INITIAL MANAGEMENT OF NEONATES WITH COMPLETE TGA

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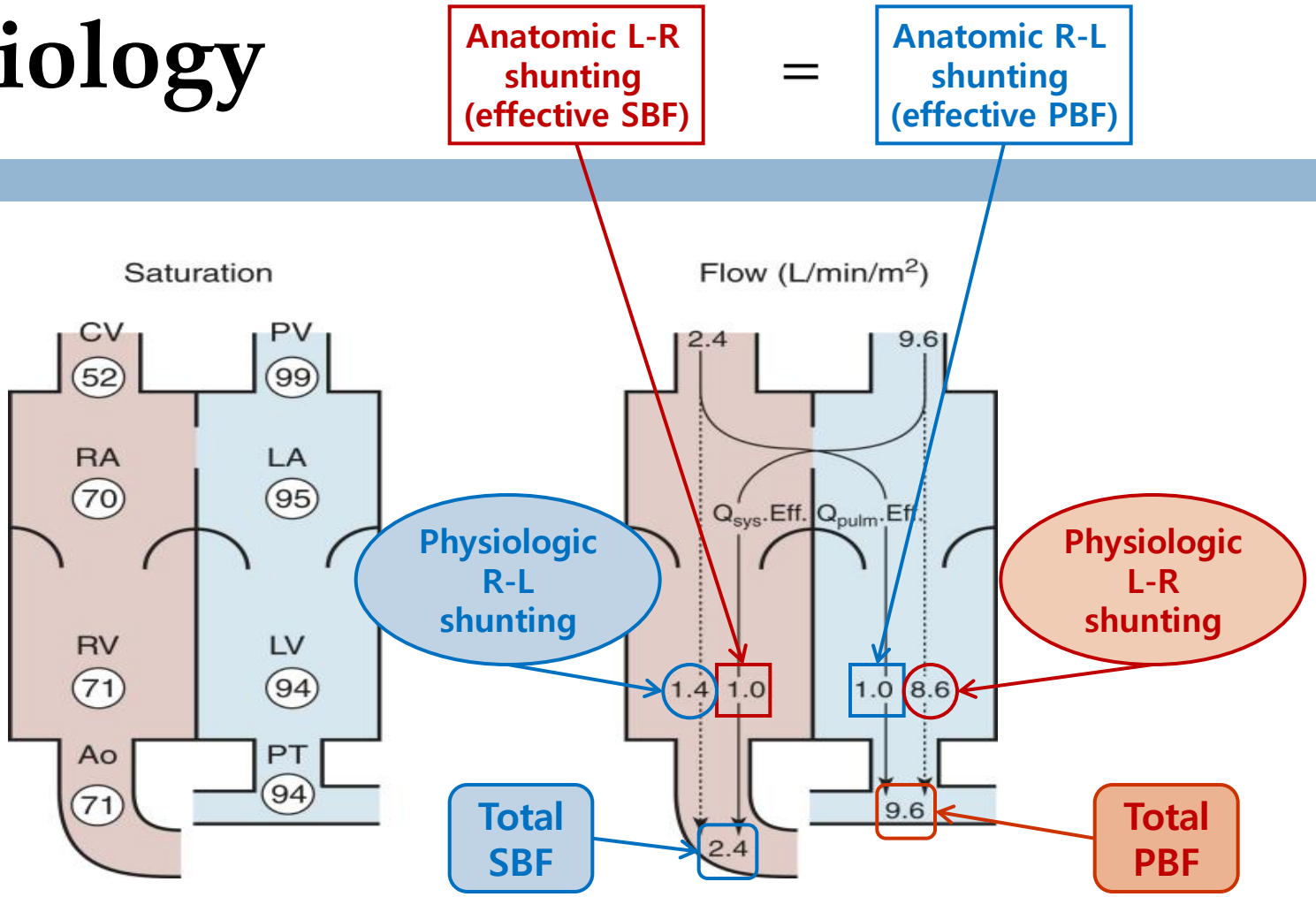
Introduction

- Parallel systemic & pulmonary circulation
- Life-threatening hypoxia
  - Effective SBF & PBF is dependent on inter-circulatory mixing.

Physiology



Saturations (*left hand panel*) and flows (*right hand panel*) within the heart of a patient with TGA and atrial mixing. Effective pulmonary (Q_{pulm}.Eff.) and systemic (Q_{sys}.Eff.) flows are equal (1 L/min/m^2), resulting from the bidirectional shunt at atrial level. However, total systemic (2.4 L/min/m^2) and total pulmonary (9.6 L/min/m^2) differ considerably such that the pulmonary-to-systemic ratio is 4 to 1. (Pediatric Cardiology Textbook 2010)

Physiology
Inter-circulatory mixing

- The extent of intercirculatory mixing in TGA depends on the number, size, and position of the anatomic communications and on total PBF.
- When the interatrial or interventricular shunting sites are of adequate size, the level of arterial oxygen saturation is influenced primarily by the pulmonary-to-systemic blood flow ratio.
- If the PBF is decreased by LVOTO or elevated PVR, the arterial oxygen saturation will be lowered, despite adequately sized anatomic shunting sites.

Clinical Manifestation
Physiologic – Clinical classification

- TGA with IVS or small VSD
  - Usually poor mixing, deep cyanosis
  - A large PDA, subsequent increased PBF may blunt cyanosis and mimic the clinical course of those with increased PBF.
- TGA with VSD
  - Increased mixing, increased PBF, CHF, only mild cyanosis
  - The presence of VSD does not ensure adequate inter-circulatory mixing and these patients may still require pre-operative interventions to establish effective mixing.
- TGA with VSD, LVOTO
  - The degree of cyanosis may not be affected by the degree of inter-circulatory mixing due to fixed restriction of PBF.
- TGA with RVOTO
  - Enough PBF & oxygenation but systemic hypoperfusion
- TGA with VSD and PVOD
  - Restricted PBF

Preoperative Evaluation

- Basic diagnosis
  - Concordant A-V & discordant V-A connection
  - Parallel relationship of the great vessels
  - D-malposed great arteries
- Semilunar valve morphology & function
  - Generally PV annulus Z-value of > - 2.5 should be sufficient to consider an ASO. (Shon YS,1998)
- The adequacy of inter-circulatory mixing
  - An absent or small (< 5 mm) PFO may require BAS.
- VSD: size, number, and location
- LVOTO: nature & degree, outlet septum malalignment
- Origin & course of the coronary arteries
- Other associated malformations, including DORV, or double inlet ventricle with discordant V-A connections

Preoperative Evaluation
Identification of high risk group

- Complex coronary anatomy
  - Intramural coronaries, single coronary ostium (risk of kinking and stretching)
- Severe malalignment of the commissures
- Multiple VSDs
- Aortic arch obstruction (usually in T-B)
- T-B with subaortic obstruction, DORV with NC-VSD
  - Multiple challenging associations in T-B: arch obstruction, side-by-side vessels, subaortic obstruction by posterior malaligned OS
- TGA with IVS > 3 weeks
- TGA with VSD and severe PH (> 6 WU)
- BWt < 2.5 kg

Preoperative Mortality in d-TGA

- Surgical mortality for ASO ≈ 2–5 % or less (Wernovsky G,1995)
- Preoperative mortality ≈ 4% in a multi-center prospective study (Kirklin JW,1992)

Preoperative Mortality in ASO Candidates (Soongswang J, et al., 1998; JACC)

- 4.1% (12/295) mortality before ASO
- 11 of 12 (3.7%) died due to consequences of inadequate interatrial mixing despite PGE1 infusion
- Contributing factors
  - Prematurity (41.7%), severe RDS (25%), PPHN (16.7%)
- Risk factors for death before surgery
  - Lower initial saturation
  - Smaller ASD
  - Worse response to PGE1 infusion
- Urgent BAS was performed in 66.7% with improved oxygenation.

Preoperative Mortality in d-TGA
Prenatal Risk Factors (Maeno YV et al. Circulation, 1999)

- Restrictive ductus arteriosus is associated with increased mortality and PH.
- Restrictive FO is associated with increased mortality.
  - Prenatally abnormal FO (fixed position, flat, and/or redundant septum primum)

TGA with Deep Cyanosis

- Deep cyanosis, hypoxemia, acidosis ± hypercabia
- TGA with IVS
  - Poor mixing; decreased effective PBF & SBF ⇒ PGE1 & BAS
- TGA with severe LVOTO
  - Decreased PBF ⇒ PGE1
- TGA with severe PH
  - Persistent hypoxemia and acidosis despite adequate anatomic communication due to poor mixing

Management

- Ensure adequate systemic perfusion & oxygen delivery
- PGE1 infusion
- Other supportive management
  - Sedation, muscle relaxant, and mechanical ventilation
  - Oxygen, acid–base correction, antibiotics
  - Correct anemia
  - Inotropics and diuretics in some patients with large inter-circulatory shunts
- BAS

Management : BAS
Role of BAS

- **TGA with IVS**
  - PGE1 ⇒ ↑ increases ductal flow
    ⇒ ↑ LA blood return & LAP
    ⇒ further closure of FO, ↓ atrial mixing, ↓ effective SBF & PBF
    ⇒ pulmonary edema & further systemic desaturation (Baylen BG,1992)
- **TGA with VSD**
  - PVR↓ ⇒ ↑ shunt from m-RV to m-LV through VSD & ↑ PBF
    ⇒ ↑ LA blood return & LAP
  - BAS can relieve increased LAP.
  - Earlier PVOD in patients with TGA with large VSD & intact atrial septum than the patient with simple large VSD

Management : BAS
Complications

- Cardiac complications of the procedure
  - Damage of atrial wall, pulmonary vein, or IVC perforation or tears or AV valve damage
  - Complete heart block, typically self-limited
  - Intracardiac rupture of the balloon
- Balloon in RA appendage
- Unable to rupture IAS in older infants, particularly those with TGA/VSD
- CNS complication

Management : BAS
CNS complications

- Increased rate of brain injury associated with BAS (McQuillen PS, UCSF, 2006)
  - In this retrospective review, it was difficult to separate out the CNS effects of the profound hypoxemia leading to the need for urgent intervention, from the CNS effects of the intervention itself. (McQuillen PS,2006)
- More recent data have shown BAS to be safe and not related to preoperative brain injury. (Petit CJ,2009; Beca J,2009; Applegate SE,2010)
  - Failure to achieve a preoperative PaO2 > 40 mmHg was associated with brain injury. (Petit CJ,2009)

Management : BAS
CNS complications

- Too high incidence of focal lesions on brain MRI
- Difficult to separate out the CNS effects of the profound hypoxemia leading to the need for urgent intervention, from the CNS effects of the intervention itself
- Need for comparison of pre- with post-BAS MRI

BAS Is Associa

- McQuillen PS,
- Twenty-nine te
surgery in a p
preoperative MRI, and all injuries were focal or multifocal. None of the patients had birth asphyxia.
- Nineteen patients (66%) required preoperative BAS. All patients with brain injury had BAS (12 of 19; risk difference, 63%; 95% confidence interval, 41-85; P=0.001). As expected on the basis of the need for BAS, these neonates had lower SaO2 (P=0.05).
- The risk of injury was not modified by the cannulation site for BAS (umbilical vs femoral, P=0.8) or by the presence of a central venous catheter (P=0.4).
- Conclusions : BAS is a major identifiable risk factor for preoperative focal brain injury in neonates with TGA. Imaging characteristics of identified brain injuries were consistent with embolism; however, the mechanism is more complex than site of vascular access for BAS or exposure to central venous catheters.

Management : BAS
Current indications & timing : Emergency BAS

- PGE1 ASAP in cyanotic patients with TGA with IVS
- Emergency BAS
  - Persistently hypoxic patients due to restrictive FO with/without pulmonary congestion even after PGE1 infusion
  - Prompt therapeutic BAS before hemodynamic and angiographic investigations
- Role of elective BAS
  - Stabilize patients' conditions
  - Decrease PGE1
  - More elective (semi-elective) operation

Management : BAS
Current indications & timing

- Potential benefits of waiting 4-7 days before an ASO
  - Allow the baby to make an effective transition from fetal to neonatal circulation
  - Allow PVR to fall
  - Allow some improvement in kidney & liver function to occur
  - Begin enteral nutrition
  - Evaluate for any additional congenital anomalies
  - Be sure the family understands the risks & benefits of the proposed surgery
- Potential risks of "delay" in surgery, with or without BAS
  - "steal" of systemic CO into lung through large PDA despite favorable systemic O2 saturation
  - Increased risk of paradoxical embolism, infection
  - Increased risk of CNS injury, especially to white matter (Petit CJ, 2009)
    - √ Recent FU neurodevelopmental outcome studies in infancy and beyond suggest that earlier elimination of hypoxemia may contribute to improved motor outcomes and brain growth in certain subgroups of patients. (Ibuki K, 2012)

Management : BAS
Current indications & timing

- Neuro-protective strategy in TGA at The Children's Hospital of Philadelphia (Moss & Adams 2012)
  - Early arterial switch operation (2-3 days of age if possible)
    - √ As soon as there is evidence of a fall in PVR (usually seen by Doppler at the ductus within 24 to 48 hours) and there are no noncardiac contraindications to surgery.
  - BAS if
    - √ there is an anticipated delay beyond this time frame,
    - √ oxygen saturations are <80% despite PGE1
  - Discontinue PGE1 after BAS
    - √ Not restarted unless there is consistent peripheral oxygen saturation of <70% (with a small or closed PDA)

Management : BAS
Prediction of need for BAS

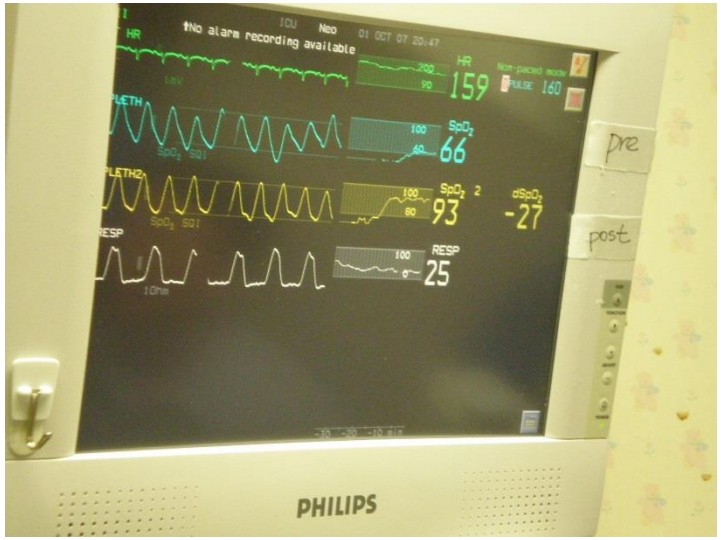
- Findings of fetal echocardiography
  - Restrictive PFO & DA (Maeno YV, 1999)
  - Hypermobile atrial septum and reverse diastolic PDA flow (Punn R, 2011)
- Inadequate increase of PaO2 despite high O2
  - When PaO2 values are <30 mmHg in room air and remain below 35 to 40 mmHg during high-oxygen-content breathing, poor intracardiac mixing is present. (Moss & Adams, 2012)

PH in TGA

- Two types of PH
  - PPHN-like PH in newborn
  - PVOD due to increased PBF

PH in TGA
PH in newborn

- Refractory hypoxemia and acidosis despite adequate anatomic communications due to inadequate mixing (at least 5-6 mm of ASD with or without BAS and PGE1)
- Reverse differential cyanosis



PH in TGA

PH in newborn

- Common occurrence of persistent PH and early progression of PVD in the infants with TGA and IVS (Viles PH,1969; Hawker RE,1974; Chang AC,1991)
- Increased O2 content in the PA (Maeno YV,1999)
  $\Rightarrow \downarrow$ PVR, retrograde diastolic flow in DA, ductal constriction
- Prenatal constriction of the DA produces anatomic changes in small pulmonary arteries similar to neonates with idiopathic PPHN (Levin DL,1979; Wild LM,1989; Murphy JD,1981).

PH in TGA

PH in newborn : Management

- Alkalinization
  - Bicarbonate if serum Na^+ level is tolerable
  - Hyperventilation
- Decrease O2 consumption
  - Paralyze and ventilator care
  - Narcotic anesthesia & neuromuscular block
- Increase O2 delivery
  - Inotropic agents; Epinephrine
- NO pre- and post-operatively
- ECMO pre- and post-operatively
- Early ASO

PH in TGA
PH due to increased PBF

- The pathogenesis of the more accelerated and wide-spread PVD in TGA is undoubtedly multifactorial. (Moss & Adams 2012)
  - Anatomic changes in small pulmonary arteries due to prenatal constriction of DA which is secondary to high PBF
  - Hypoxia related bronchial collaterals
  - Local hypoxemia, increased PBF & PA pressure by bronchial collaterals and vasoconstriction

PH in TGA

Evaluation of PH

- Sometimes difficult to measure the PAP
- Application of the Fick principle for calculating PBF and SBF in infants with TGA can have major sources of error.
  - Oxygen consumption is not normal in the severely hypoxemic infant, and assumed values are unreliable.
  - Systemic and pulmonary arteriovenous oxygen differences may be quite small; consequently, minor errors in oxygen saturation measurement introduce large errors in calculations of flow.
  - Falsely high PA oxygen saturation at proximal sampling site, and subsequently false high PBF due to distal bronchopulmonary collaterals
    - ✓ Application of the Fick principle tends to overestimate PBF and hence underestimate PVR. Therefore, calculated PVR always should be viewed as minimum values.

PH in d-TGA
PAB

- Current indications for PAB in the neonatal period
  - Complex, multiple VSDs
  - Coexisting medical conditions that cause a delay in surgery to later in infancy
- Generally the PA in infants with TGA is banded more loosely than in infants with NRGA because TGA pathophysiology requires a somewhat higher PBF for optimum inter-circulatory mixing.
- Subaortic stenosis following PAB

PH in TGA
Surgery for TGA/VSD with PVOD

- Palliative switch ± VSD partial closure versus no treatment
  - Despite the advanced pulmonary vascular changes, the pulmonary artery oxygen saturation is higher than the aortic saturation in most patients.
  - Palliative switch (either atrial or arterial) allows more effective pulmonary and systemic flows and a significantly improved systemic arterial oxygen saturation.

Neonates with TGA & Low BWt

- The ASO was accomplished without mortality in four of nine with a weight <2 kg. Early ASO may improve survival in patients weighing <2 kg.
- Early correction >> Prolonged medical supportive management waiting for growth
  (Chang AC,1994; Pawade A,1993)

Fetal Diagnosis

Impact of Fetal Diagnosis (Bonnet et al. Circulation, 1999)

	Postnatal Group	Prenatal Group	*P*
Isolated TGA	204	57	NS
Associated defects	46	11	NS
VSD	31	8	NS
VSD + CoA	14	3	NS
CoA	1	1	NS
Age at admission, h	73±210	2.2±2.8	<0.01
Mechanical ventilation	95 (38)	12 (17.6)	<0.01
Metabolic acidosis±MOF	56	8	<0.05
PGE_1 infusion	95	32	NS
BAS	168	54	NS
Preoperative mortality	15	0	<0.05
Coronary artery pattern	233 ASO	68 ASO	
Normal	168	47	NS
Abnormal	65	21	NS
Postoperative mortality	20	0	<0.01
Hospital stay, d	30±17	24±11	<0.01

VSD indicates ventricular septal defect; CoA, coarctation; MOF, multiorgan failure; PGE_1, prostaglandin E_1; BAS, balloon atrioseptotomy; and ASO, arterial switch operation. Values are n (%).

Preoperative Care of Complete TGA

Surgery !

if unstable despite medical care

TGA with Low LV Pressure
Two-Stage ASO : Disadvantages

- Persistent cyanosis after 1st stage operation
- Low output syndrome during the interval period between banding and correction
  - from a combination of acute (fixed) RV volume overload from the shunt and acute (transient) LV dysfunction from the PAB
- LV dysfunction after ASO
  - Older age at PAB and a longer PAB to ASO interval were thought to be important contributory factors to abnormal LV function. (Borow K,1984; Sievers H, 1985)
- Increased LV end-systolic pressure
- Increased incidence of AR (Boutin C, 1994)
- Increased incidence of RVOTO (Wernovsky G, 1995)

Surgery for TGA with Low LVP
Primary anatomic repair

- Empiric criteria to determine adequate LV preparation may include
  (a) an absolute LVSP that is appropriate for age,
  (b) a LVP at cardiac catheterization that is at or above 70% systemic levels (LV-to-RV ratio >0.7), or
  (c) LV muscle mass that is within the normal range for BSA. (Moss & Adams 2012)

TGA with Low LV Pressure
One- or Two-Stage ASO

- Need for LV training ?
  - no need until 4~6 weeks of age
  - 1~3M; Primary ASO ?
  - > 3 M; Staged ASO or Primary ASO with LVAD
- Staged ASO in older age;
  4 ~ 7 days after PAB