

Dear Editor

Some asthmatics show elevation of the peripheral venous oxygen pressure (PvO₂)

Bronchial asthma is a common disease, characterized by reversible narrowing and hyperresponsiveness of the airways. Evaluation of airflow limitation and airway hypersensitivity is useful for objective assessment of asthma.^{1,2} However, these tests may not be sufficient to fully elucidate the exact condition of asthma. During the course of many years of clinical experience, we noticed that some asthmatics present a contradiction by having a decent peak flow even while experiencing persistent dyspnea. We thus hypothesized that some other internal factor might be involved in the causation of some cases of dyspnea.

While searching for novel objective indices, approximately eight years ago we found marked elevation of the peripheral venous oxygen pressure (PvO₂) in an asthmatic subject. Further careful analysis led to a belief that said finding was reproducible and not erroneous, and was in fact occasionally seen in a

small number of exacerbated asthmatics.³⁻⁶ There were no signs of circulatory disturbances such as venous dilatation or peripheral temperature decline. Those deteriorating patients appeared to share several clinical features of not feeling well: lassitude, shortness of breath, palpitation and easy fatigability, combined with mild to moderate airflow limitation, and they each fulfilled the diagnostic criteria for asthma.² Besides having very high PvO₂ levels, they were intractable asthmatics who had responded poorly to a series of rescue medications and required hospitalization. Figure 1 plots the individual time-course data for PvO₂ obtained from 11 such patients without oxygen inhalation. Surprisingly, they initially showed an extraordinarily high PvO₂ (78.5 ± 16.9 Torr, $n = 11$) (median $\pm$ SD) (shown as the origin of Fig. 1), similar to that usually observed in arterial blood. The levels of PvCO₂ (38.8 ± 4.9 Torr, $n = 11$) also corresponded to the normal partial pressure of carbon dioxide in the arterial blood (PaCO₂). In clear contrast, the gas data for other severe, moderate or mild asthmatics, either stable or unstable, were within a narrow range and essentially the same as for healthy subjects (asthmatics without PvO₂ elevation: PvO₂ 22.4 ± 7.3 Torr, PvCO₂ 48.6 ± 4.7 Torr, $n = 36$;

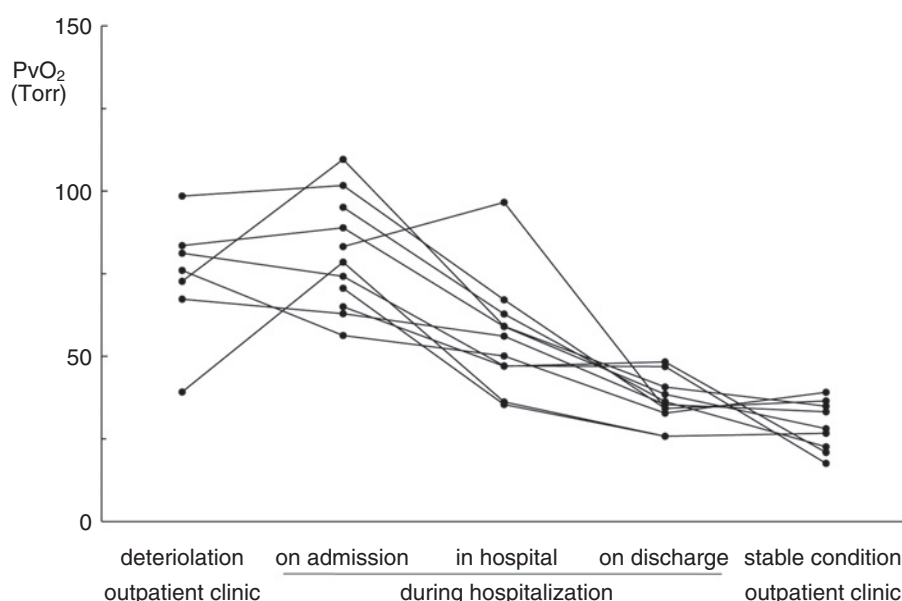


Fig. 1 Individual data for 11 consenting patients show that the PvO₂ levels were markedly elevated at the time of an emergency hospital visit and admission and gradually declined during therapy. All blood samples were obtained by venipuncture of the median cubital vein or forearm vein when blood cell and/or chemistry analysis was necessary. An aliquot of each sample was introduced directly into a gas analysis syringe and subjected to gas measurement within two minutes. The venous blood thus made no significant contact with room air, and contamination by arterial blood was unlikely. A pulse oxymeter indicated that O₂ saturation of the arterial blood was well maintained during venous blood sampling from the patients.

healthy: PvO_2 26.4 ± 10.2 Torr, $PvCO_2$ 47.8 ± 5.4 Torr, $n = 26$). As demonstrated in the figure, these very high PvO_2 levels gradually decreased, and inversely, $PvCO_2$ gradually increased (data not shown) during hospitalization, accompanied by alleviation of the dyspnea. Even high-dose systemic steroid therapy of these 11 patients failed to induce a rapid decrease in the PvO_2 level or rapid symptomatic relief. Oxygen inhalation often mildly alleviated their dyspnea. The most effective overall treatment for their symptoms, including fatigue, was rest.

We now believe that these gas analysis data clearly indicate the existence of a systemic mechanism driving PvO_2 elevation in some deteriorating asthmatics. Why and how their PvO_2 elevation occurs and is maintained, whether their airway inflammation is unique and the prevalence of such patients among asthmatics remain to be elucidated. Another important point is identification of a specific clinical biomarker in these patients that would be indicative of an elevated PvO_2 level during asthma exacerbation. At present, potentially useful clues for identifying these patients may be exertional breathlessness that seems out of proportion to the objective asthmatic state and a strangely bright red color of venous blood samples. Our preliminary analysis showed that the serum levels of lactate and pyruvate were elevated in these deteriorating patients, suggesting insufficient tissue oxygenation.⁵ We presume that a high PvO_2 level translates into an inadequate oxygen supply and decreased consumption in peripheral tissues, leading to the lassitude, shortness of breath and easy fatigability seen in these deteriorating asthmatics.

The results shown herein were presented in part at academic meetings and have been published in abstract form.³⁻⁶

Yasuyuki Sano¹, Hirokazu Yamada¹,
Chuhei Ogawa¹ and Masao Yamaguchi²

¹Department of Allergy and Respiratory Medicine, Doai Memorial Hospital and ²Division of Respiratory Medicine and Allergology, Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan
Email: cky07460@moon.odn.ne.jp

REFERENCES

1. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. Updated 2009. Available at: <http://www.ginasthma.org>.
2. *Guidelines for the Diagnosis and Management of Asthma, Expert Panel Report II, B*. Bethesda, MD: National Institutes of Health, 1997.
3. Ogawa C, Koketsu R, Ishikawa M *et al*. [Five women with cough-variant asthma whose severe dyspnea led to induction of continuous oxygen therapy (abstract)]. *Arerugi [Jpn J Allergol]* 2003;**52**:892 (in Japanese).
4. Sano Y. Severe intractable asthma with exertional breathlessness as a chief complaint [abstract]. In: *Proceedings of the 14th Congress of Interasthma Japan/North Asia*, 2004; 16-7 (partly in Japanese).
5. Horita N, Arai T, Okada Y *et al*. [Assessment of tissue hypoxia and its impact on lactate and pyruvate metabolism in asthmatics presenting breathlessness at rest (abstract)]. *[Jpn Respir Soc]* 2010;**48**:S182 (in Japanese).
6. Aoki K, Hirano R, Shimoda M *et al*. [An asthmatic patient presenting recovery from severe dyspnea and gradual normalization of elevated PvO_2 (abstract)]. *[Jpn J Pediatr Intractable Asthma and Allergic Diseases]* 2007;**5**:135 (in Japanese).