“Cardiovascular Pharmacology in Pediatric Patients with Congenital Heart Disease

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“Dr Anna Maria Henaine” declare to meeting attendees that there are no financial relationships with any for-profit companies that are directly or indirectly related to the subject of this presentation.
A normal heart has valves, arteries and chambers that carry the blood in a circulatory pattern:

Body → Heart → Lungs → Heart → Body

When all chambers and valves work correctly

↔ Blood pumped to the lungs for $O_2$ → out to body ($O_2$)

When valves, chambers, arteries and veins malformed

↔ Circulation pattern → impaired

CHD = malformations present at birth
FETAL DEVELOPMENT CHART

This chart shows vulnerability of the fetus to defects throughout 38 weeks of pregnancy. *
* = Most common site of birth defects

Adapted from Moore, 1993 and the National Organization on Fetal Alcohol Syndrome (NOFAS) 2009.

*This fetal chart shows the 38 weeks of pregnancy. Since it is difficult to know exactly when conception occurs, health care providers calculate a woman’s due date 40 weeks from the start of her last menstrual cycle.
FETAL VS NORMAL HEART

Fetal Physiology

- From Upper Body
- Right Atrium
- Right Ventricle
- Aorta
- PDA
- Left Ventricle
- From Lower Body
- From Placenta

Normal Heart

- From Upper Body
- Aorta To Body
- Right Atrium
- Right Ventricle
- To Lungs
- Left Atrium
- Left Ventricle
- From Upper Body
- From Body
NEONATAL VS ADULT CARDIAC PHYSIOLOGY

At birth, neonatal myocyte not fully developed \(\Rightarrow\) heart less able to respond to volume loading with an ↑ CO [higher proportion of fibrous tissue to contractile tissue, as compared to that of an adult]

The neonate relies heavily on Ca++ flux through the sarcolemma for myocyte function (contraction)

\[ \text{CO} = \text{HR} \times \text{SV}. \text{ Unlike adults, neonates possess a limited ability to ↑ CO by ↑ SV} \]

Neonatal CO is significantly dependent on HR (\(\Rightarrow\) less preload reserve)

Neonatal O₂ requirements >>> adult \(\Rightarrow\) neonatal heart function at near maximal capacity

Relative dominance of the sympathetic and parasympathetic system changes as the neonate develops. The parasympathetic system is fully formed shortly after birth, while the sympathetic innervation is incomplete \(\Rightarrow\) predisposition of the neonate to pronounced vagal responses (bradycardia)

Prior to anatomic closure of the foramen ovale or DA, neonates may, in times of stress, revert to a fetal pattern of circulation \(\Rightarrow\) shunting in either direction, as the balance of SVR and PVR dictate. Sepsis, hypoxia, hypercarbia, hypothermia, or pain may precipitate this by ↑ PVR [PVR approaches adult values by about 2 months of age]

Lactate is the 1\textsuperscript{st} fuel source for the immature myocardium \(\text{in contrast the adult}\) myocardium which utilizes fatty acids for energy

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ETIOLOGY

Environmental
Diabetes, rubella, SLE
Maternal intake of teratogenic agents (Li+, isotretinoin, alcohol, anticonvulsants)
Paternal age

Genetics
Numerical chromosomal abnormalities (5%): trisomy 21 (Down Syndrome), trisomy 18, trisomy 13 and monosomy X (Turner syndrome)
Microscopic deletions on chromosomes or single-gene mutations
Epidemiology

- CHD → most common ~ incidence 6-9‰
- 28% of all major congenital anomalies
- Diagnosed 8-10‰ live births in the US*
- Reported total CHD birth prevalence ↑ substantially over the last century → stable estimate of 9‰ live births in the last 15 y
- 1.35 million NN with CHD /year
- Major global health burden**

- In Lebanon, the incidence is 7-8‰ and mortality 1-6% (according to MOPH Statistic Department 2018)

*Increasing number of U.S. adults living with congenital heart defects [American Heart Association Journal Report; July 05, 2016]
**van der Linde et al. JACC Vol. 58, No. 21, 2011 Birth Prevalence of Congenital Heart Disease November 15, 2011:2241–7
CONGENITAL HEART DEFECTS: CLASSIFICATION

CHD

ACYANOTIC

Volume load
L→R shunts
- Ventricular Septal Defect
- Patent Ductus Arteriosus
- Atrial Septal Defect

Pressure load
Outflow obstruction
- Pulmonary Valve Stenosis
- Aortic Valve Stenosis
- Coarctation of the Aorta

CYANOTIC

↑ Pulmonary flow
- Transposition of the Great Arteries
- Single Ventricle
- Truncus Arteriosus

↓ Pulmonary flow
- Tetralogy of Fallot
- Pulmonary Atresia
- Tricuspid Atresia
COMPLICATIONS

- Abnormal Heart Rhythms (arrhythmias)
  - Heart pump less efficiently. In children:
    - Fast heart rate (tachycardia), the most common type found in children being **supraventricular tachycardia**
    - Slow heart rate (bradycardia)
    - Long QT Syndrome (LQTS)
    - **Wolff-Parkinson-White syndrome** (WPW syndrome)
  - **Heart Failure.** 1\textsuperscript{st} causes in children and adolescents:
    - “Over-circulation failure,” (blood mixes inside the heart)
    - “Pump failure,” (heart muscle becomes damaged and no longer contracts normally)

- **Pulmonary HTA.** CHD => more blood flow to the lungs, causing pressure to build and making heart work harder

- **Heart Valve Problems.** In some types of CHD, the heart valves are abnormal

- **Heart Infection (endocarditis)**

- **Stroke**
CONSIDERATIONS FOR THE PEDIATRIC PATIENT

**Oral administration of drugs**: most common method used in children. NN, compared with infants and older children have less acid secretion in the stomach for the 1st few weeks after birth.

GI transit time is more rapid for the 1st 5y of childhood [can affect the absorption of drugs administered in a SR preparation]

**Drug Distribution**: plasma → organs on the basis of their affinity for tissues with high water or lipid content.

In premature infants water represents 85% of BW

In 1 y old child → 60%

When the percentage of extracellular water is high (neonate ) => drug must be given in a larger dose [mg/kg basis ] to achieve the same serum concentration

**Drug Metabolism**: liver +++

Phase 1: metabolize substances by oxidase system, cyp450 system and N-demethylation pathways*

Phase 2: reactions conjugate endogenous compounds or specific drugs and their metabolites into water soluble entities by glucuronidation or acetylation

**Drug Elimination**: kidney +++

Biliary, GI and respiratory tract ±

↓renal elimination in NN {must be accounted for when dosing}
In children

- 50% of all drugs used are unlicensed or off-label, reflecting the paucity of specific trials in children

⇒ Most recommendations are based on extrapolation from adults

- There is evidence that such extrapolation may, in many circumstances, be inappropriate
1- PROSTAGLANDINS [PGE1]

PGE1 effective to dilate ductus arteriosus (regardless of age)

**Indications of PGE1**

- **↑pulmonary blood flow**: pulmonary and tricuspid atresia or pulmonary stenosis with or without shunt
- **↑systemic blood flow**: coarctation of aorta, hypoplastic left heart or interrupted aortic arch;
- **Improve mixing in cases** of TGV and LV volume by keeping the duct open in cases of TGA with intact ventricular septum

**Prostaglandin Therapy**

- PG metabolized rapidly → continuous infusion through a pump delivery system at an initial IV infusion of 0.05 µg/kg/min. For maintenance → 0.005-0.01 µg/Kg/min
- Over 2/3 of the circulating PG metabolized in a single pass through the lungs, and the metabolites are excreted by the kidneys within 24 hrs. The efficacy of the drug was assessed by a rise in SP02*

**Common side effects**: cutaneous vasodilatation, apnea or hypoventilation (21.5 to 53%) => immediate intubation and ventilation during treatment**, seizures, pyrexia and diarrhea. Flushing (10%). Edema (Furosemide 1mg/kg **per os** BID)

* Patent Ductus Arteriosus

** Patent Ductus Arteriosus

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□ **Prostaglandins E2** used to perform a better lung or kidney perfusion by opening ductus arteriosus

□ **Indications:** pulmonary atresia, hypoplastic left heart syndrome, transposition of the great arteries with or without ventricular septal defect, coarctation of the aorta and tetralogy of Fallot

□ **Dose of PGE2** infusion 0.1 µg/kg /BW/min and progressive ↓ (depending on the capillary pO₂)

□ An oral PGE2 has also been administered. The effectiveness and simplicity of oral PGE2 administration have advantages over IV, especially for long-term treatment
The immature coagulation system during infancy has age-related physiological differences in proteins that contribute to significant variation in heparin responsiveness through alterations in heparin-enhanced thrombin inhibition.
A- ANTICOAGULANTS: HEPARIN

Enhancement of thrombin inhibition [80-120% (NN 40-60%)] by the binding of heparin to AT at a specific pentasaccharide sequence on the heparin molecule.

- AT activity in NN and infants >>>>> adults [normal activity levels are not reached until at least 6 months of age] Also in sepsis, liver dysfunction, DIVC*
- Children with CHD, are at higher risk for thrombosis due to an immature coagulation system or complex surgical palliations=>frequently prescribed platelet inhibitors, LMWH, or UFH for the prevention or treatment of thromboembolic events

Serious complications of thrombosis and bleeding occur frequently following CH surgery. Subtherapeutic heparin AC can directly influence these outcomes.

- Inhibits osteoblast formation, and activates osteoclasts ↔ promote bone loss (>>adults)
- HIT is the most important non-hemorrhagic SE

LD 75 u/kg by IV injection over 10 mn
MD 28 u/kg/hr by continuous IV

- Hypothermia, hemodilution, and ↑ binding to PP will have variable effects on heparin pharmacodynamics and pharmacokinetics in children undergoing cardiac surgery

Compared with adults, UFH in younger children has a larger Vd, ↑ Cl, and a shorter dose-dependent t½.

Pharmacodynamics are age-dependent, with ↓ antithrombotic effects measured by anti-Xa and anti-IIa activity in younger children*


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B- ANTICOAGULANTS: LOW MOLECULAR WEIGHT

- LMWHs >> inhibitory activity against factor Xa than thrombin and exhibit less binding to cells and PP than heparin
- LMWH preparations have more predictable pharmacokinetic and pharmacodynamic properties, longer half-life than heparin, and associated with a lower risk of non-hemorrhagic side effects

- LMWHs administered OD or BID by SC, without coagulation monitoring
- Dosage: 1 mg/kg/dose/12h SC [Prophylactic 0.5 mg/kg/dose/12h]
- Fondaparinux, synthetic pentasaccharide, catalyzes the inhibition of factor Xa, but not thrombin, in an antithrombin-dependent fashion. Binds only to antithrombin\(\rightarrow\) fondaparinux-associated HIT or osteoporosis is unlikely to occur

- Fondaparinux exhibits complete bioavailability when administered SC, longer half-life than LMWHs, and given once daily by SC injection in fixed doses, without coagulation monitoring
C- VITAMINE K ANTAGONISTS (VKA)

VKAs are problematic in NN for several reasons*

1- The plasma levels of the vitamin K-dependent coagulation factors are physiologically ↓ to levels that are comparable to those achieved in adults receiving therapeutic amounts of VKAs with target INRs of 2.0 to 3.0

2- Infant formula is supplemented with vitamin K to prevent hemorrhagic disease of the NN. In contrast, breast milk has low concentrations of vitamin K, making breast-fed infants very sensitive to VKAs [compensated by feeding breast-fed neonates 30 to 60 mL of formula /d]

3- VKAs are only available in tablet form => can be dissolved in water (neither stability data nor critical assessment available)

4- VKAs require frequent monitoring in NN [rapidly changing physiologic values of the vitamin K-dependent coagulation proteins + frequent changes in medications and diet]

5- Little efficacy or safety information specific to their use in NN

Problems of vascular access, frequent intercurrent infections, concurrent medications, lack of liquid preparation, and poor compliance


OAC in pediatrics
Warfarin
Acenocoumarol
Phenprocoumon
Fluindione
C- VITAMINE K ANTAGONISTS

Monitoring *OAC therapy in children is difficult and requires close supervision with frequent dose adjustments**

Adverse Effects

Bleeding (3.2% patients/year)
=>IV vitamin K in doses of 30 mg/kg or immediate reversal with FFP PT complex concentrates or recombinant factor VIIa

Non-hemorrhagic complications rare tracheal calcification or hair loss

In children with HIT argatroban, bivalirudin, lepirudin, dabigatran, danaparoid, and fondaparinux

<table>
<thead>
<tr>
<th>Stage</th>
<th>Day</th>
<th>INR</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Day 1</td>
<td>1.0-1.3</td>
<td>0.2 mg/kg orally</td>
</tr>
<tr>
<td>II</td>
<td>Days 2-4</td>
<td>1.1-1.3</td>
<td>Repeat day 1 loading dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4-1.9</td>
<td>50% of day 1 loading dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0-3.0</td>
<td>50% of day 1 loading dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.1-3.5</td>
<td>25% of day 1 loading dose</td>
</tr>
<tr>
<td></td>
<td>&gt;3.5</td>
<td>Hold dosing until INR is &lt;3.5, then restart at 50% of previous dose</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Maintenance</td>
<td>1.1-1.4</td>
<td>Increase by 20% of dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4-1.9</td>
<td>Increase by 10% of dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0-3.0</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.1-3.5</td>
<td>Decrease by 10% of dose</td>
</tr>
<tr>
<td></td>
<td>&gt;3.5</td>
<td>Hold dosing until INR is &lt;3.5, then restart at 20% less than last dose</td>
<td></td>
</tr>
</tbody>
</table>

Target INR of 2.5 (INR range, 2.0 to 3.0).

Low dose: prophylactic target INR is 1.7 (range, 1.5-1.9)


IMPORTANCE OF VITAMIN K ANTAGONISTS IN PEDIATRICS

INDICATIONS
- Prophylaxis after Fontan surgery
- Mechanical prosthetic valves
- Kawasaki disease with large aneurysms
- Dilated cardiomyopathy with severe left ventricular dysfunction
- Primary pulmonary hypertension

(VKA indications extrapolated from adult series)

INTERACTIONS
- Warfarin dose needs to be ↑ when coadministered with anticonvulsants
- Other drugs interacting with warfarin: aspirin, steroids, NSAIDS, alcohol, fluconazole, metronidazole, amoxicillin, rifampicin, sulfamethoxazole-trimethoprim
- Foods: liver, broccoli, Brussels sprouts, spinach, coriander, cabbage and other green leafy vegetables

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D- ANTIPLATELET THERAPY

Thrombin

Fibrinogen

Fibrin

Thrombus

Platelet aggregation

Platelet activation

Prothrombin

Plasma clotting cascade

Tissue factor

Collagen

ADP

Aspirin

Thromboxane A₂

Clopidogrel
Prasugrel
Ticagrelor

Eptifibatide
Abciximab
Tirofiban
(GPI)

Heparin
LMWHs

Fondaparinux

Heparin
LMWHs

AT

AT

AT

Bivalirudin
Hirudin
Argatroban

Dabigatran

Rivaroxaban
Apixaban
Edoxaban

Fibrinolytics
D- ANTIPLATELET THERAPY: ASPIRIN

- Compared with adults, NN platelets are hyporeactive to thrombin, ADP/epinephrine, and Tx A2 (the result of a defect intrinsic to neonatal PLT)

- The bleeding time is short in NN because of ↑ RBC size, ↑ Ht levels and ↑ levels of von Willebrand

- **Aspirin** most common antiplatelet agent used in pediatrics. The dose of aspirin for optimal inhibition of PLT aggregation is ??

  Empirical doses of 1 to 5 mg/kg /d (max 10 mg/kg/d)

- **Adverse Effects:** Neonates may be exposed to aspirin because of maternal ingestion (treatment of preeclampsia). Clearance of aspirin is slower in NN, potentially placing them at risk for bleeding for longer periods of time.

- In older children, aspirin rarely causes important hemorrhage, except in the presence of an underlying hemostatic defect or in children also treated with AC.
D- ANTIPLATELET THERAPY: CLOPIDOGREL

- **Clopidogrel** used with increasing frequency in children
  
  Initial dose 1 mg/kg/d (effective and safe)

- Dosing strategies ⇔ rounding doses to ¼ or ½ tablets (75 mg tablets)

- Regular monitoring of liver and renal function

- The Platelet Aggregation Inhibition on Children on Clopidogrel (PICOLO) study reported that Clopidogrel 0.20 mg/kg/d in children aged birth to 24 months with cardiac disease, 80% of whom were also receiving aspirin at a mean dose of 9 mg/kg/d, achieved a platelet inhibition level (measured by % inhibition of ADP induced platelet aggregation) similar to that which was targeted in adult studies using 75 mg/d
### HEART FAILURE AND CONGENITAL HEART DEFECTS

#### ADULTS

- **Failure of the left ventricle**
  - CAD
  - HTA-induced cardiac stress
  - Arrhythmias
  - Valvular disease
  - Rheumatic heart disease (20.1%)
  - Cardiomyopathy (16.8%)
  - Cardiac procedures (0.28%)

#### CHILDREN

- **Congenital malformations**
  - Left-to-right shunts => the function of both right and left ventricles affected ⇔ high-output HF
  - Cardiomyopathy and anthracycline toxicity ⇔ low-output HF
  - Anemia 2<sup>ry</sup> to malaria and malnutrition
  - Cardiac procedures (61.4%)
HEART FAILURE AND CONGENITAL HEART DEFECTS

WHO Essential Medicines List for Children (EMLc)

- Diuretics
- Digoxin
- Beta-blockers
- ACEI
- K+ sparing diuretics
- Dopamine

Salt restriction not indicated in pediatrics and water restriction adapted to natriuresis and clinical symptoms

*Ware S and Hinton R. Heart Failure in Pediatric Patients With Congenital Heart Disease. Circulation Research. 2017;120:978-994

Etiology

- CHD
- Valve disease
- Myocarditis
- Kawasaki
- Arrhythmias
- RA/Toxins

Mechanisms

- Early Therapy
- Advanced Intervention
- Shared Mechanisms

Diagnosis

- CHD
- CNH

Surveillance

- ~20%
- 100%
- 100%
- 100%

Ventricular Dysfunction

- ~6%
- ~40%
- ~65%

Heart Failure

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A-DIURETICS

- **LOOP DIURETICS** \( \uparrow \) Na+ and water loss
  - Rapid relief from symptoms of fluid overload **BUT** their effects on disease progression and survival ??
  - ↓ risk of death and deterioration and improved exercise capacity (compared to other treatments)
  - **Furosemide** (bolus of 1 mg/kg IV; titrated based on diuresis) available in formulations suitable for pediatrics
  - **Bumetanide** (10-40 µg/kg/h) available and used in pediatrics but limited published data

- **ALDOSTERONE ANTAGONISTS** \( \downarrow \) Na+ and water retention
  - Reduced myocardial fibrosis
  - **Spironolactone** (1 mg/kg po OD or BID) in pediatric HF limited (ONLY FE<40%). Enhances effect of digoxin and thiazides and/or can be added to loop and/or thiazide diuretics (monitoring of K+)
  - No published evidence on the role of **Eplerenone**

Diuretic site of action:
1. Acetazolamide
2. Osmotic diuretics (e.g. mannitol)
3. Loop diuretics (e.g. furosemide)
4. Thiazides (e.g. HCTZ)
5. Potassium-sparing (e.g. spironolactone)
B- DIGOXIN

- Inotropic effects
- Slowed heart rate, improving balance of O₂ supply and demand
- Inhibition of sympathetic nervous system
- Inhibition of renin release
- Toxic dose 5ng/ml NN and 3 ng/ml older children
- ONLY IN L-R SHUNT NOT USED (Ineffective)
- In Renal Failure: CrCL:
  - 75 and 50 ml/mn : 2/3 dose
  - 50 and 25 ml/mn : ½ dose,
  - 25 and 10 ml/mn : ¼ dose

### Table: Total Digitalizing Dose and MD

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Digitalizing Dose † (µg/kg)</th>
<th>MD ‡ (µg/kg bid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm NN</td>
<td>20</td>
<td>2.5</td>
</tr>
<tr>
<td>Term NN</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>1 mo–2 yr</td>
<td>50–30</td>
<td>6–5</td>
</tr>
<tr>
<td>2–5 yr</td>
<td>40–30</td>
<td>5–4</td>
</tr>
<tr>
<td>6–10 yr</td>
<td>35–20</td>
<td>4–2.5</td>
</tr>
<tr>
<td>&gt; 10 yr §</td>
<td>15–10</td>
<td>2.5–1.25</td>
</tr>
</tbody>
</table>

*All doses are based on ideal BW with normal renal function. The IV dose is 75% of the oral

†The digitalizing dose is necessary when treating arrhythmias or acute HF. Usually given over 24 h with ½ of the dose given initially, followed by ¼ of the dose given twice, separated by 8- to 12-h intervals; ECG monitoring

‡The maintenance dose is 25% of the digitalizing dose, given in 2 divided doses.

§Not to exceed adult digitalizing/MD of 1-1.5 mg/0.125-0.250 mg/d

Digoxin syrup
1ml = 50 µg
C- ANGIOTENSIN ENZYME INHIBITORS

- Indications in pediatric practice
  - Myocardial dysfunction, mild-moderate valvular insufficiency and large left to right shunts (when surgery is not appropriate)
  - **Enalapril** liquid formulation challenging, whereas liquid formulation of **captopril** available
  - **Captopril** syrup 5mg/5ml or 25 mg/5ml ↔ 0.05-1.5 mg/kg/d in 2-3 divided doses (initial dose 0.3 mg/kg/d) and Enalapril (0.16 mg/kg/d)
  - Tablet formulation appropriate for older children
  - Captopril shorter duration of action ⇒ frequent administration (TID) [Enalapril OD or BID]

- ↓ 20% mortality rate on long term treatment*

- **There is very little published data on the use of ARBs in children.** The pharmacokinetics of irbesartan and losartan in hypertensive children have been reported **BUT** No published studies specifically on the use of ARBs in children with HF were identified

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D- BETA-BLOCKERS

- Slowed heart rate*, improving balance of $O_2$ supply and demand
- Reduced myocardial apoptosis and fibrosis. Anti-arrhythmic effects
- Synergism with ACE inhibitors and cannot be started directly after inotopic agents or severe CHF => USED with low doses + to diuretics

- **Carvedilol** → most widely studied in HF **BUT** higher doses relative to BW are required to provide exposure comparable to adults $\Leftrightarrow$ 1mg/kg/d for adolescents, 2mg/kg/d for children aged 2 to 11 years and 3mg/kg/d for infants (aged 28 days to 23 months). **Bisoprolol** also is used

$$([(\text{Adult Dose} \times \text{BSA of children})] / 1.73 \text{ m}^2) \{\text{BSA } (\text{m}^2 )= [(4 \times \text{BW in kg}) + 7] / (\text{BW in kg} + 90)\}$$

- **Metoprolol** → antihypertensive in children

- No published data on the use of **Nebivolol** in children with HF

- Whilst beta-blocker therapy in adults reduces sudden cardiac death, the effect of beta-blockade in children does not appear to reduce the QT interval in the same way, the significance of this is not yet known { they ↓ morbi-mortality and improvement of symptoms}
In severe HF, cardiac output and BP are low ⇔ inotropic drugs stimulate cardiac contractility + peripheral vasoconstriction.

Catecholamines → Dopamine/Dobutamine and PDE inhibitors (Milrinone and Amrinone)

Acute cardiac failure is often complicated by deterioration in renal function and worsened outcomes.

⇒ Dopamine and Dobutamine (5-20 µg/kg/mn) in cardio-renal syndrome.

PDE inhibitors {Milrinone (0.375-1 γ/kg/mn) → shorter half-life and wider therapeutic index} ⇒ significant pulmonary vasodilation; little effect on myocardial O₂ demand.

In the case of children refractory to treatment:
- Long term treatment may be limited + cardiac transplantation.
- Proceeding to transplant immediately will however often not be possible or appropriate, due to the instability of the patient, access to a transplant unit or availability of a suitable donor.

⇒ Additional supportive treatments for a period of several months inotropes used as “bridging-therapy”, (delivered in both the in-patient and out-patient settings).
4- DRUGS USED IN ARRHYTHMIAS

- Arrhythmias are a major cause of mortality and morbidity in children (ventricular tachyarrhythmias)

- >½ of children with dilated cardiomyopathy die from ventricular arrhythmias at the time of presentation and almost 2/3 of those awaiting transplantation

- There are risks associated with some antiarrhythmic medications [negative inotropic effects or have proarrhythmic effects]*

- Beta-blockers: Propranolol (0.25-1 mg/kg/dose 3-4/d); Acebutolol (5mg/kg/dose 2/d); Nadolol (25-75 mg/m²/d); Sotalol studied in children but SE affecting 20-30% of patients

- Amiodarone (type III) has been studied in children; some studies suggested it was well tolerated; others have raised concerns that the IV formulation may be linked with hypotension or collapse. Major indications are tachyarrythmias. LD per os 500 mg/m² (BSA=4BW+7/ BW+90) (for 7-8 d); MD 250 mg/m²

- Digoxin (per os only)

- Verapamil (not DOC)
PULMONARY HYPERTENSION

- **Previous KT** should be performed
- Evaluation in <2 years old patients: limited
- **Bosentan** (2mg/kg/12h (4mg/kg/d) and **Sildenafil** (0.5 mg/kg /4h (2mg/kg/4h)
- **Treprostinil** continuous SC perfusion through a pump {initial dose 2.5ng/kg/mn with progressive ↑ to reach the optimal theoretical dose at discharge ( 20 ng/kg/mn)}
- **Nitric Oxide (NO)** in acute PHTA or to evaluate the vascular pulmonary reactivity by echography
- **Nifédipine** Limited in pediatrics. Only when reactivity +++ to O₂ or NO administration
Although CHD can happen to any child, it’s not necessarily a hopeless condition.

Many of the causes can be repaired.

It’s important that parents and family members understand the causes and treatments in children.

When parents ensure that proper medical care is provided – and as newer techniques and medications become available – most children with CHD should be able to grow and lead active lives.
THANK YOU
Follow your heart & share the Love

Heartbeat « zappe avec les stars » au service des enfants cardiaques défavorisés
Key Takeaways