Discussion

Because the sulfasalazine procedure used in this study requires no special equipment for determination of acetylator phenotype, it has been described by Schroder (9) as "simplified." However, this method, like other acetylator phenotyping tests, requires the administration of a sulfonamide and collection of a urine or plasma sample a certain interval after ingestion of the drug. This has proved to be unpopular for large-scale population studies. In contrast, because the AFMU/1MX ratio approaches no maximum value and the concentrations of these metabolites are relatively insensitive to variation in oral absorption or renal excretion, the caffeine metabolite test apparently does not require careful monitoring of the amount of caffeine intake or timing of the urine collection (14). For these reasons, and because caffeinated beverages are considered food items and not drugs, subjects ordinarily do not refuse or hesitate to participate in such studies.

Owing to the excellent linearity of the relation between the above parameters for AFMU/1MX, we have shown in this report that this peak height ratio can be used to determine the acetylator phenotype in lieu of the molar concentration ratio, obviating the time and effort needed to prepare the standard curve and calculate this ratio. Indeed, by use of this approach one can accurately and reliably (Table 1) determine the acetylator phenotype in less than 30 min, which is the shortest time reported for such a test, thus making it highly suitable for population studies.

We thank the administration of the King Faisal Specialist Hospital & Research Center for its support of the pharmacokinetics research program at this institution.

References


Concentrations of Some Trace Elements (Se, Zn, Cu, Fe, Mg, K) in Blood and Heart Tissue of Patients with Coronary Heart Disease

O. Oester,1 M. Dahm,2 H. Oelert,2 and W. Prehlitz1

We measured Se, Zn, Fe, Cu, Mg, and K in blood and heart tissue of patients with coronary heart disease. Such patients have subnormal selenium concentrations in serum, whole blood, and (calculated per gram of hemoglobin) erythrocytes. Concentrations of zinc and copper in serum were also subnormal in these patients. Heart tissue collected from these patients during bypass surgery was analyzed for Se, Zn, Fe, Cu, Mg, and K; results are expressed in terms of wet weight and in relation to nitrogen and phosphorus content. Concentrations of these elements in blood are correlated with those in heart tissue. Selenium concentrations in serum correlated positively with those in tissue but not with those in erythrocytes. We found no association between concentrations of zinc, iron, copper, magnesium, and potassium in serum and the corresponding concentrations in heart tissue. There was a moderately positive correlation between the concentration of ferritin in serum and that of iron in tissue. We conclude that the turnover rate for selenium in tissue is similar to that in serum but greater than that for erythrocyte selenium. The concentrations of these six elements in heart tissue are partly correlated with the ejection fraction of the left ventricle.

Additional Keyphrases: ejection fraction · tissue analysis · atomic absorption spectrometry · ferritin

Selenium, an essential trace element, is part of the enzyme glutathione peroxidase (EC 1.11.1.9), which is involved in removal of hydrogen peroxide and lipid peroxides produced during oxidative processes in cells. Glutathione

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Peroxidase is found in all avian and mammalian tissue (1-6). Pathological symptoms of dietary selenium deficiency involving the heart are observed in many animal species. Researchers on animals report that selenium protects the heart against cardiotoxic elements, cardiotoxic xenobiotics, and viral infections affecting the heart (7-9).

Dietary selenium deficiency in Chinese people is associated with an endemic cardiomyopathy called "Keshan disease," which affects primarily children and women of child-bearing age (10, 11). Several clinical studies involving large populations have demonstrated that supplementing the diet with sodium selenite decreases the incidence of Keshan disease significantly (10-13).

In the industrialized West, dietary selenium deficiency is thought to be associated with cardiovascular disease. A prospective epidemiological study done in Finland revealed the selenium concentration in serum to be inversely related to the risk of cardiovascular disease (14, 15). However, other prospective epidemiological studies found no such association (16-19). A clinical investigation of patients with coronary arteriosclerosis noted an inverse correlation between selenium concentration in plasma and the degree of coronary arteriosclerosis (20), a finding our results do not confirm. In our studies, however, the patients with coronary heart disease had, in general, lower concentrations of selenium in serum (21) and in whole blood (22) than did the healthy controls. This was also true for patients with acute myocardial infarction (22, 23).

In all these epidemiological and clinical studies, the selenium concentration in serum was the criterion for the selenium status of the controls and patients. However, it has not yet been proved conclusively that serum selenium concentrations accurately reflect the concentration of selenium in tissue. We therefore decided to investigate the correlation, if any, between the serum selenium concentration and that in tissue. In addition, we quantified the elements zinc, iron, copper, magnesium, and potassium, also widely believed to be involved in heart diseases (24), in serum and tissue, and we report their correlations. We measured some trace-element concentrations in patients with coronary heart disease who underwent bypass surgery.

Materials and Methods

Instrumentation

We determined iron and copper in the samples after wet digestion and determined selenium in serum directly by atomic absorption spectrometry (AAS). We used a Model 5000 AAS equipped with graphite furnace (HGA 500) and Zeeman compensation (Perkin-Elmer Corp., Norwalk, CT).

To determine selenium in tissues after wet digestion, we used the Model 5000 AAS equipped with the hydride system MHS 20 (Perkin-Elmer).

To determine zinc, magnesium, and potassium in the samples after wet digestion, we used a flame atomic absorption spectrometer (Model 420; Perkin-Elmer).

For determinations of nitrogen, we used the Büchi 322 apparatus equipped with control unit 342 (Büchi, Flawil, Switzerland). Electrodeless discharge lamps (all from Perkin-Elmer) were used for determination of selenium and phosphorus, and hollow-cathode lamps for determination of zinc, copper, magnesium, iron, and potassium.

Reagents

Selenium, copper, iron, zinc, magnesium, and potassium standards (Tritosol); HNO₃, HClO₄, and H₂SO₄ ("suprapure" reagents); sodium borohydride "p.a.," sodium hydroxide, and phenanthroline were all from Merck, Darmstadt, F.R.G. As antifoaming agent we used DB 110 A (Dow Corning, Midland, MI). Doubly distilled water, obtained by using Millipore equipment (Millipore Corp., Bedford, MA), was used throughout.

Blood and Tissue Samples

Blood was sampled just before surgery by venipuncture; serum was collected by 10 min of centrifugation after the blood had clotted.

Heart-tissue samples (80-150 mg wet weight), collected from the right auricle during bypass surgery, were stored frozen (−70 °C) until analyzed. All fat and fibrous tissue was removed from the samples. The tissue samples were stored in polyethylene vessels pre-cleaned (with a 10 mL/L solution of 1 mol/L HNO₃ in Triton X-100, washed, and afterwards dried) to avoid contamination.

Determinations in Tissue

Each entire tissue sample was heated (200 °C) with 2 mL of concentrated H₂SO₄ until the reaction solution was clear. The solution was transferred into a volumetric flask and diluted to 10 mL with water. Of this solution we further digested 7 mL with 10 mL of a mixture of HNO₃/HClO₄/ H₂SO₄ (8/2/3 by vol) as described previously (25-28), using a Büchi Digestor 450. After reducing the hexavalent selenium in the reaction mixture with HCl, we transferred the solution into a 50-mL volumetric flask and quantified the selenium, copper, zinc, iron, magnesium, and potassium in this solution. The remaining 3 mL of H₂SO₄-digested sample was used to quantify nitrogen by the Kjeldahl method (44).

Selenium. Selenium was determined by hydride AAS with the MHS 20 system, with phenanthroline as the complexing agent (25-28).

Phosphorus. We determined phosphorus as described previously (20), by graphite furnace AAS, using the platform technique.

Copper and iron. We determined copper and iron by graphite furnace AAS (29), using the platform technique. The instrumental parameters for the AAS 5000 and the HGA 500 were those described previously (29).

Zinc, magnesium, and potassium. Zinc, magnesium, and potassium were determined by flame atomic absorption with the AAS 420 as described previously (29).

Determinations in Serum or Whole Blood

We determined the concentration of protein in serum by using the centrifugal analyser (Cobas Bio) and biuret reagent from Hoffmann-La Roche, Basle, Switzerland. Ferritin in serum was determined with an enzyme immunoassay from Abbott Labs., N. Chicago, IL. Iron was determined with the Cobas Bio and reagents from Hoffmann-La Roche. We determined selenium in serum and whole blood by graphite-furnace AAS, using rhodium as matrix modifier as reported previously (25, 30). Zinc and copper were determined by flame AAS (31). Magnesium and potassium were determined by a standard method, with Zeiss FL 6 atomic and emission spectrometer (Zeiss, Oberkochen, F.R.G.) (31).

Other Procedures

Erythrocyte count, hemoglobin content, and mean cell volume of the erythrocyte were determined with a Coulter S Plus (Coulter Electronics, Hialeah, FL).
The ejection fraction was determined by routine left ventricular angiography from the right anterior oblique view.

The statistical comparisons were performed with the BMDP statistics program, available from W. J. Dixon, Dept. of Biometrics, School of Medicine, Univ. of California, Los Angeles.

Control Groups

The control groups consisted of middle-aged men and women (mean age of the controls 53, SD 8 y), all employees of the University of Mainz. The control groups were matched by sex with the patients with coronary heart disease (25% women, 75% men). They were checked for liver disease, diabetes, and cardiac risk factors, both clinically and by laboratory tests. On the basis of this information, the control subjects were considered to be healthy.

Results and Discussion

Table 1 summarizes our data on trace-element concentrations in serum and whole blood of 27 patients with coronary heart disease, selected for bypass surgery. The mean age of the patients (20 men, seven women) was 54 y (SD 10, range 36–76 y). The mean age of the control group was 53 y (SD 8 y). Because the patient group included more men than women, the male patients were also compared with an age-matched male control group, but this did not change the results and all significant differences remained.

In the patient group, 13 had had coronary heart disease for one year, the other 14 for longer. Nine of the patients had never had myocardial infarction, and 18 had had myocardial infarction in the past; four of the latter had had a reinfarction in the past.

In nine patients two of the three major coronary arteries or their branches were severely affected and in 18 patients all three arteries were affected (all 27 cases had more than 75% blockage). The degree of narrowing was determined independently by two experienced cardiologists.

For all 27 patients, selenium concentrations in serum, whole blood, and erythrocytes were subnormal (Table 1). This agrees with our previously reported results for selenium in whole blood and serum of patients with coronary heart disease and patients with acute myocardial infarction (21–23). Table 1 also lists the selenium concentration in serum per gram of protein, to take into account the binding of selenium to protein, e.g., hemoglobin (27).

Separate consideration of the selenium concentrations of patients with two and three stenosed vessels showed no significant differences in serum selenium between these two groups (Table 1). This is in contrast to Moore et al. (20), who reported an inverse association between plasma selenium and the severity of coronary atherosclerosis, taking the number of stenosed vessels as the criterion for the severity of the disease. We also found a subnormal concentration of zinc and copper in serum in the patients with coronary heart disease (Table 1).

Table 2 summarizes the regression equations and correlation coefficients for the correlation of the trace-element concentrations in serum (and whole blood, for selenium) with the left ventricular ejection fraction of the heart. Our previous results had shown positive correlations of the ejection fraction of the left ventricle with the serum selenium concentrations in two different heart diseases: cardiomyopathy (33) and coronary heart disease (21). In our present

Table 1. Some Trace-Element Concentrations in Serum, Whole Blood, and Erythrocytes of Patients with Coronary Heart Disease and Healthy Controls

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Total patient group (n = 27)</th>
<th>3-vessel disease (n = 18)</th>
<th>2-vessel disease (n = 9)</th>
<th>Healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Se, μg/L</td>
<td>46 ± 19 ± 1.4</td>
<td>51 ± 23</td>
<td>43 ± 16</td>
<td>143</td>
</tr>
<tr>
<td>(28–104)</td>
<td>(30–104)</td>
<td>(28–63)</td>
<td></td>
<td>(50–90)</td>
</tr>
<tr>
<td>Serum Se, μg/g protein</td>
<td>0.94 ± 0.27</td>
<td>1.0 ± 0.24</td>
<td>0.83 ± 0.31</td>
<td>7</td>
</tr>
<tr>
<td>(0.53–1.5)</td>
<td>(0.62–1.5)</td>
<td>(0.53–1.33)</td>
<td></td>
<td>(0.65–1.25)</td>
</tr>
<tr>
<td>Whole-blood Se, μg/L</td>
<td>64 ± 16 ± 0.7</td>
<td>66 ± 23</td>
<td>63 ± 13</td>
<td>125</td>
</tr>
<tr>
<td>(42–120)</td>
<td>(42–120)</td>
<td>(45–75)</td>
<td></td>
<td>(93 ± 15)</td>
</tr>
<tr>
<td>Erythrocyte Se, μg/g Hb</td>
<td>0.29 ± 0.7 ± 0.03</td>
<td>0.28 ± 0.07</td>
<td>0.31 ± 0.1</td>
<td>49</td>
</tr>
<tr>
<td>(0.24–0.46)</td>
<td>(0.19–0.39)</td>
<td>(0.24–0.46)</td>
<td></td>
<td>(0.39 ± 0.11)</td>
</tr>
<tr>
<td>Serum iron, μg/L</td>
<td>878 ± 305</td>
<td>816 ± 300</td>
<td>1036 ± 261</td>
<td>61</td>
</tr>
<tr>
<td>(440–1310)</td>
<td>(440–1300)</td>
<td>(790–1310)</td>
<td></td>
<td>(985 ± 272)</td>
</tr>
<tr>
<td>Serum copper, μg/L</td>
<td>850 ± 230 ± 6</td>
<td>849 ± 261</td>
<td>851 ± 83</td>
<td>64</td>
</tr>
<tr>
<td>(390–1180)</td>
<td>(390–1180)</td>
<td>(710–940)</td>
<td></td>
<td>(1111 ± 340)</td>
</tr>
<tr>
<td>Serum zinc, μg/L</td>
<td>714 ± 206 ± 0.9</td>
<td>710 ± 221</td>
<td>716 ± 226</td>
<td>88</td>
</tr>
<tr>
<td>Serum magnesium, mmol/L</td>
<td>0.85 ± 0.15</td>
<td>0.9 ± 0.17</td>
<td>0.84 ± 0.1</td>
<td>50</td>
</tr>
<tr>
<td>(0.65–1.15)</td>
<td>(0.65–1.15)</td>
<td>(0.75–1.0)</td>
<td></td>
<td>(0.83 ± 0.1)</td>
</tr>
<tr>
<td>Serum potassium, mmol/L</td>
<td>4.5 ± 0.4</td>
<td>4.4 ± 0.4</td>
<td>4.6 ± 0.4</td>
<td>50</td>
</tr>
<tr>
<td>(3.1–5.2)</td>
<td>(3.1–4.9)</td>
<td>(3.2–5.2)</td>
<td></td>
<td>(4.2 ± 0.3)</td>
</tr>
</tbody>
</table>

**Table 2. Correlation of Element Concentrations (x) in Serum and Whole Blood of Patients with Coronary Heart Disease with the Ejection Fraction (y) of the Left Heart Ventricle (%)**

<table>
<thead>
<tr>
<th>Measurement (x)</th>
<th>n</th>
<th>Regression equation</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Se, μg/L</td>
<td>23</td>
<td>y = 0.15x + 55</td>
<td>0.29</td>
</tr>
<tr>
<td>Serum Se, μg/g protein</td>
<td>23</td>
<td>y = 0.14x + 49</td>
<td>0.35</td>
</tr>
<tr>
<td>Whole-blood Se, μg/L</td>
<td>20</td>
<td>y = 0.2x + 48</td>
<td>0.303</td>
</tr>
<tr>
<td>Erythrocyte Se, μg/g Hb</td>
<td>19</td>
<td>y = 0.24x + 58</td>
<td>-0.127</td>
</tr>
<tr>
<td>Serum Zn, μg/L</td>
<td>21</td>
<td>y = 1.5x + 50</td>
<td>0.288</td>
</tr>
<tr>
<td>Serum Cu, μg/L</td>
<td>21</td>
<td>y = 0.17x + 77</td>
<td>-0.472*</td>
</tr>
<tr>
<td>Serum Fe, μg/L</td>
<td>20</td>
<td>y = 0.08x + 55</td>
<td>0.223</td>
</tr>
<tr>
<td>Serum Mg, mmol/L</td>
<td>23</td>
<td>y = -9x + 77</td>
<td>-0.215</td>
</tr>
<tr>
<td>Serum K, mmol/L</td>
<td>23</td>
<td>y = -6x + 89</td>
<td>-0.239</td>
</tr>
</tbody>
</table>

* Correlation significant at P < 0.050.
Table 3. Trace-Element Concentration in Heart Tissue

<table>
<thead>
<tr>
<th>Element</th>
<th>Concen, per gram wet weight</th>
<th>Concen, per mg of nitrogen</th>
<th>Concen, per mg of phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selenium, ng</td>
<td>206 ± 71</td>
<td>10.2 ± 3.7</td>
<td>119 ± 38</td>
</tr>
<tr>
<td></td>
<td>(155 ± 30)*</td>
<td>(7.2 ± 1.4)*</td>
<td>(117 ± 23)*</td>
</tr>
<tr>
<td>Zinc, µg</td>
<td>16.2 ± 3.9</td>
<td>0.76 ± 0.2</td>
<td>9.3 ± 2.7</td>
</tr>
<tr>
<td>Copper, µg</td>
<td>3.5 ± 1.7</td>
<td>0.163 ± 0.82</td>
<td>1.9 ± 0.8</td>
</tr>
<tr>
<td>Iron, µg</td>
<td>121 ± 50</td>
<td>5.7 ± 2.3</td>
<td>65 ± 21</td>
</tr>
<tr>
<td>Potassium, mg</td>
<td>2.0 ± 0.47</td>
<td>0.100 ± 0.026</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Magnesium, µg</td>
<td>112 ± 32</td>
<td>5.7 ± 1.7</td>
<td>69 ± 19</td>
</tr>
<tr>
<td>Nitrogen, mg</td>
<td>21.8 ± 3.4 ±</td>
<td>13.0 ± 46</td>
<td></td>
</tr>
<tr>
<td>Phosphorus, mg</td>
<td>1.8 ± 0.5</td>
<td>0.087 ± 0.031</td>
<td></td>
</tr>
</tbody>
</table>

* Concentration in the left ventricle of hearts of German traffic victims (32).

If the trace-element concentrations in tissue are compared with the ejection fraction, then moderately positive correlations between the ejection fraction and the trace elements selenium, zinc, and copper are found. For phosphorus a more significant relation between the ejection fraction and the phosphorus concentrations of tissue is observed (Figure 1).

Table 4 summarizes the correlation between the selenium concentration in serum with the selenium concentration in heart tissue based on wet weight and on nitrogen and phosphorus content. The selenium concentration in serum is based on the protein concentration, because selenium is bound to proteins such as, for example, hemoglobin (27).

As seen from Table 4 and Figure 2, the serum selenium concentration is consistently and directly correlated with the tissue selenium concentration. The selenium concentration in whole blood also correlated with the tissue selenium concentration but much less significantly. The selenium concentration in the erythrocyte (based on hemoglobin) was not at all correlated with that in the tissue.

The concentrations of iron, copper, zinc, magnesium, and potassium in serum were similarly correlated with the corresponding concentrations in heart tissue, but no significant correlations were observed.

Besides the concentration of iron in serum, parameters related to the iron status in whole blood (the erythrocyte count, the hemoglobin content, and the mean erythrocyte volume) and in serum (ferritin) also were correlated with the iron tissue concentration. The serum ferritin correlated moderately and directly with the concentration of iron in tissue, whereas the other parameters were not correlated.

From these studies we conclude that the selenium concentration in serum of patients with coronary heart disease correlates directly with that in heart tissue, but that in erythrocytes (calculated per gram of hemoglobin) it does not. This difference may be due to the long mean life of the erythrocytes (ca. 100–120 days), whereas heart tissue is a relatively fast-regenerating tissue. Given our recent report (32) that the selenium concentrations in postmortem tissue samples of heart, kidney, liver, and muscle correlate directly and positively with one another, we think it very probable that the serum selenium concentration is in general a good indicator of soft-tissue selenium. A similar conclusion is supported by the data on daily dietary selenium intake in various countries (Figure 3). In New Zealand dietary selenium intake is low, in Germany (34, 35) moderate, in the

![Fig. 1. Correlation between the ejection fraction (EF) of the left ventricle of the heart with the phosphorus content of heart tissue, mg/g, wet weight basis.](image)

Table 4. Correlation of Selenium Concentration in Serum with That in Heart Tissue*

<table>
<thead>
<tr>
<th>Selenium concn in serum (µg/L)</th>
<th>Element concn in tissue (y)</th>
<th>Regression equation</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>µg/L</td>
<td>Se/g WW, ng/g</td>
<td>y = 2.3x + 104</td>
<td>0.604</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Se/mg N, ng/mg</td>
<td>y = 0.1x + 5.2</td>
<td>0.497</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Se/mg P, mg/mg</td>
<td>y = 0.7x + 86</td>
<td>0.345</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td></td>
<td>y = 3.1x - 0.02x^2 + 24</td>
<td>0.439</td>
<td>0.05</td>
</tr>
<tr>
<td>µg/L × (1 - hct)*</td>
<td>Se/g WW, ng/g</td>
<td>y = 3.4x + 105</td>
<td>0.512</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Se/mg N, ng/mg</td>
<td>y = 0.15x + 5.4</td>
<td>0.419</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Se/mg P, mg/mg</td>
<td>y = 1.5x + 72</td>
<td>0.418</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>y = 6.6x - 0.07x^2 - 9.1</td>
<td>0.522</td>
<td>0.01</td>
</tr>
<tr>
<td>µg/g protein</td>
<td>Se/g WW, ng/g</td>
<td>y = 174x + 58</td>
<td>0.660</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Se/mg N, ng/mg</td>
<td>y = 8.5x + 2.4</td>
<td>0.602</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Se/mg P, mg/mg</td>
<td>y = 75.8x + 52</td>
<td>0.540</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* Selenium concentrations in serum are given in µg/L, the total amount of element per liter of whole blood (serum selenium concentration × (1 - hct)), and in element concentration per gram of serum protein. The element concentration in the tissue is based on wet weight (WW), mg nitrogen (N), and mg phosphorus (P). Number of samples compared: 27.

Hct = Hematocrit.
Correlation of the selenium concentration in heart tissue with the selenium concentration in serum, plasma, and whole blood of countries with different daily dietary selenium intake: New Zealand (36, 37), U.S.A. (38, 40), Japan (41–43), and Germany (this study)

U.S.A. adequate, and in Japan high. Figure 3 shows a much steeper increase between the selenium in serum in heart tissue than between that in whole blood and heart tissue.

The concentrations of zinc, copper, iron, magnesium, and potassium in serum show no relevant association with those in heart tissue. This does not exclude the possibility that extreme deficiency or an overload (poisoning) of these elements could not be detected in serum or whole blood and that under these conditions also the tissue might show low or high element concentrations. Selenium, which is mostly bound in proteins—most probably as selenocysteine or selenomethionine—seems to be an exception. One explanation might be the association of selenium content and protein. This is also supported by the result that the correlation between selenium in serum and tissue is best if the serum selenium is related to the protein concentration in serum and the tissue selenium to the nitrogen content of the tissue. The tissue nitrogen content well reflects the protein content of tissue. Perhaps the relation of the selenium concentration to protein concentration (in serum based on the total-protein concentration, in the erythrocyte on the hemoglobin concentration) might be the relevant marker for diagnosis of selenium deficiency.

Fig. 4. Correlation of the ejection fraction of the left ventricle of the heart (y) with the nitrogen/phosphorus ratio in heart tissue

The concentrations of selenium, copper, zinc, and phosphorus in heart tissue are positively correlated with the left ventricular ejection fraction, a measure of the functional capacity of heart. The correlations of selenium, copper, and zinc are moderately good, but the phosphorus content is more strongly correlated with the ejection fraction (Figure 1). The phosphorus content of tissue is mostly determined by the nucleic acid content (DNA, RNA) and the phospholipid content of tissue. Nucleic acids in the cell nucleus and the cytosol, and phospholipids in the cell membrane, are all indicators of metabolically active cells. There was no relevant correlation of the nitrogen content with the ejection fraction but there was an inverse correlation with the nitrogen to phosphorus ratio (Figure 4). An increased nitrogen/phosphorus ratio could be explained by the invasion of fibrous tissue.

We express our gratitude to Mr. D. Draut for technical assistance.

References

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