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Eur Respir J 2014; 43: 1539–1541 | DOI: 10.1183/09031936.00158113 | Copyright ©ERS 2014

From the authors:

J.C. Grignola points out that the product of pulmonary vascular resistance by pulmonary vascular compliance, or time constant (RC time) of the pulmonary circulation is not truly constant, and that this impacts on the pulsatile component (W_{osc}) of right ventricular hydraulic load (W_{tot}).

He is right. But the question is, by how much? In the experimental study by PAGNAMENTA *et al.* [1], pulmonary hypertension induced by ensnarement of the pulmonary arteries, to mimic purely proximal chronic thromboembolic pulmonary hypertension (CTEPH), was associated with a decrease in RC time from 0.5 s to 0.3 s, while microembolism to mimic purely distal obstruction, like in pulmonary arterial hypertension (PAH), was associated with an increase in RC time from 0.5 s to 0.8 s. Associated changes in W_{osc}/W_{tot} went from 25% to 29% and 16%, respectively. These would be the extreme possible deviations of a fixed W_{osc}/W_{tot} of 23% calculated for all types and severities of pulmonary hypertension by SAOUTI *et al.* [2] on the basis of recovered constant RC times. In other words, W_{tot}, as an estimation of right ventricular afterload, is not always equal to 1.3 × steady-flow W (calculated as the product of mean pulmonary artery pressure and stroke volume) proposed by SAOUTI *et al.* [2], but in the range 1.2–1.4. This is not much. Furthermore, as also underscored by J.C. Grignola [1], vascular obstruction in clinical pulmonary hypertension tends to be inhomogeneous and spread over the entire vascular tree, especially in CTEPH, so that the variations of the estimate of W_{tot} would be markedly smaller, probably reduced to somewhere between 1.25 and 1.35 × steady-flow W. This corresponds to trivial variations in afterload. Unsurprisingly, as illustrated in figure 1a of J.C. Grignola's correspondence, the reported range of RC times has a minimal effect on the proportionality of systolic, mean and diastolic pulmonary artery pressures. Conversely, the near-constant RC time in pulmonary hypertension is still in marked contrast with the extensive variability of the systemic RC time [3].

The discovery of "laws of nature" in medical research clarifies understanding and is essential for bedside translation of bench research. The repeated observations by LANKHAAR *et al.* [4] that RC time is constant in the pulmonary circulation has helped considerably in the assessment of right ventricular afterload in pulmonary hypertension. But scientific truth has to be constantly rechallenged, and uncovering exceptions leads to developments of new paradigms and innovation. J.C. Grignola is to be commended for pointing out that the RC time is shortened in left heart failure with increased pulmonary venous pressure, which makes the pulmonary circulation less compliant at any given level of resistance [3], and in operable CTEPH because of increased wave reflection and proximal arterial stiffness [5]. However, the deviations are small, so that the general rule of the constancy of the RC time remains a reasonable approximation in all circumstances.

Thus, while we agree with J.C. Grignola's pertinent remarks, we humbly feel allowed to maintain our statement that the RC time of the pulmonary circulation is approximately the same in CTEPH and PAH [6], indicating surprisingly little impact of proximal obstruction-related increased wave reflection or stiffness on right ventricular afterload.

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RC time of the pulmonary circulation is approximately the same in CTEPH and PAH
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Received: Oct 06 2013 | Accepted: Oct 08 2013

Conflict of interest: Disclosures can be found alongside the online version of this article at www.erj.ersjournals.com

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Eur Respir J 2014; 43: 1541–1542 | DOI: 10.1183/09031936.00174213 | Copyright ©ERS 2014

Sleep quality as a confounding factor of maternal weight and preschool wheezing

To the Editor:

We read with great interest the recently published article by LEERMAKERS *et al.* [1] that takes an outstanding view of the relationship of maternal weight with the risk of preschool wheezing. We would like to highlight the importance of this study, as it shows a bidirectional interaction between pregnancy and childhood health. Moreover, we would like to congratulate the authors on the accomplishment of this research and suggest additional considerations for further investigations.

Currently, asthma is the most common chronic disease in children in the USA. It is noteworthy that the incidence of asthma in childhood has progressively increased, being observed 8.7% of cases in 2001 and 9.6% in 2009 [2]. For instance, 17% of children in the USA have a diagnosis of obesity and there is a higher prevalence of asthma in obese children [3]. However, the biological pathway responsible for the association of obesity with asthma is still unclear. There are several hypotheses, as discussed in the article by LEERMAKERS *et al.* [1].

We would like to discuss another important aspect on this question that refers to the impact of sleep during pregnancy on the health of both the mother and newborn. Pregnancy causes sleep changes between the first months and after the baby is born. About of 75% of mothers develop some sleep disorder in pregnancy [4], such as poor sleep quality and decreased sleep duration. In addition, pregnant mothers have an increased risk of obstructive sleep apnoea (OSA) [5]. In addition, these sleep disorders are correlated with glucose intolerance, gestational diabetes mellitus, gestational hypertension and preeclampsia [5]. It has been highlighted that diabetes in pregnancy is associated with high birth weight. Furthermore, both poor maternal sleep and OSA can lead to increased proinflammatory cytokine levels [6]. Thus, this factor could be related to increase of proinflammatory cytokine levels in mothers, which might affect the immune system of the fetus, and the risk of infectious and atopic diseases post-natally.

Breastfeeding is important for neonates, as breast milk is the primary component of the infant's diet and meets the essential nutritional requirements of the rapidly growing child. We would like to emphasise which factors may affect breastfeeding and, consequently, neonatal health. There are various bioactive factors in human colostrum and milk, such as immune cells, immunoglobulins, fatty acids, glycoproteins and antimicrobial peptides [7], that lead to inactivation of pathogens. Furthermore, there is melatonin in human milk, a hormone related to Circadian rhythms, particularly with sleep [8]. In addition, melatonin is involved in physiological and oxidative processes, including functional regulation.

The mother's behaviour could be reflected in breastfeeding and it can lead to health consequences for the baby. A study found that mothers who drank alcohol had less active sleep in their children [9]. It is well known that sleep in childhood is important for future health, as children affected by sleep disorders are more susceptible to consequences of sleep problems. There is a relationship between sleep duration during childhood, endocrine disorders and increased body mass index [10]. Sleep disorders and obesity in childhood may lead to increased proinflammatory cytokines, and this may affect the immune system and the risk of infectious and atopic diseases. For this reasons, we suggest the evaluation sleep in pregnant females.