Stage D Heart Failure: Diagnosis and Management

September 28, 2009
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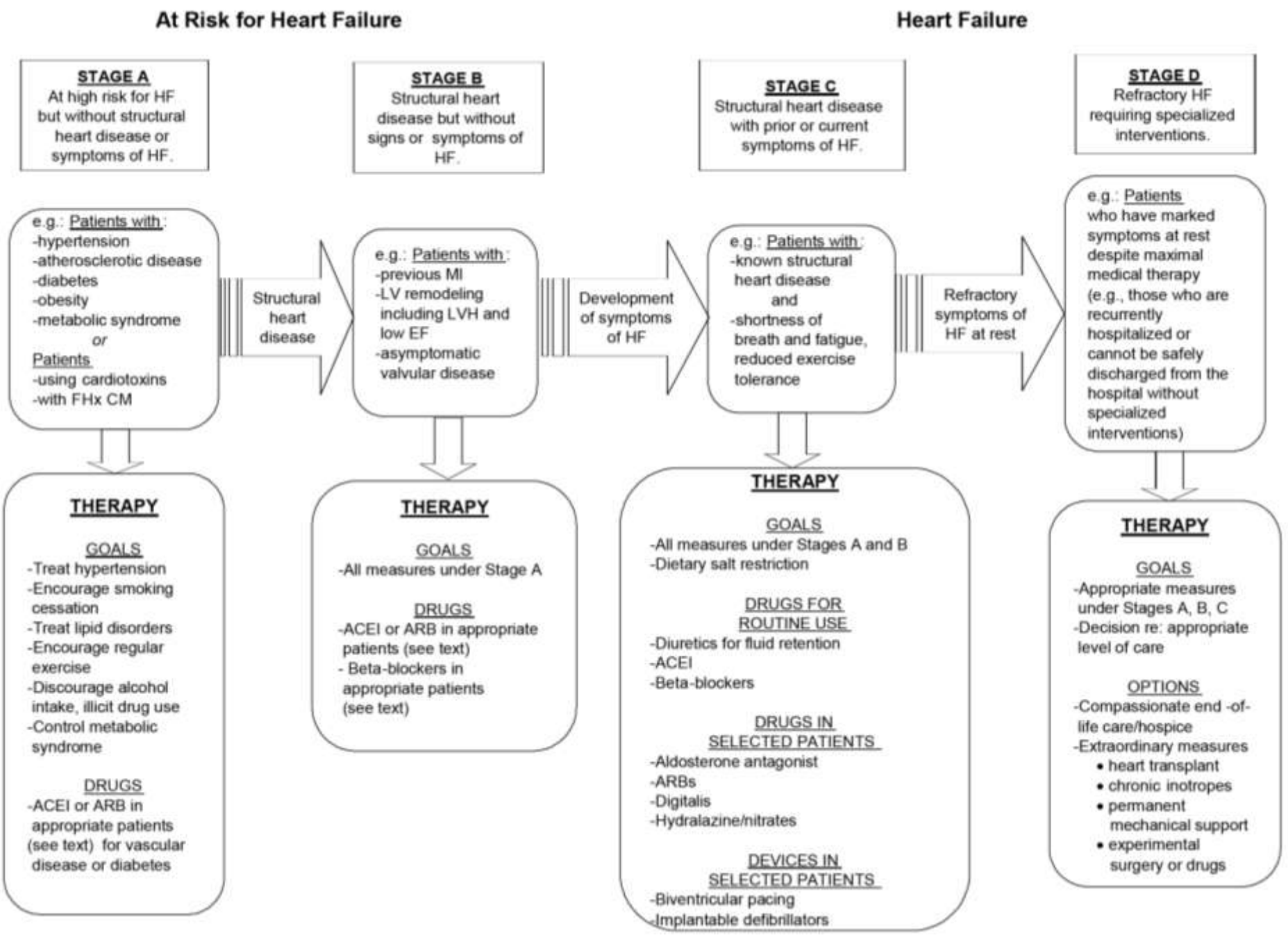
UTHSCSA and STVAHCS



Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Stage D Heart Failure

- Refractory Heart Failure
- Requiring Specialized Interventions

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Characteristics of Refractory Heart Failure

- Marked symptoms at rest
- On maximal medical therapy
- Recurrent hospitalizations
- Unable to stabilize in hospital for discharge

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Characteristics of Refractory Heart Failure Patients

- Profound fatigue
- Cannot perform most activities of daily living
- Cardiac cachexia
- Require repeated and/or prolonged hospitalizations for intense therapy

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Specialized Management in Heart Failure - Goals

- **Optimize standard medical therapy**
  - Lifestyle therapy: diet (Na, nutrients) and activity (rest), smoking, alcohol, drugs
  - Medications: ACE/ARB, B-Blocker, diuretic (solo or combination), Aldo-Antag, Dig, Hydralaz/nitrate
  - Devices: ICD, Biventricular pacing
- **Realism**: appropriate level of care

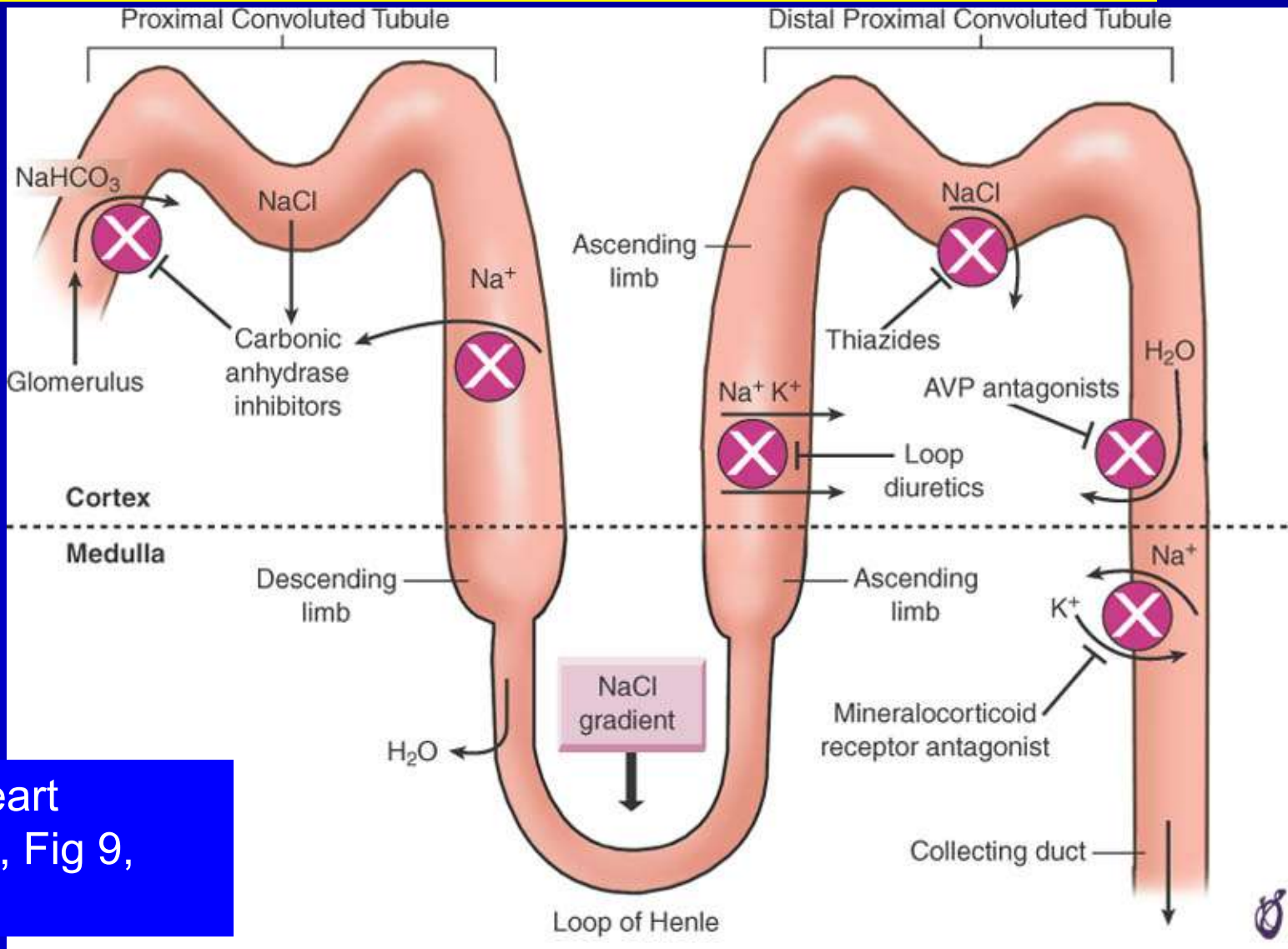
Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Meticulous Management of Fluid Status During Hospitalization - 1

- Critical step in management
- Diuretic resistance
  - Decline in renal perfusion
  - Second diuretic with complementary action
  - Addition of dopamine or dobutamine
  - Ultrafiltration or hemofiltration

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

The Nephron in HF



Braunwald's heart disease, Ch 25, Fig 9, 2008.

TABLE 25–8 | Diuretics for Treating Fluid Retention in Chronic Heart Failure*

Drug	Initial Daily Dose(s)	Maximum Total Daily Dosage	Duration of Action (hr)
Loop diuretic			
Bumetanide	0.5 to 1.0 mg once or twice	10 mg	4 to 6
Furosemide	20 to 40 mg once or twice	600 mg	6 to 8
Torsemide	10 to 20 mg once	200 mg	12 to 16
Thiazide diuretic			
Chlorothiazide	250 to 500 mg once or twice	1000 mg	6 to 12
Chlorthalidone	12.5 to 25 mg once	100 mg	24 to 72
Hydrochlorothiazide	25 mg once or twice	200 mg	6 to 12
Indapamide	2.5 mg once	5 mg	36
Metolazone	5 mg once	20 mg	12 to 24
Potassium-sparing diuretic			
Amiloride	12.5 to 25 mg once	20 mg	24
Triamterene	50 to 75 mg twice	200 mg	7 to 9
AVP antagonist†			
Satavaptan	25 mg once	50 mg once	NS
Tolvaptan	30 mg once	60 mg once	NS
Lixivaptan	125 mg twice	250 mg twice	NS
Conivaptan (IV)	20-mg IV loading dose, followed by 20 mg continuous IV infusion/day	40 IV infusion/day	7 to 9
Sequential nephron blockade			
Metolazone	2.5 to 10 mg once plus loop diuretic		
Hydrochlorothiazide	25 to 100 mg once or twice plus loop diuretic		
Chlorothiazide (IV)	500 to 1000 mg once plus loop diuretic		

*Unless indicated, all dosages are for oral diuretics.

†As of 2007, this class of agents is not FDA-approved for the management of patients with heart failure.

NS = not specified.

Modified from Hunt SA, Abraham WT, Chin MH, JL, et al: ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 112:e154, 2005.

(Modified from Hunt SA, Abraham WT, Chin MH, JL, et al: ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 112:e154, 2005.)

Braunwald's heart disease, Ch 25, Table 8, 2008.

Sorting out Diuretic Resistance

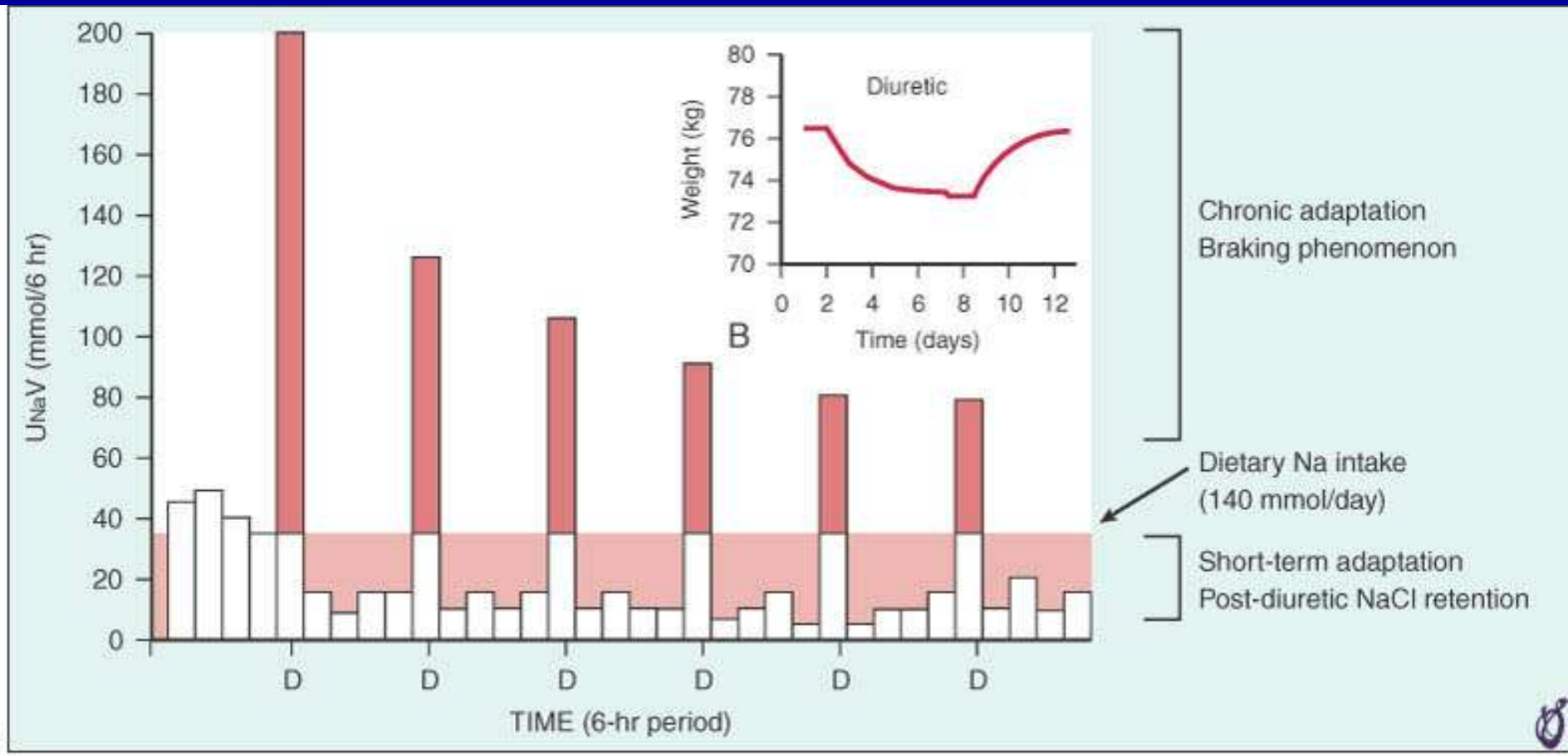
- Is the patient taking the drug?
- Is the drug being absorbed?
  - JVP elevation indicates poor absorption
- Is the blood pressure adequate to provide renal flow?
- Is renal function adequate?

Mechanisms of Diuretic Resistance

- Braking phenomenon: diuretics decrease extracellular fluid volume and activate adaptations that reduce responsiveness
  - Increase in proximal reabsorption
  - Sympathetically-mediated reduction in RBF and renin release (increase in Na reabsorption)
- Hypotension and renal hypoperfusion
- Distal convoluted tubular hypertrophy and hyperplasia due to increased delivery
- Cardiorenal syndrome

Braunwald's heart disease, Ch 25, 2008.

Braking Phenomenon



(Modified from Ellison DH: Diuretic therapy and resistance in congestive heart failure. Cardiology 96:132, 2001.)

Braunwald's heart disease, Ch 25, 2008.

Diuretic Usage

- Furosemide, max 160-200 mg dose IV, or 600 mg/da (20-40 mg IV over 1-2 minutes, then 10-40 mg/hr, or even 80-160/hr but at risk of more adverse effects)
- Second agent (later, perhaps best 3 times/wk)
  - Distal convoluted tubule: Metolazone 2-10 mg/d
  - Distal convoluted tubule: Hctz 25-100 mg/d
  - Distal convoluted tubule: Chlorothiazide 500-1000 mg IV (once or twice a day)
  - Proximal: acetazolamide 250-375 mg/da or up to 500 mg IV (up to 4 times per day) – good for alkalosis and hypokalemia
  - Collecting duct: spironolactone 100-200 mg/d
  - Collecting duct: amiloride 5-10 mg/d

UpToDate Sept 2009, furosemide. Ellison DH. Cardiology 2001;96:132-143.

Diuretic Usage

Table 2. Combination diuretic therapy

To a ceiling dose of a loop diuretic (table 1) add:

DCT diuretics

metolazone 2.5–10 mg per os daily[1]
hydrochlorothiazide (or equivalent) 25–100 mg per os daily
chlorothiazide 500–1,000 mg intravenously

Proximal tubule diuretics

acetazolamide 250–375 mg daily or up to 500 mg intravenously

Collecting duct diuretics

spironolactone 100–200 mg daily
amiloride 5–10 mg daily

[1] Metolazone is generally best given for a limited period of time (3–5 days) or should be reduced in frequency to 3 times per week once ECF volume has declined to the target level. Only in patients who remain volume expanded should full doses be continued indefinitely, based on the target weight.

Ellison DH. Cardiology 2001;96:132-143.

Diuretic Usage

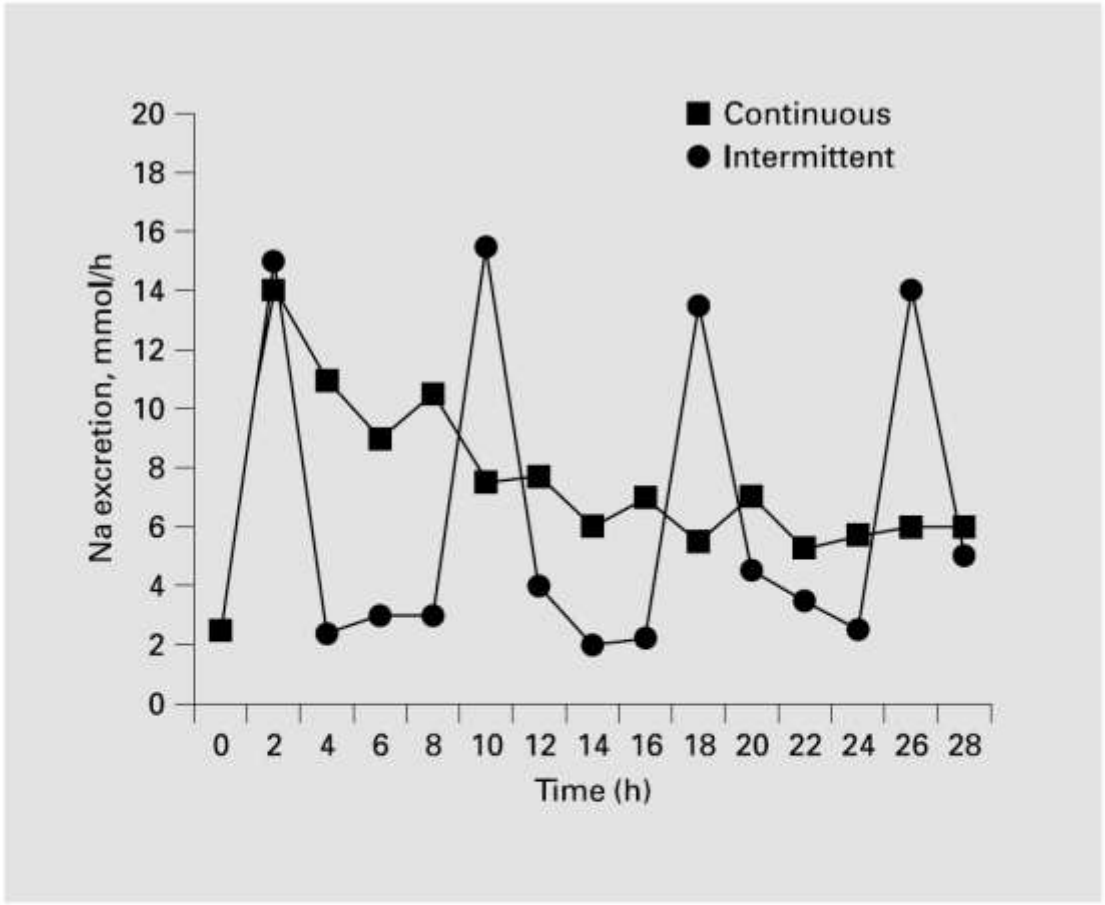


Fig. 6. Comparison of continuous-infusion versus bolus furosemide treatment of patients with chronic congestive heart failure. The squares indicate Na excretion during infusion of 2.5–3.3 mg/h furosemide following a loading dose of 30–40 mg. The circles depict urinary Na excretion following 30–40 mg of furosemide every 8 h. Total urine output was 18.5% higher during continuous infusion than bolus administration. Data are drawn from Lahav et al. [51].

Ellison DH. Cardiology 2001;96:132-143.

Diuretic Usage

Table 3. Continuous infusion of loop diuretics

	Bolus mg	Infusion rate, mg/h		
		<25 ml/min	25–75 ml/min	>75 ml/min
Furosemide	40	20 then 40	10 then 20	10
Bumetanide	1	1 then 2	0.5 then 1	0.5
Torsemide	20	10 then 20	5 then 10	5

At high continuous doses, toxicity may develop, especially during furosemide infusion in patients with impaired renal function. Doses derived from Brater [56].

Ellison DH. Cardiology 2001;96:132-143.

Meticulous Management of Fluid Status During Hospitalization - 2

- Requirements for hospital discharge
  - Stable diuretic regimen
  - Euvolemia
- Increased risk for readmission if goals not met

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Meticulous Management of Fluid Status After Hospitalization

- Weigh daily
- Diuretic dose adjustments may be made by patients based on weight changes
- Sodium restriction 2 gm Na/da
- Possibly 2 liter/da fluid restriction

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Use of Neurohormonal Inhibitors - 1

- ACE-inhibitor: increased risk for hypotension and renal insufficiency
- Beta-blocker: increased risk for exacerbation of HF symptoms
- Even low doses are beneficial
- Do not initiate use if SBP<80 or if signs of hypoperfusion
- Do not initiate beta-blocker
  - Ongoing fluid retention
  - Recent need for IV inotropes

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Use of Neurohormonal Inhibitors - 2

- Nitrate-hydralazine combination
  - Beneficial in patients not taking beta-blocker or ACE-I but less symptomatic patients than Stage D
  - Utility in Stage D unknown, but an option
  - Side-effects: headache and GI distress
- Aldosterone antagonists beneficial only if renal function is adequate and K+ is OK
- ARB beneficial if intolerant of ACE-I due to cough (and maybe angioedema) but no advantage if hypotension or renal insufficiency

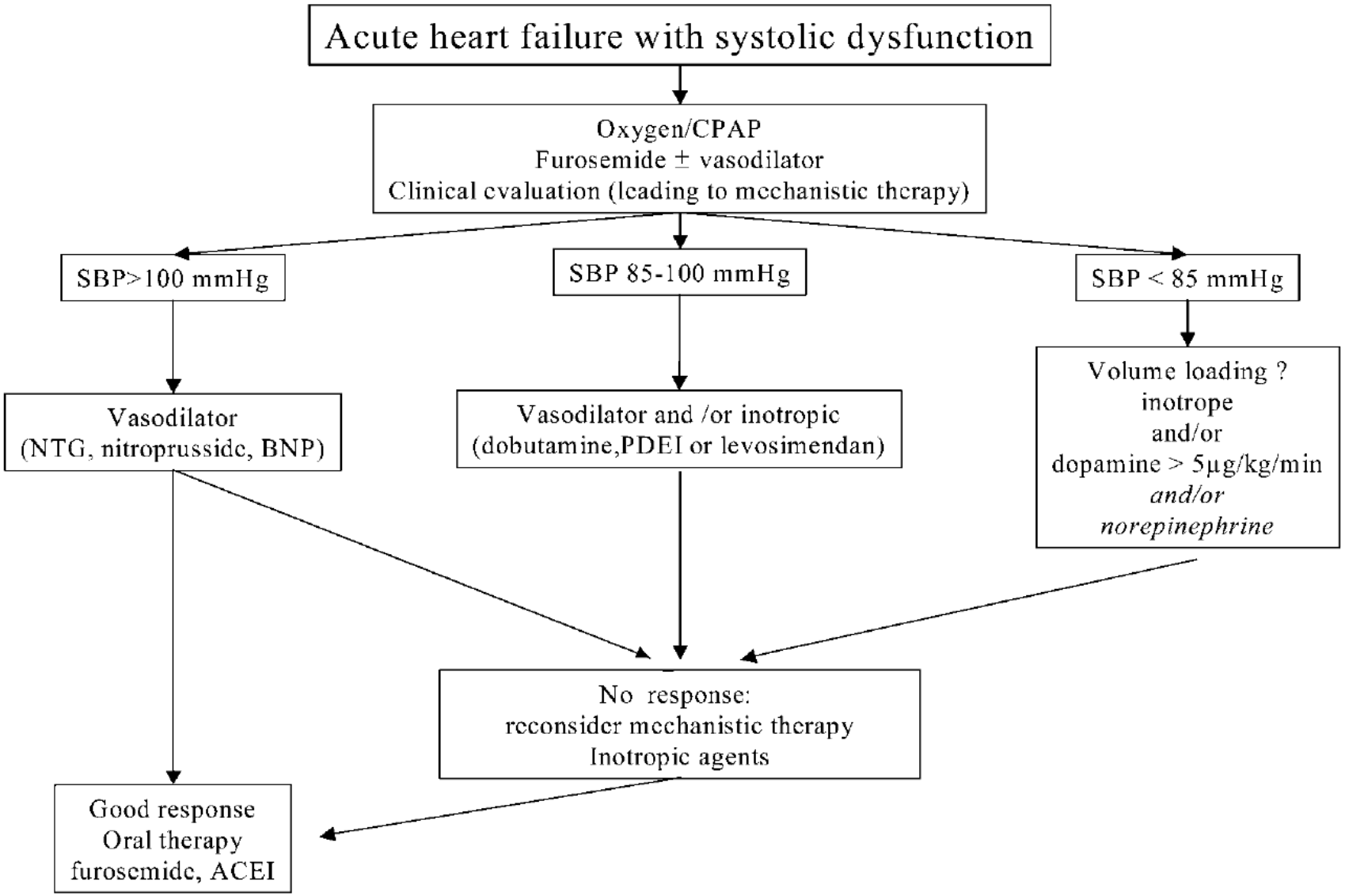
Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Use of IV Agents

- Inotropic agents
  - Dopamine
  - Dobutamine
  - Milrinone
- Vasodilator agents
  - Nitroglycerine
  - Nitroprusside
  - Nesiritide
- Generally hospitalization should continue at least 48 hr after infusions

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Rationale for Inotropes in HF



Eur Society of Cardiology. Eur Heart J. 2005;26:384-416.

Hemodynamics of Shock

Table 3
Hemodynamic parameters in shock

Type of shock	CO	PCWP	CVP	SVR	PAP	SVo_2
Cardiogenic						
LV failure	↓↓	↑↑	↑↑	↑	↑	↓
RV failure	↓↓	↔or↑	↑↑	↑	↔or↑	↓
Hypovolemic	↓↓	↓↓	↓↓	↑	↓	↓
Vasodilatory (septic)						
Early	↑↑	↓	↓	↓or↓↓	↓	↑or↑↑
Late	↔or↓	↓ or ↔	↓ or ↔	↓or↓↓	↓	↑or↑↑
Extracardiac Compressive	↓or↓↓	↔or ↓	↑↑	↑	↑↑	↓
Neurogenic	↑or↔ or↓	↓	↓	↓	↓	↓

Abbreviations: CO, cardiac output; CVP, central venous pressure; LV, left ventricle; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RV, right ventricle; SVo_2, mixed venous oxygen saturation; SVR, systemic vascular resistance.

↓-decrease, ↑-increase, ↔-equal.

London JA et al. Surg Clin N Am. 2006;86:1503.

Vasoactive Drugs in HF

Table 2
Common vasoactive agents used in cardiovascular failure

Agent	Mechanism	Dose	α	β	DA	CV effects	Notes
Norepinephrine	Direct agonist	1–12 μg/min	+++	++	0	↑ SBP, DBP ↔CO VC most vascular beds	Primary vasopressor used in VD shock
Epinephrine	Direct agonist	1–200 μg/min	++	+++	0	↑ HR, SV, CO ↑ SBP, DBP, PP, PAP VC most vascular beds	↑ MVo_2 May induce tachyarrythmias
Dopamine	Direct agonist	1–2 μg/kg/h	+	+	+++	VD renal mesenteric and coronary beds	
		2–10 μg/kg/h	++	++	+++	↑ CO, ↔ SVR	Causes NE release from nerve terminals
		10–20 μg/kg/h	+++	++	+++	↑ SVR, VC most vascular beds	May induce tachyarrythmias and ↑ MVo_2 2^{nd} line agent in VD shock
Phenylephrine	Direct agonist	20–200 μg/min	+++	0	0	↑ SVR May cause reflex bradycardia Potentially ↓ CO	Limited role in VD shock Primary agent in neurogenic shock
Dobutamine	Direct agonist	2–20 μg/kg/min	+	+++	0	↑ contractility, automaticity, CO, SV May induce hypotension by ↓ SVR	Primary inotrope in cardiogenic shock or in VD shock with myocardial depression
Milrinone	Phosphodiesterase inhibitor	50 μg/kg load 0.25–1 μg/kg/min	0	0	0	↑contractility, CO VD of systemic and pulmonary vasculature May induce hypotension	Long half-life (30–60 min) limits usefulness in acute setting

Abbreviations: CO, cardiac output; CV, cardiovascular; DA, dopamine; DBP, diastolic blood pressure; HR, heart rate; MVo_2, myocardial oxygen consumption; NE, norepinephrine; PAP, pulmonary artery pressure; PP, pulse pressure; SBP, systolic blood pressure; SV, stroke volume; SVR, systemic vascular resistance; VC, vasoconstriction; VD, vasodilation.

London JA et al. Surg Clin N Am. 2006;86:1503.

Use of IV Agents as Outpatient - 1

- Patients who cannot be weaned despite repeated attempts
- Agents that have been tried
  - Dobutamine
  - Milrinone
  - Nesiritide
- Generally in patients awaiting transplant
- Also for those who cannot otherwise be discharged

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Use of IV Agents as Outpatient - 2

- Disadvantages
  - Burden on family
  - Burden on health services
  - May increase mortality
- Advantage - may allow palliation to allow patient to die in comfort at home

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Use of Mechanical Therapies - 1

- Established: cardiac transplantation
  - Fewer than 2,500/year in US
    - Currently on the transplant list 2,861 (UNOS data)
    - 2007: 2,210 transplants in US
    - 2008: 2,192
    - 74% male, 54% over 50 yo
    - 86%, 77%, 70% (1-yr, 3-yr, 5-yr survival)
  - Indications: severe functional impairment or dependence on IV inotropic support (refractory ventricular arrhythmia or angina)

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Table 10. Indications for Cardiac Transplantation

Absolute Indications In Appropriate Patients

For hemodynamic compromise due to HF

- Refractory cardiogenic shock
- Documented dependence on IV inotropic support to maintain adequate organ perfusion
- Peak VO_2 less than 10 mL per kg per minute with achievement of anaerobic metabolism

Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention

Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities

Relative Indications

Peak VO_2 11 to 14 mL per kg per minute (or 55% predicted) and major limitation of the patient's daily activities

Recurrent unstable ischemia not amenable to other intervention

Recurrent instability of fluid balance/renal function not due to patient noncompliance with medical regimen

Insufficient Indications

Low left ventricular ejection fraction

History of functional class III or IV symptoms of HF

Peak VO_2 greater than 15 mL per kg per minute (and greater than 55% predicted) without other indications

HF indicates heart failure; IV, intravenous; and VO_2, oxygen consumption per unit time.

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Heart Transplantation

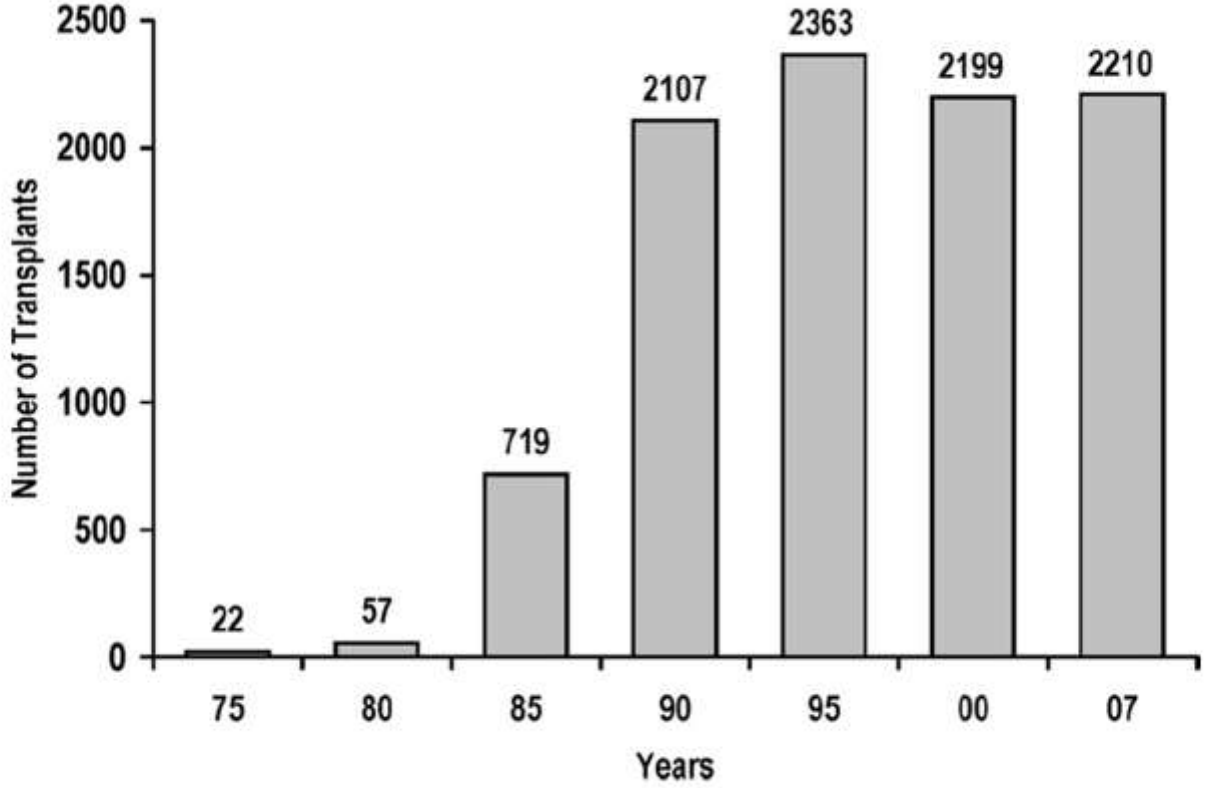
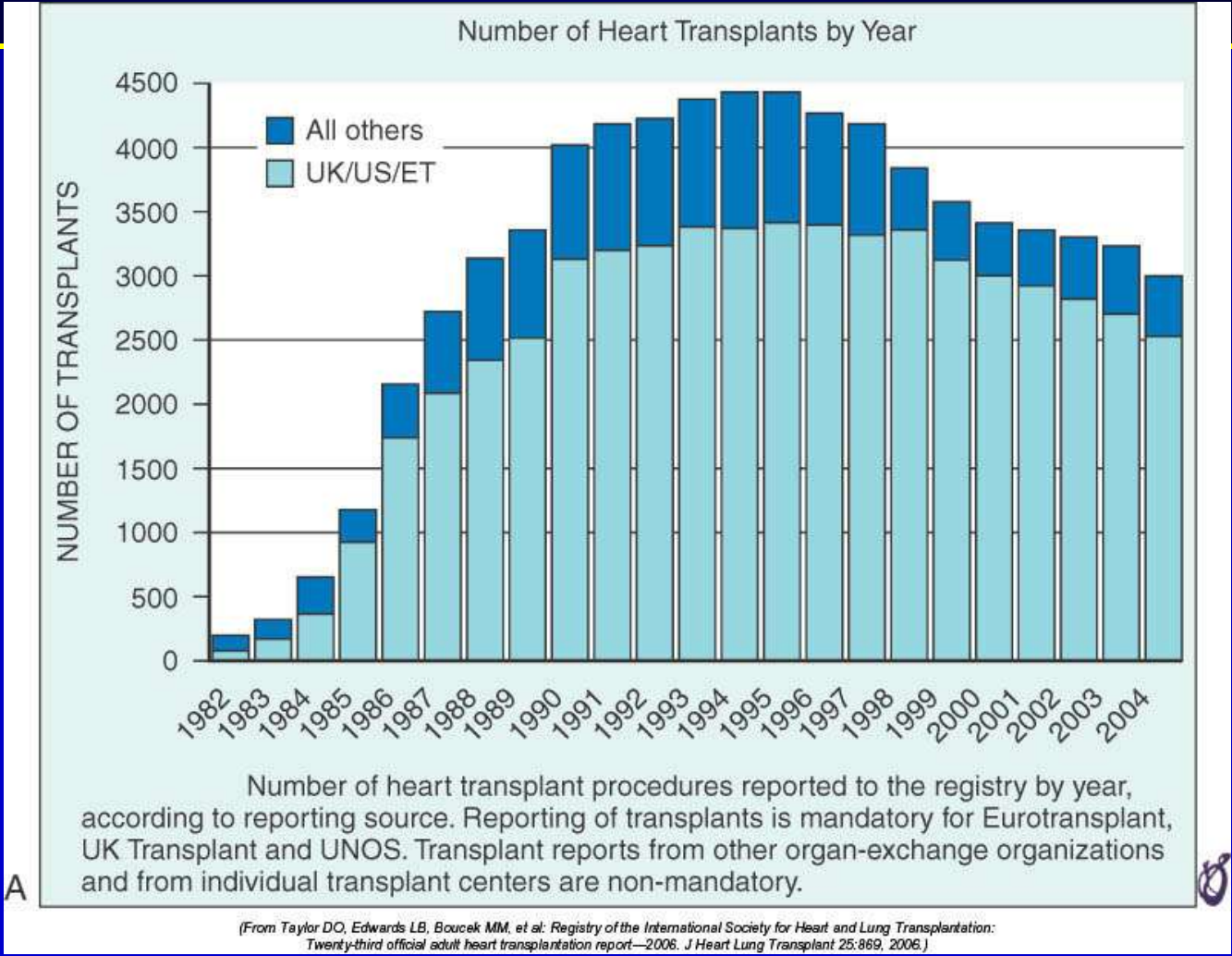


Chart 19-1. Trends in heart transplantations (UNOS: 1975–2007). Source: United Network for Organ Sharing (UNOS), scientific registry data.

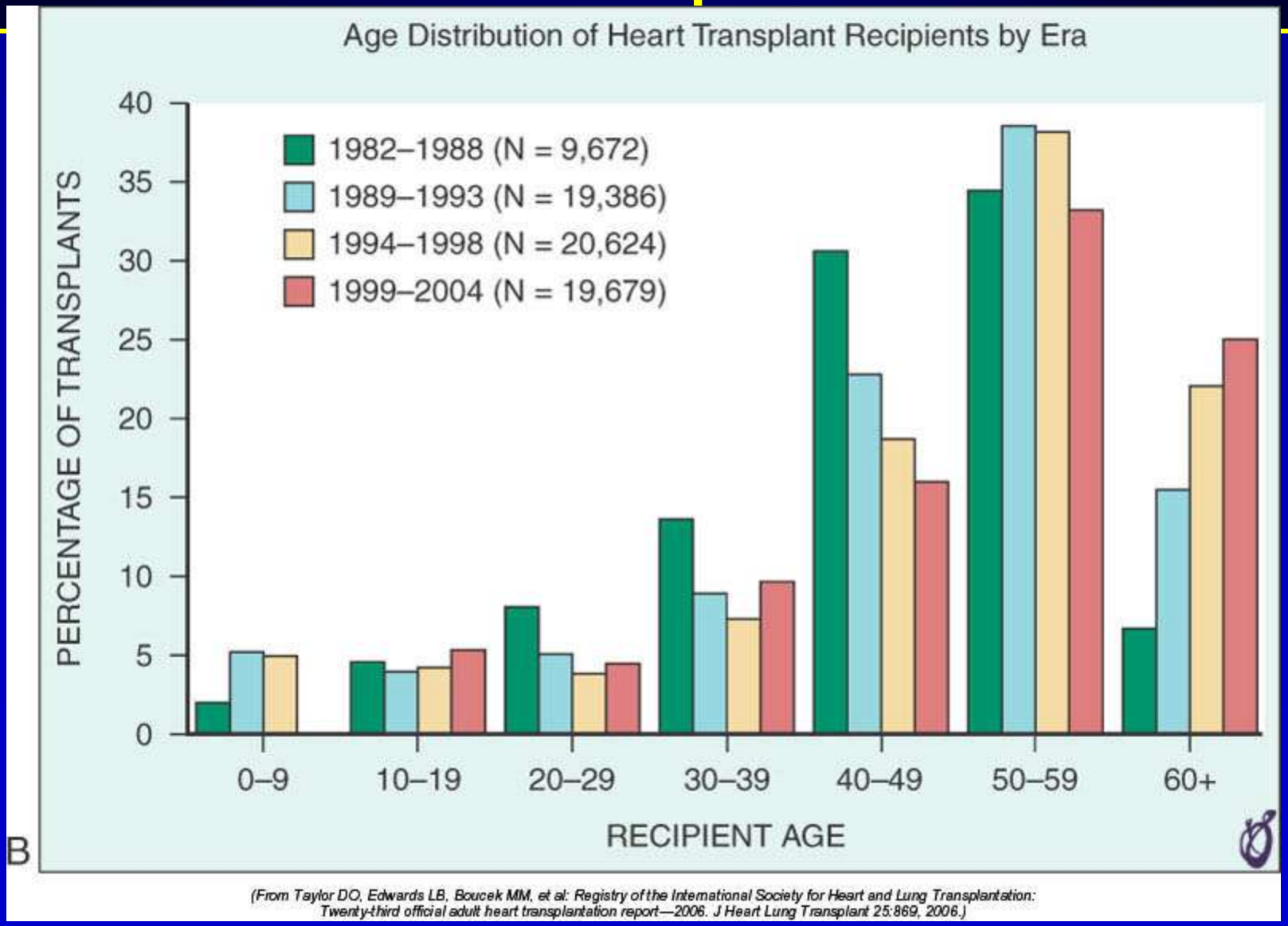
AHA Heart Disease and Stroke Statistics. 2009.

Heart Transplantation



Braunwald, Ch. 27, Fig 13A, 2008.

Heart Transplantation



(From Taylor DO, Edwards LB, Boucek MM, et al: Registry of the International Society for Heart and Lung Transplantation: Twenty-third official adult heart transplantation report—2006. J Heart Lung Transplant 25:869, 2006.)

Braunwald, Ch. 27, Fig 13A, 2008.

UNOS Status Definitions

- 1A: Inpatient mechanical circ support, ventilator, high-dose inotrope (dobutamine >7.5, milrinone >0.5)
- 1B: LVAD or inotropes
- 2: All others
- 7: Temporarily unsuitable

UNOS Policy Organ Distribution: Allocation of Thoracic Organs. June 23, 2009.

Median Transplant Survival

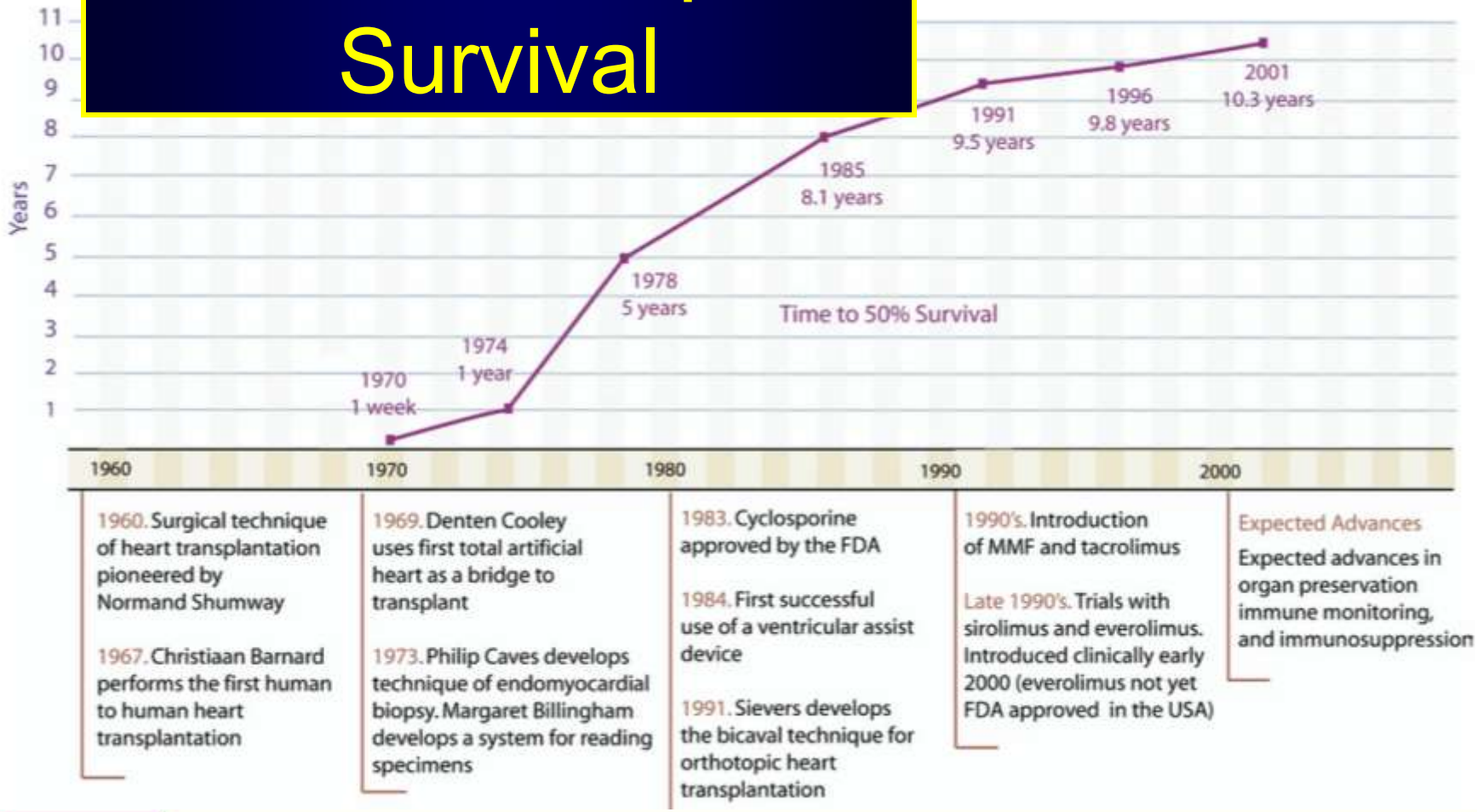
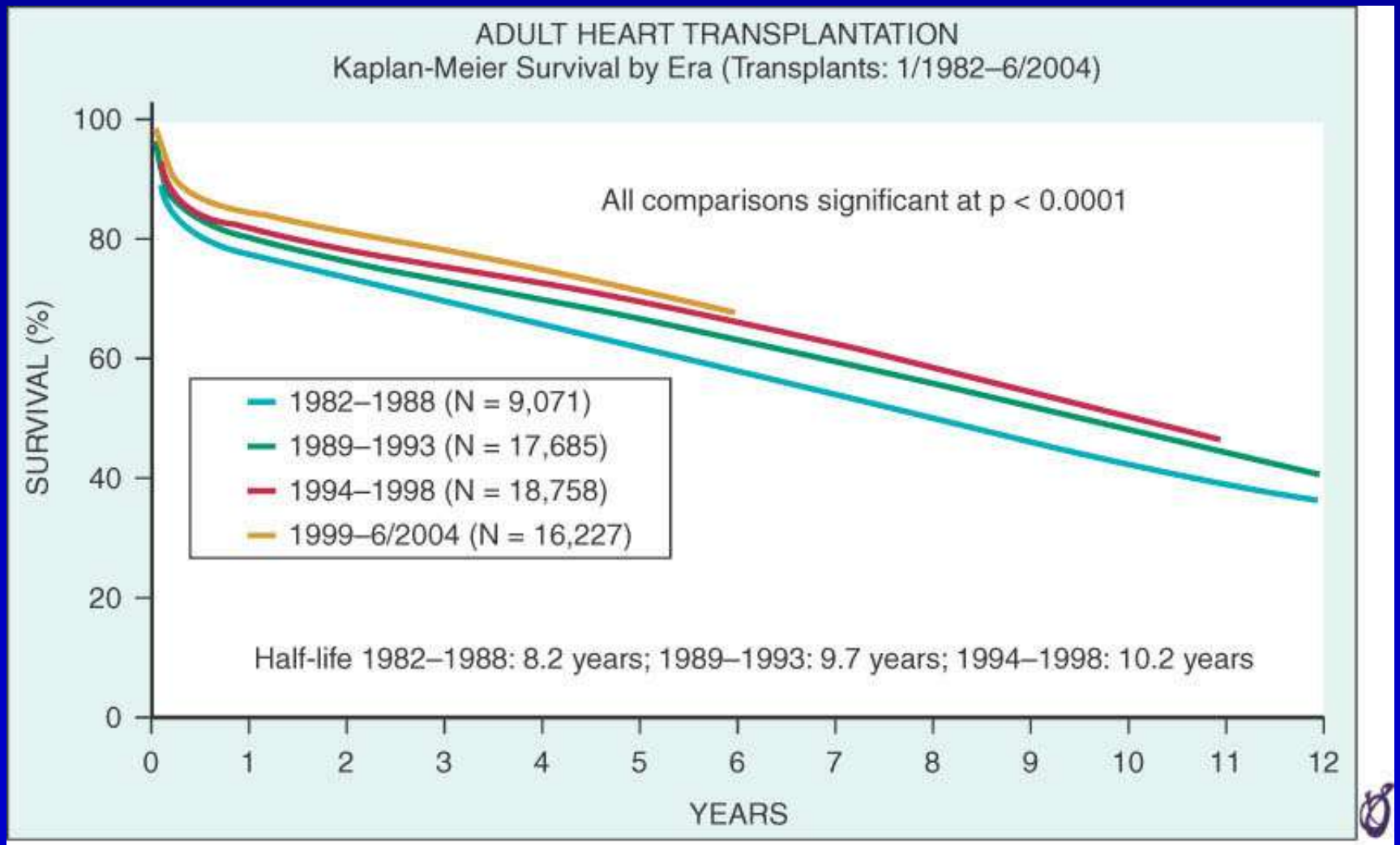


Figure 1 **Historical Perspective of Heart Transplantation**

The figure describes the major landmarks of heart transplantation associated with progressive improvement in survival. FDA = Food and Drug Administration; MMF = mycophenolate mofetil. Adapted, with permission, from Hunt (1).

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Heart Transplantation



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Braunwald, Ch. 27, Fig 13A, 2008.

Immunology in Transplantation

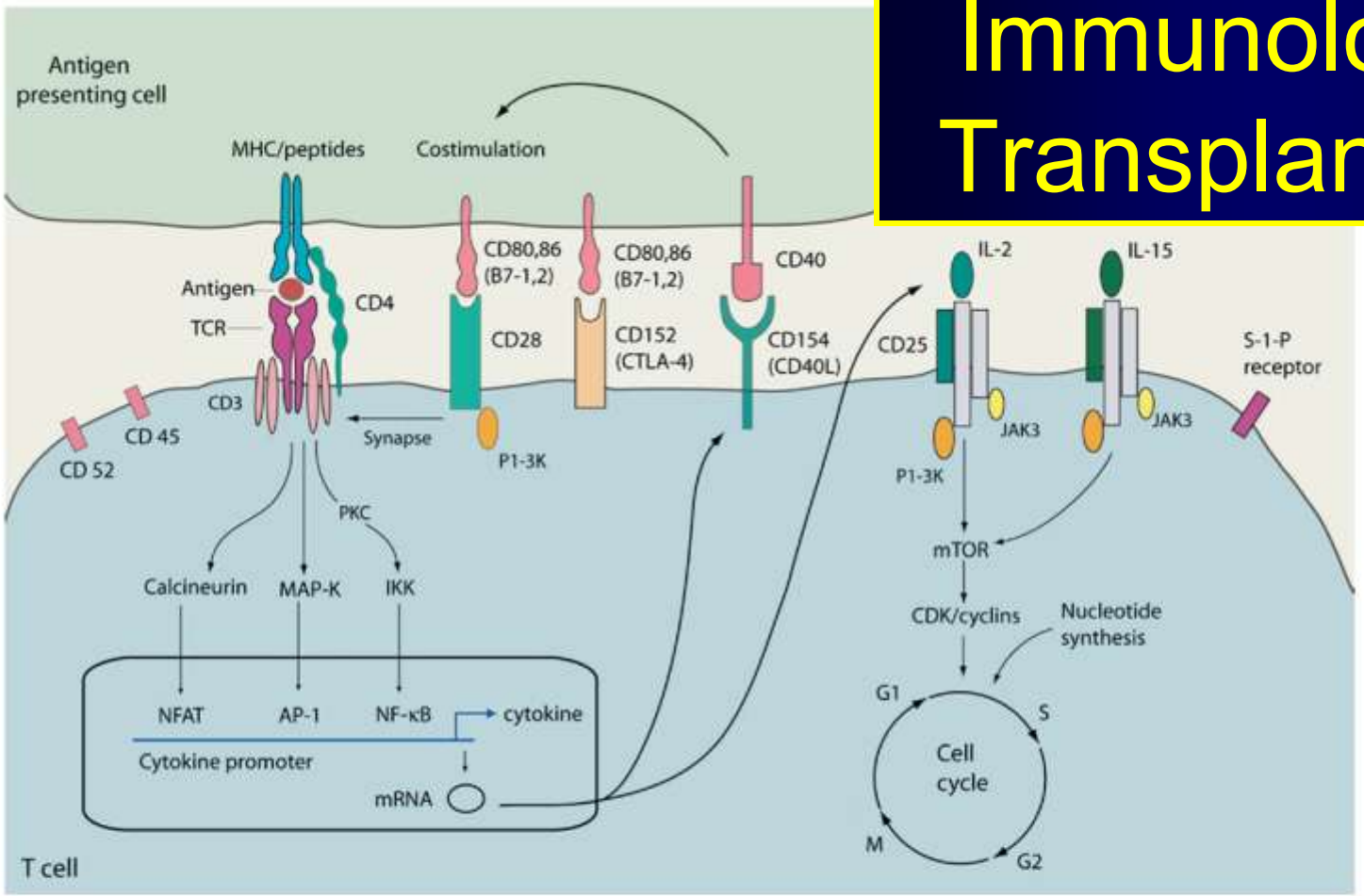


Figure 2 **Steps in T Cell Activation**

The alloimmune response often requires activation of multiple signaling pathways. The first signal is provided when antigen-presenting cells and antigens activate the T cell receptor. Costimulation (signal 2) occurs when CD80 (B7-1) and CD86 (B7-2) on the antigen-presenting cells engage CD28. Both signals activate important signal transduction pathways (calcineurin, RAS-mitogen-activated protein kinase [MAP-K] pathway, and the nuclear factor-kappa B [NF-kB] pathway). These pathways lead to the expression of many molecules, including interleukin (IL)-2 and IL-15. Interleukin-2 and other cytokines then activate the "target of rapamycin" pathway to provide the trigger for cell proliferation (signal 3). AP-1 = activating protein 1; CDK = cyclins-dependent protein kinase; IKK = serine-threonine protein kinase; JAK3 = Janus kinase 3; MHC = myosin heavy chain; mRNA = messenger ribonucleic acid; mTOR = mammalian target of rapamycin; NFAT = nuclear factor of activated T cells; PKC = protein kinase C; S-1-P = sphingosine-1-phosphate; TCR = T cell receptor. Adapted, with permission, from Halloran (28).

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Table 1 Immunosuppressive Agents in Heart Transplantation

Immunosuppressive Agent	Target Class	Comment
Glucorticosteroid	Multiple targets including inhibition of APC and nuclear transcription	Usually weaned during the first year
Calcineurin inhibitors		
Cyclosporine	Cyclophilin	Cyclosporine favored in patients with poorly controlled diabetes mellitus; tacrolimus may be associated with decreased rejection episodes
Tacrolimus	FKBP12	
Mycophenolate mofetil	Purine synthesis inhibitors	Has replaced azathioprine in combination regimens
Proliferation signal inhibitors	Target-of-rapamycin	Sirolimus may reduce the progression of allograft vasculopathy and malignancy; associated with poor wound healing
Sirolimus		
Everolimus (not yet FDA approved)		
Polyclonal antibody: horse or rabbit antithymocyte globulin	Depleting antibodies against T cells	Selective use in the treatment of severe cellular rejection or in induction therapy
Rituximab	B-cell–depleting monoclonal anti-CD20 antibody	Selective use in the treatment of humoral rejection
Daclizumab, basiliximab	Anti-CD25 antibody	Selective use for induction therapy
Alemtuzumab	Anti-CD52 antibody	Selective use for induction therapy (preliminary experience in heart transplantation), case reports of its use in refractory rejection
Intravenous immunoglobulin	Multiple sites of actions including interference with F_c receptors on the cells of the reticuloendothelial system	Selective use in the treatment of humoral rejection or sensitized patients
CTLA-4-Ig (LEA29Y) (fusion protein)	Costimulation signal inhibitor	In phase III trials in renal transplantation

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Table 2 Maintenance Regimens Used in Heart Transplantation

Regimens*	Indication or Characteristic
Calcineurin inhibitor and mycophenolate mofetil Cyclosporine, tacrolimus	Most common regimen used; older transplant patients may still be on a calcineurin inhibitor and azathioprine combination
Calcineurin inhibitor and proliferation signal inhibitor Sirolimus, everolimus	Regimen often considered in patients with established allograft vasculopathy or malignancy
Mycophenolate mofetil and proliferation signal inhibitor	Calcineurin-free regimen considered in patients with severe renal insufficiency
Tacrolimus monotherapy	Preliminary data suggest the safety of tacrolimus monotherapy in heart transplantation (45)

*Corticosteroids usually part of all regimens during the first year.

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Table 3 Immune and Functional Monitoring of Heart Transplant Recipients

Monitoring Tool	Type	Value
Endomyocardial biopsy	Histology and immunohistochemistry	Time-honored gold standard for the diagnosis of rejection; disadvantage of being invasive and susceptible to sampling errors and variability in interpretation
Drug monitoring and pharmacogenomics	Drug level or AUC	Trough levels are usually monitored for practical reasons although peak levels usually correlate better with AUC; gene polymorphisms of CYP3A5 and MDR1 correlate with calcineurin inhibitor levels
Functional monitoring	Diastolic parameters	Moderate correlation with significant rejection
	Tissue Doppler	Δ tissue Doppler systolic velocities are sensitive although less specific for the diagnosis of significant rejection
	BNP	Correlates with significant rejection; no specific threshold has good discrimination capacity
Genomic markers of rejection	AlloMap* gene expression profiling test	Sensitive marker for cellular rejection although lower specificity; not validated for AMR
T cell functional assays	1) ImmuKnow	Marker of T cell activation, currently under validation in heart transplantation
	2) Elispot	Marker of cytokine-producing T cells; currently under validation
Antibody monitoring	DSA	The presence of DSA has been associated with an increased risk of rejection and allograft vasculopathy

Maybe just first 5 years

*XDx, Brisbane, California.

AMR = antibody-mediated rejection; AUC = area under the curve; BNP = B-type natriuretic peptide; DSA = donor-specific antibodies.

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Issues in Transplantation

- Graft vasculopathy – most common cause of late graft failure, second cause of late death
- Malignancies – most common cause of late death; lymphoproliferative, aggressive skin
- Renal failure (CNI-free regimens)
- Induction of organ tolerance

Hunt SA et al. J Am Coll Cardiol. 2008;52:587-98.

Use of Mechanical Therapies - 2

- Developing:
  - Mitral surgery for annular dilation for symptoms (no proof for symptoms, LV fcn, mort)
  - Cardiomyoplasty, LV aneurysmectomy
  - Mechanical circulatory assist devices (intense investigation) – best for short term reversible (acute MI, myocarditis, postcardiotomy)

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

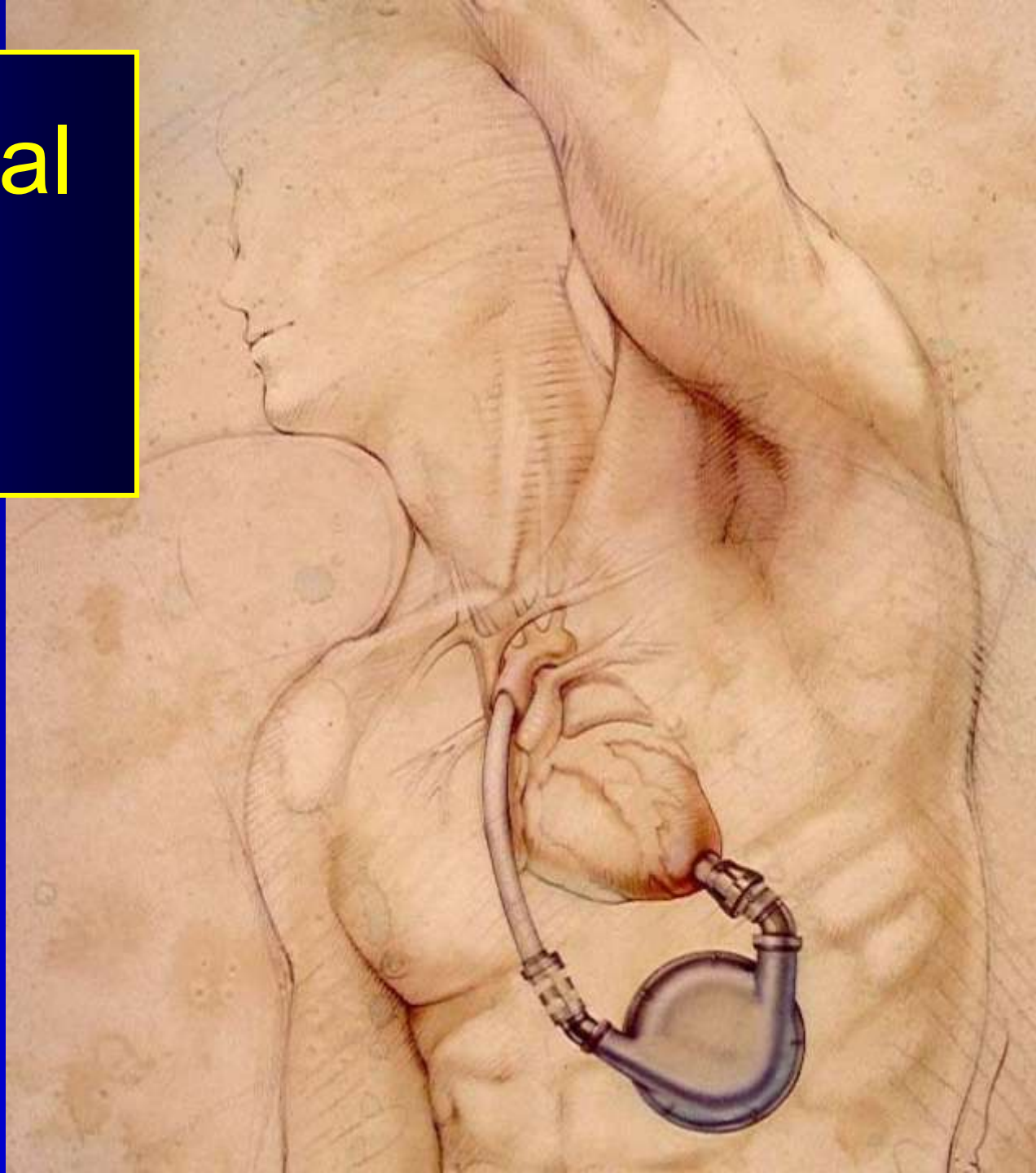
Mechanical Assist Devices

- First Generation pulsatile volume displacement pumps, large, designed for about 1 year durability
  - Heartmate I (5,000 pts)
  - Thoratec PVAD (paracorporeal VAD, 3,000 pts, now an IVAD=implantable)
  - Novocor (1,600 pts)

- Second Generation axial flow pumps, smaller, nonpulsatile
  - Heartmate II (1,200 pts)
  - Jarvik 2000
  - Berlin Heart Incor
  - MicroMed DeBakey VAD
- Third Generation bearingless continuous flow pumps with impeller that is magnetic levitation or hydrodynamically suspended
  - Heartware
  - Ventrassist
  - Duraheart VAD
  - Terumo

Birks EJ. Heart. July 16, 2009 on line.

Mechanical Assist Devices



Heartmate I

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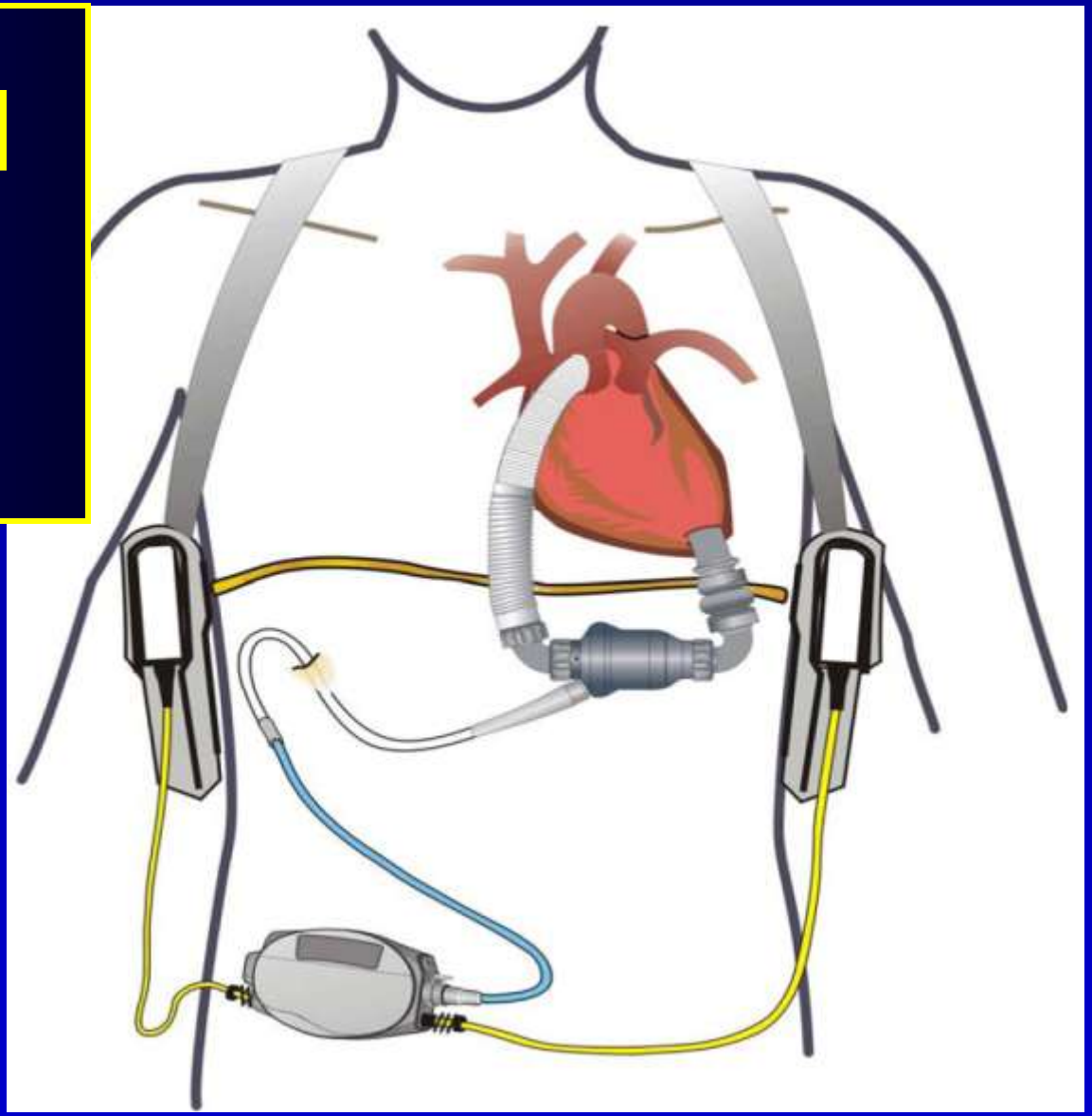
Mechanical Assist Devices

Heartmate II

Birks EJ. Heart. July 16, 2009 on line.

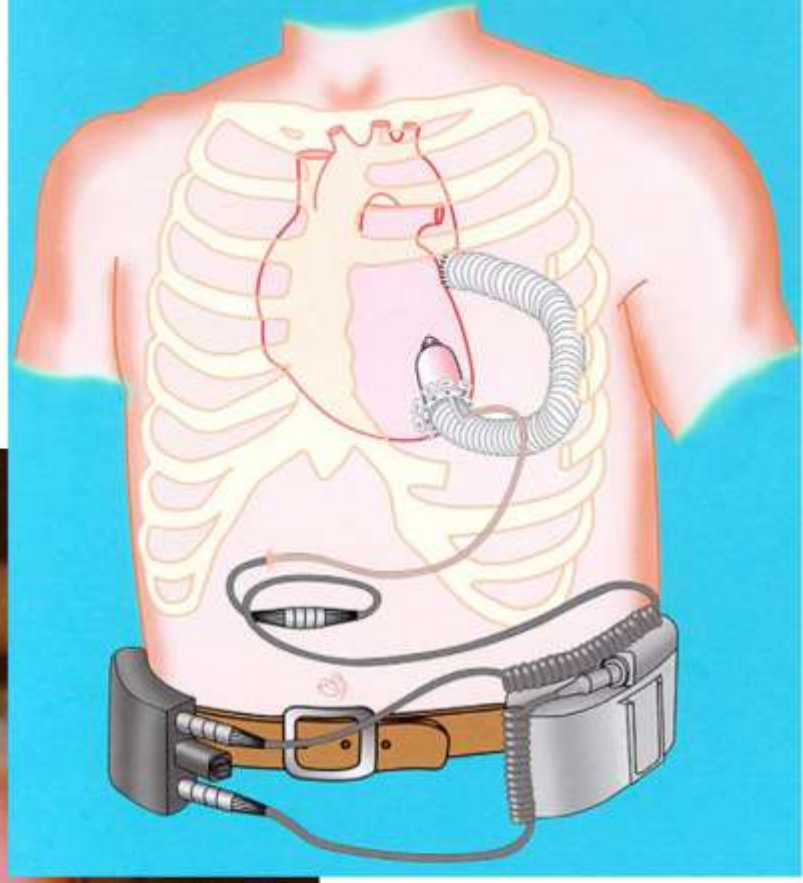
Mechanical Assist Devices

Heartmate II



Birks EJ. Heart. July 16, 2009 on line.

Mechanical Assist Devices

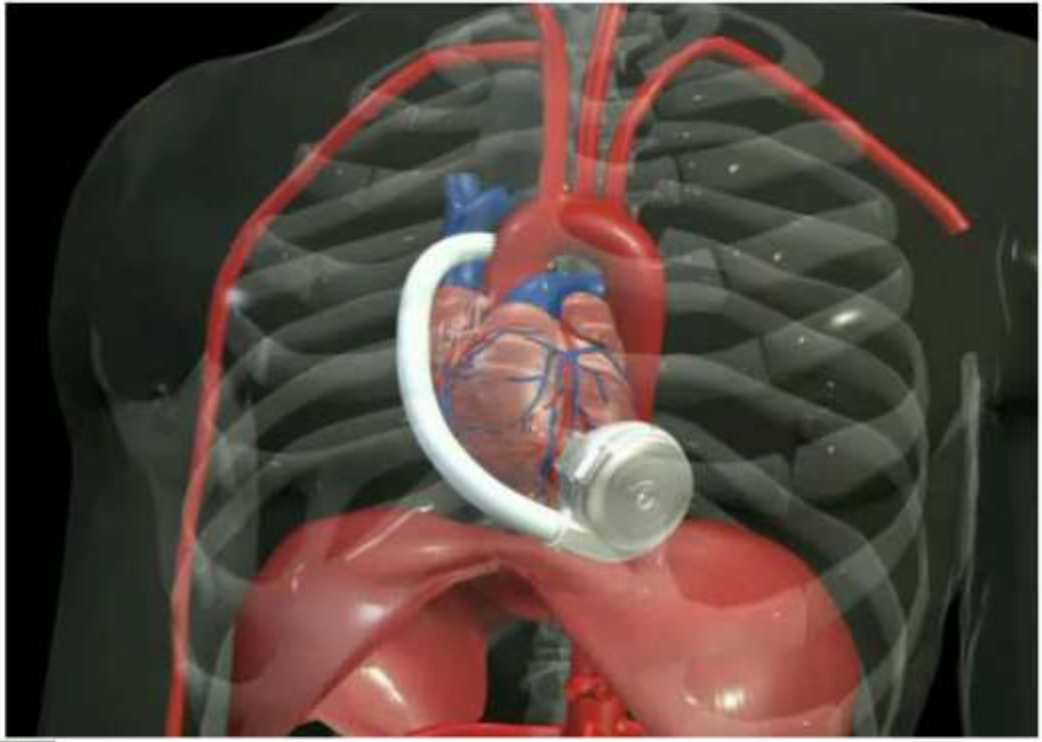


Jarvik 2000: placed in the LV

Figure 3b

Birks EJ. Heart. July 16, 2009 on line.

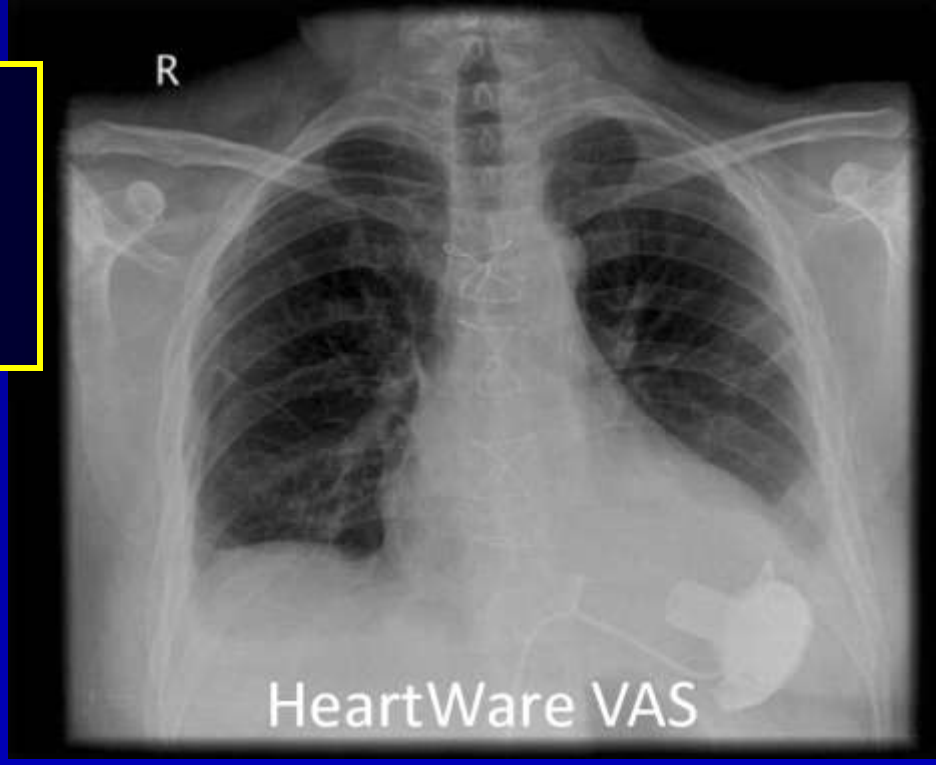
Mechanical Assist Devices

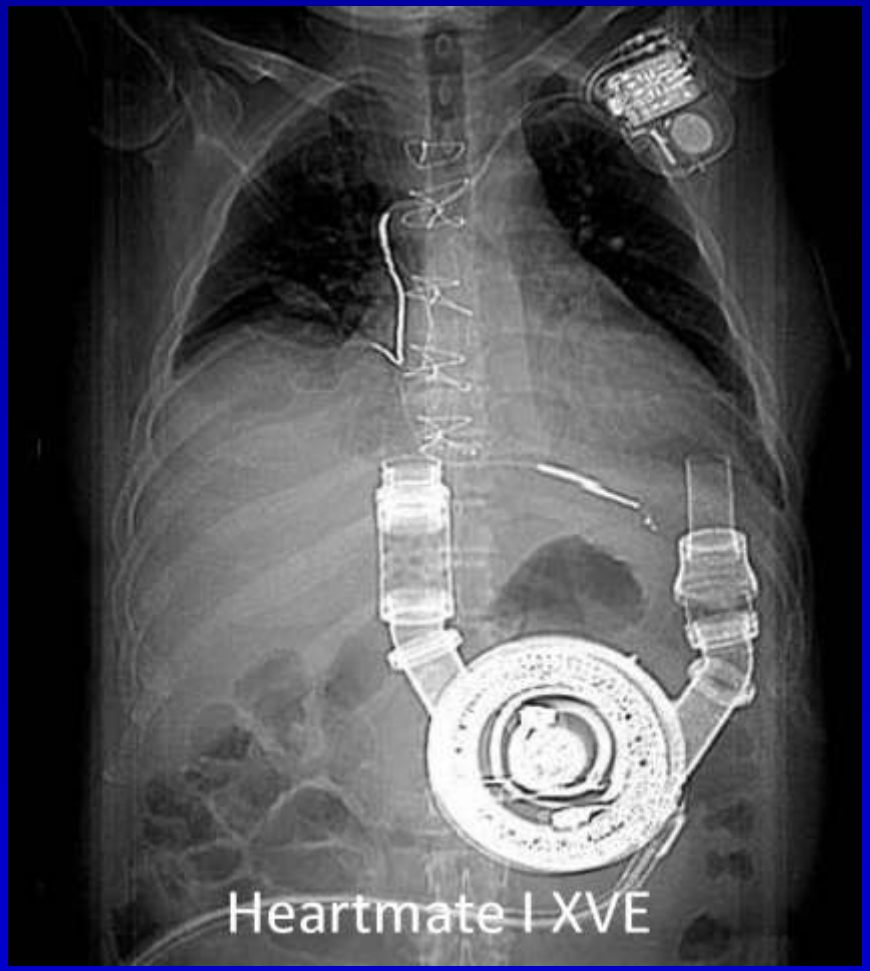


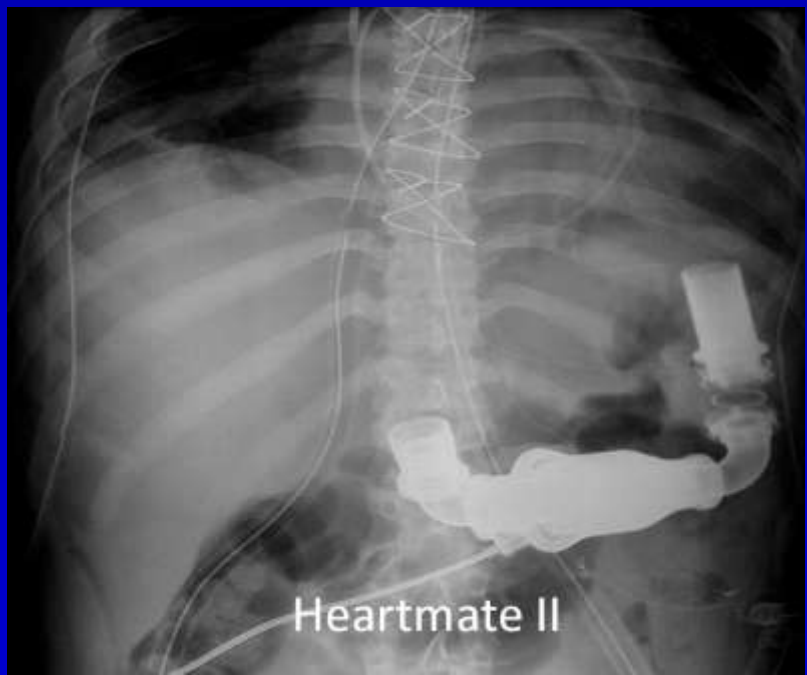
Heartware

Figure 4

Mechanical Assist Devices







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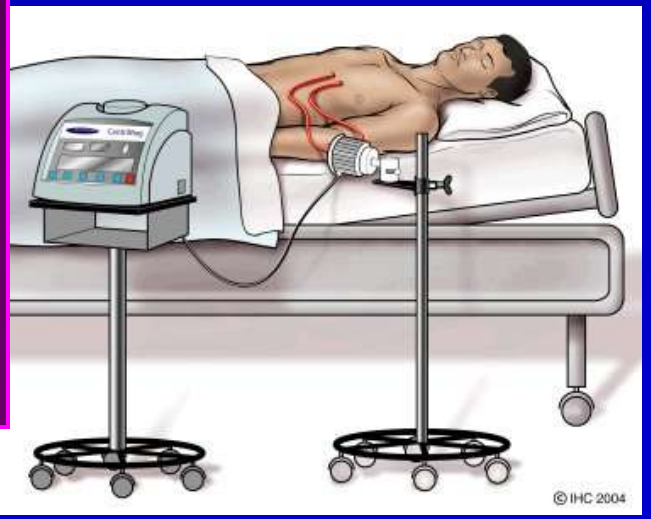
Assist Device Indications - 1

- Bridge to transplant when transplant unavailable or when patient complications are prohibitive for transplant (renal failure, nutritional status, pulmonary vascular resistance improvements may take weeks to months) – improves probability of survival to transplant
- Bridge to recovery – small number of patients (clenbuterol induces hypertrophy)

Birks EJ. Heart. July 16, 2009 on line.

Assist Device Indications - 2

- Destination therapy: Heartmate VE
  - Nov 2002 FDA approved
  - Oct 2003 Medicare approved
  - Not funded in UK
- Bridge to decision: moribund patients short term VAD (Levitronix CentriMag LVAS – not yet US approved for longer than 6 hr) to see if recovery to level of candidacy for LVAD occurs



Birks EJ. Heart. July 16, 2009 on line.

Mechanical Circulatory Assist

- Established efficacy as destination therapy: Rematch trial (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure)
  - 129 patients randomized
  - 2-year survival: medical=6%, device=23% (Heartmate I)
  - Complications: bleeding, infection, thromboembolism, device failure (sepsis 41% and device failure 17% of deaths)
  - Anticipated to benefit those with expected 1-year survival<50%
  - Bridge to recovery?

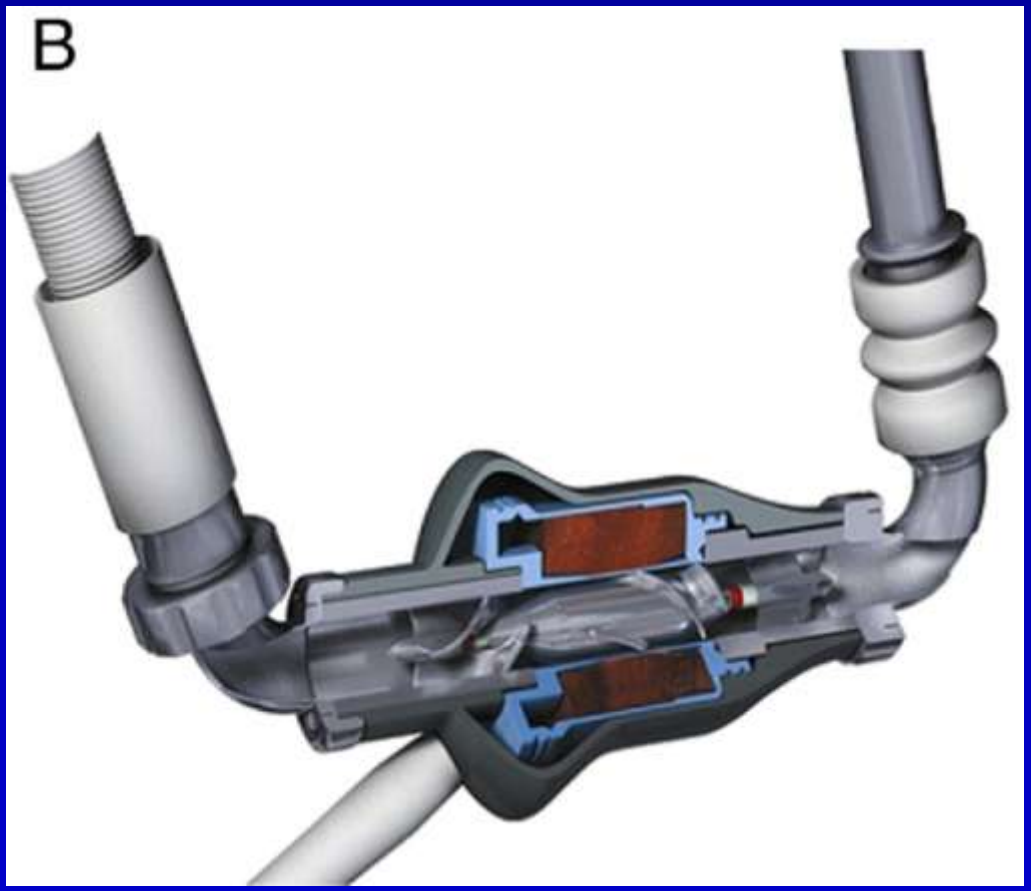
Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

Heart Mate II

- 281 patients with 18 mo f/u or endpoint
- 54 yo, mostly men, mostly nonischemic CM, most on inotropes, 45% IABP
- Death:20%, Sepsis 4%, stroke 4% (equal hemorrhagic and ischemic), right heart failure 3%, device failure 3% (7 patients: 2 pump thrombosis, 1 twisted inflow graft, 1 outflow disconnect, 1 severed percutaneous lead, 2 power loss), MSOF 2%, bleeding 1%, other 3%
- Nonfatal adverse events: bleeding requiring transfusion and surgery, stroke, esp ischemic,

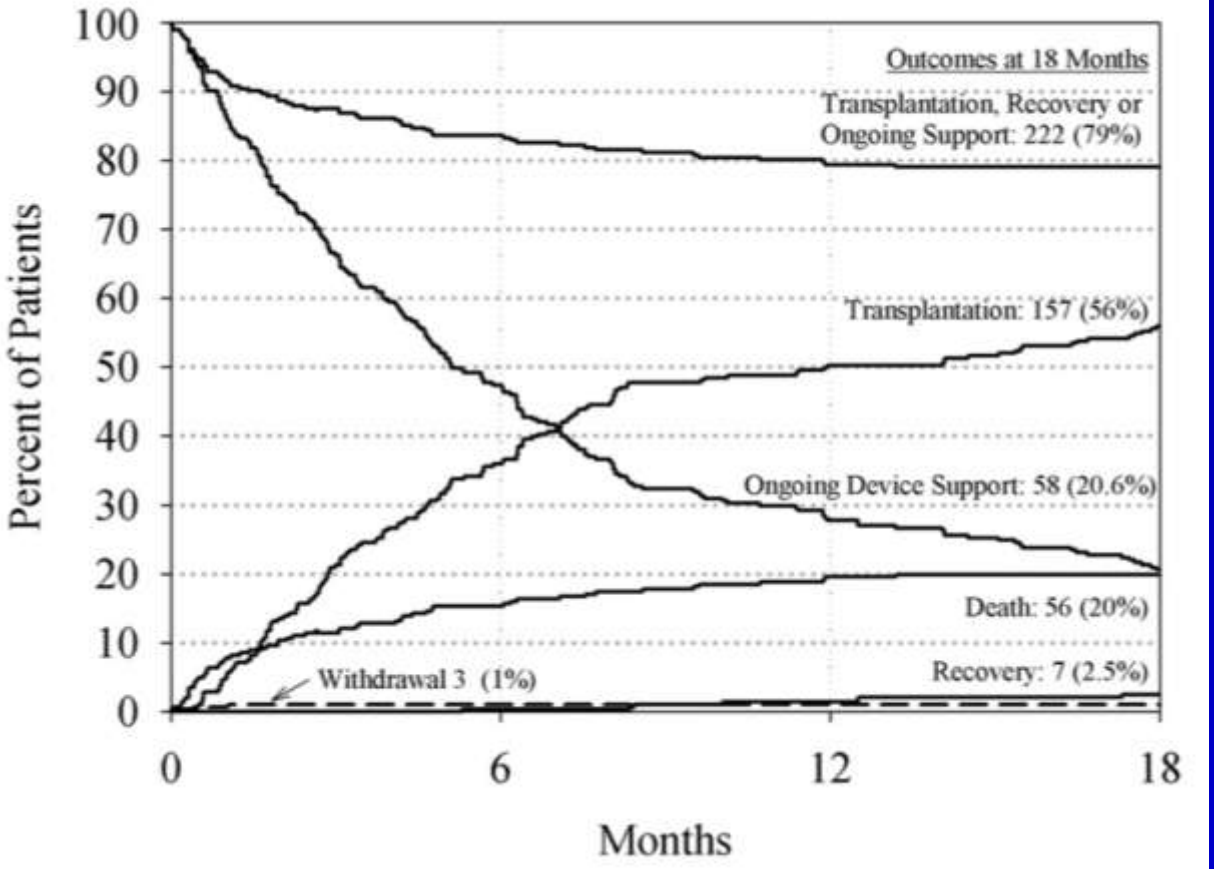
Pagani FD et al. J Am Coll Cardiol. 2009;54:312-21.

Heart Mate II



Pagani FD et al. J Am Coll Cardiol. 2009;54:312-21.

Heart Mate II



Is nonpulsatile flow acceptible to the human body long-term?

Figure 2 **Outcomes for 281 Patients After Implantation of the Continuous-Flow Left Ventricular Assist Device**

Competing outcomes analysis of patients undergoing implantation of the continuous-flow left ventricular assist device for the first 18 months after device implantation.

Pagani FD et al. J Am Coll Cardiol. 2009;54:312-21.

Assist Device Complications

- Acute: periop hemorrhage, right heart failure, abdominal complications
- Later: infection, thromboembolism, hemolysis, device failure
- All except heartmate I require anticoagulation (warfarin)

Birks EJ. Heart. July 16, 2009 on line.

Specialized Intervention in Heart Failure - Options

- **Compassionate end-of-life care/hospice**
- **Extraordinary measures**
  - Heart transplant
  - Chronic inotropes
  - Permanent mechanical support
  - Experimental surgery or drugs

Jessup M et al. ACC/AHA Update Guideline for Mgmt of Heart Failure. 2009.

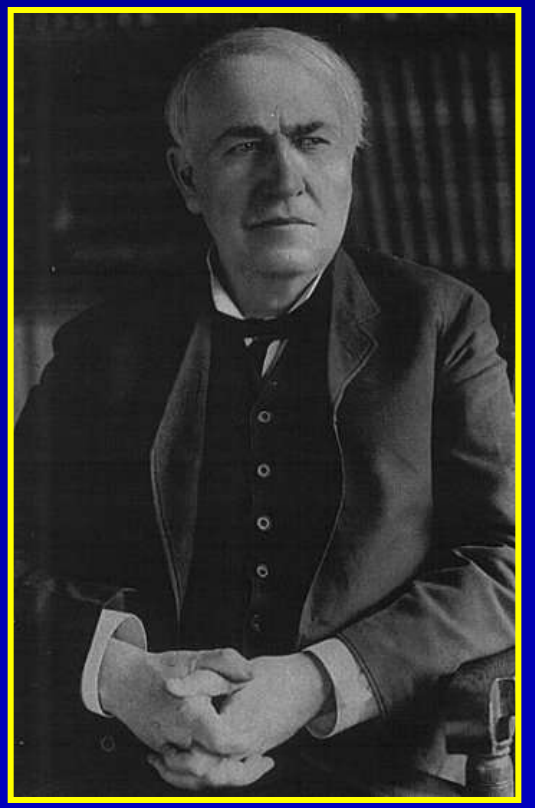
Predictors of Adverse Outcome

- BUN elevation
- lower SBP
- male gender
- previous hospitalizations
- worse NYHA class
- Hyponatremia
- elevated RA pressure and PAW pressure

- S3 as outpatient
- narrow pulse pressure
- Tachycardia
- positive troponin
- BNP>1100
- failure of BNP to fall with inpatient treatment
- discharge BNP>430

Jain P. et al. Am Heart J. 2003;145:S3-17

Thomas Alva Edison
1847-1931



- His next development was a new type of storage battery, which Edison hoped would replace conventional batteries in the rapidly growing automobile industry. It is typical of him that even after his first 8,000 experiments failed, he said, **"Well, at least we know 8,000 things that don't work."** Although Edison's battery turned out to be unsuitable for cars, it did succeed in railroad and marine shipping applications, which required batteries with longer life and greater durability.

http://www.madehow.com/inventorbios/22/Thomas-Alva-Edison.html

Things that don't work in HF

- Calcium sensitizers – levosimendan
- Nitric oxide synthase inhibitors – tilarginine acetate (L-NMMA) in shock
- Vasopressin antagonists - -vaptans
- Endothelin antagonists - -sentans
- ?EECP

Tidbits in Heart Failure

- Sauna bathing may be beneficial
- Moxonidine, a central sympathetic inhibitor, is adverse

ADHF Management Summary from Braunwald 2005

- Begin with IV diuretics
- If poor perfusion or poor response, add dobutamine or nesiritide (milrinone only if EDP>15 because of vasodilation lowering preload, but choice if β-blocker)
- If poor response – PA catheter, consider dobutamine plus milrinone
- After optimization of inotropes, can add vasodilator if SVR or PVR high – NTP or NTG can be used instead of inotrope if SVR is high
- If BP is too low, dopamine, but its beta is weak and tachyphylaxis is in 12 hr, or vasopressin

Bristow MR et al. "Management of heart failure" in Braunwald's Heart Disease, 7th ed. p. 613.

Questions?

NYHA (New York Heart Association) Functional Classification

- Class I – symptoms at level of exertion that would cause symptoms in normal people
- Class II – symptoms at ordinary exertion
- Class III – symptoms at less than ordinary exertion
- Class IV – symptoms at rest

Factors Affecting Symptoms in HF

- LV systolic function
- LV diastolic function
- RV function
- Pericardial restraint
- Valvular regurgitation
- Noncardiac factors (peripheral vascular, pulmonary, muscular, neurohormonal, autonomic)