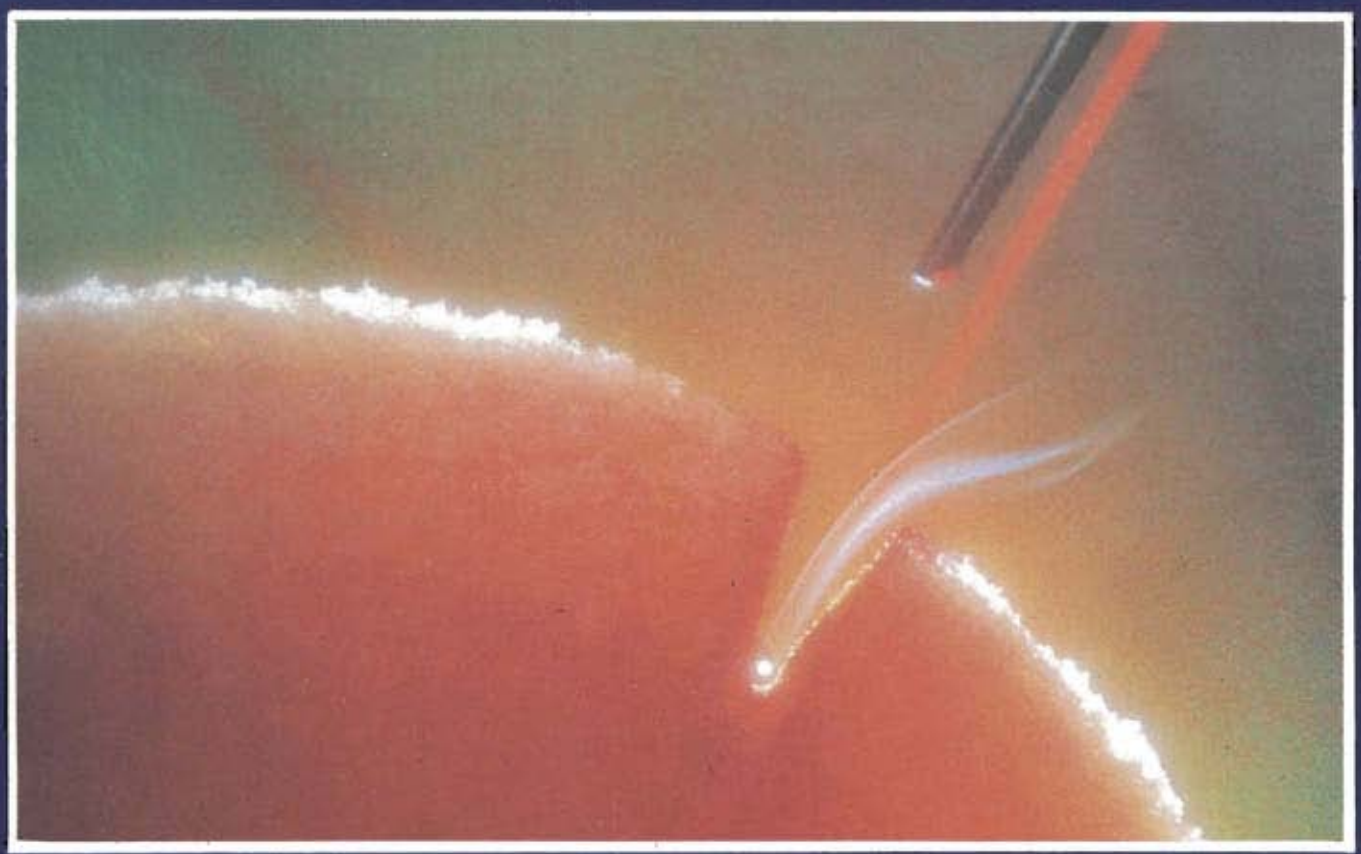
Vol. 2, No. 3, July-Aug 1994 Reg. No. 30/AL/92/TC Rs. 50.00

BIO MED

Magazine for Medical Update



LASERS IN

- SURGERY
- PHYSIOTHERAPY
- UROLOGY
- OPTHALMOLOGY
- GYNECOLOGY

INFORMATIVE ARTICLE

OXYGEN DISTRESS DURING ROUTINE BICARBONATE HEMODIALYSIS

During a pilot project monitoring 56 hemodialysis patients, values of pO_2 measured in the arterial line (pO_2(al)) of less than 8 kPa (60 mmHg) were recorded for 14.2% of the monitored time. Severe hypoxia like this demands treatment, but remains unnoticed during routine hemodialysis.

Dr. Anders Lassen Nielsen.

Hypoxia during hemodialysis is a fact!

It is a well-known fact that hypoxia occurs during hemodialysis (HD) [1]. Some other serious clinical aspects of recurrent cases of dialysis associated hypoxia (DAH) have previously been mentioned [2]. We have dealt with some of the analytical considerations that should be made in connection with the monitoring of patients during HD [2].

Why the cause of hypoxia has not been determined

Since hypoxia during HD was first reported by Johnson et al. in the early 70's, more than two hundred articles concerning hypoxia during dialysis with acetate or bicarbonate have been published [1]. Despite all these investigations the causes have never been explained. The reports have given conflicting data and caused confusion [1,3] because:

1. In the first place, we have a multifactorial complex of problems. Several mechanisms have been suggested. From the literature there is a consensus of opinion regarding the most important factors: dialysis membrane bio-incompatibility and "CO_2 unloading". The term "CO_2 unloading" covers reflex hypoventilation caused by a CO_2 loss across the dialysis membrane, and/or CO_2 consumption caused by acetate metabolism (acetate dialysis) or as compensation for alkalemia induced by "high" bicarbonate dialysate (bicarbonate dialysis) [4]. Furthermore, many other factors come into play which contribute to the confusion, e.g., the left shift of the oxygen dissociation curve (ODC) caused by the Bohr effect during HD as the patient is made alkalotic, or the direct depressive effect of even the smallest amounts of acetate on the heart-lung function as well as changed metabolism.
2. Another cause is the fact that practically all investigations have been made on a relatively limited number of patients [1], with different patient categories and under varying treatment regimes.
3. With existing technology, it has only been possible to make a limited number of spot measurements during a single HD treatment. No particular interest has been attached to inter and intra-patient variation.
4. The picture is further complicated by inconsistent and inaccurate use of terms used to describe data and results. Terms like hypoxia, hypoxemia and tissue hypoxia are often used as synonyms. Another confusion of terms is caused by the use of "arterial" and "venous". Sometimes the term refers to actual arterial or venous blood, at other times to the blood lines where "arterial" means the blood in the lines from the patient to the dialyzer (unpurified blood)and "venous" refers to the blood in the lines from the patient. These terms are often mixed up with the occurrence of recirculation causing even greater confusion. There are therefore many good reasons why the complex of causes of DAH are far from being mapped.

How to get on?

The first three reasons for our lack of knowledge can only be found through continued research and performance of more major, controlled experiments. The fourth reason can be dealt with immediately.

Terminology of oxygen status

As to inconsistent and inadequate terminology, we can all be more careful using terms and using them stringently and consistently. It is important to indicate exactly where and under what circumstances certain measurements have been made. In many articles the term pO_2 is used, and it is evident that most authors find this term unambiguous, but is it? A recommendation is to use the terminology of oxygen status described by Wandrup [5]. If the following abbreviations are used:

al: arterial line (line leading blood to the dialyzer)

vl: venous line (line leading blood from the dialyzer)

it is always certain that pO_2 (al) is the oxygen tension measured in the line with blood to the dialyzer, and the pO_2(a) is the oxygen tension measured in an artery. That it is ordinarily safe to interpret blood gas parameters obtained from the "arterial" bloodlines as equivalent to those obtained using a conventional arterial puncture [6], does not mean that it is unnecessary to define exactly where the samples have been taken from.

Terminology of recirculation

The most common access to blood vessels in connection with HD is the arterio-venous fistula. In order to prevent misunderstandings and confusion it is recommended that the following definitions be used (Fig. 1) when describing blood gases during HD:

mixed venous: arterial blood mixed with blood from veins;

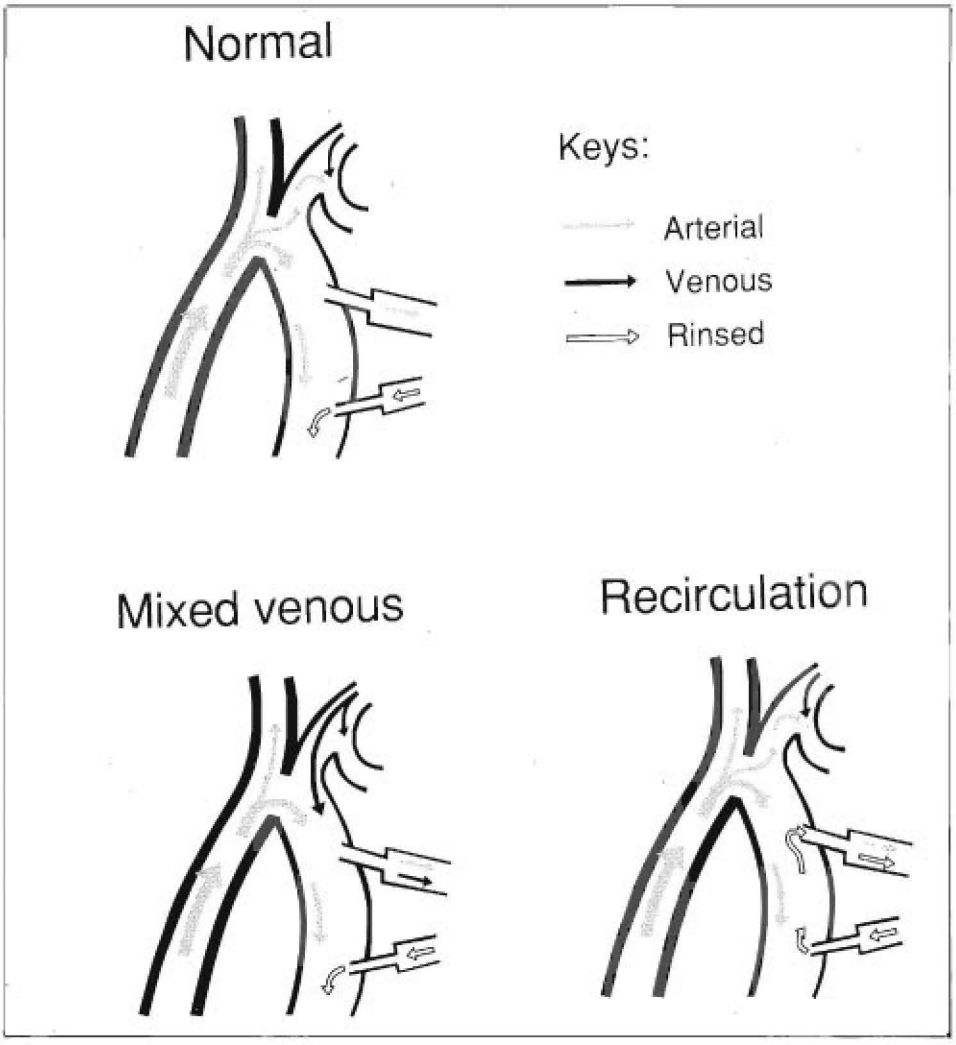
recirculation: mixing with blood that is returned from the dialyzer, i.e., fistula blood mixed with blood from the "venous blood line"(vl).

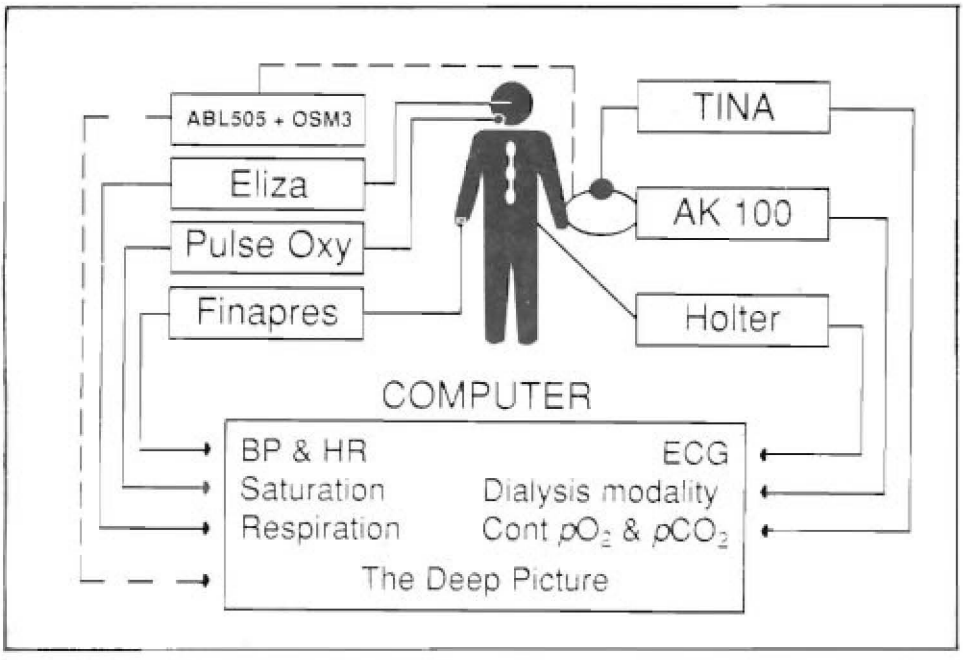
The CORD setup

The CORD project was started with the purpose of evaluating the advantages of continuously monitoring $pO_2$2(al) and pCO_2(al) during HD. CORD is an abbreviation of Continuous Oxygen Registration during Dialysis. It is a cooperation project between the nephrological departments at Hvidovre University Hospital (Copenhagen, Denmark), Lund University Hospital and Park Clinic (Lund, Sweden), and industry represented by Radiometer A/S (Copenhagen, Denmark), and Gambro AB (Lund, Sweden). Further, the project has received financial support from Nyreforeningen (the Danish Renal Association), Anna og Jakob Jakobsens Legat (a private foundation), NOVO's research fund and Cilag A/S.

A standard module (Fig.2) and a standard protocol for collecting the relevant data in connection with investigations into oxygen status and the causes of hypoxia during HD has been developed. A disposable chamber, mounted after the heparin-inlet on the arterial blood line (taking blood from the patient to the dialyzer), was developed for experimental use. In this chamber, a combined pCO_2 and pO_2 electrode is installed to directly measure the blood in the blood line across a 100 SYMBOL 109 f "Symbol"m nylonreinforced silicone membrane. The electrodes are connected to a modified TINAO(Transcutaneous Monitor, Radiometer A/S) to enable continuous monitoring of pO_2(al) and pCO_2(al).

The CORD module further consists of an ordinary PC for which an interface protocol for on-line logging of data (sampling every 5 sec) has been developed. The TINA and the dialysis monitor AK100 (Gambro AB) are





interfaced with the computer so that all parameters are logged. A few of these parameters should be mentioned: fluid removal, blood-flow, blood-detector and added bicarbonate.

Further, the following equipment is interfaced: a Finapress(OHMEDA)- to measure the blood pressure and pulse rate; and ELIZA (Endtidal-CO_2-meter, breathing frequency, Engstrvm) — to register the respiration; a pulse oximeter (OXIO, Radiometer A/S — to measure the oxygen saturation and pulse rate; and a Holter-monitor — to monitor the electrocardiogram.

To validate the continuous measurements of pO_2(al) and pCO_2(al) and measurement of oxygen status of the blood, blood samples are drawn regularly using a heparinized, ventilated syringe for arterial sampling (QS90™, Radiometer A/S) through a pipe stub in the arterial line. These blood samples are determined in duplicate on an ABL505 + OSM3 (Blood gas analyzer + Oximeter, Radiometer A/S) placed close to the patient to minimize pre-analytical errors [7]. Fig. 3 shows a continuous pO_2(al) and pCO_2(al) from TINA, compared with the circular markings of pO_2(al) and pCO_2(al)results from the ABL.

Results

Previous investigations have concentrated on the "average" fall in oxygen tension during HD by means of discrete samples. During continuous measurements in the chamber, we were interested in finding the duration for which pO_2(al) was below 9 kPa (67.5 mmHg) and 8 kPa (60.0 mmHg), respectively [8]. In a pilot project we logged data from the bicarbonate HD treatment of 56 unselected patients in all. Data was logged for a total of 10,819 min. (app. 69 1/3 h) which corresponds to 38.4% of the time, pO_2(al) values below 9 kPa (67.5 mmHg) were registered. For 1,533 min. (app. 26 h) which corresponds to 14.2% of the time, pO_2(al) values below 8 kPa (60.0 mmHg) were registered (Fig.4).

Discussion

Hardly anybody would fail to intervene at a pO_2(a) below 8 kPa (60.0 mmHg) [9,10]. One could object that pO_2(al) was measured instead of pO_2(a). As mentioned before, it is safe to consider pO_2(al) as being identical to pO_2(a) for patients with a well functioning fistula. There were 26 h (14.2 % of the time) of hypoxia that demanded treatment-hypoxia that was almost always reflected in uncharacteristic and diffuse symptoms such as nausea, vomiting, headaches and cramps.

Cardiovascular mortality

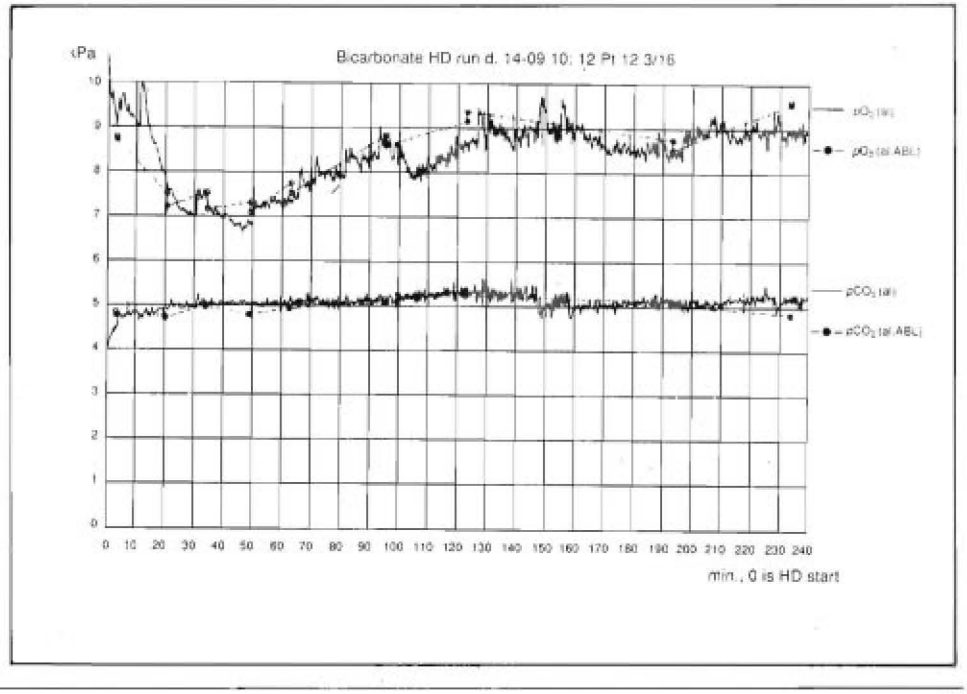
Cardiovascular diseases remain the most common cause of death in RRT (Renal Replacement Therapy) patients.

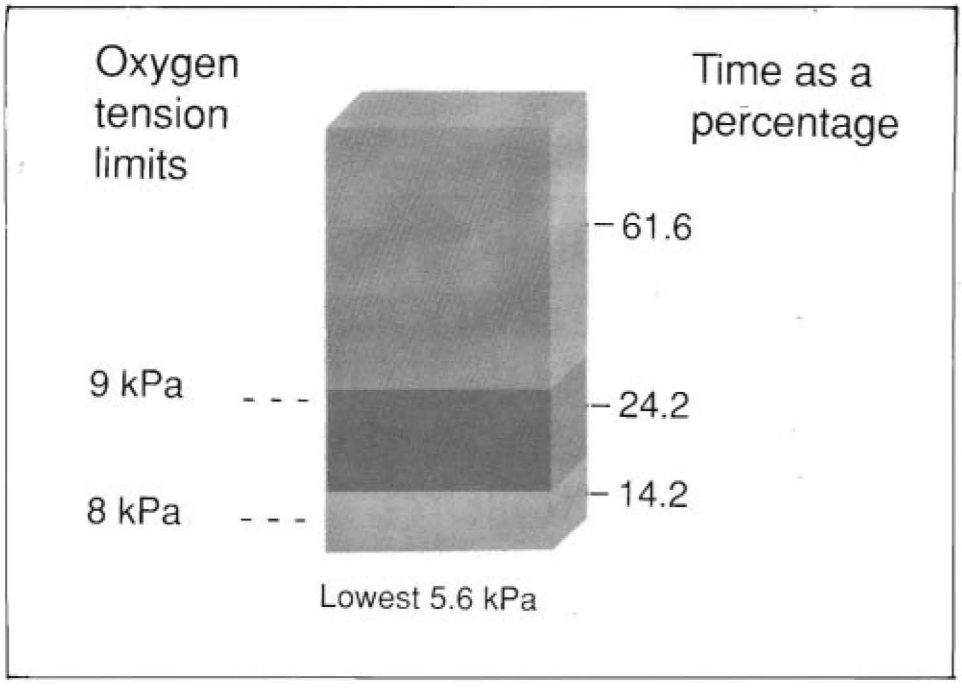
There is a 16-19 fold increase in the death rate from myocardial ischemia and infarction. This increase is present in all age groups, sexes and in both diabetic as well as non-diabetic RRT patients [11,12].

Is hypoxia to blame?

From the sleep apnoea syndrome it is known that there is a high risk of sudden heart arrhythmia and increased cardiovascular mortality due to hypoxemia [13]. It has previously been described how, in certain cases, an oxygen supplement can prevent these symptoms [14].

In this study of the 56 unselected





patients, it was clear that there was a large inter-patient variation; some patients showed practically no fall in pO_2(al), others showed short declines, while some patients show massive continuous falls. However, it should be stressed that measurement of oxygen tension is just one of the parameters necessary for the evaluation of a patient's oxygen status.

Conclusion

Hypoxia during HD is critical, and within the individual departments, the introduction of routine measurements of blood gases during HD should be seriously considered. As a minimum, patients with an increased risk of DAH, e.g., patients with extremes of age, presence of Cardio-and/or pulmonary diseases, should be measured with a view to immediate intervention. Further investigations are needed to explain the causes and co-factors of DAH.

Measurement of oxygen tension alone seems to be insufficient. The Deep Picture, which includes the oximetry parameters, is required to get a full understanding of a patient's oxygen status. This provides the important parameter: oxygen concentration (ctO_2).

In future issues, we hope to be able to tell about our results from the CORD project, among other things, the course of the ODC curve during HD, the dyshemoglobins, and oxygen status.

References:

1. Cardosa M, Vinay P, Vinet B, et al. Am J Kidney Dis 1988; 11(4):281-97
2. Lassen Nielsen A, Jensen HAE, Wandrup JH. Oxygen status: A clinical problem during routine hemodialysis? Blood Gas News 1993; 2(1): 3-5
3. De Broe ME, Heyrman RM, De Baker WA et al. Pathogenesis of dialysis-induced hypoxemia. A short overview. Kid Int 1988; suppl. 24:S57-S61.
4. Ross EA, Nissenson AR. Dialysis-associated hypoxia: Insight into pathophysiology and prevention. Seminars in Dialysis 1988; 1(1):33-39.
5. Wandrup JH. Physiochemical logic and simple symbol terminology of oxygen status. Blood Gas News 1993; 2(1):9-11.
6. Lassen Nielsen A, Brinkenfeldt H, Thunedborg P et al. Assessment of acid base and oxygen status during routine hemodialysis. In press.
7. Avoid errors in arterial blood sampling. Radiometer A/S, Denmark 1992:1-13.
8. Lassen Nielsen A, Jensen HAE, Lokkegaard N et al. Severe hypoxia during hemodialysis. Abstract from the XXIXth Congress of EDTA 1992:130.
9. Ingram Jr. RH. Adult respiratory distress syndrome. In: Wilson JD, Braunwald E, Isselbacher KJ, Petersdorf RG, Martin JB, Fauci AS, Root RK (eds.). Harrison's Principles of Internal Medicine, 12th ed. New York: McGraw-Hill, 1991:1123.
10. Shapiro BA, Harrison RA, Cane RD, Kozlowski-Templin R. Clinical application of blood gases, 4th ed. Chicago: Year Book Medical Publishers, Inc., 1989-82.
11. Raine AEG, Margreiter R, Brunner FP et al. Report on management of renal failure in Europe, XXII, 1991. Nephrol Dial Transplant Suppl 1992;2:7-35.
12. Sforzinin S, Latini R, Mingardi G et al. Ventricular arrhythmias and four-year mortality in haemodialysis patients. Lancet 1992;339:212-13.
13. Rossner S, Lagerstrand L, Persson HE et al. The sleep apnoea syndrome in obesity: Risk of sudden death. J Intern Med 1991;230: 135-41.
14. Ahmad S. Pangel M, Shen M et al. Effects of oxygen administration on the manifestations of acetate intolerance in dialysis patients. Am J Nephrol 1982; 2:256-60.

Anders Lassen Nielsen, MD
Department of Nephrology,
Copenhagen University Hospital Huidovre
DK-2650 Huidovre, Denmark