PULMONARY DIFFUSING CAPACITY IN URAEMIA

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Lung affection in uraemia often remains undiscovered. It manifests itself at least with the onset of alveolar pulmonary oedema (Fig. 1) in patients suffering from marked dyspnoea, where tachypnoea, râles and typical X-ray pictures with diffuse butterfly shadow, leaving the periphery free, are found. However, although in many patients the pulmonary oedema is asymptomatic, and physical examination of the lungs remains normal, the X-ray picture may show interstitial pulmonary oedema (Fig. 2). The present study was undertaken in order to establish whether marked forms of respiratory disturbances are present and detectable in patients with renal failure. In the literature only Erlanson et al. (1961) and Fritz and Lindquist (1961) referred to some aspects of this problem.

![Fig. 1. Alveolar uraemic pulmonary oedema.](image)

**Material and methods**

The study includes 17 patients, aged 24 to 59 years. Their clinical diagnoses are shown in the third figure. Out of 15 males and 2 females, two patients suffered from chronic renal failure due to chronic glomerulonephritis, the other 15 had acute renal failure from various causes. In only 5 of them was interstitial pulmonary oedema revealed by radiology. Nine patients were investigated within 3 months, 8 subjects as late as 9 months after the onset of the disease. In all patients the non-protein nitrogen (NPN) exceeded 100 mg per 100 ml and renal function was markedly impaired at the time of the study.

For spirometry the Prema expirator was used. The functional residual capacity and the 7
minutes nitrogen wash-out values were estimated using the open-circuit method. The nitrogen concentration was measured with the Godart nitrograph. The oxygen saturation of haemoglobin was measured in a Kipp haemoreflector. The oxygen tension was measured with a Beckmann Gas Analysator, using a Clark's electrode. The pH and Pco₂ were determined with a micro-Astrup apparatus. For determination of pulmonary diffusing capacity the steady state carbon monoxide method according to Krogh and modified by Bates was used, by means of the Godart Diffusiontest. The membrane component and the pulmonary capillary blood volume were estimated by the method described by Roughton, Forster and McNeil (1965).

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>ac. glomerulonephritis</td>
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</tr>
<tr>
<td>chron. glomerulonephritis</td>
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<td>intoxication</td>
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<td>crush syndrome</td>
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</tr>
<tr>
<td>postoperative</td>
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<tr>
<td><strong>total</strong></td>
<td><strong>17</strong></td>
</tr>
</tbody>
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*Fig. 3. Clinical diagnosis: includes 17 uraemic patients.*

*Results*

(Fig. 4). A decreased vital capacity (VC), residual volume (RV) and total lung capacity (TLC) were found. The forced expiratory ventilation per sec (FEV₁,₀) was slightly decreased and residual volume/total lung capacity-ratio (RV/TLC in %) was normal. From these values, in 37 per cent of patients there was a suggestion of the presence of a restrictive pneumopathy. In some of the patients the vital capacity (VC) was elevated. Only in one person suffering from chronic bronchitis, a pathologic elevation of RV/TLC ratio and of lung clearance index was found, in other patients it was normal. In 66% of patients a decrease of FEV was present. These evaluations point to the presence of a restriction lesion of ventilation or to an elasticity disorder.
Fig. 4. Spirometric values. Vital capacity—per cent of predicted values, forced expiratory ventilation per 1 sec in percentage of vital capacity, residual volume to total lung capacity-ratio. Normal and limit values are marked by a line.

Fig. 5. Blood gases and pH. Oxygen saturation, arterial oxygen tension, arterial carbon dioxide tension and pH.

(Fig. 5). 80% of patients showed a decreased oxygen tension, less marked in 25%, more marked in 55%, with a decrease below 80 torr. The oxygen saturation was examined in 13 persons, in 15% it was normal, in the other 85% it was decreased. The hypoxaemia persisted several months or years after the onset of uraemia. The arterial carbon dioxide tension was slightly elevated in 20% of the patients. The pH values were below 7.380 in 60% of the subjects.

(Fig. 6). Total pulmonary diffusing capacity (Dl/co) was decreased in 88% of subjects, and normal in 12%. The decrease averaged 55.3%. Empty circles correspond to the patients who were not dialysed, half black circles with 1 to 2 dialyses and dots to patients with three or more. No correlation was found between the changes of total pulmonary diffusing capacity and the number of the dialyses.

The membrane component of the diffusing capacity (Dm) was decreased in 64% of the patients in whom it was investigated. The decrease averaged 58.6% of the predicted value.
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The empty circles correspond to patients with NPN lower than 200 mg%, half black circles to patients with NPN from 201 mg% to 250 mg% and dots to patients with NPN above 250 mg%. No correlation between azotemia and membrane component of diffusion was found.

The pulmonary capillary volume (Vc) was found to be decreased in 73% of 11 investigated subjects. The decrease averaged 51.8%. The patients with haemoglobin less than 8.5 g% are marked with empty circles, with hemoglobin from 8.6 g% to 11.5 g% with half black circles, and patients with haemoglobin concentration above 11.5 g% with dots. No correlation between haemoglobin concentration and the pulmonary capillary volume was found.

From the present results it seems very probable that the alveolocapillary membrane is changed in the course of renal failure. The mechanism is not known. It can be explained as being due to the proliferative interstitial pulmonary changes and hyalinization of the alveolar membrane occurring in the presence of a defect of the activator of plasminogen in the lungs. The depression of the vascular component of diffusing capacity may perhaps be explained by changes of the pulmonary elasticity and by accelerated circulation, due to anaemia, although no relation with haemoglobin concentration was found in the present study.

Summary

In 17 patients suffering from uraemia, spirometry, gas exchange and diffusing capacity and its components were investigated. In 67% a decrease of FEV1.0 and a decrease of arterial oxygen tension in 80% of subjects was found. A markedly decreased diffusing capacity was found in 87% of individuals. Both components of diffusing capacity were decreased, the membrane component in 64% and the capillary component in 73%.

Résumé

Diffusion alvéolo-capillaire des urémiques.

Les fonctions pulmonaires ont été examinées chez 17 malades souffrant d'insuffisance rénale. La spirographie, les échanges gazeux et la capacité de diffusion pulmonaire ont été mesurés. Le volume expiratoire maximal-seconde a été abaissé chez 67% de malades, la tension artérielle d'oxygène a été abaissée chez 80% des sujets et la diffusion alvéolo-capillaire chez 87%. L'affection touchait l'élément membraneux de la diffusion et aussi le volume sanguin capillaire.
REFERENCES


DISCUSSION

The Chairman: Thank you, Dr. Jirka.

Although Dr. Jirka would not like to be pressed too much on the evidence here which he has not himself participated in, we might perhaps have some comments from the floor anyhow.

Is there anybody who wants to make comments on this paper?

Merrill (Boston): We have seen one patient who had twenty months of chronic dialysis, who developed this syndrome and went on inexorably to pulmonary fibrosis and death.

At autopsy, he had diffuse pulmonary fibrosis for which we found no specific cause, which certainly could explain the kind of defect which was noted here and in our patient.

I wonder whether any other members of this audience have seen such a case?

The Chairman: Dr. Scribner, did you notice that?

Scribner (Seattle): We have not seen this problem in any of our patients so far.

The Chairman: Dr. Shaldon, did you see it?

Shaldon (London): It does not appear to be present.

The Chairman: Anybody else working on long-term haemodialysis who has had similar experience to that of Dr. Merrill?

Kenward (Birmingham): Dr. Parsons had a similar case to this in Leeds on one of his transplant cases. The problem was obscured by the fact that the patient was on immunosuppressives.

But this girl died of diffuse pulmonary interstitial fibrosis, when the kidney was apparently still functioning relatively well.

Lindqvist (Sweden): It would have been interesting to follow one patient for a long time with many investigations, to see if a different water content of the lungs can change the situation.

The Chairman: As far as I can see from what Dr. Jirka told us, this contained a study of both acute and chronic patients. Is that right, Dr. Jirka?

Jirka (Prague): Yes.

The Chairman: In the acute cases, there might have been a lot of patients, as Dr. Lindqvist said, who may have been more or less overhydrated, and there might have been changes in their pulmonary function just due to that fact, changes which may have been improved, following dehydration by dialysis.

Do you know whether they were followed, as Dr. Lindqvist asked?

Jirka (Prague): I am sorry, I did not have too much time to discuss the details with the authors. As far as I know there were not only patients with acute renal failure but also with
chronic renal failure. A part of the patients, I think the majority, was investigated as late as eight or nine months after the onset of the improvement, which means that also patients on repeated dialysis, who were dialysed several times, were included in the study.

As far as the comparison between the pre-dialysis and post-dialysis situation is concerned, I do not know, whether this was compared or not.

The Chairman: Thank you. Any other comments?

MacDonald (Brooklyn): Patients acutely ill frequently have pulmonary problems that are not very clear.

Goldsmith (Liverpool): One wonders whether there is any analogy between Dr. Merrill’s case and the syndrome of hexamethonium lung which has been described several times, in which a progressive fibrosis is thought to be due to recurrent minor pulmonary oedema.

The Chairman: Did your patient have hexamethonium Dr. Merrill?

Merrill (Boston): No.

The Chairman: He was off drugs actually, was he not?

Merrill (Boston): He had other drugs but none of the other patients on similar drugs for longer periods of time have had anything like this, and we were at a loss to explain it. We of course thought of the drug aspect but other patients on similar regimens have not developed this.

Kerr (Newcastle): I believe that one interpretation of hexamethonium lung, is that it has nothing to do with hexamethonium, but is due to recurrent episodes of pulmonary oedema from uncontrolled hypertension.

Did Dr. Merrill’s case have controlled hypertension or uncontrolled?

Merrill (Boston): It was another point that we considered. The patient did have hypertension but his defect was one of diffusion. His vital capacity, as Dr. Jirka has shown, was pretty good, and it was purely one of diffusion.

In the autopsy findings, there was one which seemed to be an alveolar-capillary block.