Pulmonary Hypertension: Not (by any stretch of the imagination) Just a Pediatric Problem

William Clarke, MD, MSc, FAAP
Associate Professor of Pediatrics and Anesthesiology
Medical College of Wisconsin

Flow

Pressure Difference

0

Flow

0

 Increasing Flow in a Garden Hose

Pressure Difference

0

Flow
Increasing Cardiac output in the Systemic Circulation

Pressure

Flow

270

Ohm's Law: E=IR
Resistance = Voltage Drop / Current Flow
Vascular Resistance = Change in pressure / Change in Flow
Systemic Circulation (Systolic pressure)

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>270</td>
<td></td>
</tr>
</tbody>
</table>

R = Pressure Change / Zero Flow Change

Increasing Flow in the Pulmonary Circulation

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Since:
1) Resistance = Pressure Change / Flow Change
2) And since Pressure changes very little for large flow changes
Then, in the Normal lung
3) PVR FALLS with increasing Flow

Increasing Flow in the Pulmonary Circulation

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Mechanisms for Control of Pulmonary Vascular Tone

Dilation

- NO
  - Guanylate cyclase
  - cyclic GMP
  - Ca$^{2+}$ in smooth muscle

Constriction

- PGI$_2$
  - Adenylate cyclase
  - cyclic AMP
  - Ca$^{2+}$ in smooth muscle

- Endothelin A or B
  - Endothelin receptor
- Thromboxane
  - Thromboxane receptor
  - Change in K+ channels

The Pathology of Pulmonary Hypertension

1) PH is categorized as “Primary” — which means we don’t know what caused it — and “Secondary” — which means we do know what caused it.

2) Irrespective of etiology most PH:
   1) starts as vaso-spastic where the endothelium emit agents which constrict the vascular smooth muscle and then
   2) progresses into vaso-occlusive where the endothelium changes phenotype and begins to grow and then occludes the vessel

3) Thrombotic PH is the most feared as it leads to relatively rapid occlusion of the vessels and rapid RV load

Figure 5. Representative photomicrographs of sequential changes in pulmonary arterial lesions that follow Heath-Edwards classification observed in various stages of SU5416/normoxia/hypoxia-exposed severe PAH rats.

Abe K et al. Circulation. 2010;121:2747-2754

Copyright © American Heart Association, Inc. All rights reserved.
With the Development of Pulmonary Hypertension
The Key Points in Understanding the Pathophysiology of PH

1) People with moderate to advanced PH show symptoms of low cardiac output and eventually die of insufficient cardiac output.

2) The pulmonary artery pressure tells you next to nothing about the state of a patient with moderate to advanced PH.

The Shape of Ventricles Means they Handle pressure Loads Very Differently: Circular LV Distributes Wall Stress

The Shape of Ventricles Means they Handle pressure Loads Very Differently: Asymmetric RV leads to different stress in free wall vs septum.
LV Concentric Hypertrophy

RV Asymmetric Hypertrophy Leads to Huge Free Wall Stress and Dilation

The RV in Severe PH
Treatment of Pulmonary Hypertension

**Dilation**

- NO
- Guanylate cyclase
- cGMP
- Ca++ in smooth muscle

**Constriction**

- Endothelin A or B
- Endothelin Receptor
- Thromboxane
- Thromboxane Receptor
- Change in K+ channels

- Ca++ in smooth muscle

**Treatment of Pulmonary Hypertension**

**Constriction**

- Bosantan and other "santans"
- Ca++ channel blockers; "worked or killed"

**Dilation**

- Continuous infusion of PGI2 or analogue: "prost" PGI2
- NO administration
- NO
- Guanylate cyclase
- cGMP
- Ca++ in smooth muscle
**Treatment of Pulmonary Hypertension**

Dilation

- NO
- Guanylate cyclase
  - cGMP
  - cGMP (inactive)

- PGI₂
- Adenylate Cyclase
  - cAMP
  - cAMP (inactive)

- Ca²⁺ in smooth muscle
  - PDE₅
  - PDE₃

- Aminon, milrinone
- Tadalafil, sildenafil

**The Developing Understanding of Treating PH**

- We started using these drugs as they were "vasodilators"
- We found out that more importantly, these drugs can reverse the phenotypic changes of PH after years of therapy
- PH is a curable disease in some patients

**A Caveat**

- For reasons we don’t understand, in many patients there is an acute, severe vaso-constriction of these drugs are stopped, even in patients who have been on them for years

_Never stop these drugs for your anesthetic for any reason_
Anesthesia In Patients with PH: Pre-operative 1

- You are well aware of the risk of PH and RV overload in patients with advance COPD

- Be suspicious of occult PH in patients with autoimmune diseases such as scleroderma, MCTD and anti-phospholipid antibody syndrome/lupus

- In pediatrics, pulmonary hypertension is most common in kids with high pulmonary flows, usually not present significantly until 2nd decade

Anesthesia In Patients with PH: Pre-operative 2

Patients with known PH as usually followed with echocardiograms and these can tell you a LOT:

1) Look at the size and shape of the RV; is there LVOT impingement?

2) Look at the description of the RV function; stressed RVs will have areas of asynchronous contraction. This is a VERY bad sign!

3) Look at the estimated RV peak pressure; this is calculated from the tricuspid regurgitation velocity (in m/sec)

Anesthesia In Patients with PH: Preoperative: 3

Tricuspid Regurgitation Velocity

1) As the RV dilates the tricuspid annulus dilates and TR becomes progressively greater

2) The TR velocity (“backwards” into the RA) is an estimate of peak RV Pressure
Color Doppler of TR Jet

Anesthesia In Patients with PH: Tricuspid Regurgitation Velocity

Estimated Peak RV pressure = 4x(TR velocity in m/sec)^2 + est RA pressure

Example: “measured TR velocity is 4.2 m/sec, CVP estimated as 15”

\[ RV_{peak} = 4 \times (4.2)^2 + 15 \] or 88 mmHg

Anesthesia In Patients with PH: Pre-operative: 4

But, like so many things in Anesthesia, clinical signs and symptoms and your patient’s history is the best assessment of functional status....

“The Patsy Questions”:

1) Can you walk from the car without stopping?
2) Can you carry a bag of groceries from the car?
3) Can you walk up steps to the house from the car carrying the groceries?
Anesthesia In Patients with PH: Intraoperative Monitoring

- You probably are going to want an arterial line
- If you have NIRS as a non-invasive estimate of perfusion that can be very helpful
- Do NOT use a PA catheter:
  - you probably won’t get it in or have it stay due to TR
  - the more you want it the less likely you’ll get it in
  - the RV is incredibly irritable and intractable V fib is well described when trying to put in PA catheters in patients with PH

Intraoperative Anesthetic Management

- There is no absolutely “wrong” or absolutely “right” way to do these anesthetics
- These are sick, stressed RVs but they do respond to modest dose inotropes
- Patients do NOT tolerate RV preload drop or LV afterload drop (septal obstruction of LVOT)
- Ketamine is known to have NO affect on PVR, it is my choice for induction and during case; midazolam doesn’t affect PVR
- N₂O raises normal PVR, probably doesn’t do much to already high PVR
- All but the very sickest patients will tolerate some volatile agent if SVR is maintained