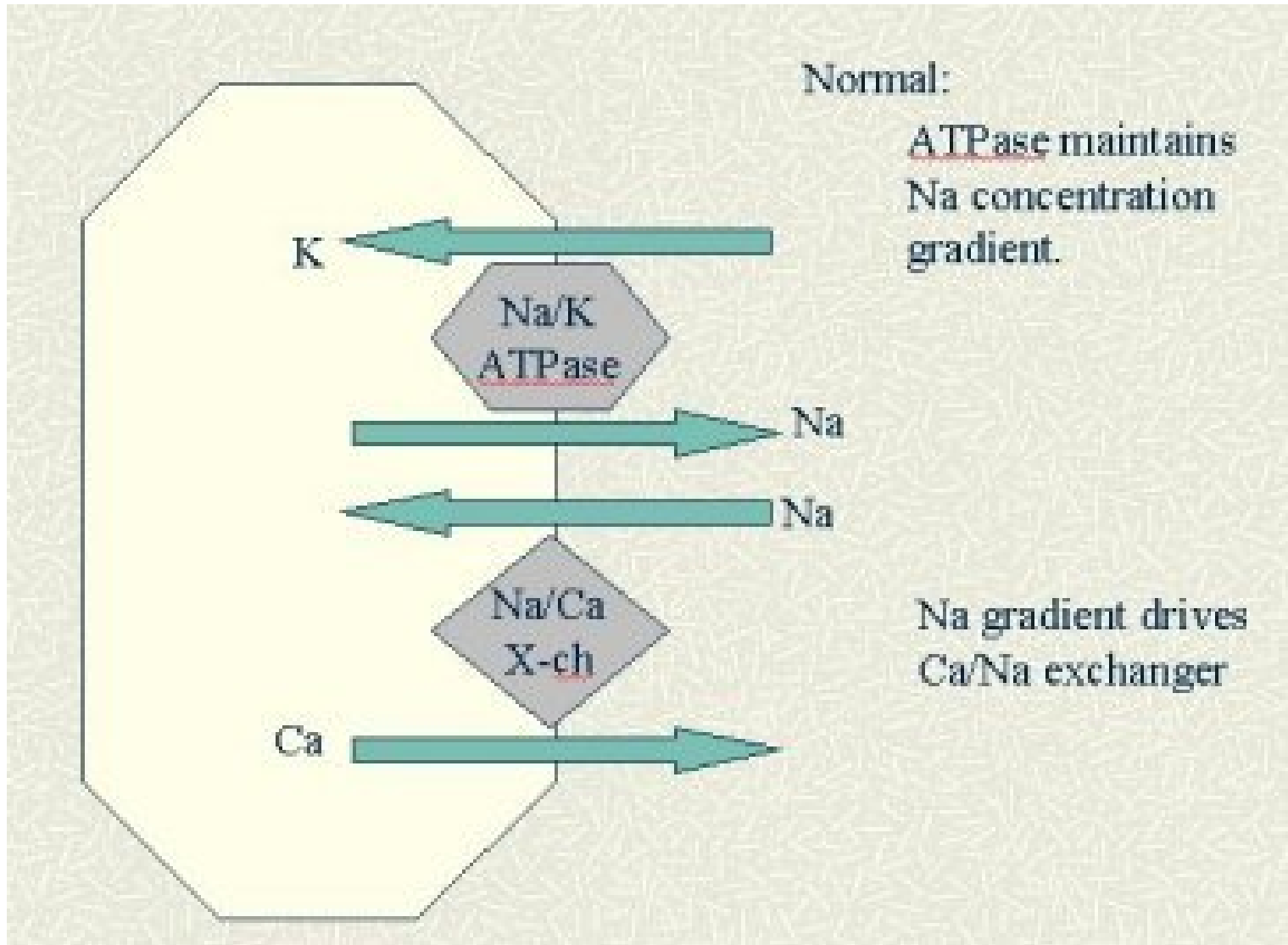
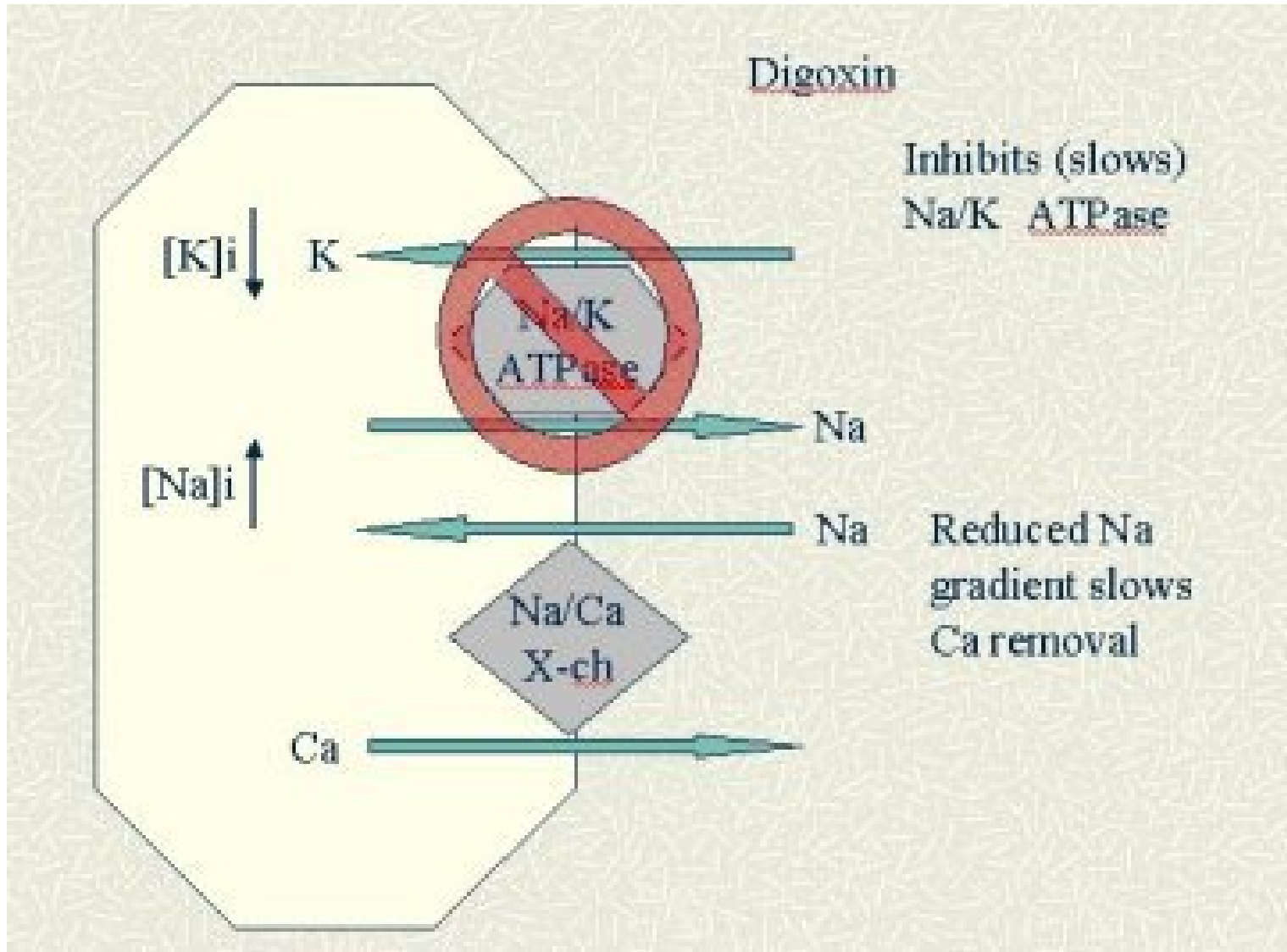


# Brief review of digoxin poisoning

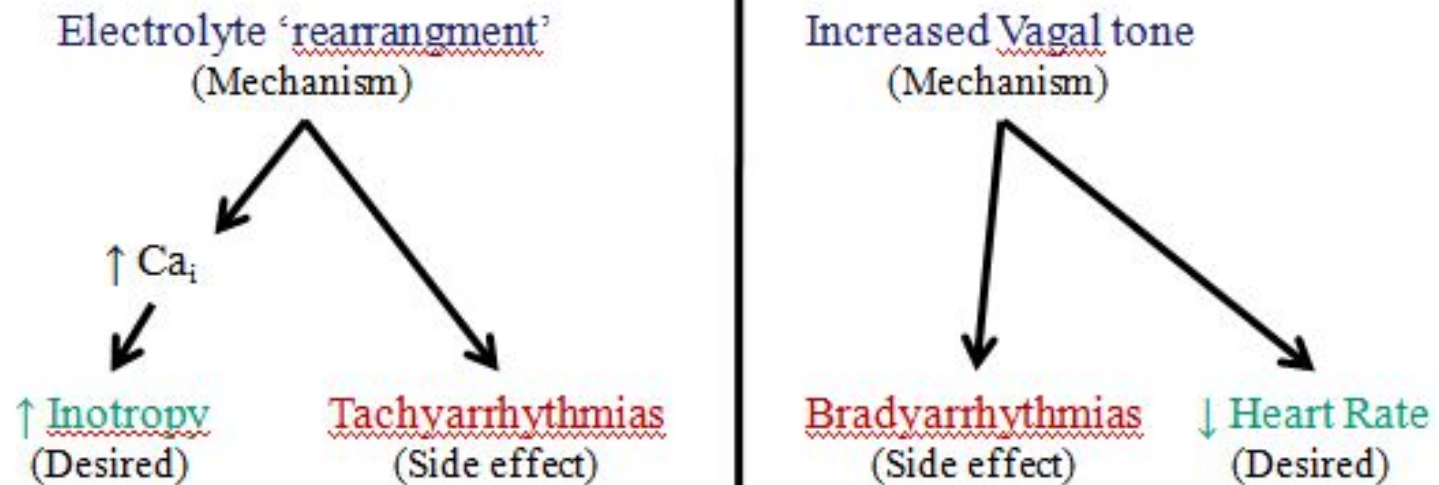
# Pharmacokinetics

- $V_d = 4-7 \text{ L/kg}$
- Half-life 36-48 hrs
- Protein binding 25%
- Extensive tissue binding
- Elimination mainly by kidney
- Large molecular weight 780g/mol





## Digoxin mechanisms of action



- Premature ventricular depolarizations
- nodal rhythms
- AV dissociation

# Other toxicity

- GI toxicity (due to vagal effects)
  - Anorexia
  - Abdominal pain / discomfort
  - Diarrhea
  - Vomiting
- Headache / visual disturbance
- Hyperkalemia (acute toxicity)

# Management

- Stop digoxin
- Mainly supportive management
- Treatment of arrhythmias
- Treatment of hypokalemia
- *Digoxin Immune Fab*
- Activated charcoal (acute toxicity) / MDAC

# Digoxin Immune Fab

- Antidote
- Immunoglobulin fragments from sheep immunized with digoxin derivative
- DigiFab / Digibind 38mg/vial
- Digitalis Antidote (doubled)
  - **Digibind** - GlaxoSmithKline; Institute of Pharmaceutical Research and Technology
  - **Digidot** - Roche
  - **DigiFab** - Protherics; Institute of Pharmaceutical Research and Technology
  - **Digitalis Antidot** - Roche
  - **Digitalis Antidote** - Roche



# Pharmacology

- Binding digoxin (80:1 in terms of mass)
- Prohibit digoxin from binding to receptor site
- Complex accumulated in blood
- Excreted via kidney



# Indications

- Severe toxicity
  - Ventricular dysrhythmias, bradyarrhythmias, 2nd / 3rd degree heart block
- Refractory hypotension
- Acute toxicity
  - Hyperkalemia
  - >10mg (adult) / >4mg (child)
  - >10ng/ml (12nmol/L)
- Chronic toxicity
  - >6ng/ml (adult) / >4ng/ml (child)
- Failed conventional treatment

# Dose of DigiFab / Digibind (vial)

- *Concentration* (ng/mL) x *body weight* (kg) / 100
- *Ingested dose* (mg) / 0.5
- Critical / cardiac arrest patients 10–20 vials
  
- Consider
  - Repeated dose
  - Plasma exchange

# **Treatment of 150 Cases of Life-Threatening Digitalis Intoxication With Digoxin-Specific Fab Antibody Fragments**

## **Final Report of a Multicenter Study**

Elliott M. Antman, MD, Thomas L. Wenger, MD, Vincent P. Butler Jr., MD,  
Edgar Haber, MD, and Thomas W. Smith, MD

**(Circulation 1990;81:1744-1752)**

- 150 patients
- Neonate – 94yo
- Digibind

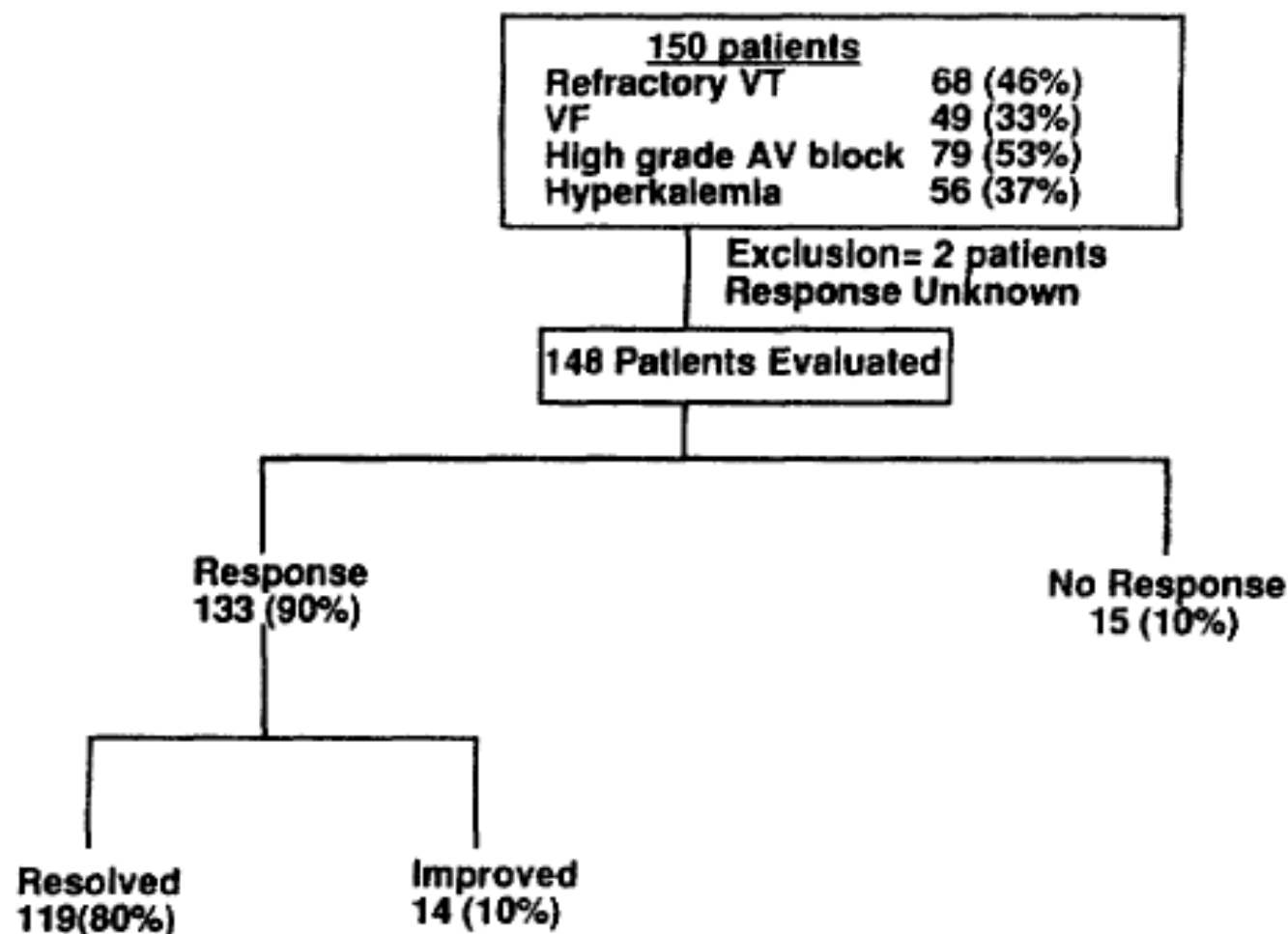
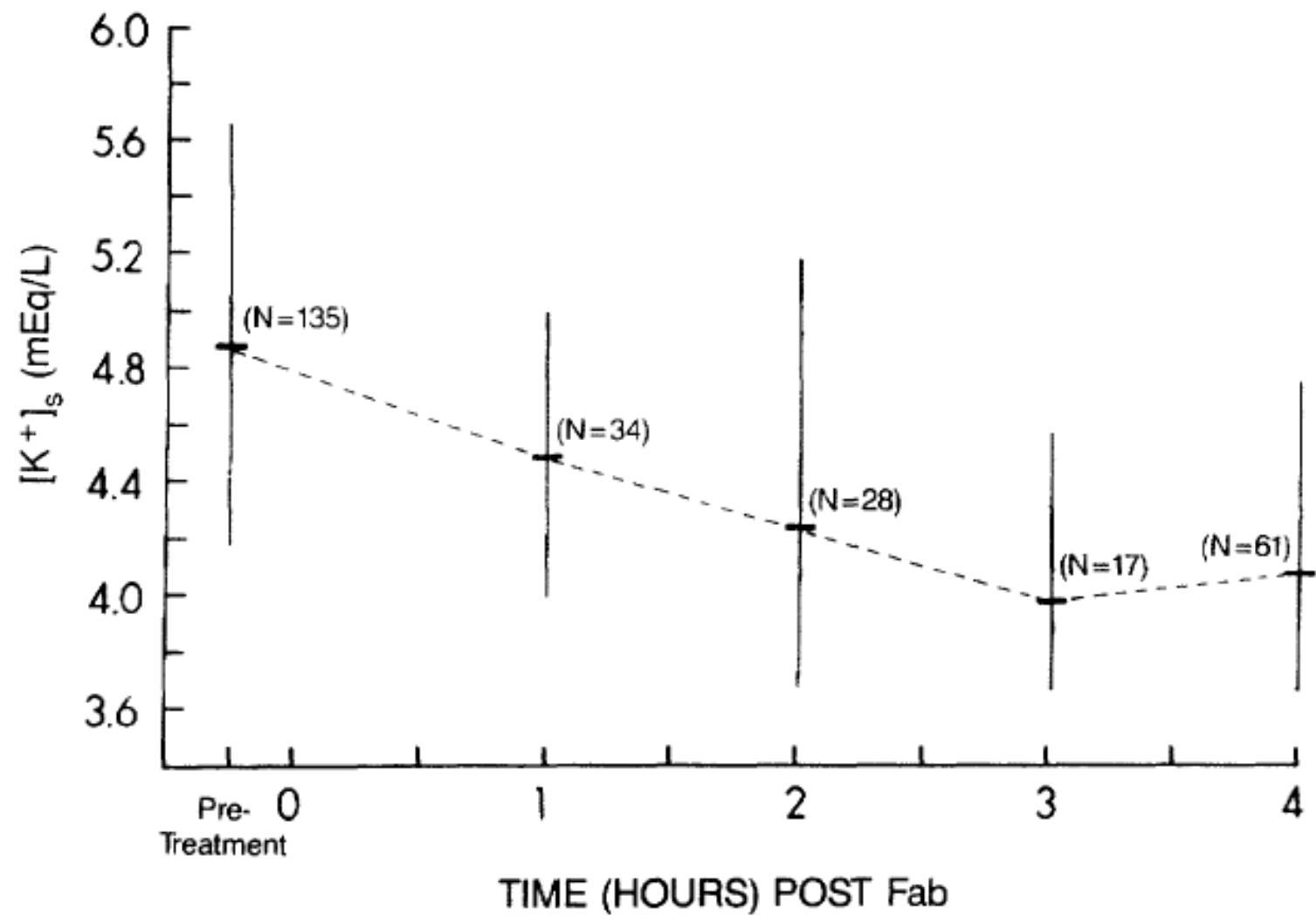


FIGURE 1. *Clinical response to Fab fragment treatment in 150 patients with potentially life-threatening digitalis intoxication. VT, ventricular tachycardia; VF, ventricular fibrillation; AV, atrioventricular.*

# Results

- Median time of response 19 minutes (after termination of infusion)
- 75% response within 60 minutes
- Complete recovery usually within 4 hours
- 30/56 cardiac arrest patients survived hospitalization (54%)
- 14 (9%) with adverse reaction



# DigiFab vs. Digibind

- Half-life 15 vs. 23 hours
- Equally effective in reversal of cardiac toxicity / hyperkalemia in rat models

**Dart RC, Garcia RA, & Shannon M: A comparison of the efficacy of Digibind(R) to a new digoxin specific fab (Digitab(TM)). J Toxicol-Clin Toxicol 1995; 33:498**



# Side effects

- *Hypokalemia*
- *Aggravated heart failure*
- Loss of control of ventricular rate (digoxin effect)
- Allergic reaction

Thank you