Response

To the Editor:

I appreciate Dr Besada’s interest in our article on the potential risks of developing Pneumocystis pneumonia (PCP) in immunocompromised patients receiving rituximab. We too wish to know the overall incidence of this often lethal complication following the administration of this medication. Unfortunately, under the design of the study, this is not currently possible. During this time frame, a significant number of patients received rituximab at outside institutions either before or after care at the Mayo Clinic. Thus, there were no means to accurately obtain the total number of patients who were exposed to rituximab over this time period in the entire patient population. We simply raised concern that PCP may develop as a complication in patients receiving rituximab and that this infection has a high attendant mortality (about 30%). Our experience is that in infancy, sleeping is not an essential prerequisite for the development of glossoptosis apnea. 3 The main difference is that in infancy, sleeping is not an essential prerequisite for the development of glossoptosis apnea. 3 The study of breathing patterns during respiratory distress shows that these infants present recurrent obstructed inspiratory efforts (an equivalent of Müller maneuver). The obstructed inspiration is followed by a prolonged and interrupted expiratory flow, despite a positive expiratory intrathoracic pressure (an equivalent of Valsalva maneuver), and then by a retarded expiratory flow (grunting expiration). 4 The association between obstructive apnea and respiratory grunt suggests that the functional upper airway obstruction

Pathophysiology of Intrapulmonary Right-to-Left Shunt in Infants With Obstructive Apnea

To the Editor:

We read with great interest the article by Shaikh et al in CHEST (January 2013). The authors concluded that in adults with severe sleep apnea syndrome, closure of the patent foramen ovale is not followed by a reduction in nocturnal desaturation, suggesting the coexistence of an alternative mechanism of residual right-to-left shunt (RLS). Here we propose a potential source of residual RLS.

In infants with Pierre Robin syndrome, with choanal atresia/stenosis, or with esophageal atresia, the pathogenic mechanism of glossoptosis apnea is similar to that of sleep apnea. 4 The main difference is that in infancy, sleeping is not an essential prerequisite for the development of glossoptosis apnea. 5 The study of breathing patterns during respiratory distress shows that these infants present recurrent obstructed inspiratory efforts (an equivalent of Müller maneuver). The obstructed inspiration is followed by a prolonged and interrupted expiratory flow, despite a positive expiratory intrathoracic pressure (an equivalent of Valsalva maneuver), and then by a retarded expiratory flow (grunting expiration). 4 The association between obstructive apnea and respiratory grunt suggests that the functional upper airway obstruction...
may cause a lower airway instability. Grunting expiration is a breathing strategy to defend lung volume and lower airway patency by forcing gas into the peripheral airways.

Infants with glottisosis aspnea/hypopnea rarely experience severe complications, including hypoxemia and hypercapnia, pulmonary hypertension, anoxic brain damage, cor pulmonale, and sudden death. They frequently experience a blood gas derangement characterized by a degree of hypoxemia greater than the degree of hypercapnia and a hypoxemia relatively resistant to oxygen administration. Increasing $FIO_2$ required to maintain $PO_2$ between 60 and 80 mm Hg results in a considerable increase in alveolar-arterial oxygen difference (Fig 1). No lung opacities or only small areas of collapse or consolidation are usually found on chest radiographs. Oxygen compared with other gases is more rapidly absorbed from the alveoli. Therefore, the most likely explanation for such large alveolar-arterial oxygen differences is that the high oxygen concentration in the inspired air converts in pulmonary RLS. From the results of our research group studies, we speculate that an intrapulmonary RLS may be the source of residual A-aO$_2$ in some adults with sleep apnea undergoing closure of patent foramen ovale.

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**Financial/Nonfinancial disclosures:** The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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**DOI:** 10.1378/chest.13-0566

**REFERENCES**


**An Algorithm for Approaching Mediastinal Lymphadenopathy in Pulmonary Hypertension**

To the Editor:

The recently published article by Mona et al (February 2013) is timely but raises more questions about how to study patients with mediastinal lymphadenopathy (MLAD) and idiopathic pulmonary arterial hypertension (IPAH). It would be particularly helpful for clinicians who treat such patients to be able to perform a risk assessment of the need for mediastinal sampling in a patient group where even minimally invasive endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) or conventional TBNA is likely to be tolerated less well compared with patients without IPAH. That said, EBUS-TBNA (or conventional TBNA) do provide less invasive alternatives to mediastinoscopy.

A plethora of guidelines exist regarding the approach to pulmonary nodules and MLAD in the context of lung cancer or malignancy. However, there seems to be a need for guidelines on the approach to idiopathic or unexplained MLAD (without the context of a known cancer) and prospective controlled studies of adequate size to clarify whether conservative monitoring of patients with IPAH and MLAD between 1 and 2 cm with an effusion misses any significant mediastinal pathology. For patients with MLAD $> 2$ cm with IPAH, a safer option might be to perform the less invasive neck ultrasound biopsy first before using EBUS-TBNA or conventional TBNA because it is known that there is a high incidence of pathologic suprACLavicular lymphadenopathy in patients with MLAD, even though this may not be apparent on CT scan of the neck, as ultrasound is superior in this regard. In addition, IPAH represents one of many nonmalignant disorders where MLAD occurs; others would include bronchiectasis, pulmonary veno-occlusive disease, congestive cardiac failure, interstitial lung disease (without granulomatous disease), and reactive infective adenopathy, to name a few. In many of these disorders, pulmonary hypertension may be present, and avoiding invasive EBUS-TBNA sampling might be preferable (unless a specific treatable diagnosis, eg, mycobacterial infection, could be achieved). Could it be that the predominant mechanism for MLAD in all these conditions is actually from elevated right-sided (rather than left-sided) pressures?

In summary, further guidance on a stratified, sequential approach to the investigation of MLAD in suspected benign disorders with pulmonary hypertension would be welcome, reserving EBUS-TBNA or conventional TBNA for situations where neck ultrasound biopsy is unhelpful. Mediastinoscopy should also be reserved for cases where EBUS-TBNA or conventional TBNA is nondiagnostic and the pretest clinical probability of malignancy or treatable mediastinal pathology outweighs the risk of performing mediastinoscopy in the presence of significant pulmonary hypertension.