

Pulmonary Hypertension

Ken Whyte

Regional Pulmonary Vascular Clinic

With acknowledgement to:

Dr Engin Ahmed @ CMDHB

**Dr Alastair McGeorge & CVICU @
Auckland City Hospital**



**Green Lane Respiratory
Service, ADHB**

Aims & outline

- PH:
 - Pulmonary circulation
 - Definition
 - Classification
 - Pathophysiology
 - Targeted Treatment
 - Cycle of RV death
- PH & Anaesthesia:
 - Non cardiac surgery
 - Incidence
 - Aetiology
 - The traps in the pathophysiology
- PH & ICU:
 - Management



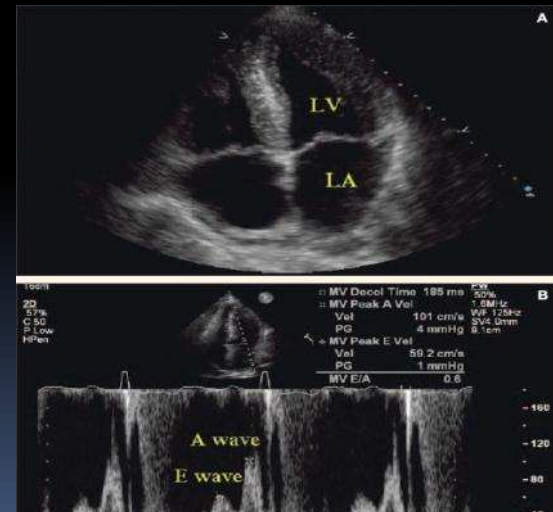


© 2007 Tribune Media Services, Inc. All rights reserved.

3/27

"I know nothing about the subject,
but I'm happy to give you my expert opinion."

The Problem?



PH is the 4th commonest CV diagnosis in US & Europe

Pulmonary circulation: Physiology of “Lesser Circulation”

- All the cardiac output has to go through the lungs;
- has to be able to cope with large variations in cardiac output with exercise;
- low pressure, low impedance & highly compliant system;
- Ventriculo-arterial coupling determines function;
- right ventricle is not designed for either a very high pressure or a very high work load;



maintaining V/Q to close to 1:1 throughout!

Right Ventricle: Physiology

- Almost an addendum to the left ventricle?
- shares the interventricular septum & pericardial sac so high pressures can affect the left if severe;
- was hypertrophied at birth & involuted therefore is capable of both hypertrophy and re-modelling to large extent;
- Volume not pressure pump;
- RV myocytes are embryologically & morphologically different from LV, also ischaemic resistant;

Endogenous vasodilators

- Nitric oxide (NO)
 - Produced by endothelium-derived pulmonary NO synthase (eNOS)
 - NO activates guanylate cyclase, which makes cGMP, which activates cGMP kinase, which opens K⁺ channels leading to membrane depolarisation and inhibition of Ca⁺⁺ influx
- Prostacyclin (PGI₂)
 - Metabolite of arachidonic acid, produced by vascular endothelium
 - Potent vasodilator with antithrombotic and antiproliferative effects
 - Activates adenylate cyclase to increase intracellular cAMP
 - Increases endothelial expression of NOS

Table 3 Haemodynamic definitions of pulmonary hypertension^a

Definition	Characteristics	Clinical group(s) ^b
Pulmonary hypertension (PH)	Mean PAP ≥ 25 mmHg	All
Pre-capillary PH	Mean PAP ≥ 25 mmHg PWP ≤ 15 mmHg CO normal or reduced ^c	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	Mean PAP ≥ 25 mmHg PWP > 15 mmHg CO normal or reduced ^c	2. PH due to left heart disease
Passive	TPG ≤ 12 mmHg	
Reactive (out of proportion)	TPG > 12 mmHg	

Definition of Pulmonary Hypertension

Mean pulmonary artery pressure (mPAP) at rest ≥ 25 mmHg

$$\text{Mean PAP} = \text{Flow} \times \text{PVR} + \text{LAP}$$

MEANING OF TRICUSPID REGURGITATION VELOCITY > 2.5 m/s?

Increased Flow

**Hyperdynamic
state**

**Pap > 25 mmHg
PVR < 2 UI or 160
dynes**

Increased LAP

LV Dysfunction

**Pap > 25 mmHg
Pcwp > 15 mmHg**

PCWP can mislead!

Increased PVR

**Pulmonary artery
hypertension**

**Pap > 25 mmHg
PVR > 2 UI or 160
dynes**

Definition of Pulmonary Hypertension

Mean pulmonary artery pressure (mPAP) at rest ≥ 25 mmHg

$$\text{Mean PAP} = \text{Flow} \times \text{PVR} + \text{LAP}$$

MEANING OF TRICUSPID REGURGITATION VELOCITY > 2.5 m/s?

Increased Flow

**Hyperdynamic
state**

**Pap > 25 mmHg
PVR < 2 UI or 160
dynes**

Increased LAP

LV Dysfunction

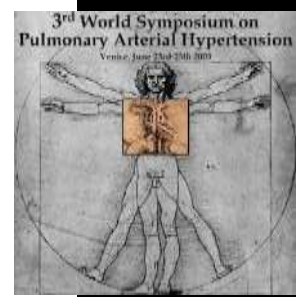
**Pap > 25 mmHg
Pcwp > 15 mmHg**

PCWP can mislead!

Increased PVR

**Pulmonary artery
hypertension**

**Pap > 25 mmHg
PVR > 2 UI or 160
dynes**



PULMONARY HYPERTENSION DIAGNOSTIC CLASSIFICATION

(Simonneau et al. J Am Coll Cardiol 2004)

1. Pulmonary Arterial Hypertension

Idiopathic PAH

Familial PAH

Related to:

- Connective tissue diseases
- HIV infection
- Portal hypertension
- Anorexigens
- Congenital Heart Diseases

• PPHN

• PAH with venulae/cap inv (PVOD)

2. PH with Left Heart Disease

- Atrial or Ventricular
- Valvular

3. PH with Lung Diseases/Hypoxemia

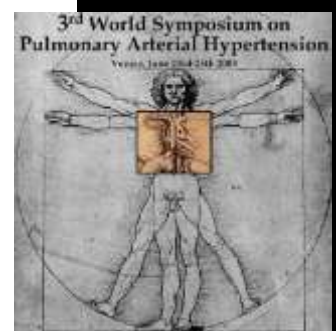
- COPD
- Interstitial Lung Diseases
- Sleep-disordered breathing
- Developmental Abnormalities

4. PH due to Chronic Thrombotic and/or Embolic Disease

- TE obstruction of proximal PA
- TE obstruction of distal PA
- Non Thrombotic Pulmonary Embolism

5. Miscellaneous

- Histiocytosis X, Sarcoidosis
- Compression of pulmonary vessels (fibrosis, mediastinitis, tumor, adenopathy)...



THERAPEUTIC CONSEQUENCES OF THE DIAGNOSTIC CLASSIFICATION (updated 3rd WSPAH-Venice 2003)

1. Pulmonary Arterial Hypertension

- Calcium channel blockers in responders
- Prostacyclin derivatives
- Endothelin receptor antagonists
- Phosphodiesterase inhibitors

2. PH with Left Heart Disease

- Beta blockers
- ACE inhibitors ...

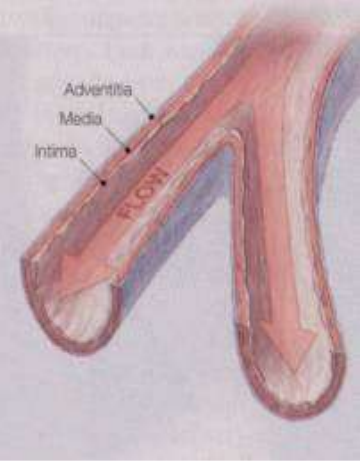
3. PH with Lung Diseases/Hypoxemia

- Oxygen
- CPAP...

4. PH due to Chronic Thrombotic and/or Embolic Disease

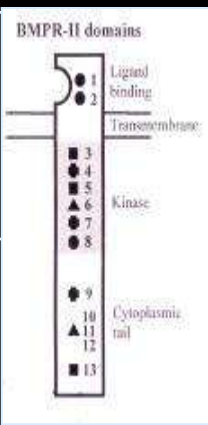
- Pulmonary endarterectomy





RISK FACTOR
(autoimmunity, HIV, drugs, toxins...)

GENETIC PREDISPOSITION
(BMP2, ALK-1, 5-HTT..)

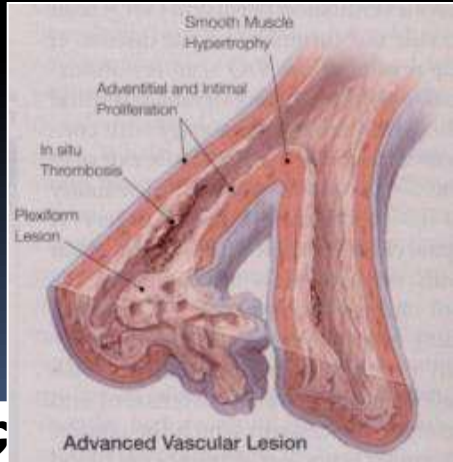
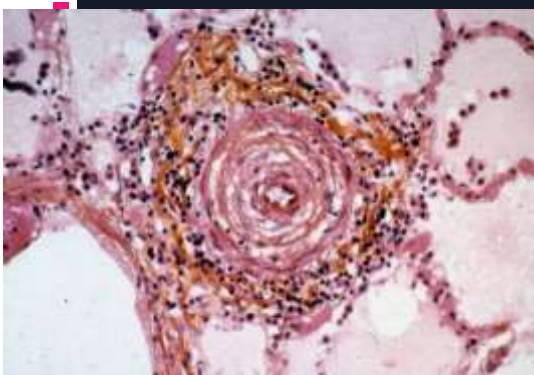


PULMONARY VASCULAR DYSFUNCTION

Endothelial cell dysfunction
(NO, PgI2, ET-1...)

Smooth muscle cell dysfunction
(Kv1.5...)

INFLAMMATION/REMODELING
(IL-1, IL-6, PDGF, Chemokines...)



PULMONARY VASCULAR REMODELING DISEASE PROGRESSION

The soup of PAH

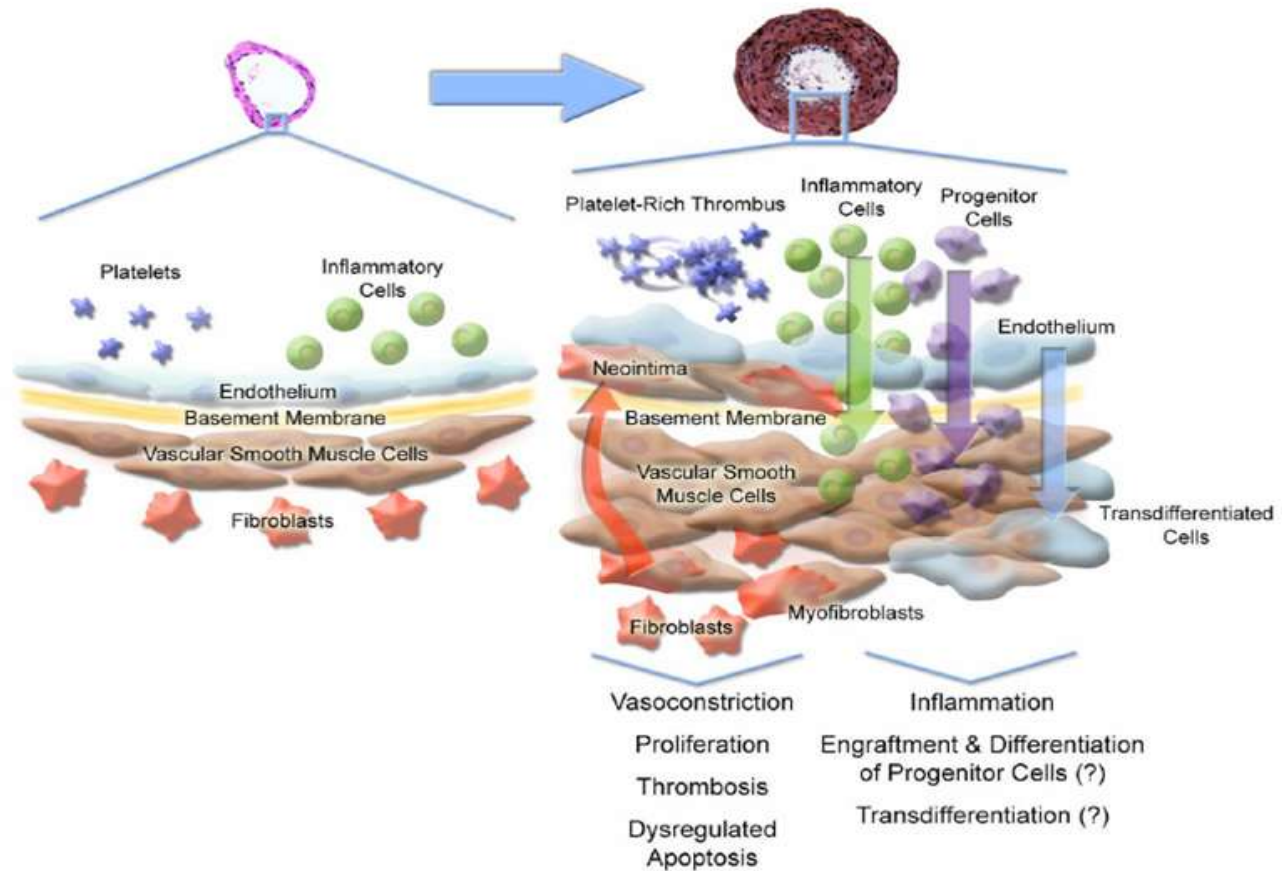
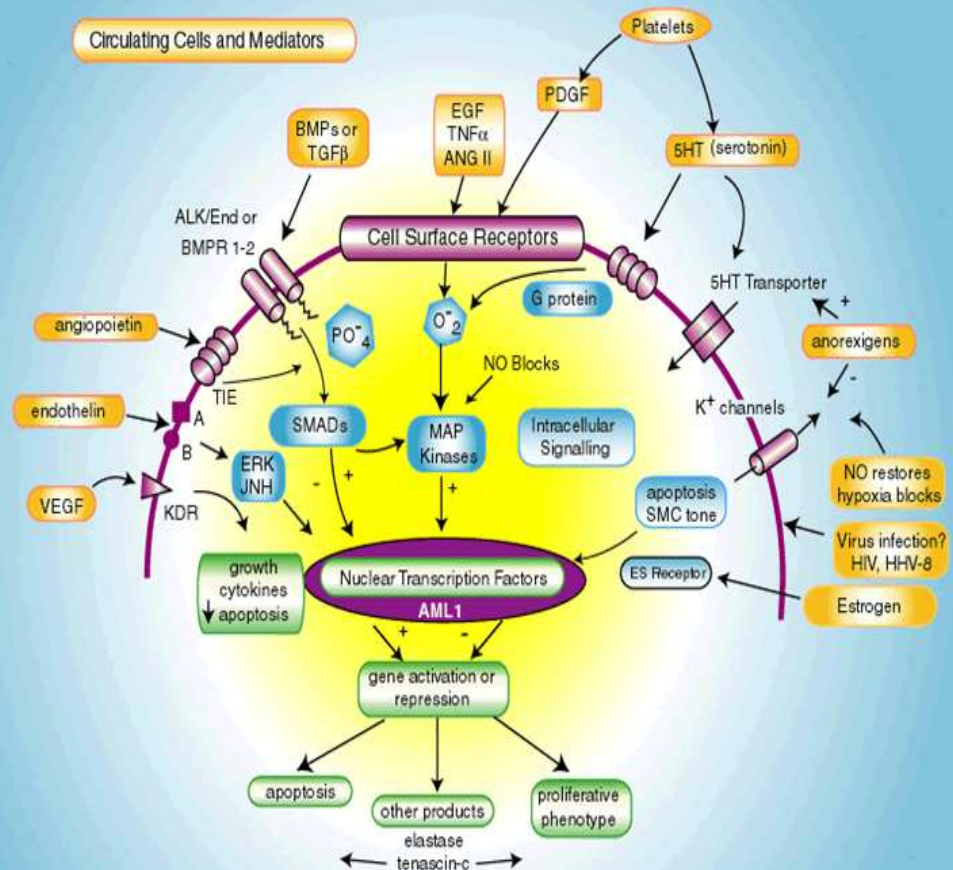
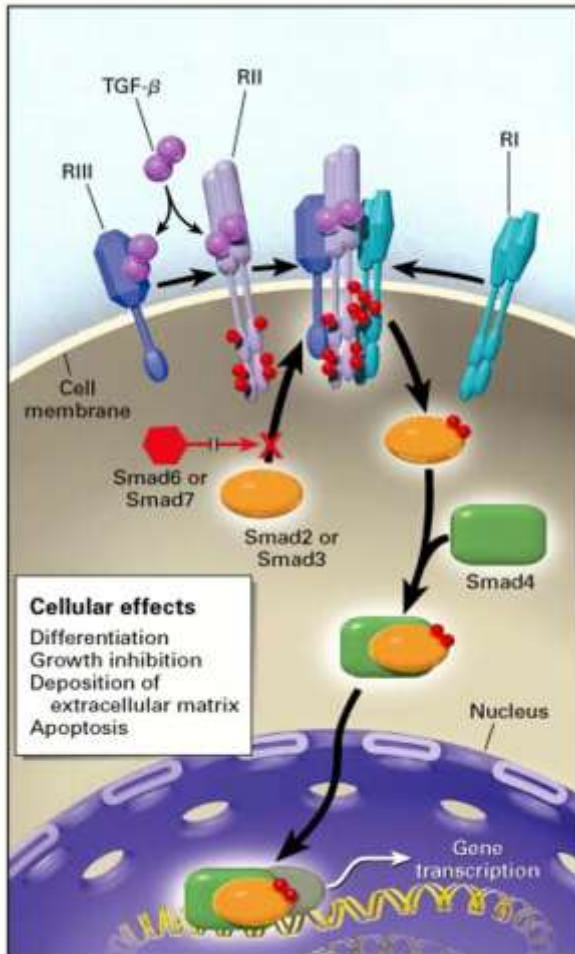
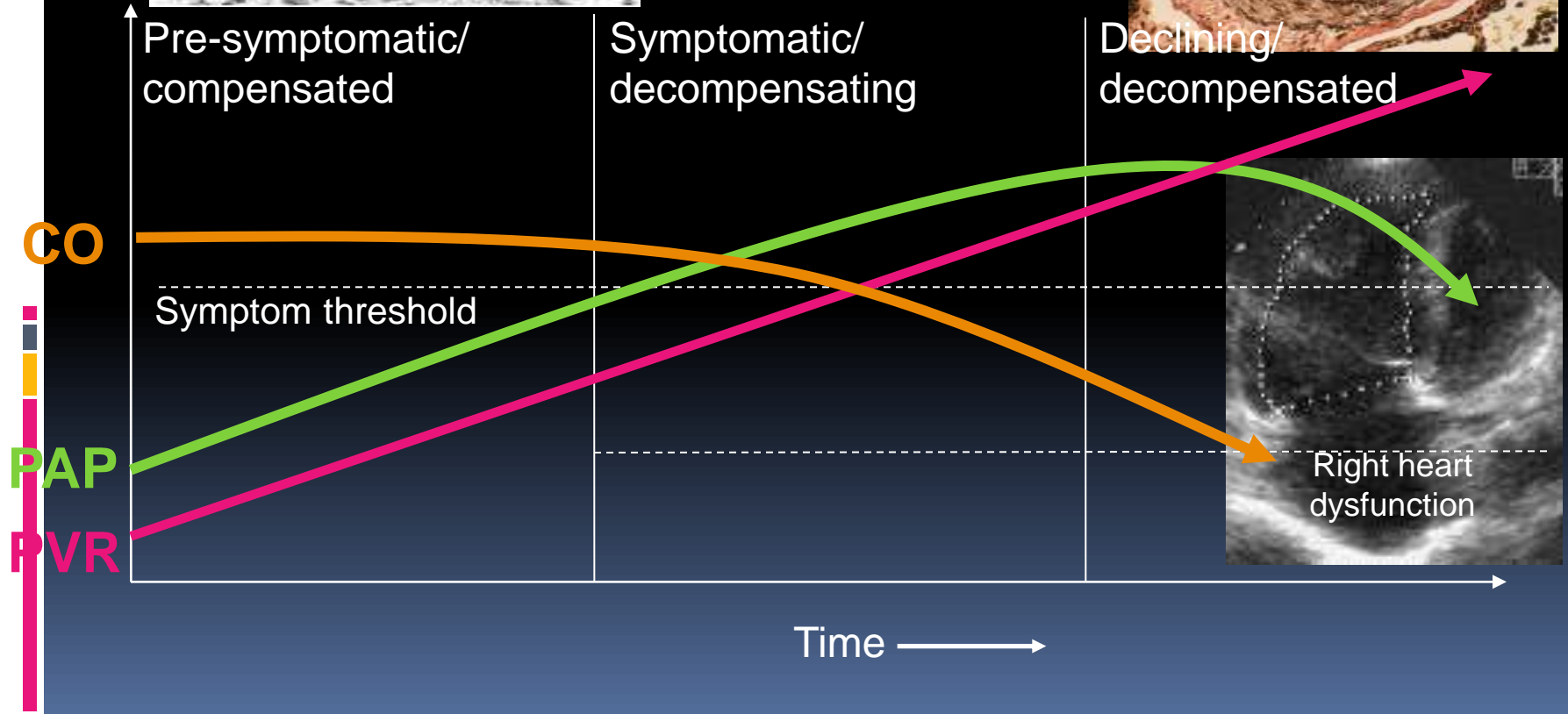
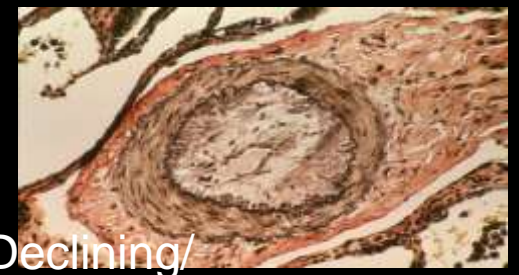


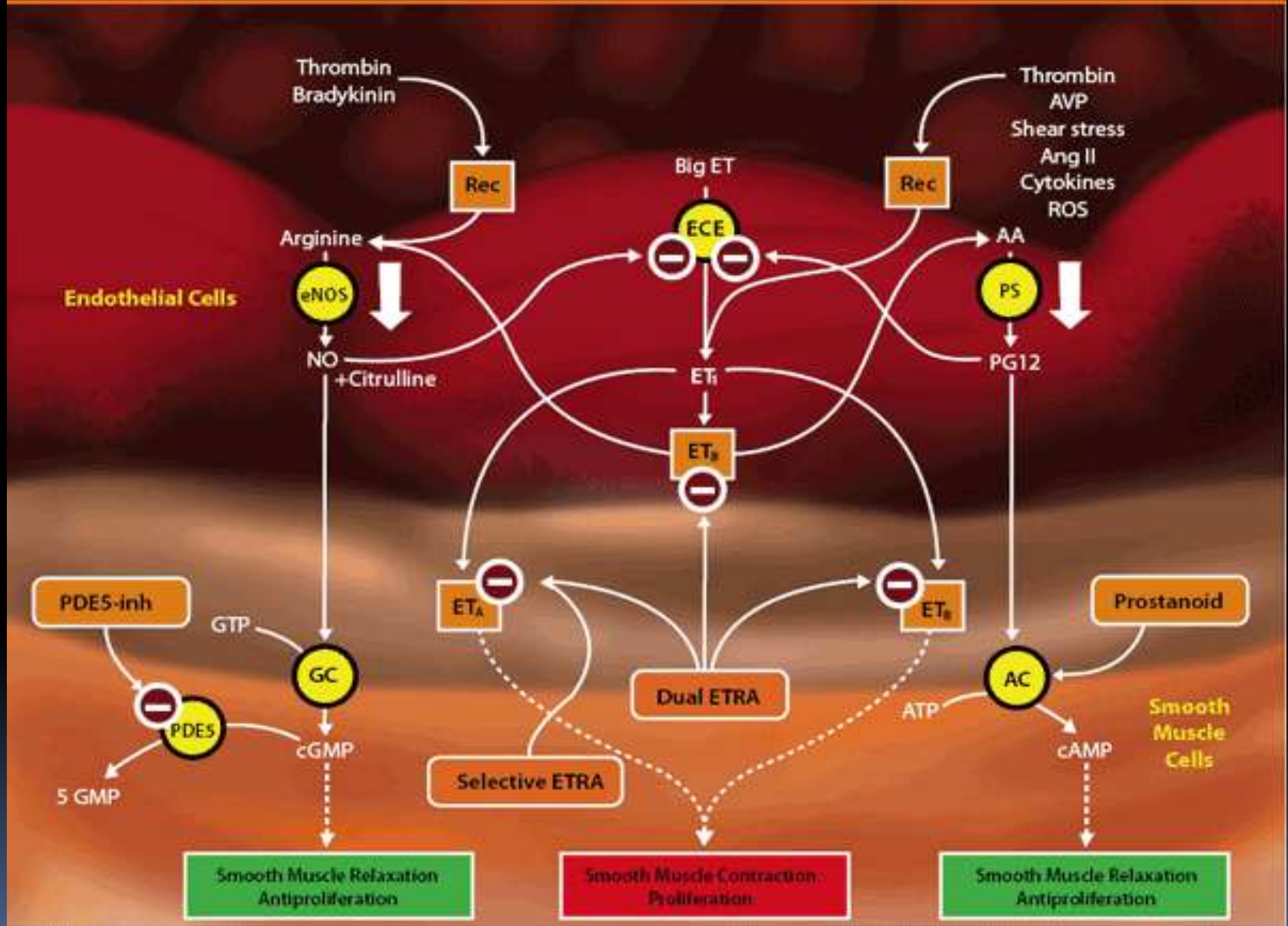
Figure 1. Pulmonary Arterial Pathobiology Involves the Coordinate Action of Multiple Cell Types

The soup of PAH



Schematic progression of PAH



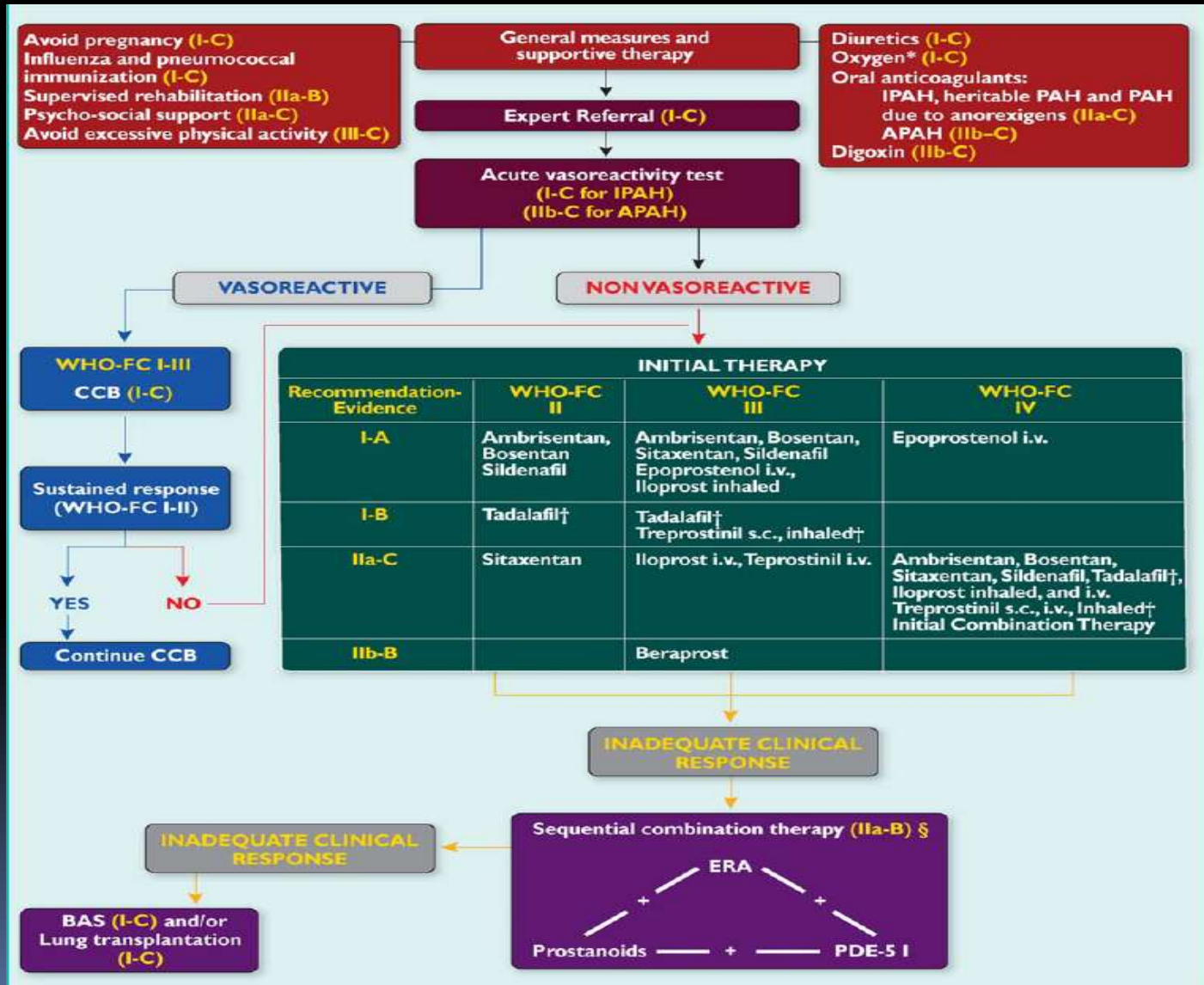


Achievements with Monotherapy (IV/inhaled prostanoid/PDE5/ERA)

Endpoint	Benefit at 12 months
SMW	+30 to +50m
Functional Class	20 - 40% red by 1 - 2 FC
Time to clin. worsening	Increased
Hemodynamics	PAP -2 to -6%
	CO +20 to 30%
Survival	20 - 30% improvement

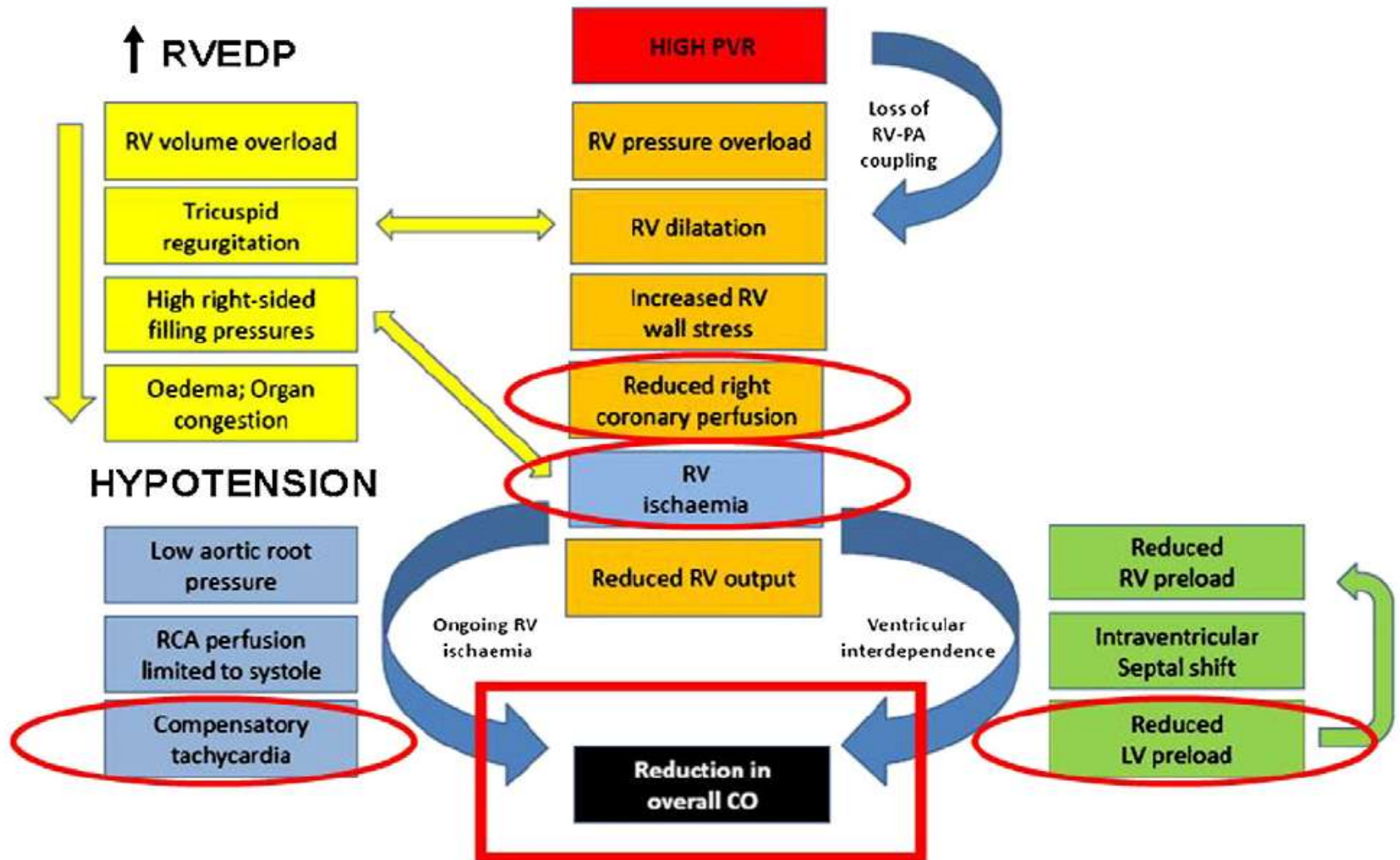
...mortality reduced to around 10% per annum in iPAH – but for how long?

Treatment Algorithms for PAH



Cycle of RV death

PH and RV Failure: The Downward Spiral



Pulmonary Hypertension & Anaesthesia -Why should you be scared?



PH patients & non-cardiac surgery

Price LF et al, Eur Resp J 2010;35:1295

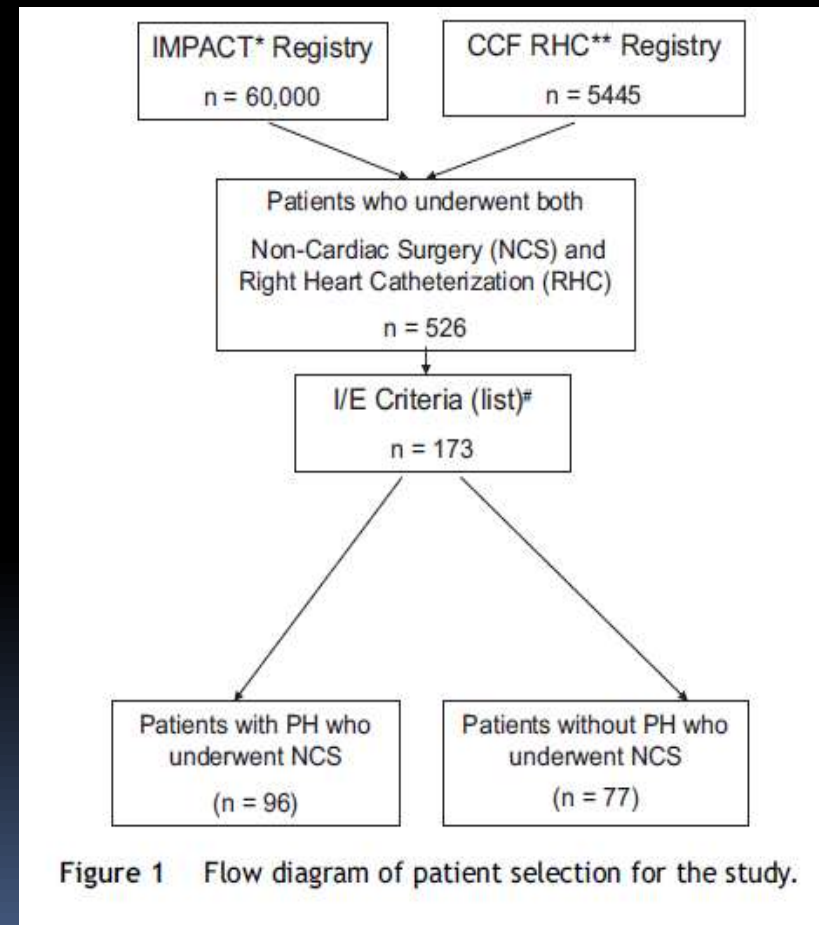
- Retrospective, n=28 proven PAH patients
- emergency & non-emergency non-obstetric non-cardiac surgery, 75% NYHA I-II, 50% major surgery v minor surgery;
- Peri-operative complications related to PH
- Most complications occurred within 48hrs

obstetric surgery. In this cohort of well-characterised patients with mostly mild-to-moderate PAH and non-operable CTEPH, overall perioperative mortality was 7%, and the incidence of perioperative complications up to day 28 was 29%. These are relatively high adverse event rates despite operating on mostly nonsevere patients in an experienced PH centre.

Type of PH crucial to risk

Kaw et al, Respir Med 2011;105:619-624

- Different approach – 5445 patients who had [®] HC over 5 yrs
- N=173 had [®] HC and non-cardiac surgery (NCS) within 2 yrs & identified 96 patients with PH & NCS.



Type of PH crucial to risk

Kaw et al, Respir Med 2011;105:619-624

Table 3 Perioperative complications by pathophysiologic category of PH.

Type of PH	N	Postop morbidity	Postop mortality
Pulmonary Arterial Hypertension ^a	12	5(41)	1(8)
Pulmonary Venous Hypertension ^b	38	6(16)	—
Mixed Pulmonary Hypertension ^c	46	11(24)	—

^a (PCWP<15; PVR>3).

^b (PCWP>15; PVR<3).

^c (PCWP>15; PVR>3).

Table 4 Multiple logistic regression for morbidity and mortality in all patients. (Area under ROC curve: .85).

Variable	OR ^a	P-value
Age	1.04	.09
ASA class (>2/≤2)	4.2	.02
Surgical risk class		.06
2/1	1.7	
3/1	5.8	
CRI	3.2	.03
PH	15.3	.001

ASA Class: American Society of Anesthesiology Class; CRI: Chronic.

Renal insufficiency; PH: Pulmonary Hypertension.

^a OR (Yes/No).

Table 3 Haemodynamic definitions of pulmonary hypertension^a

Definition	Characteristics	Clinical group(s) ^b
Pulmonary hypertension (PH)	Mean PAP ≥ 25 mmHg	All
Pre-capillary PH	Mean PAP ≥ 25 mmHg PWP ≤ 15 mmHg CO normal or reduced ^c	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	Mean PAP ≥ 25 mmHg PWP > 15 mmHg CO normal or reduced ^c	2. PH due to left heart disease
Passive	TPG ≤ 12 mmHg	
Reactive (out of proportion)	TPG > 12 mmHg	

The problem: PH is common

- 4th commonest cardiovascular diagnosis in US & Europe;
- Commonest cause of PH:
 - Age & hypertension
 - LV compliance falls six-fold with age
 - Systolic function often well preserved in elderly
 - Diastolic dysfunction difficult to define and detect.
- Many post-capillary PH patients have mild to moderate PH (RVSP 40-65mmHg)

The reality in anaesthesia?

Lai HC et al, BJA 2007; 99:184-190

- Tertiary hospital, 5yrs, 64,000 patients;
- 9,593 echo <30 days pre-op;
- 62 had severe PH (RVSP>70mmHg) \bar{x} =78.8 (70-120mmHg)
- Matched controls
- Intraop & postop events + 28 day death rate

Table 5 Postoperative major adverse events of all patients in both groups. *Some patients encountered more than one adverse event. **Both were fatal ventricular arrhythmias despite cardioversion/defibrillation; ***2-28 days after surgery

	Control (n=62)	PH (n=62)	P-value
Morbidity (%)	2 [3.2]	15 [24.2]*	0.002
Heart failure (%)	0 [0]	6 [9.7]	0.028
Delayed tracheal extubation >24 h (%)	2 [3.2]	13 [21]	0.004
Stroke (%)	0 [0]	1 [1.6]	NS
Myocardial ischaemia/infarction (%)	0 [0]	1 [1.6]	NS
Major arrhythmia (%)	0 [0]	2 [3.2]**	NS
Mortality (in-hospital death, %)	0 [0]	6 [9.7]***	0.028

The reality in anaesthesia?

Lai HC et al, BJA 2007;99:184-190

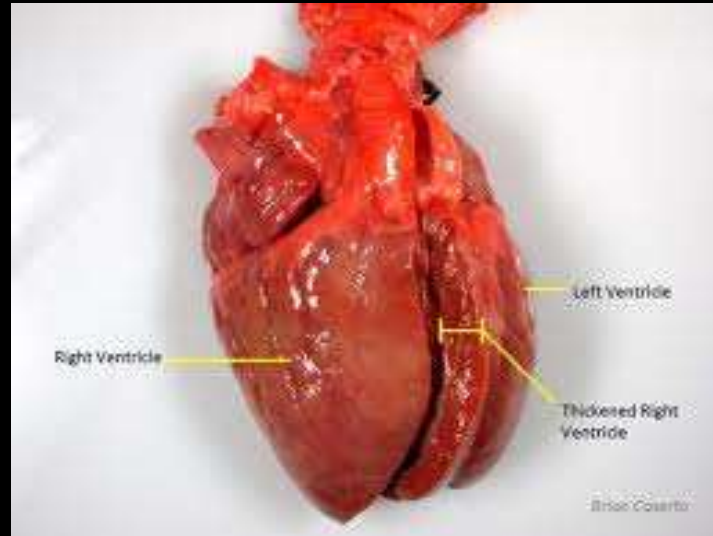
- 0.67% of patients coming to surgery had severe PH
- 0.1% had PAH & 0.1% had indeterminate cause
- 0.3% had post capillary PH (left heart)
- 0.1% had lung disease related pre-capillary

	<i>n</i> (total=62)
Pulmonary arterial (%)	11 [17.7]
Collagen disease	4**
Portal hypertension	5
Left to right shunt	2***
Pulmonary venous	
Left-sided atrial or ventricular (%)	27 [43.5]
Left-ventricular failure	13
Hypertrophic cardiomyopathy	2
Valvular disease	12
Mitral regurgitation/stenosis	5/2
Aortic regurgitation/stenosis	3/2
Respiratory disease or hypoxemia (%)	13 [21]
Chronic pulmonary embolism (%)	2 [3.2]
Undetermined (%) [†]	9 [14.5]

The physiological challenge?

Right ventricle:

- **Pre-load:** dependent
- **Contractility:**
 - ?where on Starling curve
 - Sympathetic drive +
 - Uncoupled
 - Reduced coronary flow
- **Afterload:**
 - High
 - ?cannot be lowered
 - Can be increased



Left ventricle:

- **Pre-load:** reduced?
- **Contractility:**
 - Squashed
 - Prolonged RV contraction
 - Sympathetic drive +
- **Afterload:**
 - If SVR drops then RV filling compromised

The physiological challenge?

Right ventricle:

- Pre-load: dependent
- Contractility:
 - ?where on Starling curve
 - Sympathetic drive +
 - Uncoupled
 - Reduced coronary flow
- Afterload:
 - High
 - ?cannot be lowered
 - Can be increased

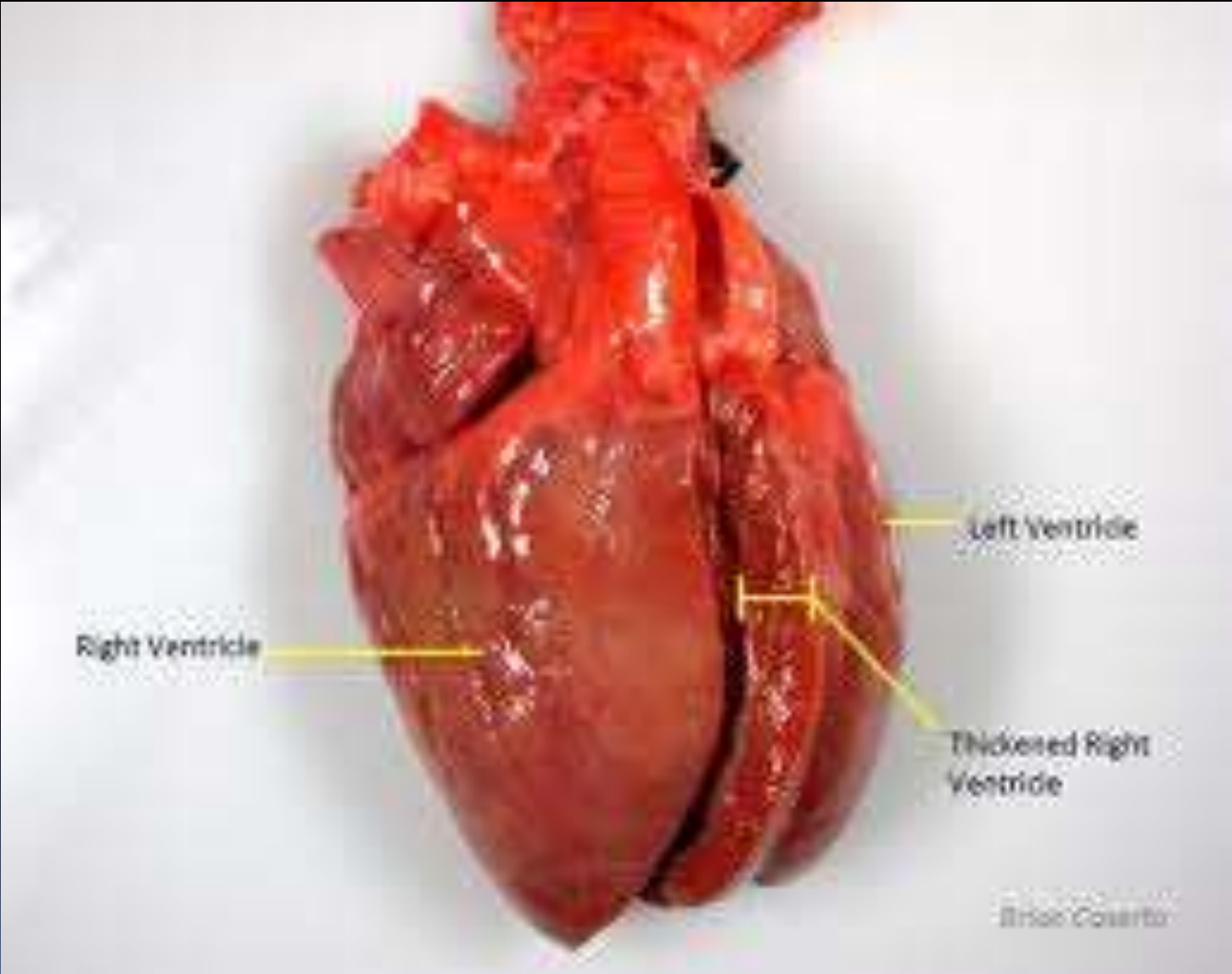


Left ventricle:

- Pre-load: reduced?

Inhaled Agents:

- No clinical trials assessing different volatiles
- All volatiles may worsen RV dysfunction by decreasing preload, afterload and contractility
- Sevoflurane & isoflurane do not adversely affect PVR (neither did halothane or enflurane!)
- Sevo decreases PAP more than iso
- PVR is increased by both nitrous (not in paed) and desflurane



Right Ventricle

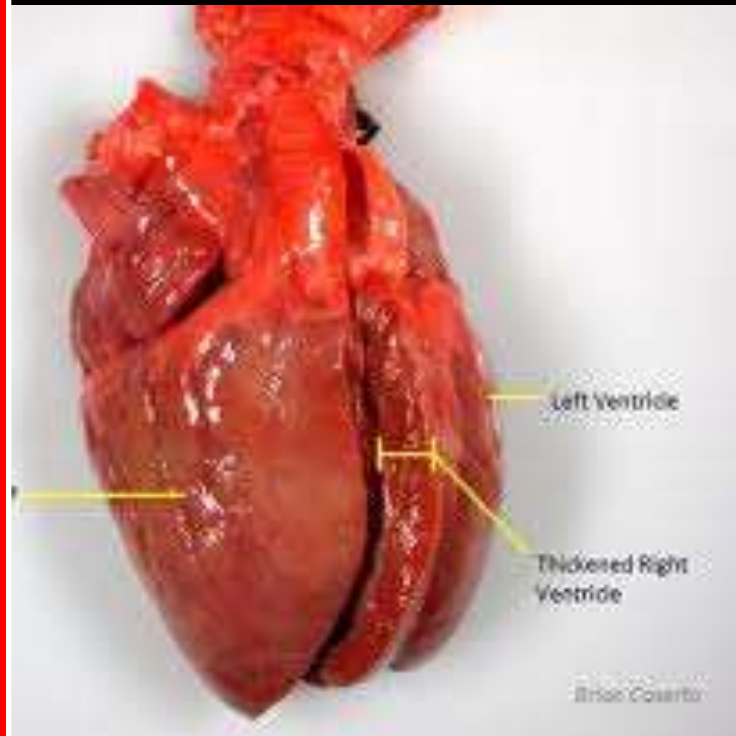
Left Ventricle

Thickened Right Ventricle

Brian Cosetta

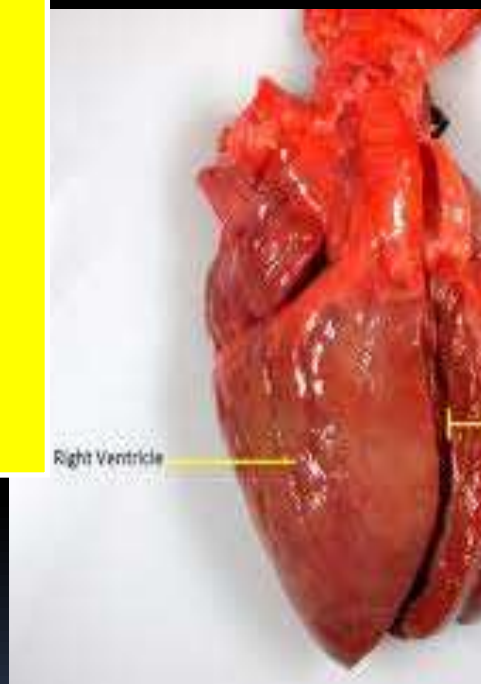
Induction:

- Prone to hypotension and cardiovascular collapse
- High baseline sympathetic tone
- Etomidate is apparently ideal
- Intubation may exacerbate the hypotension if causes further sympathetic stimulation



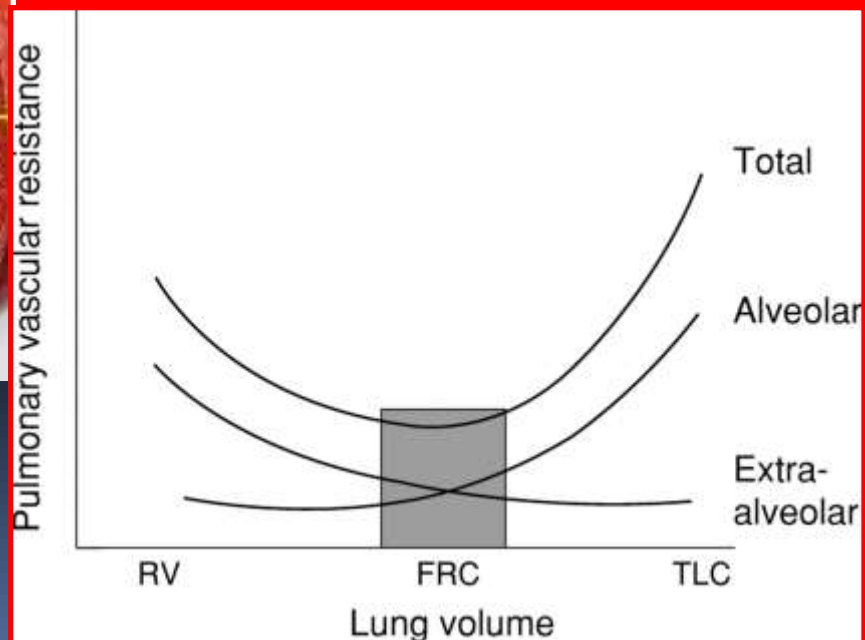
Induction:

- Prone to hypotension and cardiovascular collapse
- High baseline sympathetic tone
- Etomidate is apparently ideal
- Intubation may exacerbate the hypotension if causes further sympathetic stimulation



Ventilation:

- Avoid atelectasis so adequate levels of PEEP
- Moderate V_t , avoid high PIP so increase RR to maintain MV
- High FiO_2
- Hypocarbica is a potent pulmonary vasodilator



Induction:

- Prone to hypotension and cardiovascular collapse
- High baseline sympathetic tone
- Etomidate is apparently ideal
- Intubation may exacerbate the hypotension if causes further sympathetic stimulation

Ventilation:

- Low levels of PEEP
- Moderate Vt
- High FiO₂
- Hypocarbica is a potent pulmonary vasodilator

Emergence:

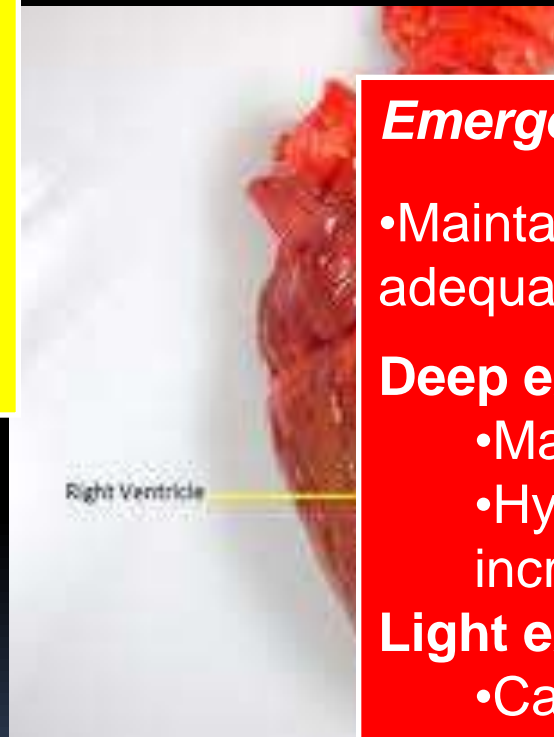
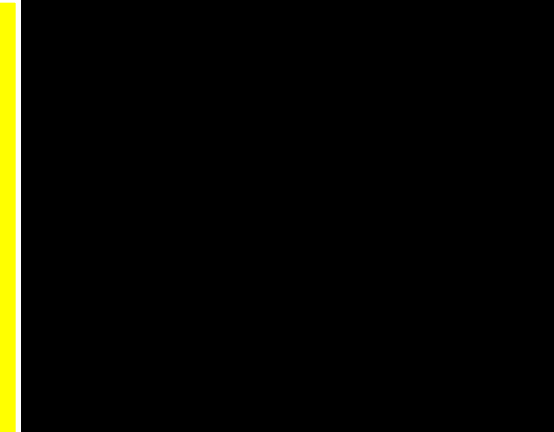
- Maintaining haemodynamic stability and adequate ventilation can be difficult

Deep extubation?

- May decrease SVR, contractility
- Hypoxia and hypercarbia will increase PVR

Light extubation?

- Can cause severe pulmonary vasoconstriction
- Need tube tolerance without increased sympathetic tone
- ***May need ongoing ventilation***



Management Strategies: KISS

- Treat precipitating factors eg Sepsis
- Obtain background info:
 - Type of PH if known
 - Functional status
 - Current therapy
 - Further therapy available?
 - Transplant candidate?
- Pre-operatively set ceiling of care:
 - Discuss with ICU
 - Discuss with PH unit if known to them
- Transfer if appropriate?
- Optimize volume status: avoid filling or offloading unless clear indication
- Augment CO
- Reduce PVR
 - Treat reversible factors
 - Metabolic state: anaemia, acidosis, hypoxaemia
 - Respiratory failure: limit Pplat (lung protection) but beware hypercarbia increasing PVR
 - Reduce sympathetic stimulation
 - Pulmonary vasodilators – inhaled (NO or prostanoid) vs IV
- Maintain adequate SVR
 - Keep PVR \ll SVR – Use pressors if necessary

Emergency surgery & PH on echo: What should you do?

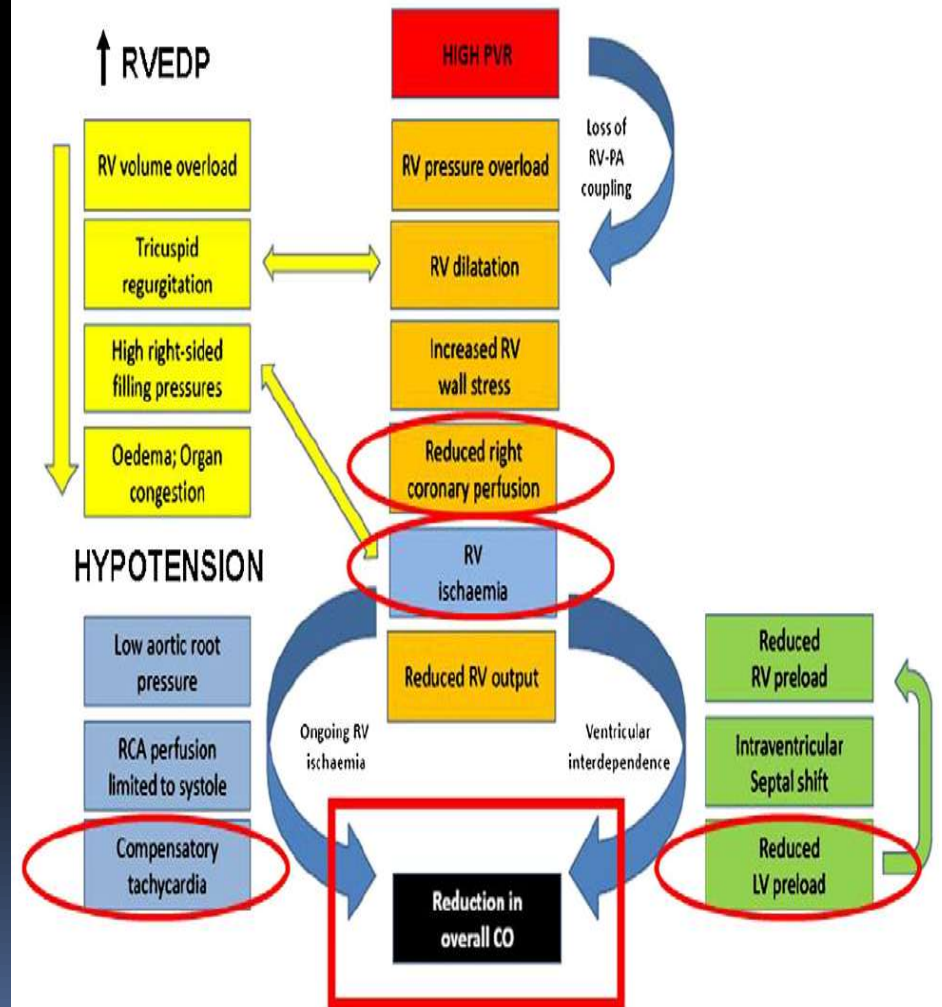
- Is the cause of the PH known? How severe is the PH?
- Lung disease? - If Yes probably bad lung disease if PH present
- If no known cause then “scuttle” to pre-test probability:
 - Age – diastolic dysfunction part of normal ageing
 - AF
 - Left heart disease (any mitral disease?)
 - Left atrial enlargement
 - Normal LVEF?
 - If Yes – diastolic dysfunction on echo?
 - If No – long standing hypertension, concentric LVH or ECG changes of LVH?
 - Obese?
- If Yes to 2 or more near certain post capillary PH and then approach as high risk cardiac case. If one positive odds still strongly favour post capillary PH & “assume”

Faced with RV death cycle: ICU?

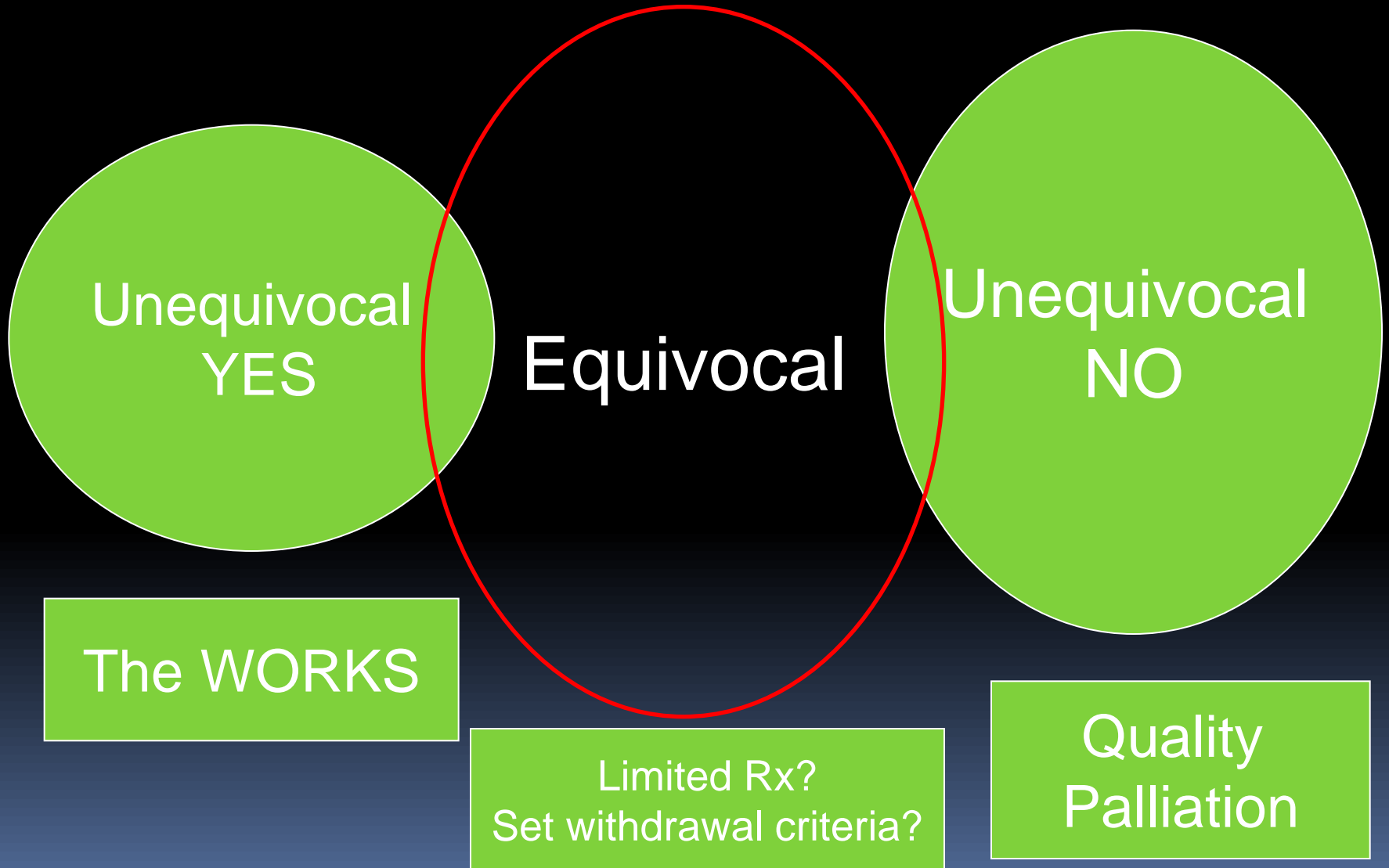
Salvage realistic prospect?

- Monitor
- Dobutamine?
 - Contractility increases
 - Decreases RV & LV afterload
 - HR response concern
- Vasopressin?
 - Systemic vasoconstriction & pulm vasodilator
- Inotropic support?
 - Noradrenaline but HR ↑
- Inodilators:
 - Milrinone
 - Levosimendan
- IV prostanoid for pulmonary vasodilation

PH and RV Failure: The Downward Spiral



Playing God?



1. Treat triggering factors and provide supportive care

- Treat infections, anemia, arrhythmias, comorbidities
- Rule out pulmonary embolism, myocardial infarction, other conditions
- Oxygen ($\text{SaO}_2 > 90\%$)
- Avoid intubation, if possible
- Contact PH referral center

2. Optimize fluid balance

- Administer fluids if hypovolemia is present/suspected
- Administer IV diuretics (or use hemofiltration) if fluid excess is present

3. Reduce RV afterload

- IV prostanoids (epoprostenol, treprostinil, iloprost) are treatment of choice
- Alternatives include IV or oral PDE-5 inhibitors or inhaled vasodilators (NO, iloprost)

4. Optimize cardiac output

- If 1-3 are insufficient:
- Dobutamine
 - $\text{ScvO}_2 > 70\%$
 - $\text{SvO}_2 > 65\%$
 - $\text{CI} > 2.0 \text{ l/min/m}^2$
 - Alternatives include levosimendan or PDE-3 inhibitors (may cause systemic hypotension)

28

5. Optimize perfusion pressure

- If 1-4 are insufficient:
- Norepinephrine or vasopressin

6. Consider lung transplantation

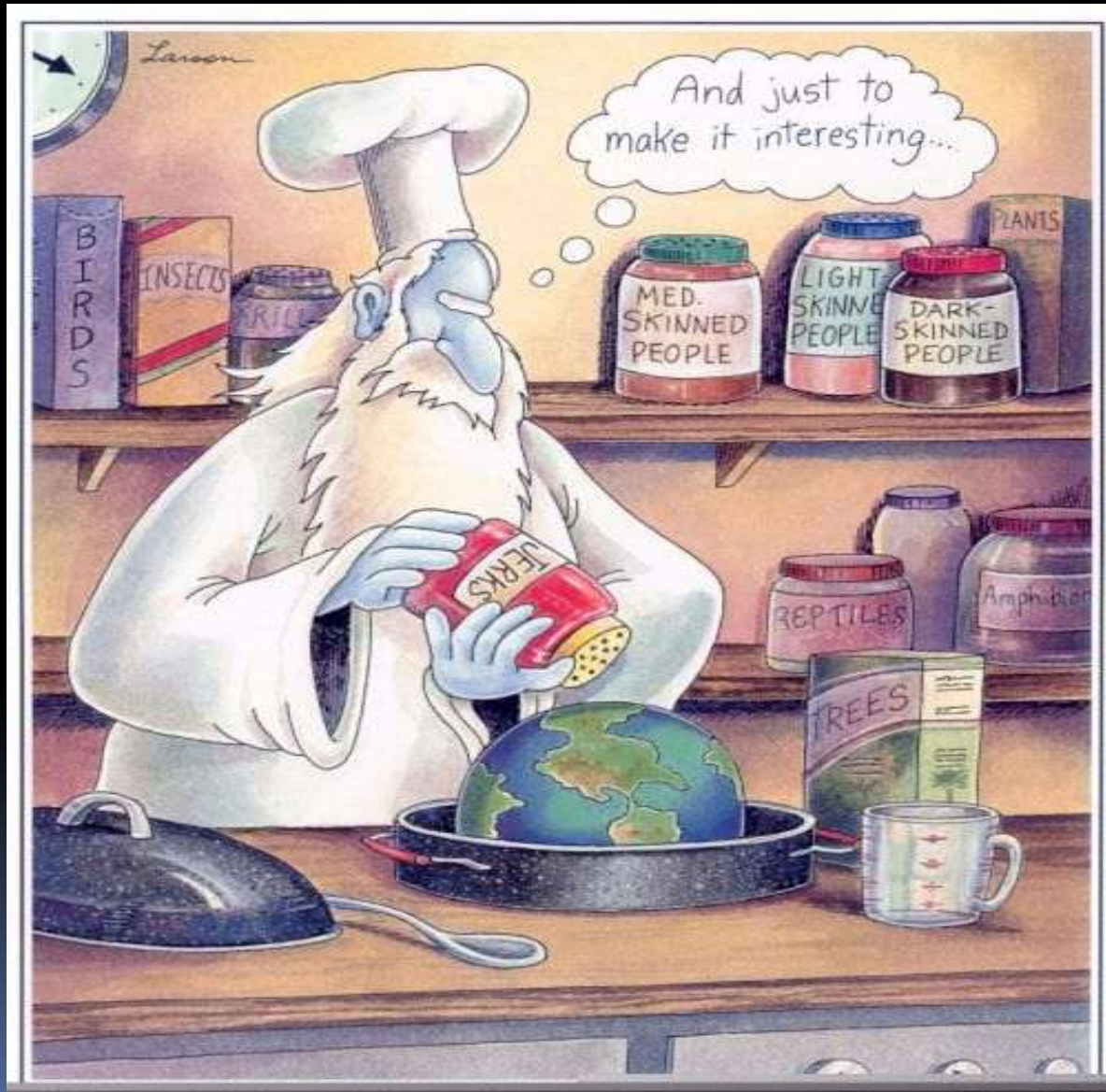
- If 1-5 are insufficient:
- Lung transplantation possible?
 - Consider extracorporeal life support

&

PRAY

Hoepfer & Granton
AJRCCM 2011

Pulmonary Hypertension interesting?



The really difficult questions?

- Who should anaesthetise PAH patients?
- When should we say anaesthesia too risky?
 - NYHA/WHO class
 - Type of anaesthesia
 - Swan Ganz mandatory
 - Inhaled NO in theatre & post op ICU
 - iNO and dobutamine “salvage”

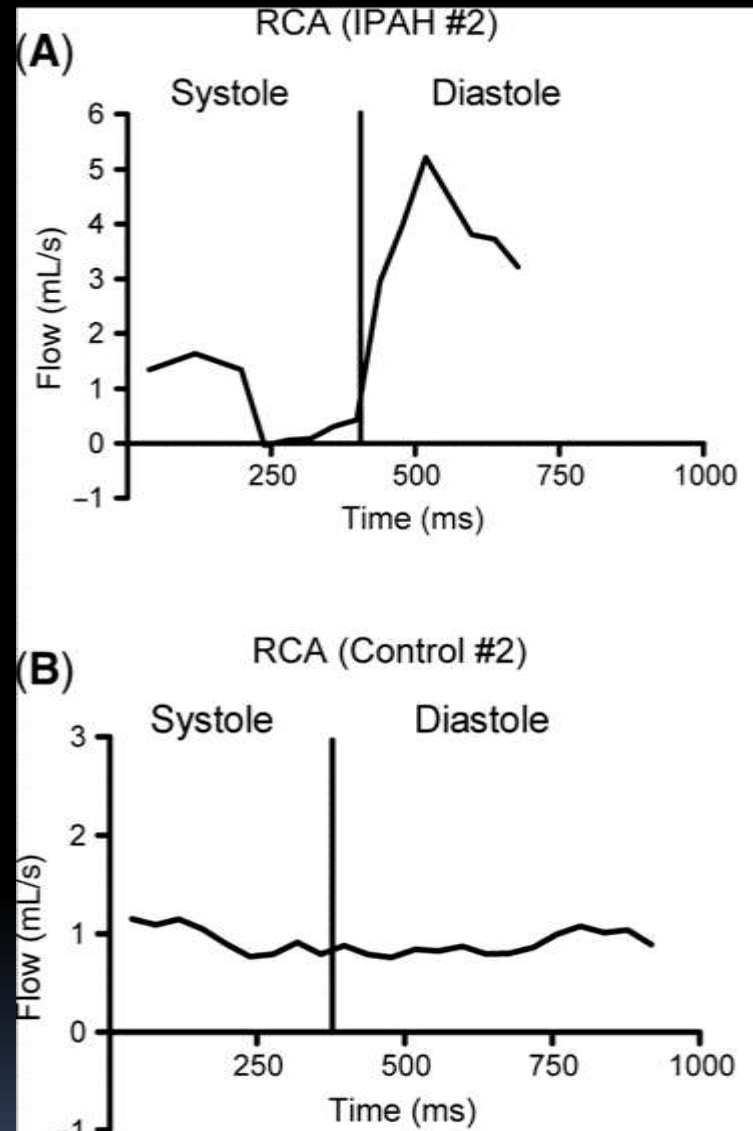
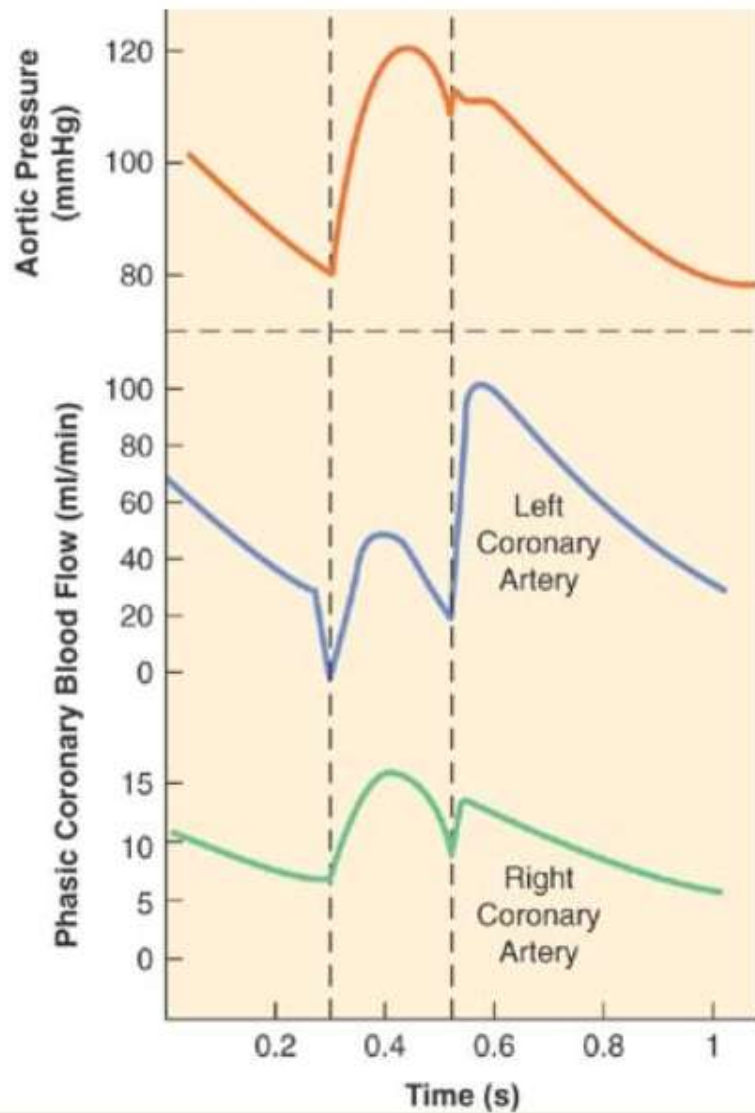
Regional

- Peripheral Nerve Blocks
 - Avoids GA and CNB
- Neuraxial
 - Need to spare respiratory function
 - Beware decreases in SVR
 - Slow titration preferred vs single shot
 - Can use thoracic epidurals if titrated
 - Intrathecal/ epidural opiates can be very effective
- Avoid excess sedation
 - SVR may decrease, hypercarbia

PAH and obstetric surgery

Historically maternal mortality 36-50% but more recently 25%, often deteriorate post-partum (autotransfusion)

study for this reason. However, useful experience with obstetric RA can be extrapolated to the nonobstetric setting. Successful incremental regional blockade has been used in PAH obstetric deliveries [21], and is well tolerated by mothers with PH [31]. RA was previously thought harmful in patients with PH because of the haemodynamic compromise following sympathetic blockade; however, using a low intrathecal dose minimises this potential drop in afterload, and careful incremental epidural top-ups are well tolerated. RA techniques



Drug	Dose	Half-life (duration of action)	Potential adverse effects
Intravenous			
Prostacyclin (Epoprostenol, Flolan)	Start at 1 ng/kg/min; titrate upward in 2-ng/kg/min increments according to effect	3-5 minutes (10 minutes)	Systemic hypotension, worsening oxygenation (increased V/Q mismatch), antiplatelet effect, headache, flushing, jaw pain, nausea, diarrhea
Iloprost	1-5 ng/kg/min	30 minutes	Similar to Flolan; also syncope (5%)
Sildenafil [325] (NB off-license use in hemodynamically unstable patients)	Low dose, 0.05 mg/kg; high dose, 0.43 mg/kg (comes as 0.8 mg/ml)	3-5 hours	Hypotension: caution if fluid depleted, severe LV-outflow obstruction, autonomic dysfunction. Hypoxemia due to V/Q mismatch. Common: headache, flushing, diarrhea, epistaxis, tremor. Rare but important: anterior ischemic optic neuropathy
Milrinone	50 µg/kg over 10 minutes followed by 0.375-0.75 µg/kg/min infusion	1-2 hours	Tachyarrhythmias, hypotension
Adenosine	50-350 µg/kg/min, titrate up in 50 µg/kg/min increments	5-10 seconds (2 minutes)	Bradycardia, bronchospasm, chest pain
Inhaled (preferred; Note variable absorption likely)			
Prostacyclin (Epoprostenol, Flolan) [286,303]	0.2-0.3 ml/min of 10-20 µg/ml nebulized into inspiratory limb of ventilator circuit (30-40 ng/kg/min)	3-5 minutes	As above but less hypotension and improved oxygenation compared with intravenous use
Iloprost [275]	2.5-5 µg 6-9 times/day, 1 mg/ml milrinone into the ventilator circuit at 0.2-0.3 ml/min for 10-20 minutes	30 minutes	As above and bronchospasm
Milrinone [176,178,179] NO	5-80 ppm continuously	1-2 hours 15-30 seconds (5 minutes)	Less systemic hypotension than with IV milrinone Methemoglobinemia; withdrawal PH
ORAL (rarely in ICU)			
Bosentan	62.5-125 mg b.d.	5 hours	Liver-function test abnormalities; drug interactions; edema
Sildenafil	0.25-0.75 mg/kg 4 hrly	3-4 hours	As above; less hypotension and hypoxemia in stable patients

Inodilators

- Increase contractility
- Decrease SVR
- Decrease PVR
- Co-administration of pressors may be necessary

Levosimendan

- Sensitizes troponin to calcium
- Inhibits PDE III
- Potassium channel opener
- Improves diastolic function and contractility without increased oxygen consumption
- Vasodilates
- Clinically improves RV failure and decrease PVR
- Promising

Levosimendan

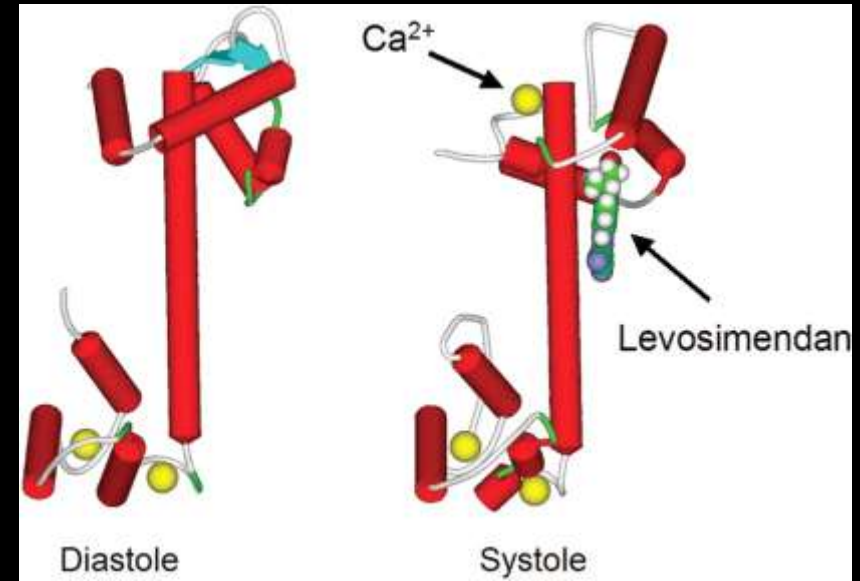
Primary mechanism:

In diastole the binding pocket is not exposed.

In systole Ca^{2+} binds to troponin C and exposes a hydrophobic binding pocket. Levosimendan stabilizes troponin C and prolongs the binding of Ca^{2+} .

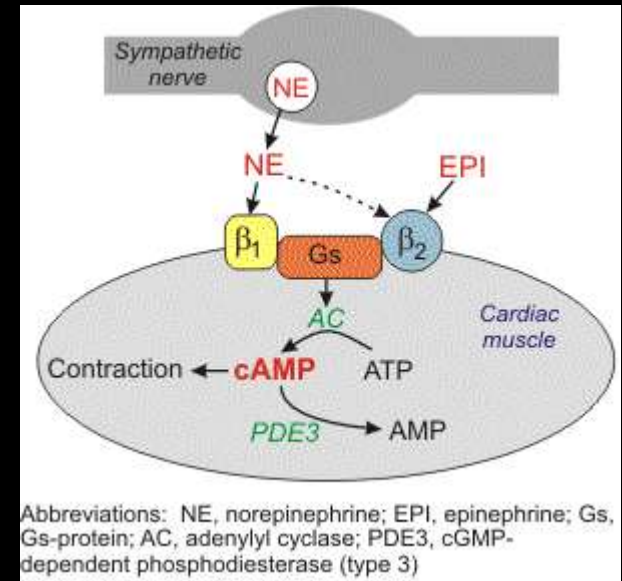
Dual mechanism:

Also has 'anti-ischaemic' effect via ATP-dependent K^{+} channel activation in cardiac myocytes.



Milrinone

- cAMP PDE III inhibitor
- Inotropy
- Chronotropy
- Dromotropy
(conduction velocity)
- Peripheral vasodilatation
- (Decrease platelet aggregation)



Management Strategies

- Prevention
- Detection
- Treatment

Lai et al BJA 2007

- Tertiary institute in Taiwan
- 1999 to 2004
- 63964 patients in total for non cardiac surgical procedure
- 9593 pts echo evaluation 30 days prior to surgery
- 62 pts had echo evidence of **RVSP >70 mmHg** and were not intubated pre-op
- Mean RVSP 78.8 (70-122mmHg)
- Controls were matched & RVSP<35mmHg
- Intraop and post op events and 28 day mortality

Demographics

	Control	PH	P-value
<i>n</i>	62	62	
Male (%) [*]	38 [61.3]	38 [61.3]	NS
Age (yr) [*]	67 (14)[27–94]	67 (15)[26–91]	NS
Hypertension (%)	26 [41.9]	20 [32.3]	NS
DM (%)	10 [16.1]	20 [32.3]	0.059
CAD (%) ^{**}	11 [17.7]	12 [19.4]	NS
LVEF (%) [*]	48 (11)[17–55]	48 (11)[19–57]	NS
Chronic pulmonary disease (%)	7 [11.3]	10 [16.1]	NS
Renal dysfunction (%)	3 [4.8]	3 [4.8]	NS
PASP (mm Hg)	32.3 (4.0)[70–122]	78.8 (9.4)[20–35]	<0.001

Aetiology of PH

	<i>n</i> (total=62)
Pulmonary arterial (%)	11 [17.7]
Collagen disease	4 ^{**}
Portal hypertension	5
Left to right shunt	2 ^{***}
Pulmonary venous	
Left-sided atrial or ventricular (%)	27 [43.5]
Left-ventricular failure	13
Hypertrophic cardiomyopathy	2
Valvular disease	12
Mitral regurgitation/stenosis	5/2
Aortic regurgitation/stenosis	3/2
Respiratory disease or hypoxemia (%)	13 [21]
Chronic pulmonary embolism (%)	2 [3.2]
Undetermined (%) [†]	9 [14.5]

Post-operative events

Table 5 Postoperative major adverse events of all patients in both groups. *Some patients encountered more than one adverse event. **Both were fatal ventricular arrhythmias despite cardioversion/defibrillation; ***2–28 days after surgery

	Control (n=62)	PH (n=62)	P-value
Morbidity (%)	2 [3.2]	15 [24.2]*	0.002
Heart failure (%)	0 [0]	6 [9.7]	0.028
Delayed tracheal extubation >24 h (%)	2 [3.2]	13 [21]	0.004
Stroke (%)	0 [0]	1 [1.6]	NS
Myocardial ischaemia/infarction (%)	0 [0]	1 [1.6]	NS
Major arrhythmia (%)	0 [0]	2 [3.2]**	NS
Mortality (in-hospital death, %)	0 [0]	6 [9.7]***	0.028

Optimize therapy

- Involve pulmonary hypertension specialist
- Optimize underlying disease
- Treat RV overload if any
- Continue chronic PH therapy
- Consider starting and stabilising PH therapy
- Do it somewhere else??

Inhaled Agents

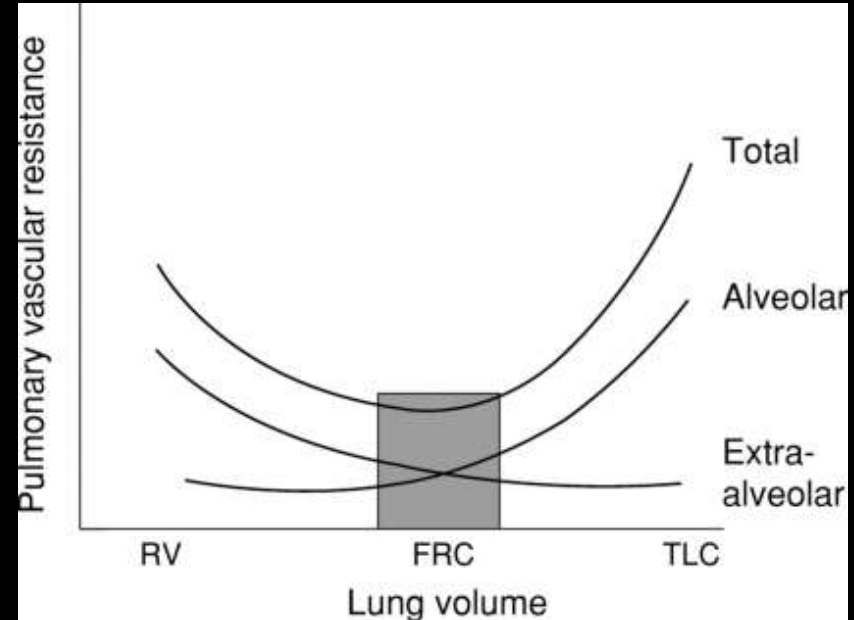
- No clinical trials assessing different volatiles
- All volatiles may worsen RV dysfunction by decreasing preload, afterload and contractility
- Sevoflurane & isoflurane do not adversely affect PVR (neither did halothane or enflurane!)
- Sevo decreases PAP more than iso
- PVR is increased by both nitrous (not in paed) and desflurane
- HPV ?? Not clinically relevant < 1 MAC

Induction

- Prone to hypotension and cardiovascular collapse
 - High baseline sympathetic tone
 - Etomidate is apparently ideal
 - Intubation may exacerbate the hypotension if causes further sympathetic stimulation

Ventilation

- Low levels of PEEP
- Moderate V_t
- High FiO_2
- Hypocarbica is a potent pulmonary vasodilator



Emergence

- Maintaining haemodynamic stability and adequate ventilation can be difficult
 - Deep extubation
 - May decrease SVR, contractility
 - Hypoxia and hypercarbia will increase PVR
 - Light extubation
 - Can cause severe pulmonary vasoconstriction
 - Need tube tolerance without increased sympathetic tone
- May need ongoing ventilation

Management Strategies

- Optimize volume status: avoid filling +/- offload
- Augment CO
- Reduce PVR
 - Pulmonary vasodilators – inhaled vs IV
 - Treat reversible factors
 - Metabolic state: anaemia, acidosis, hypoxaemia
 - Respiratory failure: limit Pplat (lung protection) but beware hypercarbia increasing PVR
 - Reduce sympathetic stimulation
- Maintain adequate SVR
 - Keep $PVR \ll SVR$
 - Use pressors if needed

Why should you be scared?



Definition of complications

Price LF et al, Eur Resp J 2010;35:1295

- Major PAH complications:
 - Death
 - Right heart failure:
 - Inotropes
 - iNO
 - Increased pulm vasodilatory Rx
- Minor PAH complications:
 - Hypoxia requiring intervention
 - Isolated hypotension
 - RH failure not requiring inotropes etc

PH patients & non-cardiac surgery

obstetric surgery. In this cohort of well-characterised patients with mostly mild-to-moderate PAH and non-operable CTEPH, overall perioperative mortality was 7%, and the incidence of perioperative complications up to day 28 was 29%. These are relatively high adverse event rates despite operating on mostly nonsevere patients in an experienced PH centre.

However patients who survived appeared to regain their previous level of function after surgery.

Emergency surgery carried a high risk (50% mortality, n=4)

What kills PAH patients?

TABLE 1

Causes of death in 99 patients with pulmonary arterial hypertension in UZ Leuven, Belgium

Sudden death	18
Pulmonary hypertension crisis	1
Respiratory failure	2
Pneumonia	3
Massive haemoptysis	1
Liver failure	3
Atrial septostomy	1
Acute pulmonary embolism	1
Ischaemic colitis	1
Medication withdrawal	1
Right ventricular failure	32
Hyperthyroidism	1
Sepsis	8
Bleeding (other)	2
Intracranial bleeding	2
Liver transplantation	1
Anaesthesia	2
Cancer	3
Myocardial infarction	1
Unknown	15

Table 5 Pulmonary vascular properties of vasoactive agents

	CI	PVR	SVR	PVR/SVR	Tachycardia	Renal ^a /metabolic
Vasopressors				Dose related		
NE	+	+	++	+/-	+	Lactic acidosis
PHE	-	++	+	+	-	-
Low-dose AVP	+/-	+/-	++	-	-	Diuresis ++
Inotropes						
Dobutamine <5 µg/kg/min	++	-	-	-	+	
Dopamine	+	+/-	+	+	++	Natriuresis
Epinephrine	++	-	++	-	++	Lactic acidosis
Inodilators						
PDE IIIs	++	-	-	-	+/-	-
Levosimendan	++	-	-	-	-	-

AVP, arginine vasopressin; NE, norepinephrine; PDE IIIs, phosphodiesterase inhibitors; PHE, phenylephrine. ^aRenal blood flow is likely to improve with increased cardiac output and systemic blood pressure with all agents.

Prospective study – Sztrymf et al, ERJ 2010;35:1286-1293

TABLE 3 Clinical and biochemical data at admission according to survival in the intensive care unit

	Nonsurvivors	Survivors	p-value
Patients n	19	27	
Triggering factor (yes/no) n	9/19	14/27	0.8
Mean systemic arterial pressure mmHg	64 (32–95)	67 (43–91)	0.9
Cardiac frequency beats·min ⁻¹	112 (42–144)	110 (82–151)	0.9
Diuresis mL·day ⁻¹	1500 (100–8500)	1550 (500–3900)	0.7
Furosemide dose mg·day ⁻¹	250 (60–1500)	170 (40–1000)	0.04
Serum level of creatinine μmol·L ⁻¹	112 (76–446)	95 (53–204)	0.04
BNP pg·mL ⁻¹	1415 (449–3550)	628 (87–1460)	0.0007
C-reactive protein mg·L ⁻¹	40 (0–277)	12 (0–200)	0.01
Troponin Ic ng·mL ⁻¹	0 (0–7.35)	0 (0–1.14)	0.4
SAPS II	32 (11–49)	22 (6–43)	0.001

BNP: brain natriuretic peptide; SAPS II: simplified acute physiology score II.

Prospective study – Sztrymf et al, ERJ 2010;35:1286-1293

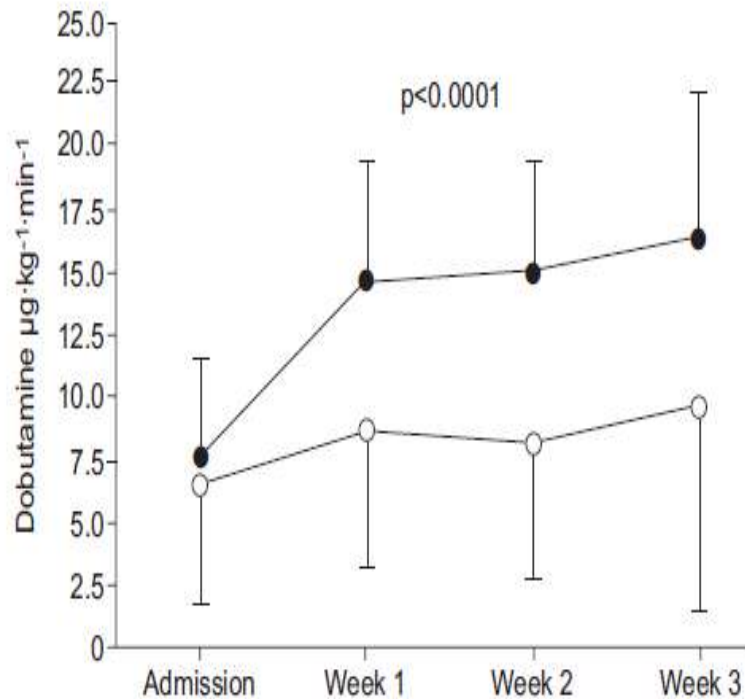


FIGURE 3. Changes in dobutamine doses according to survival in the intensive care unit (ICU): patients discharged from the ICU (survivors; ○) or patients who died in ICU (nonsurvivors; ●).

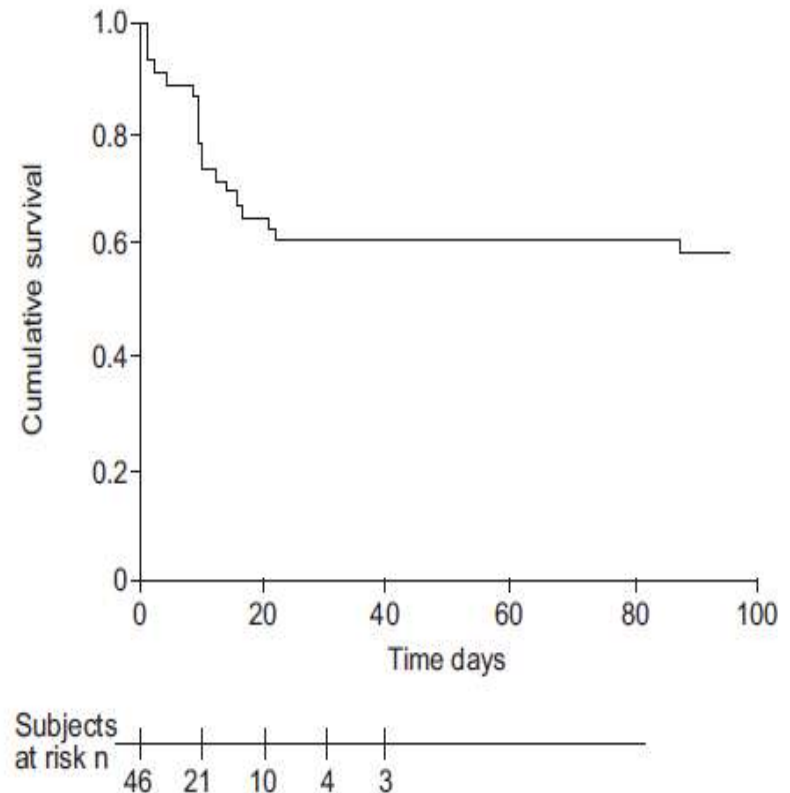
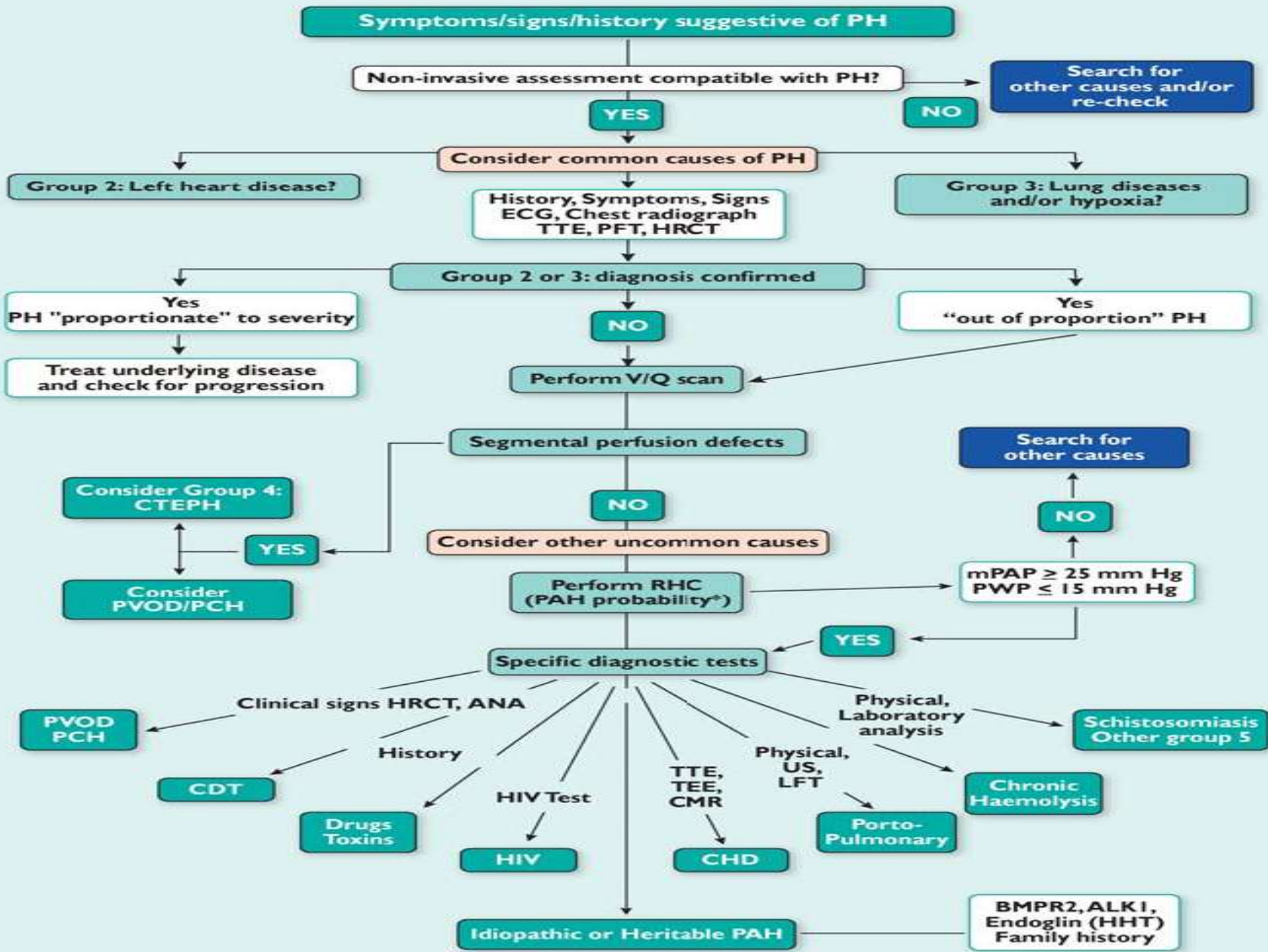


FIGURE 1. Survival in overall population.

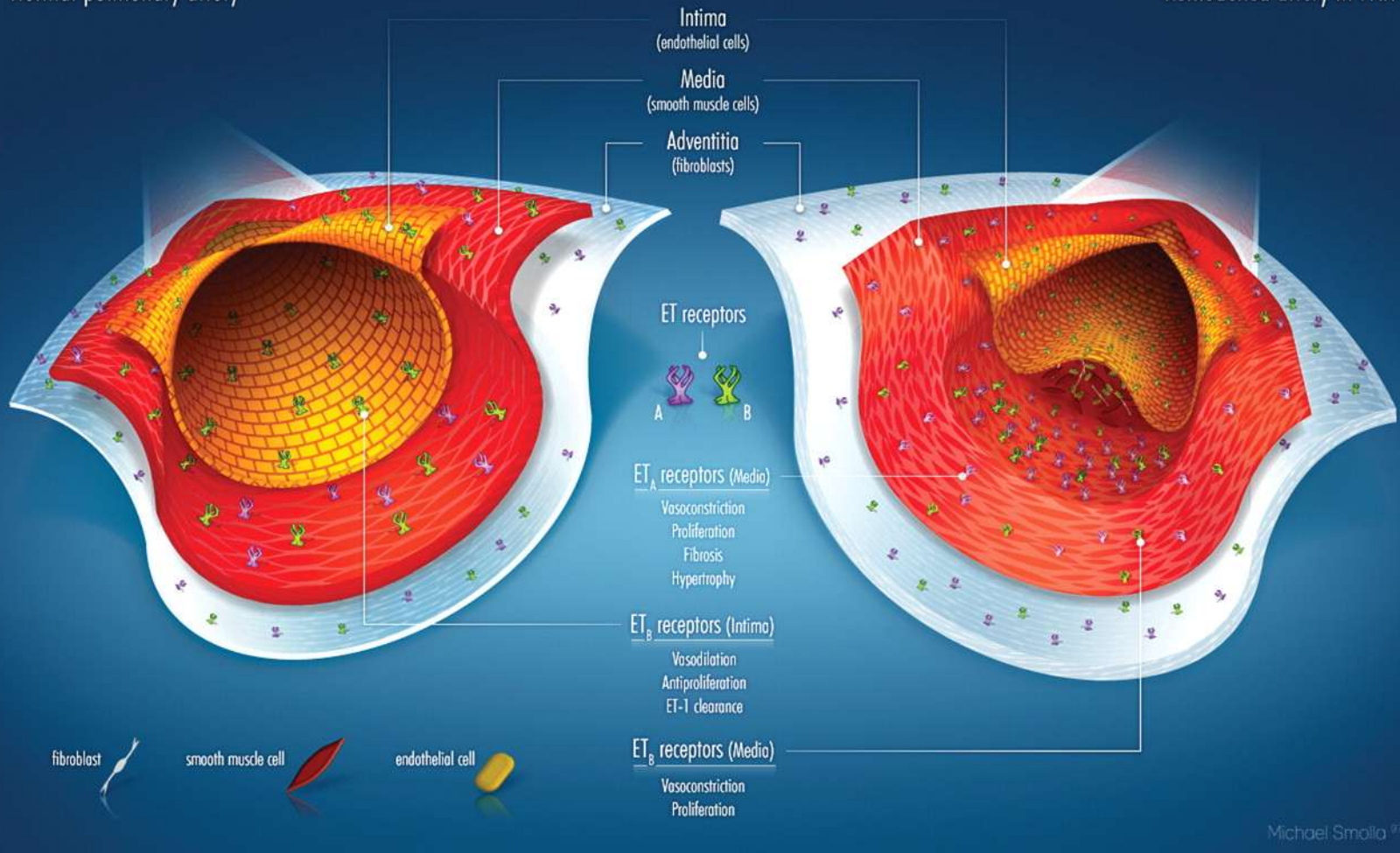


Lai et al BJA 2007

- Tertiary institute in Taiwan
- 1999 to 2004
- 63964 patients in total for non cardiac surgical procedure
- 9593 pts echo evaluation 30 days prior to surgery
- 62 pts had echo evidence of **RVSP >70 mmHg** and were not intubated pre-op
- Mean RVSP 78.8 (70-122mmHg)
- Controls were matched & RVSP<35mmHg
- Intraop and post op events and 28 day mortality

Normal pulmonary artery

Remodelled artery in PAH

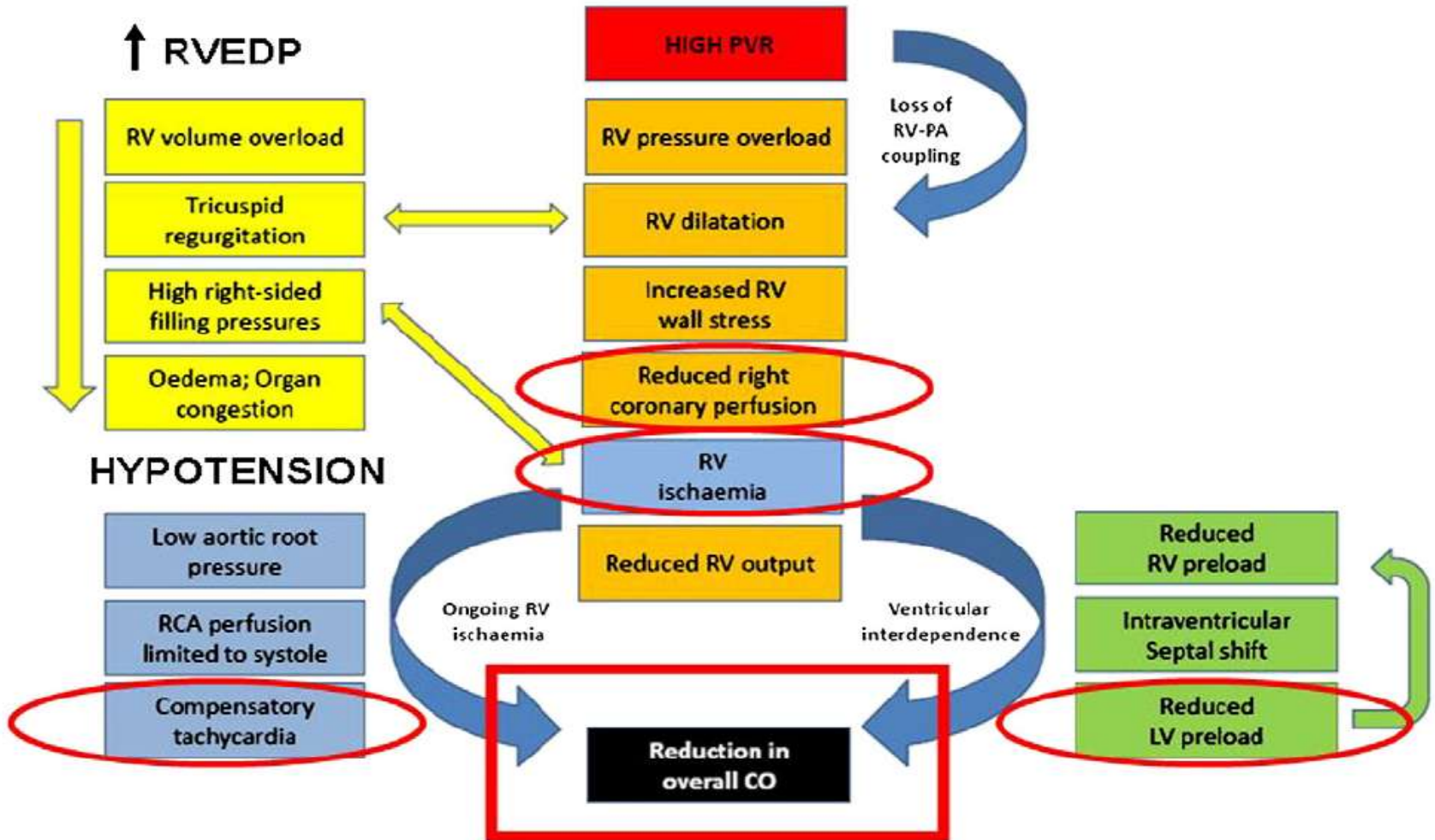


Michael Smolnik ⁹⁷

Opitz C F et al. Eur Heart J 2008;eurheartj.ehn234

Cycle of RV death

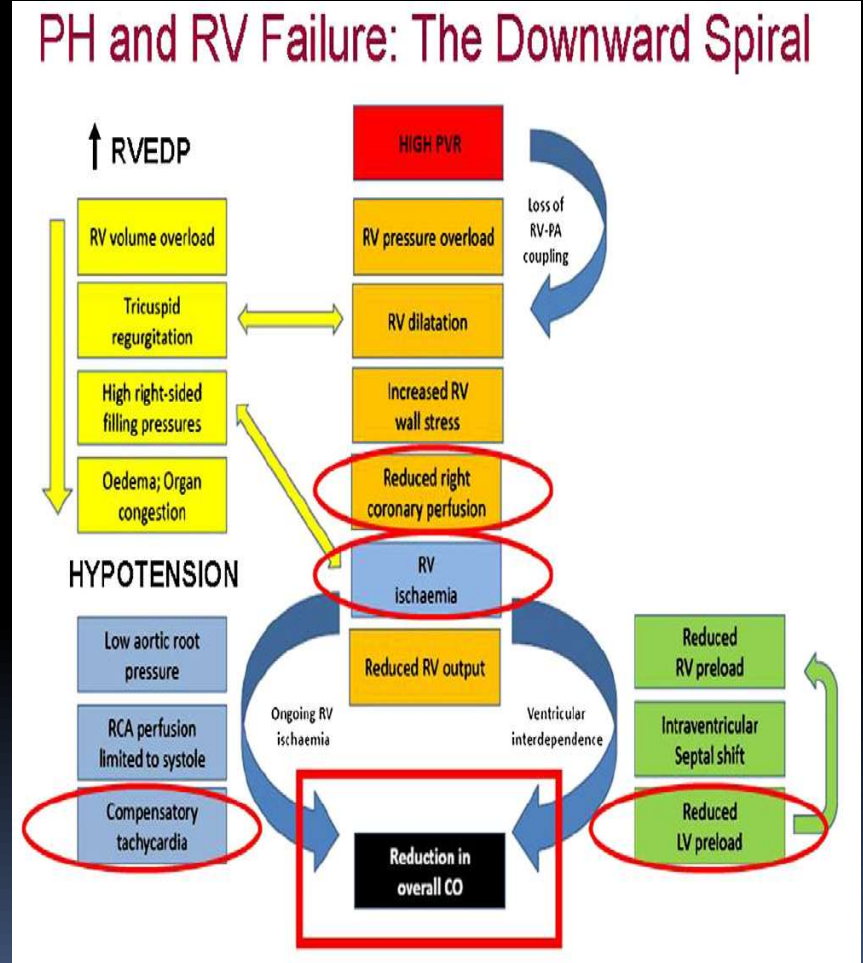
PH and RV Failure: The Downward Spiral



Faced with RV death cycle: ICU?

Salvage realistic prospect?

- Monitor
- Dobutamine?
 - Contractility increases
 - Decreases RV & LV afterload
 - HR response concern
- Vasopressin?
 - Systemic vasoconstriction & pulm vasodilator
- Inotropic support?
 - Nor-epinephrine but HR increase
 - Inodilators:
 - Milrinone
 - Levosimendan
- IV prostanoid for pulmonary vasodilation



WHAT TO DO WHEN THE SHIT HITS THE FAN

Are you prepared to deal with:

Right ventricular failure?

Earthquakes? Fires? Flooding? Civil unrest?

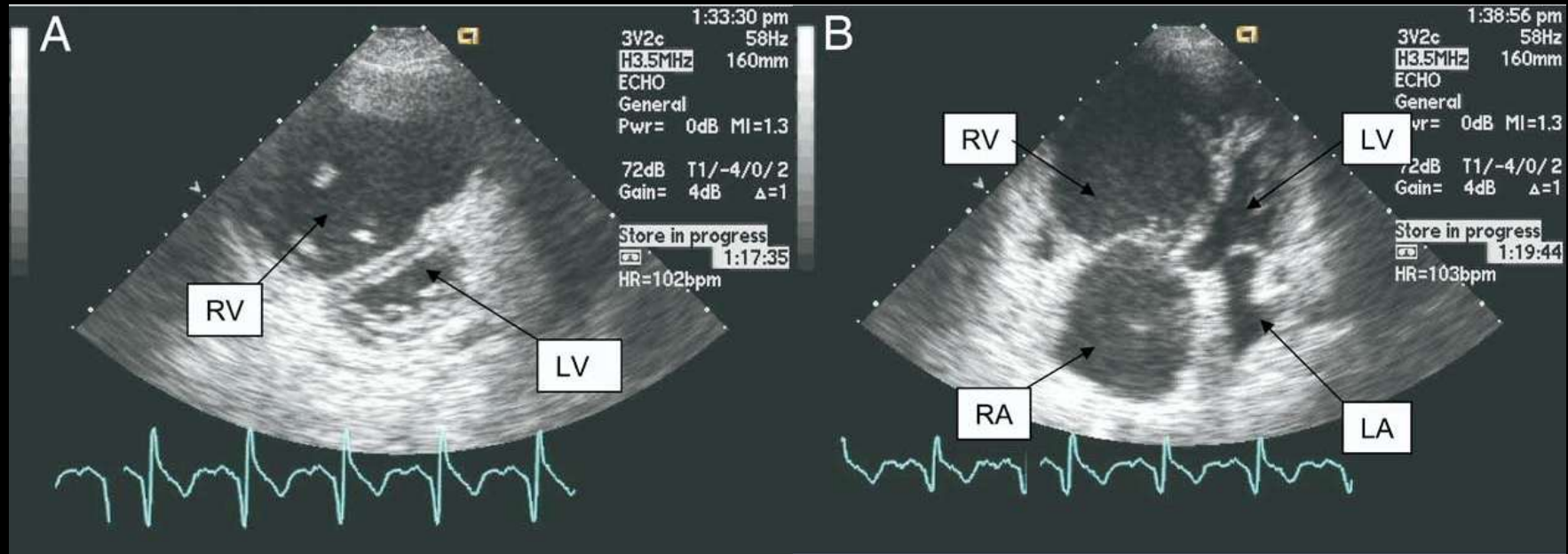
David Black



Normal RV

- Smaller and thin walled compared to LV
- Crescent shaped in X section
- 1/6 of the LV's work and pressure
- Little variation in PAP
- Driving pressure for coronary flow is Aortic root pressure – Intraventricular pressure, therefore, flow is throughout the cardiac cycle
- RV systolic function augmented by IVS bulging into the RV during systole

Common TTE findings



(A) Parasternal short axis view. (B) Apical 4 chamber view. Common echocardiographic findings in PAH include: right atrial enlargement; right ventricular enlargement; abnormal contour, flattening, or reverse curvature of the interventricular septum; and underfilled left heart chambers.

References

- Pulmonary Vascular And Right Ventricular Dysfunction In Adult Critical Care: Current And Emerging Options For Management: A Systematic Review.
Price et al. Crit Care 2010, 14:R169
- Anaesthesia and Right Ventricular Failure.
Forrest. Anaesthesia and Intensive Care 2009; 37(3): 370-385
- Anaesthesia For Patients With Pulmonary Hypertension.
Pritts & Pearl. Curr Opin Anaesthesiol 2010; 23: 411-416
- Intraoperative Management Of Pulmonary Hypertension And Associated Right Heart Failure.
Gordon et al. Curr Opin Anaesthesiol 2009; 23: 49-56
- ACCF/ AHA 2009 Expert Consensus Document on Pulmonary Hypertension:
<http://content.onlinejacc.org/cgi/content/full/53/17/1573>
J Am Coll Cardiol 2009; 53; 1573-1619
- Noncardiothoracic Nonobstetric Surgery In Mild To Moderate Pulmonary Hypertension.
Price et al. Eur Resp J 2010; 35: 1294-1302
- Severe Pulmonary Hypertension Complicates Postoperative Outcome Of Non Cardiac Surgery.
Lai et al. BJA 2007; 99 (2): 184-190
- Right Coronary Artery Flow Impairment In Patients With Pulmonary Hypertension
Van Wolferen et al. Eur Heart J 2008; 29: 120-127
- Respiratory Physiology The Essentials
West JB 2008: 8th edition
- Miller's Anaesthesia
Miller et al 2009: 7th edition