increased glomerular filtration rate (GFR), biochemical changes in the urine and blood, increased frequency of urination, urinary stasis, and urinary tract infections.

There is an increase in renal plasma flow by about 50% to 80 % and in GFR by 50%.[40] The increase in the

renal plasma flow is due to the generalized increase in blood volume. There is increased creatinine clearance and uric acid and urea excretion resulting in a slight decline in serum creatinine and blood urea nitrogen (BUN) levels.[3,41] There is also frequency of urination usually during the second half of gestation due to altered osmoregulation (decrease in plasma osmolality). Human chorionic gonodotropin (hCG), may be involved in the osmoregulatory changes of pregnancy.[42] In addition, 1% to 2% of pregnant women have hypotonic bladder, urinary stasis, and pyelonephritis.[20,41,42] It is advisable to ask the patient to void the bladder just prior to starting the dental procedure.

Endocrine changes

Female sex hormones (estrogen, progesterone, and human gonadotrophin) are secreted primarily by the placenta. These hormones are responsible for most of the physiologic changes during pregnancy. In addition, there is also an increase in thyroxine, steroids, and insulin levels. The thyroid gland increases in size by up to 50%. There is an increase in serum thyroid binding globulin, and thyroxine due to the placental secretion of human chorionic thyrotropin (a specific thyroid-stimulating hormone).[43] There is an increase in the circulating 1,25, dihydroxy-cholecaliciferol (vitamin D) levels due an increase in circulating serum parathyroid hormone levels by up to 50%.[44,45] Corticosteroid levels are increased moderately. There is a 2-fold increase in aldosterone and a 3-fold increase in cortisol levels.[46,47]

Estrogen and progesterone are insulin antagonists and the increased levels of these hormones lead to insulin resistance, thus insulin levels are elevated in pregnant women to compensate for this resistance. About 45% of pregnant women are unable to produce sufficient amounts of insulin to overcome the antagonist action of estrogen and progesterone, and as a result develop gestational diabetes. Women who are obese and with a positive family history of type II diabetes mellitus have a higher risk of developing gestational diabetes.[8]

Oral and facial changes

Oral changes seen in pregnancy include gingivitis, gingival hyperplasia, pyogenic granuloma, and salivary changes. Increased facial pigmentation is also seen. Elevated circulating estrogen, which causes increased capillary permeability, predisposes pregnant women to gingivitis and gingival hyperplasia.[48,49] Pregnancy gingivitis usually affects marginal and interdental papilla[50] and is related to preexisting gingivitis. Good oral hygiene can help to prevent or reduce the severity of the hormone-mediated inflammatory oral changes. Pregnancy does not cause periodontal disease but does worsen an existing condition.[51]

Pyogenic granuloma (pregnancy tumor) occurs in about 1% to 5% of pregnant women.[52] Increased angiogenesis, due to sex hormones coupled with gingival irritation by local factors such as plaque, is believed to cause pyogenic granuloma.[53] It occurs mainly on the labial aspect of the interdental papilla. It can happen at any time during pregnancy, but is reported to be most common in first pregnancies, during the first and the second trimesters[52] and may regress after the child's birth.[50] Erosion of teeth on lingual and palatal surfaces of incisors has been mentioned in a case report,[54] but to our knowledge there is no clinical study available to support this finding.

The main salivary changes in pregnancy involve its flow, composition, pH, and hormone levels. Cross-sectional studies show a reduced whole stimulated salivary flow rate in pregnant women, but longitudinal studies show that there is no change in the whole stimulated salivary flow rate.[52]

The change in composition of the saliva includes a decrease in sodium and pH, and an increase in potassium, protein, and estrogen levels.[52,55] Salivary estrogen level has been suggested as a screening test to detect the risk potential for preterm labor. Salivary estrogen levels are higher in the women destined to have preterm babies than in women having normal term deliveries.[56,57]

Salivary estrogen also increases the proliferation and desquamation of the oral mucosa and an increase in subgingival crevicular fluid levels. The desquamating cells provide a suitable environment for bacterial growth by providing nutrition predisposing the pregnant woman to dental caries.[52]

There is an increase in facial pigmentation called melasma or the "mask of pregnancy," appearing as bilateral brown patches in the mid-face.[58] These facial changes begin during the first trimester[59] and are seen in up to 73% of pregnant women.[58] The etiology of this condition is unknown, but is believed to be related to the increase in serum estrogen and progesterone.[60] Melasma usually resolves after parturition.[50]

Recent studies suggest a link between periodontal disease and preterm low birth weight. Lopez et al,[61] in an investigation of 400 women who had gingivitis and periodontal disease, found a positive correlation between periodontal disease and low birth weight. Periodontal disease seemed to be an independent risk factor for low birth weight, and was decreased by good oral hygiene and periodontal treatment.[61]Although a positive correlation between periodontal diseases and low birth weight has been reported, causal explanation has not been found in several animal and human case-control studies.[62]

Table II. Estimated radiation exposure to the human body in Gray (Gy)[14,67,70]

Radiographs	*Exposure in Gy*
Full month series (18 intraoral, D film, lead apron)	1×10^{-5}
Panoramic film	15×10^{-5}
Daily radiation (cosmic)	4×10^{-4}
Skull	4×10^{-3}
Chest	8×10^{-3}

RADIOGRAPHS, PREGNANCY, AND THE FETUS

X-rays are a type of electromagnetic radiation that have the ability to ionize material through which it passes. Ionizing living matter results in damage to cells or DNA. Depending on the amount of radiation and the stage of pregnancy, damage to fetal cells may result in miscarriage, birth defects, or mental impairment. Dental radiographs may be prescribed during pregnancy, because radiation exposure to the fetus in utero is negligible.[63] The dose to the fetus is about 1/50 000 of the direct exposure to the head.[63] As a consequence, the effective body dose from the full mouth series of D speed films is less than 1×10^{-6} Gy (Table II). This is less than 2.5 hours of average daily background radiation in the United States. It is about the same amount of additional daily background radiation exposure received by Denver residents due to decreased atmospheric density and reduced absorption of cosmic radiation relative to a sea level location. It is significant to note that there is no increase in fetal abnormalities in Denver relative to other locations in United States.[64] Principal fetal abnormalities produced by radiation are almost certainly the consequence of damage to cells and would therefore be consistent with a threshold dose, for example mental retardation.[65] Using the most recent dosimetric data for atomic bomb survivors, a dose response relationship is consistent with a threshold of 0.12 to 0.20 Gy. The risk of teratogenesis from a dental exposure is therefore nil with a threshold safety factor of 10 000×.[64]

Teratogenecity of radiation depends on fetal age and the dose of radiation.[66] The greatest risk to the fetus for teratogenecity and death is during the first 10 days after conception. The most critical period of fetal development is between 4 and 18 weeks after conception. The chance of fetal teratogenecity with an exposure of 0.01Gy is about 0.1% and radiation doses of up to 0.05 Gy or less are not associated with significant increase in tetratogenecity.[67] The National Commission for Radiation Protection (NCRP) recommends that the cumulative fetal dose should not exceed 0.005 Gy.[68] Fetal exposure to radiation of more than 0.20 Gy will cause microcephaly and mental retardation.[66]

Radiographs employed in dentistry such as the panoramic and full mouth intraoral series are generally safe during pregnancy. The average radiation doses absorbed by the fetus in panoramic and full mouth radiographs are 1.5×10^{-4} Gy and 10^{-5} Gy respectively (Table II). The dental radiation received is also 40-fold less than the naturally occurring background radiation.[67,68] Although the risk of teratogenecity is exceedingly low with dental radiographs, the amount of radiation exposure to the pregnant mother and fetus can and must be minimized even further by using bitewing radiographs instead of panoramic radiographs, using high-speed films (E speed), the use of rectangular collimation instead of circular collimation, properly collimated beam, and lead aprons over the abdomen.[69-72] Following all the above-mentioned precautions will further reduce the patient's radiation exposure.[70]

The ability of the lead apron to significantly add to the reduction of the nominal dose from maternal dental diagnostic imaging is debatable.[73]Although the use of a lead apron is recommended by the American Dental Association (ADA), its utility is primarily psychological.

The ADA endorses US Food and Drug Administration (FDA) selection criteria for dental x-ray exposures, which states that "dental radiographs for pregnant patients may be prescribed according to the usual and customary selection criteria."[74] While considering potential risks of diagnostic imaging, the potential benefits must be considered. Radiography facilitates an accurate diagnosis. This in turn will lead to maintenance of health or timely initiation of corrective therapy when needed. Incomplete or inaccurate diagnosis delays appropriate therapy and may lead to inappropriate management, and further deterioration and complication become more likely.

DRUGS

Drugs are absorbed easily during pregnancy as the serum concentration for drug binding is lower than in the nonpregnant state.[75] There is also a higher volume of drug distribution, lower maximum plasma concentration, lower plasma half-life, higher lipid solubility, and a higher clearance of the drugs.[75] All these factors allow for easy transfer of an unbound drug across the placenta exposing the fetus to the drugs. Certain drugs are known to cause miscarriage, teratogenecity, and low birth weight of the fetus.[76] Therefore, caution should be exercised when prescribing drugs to a pregnant women. Most drugs are excreted in breast milk, exposing the newborn to the drugs. Neonatal toxicity depends on the chemical properties, dose, frequency, duration of exposure to the drugs, and amount of milk consumed.[75]

The FDA has categorized the potential for drugs to cause birth defects, providing definitive guidelines for prescribing drugs during pregnancy.[77] They are as follows:

Category A—Controlled human studies indicate no apparent risk to the fetus. The possibility of risk to the fetus is remote.

Category B—Animal studies do not indicate fetal risk. Well-controlled human studies have failed to demonstrate a risk

Category C—Animal studies show an adverse effect on the fetus but there are no controlled studies in humans. The benefits from use of such drugs may be acceptable.

Category D—Evidence of human risk, but in certain circumstances the use of such a drug may be acceptable in pregnant women despite its potential risk.

Category X—Risk of use in pregnant women clearly outweighs possible benefits.

Analgesics

Acetaminophen, FDA category B, is the most useful analgesic to be used during pregnancy.[7,78-80] It can be used in any stage of pregnancy and in nursing mothers.[76] Maternal anemia and fetal renal disease was reported, however, used in high doses. [7]

Certain opioid analgesics (oxycodone, morphine, or propoxyphene) can be used during pregnancy and lactation.[76] However, chronic use of narcotics may result in growth retardation and physical dependency. Opioids pass the placental barrier and are excreted in the breast milk. The American Academy of Pediatrics has classified opioids to be compatible with breast feeding.[81]

Aspirin is FDA category C. It is a prostaglandin inhibitor and it is known to cause constriction of the ductus arteriosus. It is also secreted in the breast milk. Therefore, it should be avoided particularly during the third trimester of pregnancy and while nursing.[76,79,80]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are also prostaglandin synthesis inhibitors. The prostaglandins act on the smooth muscles in the endometrial lining and contribute to the expulsion of the embryo. They are also involved in maintaining the patency of the ductus arteriosus in the fetal heart.[82] There is no significant association between using NSAIDs during pregnancy and an increased risk of congenital defect, low birth weight, and premature birth, but there is an increased risk of miscarriage.[82] Janssen and Genta[83] recommend that NSAIDs be given during pregnancy in the lowest effective dose intermittently, only if needed, and should be discontinued 6 to 8 weeks before delivery.[83] Maternal effect of NSAIDs are reported to cause prolongation of pregnancy in the third trimester and causes premature closure of the ductus arteriosus, leading to pulmonary hypertension, respiratory problems, renal dysfunction, and hemostatic abnormalities in the fetus, but teratogenecity has not been found. [84] NSAIDs are excreted in small amounts into breast milk with small risk for adverse effects in the infant.[84] Gastrointestinal complications are known to be caused by NSAIDs and are aggravated during pregnancy.

Local anesthetics

Most local anesthetics used in dentistry are FDA class B, except mepivacaine and bupivacaine, which are FDA class C. Local anesthetics pass the placental barrier by passive diffusion, but most of them are considered to be safe and nonteratogenic.[78] The most widely used local anesthetics belong to the chemical class the amides (bupivacaine, prilocaine, lidocaine) (Table III). The blood concentrations of amide local anesthetics are dependent on the presence of a 1-acid glycoprotein. This glycoprotein is necessary for the local anesthetic to be metabolized. During pregnancy the level of a 1-acid glycoprotein is reduced leading to increased free local anesthetic level in the plasma. This increases the possibility of fetal toxicity, especially in long-acting amides such as bupivicaine.[85,86] Therefore, use of longer-acting amide local anesthetics is not recommended. When a short-acting amide such as lidocaine was used in rats at the dose of 6.6 times higher than the maximum dose allowed in humans, no fetal harm was observed.[85] Therefore, the administration of lidocaine in the doses used in dentistry is safe in pregnant and nursing women.

The use of epinephrine, a naturally occurring hormone, in local anesthesia in the doses used for dental treatment is not associated with fetal abnormality, and is considered to be safe during pregnancy.[7] Although epinephrine is not teratogenic, caution should be taken to avoid accidental intravenous administration.[78] There is no contraindication to using local anesthetics in a nursing mother, except cocaine, which is absolutely contraindicated.[87]

Antibiotics

Beta-lactam ring−derived antibiotics (penicillins and cephalosporins) are the first-choice antibiotics for orofacial infections. They are categorized as FDA class B drugs. These antibiotics cross the placenta but are known to be safe when used in pregnancy.[88]

Macrolides (erythromycin, clindamycin, azithromycin) are categorized as FDA class B drugs. They pass the placental barrier but only in small amounts. Therefore, they are recommended for use in pregnant women who are allergic to penicillin. Clarithromycin, also a macrolide, is categorized as FDA class C. It is mostly recommended for use in pregnant HIV patients for the treatment of *Mycobacterium avium* complex (MAC).[85,88]

Tetracyclines are classified FDA category D, and thus should only be used when there is no other alternative treatment available, such as in the treatment of a patient with syphilis who has an allergy to penicillin.[88] Aminoglycosides (streptomycin, gentamycin) are

Table III. Common drugs used in dentistry[14,75-81,85]

Drugs	*FDA category*	*Use in pregnancy*	*Use in nursing*	*Possible side effects*
Analgesics				
Acetaminophen	B	Yes	Yes	Not reported
Aspirin	C	Not in 3rd trimester	No	Postpartum hemorrhage
Ibuprofen	B	Not in 3rd trimester	Yes	Delayed labor
Naproxen	B/D**	Not in 2nd 1/2 of pregnancy	Yes	Delayed labor
Codeine	C	With caution	Yes	Multiple birth defects
Oxycodone	B	With caution	With caution	NRD
Hydrocodone	C/D*	With caution	With caution	NRD
Morphine	B	Yes	Yes	Respiratory depression
Propoxyphene	C	With caution	Yes	Not reported
Meperidine	B	Yes	Yes	Not reported
Pentazocine	C	With caution	With caution	Not reported
Antibiotics				
Amoxicillin	B	Yes	Yes	Not reported
Metronidazole	B	Yes	Yes	Not reported
Erythromycin	B	Yes	Yes	Not reported
Penicillin v	B	Yes	Yes	Not reported
Cephalosporins	B	Yes	Yes	Not reported
Gentamycin	C	Yes	Yes	Fetal ototoxicity
Clindamycin	B	Yes	Yes	Not Reported
Tetracycline	D	No	No	Discoloration teeth
Chloramphenicol	X	No	No	Maternal toxicity/fetal death
Chlorhexidine	B	No data	No data	Not reported
Antifungals				
Nystatin	B	Yes	Yes	Not Reported
Clotrimazole	B	Yes	Yes	Not Reported
Fluconazole	C	With caution	With caution	Not Reported
Ketoconazole	C	With caution	No	Fetal toxicity
Local Anesthetics				
Lidocaine	B	Yes	Yes	Not reported
Mepivacaine	C	With caution	Yes	Fetal bradycardia
Prilocaine	B	Yes	Yes	Not reported
Bupivacaine	C	With caution	Yes	Fetal bradycardia
Etidocaine	B	Yes	Yes	Not reported
Corticosteroids				
Prednisolone	B	Yes	Yes	Not reported
Sedative/Hypnotics				
Nitrous oxide	Not assigned	Not in 1st trimester (**)	Yes	Spontaneous abortions
Barbiturate	D	Avoid	No	NRD
Benzodiazepines	D	No	No	Cleft lip/palate

*Note: D indicates caution: if used for prolonged period of time, or high doses.
**NRD: neonatal respiratory depression.

categorized FDA class C drugs. They pass the placental barrier readily but there have been no documented reports of neonatal toxicity from exposure to aminoglycosides in humans.

Chlorhexidine is categorized as a class B drug by the FDA and is safe to use during pregnancy and lactation.

Antifungal drugs

Nystatin and clotrimazol are FDA class B drugs and they are considered to be safe during pregnancy and lactation. Ketoconazole and fluconazole are FDA class C. Ketoconazole is secreted in breast milk and is reported to cause adrenal insufficiency and hepatotoxicity in newborns, therefore it should be avoided during nursing.[80] There are no reported adverse effects of using fluconazole during nursing.[85]

Corticosteroids

Corticosteroids are FDA category C drugs. Corticosteroids are commonly used to treat various inflammatory oral conditions. Corticosteroids are generally used as local topical preparations (ointments, mouth washes, lozenges) in treating inflammatory oral conditions. When systemic corticosteroids are used to treat oral conditions, they are usually given in moderate to high doses (25-40 mg/day) for a short duration. The complications arising from using systemic

corticosteroids in a pregnant woman are the same as those that may occur in a nonpregnant individual.

In addition, pregnancy-specific complications that arise are premature rupture of embryonic membranes, hypertension, and gestational diabetes mellitus.[89] When administered systemically, the lowest effective dosage should be given and the fetus should be monitored for infections and adrenal insufficiency.[90]

Generally the use of local and topical corticosteroids is safe in pregnant and lactating women. Corticosteroids cross the placental barrier and for this reason the lowest possible dose that would control the disease should be given.[83] Although the incidence of adrenal suppression and infections are low, fetal monitoring is necessary.[90] The current thinking is that antenatal corticosteroid administration reduces neonatal morbidity in preterm infants.[91] The American College of Obstetricians and Gynecologists Committee on Obstetric Practice supports a single course of corticosteroids to all pregnant women between 24 and 34 weeks of gestation who are at risk to preterm delivery within 7 days.[92] Despite the secretion of corticosteroids in the breast milk, the American Academy of Pediatrics Committee on Drugs recommends using prednisone and prednisolone in nursing mothers when it is indicated.[81] Information on the use of other corticosteroids such as dexamethasone and betamethasone are not available.[83] Nursing mothers on high doses of steroids can wait up to 4 hours before nursing as this may reduce the amount of steroids in the milk.[81,93]

Sedatives and hypnotics

Nitrous oxide (N_2O) has not been classified into any category by the FDA and its use in pregnancy is controversial due to unproven deleterious effects on the pregnant woman and fetus. Nitrous oxide inhibits methionine synthetase activity in rats, but it is not known to affect humans. Nitrous oxide also causes vasoconstriction and may reduce uterine blood supply. Chronic exposure of pregnant dental health workers to N_2O for more than 3 hours without the use of scavengers has resulted in decreased fertility and spontaneous abortions.[94] The National Institute of Occupational Safety and Health recommends that proper ventilation (10 or more room air exchanges per hour), scavenging systems (vacuum up to 45 L/min), appropriate mask sizes, regular air sampling, and low exposure of 25 parts per million to be used when pregnant health care workers are involved.[80,95] A recent systemic review suggests that 50% N_2O is safe for use in parturient women, their newborns, and health care workers in attendance during its administration.[96] There are no reports of N_2O secretion and its impact in breast-feeding, but this has not been studied.[96] If N_2O is required, it is better given in the second and third trimesters, to be administered for less than 30 minutes with at least 50% oxygen.[97]

Barbiturates and benzodiazepines are categorized as FDA class D drugs and should be avoided during pregnancy and nursing.

SPONTANEOUS ABORTION AND PRETERM LABOR

Spontaneous abortion is the most common complication of pregnancy. It occurs in 10% to 15% of all pregnancies and is common during the first trimester.[98] It has been estimated that 2% to 5% of women have 3 or more miscarriages.[98] Vaginal bleeding associated with cramping during pregnancy may be the first clinical sign of spontaneous abortion.[99] Minor contractions without bleeding (Braxton-Hicks contractions), which subside spontaneously or contractions when a patient shifts position do not indicate an emergency.[100] In the case of vaginal bleeding with or without powerful contractions, the patient should be positioned on her left side. Oxygen is administered and emergency medical services are activated.[101]

Preterm labor comprises 6% to 10% of all births in Western countries and is characterized by back pain or discomfort, pelvic and/or abdominal pressure, or vaginal discharge.[99,102] Spontaneous labor may begin at any stage during the pregnancy. In the event of the patient having symptoms in the dental office, the patient should be placed in a reclined and comfortable position and vital signs should be monitered. Emergency medical services and the patient's obstetrician should be notified immediately.

DENTAL MANAGEMENT GUIDELINES

First trimester (conception to 14th week)

The most critical and rapid cell division and active organogenesis occur between the second and the eighth week of postconception. Therefore, the greater risk of susceptibility to stress and teratogens occurs during this time and 50% to 75% of all spontaneous abortions occur during this period.[35]

The recommendations are:

1. Educate the patient about maternal oral changes during pregnancy.
2. Emphasize strict oral hygiene instructions and thereby plaque control.
3. Limit dental treatment to periodontal prophylaxis and emergency treatments only.
4. Avoid routine radiographs. Use selectively and when needed.

Second trimester (14th to 28th week)

Organogenesis is completed and therefore the risk to the fetus is low. This is the safest period for providing dental care during pregnancy.

The recommendations are:

1. Oral hygiene, instruction, and plaque control.
2. Scaling, polishing, and curettage may be performed if necessary.
3. Control of active oral diseases, if any.
4. Elective dental care is safe.
5. Avoid routine radiographs. Use selectively and when needed.

Third trimester (29th week until childbirth)

Although there is no risk to the fetus during this trimester, the pregnant mother may experience an increasing level of discomfort. Short dental appointments should be scheduled with appropriate positioning while in the chair to prevent supine hypotension. It is safe to perform routine dental treatment in the early part of the third trimester, but from the middle of the third trimester routine dental treatment should be avoided.

The recommendations are:

1. Oral hygiene, instruction, and plaque control.
2. Scaling, polishing, and curettage may be performed if necessary.
3. Avoid elective dental care during the second half of the third trimester.
4. Avoid routine radiographs. Use selectively and when needed.

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