



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PPHN - clinical vs regulatory needs

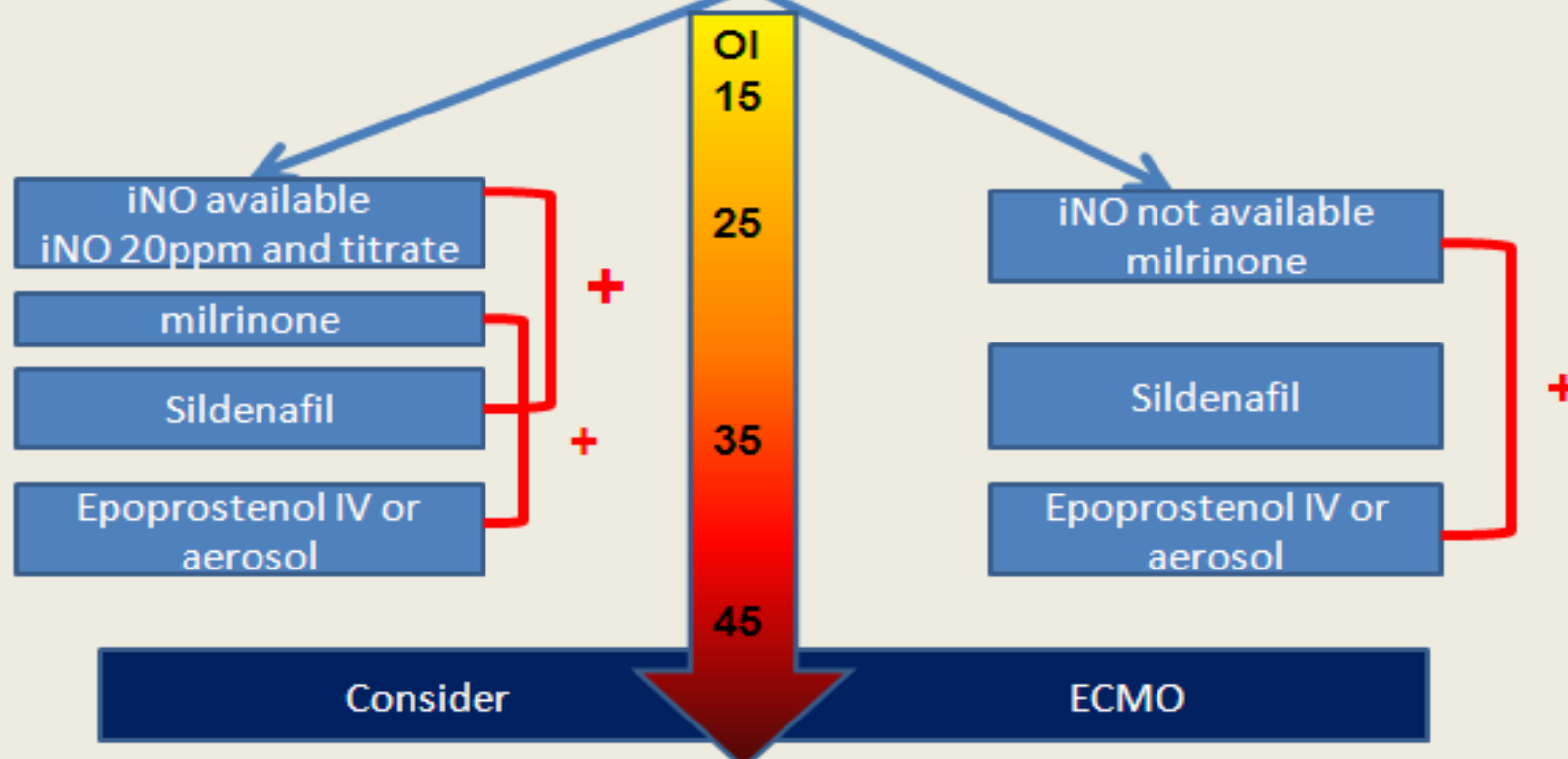
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Treatment of PPHN (Hugo Devlieger, KUL Leuven, 2009)

Optimization of lung recruitment (HFO)
Inotropic support (dopamine, norepinephrine)
Sedation and analgesia
Correct acidosis





Ru-Jeng Teng et al. (*Journal of the Formosan Medical Association, 2013*)

Table 1 Classification of persistent pulmonary hypertension of the newborn (PPHN).

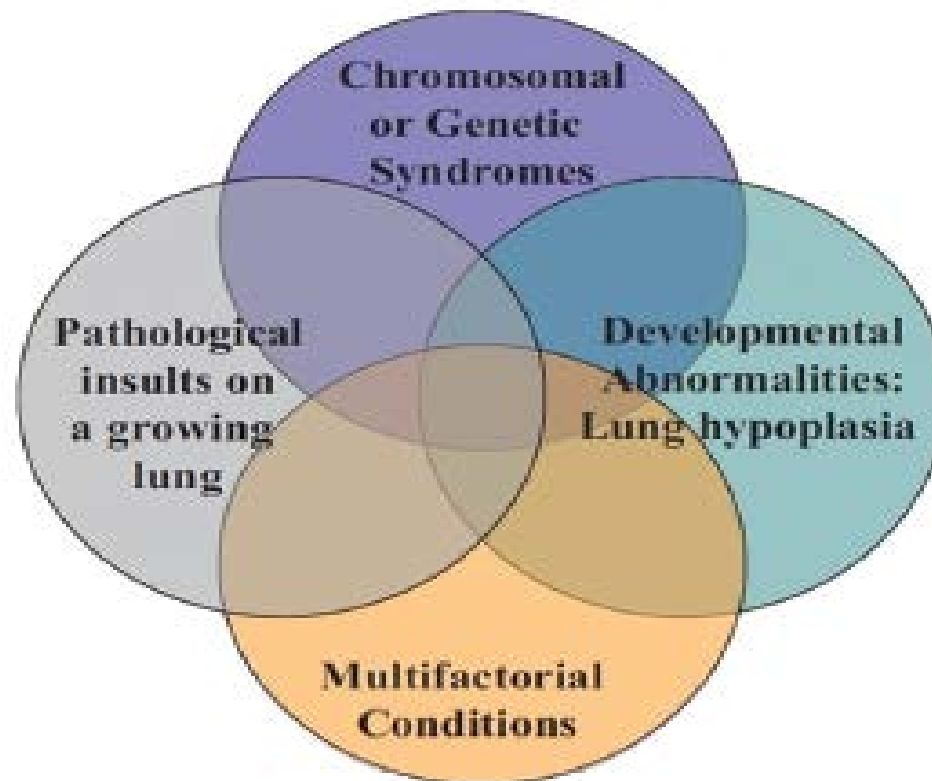
- Abnormally constricted pulmonary vasculature caused by parenchymal diseases:
 - Meconium aspiration syndrome
 - Respiratory distress syndrome³⁰
 - Pneumonia
- Hypoplastic pulmonary vasculature:
 - Congenital diaphragmatic hernia
 - Lung hypoplasia
- Normal parenchyma with remodeled pulmonary vasculature:
 - Idiopathic PPHN
 - Congenital heart disease
 - Hypoxic–ischemic encephalopathy, chronic
 - Others



Clinical trials in neonates and children: Report of the pulmonary hypertension academic research consortium pediatric advisory committee

*Ian Adata¹, Sheila G. Haworth², Max Wegner³, Robyn J. Barst⁴, Dunbar Ivy⁵, Kurt R. Stenmark⁶,
Abraham Karkowsky⁶, Erika Rosenzweig⁶, and Christopher Aguilar⁷*

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**GUIDELINE ON THE CLINICAL INVESTIGATIONS OF MEDICINAL PRODUCTS FOR
THE TREATMENT OF PULMONARY ARTERIAL HYPERTENSION**

1. Pulmonary arterial hypertension (PAH)

1.1. Idiopathic PAH

1.2. Heritable

1.2.1. BMPR2

1.2.2. ALK1, endoglin (with or without hereditary hemorrhagic telangiectasia)

1.2.3. Unknown

1.3. Drug- and toxin-induced

1.4. Associated with

1.4.1. Connective tissue diseases

1.4.2. HIV infection

1.4.3. Portal hypertension

1.4.4. Congenital heart diseases

1.4.5. Schistosomiasis

1.4.6. Chronic hemolytic anemia

1.5 Persistent pulmonary hypertension of the newborn



Updated Clinical Classification of Pulmonary Hypertension

Table 1 Updated Classification of Pulmonary Hypertension*

1 Pulmonary arterial hypertension

1.1 Idiopathic PAH

1.2 Heritable PAH

1.2.1 BMPR2

1.2.2 ALK-1, ENG, SMAD9, CAV1, KCNK3

1.2.3 Unknown

1.3 Drug and toxin induced

1.4 Associated with:

1.4.1 Connective tissue disease

1.4.2 HIV infection

1.4.3 Portal hypertension

1.4.4 Congenital heart diseases

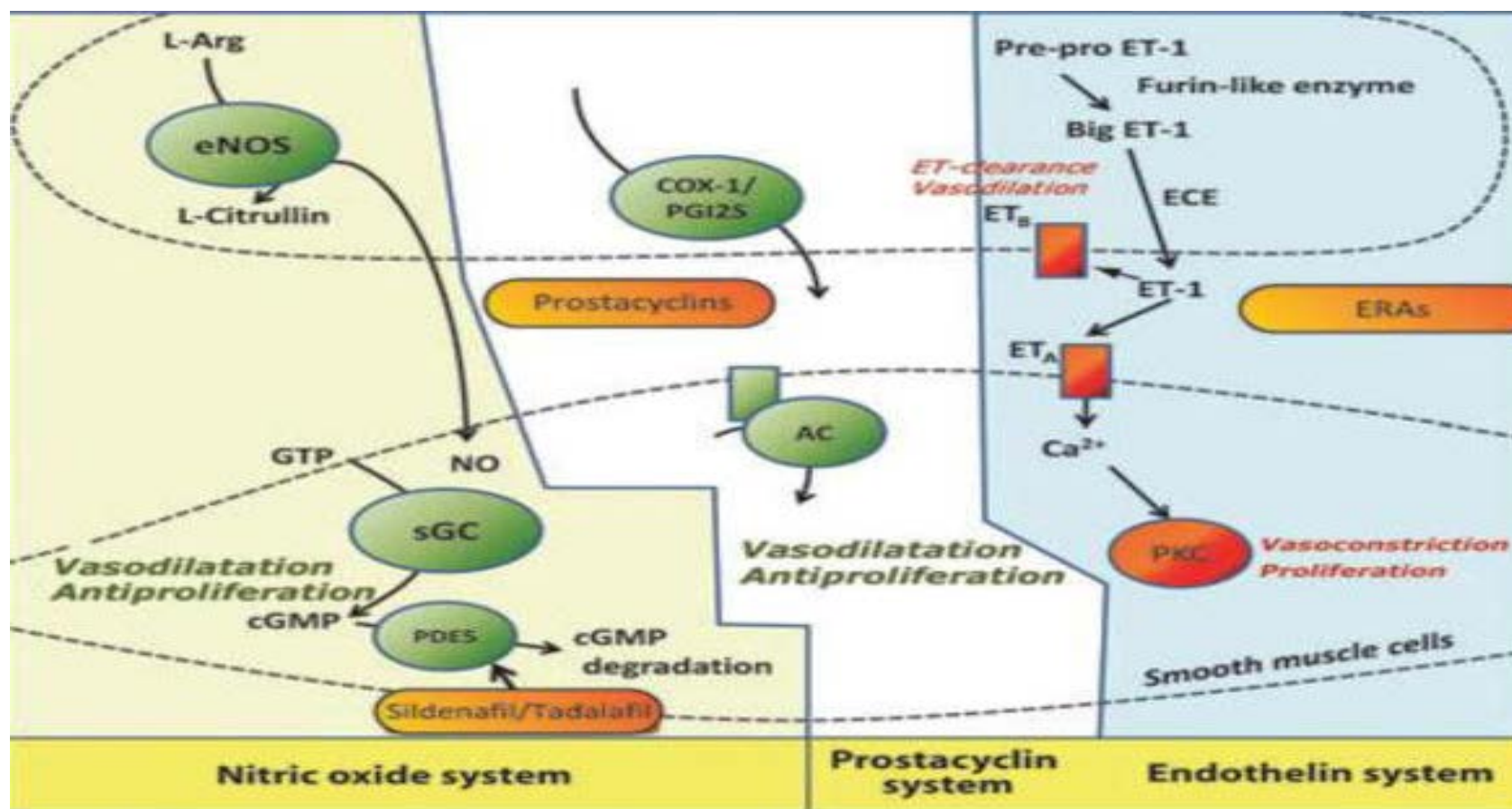
1.4.5 Schistosomiasis

1' Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

1'' Persistent pulmonary hypertension of the newborn (PPHN)



Vorhies EE, Ivy DD. Drug Treatment of PAH in Children. *Paediatric drugs*. 2014





PPHN – current questions

- If there is unmet therapeutic need ??
- What is current standard of care??
- If CTs in PPHN should be included into development of new drugs for PAH??
- Design of CTs in PPHN
- End points
- Duration of studies
- Duration of follow-up