

# Pharmacological treatment of heart failure

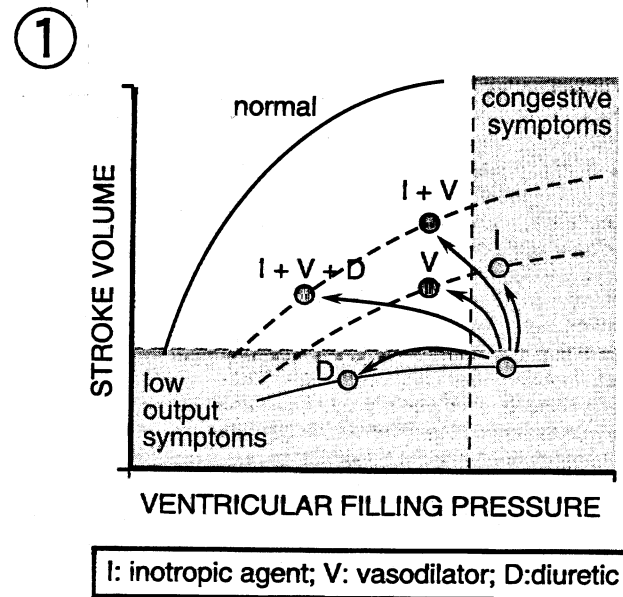


Figure 34-2. Physiological response to pharmacological interventions in heart failure.

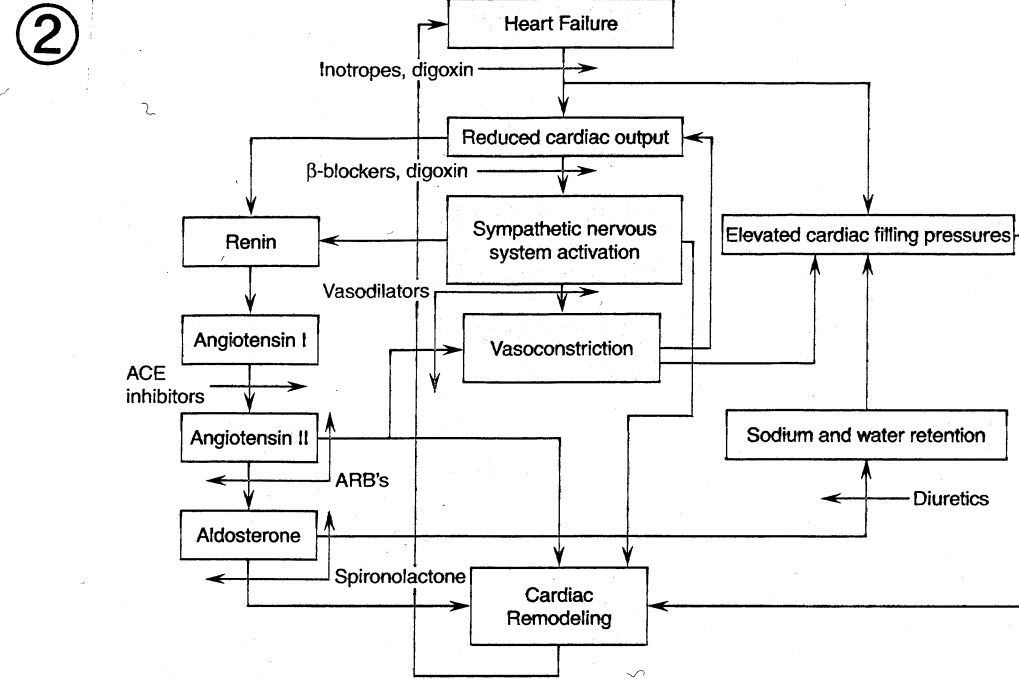


Figure 34-1. Pathophysiological mechanisms of heart failure and major sites of drug action.

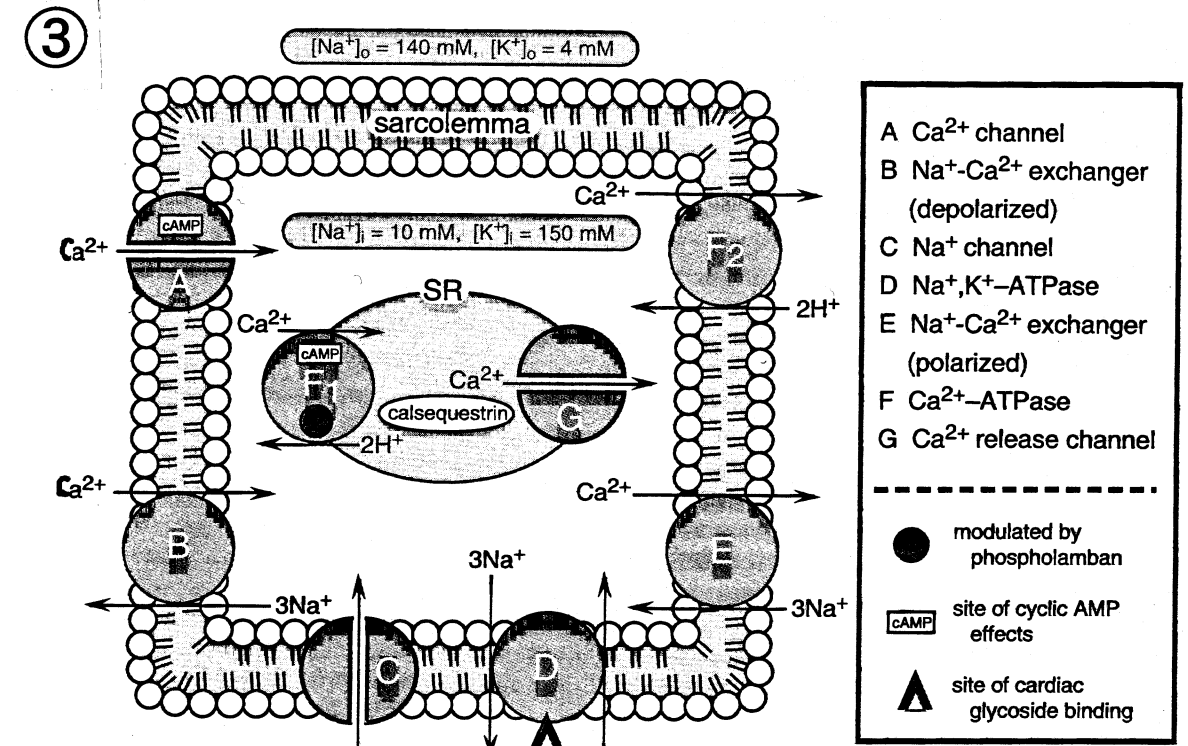


Figure 34-3. Sarcoplasmic exchange of Na<sup>+</sup> and Ca<sup>2+</sup> during cell depolarization and repolarization.

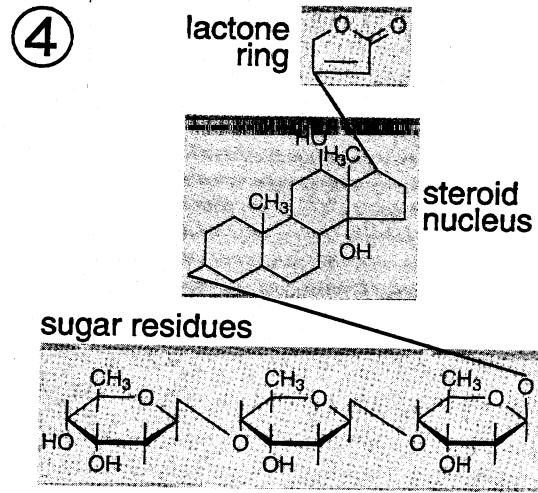


Figure 34-1. Structure of digoxin.

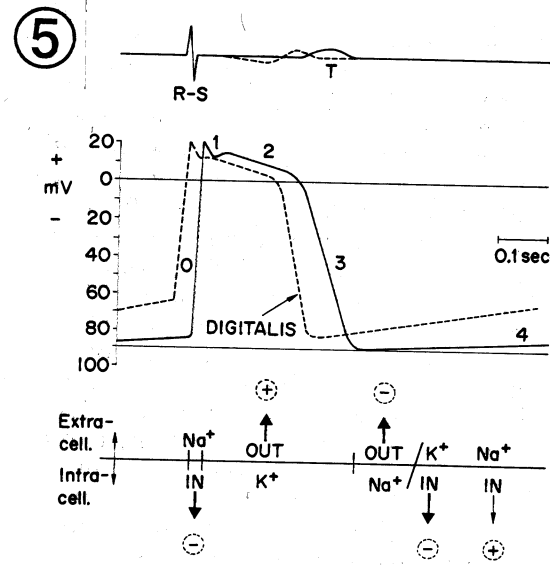


Figure 31-4. Effects of digitalis on subsidiary pacemaker activity.

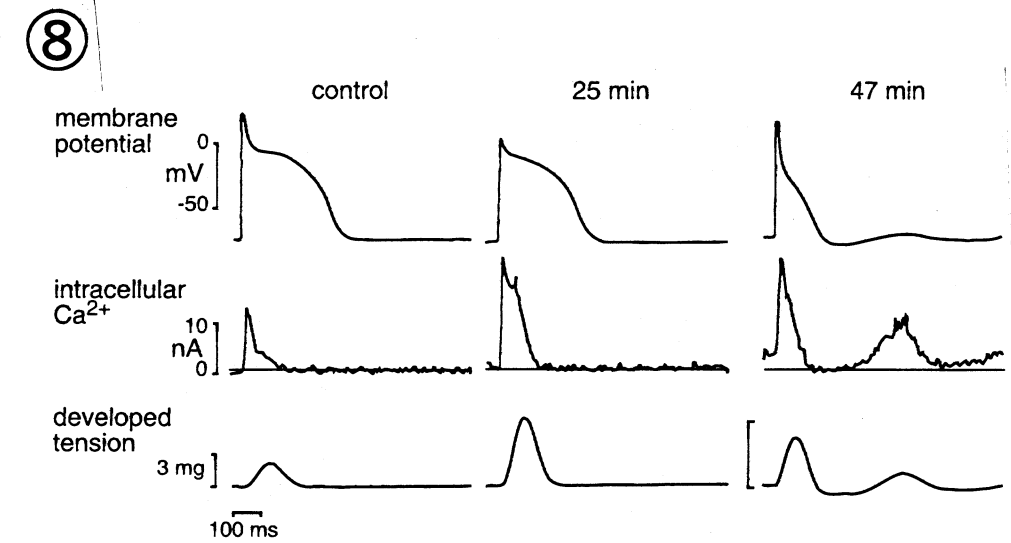
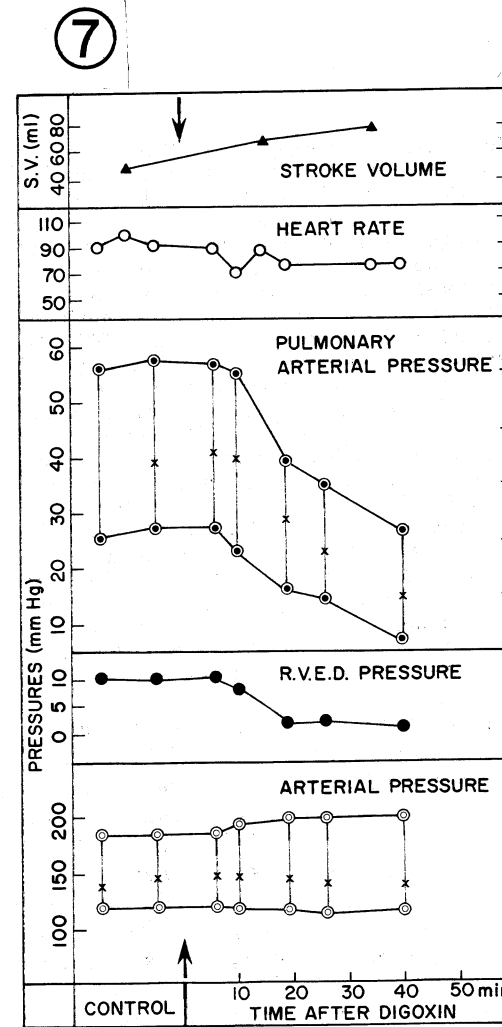


Figure 34-5. Role of intracellular calcium in mediating inotropic and toxic electrophysiological effects of cardiac glycosides.

6 Table 31-3. AVERAGE PHARMACOKINETIC VALUES AND DOSES FOR CARDIAC GLYCOSIDES

|                                   | DIGITOXIN       | DIGOXIN       | DESLANOSIDE  | OUABAIN        |
|-----------------------------------|-----------------|---------------|--------------|----------------|
| Gastrointestinal absorption       | 90-100%         | 60-85%        | Unreliable   | Unreliable     |
| Onset of action *                 | ½-2 hr          | 15-30 min     | 10-30 min    | 5-10 min       |
| Peak effect *                     | 4-12 hr         | 1-5 hr        | 1-2 hr       | ½-2 hr         |
| Plasma concentration, ng/ml       |                 |               |              |                |
| Therapeutic                       | 14-26           | 0.8-1.6       |              |                |
| Toxic                             | > 34            | > 2.4         |              |                |
| Plasma half-life *                | 5-7 days        | 36 hr         | 36 hr        | 21 hr          |
| Excretory pathway                 | Hepatic → Renal | Renal         | Renal        | Renal          |
| Total digitalizing dose (adult) † |                 |               |              |                |
| Oral                              | 1.2-1.6 mg ‡    | 2.0-3.0 mg §  |              |                |
| Intravenous                       | 1.2-1.6 mg †    | 0.75-1.5 mg ¶ | 1.2-1.6 mg # | 0.25-0.5 mg ** |
| Daily oral maintenance dose       | 0.05-0.2 mg     | 0.25-0.75 mg  |              |                |

\* All time values are based on intravenous administration of a single digitalizing dose.

† The values given represent average doses or ranges for complete digitalization; the requirements of individual patients may depart considerably from these figures. For the overwhelming majority of patients, only a fraction of the digitalizing dose should be given initially, followed by subsequent fractional doses at appropriate intervals, as indicated for the individual drugs. For complete discussion, see text.

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| NYHA Functional Class          | I            | II  | III          | IV           |
|--------------------------------|--------------|---|--------------|--------------|
|                                | Mild HF      |   |              | Severe HF    |
| Diuretics                      | Consider use | Consider use                                    | Consider use | Consider use |
| ACE inhibitors                 | Consider use | Consider use                                    | Consider use | Consider use |
| β-receptor blockers            | Consider use | Consider use                                    | Consider use | Consider use |
| Digoxin - atrial fibrillation  | Consider use | Consider use                                    | Consider use | Consider use |
| Digoxin - sinus rhythm         |              | Consider use                                    |              |              |
| Spironolactone                 |              | Consider use                                    |              |              |
| ARB                            |              | Intolerant of ACE inhibitor-cough or angioedema |              |              |
| Hydralazine/nitrates           |              | Intolerant of ACE inhibitor                     |              |              |
| Warfarin - atrial fibrillation | Consider use | Consider use                                    | Consider use | Consider use |
| Warfarin - sinus rhythm        | Consider use | Consider use                                    | Consider use | Consider use |

Figure 34-10. Guidelines for pharmacological management of ambulatory patients with heart failure.

As the number of options for the drug therapy of heart failure increases, it has become more important to determine, based in most cases on evidence from clinical trials, the optimal usage of these drugs. Shown are recommendations for the pharmacological management of left ventricular systolic dysfunction as formulated by the Heart Failure Society of America. Blue boxes represent groups in which drugs should be routinely administered. Gray boxes represent groups in whom drug use should be considered. (ACE inhibitor = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; HF = heart failure) (Adapted from Heart Failure Society of America, 1999, with permission.)