Concentrations of Arsenic, Manganese and Selenium in Peripheral Nervous Tissue of Patients with Uraemia and a Control Group

P. CHRISTOFFERSEN*, ELSE DAMSGAARD†, K. HEYDORN†, N. A. LARSEN*, B. NIELSEN* and H. PAKKENBERG*

* Copenhagen Kommunehospital, Denmark
† The Isotope Laboratory of the Danish Atomic Energy Commission’s Research Establishment, Riso, Denmark

Prompted by the report of Bergström and Wester (1966) to this association that the serum arsenic concentration in uraemic patients was ten times higher than in normal controls, and that the high serum level could be reduced by dialysis, we decided to investigate the possible relationship between abnormal concentrations of trace elements in the tissues of uraemic patients and the development of uraemic polyneuropathy. So far our results have been negative.

Among the trace elements we chose arsenic, manganese and selenium. One reason for this choice was that the concentrations of these three elements could be determined from a single sample of tissue. Other reasons were the elevated serum arsenic concentration in uraemic patients (Brune et al, 1966) and the occurrence of a peripheral polyneuropathy in chronic arsenic poisoning (Harvey, 1965). Chronic manganese poisoning is characterized by a wide variety of neurological symptoms (Mena et al, 1967), and in domestic animals both deficiency and excess of selenium are known to cause neuro-muscular disorders.

METHODS
Specimens for determination of trace element concentrations were taken at autopsy from the pelvic part of the sciatic nerve. Each sample had a weight of about one gram. No metal of any kind was allowed near the specimen. The excision of the samples was performed with plastic knives. The specimens were placed in polyethylene containers and immediately put in a deep-freeze, where they remained until the analysis could be carried out.

The determination of manganese, arsenic and selenium was carried out by neutron activation analysis (Heydorn, 1967) by two of the authors. Samples of one gram were irradiated in the Danish reactor DR 2 at a thermal
neutron flux of $7 \times 10^{12}$ n/cm$^2 \times$ sec for a period of one hour. A radio-
chemical procedure was developed for the separation of these elements after
decomposition of the irradiated material in nitric-sulphuric acid, and measure-
ment of Mn-56, As-76 and Se-81m was done by $\gamma$-ray spectroscopy. Chemical
yield was determined by the addition of Mn-54 tracer, and by re-irradiation of
the separated arsenic and selenium samples. All results are expressed as
parts per billion (p.p.b.) of wet tissue weight.

TABLE I. Distribution of uraemic and control patients according
to sex, duration of renal insufficiency, dialysis treatment
and the presence of polyneuropathy

<table>
<thead>
<tr>
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<th>Sex</th>
<th>Duration of renal insufficiency</th>
<th>Regular dialysis treatment</th>
<th>Uraemic polyneuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>&gt; 5 years</td>
<td>&lt; 5 years</td>
<td>unknown</td>
</tr>
<tr>
<td>Group of uraemic patients</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Group of control patients</td>
<td>3</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

MATERIAL
The clinical data of the patients examined are shown in Table I. The group
of uraemic patients consisted of one woman and five men. Their average age
was 34 years with a range from 19 to 53 years.

In four of the patients an abnormal serum creatinine concentration was
found more than five years before their death. In one patient the duration of
renal insufficiency was three years, and in the last, the duration could not be
established.

Terminally four of the patients were treated with regular peritoneal dia-
lysis for four to eight months. The two other patients received but a few dia-
lyses.

Regular monthly clinical examinations of the uraemic patients by the
neurologist of our group showed a slight polyneuropathy in two patients and
a moderate, rapidly progressing polyneuropathy in one. Three patients had
no clinical signs or symptoms of uraemic polyneuropathy. The polyneuro-
pathy appeared two to four months before death.

Our control group consisted of seven patients with neither clinical nor
autopsy evidence of renal disease and without complaints or signs related to
polyneuropathy. The previous histories of these patients contained no dis-
eases known to be associated with peripheral nerve affections. The age of
the patients ranged from 20 to 86 years with a mean value of 51 years.

From the uraemic patients specimens for neuropathological examination
by light microscopy were taken from the contralateral sciatic nerve at the
same level as that of the specimens for neutron activation analysis. No patho-
logical changes were found in the nerves of the patients without clinically
detectable polyneuropathy. Figure 1 shows a cross section of the sciatic
Figure 1. Cross section of the sciatic nerve from one of the uraemic patients without clinically detectable polyneuropathy. The myelin sheaths are well preserved and uniformly stained. (Stain: osmic acid. Magnification: x 250)

Figure 2. Cross section of the sciatic nerve from the patient with clinically pronounced uraemic polyneuropathy. The poor staining quality of the fragmented myelin sheaths is evident. Some myelinated nerve fibres have disappeared. (Stain: osmic acid. Magnification: x 250)
nerve from one of these patients. The osmic acid stain shows myelin sheaths that are equally and uniformly stained.

The specimens from patients with polyneuropathy usually show demyelination with a relative sparing of the axis cylinders. In our three patients with uraemic polyneuropathy the degree of nerve degeneration correlated well with the severity of the clinical symptoms and signs. Figure 2 shows a cross section of the sciatic nerve from the patient with the most pronounced polyneuropathy.

RESULTS
We have tried to correlate the concentrations of the trace elements to several factors, including uraemia, uraemic polyneuropathy, age and sex of the patients.

**TABLE II.** Mean concentration of arsenic, manganese and selenium in peripheral nervous tissue (parts per billion of wet tissue weight)

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<tbody>
<tr>
<td>Group of uraemic patients</td>
<td>6</td>
<td>8.3 (± 0.9)</td>
<td>49 (± 19)</td>
<td>93 (± 12)</td>
</tr>
<tr>
<td>Group of control patients</td>
<td>7</td>
<td>8.2 (± 1.0)</td>
<td>72 (± 20)</td>
<td>119 (± 29)</td>
</tr>
</tbody>
</table>

Table II shows the mean concentrations of arsenic, manganese and selenium of the peripheral nervous tissue in the patients dying from chronic uraemia and in the control group. The difference between the two groups does not reach statistical significance for any of the three elements.

Polyneuropathy likewise does not seem to influence the level of the three elements in peripheral nervous tissue. Table III shows the patient material

**TABLE III.** Mean concentrations of arsenic, manganese and selenium in peripheral nervous tissue. Patients with uraemic polyneuropathy are compared to patients without clinically detectable nephropathy

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<tr>
<td>Group of uraemic patients with polyneuropathy</td>
<td>3</td>
<td>8.7 (± 1.2)</td>
<td>43 (± 15)</td>
<td>89 (± 18)</td>
</tr>
<tr>
<td>Control group + group of uraemic patients without polyneuropathy</td>
<td>10</td>
<td>8.1 (± 0.9)</td>
<td>67 (± 23)</td>
<td>112 (± 29)</td>
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</table>
divided into a group with polyneuropathy and a group without polyneuropathy. The differences between the mean concentrations for these two groups are not significant.

Furthermore we have compared the mean concentrations of the three trace elements in peripheral nervous tissue of patients younger than 45 years to those of patients above that age, and the mean concentrations of the men to those of the women. In no case was the difference of statistical significance.

With the reservation imposed by the small number of patients hitherto examined, we must conclude that neither uraemia nor the existence of a uraemic polyneuropathy are associated with significant changes in the concentrations of arsenic, manganese and selenium within the proximal part of the sciatic nerve.

We are continuing our investigation, however, both to increase the number of patients examined and to see if different concentrations of the trace elements may be found in peripheral nerves of a more distal position or in the central nervous system.

REFERENCES