

TABLE 2

ADVERSE DRUG INTERACTIONS IN DENTISTRY: ANTIBIOTICS.

POSSIBLE DRUG INTERACTION	SIGNIFICANCE RATING	MECHANISM AND CLINICAL PRESENTATION
Bactericidal antibiotics with bacteriostatic antibiotics	2	Theoretically, bactericidal drugs work best when microbes are actively growing. By inhibiting cell growth, bacteriostatic agents may antagonize the bactericidal agent. This interaction is not consistently demonstrated clinically.
Tetracyclines with products that contain divalent or trivalent cations	2	Tetracycline molecules chelate divalent and trivalent cations, impairing antibiotic absorption. In addition, antacids can raise the gastrointestinal pH, also impairing absorption. Serum tetracycline levels can be reduced 20 to 100 percent, leading to poor antibiotic efficacy.
Metronidazole with alcohol	2	Metronidazole produces a disulfiram effect by inhibiting the enzyme acetaldehyde dehydrogenase. Acetaldehyde accumulation can lead to facial flushing, headache, palpitation and nausea.
Metronidazole with lithium	1	Metronidazole inhibits the renal excretion of lithium, leading to elevated lithium blood concentrations. Lithium toxicity— as manifested by confusion, ataxia and kidney damage— can result.
Tetracyclines with lithium	4	Metronidazole inhibits the renal excretion of lithium, leading to elevated lithium blood concentrations. Lithium toxicity— as manifested by confusion, ataxia and kidney damage— can result. A single case report describes elevated lithium blood concentrations and lithium toxicity with concomitant tetracycline administration. ²⁵ Another report ²⁶ and a clinical research study ²⁷ do not support the interaction.
Erythromycin or tetracyclines with digoxin	1	These antibiotics can reduce the gut flora, in particular <i>Eubacterium lentum</i> , which metabolize a significant amount of oral digoxin in 10 percent of patients taking the drug. Elevated concentrations of digoxin can occur in such patients, leading to digitalis toxicity, as manifested by salivation, visual disturbances and arrhythmias.
Tetracyclines or other broad-spectrum antibiotics with warfarin or anisindione	4	Broad-spectrum antibiotics are hypothesized to reduce the gut flora that normally synthesize vitamin K, a necessary cofactor for clotting. Since warfarin's and anisindione's anticoagulant mechanism involves an antagonism of vitamin K-dependent clotting factors, an increased risk of bleeding may occur. Interaction appears significant only in patients with poor vitamin K intake.
Erythromycin, clarithromycin or metronidazole with warfarin or anisindione	1	These antibiotics decrease the metabolism of warfarin and anisindione and can significantly increase prothrombin times and increase the risk of serious bleeding in anticoagulated patients. Signs of this adverse interaction include hematuria, bruising and hematoma formation.

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above 2.5 mEq/L.² In addition, elevated blood lithium concentrations can lead to renal dysfunction, often in the form of nephrogenic diabetes insipidus,

resulting in excessive excretion of dilute urine.^{2,21}

Three cases have been reported in the literature in which the administration of metro-

nidazole for one week (500-1,000 milligrams daily) apparently induced elevations in lithium blood concentrations with concomitant toxicity.^{22,23} In

TABLE 2 CONTINUED

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POSSIBLE DRUG INTERACTION	SIGNIFICANCE RATING	MECHANISM AND CLINICAL PRESENTATION
Erythromycin, clarithromycin, ketoconazole or itraconazole with a host of other drugs that are metabolized by the CYP3A4 and CYP1A2 system in the gut wall and liver	Depends on interacting drug (see below)	These antimicrobial agents block the metabolism and thus increase blood levels of a number of drugs. Severity of the reaction depends on the therapeutic index of the interacting drug.
Astemizole, terfenadine or cisapride	1	Life-threatening ventricular arrhythmias (torsades de pointes). Metronidazole also increases cisapride blood levels.
Alfentanil	1	Enhanced and/or prolonged respiratory depression. Ketoconazole not implicated.
Bromocriptine	1	Increased risk of adverse central nervous system effects, dyskinesias and hypotension.
Carbamazepine	1	Increased risk of ataxia, vertigo, drowsiness and confusion. Cardiac arrest reported in one child taking erythromycin. ⁶⁸
Cyclosporine	1	Enhanced immunosuppression and nephrotoxicity.
Felodipine and possibly other calcium-channel blockers	1	Increased risk of hypotension, tachycardia and edema.
Methylprednisolone or prednisone	1	Increased risk of Cushing's syndrome and immunosuppression.
Theophylline	1	Increased risk of tachycardia, cardiac arrhythmias, tremors and seizures. Ketoconazole not implicated in this interaction.
Lovastatin and possibly other -statins	1	Muscle pain and rhabdomyolysis (skeletal muscle lysis). Pharmacokinetic interaction demonstrated for azole antifungal drugs.
Triazolam or oral midazolam	2	Marked increases in blood levels of both benzodiazepines when taken by mouth, leading to increases in sedative depth and duration.
Disopyramide	4	A few clinical reports of arrhythmias or heart block with concurrent erythromycin use. Definitive pharmacokinetic studies are needed.
Penicillins, cephalosporins, erythromycin, clarithromycin, tetracyclines, metronidazole with combined estrogen and progestin oral contraceptives	4	Sporadic case reports have implicated the concomitant ingestion of antibiotics and oral contraceptives with unwanted pregnancies. It is theorized that antibiotics, by decimating the normal gut flora, can interfere with the enterohepatic recycling of the estrogen component of oral contraceptives, thereby leading to subtherapeutic blood levels and ovulation. With the exception of the antituberculosis drug rifampin, clinical studies have failed to demonstrate an interaction.

one woman, lithium blood concentrations increased from 1.3 mEq/L to 1.9 mEq/L. She developed signs (such as ataxia, mental clouding and muscle weakness) of lithium toxicity.²² In

another woman, lithium blood concentrations were elevated to a lesser degree (from 1.1 mEq/L to 1.3 mEq/L), but she developed persistent polyuria and nocturia, indicative of kidney

damage.²³ In a third female patient, lithium blood concentrations increased dramatically from 0.9 mEq/L to 2.0 mEq/L. She was admitted to the hospital because of severe confusion