4. Check for pregnancy; avoid drug/use with extreme caution during first 2 trimesters.
5. Give in high enough doses for anti-inflammatory effects when needed; use lower dose for analgesic effects. Reduce dose by half in those over 65 years old.
6. Monitor BP, CBC, renal and LFTs; reduce dose with dysfunction and assess for bleeding.

CLIENT/FAMILY TEACHING
1. May give with water, milk, or meals to reduce gastric irritation. Do not crush or chew tablets.
2. Report adverse effects, unusual bruising/bleeding, or lack of response; may inhibit platelets which is reversible with drug discontinuation. Do not give with acetaminophen or aspirin.
3. May cause dizziness or drowsiness; use care when operating machinery or driving.
4. Report stool color changes or diarrhea; can cause electrolyte imbalance or GI bleed.
5. Must take on a regular basis to sustain anti-inflammatory effect.
6. NSAIDs may cause an increased risk of serious CV thrombotic events, MI, and stroke, which can be fatal. Drug can precipitate Reye’s syndrome.
7. Pregnant women should avoid use late in pregnancy.
8. Keep all F/U to assess response, labs and for adverse SE. Drug dose needs to be adjusted according to age, condition, and changes in disease activity.

OUTCOMES/EVALUATE
↓ Pain/inflammation; ↑ joint mobility

**Digoxin**
(di-h-JOX-in)

**Classification(s):** Cardiac glycoside

**Pregnancy Category:** A

**Rx:** Digoxin, Digoxin Injection Pediatric.

**Rx:** Apo-Digoxin, Digoxin Injection C.S.D., Digoxin Pediatric Injection C.S.D., PMS-Digoxin.

**INDICATIONS/USES**
(1) CHF, including that due to venous congestion, edema, dyspnea, orthopnea, and cardiac arrhythmia. May be drug of choice for CHF because of rapid onset, relatively short duration, and ability to be administered PO or IV. (2) Control of rapid ventricular contraction rate in clients with atrial fibrillation or flutter. (3) Slow HR in sinus tachycardia due to CHF. (4) SVT. (5) Prophylaxis and treatment of recurrent paroxysmal atrial tachycardia with paroxysmal AV junctional rhythm. (6) Cardiogenic shock (value not established).

**ACTION/KINETICS**

**Action**

Increases the force and velocity of myocardial contraction (positive inotropic effect) by increasing total peripheral resistance. This effect is due to inhibition of sodium/potassium-ATPase in the sarcolemmal membrane, which alters excitation-contraction coupling. Inhibiting sodium/potassium-ATPase results in increased calcium influx and increased release of free calcium ions within the myocardial cells, which then potentiate the contractility of cardiac muscle fibers. Digoxin also decreases HR, decreases the rate of conduction, and increases the refractory period of the AV node due to an increase in parasympathetic tone and a decrease in sympathetic tone. Clinical effects are not seen until steady-state plasma levels are reached. The initial dose of digoxin is larger (loading dose) and is traditionally referred to as the digitalizing dose; subsequent doses are referred to as maintenance doses.

**Pharmacokinetics**

**Onset, PO:** 0.5–2 hr; **time to peak effect:** 2–6 hr. **Duration:** Over 24 hr. **Onset, IV:** 5–30 min; **time to peak effect:** 1–4 hr. **Duration:** 6 days. **t1/2:** 30–40 hr. **Therapeutic serum level:** 0.5–2.0 ng/mL. Serum levels above 2.5 ng/mL indicate toxicity. Fifty percent to 70% is excreted unchanged by the kidneys. Bioavailability depends on the dosage form: Tablets (60–80%) and elixir (70–85%). Thus, changing dosage forms may require dosage adjustments. **Plasma protein binding:** 20–25%.

**CONTRAINDICATIONS**

Ventricular fibrillation or tachycardia (unless congestive failure supervenes after protracted episode not due to digitalis), in presence of digoxin toxicity, hypersensitivity to cardiac glycosides, beriberi heart disease, certain cases of hypersensitive carotid sinus syndrome.
SPECIAL CONCERNS

- Use with caution in clients with ischemic heart disease, acute myocarditis, hypertrophic subaortic stenosis, hypoxic or myxedematous states, Adams-Stokes or carotid sinus syndromes, cardiac amyloidosis, or cyanotic heart and lung disease, including emphysema and partial heart block.
- Also use with caution and at reduced dosage in elderly, debilitated clients, pregnant women and nursing mothers, and newborn, term, or premature infants who have immature renal and hepatic function and in reduced renal and/or hepatic function.
- Those with carditis associated with rheumatic fever or viral myocarditis are especially sensitive to digoxin-induced disturbances in rhythm.
- Electric pacemakers may sensitize the myocardium to cardiac glycosides.
- The t½ of digoxin is prolonged in the elderly; anticipate smaller doses.
- Be especially alert to cardiac arrhythmias in children. This sign of toxicity occurs more frequently in children than in adults.

SIDE EFFECTS

Most Common
Tachycardia, headache, dizziness, mental disturbances, N&V, diarrhea, anorexia, blurred or yellow vision.

Digoxin is extremely toxic and has caused death even in clients who have received the drug for long periods of time. There is a narrow margin of safety between an effective therapeutic dose and a toxic dose. Overdosage caused by the cumulative effects of the drug is a constant danger in therapy. Digoxin toxicity is characterized by a wide variety of symptoms, which are hard to differentiate from those of the cardiac disease itself. One of the most serious side effects of digoxin is hypokalemia. This may lead to cardiac arrhythmias, muscle weakness, hypotension, and respiratory distress. Other agents causing hypokalemia reinforce this effect and increase the chance of digitalis toxicity. Such reactions may occur in clients who have been on digoxin maintenance for a long time.

CV: Changes in the rate, rhythm, and irritability of the heart and the mechanism of the heartbeat. Extrasystoles, bigeminal pulse, coupled rhythm, ectopic beat, and other forms of arrhythmias have been noted. Death most often results from ventricular fibrillation. Discontinue digoxin in adults when pulse rate falls below 60 beats/min. All cardiac changes are best detected by the ECG, which is also most useful in clients suffering from intoxication. Acute hemorrhage. GI: Anorexia, N&V, excessive salivation, epigastric distress, abdominal pain, diarrhea, bowel necrosis. Clients on digoxin therapy may experience two vomiting stages. The first is an early sign of toxicity and is a direct effect of digoxin on the GI tract. Late vomiting indicates stimulation of the vomiting center of the brain, which occurs after the heart muscle has been saturated with digoxin. CNS: Headaches, fatigue, lassitude, irritability, malaise, muscle weakness, insomnia, stupor. Psychotomimetic effects (especially in elderly or arteriosclerotic clients or neonates) including disorientation, confusion, depression, aphasia, delirium, hallucinations, and, rarely, convulsions. Neuromuscular: Neurologic pain involving the lower third of the face and lumbar areas, paresthesia. Visual disturbances: Blurred vision, flickering dots, white halos, borders around dark objects, diplopia, ambyopia, color perception changes. Hypersensitivity: Skin reactions (urticaria, fever, pruritus, facial and angioneurotic edema). Miscellaneous: Chest pain, coldness of extremities.

LABORATORY TEST CONSIDERATIONS

May ↓ PT. Alters tests for 17-ketosteroids and 17-hydroxycorticosteroids.

OVERDOSE MANAGEMENT

Symptoms: Adults: The relationship of digoxin levels to symptoms of toxicity varies significantly from client to client; thus, it is not possible to identify digoxin levels that would define toxicity accurately. Toxicity: GI: Anorexia, N&V, diarrhea, abdominal discomfort, or pain. CNS: Blurred, yellow, or green vision and halo effect; headache, weakness, drowsiness, mental depression, apathy, restlessness, disorientation, confusion, seizures, EEG abnormalities, delirium, hallucinations, neuralgia, psychosis. CV: VT, unifocal or multiformal PVCs (especially in bigeminal or trigeminal patterns), paroxysmal/nonparoxysmal nodal rhythms, AV dissociation, accelerated junctional rhythm, excessive slowing of the pulse, AV block (may proceed to complete block), atrial fibrillation, ventricular fibrillation (most common cause of death).
**Children:** Visual disturbances, headache, weakness, apathy, and psychosis occur but may be difficult to recognize. CV: Conduction disturbances, supraventricular tachyarrhythmias (e.g., AV block), atrial tachycardia with or without block, nodal tachycardia, unifocal or multifocal ventricular premature contractions, ventricular tachycardia, sinus bradycardia (especially in infants).

**Treatment:**
- Discontinue drug, admit to ICU for continuous ECG monitoring.
- If serum potassium is below normal, KCl should be administered in divided PO doses totaling 3–6 grams (40–80 mEq). Potassium should not be used when severe or complete heart block is due to digoxin and not related to tachycardia.
- Atropine: A dose of 0.01 mg/kg IV to treat severe sinus bradycardia or slow ventricular rate due to secondary AV block.
- Cholestyramine, colestipol, activated charcoal: To bind digoxin in the intestine, thus preventing enterohepatic recirculation.
- Digoxin immune FAB: See drug entry. Given in approximate equimolar quantities as digoxin, it reverses S&S of toxicity, often with improvement within 30 min.
- Lidocaine: A dose of 1 mg/kg given over 5 min followed by an infusion of 15–50 mcg/kg/min to maintain normal cardiac rhythm.
- Phenytoin: For atrial or ventricular arrhythmias unresponsive to potassium, can give a dose of 0.5 mg/kg at a rate not exceeding 50 mg/min (given at 1–2 hr intervals). The maximum dose should not exceed 10 mg/kg/day.
- Countershock: A direct-current countershock can be used only as a last resort. If required, initiate at low voltage levels. **Treatment:** In Children: Give potassium in divided doses totaling 1–1.5 mEq/kg (if correction of arrhythmia is urgent, a dose of 0.5 mEq/kg/hr can be used) with careful monitoring of the ECG. The potassium IV solution should be dilute to avoid local irritation although IV fluid overload must be avoided.

**DRUG INTERACTIONS**

The following drugs increase serum digoxin levels, leading to possible toxicity: Aminoglycosides, ami-iodarone, anticholinergics, atorvastatin, benzodi-azepines, captopril, clarithromycin, diltiazem, di-pyridamole, erythromycin, esmolol, flecainide, hydroxychloroquine, ibuprofen, indomethacin, itraconazole, nifedipine, quinidine, quinine, telmisartan, tetracyclines, tolbutamide, verapamil.

**Albuterol** / Digoxin binding to skeletal muscle

**Aloe** / Potential for digoxin effect R/T aloe-induced hypokalemia

**Amiloride** / Digoxin inotropic effect

**Amphotericin B** / Potential for cardiac arrhythmias following parenteral calcium

**Aminoglycosides** / Digoxin effect R/T GI tract absorption

**Aminosalicylic acid** / Digoxin effect R/T GI tract absorption

**Aminosalicylic acid** / Digoxin effect R/T GI tract absorption

**Amphotericin B** / Potential for cardiac arrhythmias following parenteral calcium

**Antacids** / Digoxin effect R/T GI tract absorption

**Beta-blockers** / Complete heart block possible

**Buckthorn bark/berry** / Potential for digoxin effect R/T to buckthorn-induced hypokalemia

**Calcium preparations** / Cardiac arrhythmias following parenteral calcium

**Chamomile flower** / Potential for digoxin effect R/T to chamomile-induced hypokalemia

**Chlorthalidone** / K+ and Mg++ loss with chance of digitalis toxicity

**Chloretamyl** / Binds digoxin in the intestine and its absorption

**Colestipol** / Binds digoxin in the intestine and its absorption

**Disopyramide** / May alter effect of digoxin

**Ephedra** / Chance of cardiac arrhythmias

**Ephedrine** / Chance of cardiac arrhythmias

**Epinephrine** / Chance of cardiac arrhythmias

**Ethacrynic acid** / K+ and Mg++ loss with chance of digitalis toxicity

**Fluoxetine** / Possible serum digoxin levels

**Furosemide** / K+ and Mg++ loss with chance of digoxin toxicity

**German chamomile flower** / Potential for digoxin effect R/T to chamomile-induced hypokalemia

**Ginseng** / Digoxin levels

**Glucose infusions** / Large infusions of glucose may cause K+ and chance of digoxin toxicity
Grapefruit juice / ↑ Digoxin bioavailability; do not take digoxin with grapefruit juice

Hawthorn / Potential of digoxin effect

Hypoglycemic drugs / ↓ Effect of digitalis glycosides R/T ↑ liver breakdown

Iceland moss / Potential for ↑ digoxin effect R/T to iceland moss-induced hypokalemia

Indian snakeroot / ↑ Risk of bradycardia

Ivy leaf / Potential for ↑ digoxin effect R/T to ivy-leaf-induced hypokalemia

Levethyroxine / ↓ Serum levels and therapeutic digoxin effect

Licorice / Potential for ↑ digoxin effect R/T to licorice-induced hypokalemia

Marshmallow root / Potential for ↑ digoxin effect R/T to marshmallow-root-induced hypokalemia

Methimazole / ↑ Chance of toxic effects of digitalis

Metoclopramide / ↓ Digoxin effect R/T ↓ GI tract absorption

Muscle relaxants, nondepolarizing / ↑ Risk of cardiac arrhythmias

Penicillamine / ↓ Serum digoxin levels

Propranolol / Potentiates digitalis-induced bradycardia

Rhubarb root / Potential for ↑ digoxin effect R/T to rhubarb-root-induced hypokalemia

St. John’s wort / ↓ Digoxin plasma levels R/T ↑ renal excretion

Sarsaparilla root / Potential for ↑ absorption of digoxin

Senna pod/leaf / Potential for ↑ digoxin effect R/T to senna-induced hypokalemia

Spirinolactone / Either ↑ or ↓ toxic effects of digoxin

Sucinylcholine / ↑ Chance of cardiac arrhythmias

Sulfasalazine / ↓ Digoxin effect R/T ↓ GI tract absorption

Sympathomimetics / ↑ Chance of cardiac arrhythmias

Thiazides / ↑ K+ and Mg&dbnbsp lose with ↑ chance of digoxin toxicity

Thioamines / ↑ Effect and toxicity of digoxin

Thyroid / ↓ Digoxin effect

Triamterene / ↑ Digoxin effects

HOW SUPPLIED

Elixir, Pediatric: 0.05 mg/mL; Injection: 0.1 mg/mL (pediatric), 0.25 mg/mL; Tablets: 0.125 mg, 0.25 mg.

DOSAGE

ELIXIR; TABLETS

Digitalization: Rapid.

Adults: A total of 0.75–1.25 mg divided into two or more doses each given at 6–8-hr intervals.

Digitalization: Slow.

Adults: 0.125–0.5 mg/day for 7 days. Pediatric. (Digitalizing dose is divided into two or more doses and given at 6–8-hr intervals.) Children, 10 years and older, rapid or slow: Same as adult dose. 5–10 years: 0.02–0.035 mg/kg. 2–5 years: 0.03–0.05 mg/kg. Premature and newborn infants to 1 month: 0.02–0.035 mg/kg.

Maintenance.

Adults: 0.125–0.5 mg/day. Pediatric: One-fifth to one-third the total digitalizing dose daily. NOTE: An alternate regimen (referred to as the ‘small-dose’ method) is 0.017 mg/kg/day. This dose causes less toxicity.

IV

Digitalization.

Adults: Same as tablets. Maintenance: 0.125–0.5 mg/day in divided doses or as a single dose. Pediatric: Same as tablets.

NURSING IMPLICATIONS

IMPLEMENTATION/ADMINISTRATION/STORAGE

1. Measure liquids precisely using calibrated dropper/syringe.

2. Obtain written parameters for high/low pulse rates, at which cardiac glycosides are to be held; changes in rate or rhythm may indicate toxicity.

3. Differences in bioavailability have been noted between products; monitor when changing from one product to another.

4. If switching from tablets or elixir to the parenteral route, expect reduction in dosage; absorption is much higher with the parenteral form.

5. Protect from light.

6. COMPATIBILITY Give IV injections over 5 min (or longer) either undiluted or diluted
Digoxin

fourfold or greater with sterile water for injection. 0.9% NaCl, RL injection, or DSW.

7. **INCOMPATIBILITY** Administer separately.

**ASSESSMENT**

1. List type, onset, characteristics of S&S. If administered for heart failure, note causes; ensure failure not solely related to diastolic dysfunction; drug’s positive inotropic effect may increase cardiac outflow obstruction with hypertrophic cardiomyopathy.

2. List drugs prescribed that would adversely interact with digoxin and monitor; diuretics may increase toxicity.

3. Assess for hyper/hypothyroidism; hypothyroid sensitive to glycosides while hyperthyroid may require a higher dose of drug.

4. Obtain ECG; note rhythm/rate. Check apical pulse for 1 full min before administering. Identify when to withhold dose i.e., HR <60 bpm in adult, <70 bpm in child, or <90 bpm in infant.

5. Document cardiopulmonary findings; note presence of S3, JVD, HJR, displaced PMI, HR above 100 bpm, rales, peripheral edema, DOE, PND, and echo, MUGA, cardiac catheterization findings. Note NYHA Classification.

6. Observe S&S of toxicity (N&V, abdominal pain, anorexia, confusion, visual disturbances, bradycardia, ECG changes, arrhythmias, headache, seizure). With elderly-- rate of drug elimination is slower.

7. Monitor closely during digitalization:
   - Observe for bradycardia/arrhythmias, count apical rate for at least 1 min before administering drug. Obtain written parameters (e.g., HR >60 bpm) for drug administration.
   - Anticipate more than once-daily dosing in most children (up to age 10) R/T higher metabolic activity.
   - With coworker simultaneously take apical and radial pulse for 1 min; report pulse deficit (e.g., the wrist rate is less than the apical rate); may indicate adverse drug reaction.
   - Monitor weights and I&O; check for edema. Adequate intake will help prevent cumulative toxic drug effects.
   - If taking non-potassium-sparing diuretics as well as digoxin, will need potassium supplements. Provide the most palatable preparation available. (Liquid potassium preparations usually bitter.)

8. When given to newborns, use monitor to identify early evidence of toxicity: excessive slowing of sinus rate, sinoatrial arrest, prolonged PR interval.

9. Monitor digoxin levels periodically, assess for S&S of toxicity; draw specimen more than 6 hr after last dose.

10.**CLIENT/FAMILY TEACHING**

1. Take at the same time each day; after meals to lessen gastric irritation. Do not take with grapefruit juice.

2. Maintain written record of pulse rates and weights; review guidelines for withholding medication and reporting abnormal pulse rates. Report Wt gains of >2 lb/day or >5 lb/week.

3. Do not change brands; different preparations have variations in bioavailability and may cause toxicity or loss of effect.

4. Follow directions carefully for taking medication. If one dose is accidentally missed, do not double up on the next dose.

5. Report adverse effects or toxic drug symptoms: Anorexia, N&V, abdominal pain and diarrhea are often early symptoms due to the toxic effects on the GI tract and brain. Disorientation, agitation, visual disturbances, changes in color perception, irregular heartbeat, and hallucinations may also occur.


7. Consult provider before taking any other medications, whether prescribed or OTC, because
Digoxin Immune Fab

**Classification(s):** Antidote for digoxin poisoning

**Pregnancy Category:** C

**Rx:** DigiFab, Digibind.

**INDICATIONS/USES**

Life-threatening digoxin toxicity or overdosage. Symptoms of toxicity include severe sinus bradycardia, second- or third-degree heart block that does not respond to atropine, ventricular tachycardia, and ventricular fibrillation.

**NOTE:** Cardiac arrest can be expected if a healthy adult ingests more than 10 mg digoxin or a healthy child ingests more than 4 mg. Also, steady-state serum concentrations of digoxin greater than 10 ng/mL or potassium concentrations greater than 5 mEq/L as a result of digoxin therapy require use of digoxin immune Fab. (Ovine)

**ACTION/KINETICS**

**Action**

Digoxin immune Fab are antibodies that bind to digoxin making them unavailable to bind at their site of action. In cases of digoxin toxicity, the antibodies bind to digoxin and the complex is excreted through the kidneys. As serum levels of digoxin decrease, digoxin bound to tissue is released into the serum to maintain equilibrium and this is then bound and excreted. The net result is a decrease in both tissue and serum digoxin.

**Pharmacokinetics**

**Onset:** Less than 1 min. Improvement in signs of toxicity occurs within 30 min. $t_{1/2}$ 15–20 hr (after IV administration). Each vial contains either 38 mg or 40 mg of pure digoxin immune Fab, which will bind approximately 0.5 mg digoxin.

**SPECIAL CONCERNS**

- Use with caution during lactation.
- Use in infants only if benefits outweigh risks.
- Clients sensitive to products of sheep origin may also be sensitive to digoxin immune Fab. Skin testing may be appropriate for high-risk clients.

**SIDE EFFECTS**

**Most Common**

- Hypokalemia.

**Miscellaneous:** Hypokalemia. Rarely, hypersensitivity reactions occur, including fever and anaphylaxis.

**HOW SUPPLIED**

- **Digibind:** Injection: 38 mg/vial.
- **DigiFab:** Injection: 40 mg/vial.

**DOSAGE**

**IV**

Dosage depends on the serum digoxin concentration. A large dose has a faster onset, but there is an increased risk of allergic or febrile reactions. The package insert should be carefully consulted.

**Acute ingestion of an unknown amount of digoxin.**

- **Adults and children:** 20 vials (760 mg Digibind or 800 mg DigiFab). In small children, monitor the amount of overload.

**Toxicity during chronic therapy.**

- **Adults:** 6 vials (228 mg of Digibind or 240 mg DigiFab) is usually enough to reverse most cases of toxicity. **Children,** <20 kg: A single vial (38 mg Digibind or 40 mg DigiFab) should be sufficient.

**NURSING IMPLICATIONS**

**IMPLEMENTATION/ADMINISTRATION/STORAGE**

1. **IV** Dose of antidote estimated based on ingested digoxin differs significantly from that...