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Strategies to increase the lung donors′ pool

To the Editors:

In a recent issue of the *European Respiratory Journal*, DE PERROT *et al*. [1] suggested various strategies in order to increase the number of lung donors. Among these strategies, the extension of the lung donors′ selection criteria was discussed. We would like to stress some points in a subtype of marginal donors. Most of the transplant coordination centres are reluctant to consider donors who present with brain death after a toxic exposure.

Data available from the organ procurement organisations are scarce. Cumulative data recovered from January 1988 to March 2004 by the US Organ Procurement and Transplantation Network revealed that, among the 10,981 lung donors recorded within the interval, the mechanism of death was drug intoxication in only 92 cases (<1%). Similarly, the experience published by Eurotransplant (Austria, Belgium, Germany, Luxemburg and The Netherlands) is extremely limited. In 1996, a total of 168 lung transplantations were performed. The cause of death was mentioned as suicide for 15 donors (9%). As suicide may have also included deaths secondary to gunshots, hanging or drowning, the overall percentage of intoxicated donors appears to be very low in this report.

In our centre (Dept of Intensive Care, Cliniques St-Luc, Université catholique de Louvain, Brussels, Belgium), from 293 organ donors, 864 organs were procured between January 1989 and December 1997. In contrast to the previous data, 21 (7%) of our patients had developed brain death after acute poisoning [2]. A large number of intoxicants were used: cyanide, carbon monoxide, tricyclic antidepressants, barbiturates, paracetamol, insulin, and methanol. The outcome of the recipients of various organs was excellent. Bipulmonary transplantation was possible from a donor who died from methanol poisoning [3]. In the rejected cases, the lungs were not harvested for reasons that were independent from a toxic origin.

It is our experience that poisoned donors are often discarded *a priori* from organ donation, for fear of transferring the poisoning to the recipient with resultant organ dysfunction. However, the lung is seldom the main target organ of acute poisoning, with the notable exception of paraquat. Lung donation should be possible after acute overdose with the most frequent pharmaceutical drugs, including psychotropes.

Although there are data suggesting tricyclic antidepressants (TCA) accumulation in the lungs of a limited number of healthy volunteers, these data should not be extrapolated to transplant patients without caution [4]. There are data suggesting the feasibility of liver transplant in patients who died of TCA overdose and in whom TCA accumulation in the liver was demonstrated [5]. Accordingly, we believe that TCA overdose *per se* should not preclude a lung transplant.

Whereas fatalities after carbon monoxide exposure remain common, few numbers of lung transplantations have been reported [6]. It seems important to identify the source of carbon monoxide poisoning. Whilst various pulmonary lesions have been described following smoke inhalation, pure carbon monoxide poisoning is unlikely to be associated with chemical smoke-inhalation injury to the lung and lower airways [7].

Deaths in young donors are now frequently observed among illicit substance abusers. Successful lung transplantation has been performed from a donor who died after methylenedioxymethamphetamine ("ecstasy") exposure [8]. From a toxicological point of view, there is no reason to exclude ecstasy-intoxicated donors, provided that the commonly accepted criteria for organ donation are fulfilled.

In contrast, methadone has been reported to accumulate not only in the kidneys, spleen and liver, but also in the lungs. This should be particularly true in patients under maintenance therapy with multiple dosing. Acute lung injury is a rare but possible complication of acute methadone overdose [9].

The issue of organ donation after chronic use of inhaled drugs is still controversial. The pulmonary complications of inhaled cocaine are characterised by lesions of the alveolar wall and of the pulmonary microcirculation [10–12]. Short-term exposure to cocaine may enhance the production of interleukin-8, a potent polymorphonuclear chemoattractant and neutrophil-activating factor, associated with both acute and chronic lung injury [12]. These data clearly preclude lung donation in these cases.

Regular marijuana smoking can induce alterations in the structure and function of alveolar macrophages, and these patients′ lungs are unsuitable for transplantation [13]. This

restriction does not apply to the occasional marijuana smoker.

In conclusion, lung donation after fatal acute poisoning, although difficult, could be considered in selected cases of poisoning by pharmaceutical drugs that are not associated with lung injury and in selected cases of pure carbon monoxide intoxication. Oral ecstasy poisoning, as well as occasional marijuana smoking, do not appear to be an absolute contraindication.

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End points for pulmonary arterial hypertension: a way backward

To the Editors:

In the June 2004 issue of the *European Respiratory Journal*, PEACOCK *et al.* [1] recognised the need for end points, other than the assessment of functional capacity with the 6 min walking test, in pulmonary arterial hypertension (PAH) clinical trials. In their looking forward, the authors did not mention any role of the diffusing lung capacity for carbon monoxide (*D*L,CO) test, which was originally devised in 1909–1915 [2]. However, as recently reviewed [2, 3], the measurement of lung gas transfer for CO (*T*L,CO) holds some premise into the evaluation of patients with PAH. In daily clinical practice, *T*L,CO is derived from the product of constant rate of alveolar to blood CO uptake and the accessible alveolar volume, which is usually preserved in PAH; the examination of these two components allows exploration of the pathophysiological mechanism of *T*L,CO decrease at any time, due to pulmonary vascular abnormalities. Furthermore, the physiology of CO transfer is governed by the Roughton-Forster equation [4], partitioning the resistances to CO into membrane and red cell contributions, the latter accounting with appropriate calculations for 70–80% of total resistance [3]. Moreover, the *D*L for CO or another suitable gas with greater haemoglobin affinity, such as nitric oxide, could be assessed at rest and during exercise, in combination with noninvasive measurement of cardiac output, providing sensitive indicators of the diffusive oxygen transport effectiveness, and structural alteration of the alveolar-capillary barrier [5, 6]. Therefore, it seems logical to assume abnormalities in *D*L recruitment (or *D*L/cardiac output ratio) occurring in PAH before chronic cardiac consequences would be detected during echocardiography. Accordingly, *D*L,CO decrease at rest is present in 80% of PAH patients [7], and it is significantly related to the main cardiopulmonary exercise test parameters of aerobic function [8], which, in turn, are relevant to the prognosis of PAH [9].

In conclusion, following the authors' suggestions, we believe that diffusing lung capacity tests, combined in parallel with other markers, should receive consideration for as broader an application as possible for markers of pulmonary arterial hypertension. Hopefully, a view backward may widen the way forward.

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