Enzymes in Renal Diseases

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ABSTRACT

Recent progress is reviewed in the diagnostic enzymology of renal diseases. Enzyme determinations in blood serum are of little value. Activity increases during hemodialysis are most likely due to fluid redistribution. Enzymes are transported from the interstitium via the lymph into the intravascular space where they accumulate.

Determination in the urine of enzymes of the brushborder of the proximal convoluted tubules (e.g., alanine aminopeptidases) and lysosomal enzymes (e.g., β-glucuronidase) aid in the recognition and differential diagnosis of renal diseases. A pattern consisting of alanine aminopeptidase, β-glucuronidase, lysozyme and protein appears to be of particular value.

A recently proposed working hypothesis links enzymuria to the reabsorption in the nephron of lysosomotropic agents, including protein.

Enzyme activity changes in the renal cortex during the acute rejection of kidney transplants in the cat suggest that the kidney loses its potential for fatty acid oxidation, citrate cycle, gluconeogenesis and amino acid transamination and deamination. The potential for glycolysis and hexose monophosphate shunt is maintained. Rejected human kidney transplants show a similar enzyme pattern. More research is necessary before enzyme determinations in renal tissue may be recommended as aids in assessment of the viability of a renal transplant or a conserved kidney prior to transplantation.

In this review of diagnostic enzymology in renal diseases which is limited to more recent perceptions, the subject is divided into three parts: (1) enzymes in blood plasma; (2) enzymes in urine; (3) enzymes in renal tissue.

Enzymes in Blood Plasma

It appears as if diagnostic enzymology in blood plasma offers little in the recognition and differential diagnosis of renal diseases, with the exception perhaps of the renal infarct. However, some recent observations are worth to be mentioned on enzyme activity changes in the serum in chronic renal failure treated with hemodialysis. In 1968 Ringoire reported that LDH-5 (M₄) increases in serum directly following hemodialysis. He believed that this
isoenzyme originated from the diseased kidneys,* despite the fact that human kidney contains comparatively little LDH-5.20 Enzyme activity changes in serum during hemodialysis were reinvestigated in this laboratory, and the scope was broadened to include 11 enzymes.†

AlAT, ALD, AspAT, GGTP, GLDH, G-6-PD, LAP, LDH, MDH, PGDH and SDH were determined in 16 patients over a period of about one year. The total number of dialyses were 82, varying from 1 to 14 for each patient.10

Frequency and direction of the activity changes are shown in figure 1. The considerable differences must be noted which were found between the enzymes. In figure 2 are shown the plotted means of the activities before and after hemodialysis. The changes were statistically significant except for G-6-PDH and PGDH. Again, the differences must be noted between the relative extent of the activity elevations. The mean increase for MDH was about 58 percent as compared to 25 percent for AspAT and less than 10 percent for LAP.

The results rule out simple hemoconcentration as the cause for enzyme activity increases, as has been found in the acute decrease of the plasma volume.11 Blood cells, which are exposed to a considerable mechanical stress during hemodialysis, and the diseased kidneys could be excluded as possible sources of the enzymes. Their respective enzyme activity patterns were inconsistent with the pattern of activity increase in plasma. There is further and direct evidence against the diseased kidneys as enzyme source; the activity changes in plasma following hemodialysis were the same before and after bilateral nephrectomy.

Activity increases of enzymes following hemodialysis could theoretically be caused by the removal of inhibitors. It was confirmed by the present authors that in vitro dialysis of serum from patients and healthy persons against the

* See pages 202 to 206 in reference #25.
† Abbreviation of enzymes with classification numbers (1972) AAP = alanine aminopeptidase, 3.4.11.2 (aminopeptidase, microsomal); AlAT = alanine aminotransferase, 2.6.1.2; ALD = aldolase, 4.1.2.13; AspAT = aspartate aminotransferase, 2.6.1.1; CPK = creatine kinase, 2.7.3.2; GGTP = gammaglutamyl transpeptidase, 2.3.2.2; GLDH = glutamate dehydrogenase, 1.4.1.2; β-Glu = β-glucuronidase, 3.2.1.31; G-6-PDH = glucose-6-phosphate dehydrogenase, 1.1.1.49; LAP = leucine aminopeptidase, 3.4.11.1 (aminopeptidase, cytosol); LDH = lactate dehydrogenase, 1.1.1.27; MDH = malate dehydrogenase, 1.1.1.37; NAG = β-N-acetylglucosaminidase, 3.2.1.30; PGDH = phosphogluconate dehydrogenase, 1.1.1.44; SDH = sorbitol dehydrogenase (= iditol dehydrogenase), 1.1.1.14.
dialysis medium had no significant effect on the enzyme activities.

Although the plasma volume remains constant in most instances during hemodialysis, the organism loses intracellularly and interstitially retained water. It is conceivable that with the redistribution of fluid, enzymes are transported via the lymph from the interstitium into the intravascular space where they accumulate during hemodialysis. It is known from animal experiments that the enzyme patterns of the lymph (as the reservoir of the interstitial fluid) differ considerably from that of the blood plasma. An increased flux of enzyme containing lymph into the plasma must therefore result in changes of the intravascular enzyme activity pattern.

Although there is no evidence at present, another reason for the observed effect should be considered,—namely a temporary inhibition of the elimination of enzymes during hemodialysis.

Wong et al also reported pre- and post-hemodialysis data on 29 patients with endstage renal failure. Statistically significant activity increases were found for amylase (10 percent), LDH (20 percent) and alkaline phosphatase (7 percent). Rises of AspAT (5 percent) and CPK (8 percent) were not significant. Since serum albumin was also increased by 14 percent, it is believed that the activity changes were the result of hemoconcentration. It should not be forgotten, however, that plasma proteins are as much subject to redistribution between the interstitial and intravascular space as the enzyme proteins.

**Enzymes in the Urine**

Three comprehensive reviews of enzymes in the urine have been published within the past decade. In addition, the proceedings of the symposium, “Enzymes in Urine and Kidney,” deal with many different aspects of enzymuria not only in the papers, but also in the printed discussions.

From the author’s review, the conclusions about the origin of enzymes in urine can be summarized as follows: Renal tissue must be regarded as the main source of enzymes in the urine. The comparison of quantitative enzyme activity and distribution patterns in the nephron with the activity patterns in urine may help to localize lesions within the nephron. Of the enzymes present in serum, only those with molecular weights smaller than about 69,000 are filtered in the glomeruli; small amounts which escape reabsorption in the nephron appear in the final urine. Increased renal clearance of serum enzymes in renal diseases should depend, at least theoretically, on the type of protein clearance of which selective and more or less unselective types are distinguished.

In the selective type only the smaller of the serum proteins pass the glomerular filter. In the most extreme unselective type, however, the urine contains proteins in proportions almost equal to serum. It is possible to roughly estimate how much LDH of the serum would appear in the urine in unselective protein clearance. One milliliter of serum with 70 mg of total protein contains approximately 100 mU of LDH. Consequently, in proteinuria about 1,400 mU would be excreted per gram of protein. This amounts to only about 10 to 20 percent of the normal LDH activity present in the 24 hour urine volume (upper limit about 13,000 under comparable assay conditions).

Although erythrocytes and leucocytes are potential sources of certain enzymes in urine, their contribution has probably been overestimated. Microorganisms apparently do not contribute to the enzymes most commonly measured in the urine.
As the result of the literature review and personal laboratory experience, a rather cautious view has been expressed by the author as to the value of enzyme measurements in the urine in the diagnosis and differential diagnosis of renal diseases. Not only does urine constitute a very unfavorable environment for enzymes, but it also contains enzyme inhibitors, not all of which can be removed by dialysis. Most importantly, enzymuria is rather unspecific in renal diseases and enzymes may also be elevated in extra-renal diseases.

More recent experiences have confirmed that little can be gained from measuring metabolic enzymes such as LDH, MDH, AspAT and others in the urine. The focus shall therefore be on enzymes of the brushborder of the proximal convoluted tubules (GGTP and AAP), on lysosomal enzymes (β-Glu and NAG) and on lysozyme which, owing to its molecular weight of approximately 15,000, is filtered in the glomeruli and almost quantitatively reabsorbed by the intact nephron. Rather then giving another comprehensive review, publications were selected which, in the author's opinion, indicate that urinary enzymes may eventually find their place in the diagnostic enzymology of renal disease.

For the removal of inhibitors the dialysis of the urine may be replaced by gel filtration. Since the urinary excretion of enzymes varies with the fluid volume, timed urine collections (8 hrs overnight or 24 hrs) are necessary to eliminate the effect of diurnal variations. Several investigators now use urinary creatinine as this reference for enzyme quantitation; this makes possible the use of spot urine samples.

To weigh the excretion of tubular enzymes in kidney diseases it is useful to consider two patho-biochemical principles: (1) alterations of the cell membrane and (2) changes of the rate of enzyme synthesis in tubular cells. In acute lesions, disturbances are expected of the integrity of the cell membranes and, consequently, of the increased excretion of tubular enzymes. In chronic processes of long duration with a predominantly degenerative component, the biosynthesis of enzymes may be impaired and the urinary excretion of tubular enzymes reduced.

**Gamma Glutamyl Transpeptidase**

Methodical details for the determination of GGTP in the urine with L-γ-glutamyl-p-nitroanilid as substrate were published by Szasz. Urine contains heatstable dialyzable inhibitors. Inhibition shows considerable inter- and intra-individual (from day to day) fluctuations and is more pronounced in males than in females. The maximum inhibition may be as high as 70 percent. The GGTP activity in urines of males is about 50 percent higher than in the urine of females. The excretion during the night is higher than during the day.

GGTP excretion was studied in kidney diseases by Levy and Dubach, Thiele and Kley et al. These investigations have several results in common: (1) a positive correlation between GGTP excretion and creatinine clearance (Ccr) and urea clearance, respectively, both in the presence and absence of renal diseases; (2) diminished excretion in patients with chronic nephropathies, in proportion to the remaining active parenchyma; and (3) a normal or increased excretion in acute renal diseases.

When Thiele expressed his data on patients with chronic kidney diseases as the ratio GGTP/Ccr, he found that 80 percent were outside the normal tolerance limits while only 37 percent were above the normal limits when GGTP activity was calculated per unit urine volume. Similar observations were made by Beck
and Chaudrin with GGTP\textsuperscript{9} and by Farr et al in regard to lysozyme excretion.\textsuperscript{9} The ratio GGTP/C\textsubscript{cr} was described as a useful parameter in recognizing the rejection of renal transplants.\textsuperscript{29}

The activity of GGTP in renal cortex and medulla is very much higher than in other tissues, except in leucocytes.* In malignant renal tumors, the activity is much lower than in healthy tissue.\textsuperscript{2,15} Hautmann et al\textsuperscript{15} found, in all 16 cases which they studied, a significantly reduced excretion of GGTP in catheter urine from the side of the tumor. LDH in urine was elevated in all 16 cases. Other enzymes from a larger pattern showed less frequent and mostly less pronounced increases in the urine.

\section*{N-Acetyl-\(\beta\)-Glucosaminidase}

The urinary excretion of NAG was studied by Wellwood et al\textsuperscript{32} in 36 patients with acute and chronic renal diseases. NAG was found to be a sensitive indicator of renal damage. Extremely high values were observed in acute renal failure following hypotensive episodes. In chronic pyelonephritis, the urinary NAG activity was normal when serum creatinine was normal, but it was increased with creatinine retention. In chronic glomerulonephritis, the urinary NAG elevation was independent of the serum creatinine levels. This enzyme behaves very similar to \(\beta\)-Glu (table II). An elevation of urinary NAG may be the first evidence of acute renal transplant rejection and more reliable than activity changes of other enzymes.\textsuperscript{31}

\section*{\(\beta\)-Glucuronidase}

Gonick et al\textsuperscript{13} investigated the urinary excretion of \(\beta\)-glu in 245 patients with renal diseases of diverse causes. According to their results (table I), it appears possible to distinguish active from inactive forms of renal diseases, to distinguish carcinomas from cysts and to detect renal graft rejections. The results agree well with those shown in table II.

\subsection*{Alanine Aminopeptidase}

This enzyme is present in many organs and in serum and urine of healthy persons while in the kidney it is concentrated in the brush border of the proximal convolutions. The AAP of the serum has the same fast electrophoretic mobility towards the anode as the liver-AAP, while the AAP in urine moves slightly towards the cathode, as does the renal AAP. Both the enzymes in urine and in kidney have identical immunochemical and biochemical characteristics. The molecular weight of AAP is approximately 230,000 and the enzyme is not filtered by the intact glomeruli. The appearance of the serum fraction in certain renal diseases with massive proteinuria has been demonstrated.\textsuperscript{23} Urinary excretion of AAP appears to be a sensitive indicator of tubular damage, more sensitive than the excretion of other brush-border enzymes, AP and GGTP. Peters et al\textsuperscript{23} have demonstrated that the determination of AAP isoenzymes in the urine can improve the diagnostic value of AAP in renal diseases. In this pilot study with 67 patients, total urinary AAP was elevated in most cases of acute and chronic renal diseases. In predominantly tubular nephropathies, the kidney AAP prevailed; however, in predominantly glomerular diseases the serum enzyme was found in addition to the kidney fraction or, in a few instances, the serum fraction only. The excretion of the serum-AAP was associated with massive proteinuria and disappeared from the urine after remissions.
TABLE I

Statistical Summary of Urinary β-Glucuronidase Activities*

<table>
<thead>
<tr>
<th>Disease</th>
<th>n</th>
<th>&gt;30</th>
<th>&lt;30</th>
<th>Mean</th>
<th>SD</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals</td>
<td>41</td>
<td>1</td>
<td>40</td>
<td>14.4</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Active glomerulonephritis§</td>
<td>38</td>
<td>31</td>
<td>7</td>
<td>70.0</td>
<td>50.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inactive glomerulonephritis</td>
<td>25</td>
<td>9</td>
<td>16</td>
<td>32.4</td>
<td>20.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>44.3</td>
<td>25.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Active pyelonephritis§</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td>61.9</td>
<td>39.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inactive pyelonephritis</td>
<td>13</td>
<td>2</td>
<td>11</td>
<td>24.0</td>
<td>7.8</td>
<td>NS</td>
</tr>
<tr>
<td>Acute tubular necrosis</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>148.1</td>
<td>158.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal adenocarcinoma</td>
<td>17</td>
<td>17</td>
<td>0</td>
<td>42.8</td>
<td>6.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal cysts</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>17.9</td>
<td>12.8</td>
<td>NS</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>17</td>
<td>8</td>
<td>9</td>
<td>35.2</td>
<td>21.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>1 to 3 days post transplant</td>
<td>27</td>
<td>27</td>
<td>0</td>
<td>102.9</td>
<td>38.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3 weeks post transplant</td>
<td>22</td>
<td>16</td>
<td>6</td>
<td>32.2</td>
<td>9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute homograft rejection</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td>144.2</td>
<td>124.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Observation of patients with various renal diseases.
†X² for multiple comparisons.
§Comparison of active vs inactive glomerulonephritis: P<0.001.
#Comparison of active vs inactive pyelonephritis: P<0.001.

The group of patients with both serum and tubular AAP in urine could be divided into two subgroups, I and II. In subgroup I, the tubular fraction either prevailed or was slightly lower than the serum AAP. In subgroup II, the serum enzyme was stronger and the renal fraction was close to the "normal" range. The authors emphasize that this should not be interpreted as the indication of an intact tubular epithelium but rather as a sign of cell degeneration with impaired enzyme biosynthesis. In the few cases with advanced renal disease in which only the serum AAP was present in the urine, the tubular degeneration had probably reached the stage of severely reduced enzyme synthesis.

The parenteral application of manitol, dextran, certain x-ray contrast media and aminoglycoside antibiotics provokes the release of enzymes into the urine. They have no effect, however, on the healthy kidney. Of the three enzymes, AAP, β-Glu and Lysozyme, a regular but transitory

TABLE II

Protein and Enzyme Constellations in Renal and Primary Extrarenal Diseases

<table>
<thead>
<tr>
<th>Disease Group</th>
<th>Proteinuria</th>
<th>Aminopeptidase</th>
<th>β-Glucuronidase</th>
<th>Lysozyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute renal failure</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>x</td>
</tr>
<tr>
<td>Pyelonephritis, acute exacerbation</td>
<td>+</td>
<td>+</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Chronic pyelonephritis without retention</td>
<td>x</td>
<td>x</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic pyelonephritis with retention</td>
<td>x</td>
<td>x</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic glomerulonephritis with nephrotic syndrome</td>
<td>++</td>
<td>+</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Chronic glomerulonephritis without retention</td>
<td>x</td>
<td>x</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic glomerulonephritis with retention</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hyperthyreosis</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Virus hepatitis (one week)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Benign bile duct occlusion</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Malignant bile duct occlusion</td>
<td>x</td>
<td>++</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
elevation was observed of the renal AAP in patients with chronic pyelonephritis together with various degrees of proteinuria. Additional material may be found in the bibliography of Burchardt et al.4

**Lysosomotropism and Enzymuria**

Burchardt et al3 proposed an interesting and stimulating working hypothesis for the changes of enzyme excretion in the urine. This hypothesis links enzymuria to lysosomotropism, which was recently reviewed by DeDuve and coworkers.5

Among the lysosomotropic substances which were found to provoke enzymuria are mannitol, dextran, certain x-ray contrast media, aminoglycosid antibiotics, bile acids and proteins.3,4

Out of a larger spectrum of enzymes which are elevated in various diseases and after the administration of lysosomotropic agents,4 Burchardt et al3 selected AAP (representative of the brushborder enzymes), β-Glu (lysosomal enzyme) and lysozyme (filtered in the glomeruli and reabsorbed by the tubular epithelium).

The activity pattern of these enzymes, together with the degree of protein excretion, provides information in renal and primary extrarenal diseases and allows one to assess the type of glomerular and tubular lesions. As may be expected, this pattern does not permit one to draw conclusions as to the nosologic diagnosis (table II).

These results and observed effects of lysosomotropic agents provided an explanation of the release of enzymes into the urine (see also figure 3). The lysosomotropic substances in the primary urine, including the physiologically filtered serum proteins, are taken up into the tubular cells by endocytosis (pinocytosis). The endocytic vesicles combine with lysosomes which contain digestive enzymes. As is pointed out by DeDuve, overdosing of the lysosomes, particularly after administration of slowly or undigestable substances, may lead to severe degenerative alterations of the cells.

The process of endocytosis and digestion, according to the theory of Burchardt et al, entails the release of cell enzymes into the urine. Increased glomular filtration of lysosomotropic agents, e.g., protein causes increased release of enzymes.

The reabsorption of filtered protein and lysozyme is reduced in cases of a domineering atrophy of the tubular cells and results in proteinuria and lysozymuria with a relatively low excretion of lysosomal (digestive) enzymes. In acute renal failure, as is to be expected, all groups of enzymes appear for a short period of time in large amounts in the urine. In nephropathies with equally increased protein filtration and reabsorption, digestive cell enzymes may be elevated without concomitant proteinuria. A correlation can therefore not be expected between protein and enzyme excretion. It is not necessary, in the author's opinion, to assume that enzyme release inevitably depends on tubular cell lesions which are associated with reduced tubular function.

In reviewing this working hypothesis which Burchardt et al. have put forward for discussion, there are no difficulties in understanding the proposed mechanisms under pathological conditions, i.e., increased filtration of protein and/or lysosomotropic substances. Considering the physiological excretion of brushborder and lysosomal enzymes, however, one may wonder if the normal protein reabsorption can actually be held responsible. Could the normal amounts of tubular cell enzymes in the urine not be explained sufficiently by physiological cell turnover?

Other questions concern cytoplasmic enzymes. The theory mentions brushborder and lysosomal enzymes. It has been observed that lysosomes, after "ingesting" of lysosomotropic substances, are extruded into the tubular lumen (exostosis). This would explain the appearance in the
Figure 3. Concept of the correlation between the reabsorption of lysosomotropic agents by the tubular epithelium and urinary excretion of protein and enzymes.

- E = tubular enzymes; □ P = protein; □ Lys = lysozyme; □ lysosomotropic agents.

- A. Physiological condition: tubular reabsorption of protein filtered in small amounts by the glomeruli; consecutive release of small amounts of cell enzymes; lysozyme filtered by the glomeruli is almost completely reabsorbed.

- B. Increased glomerular filtration of protein with increased reabsorption and increased release of cell enzymes.

- C. Filtration of lysosomotropic agents which compete with protein in the reabsorption; the excretion of protein and cell enzymes is increased.

- D. Nephrocirrhosis of various genesis: the protein concentration is elevated in the reduced volume of the glomerular filtrate; the reabsorption of protein is diminished; depending on the degree of the tubular epithelium the release of cell enzymes is decreased; the reabsorption of lysozyme is diminished.

- E. Caused by the disintegration of the tubular cells serum and cell enzymes and serum and structural proteins appear in large amounts in the final urine.

Enzymes in Renal Tissue

Although quantitative activity and distribution patterns have been determined in the human nephron, observations in renal diseases are scarce. The results do not correlate with certainty the enzyme activity changes with functional impairments.

In a cooperative study, enzyme changes correlated with functional and morphological parameters have been investigated during the acute rejection of kidney transplants in the cat. The enzyme pattern was selected so as to permit an assessment of the potentials of various metabolic pathways. Directly after unilateral nephrectomy, a kidney from a donor animal was transplanted. Enzymes were determined in the transplanted kidney and the contralateral kidneys of both the recipient and the donor. Two to three animals were sacrificed on each of the ten days following the transplantation. Owing to the number of samples that had to be processed, nephron dissection was done only in selected cases. In the remainder, enzyme activities were determined in extracts from the renal cortex. The results suggest that during acute rejection, the kidney loses its potential for fatty acid oxidation, citrate cycle, gluconeogenesis and amino acid trans-
and deamination. In addition, the potentials of glycolysis and hexose monophosphate shunt are maintained.

A representative example, e.g., the activity changes of hydroxyacyl CoA dehydrogenase (fatty acid oxidation), is shown in figure 4. Note that the activity in the healthy contralateral kidney increases slightly (compensation?). The changes are about equal in the proximal and distal convolutions as determined in microdissected samples of these nephron structures. A comprehensive publication is in preparation including light- and electron-microscopy, scintigraphy and other functional parameters. Preliminary results are available.22

Preliminary studies in this laboratory on acutely rejected human renal transplants showed very similar results. Gregoire and Gepts14 found the same trend of enzyme activity changes in the dissected parts of the nephron of long surviving human kidney transplants. The transplants had to be removed because of progressive and irreversible renal failure.

It is conceivable that an “enzyme status” which permits the assessment of metabolic changes in the transplanted kidney may help in making the decision as to whether or not a transplant should be removed during a rejection crisis. Tissue in amounts obtained by needle biopsy are more than sufficient to determine enzymes in dissected parts of the nephron with ultramicro techniques. These investigations can be done only in laboratories that specialize in these methods. More research with human transplants is essential before this technique may be recommended as a diagnostic procedure.

This concept may also be applied to assess the viability of conserved kidneys prior to transplantation. This type of research is costly and, regrettably, funds are not readily available at the present time.

References


