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LETTERS

Chronic thromboembolic pulmonary hypertension and upper limb thrombosis

To the Editor:

In a recent *Point of View* article I puzzled over the apparent association between chronic thromboembolic pulmonary hypertension (CTEPH) and upper extremity deep vein thrombosis, an association which was less evident with lower limb venous thrombosis [1].

Some subsequent publications may be relevant to this issue. WOLF *et al.* [2] have recently demonstrated again the prevalence of high titres of antiphospholipid antibodies in patients with CTEPH. HERON *et al.* [3] also showed for the first time that these antibodies (and Protein S deficiency, which is probably syergistic) are also common among patients with idiopathic upper-extremity deep vein thrombosis [4]. Antiphospholipid antibodies are a well established cause of arterial and venous thrombosis, often at relatively unusual sites [5]. It seems likely that the antiphospholipid syndrome might explain this apparent association, either by the formation of venous thrombi which embolize to the lungs, or as seems more likely, by stimulating parallel prothrombotic changes in the venous and pulmonary arterial systems. Many of the "pulmonary emboli" which are diagnosed in this context, particularly in young females, might actually be longstanding pulmonary artery thrombosis which is unmasked by coincidental nonspecific chest symptoms. Whether the final diagnosis in these cases is embolism or pulmonary artery thrombosis seems to be largely a matter of individual preference [6]. The antiphospholipid syndrome may well prove to be the key which unlocks many previously mysterious conditions [7].

Recently, another potentially arteriopathic association of severe pulmonary hypertension has been added to the growing list, in the form of hyperuricaemia [8].

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Circulating endothelin-1 and obstructive sleep apnoea

To the Editor:

We read with great interest the article by GRIMPEN *et al.* [1] entitled "Endothelin-1 plasma levels are not elevated in patients with obstructive sleep apnoea". Although we appreciate the hard work done, we feel that the authors have extended their conclusions beyond the study undertaken.

Elevated plasma endothelin-1 (ET-1) 1evels are a nonspecific marker of endothelial dysfunction due to cardiovascular, renal or pulmonary disease. As far as we are aware, there is no dose/response relationship depending on the number of pathological conditions that have caused the endothelial dysfunction. Neither is there reason to assume that a patient with hypertension, coronary artery disease (CAD) and obstructive sleep apnoea (OSA) will have a higher ET-1 1evel than a control with only hypertension and CAD. The problem cannot be resolved by matching control subjects with hypertension or CAD.

The study of PHILLIPS *et al.* [2] (January 1999), reporting a significant increase in ET-1 levels after 4 h of untreated severe OSA and a decrease after 5 h of nasal continuous positive airway pressure, was not cited. While discussing our preliminary report [3], GRIMPEN *et al.* [1] did not mention important differences in patient groups: our patients had more severe OSA and a higher body mass index. They were also 12 yrs younger, nonsmokers not receiving medication and had no chronic diseases other than OSA (and hypertension in the hypertensive group), whereas the majority of the patients and controls in the study of GRIMPEN *et al.* [1] received medication for cardiovascular diseases.

It would be interesting to know the smoking history of the patients and controls. Smoking causes endothelial dysfunction even in the absence of hypertension or CAD [4]. Elevated ET-1 levels have been reported in chronic obstructive pulmonary disease without coexisting pulmonary hypertension [5]. As the authors stated, mild pulmonary hypertension is often seen in patients with OSA. We are not aware of reports comparing ET-1 levels in venous and arterial blood in patients with this type of secondary pulmonary hypertension.

In future studies, it may be useful to focus on younger age groups in earlier stages of obstructive sleep apnoea and endothelial dysfunction. Before stating that "endothelin-1 plasma levels are not elevated in patients with obstructive sleep apnoea", arterial endothelin-1 levels should be measured in

conjunction with apnoeas in patients without other sustained cardiovascular diseases.

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