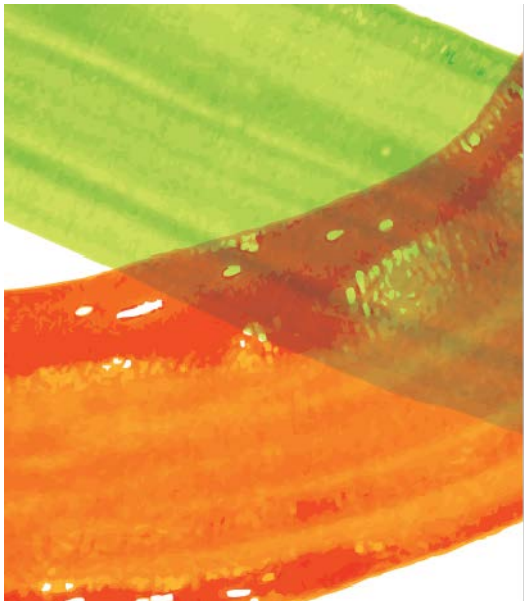
The Children's Hospital of San Antonio™
CHRISTUS Health

Why Children Are Not Small Adults? Treatment of Pediatric Patients Needing Mechanical Circulatory Support

Baylor College of Medicine

Utpal S Bhalala, MD, FAAP
Assistant Professor and Director of Research
Pediatric Critical Care Medicine
Associate Medical Director, Volker Clinical Research Center
The Children's Hospital of San Antonio
Baylor College of Medicine



The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

No Disclosures to Report

Learning Objectives

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

1. Learn “why children are not little adults”
2. Compare and contrast the differences between mechanical circulatory support in adults and pediatrics with advanced cardiovascular disease
3. Discuss novel treatment modalities for pediatric patients with advanced heart disease

Not within the scope of this talk

The Children's Hospital of San Antonio
CHRISTUS Health

Baylor College of Medicine

-Timing of Mechanical Circulatory Support (MCS) in relation to cardiac failure

-Practical perks while managing patients on MCS

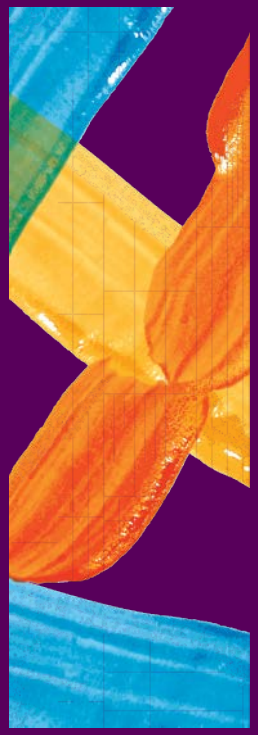
-Anticoagulation management of patients supported on MCS

-Serious infectious complications of MCS and management of infections

-Ethical and social considerations

-Withdrawal of life support considerations for children supported on MCS

Why Children Are Not Small Adults?



Children are not little adults

CHILDREN ARE NOT LITTLE ADULTS

Giotto, National Gallery, Washington DC

Raphael, National Gallery of Art, Washington, DC

Children are not little adults

CHILDREN ARE NOT LITTLE ADULTS

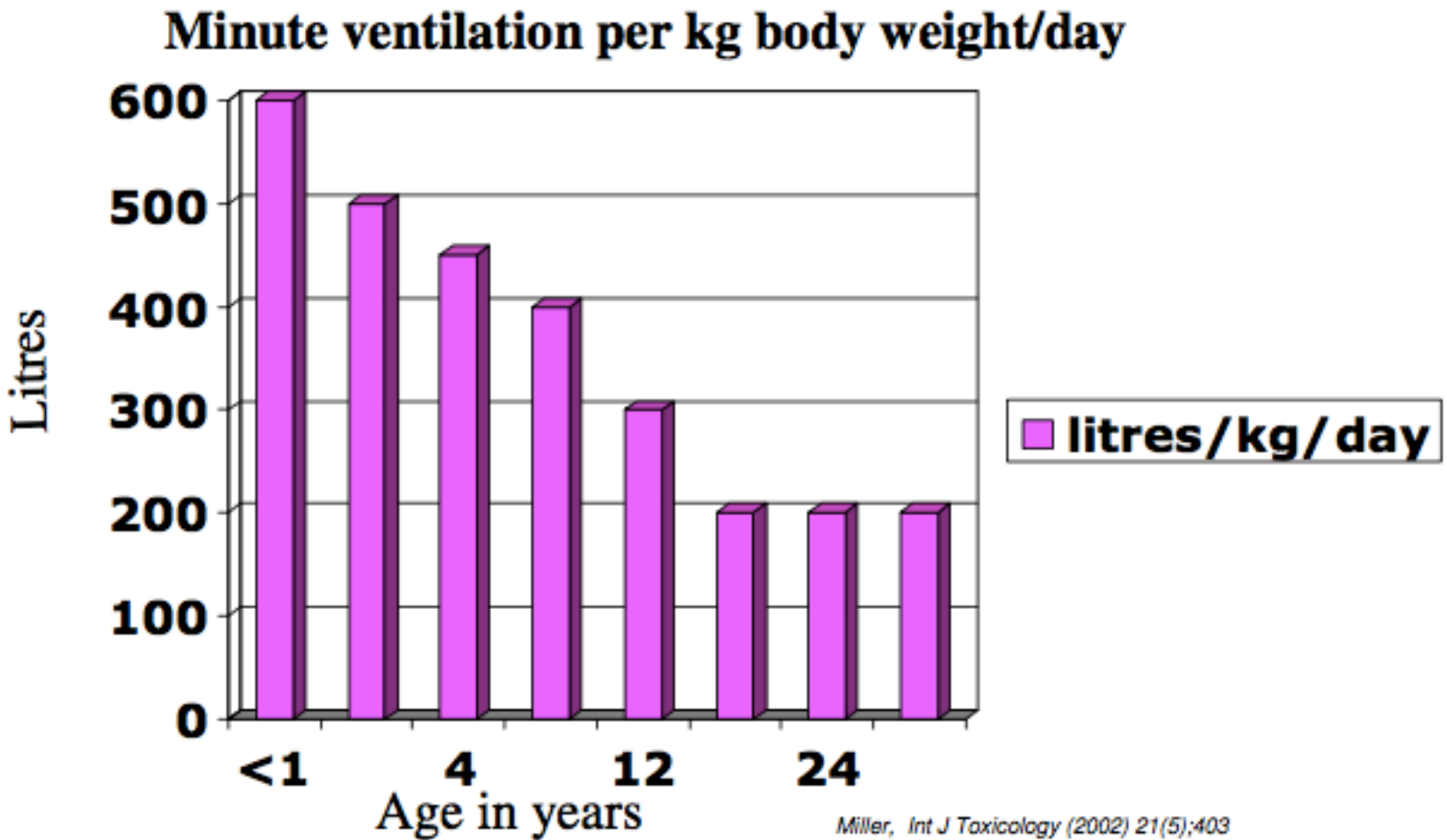
Raphael, National Gallery of Art, Washington, DC

1. **Different and unique exposures**
2. **Dynamic developmental physiology**
3. **Longer life expectancy**
4. **Politically powerless**

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

OXYGEN DEMAND

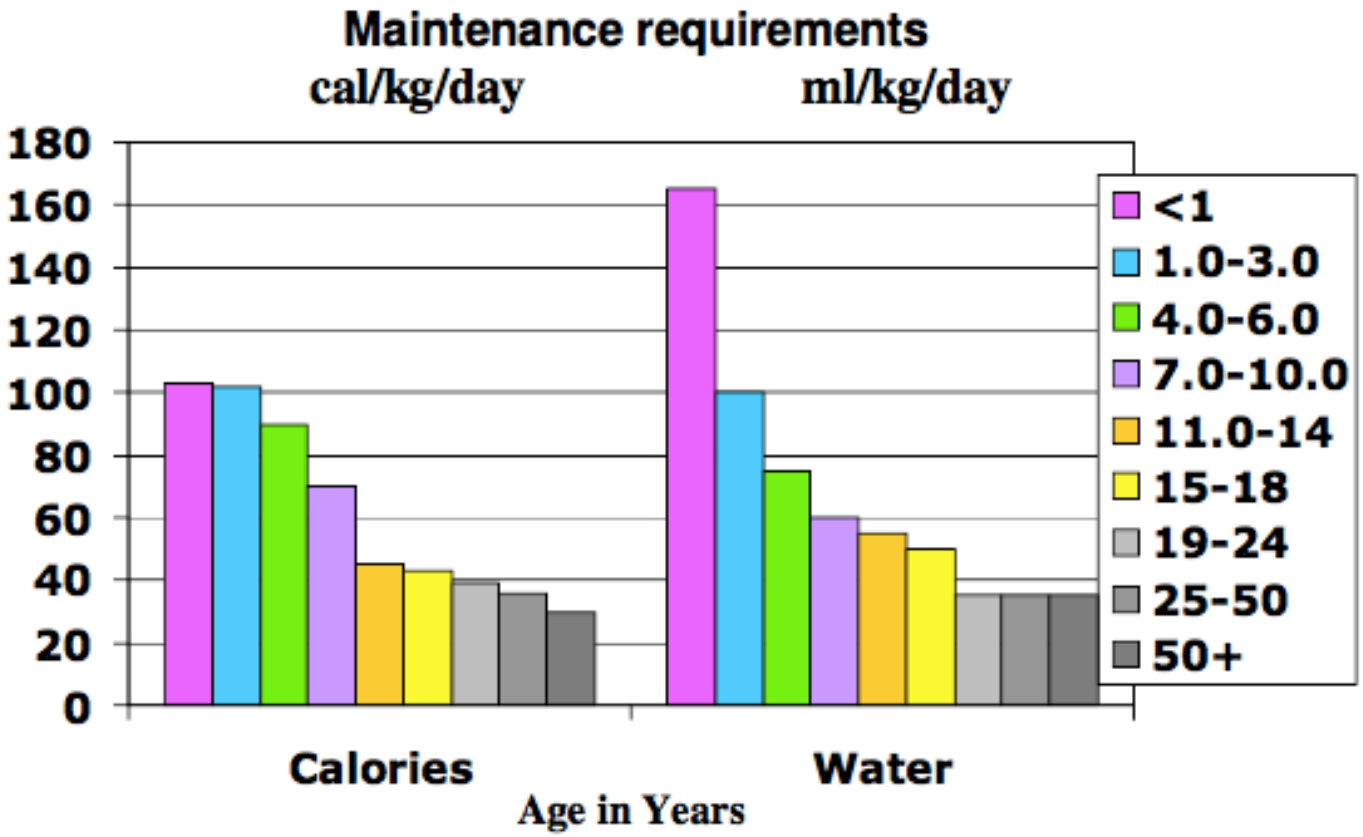


Miller, Int J Toxicology (2002) 21(5);403

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

CALORIE AND WATER NEEDS



Children are not little adults

	Heart
Children	Normal coronary arteries Glucose for energy source Diminished sensitivity to insulin Greater ability to store glycogen Smaller cardiac dimensions Right ventricular dominance Typical dysrhythmia: supraventricular tachycardia
Adults	Coronary artery disease Hypertension Long-chain fatty acids as energy source Left ventricular dominance Typical dysrhythmia: ventricular fibrillation

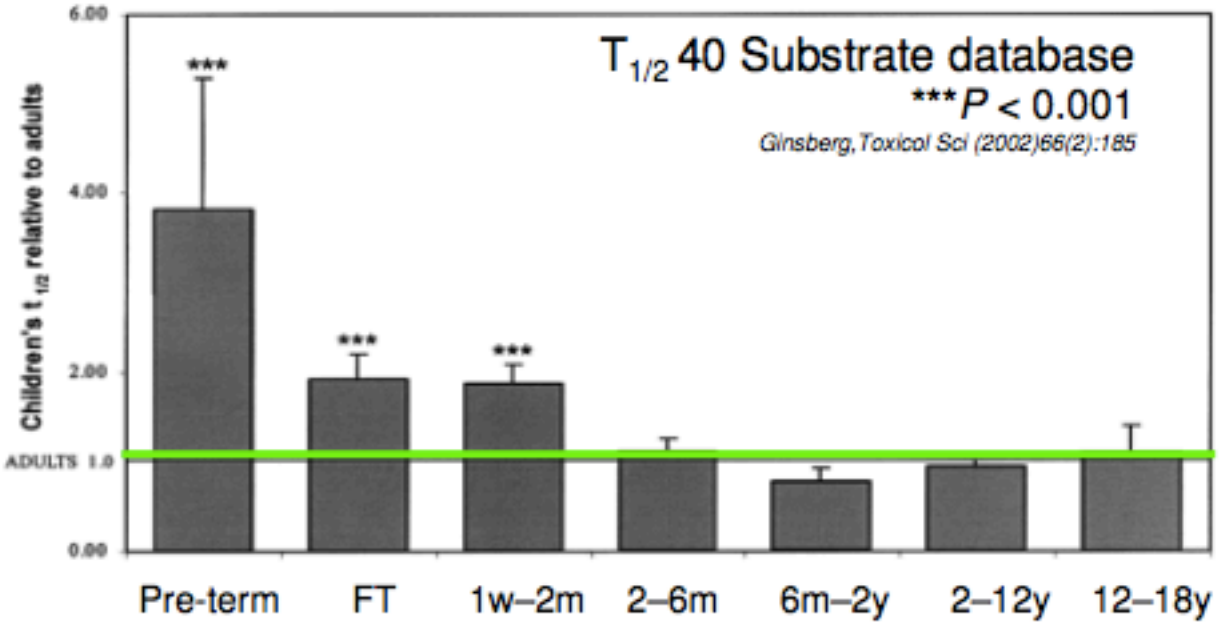
The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

LESSONS LEARNED FROM PHARMACEUTICALS

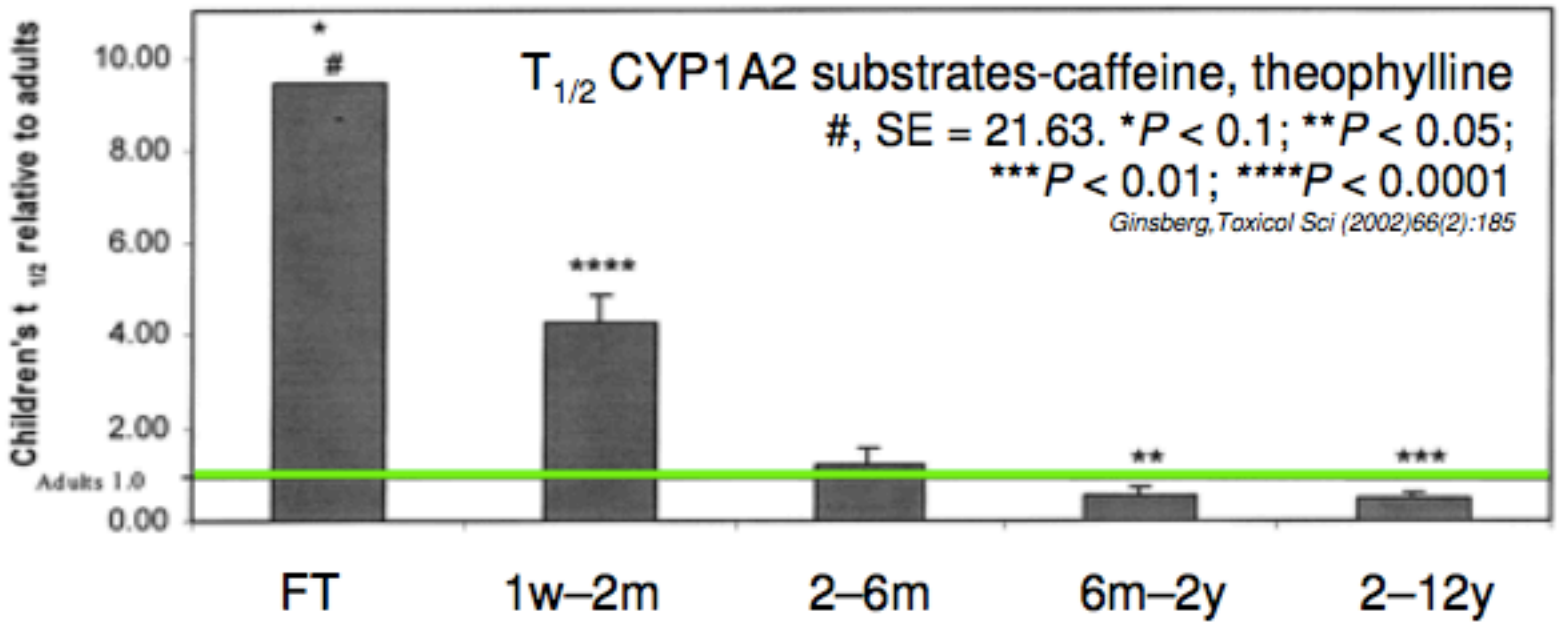


- In the aggregate, slower elimination in the very young
- No statistical difference after 2 months
- Children's PK Database *(www.clarku.edu/faculty/dhattis)*

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

LESSONS LEARNED FROM PHARMACEUTICALS



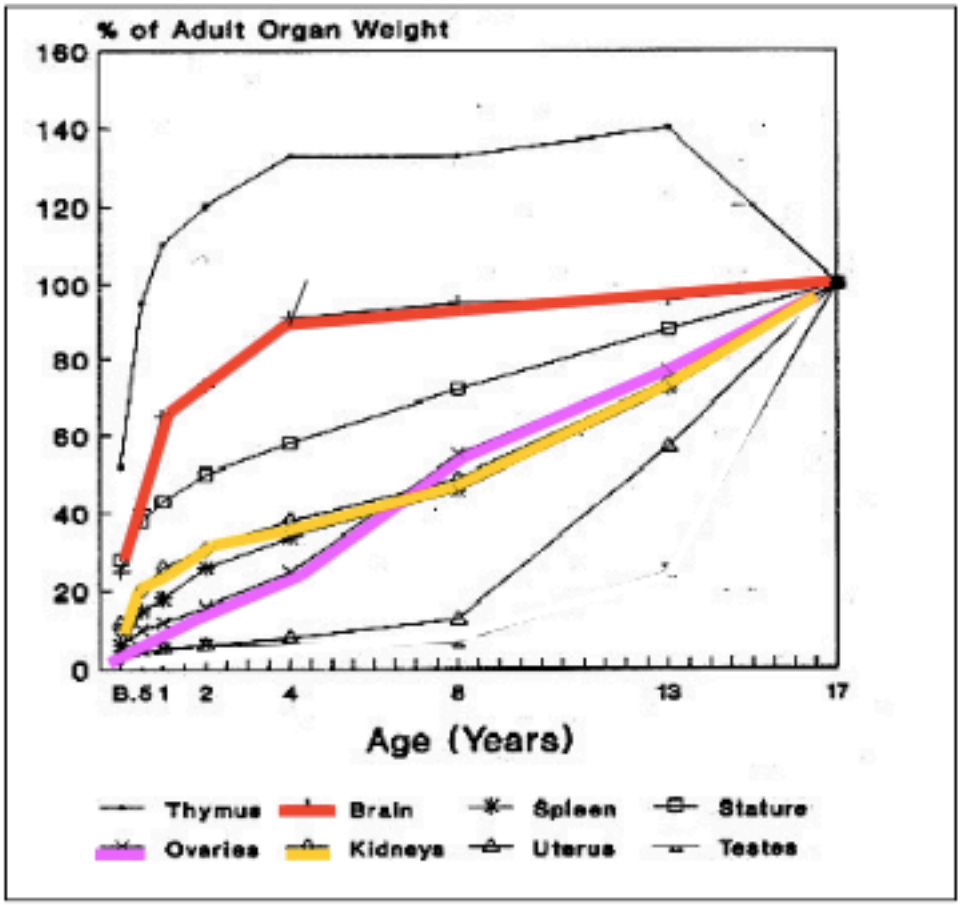
- High variability even for closely related drugs
- Neonate/adult difference for caffeine 13X greater than for theophylline

Generalizations are not possible!

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

WINDOWS OF DEVELOPMENT: BIRTH TO ADOLESCENCE



Altman eds, FASEB, 1962

- **Vital organ growth**
  - Brain
  - Lungs
  - Kidneys
  - Reproductive organs
- **Physiological function**
  - Central nervous system
  - Immune system
  - Endocrine system

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

NEURODEVELOPMENT: CONTINUES THROUGH PUBERTY!

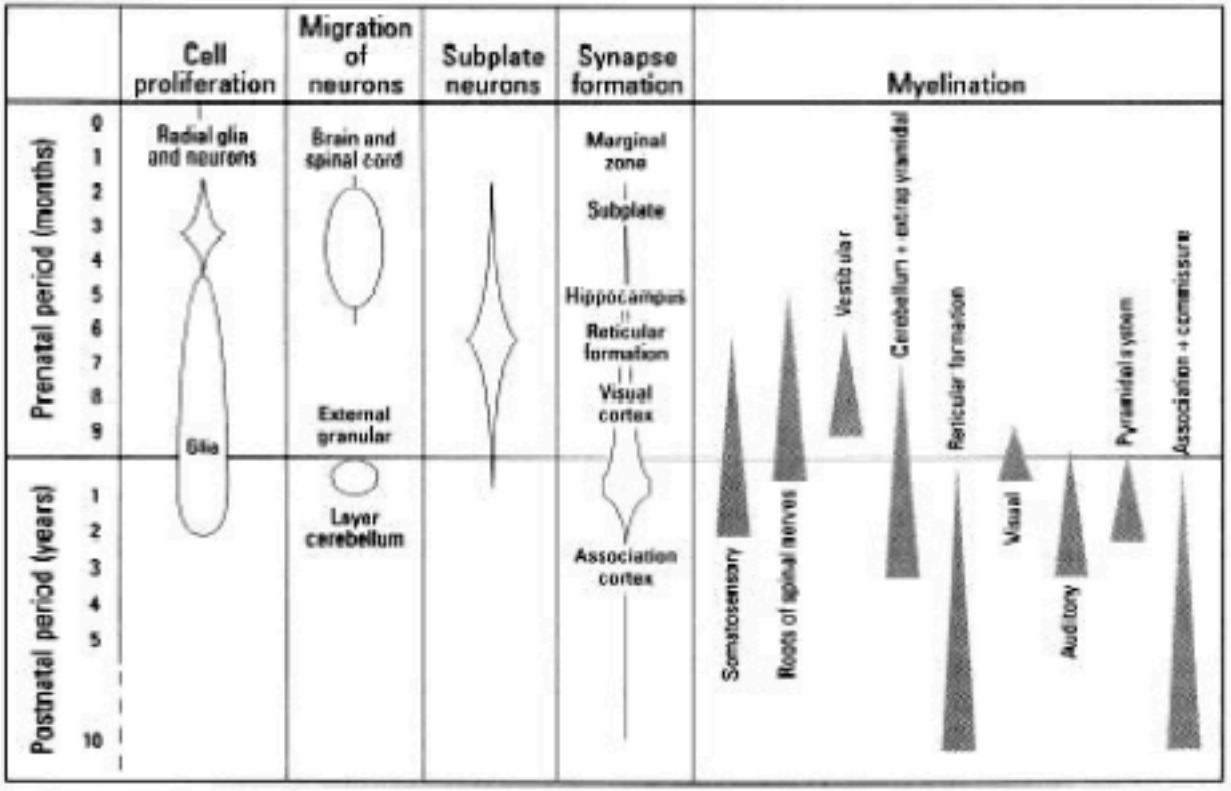


Figure 2. Comparison of timelines for developmental processes in humans. The prenatal period is scaled in months and the postnatal development is scaled in years. Adapted from Herschkowitz et al. (*16*) and reprinted with permission of Hippokrates Verlag GmbH.

- Growth 4–17 yrs in fibre tracts for motor and speech
- Activity alters architecture
- Adolescence extensive elimination of some synapses
- Redistribution of neurotransmitters

Rice,EHP, (2000) 108 (3), 511

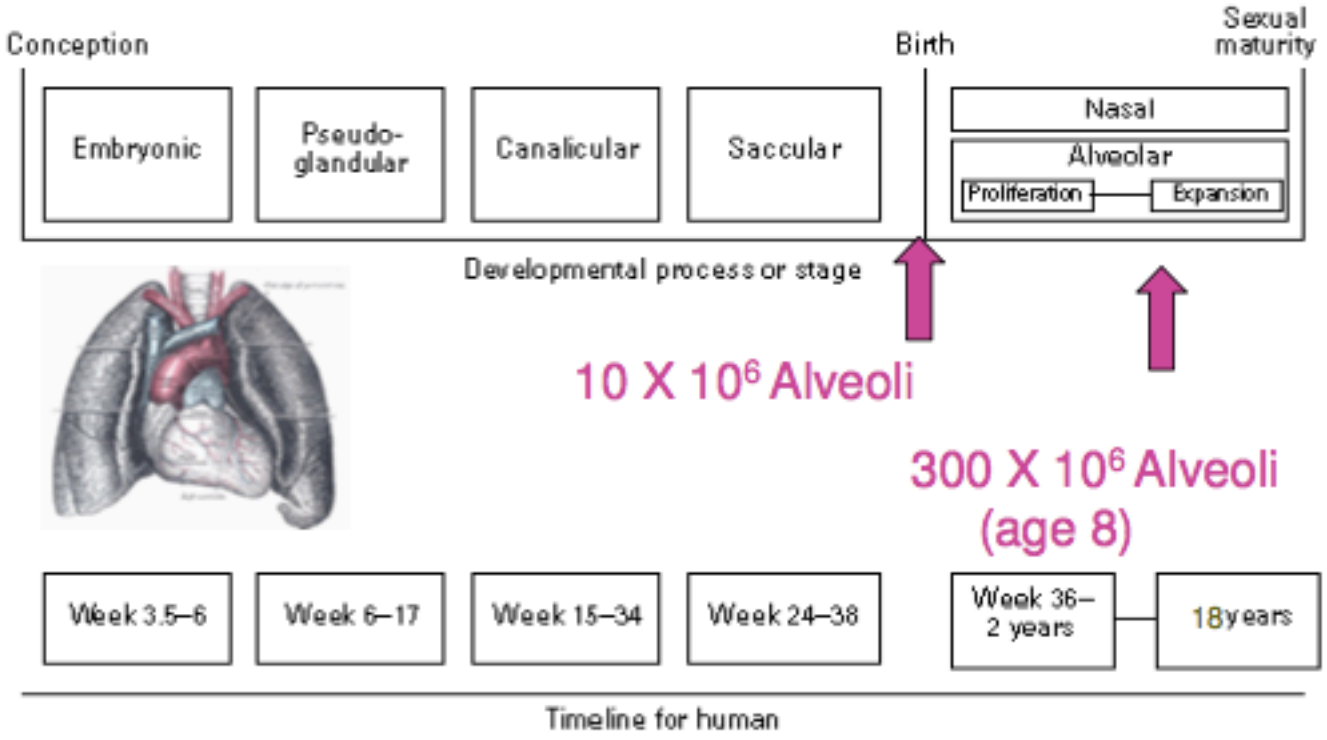
The Children's Hospital of San Antonio

Baylor College of

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

RESPIRATORY DEVELOPMENT: CONTINUES THROUGH LINEAR GROWTH

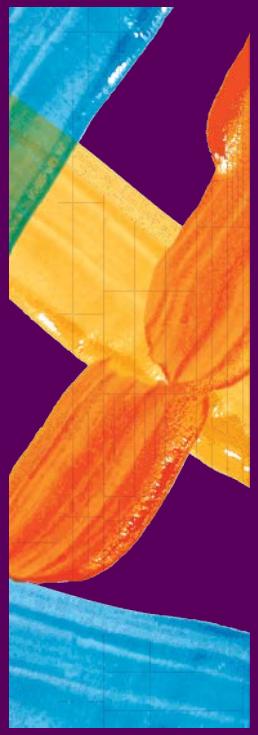


Growth
- Tobacco smoke
- Particulates
- Ozone

Function
- Indoor air
- Ozone

Dietetr,. *EHP*, 2000,108 (3): 483.

Pediatric Heart Failure



Pediatric Heart Failure

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

- In contrast to adults with HF, children with HF vary in size, anatomy (congenital heart disease), and total number.
- As the pediatric population living with HF expands, increasing demands on alternatives to ECMO have arisen.
- These factors pose significant technological and financial concerns on the development of alternative forms of Mechanical Circulatory Support (MCS) for children with HF.

Pediatric Heart Failure

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

- Mechanical Circulatory Support (MCS) is the use of a mechanical pump/s to support a weakened heart muscle.
    - Ventricular Assist Device (VAD) to assist a weakened ventricle
    - Total Artifical Heart (TAH) to replace biventricular failing heart

Mechanical Circulatory Support (MCS)

The Children's Hospital of San Antonio
CHRISTUS Health

Baylor College of Medicine

- Mechanical Circulatory Support (MCS) can be used in the following roles:
  - Bridge to Transplant (BTT)
  - Bridge to Recovery (BTR)
  - Bridge to Decision/Candidacy (BTD)
  - Chronic Therapy

ECMO

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Adults are just Big Kids

ECMO

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Size of Circuit Components Based on Patient Weight

Weight (kg)	2-8	8-12	12-20	20-30	>30
Tubing size	1/4"	3/8"	3/8"	3/8"	1/2"
Race way tubing	1/4"	3/8"	3/8"	3/8"	1/2"
Bladder	1/4"	3/8"	3/8"	3/8"	3/8"
Oxygenator (sqm)	0.8	1.5	2.5	3.5	4.5[1]
Venous cannula[2]	10-14	16	18	20	22

ECMO

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Pediatric ECMO Management: Flow

- Infants: 120-150 cc/kg/min
- Children: 100-120 cc/kg/min
- Adults: 70-80 cc/kg/min
- Attempt to reach maximal flow early in run to determine buffer

Adult Mechanical Circulatory Support (MCS)

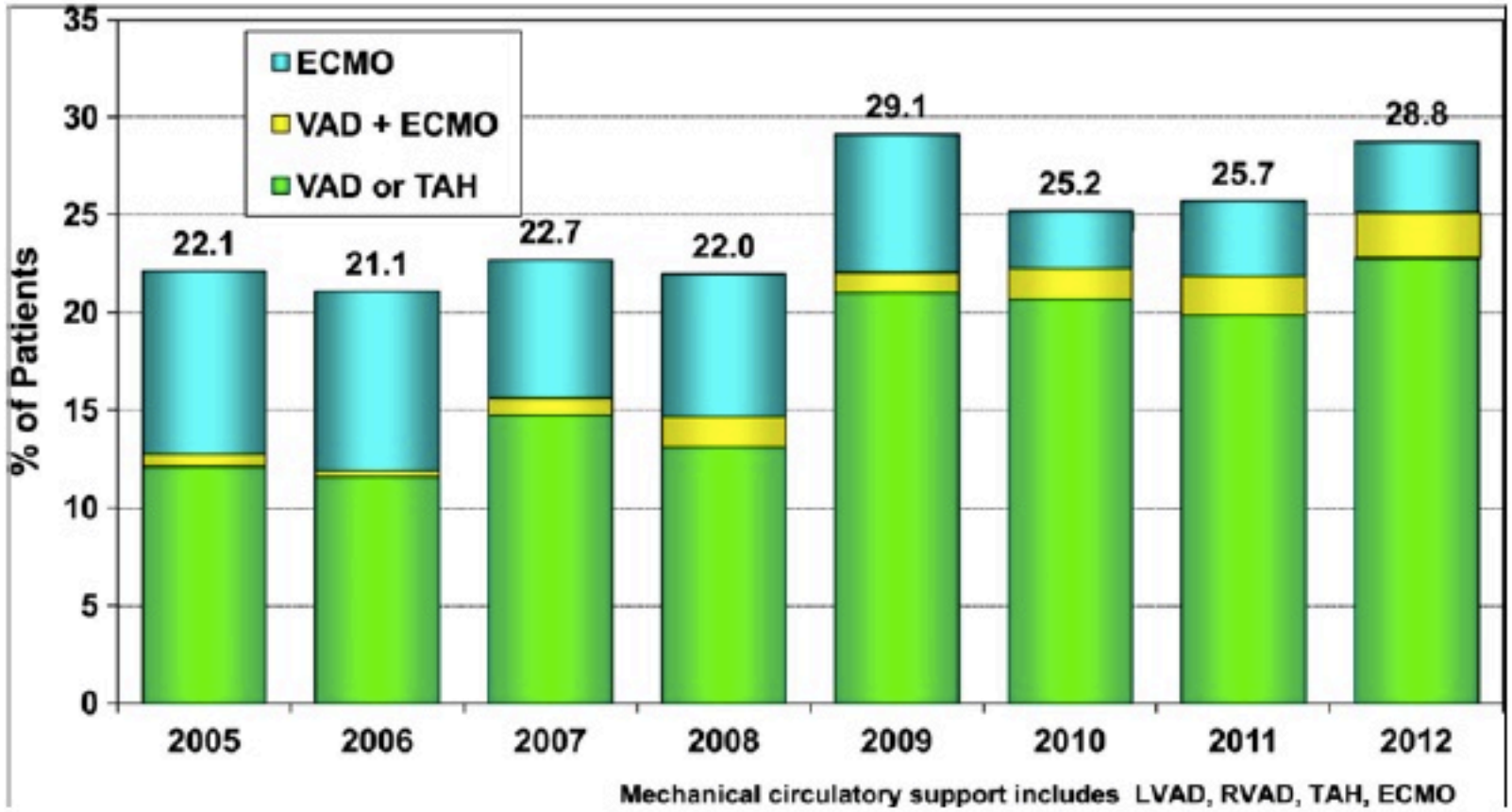
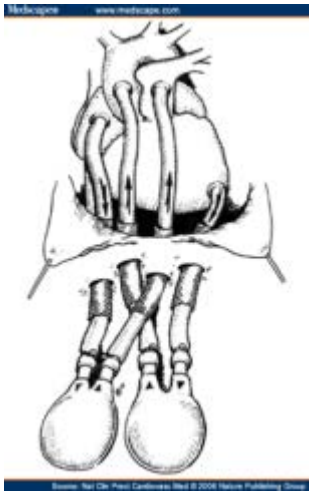


Figure 5: Percentage of patients bridged with mechanical circulatory support by year (transplants: January 2005-December 2012).

- ECMO= extracorporeal membrane oxygenation; LVAD= left ventricular assist device; RVAD= right ventricular assist device; TAH= total artificial heart; VAD= ventricular assist device.
- Reprinted with permission from Benden et al. [88]

EXCOR Berlin Heart

- Uni - or Bi- Ventricular Support
- Longest application > 1000 days
- Wide selection of blood pumps and cannulas
- Specially designed small pumps and cannulas for infants and children
- Easy visual inspection of the blood pumps (pump performance and/or deposit formation)
- Paracorporeal design allows for ease of exchange due to upsize or thrombus



EXCOR Berlin Heart

The Children's Hospital of San Antonio
CHRISTUS Health

Baylor College of Medicine

Paracorporeal ventricular assist device (VAD)

IKUS® driving unit

EXCOR Berlin Heart

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

EXCOR® Ikus Driving Unit

- Electro pneumatic driving unit
- Suitable for all EXCOR® blood pumps
- Uni- and biventricular operation
- Battery back-up
- Hand pump provided for emergency use
- Various operating modes for BVAD support

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prospective Trial of a Pediatric Ventricular Assist Device

Charles D. Fraser, Jr., M.D., Robert D.B. Jaquiss, M.D., David N. Rosenthal, M.D., Tilman Humpl, M.D., Ph.D., Charles E. Canter, M.D., Eugene H. Blackstone, M.D., David C. Naftel, Ph.D., Rebecca N. Ichord, M.D., Lisa Bomgaars, M.D., James S. Tweddell, M.D., M. Patricia Massicotte, M.D., Mark W. Turrentine, M.D., Gordon A. Cohen, M.D., Ph.D., Eric J. Devaney, M.D., F. Bennett Pearce, M.D., Kathleen E. Carberry, R.N., M.P.H., Robert Kroslowitz, B.S., and Christopher S. Almond, M.D., M.P.H., for the Berlin Heart Study Investigators

EXCOR Berlin Heart

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

- EXCOR Berlin Heart IDE study led to FDA approval of the device in U.S.A. on December 16, 2011
- Although this study showed a significant mortality benefit, significant morbidity remained
    - Bleeding 44%
    - Stroke 29%

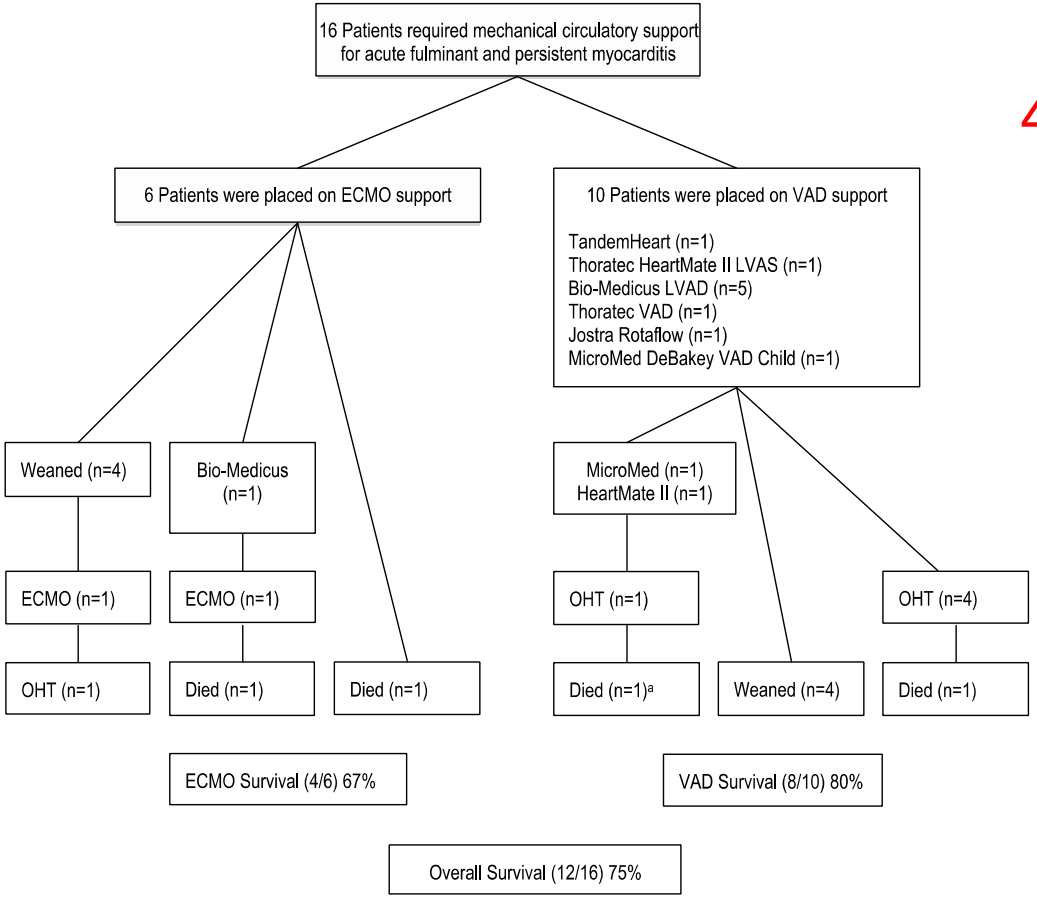
Journal of Cardiac Failure Vol. 17 No. 6 2011

Effectiveness of Mechanical Circulatory Support in Children With Acute Fulminant and Persistent Myocarditis

IVAN WILMOT, MD,[1] DAVID L. S. MORALES, MD,[2] JACK F. PRICE, MD,[1] JOSEPH W. ROSSANO, MD,[1] JEFFREY J. KIM, MD,[1] JAMIE A. DECKER, MD,[1] MARY CLAIRE MCGARRY, CCP, RRT, BS, LP,[2] SUSAN W. DENFIELD, MD, FACC,[1] WILLIAM J. DREYER, MD, FACC,[1] JEFFREY A. TOWBIN, MD,[1,3] AND JOHN L. JEFFERIES, MD, MPH, FACC[1,3]

Houston, Texas

44% BTR



67% ECMO Survival

80% VAD Survival

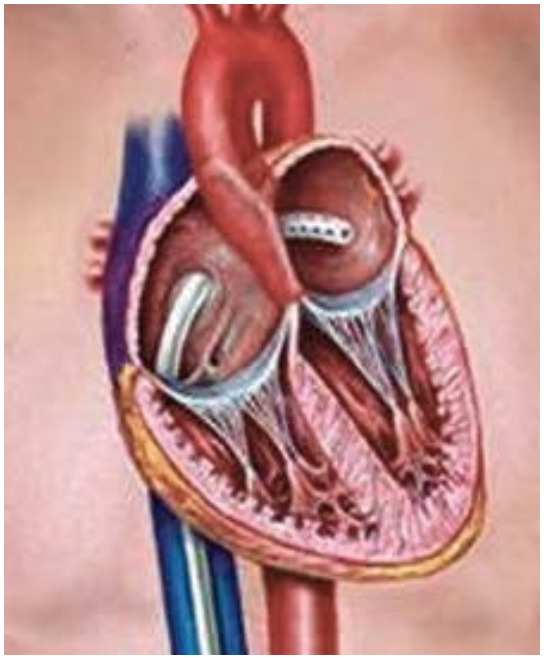
Wilmot et al. J Car Fail. 2011

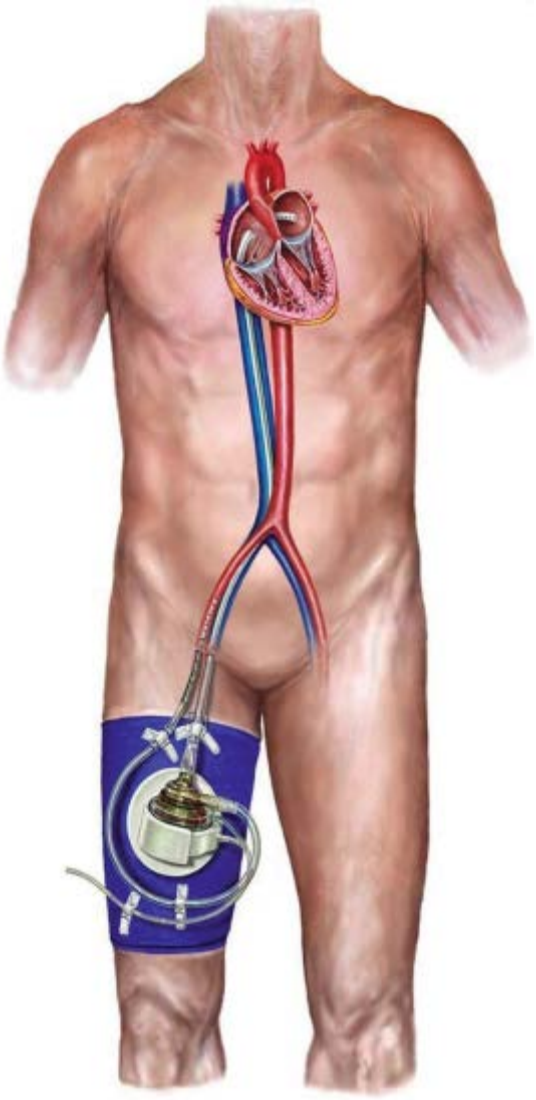
TandemHeart®

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Percutaneous placed
short-term LVAD





Courtesy of Cardiac Assist Inc, Pittsburg, PA

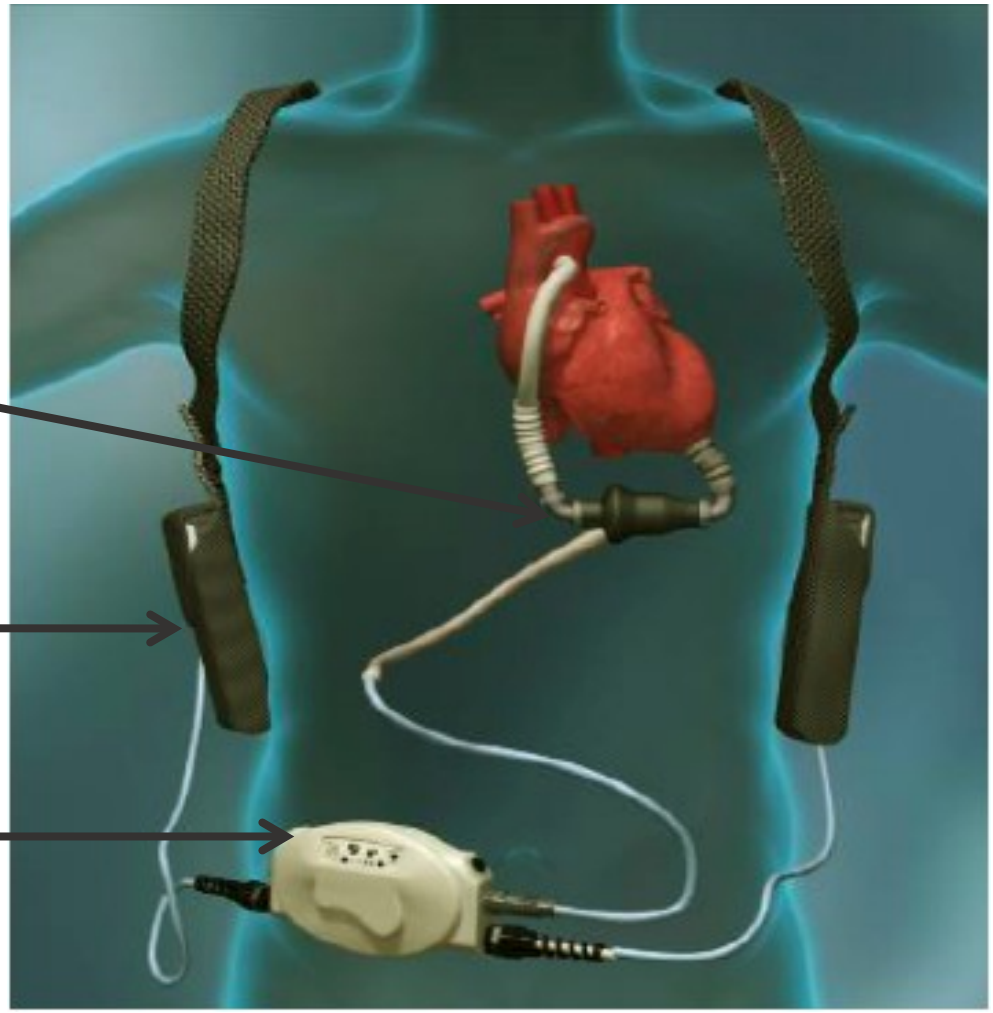
HeartMate II LVAD

The Children's Hospital of San Antonio
CHRISTUS Health
Baylor College of Medicine

Surgically placed long-term LVAD

Battery pack

External console



Pediatric MCS

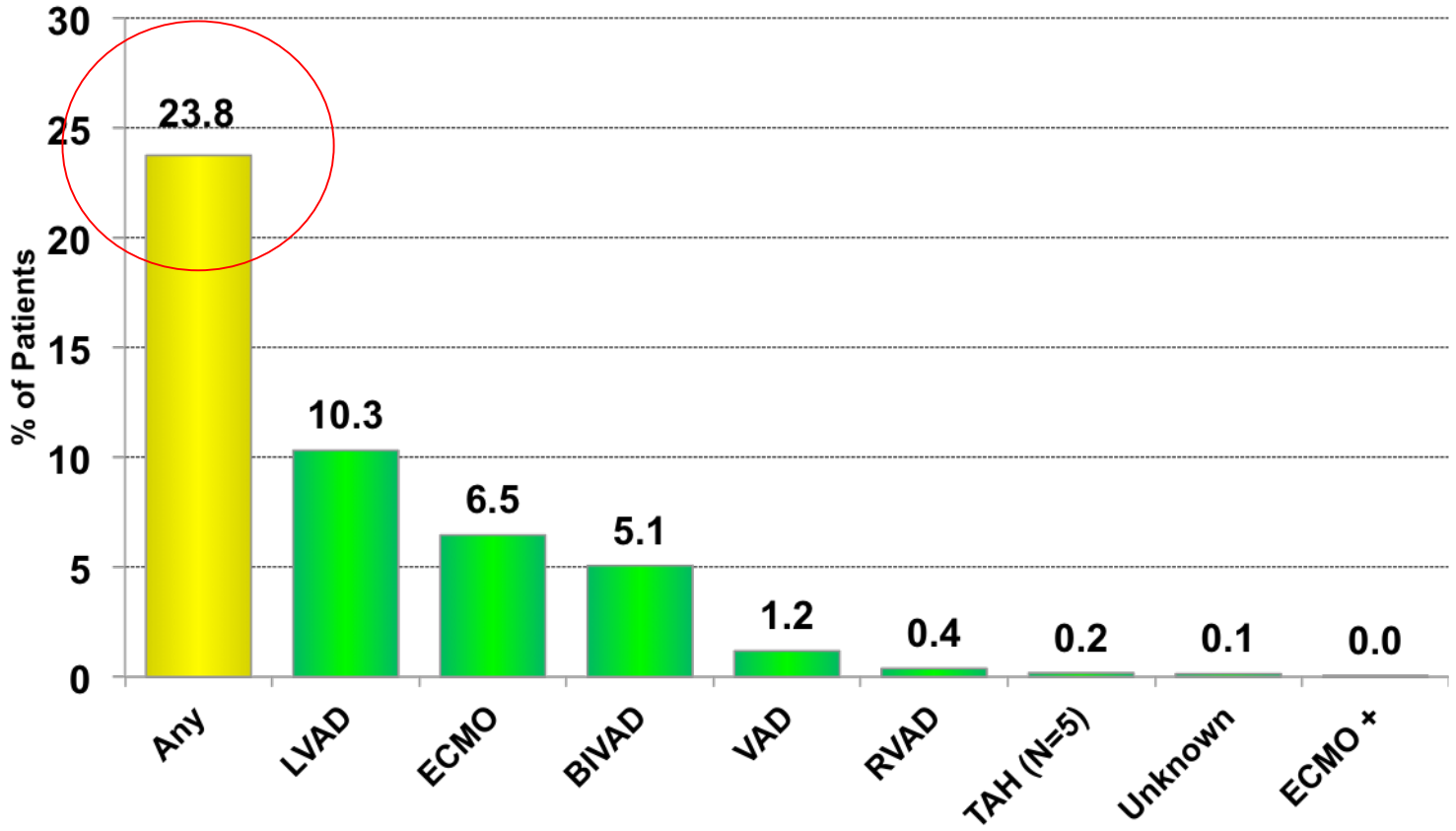
- Increasing literature reports show promising VAD results in the pediatric HF population.
- In the setting of limited heart transplant donors, and increasing numbers of children with HF, many centers are utilizing VAD's as a bridge to transplant (BTT).

Chen et al. Eur J Cardiothorac Surg 2005
Lorts et al. Curr Opin Organ Transplant 2015

Increased Number of Participating Centers in PediMACS

Blume et al-AHA 2014

ISHLT BTT with MCS (2004-2013)



Pediatric MCS

- With the increased utilization of MCS in the pediatric HF population, the ISHLT recently released updated Guidelines for the Management of Pediatric HF in 2014.
- These guidelines include MCS use in the pediatric HF population including indications for MCS, patient selection, timing of implant, device selection, and recommendations.

ISHLT Guidelines for the Management of Pediatric Heart Failure, 2014

Pediatric MCS

- MCS is reserved for children with acute life-threatening cardiovascular events or severe HF symptoms despite maximal medical therapy.
- MCS should be considered if a child requires inotropic infusions to maintain cardiovascular stability and other organ systems begin to be compromised.

ISHLT Guidelines for Management of Pediatric Heart Failure, 2014

Special Pediatric MCS Considerations

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

- An increased interest in *chronic therapy* for pediatric patients
  - Muscular dystrophy
  - Cancer patients post chemotherapy
  - Patients with contraindications to transplant (elevated pulmonary vascular resistance)

Conclusions

- Although children with HF refractory to medical therapy have limited options, recent advances in MCS can provide superior outcomes when used as a bridge to transplant (BTT).
- The Berlin Heart EXCOR VAD provide a MCS option for both infants and children, however morbidity concerns remain.
- MCS can be used successfully as a bridge to transplant (BTT), bridge to recovery (BTR), and bridge to decision (BTD).

Conclusions

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

- 2014 ISHLT Guidelines for the Management of Pediatric HF include indications for MCS, patient selection, timing of implant, device selection, and recommendations.
- There is an increasing interest in MCS as a chronic therapy in pediatrics.
- The future of MCS in children appears promising with increasing options available in this vulnerable population

Learning Assessment Question 1

The Children's Hospital of San Antonio
CHRISTUS Health

Baylor College of Medicine

What is the most important mechanism by which children improve their cardiac output in contrast to adults?

A) Increase in hear rate

B) Increase in stroke volume

C) A and B

D) Neither A not B

Learning Assessment Question 2

Duration of CPR prior to ECPR is an important determinant of outcomes of ECPR?

A) True

B) False

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Children are not little adults

We hold our future in our hands and it is our children

The Children's Hospital of San Antonio™
CHRISTUS Health

Baylor College of Medicine

Thank You!