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Review

Cardiorespiratory Interactions in Paediatrics ‘It’s (almost always) the circulation stupid!’

M.L. Rigby [1,*], M. Rosenthal [2]

[1] Department of paediatric cardiology, Royal Brompton Hospital, London SW3 6NP, UK
[2] Department of respiratory paediatrics, Royal Brompton Hospital, London SW3 6NP, UK

EDUCATIONAL AIMS

To provide the reader with a pragmatic approach to disentangle conflicts of diagnosis in ventilatory and circulatory disorders. The reader will come to appreciate:

- The variability of cardiopulmonary interactions.
- The numerous possible causes.
- A logical approach to diagnosis.

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SUMMARY

The interaction of the heart and lungs is probably the most important aspect of life and survival. Fortunately, it is not difficult to understand the fundamentals. The purpose of the lungs and their ventilation is to present oxygen to the circulation via the alveoli and to receive carbon dioxide from the circulation and then expel it. The relations of the heart and lungs and the matching of blood flow to the various organs with ventilation and lung perfusion may be disrupted by a variety of congenital or acquired heart malformations. They include those giving rise to an increased or reduced pulmonary blood flow, elevated pulmonary venous pressure or external physical pressure on the airways or lung parenchyma. Respiratory disorders which compromise cardiac function include states with reduced alveolar ventilation, those with a barrier to ventilation or perfusion, ventilation/perfusion mismatch and pulmonary vascular disease. There is also a fascinating group in which congenital disorders of the heart and lung co-exist to produce very particular modes of abnormal cardiopulmonary interaction.

INTRODUCTION

Although cardiovascular and respiratory disorders often produce the same symptoms in infants and children, with basic examination you might believe the distinction should be obvious, but in practice things are rarely so simple. This is probably because major heart disease may be complicated by respiratory complications and lung disease may masquerade as cardiac or have cardiovascular complications. For example symptomatic major cardiac disorders without a heart murmur may be presumed to be respiratory in origin. Congenital pulmonary lymphangiectasia may be associated with a chronic and recurrent pericardial effusion [1]. Confusion may also arise when arterial desaturation occurs in the presence of a normal heart because of pulmonary arteriovenous fistulae [2]. Occasionally congenital heart and pulmonary malformations may coexist. There is also an association between cystic fibrosis and myocardial fibrosis and cardiomyopathy but congenital heart disease is hardly ever encountered [3].

Of course asthma, the most common respiratory disorder, is poorly tolerated by patients with cyanotic heart disease and conditions with a high pulmonary blood flow or vice versa. In our institution chest physicians and cardiologists frequently argue about which is more important. So this article sets out how the

* Corresponding author.
E-mail addresses: michael.rigby@rbht.nhs.uk (M.L. Rigby), m.rosenthal@rbht.nhs.uk (M. Rosenthal).

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respiratory system may affect the cardiovascular system but more likely how the cardiovascular system may affect the respiratory system.

The purpose of the heart and circulation is to deliver oxygen and nutrients to the organs and to remove waste, especially carbon dioxide. Organ requirements can be relatively constant or at other times demand greater perfusion, oxygen delivery and carbon dioxide removal.

The key word is matching; the matching of delivery/removal to the organ's needs, and the matching of the (pulmonary) circulation to the (alveolar) ventilation and vice versa both in proximity and quantity. The hormonal, neural and molecular control mechanisms leading to this matching are highly complex and beyond the scope of this paper. Given the inevitably intimate embryological relationship in development, abnormalities will not necessarily neatly sub-divide into ventilatory or circulatory but may well have both elements in either origin or consequence. Nevertheless broad categories can be devised [Table 1].

To avoid turgid descriptions or exhaustive lists of all possible problems we will highlight key areas to illustrate the mantra that all these issues boil down to matching. Pulmonary hypertension in general and Trisomy 21 in particular probably best illustrate this.

PULMONARY HYPERTENSION WITH/WITHOUT TRISOMY 21

Pulmonary hypertension (Proximal pulmonary arterial pressure greater than 30/15 mmHg) is a disorder of distal pulmonary arteries leading to a progressive increase in pulmonary vascular resistance. The consequences are eventually reduced pulmonary blood flow, diminished cardiac output and a classic example of ventilation perfusion mismatch. With an intracardiac communication right to left shunting results in progressive cyanosis (Eisenmenger's syndrome). The initial effect on the heart itself is right ventricular hypertrophy but in time right ventricular failure, cardiac arrhythmias or sudden death will occur.

The recent worldwide TOPP registry study (Tracking of outcome and practice in paediatric pulmonary hypertension included 362 children confirmed by catheterisation (359) or histology (Group 3) [4]. Over 50% were idiopathic or familial, about a third were secondary to congenital heart disease and only 42/362 (12%) had pulmonary arterial hypertension (PAH) due to respiratory causes or hypoxaemia. The remainder included almost single cases of liver disease, connective tissue disease, HIV and 6 cases of pulmonary veno-occlusive disease. Breaking these respiratory cases down (Table 2) showed that bronchopulmonary dysplasia and interstitial lung disease comprised 25% each. Clearly ascertainment bias may be present as many will be not be diagnosed so formally. There was a slight excess of females (1.4 to 1) irrespective of causation. The risk of associated Trisomy 21 was very high with 9/42 (21%) having Trisomy 21 in this respiratory cause group, very similar to the 23% in the congenital heart disease cause group.

The reasons why Trisomy 21 adds such an increased risk for the development of pulmonary hypertension are not really known and are likely to be multifactorial. Factors to consider in children with Trisomy 21 include:

a) Their increased risk of congenital heart disease with left to right shunts (Group 1) such as atrioventricular septal defect (AVSD).
   Plus
b) Their incidence of obstructive sleep apnoea is very high [5,6], at least 80% (Group 4)
   Plus
c) Their risk of overt/covert food aspiration is much greater (groups 4,5 possibly 6)
   Plus
d) The risk of significant gastroesophageal reflux disease (GORD) is much greater than children without Trisomy 21. (Group 4)
   Plus
e) There is an increased risk of interstitial lung disease (Group 5)

Even without congenital heart disease, the cumulative risk factors seem a likely explanation for the registry findings. In our experience, even accepting a skewed denominator, 50% of all Trisomy 21 infants we see, with or without a known cardiac defect, have silent aspiration on videoflouroscopy which would not be picked up on a feeding history. These cited risk factors demand very close attention in all Trisomy 21 infants with or without a known cardiac defect with low thresholds for early and repeated sleep studies, speech and language assessments together with videoflouroscopy and early recourse to GORD therapy [7]. Adenotonsillectomy for obstructive sleep symptoms has a lower (c.20%) "cure" rate than in non-trisomy 21 children and therefore the requirement for non-invasive CPAP will be higher. Regarding interstitial lung disease, high resolution CT scans of the lungs can trap the reader, or at least these authors, showing a picture indistinguishable from ILD which on open lung biopsy was solely attributed to aspiration.

The respiratory system extends from the tip of the nose to the alveolus and the fundamental impact this system may have on the cardiovascular system is the causing or exacerbating of pulmonary hypertension. The biggest driver of this is hypoxia and to a lesser extent hypercapnia. This hypoxia may well be intermittent and

Table 2
Respiratory causes (42/362, 12%) of catheter confirmed pulmonary arterial hypertension in children from the TOPP (tracking outcomes and practice in paediatric pulmonary hypertension) registry [4].

	42/362
Bronchopulmonary Dysplasia/Chronic lung disease of prematurity	11 (26%)
Interstitial Lung disease	10 (24%)
High Altitude	7 (17%)
Obstructive Sleep Apnoea/Disordered breathing	5 (12%)
Congenital Pulmonary Hypoplasia	5 (12%)
Congenital Diaphragmatic hernia	4 (10%)
Kyphoscoliosis	2 (5%)
Other	2 (5%)

Table 1
Typical problems of circulation, ventilation or both, resulting in matching issues. The Group numbers will be used in the text to highlight the many possible interactions.

Circulation	Ventilatory	Both
1. Excess pulmonary blood flow. Eg left to right shunts, common mixing situations without pulmonary stenosis	4. Reduced (alveolar) ventilation eg airway abnormalities, neuro- and neuromuscular disease, hypoplasia	6. Ventilation/perfusion mismatch (proximity) eg hypoplasias/asthma/absent pulmonary arteries
2. Reduced pulmonary blood flow. eg right to left shunts, tetralogy of Fallot, pulmonary arteriovenous fistulas	5. Increased ventilation/perfusion barrier eg interstitial lung disease/ pulmonary hypertension	7. Pulmonary vascular disease (see 1,3,5,6)
3. Raised pulmonary venous pressure eg Left sided obstruction, cardiomyopathy		8. Physical Compression effects of the circulation on ventilation eg vascular ring/scoliosis