Levels of Serum Ribonuclease as an Indicator of Renal Insufficiency in Patients with Leukemia

Richard L. Humphrey, Timothy P. Karpetsky, Edward A. Neuwelt, and Carl C. Levy

SUMMARY

Serum ribonuclease (RNase) levels were measured in 29 patients with leukemia at various times during their illness and compared with 54 normal controls and 28 nonleukemic patients on chronic hemodialysis. Eighty-three percent of the leukemic patients examined before therapy and with normal rates of glomerular filtration (as defined by creatinine clearance greater than 60 ml/min) had RNase levels that fell within the mean ± 2σ for the normal controls. Sixty-one percent of the leukemic patients, studied at various times during the course of their illness, who had a creatinine clearance of >60 ml/min had RNase levels in the normal range. Ninety-three percent of the leukemic patients studied with a creatinine clearance of <60 ml/min had RNase levels above the range established for the normal controls. Patients without leukemia, but on hemodialysis for chronic renal failure of varied etiologies, had markedly elevated serum RNase levels. A strong correlation between RNase levels and renal insufficiency is therefore demonstrated, illustrating that changes in RNase levels over periods of time depend on the rate of glomerular filtration and are not related to the extent of leukemia. The enzyme responsible for enhanced RNase activity as glomerular filtration rate declines is shown to be antigenically similar, if not identical, to the enzyme found in normal human plasma. In conclusion, serum RNase levels are an indication of the rate of glomerular filtration and are not a biomarker for the presence or extent of leukemia.

INTRODUCTION

In an earlier report, the extensive purification and characterization of an RNase from human plasma have been described. The enzyme, exhibiting a strong predilection for the hydrolysis of internucleotide bonds containing cytidylic acid, is in many respects quite similar to other RNases isolated from a number of sources. Enzyme activity may, for example, be regulated by changes in ionic strength, by additions of polyamines to the reaction mixture, and by the naturally occurring polynucleotide, polyadenylic acid.

Enhanced levels of the RNase have been reported in patients suffering a variety of disorders including neoplastic ones. Of special interest in this latter category is that the high plasma RNase levels obtained in certain types of leukemia (1, 5, 26, 33, 34) have been suggested as a potential diagnostic biomarker for this disease. A similar proposal, using plasma RNase activity as an indicator of disease or as an index of response to therapy, has been made for multiple myeloma. However, renal impairment is often seen as a characteristic feature of this disease. Since plasma RNase levels are known to rise significantly in a variety of renal disorders, it has been suggested and demonstrated subsequently that plasma RNase levels from multiple myeloma patients correlate well with values and reflect, therefore, rate of glomerular filtration and cannot be used either to indicate the presence of, or the extent of, plasma cell tumor. Since renal failure was not evaluated in the leukemia studies mentioned above, we examined RNase levels in patients with the acute and chronic forms of both lymphocytic and myelogenous leukemia, many of whom had concurrent renal impairment of various etiologies. Our findings indicated that in the great majority of cases studied, there was a direct relationship between plasma RNase levels and the status of the rate of glomerular filtration as estimated by CCr. Thus, irrespective of the type of leukemia studied, plasma RNase levels were elevated if there was concomitant renal insufficiency. Furthermore, because at least 2 antigenically distinct classes of human RNases exist, the enzyme produced in cases of renal failure was tested immunologically. These studies revealed that the elevated levels of RNase result from production of an enzyme that is antigenically similar, if not identical, to that normally present in human plasma.

MATERIALS AND METHODS

Normal Controls

Sera were obtained from volunteer blood donors in The Johns Hopkins Blood Bank or from volunteer donors in the leukopheresis program at The Johns Hopkins Oncology Center Research Unit.

Cancer Patient Population

Sera and/or plasma samples (anticoagulated with 144 mg

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2 To whom requests for reprints should be addressed.
3 Present address: Division of Neurosurgery, University of Texas Southwestern Medical School, Dallas, Texas 75235.
4 The abbreviations used are: CCR, creatinine clearance; BSA, bovine serum albumin.
tripotassium EDTA per dl) were obtained from patients undergoing investigation and/or treatment at The Johns Hopkins Oncology Center Research Unit located at The Baltimore City Hospitals and were stored frozen (−20°) until studied. There were 13 patients with acute myelogenous leukemia, 10 patients with acute lymphocytic leukemia, 6 patients with chronic myelogenous leukemia, and 20 patients with multiple myeloma. All studies were done at least 4 weeks after prior chemotherapy. Eighteen patients were studied. There were 13 patients with acute myelogenous leukemia, 10 patients with acute lymphocytic leukemia, 6 patients with chronic myelogenous leukemia, and 20 patients with multiple myeloma. All studies were done at least 4 weeks after prior chemotherapy. Eighteen patients were selected for more intensive analysis and were studied at intervals of 1 to 3 days throughout the course of their hospitalization and treatment.

**Patients with Renal Failure**

Sera were obtained from 28 patients during the course of routine studies performed while they were on chronic periodic hemodialysis in the Renal Unit at The Baltimore City Hospitals.

**Routine Chemistry Determinations**

Serum and urine creatinine levels and C_{cr} from 24-hr urine collections were determined by the clinical laboratories at The Baltimore City Hospitals, using standard techniques. C_{cr} determinations were performed on days bracketing the day on which an RNase level was measured. Anomalous values of C_{cr}, due to incomplete collections of urine, were rejected.

**Reagents**

Potassium polycytidylate was obtained from P-L Biochemicals, Inc., Milwaukee, Wis. BSA was obtained from Miles Laboratories, Inc., Elkhart, Ind. Pharmacia Fine Chemicals, Piscataway, N. J., provided cyanogen bromide-activated Sepharose 4B. The supplier of yeast RNA (Type XI) was Sigma Chemical Co., St. Louis, Mo.

**Assay of Human Serum RNases**

**Plasma-Type Enzyme.** The standard assay system contained 1.5 μmoles of potassium polycytidylate, 100 μmoles of Tris-HCl buffer, pH 7.5, 0.5 mg of BSA, and enzyme in a total reaction volume of 1 ml. After incubation for 7.5 min at 25°, the reaction was stopped by the addition of 1 ml of 2 N perchloric acid, and the reaction tube was chilled for at least 10 min in an ice bath. The cloudy reaction mixture was clarified by centrifugation (10 min at 45,000 × g), and the absorbance of the acid-soluble nucleotides was measured at 260 nm (32). One unit of RNase activity is defined as that amount of enzyme needed to produce an increase in absorbance of 1.0 under the conditions of the assay. All determinations were done in triplicate, with a standard error of the mean that was, in all cases, less than 10% of the mean. If the increase in absorbance of the acid-soluble nucleotides generated during the assay procedure was less than 1.8 absorbance units at 260 nm, a linear relationship between enzyme concentration and the increase in absorbance was found. Therefore, where applicable, the enzyme solution was diluted with distilled water to assure that the increase in absorbance as a result of the assay procedure would be less than 1.8 absorbance units. This assay procedure was utilized to obtain the data displayed in Charts 1 to 6.

**Liver-Spleen-type Enzyme.** The standard assay system for the liver-spleen-type enzyme differed from that of the plasma-type RNase in that the reaction mixture contained 0.25 mg of yeast RNA, 100 μmoles of sodium phosphate buffer (pH 6.0), 0.5 mg of BSA, and enzyme in 1 ml. After incubation at 25° for 15 min, enzyme activity was determined as above.

**Preparation of Immobilized Antisera**

Antisera to human liver RNase and to human pancreatic RNase were prepared by independently injecting each purified enzyme (9, 32) directly into the popliteal lymph nodes of New Zealand White rabbits (29). In each case, the presence of antibody was verified by precipitation of immune complexes with 33% saturated cold (NH₄)₂SO₄ solution (29). The respective antisera, as well as preimmunization sera, were conjugated independently to cyanogen bromide-activated Sepharose 4B as described previously (28).

**Binding of RNases to Immobilized Antisera**

The standard reaction mixture for measuring enzyme binding to antibody consisted of 4.5 units of enzyme, 0.9 mg of BSA, and sufficient 0.85% sodium chloride solution to bring the volume to 0.4 ml. To this mixture was added 0.2 ml of either pre- or postimmunization serum conjugated to Sepharose 4B and 0.4 ml of 0.02 M Tris-HCl buffer, pH 7.5. After incubation at 4° for 30 min, the Sepharose was allowed to settle, and an aliquot (0.3 ml) of the supernatant solution was examined for both liver-spleen and plasma types of RNase activity as described above.

**RESULTS**

**Correlation of Renal Function and Serum RNase Concentration.** The distribution of RNase levels did not vary significantly with the form of leukemia studied (Chart 1). Therefore, results obtained from patients with different types of leukemia were pooled and examined from the viewpoint of rates of glomerular filtration (estimated by C_{cr}). The patients with leukemia having C_{cr} > 60 ml/min had serum RNase levels that ranged from 28.0 ± 0.3 to 154.0 ± 4.8 units/ml/min, with a mean of 70.3 ± 88.0 units/ml/min (2σ). Serum RNase levels for a control group of 54 normal individuals varied from 26.2 ± 0.6 to 70.4 ± 1.0 units/ml/min, with a mean of 43.6 ± 2.0 (2σ). When these 2 groups were compared by means of the Student t test, it was found that they were statistically distinct (p < 0.0005). However, there is considerable overlap between the 2 groups. If, for example, elevated RNase activity is defined as activity which is greater than the mean + 2σ (= 64.4 units/ml/min) of the normal control group (5), then, by this criterion, there are only 17 of 44 cases of elevated RNase levels in the group of patients with leukemia and having a C_{cr} > 60 ml/min (Chart 1). Thus, at a 95% confidence level, 61.4% of these leukemias had RNase levels encompassed by the normal region. It is important to note, moreover, that for 10 of these 17
Serum RNase and Renal Insufficiency in Leukemia

Cases in which RNase levels were elevated, the CCr was somewhat reduced (60 to 90 ml/min). When leukemics having CCr < 90 ml/min were considered (25 determinations), it was found that 60% of these patients had RNase levels within normal limits (95% confidence level). These leuke

mics had RNase levels that ranged from 28.0 ± 0.3 to 110.0 ± 1.5 units/ml/min, with a mean of 53.3 ± 43.0 units/ml/min (2σ). If the 2 highest levels of RNase from this population are not included, the range is 28.0 ± 0.3 to 79.5 ± 0.8 units/ml/min and a comparison of RNase levels for this group of patients with those obtained from the 54 normal subjects, whereas 28 patients with renal failure were examined for concentrations of this enzyme (see text for details).

RNase levels in sera from 20 patients with leukemia (acute myelogenous, 9; chronic myelogenous, 4; acute lymphocytic, 7) who had not yet received treatment ranged from 30.0 ± 0.6 to 194.0 ± 15.1 units/ml/min with a mean of 60.0 ± 71.2 (2σ). In 5 cases, RNase activities exceeded 64.4 units/ml/min; however, of these, 2 had CCr < 60 ml/min. Comparison of the RNase levels for pretreatment patients with those obtained from patients with leukemia having CCr > 60 ml/min indicates that these 2 groups are statistically indistinguishable (p = 0.37).

The leukemia patients with renal insufficiency, as determined by CCr < 60 ml/min, had RNase levels that ranged from 67.9 ± 7.2 to 698.2 ± 24.2 units/ml/min, with a mean of 205.2 ± 266 (2σ). This group is quite different from either the normal controls or the leukemia patients with normal rates of glomerular filtration (p < 0.0005) (Chart 1).

To further illustrate the effect of renal insufficiency on RNase levels, concentrations of the enzyme were measured in sera obtained from 28 patients on chronic hemodialysis and ranged from 441.2 ± 18.2 to 1729.0 ± 42.0 units/ml/min with a mean of 836.7 ± 516.8 (2σ) (Chart 1). None of these patients had leukemia, and the etiologies of their renal insufficiency included 9 patients with chronic glomerulonephritis, 7 with diabetic nephrosclerosis, 6 hypertensives, 3 of uncertain etiology, and 1 each with sickle cell disease, congenital malformation, and chronic pyelonephritis. Five patients had bilateral nephrectomies at the time they were studied, and all of the others had CCr estimated at <5 ml/min and required at least 2 and more often 3 hemodialysis treatments per week. In this group, which differed from all of the 3 previous groups (p < 0.0005) with respect to the levels of RNase present, an attempt was made to correlate the level of RNase with other clinical features of the patient. Sex, race, age, and body weight failed to demonstrate any relationship. However, 5 of the 8 patients with the highest levels of RNase had bilateral nephrectomies.

The relationship of the degree of renal insufficiency to the level of serum RNase was examined further by plotting RNase levels against either CCr or serum creatinine levels (Chart 2). A strong correlation was found between the indicator of renal insufficiency and RNase concentration. In general, elevations of the enzyme accompanied either increasing plasma creatinine concentrations or declining values of CCr. There was a marked rise, for example, in plasma RNase concentrations in patients exhibiting moderate depressions in CCr: if CCr is greater than 90 ml/min, the mean RNase level is 53.3 ± 43.0 units/ml/min (2σ), whereas for CCr values ranging from 47 to 65 ml/min, the average enzyme activity is 130 ± 48.8 units/ml/min. Examination of the increases in RNase level as creatinine is elevated (Chart 2, inset) reveals that, over the range of creatinine considered normal (0.3 to 1.6 mg/dl), there is a particularly sharp rise in the concentration of enzyme. In this region, small fluctuations of plasma creatinine are reflected, in approximately linear fashion, by large changes in RNase levels. A simple method for determining an upper limit for an RNase level at a particular creatinine concentration is thus available from consideration of these data. The linear approximation between RNase and creatinine levels (0.3 to 2.0 mg/dl) is expressed by the equation:

\[
\text{RNase activity (units/ml/min)} = \frac{135.6 \cdot \text{Cr (mg/dl)}}{-46.2 \pm 92.6 \text{ (2σ)}}
\]

(Chart 2, inset, bottom broken line). Thus, to a 95% confidence level, if RNase activity > [136·Cr] + 46.4, the enzyme concentration is greater than that anticipated on the basis of renal insufficiency alone (Chart 2, inset, top broken line). An attempt was made to find some common features among...
The constants $A$, $B$, and $D$ were determined to be $-113.2$, $32,820$, and $80.9$, respectively, through use of the MLAB program (17, 18). Inset, variation of RNase concentration with level of creatinine. The best fit to the equation:

$$\text{Units RNase activity/ml/min} = \frac{B}{Cc} + D$$

is plotted as a solid line ($A = 2.42 \times 10^{-3}$, $B = 3.93 \times 10^{-3}$, $D = -0.49$). The bottom broken line displays the least-squares regression equation of RNase activity on creatinine levels (for the region creatinine = $0.3 - 1.8$ mg/dl). Units RNase activity/ml/min = $135.6 \times$ creatinine (mg/dl) $+ 46.2$. Elevated RNase activities that, to a 95% confidence level, cannot be accounted for by increased creatinine alone, lie above the top broken line: Units RNase activity/ml/min = $135.6 \times$ creatinine (mg/dl) $+ 46.4$ (see text for details).

Although changes in serum RNase levels have been suggested to be of potential diagnostic value for certain types of leukemia (5), our results from either patients with leukemia who had not received treatment or from patient time-course studies demonstrate that there is no indication that plasma RNase levels may be utilized as a biomarker for the presence of leukemia or as an index of the response to therapy for that neoplastic disease. Instead, as demonstrated by Charts 2 to 6, there is a direct relationship between RNase activity and serum creatinine levels or $C_{Cr}$. Decreasing rates of glomerular filtration, regardless of etiology, resulted in a precipitous rise in levels of 1 type of human RNase. The enzyme responsible for enhanced RNase activity as the $C_{Cr}$ decreases is antigenically similar, if not identical, to the enzyme found in normal human plasma. A 2nd immunological class of RNases, found normally in a number of human tissues (9, 27) was not detected in significant quantities in either normal control plasma or in the pathological samples examined.

The pathogenesis of the elevated RNase levels in those patients with renal failure is not clear. The RNase from human plasma has a molecular weight of approximately 32,000 daltons and, therefore, will pass across the normal glomerular basement membrane (32). Renal damage that decreases glomerular filtration would lower the rate of fil-
tration of RNase and concomitantly raise the plasma level of the enzyme. It has been suggested that the kidney is the sole source of plasma RNase (15). However, this seems unlikely in view of the fact that patients having bilateral nephrectomies had the highest levels of this RNase. This is not to say that parenchymal kidney damage does not contribute to elevations in the enzyme. Thus, serum levels of RNase are, in all probability, determined by cellular synthesis and degradation, as well as by glomerular filtration.

The results of the present study and, additionally, those from previous work dealing with multiple myeloma (16) indicate clearly the dependency of plasma RNase levels on the status of the patient’s renal insufficiency. It is interesting to note, on the other hand, that concentrations of serum RNase are abnormally elevated in patients with pancreatic cancer, and, consequently, levels of this enzyme have been suggested as a biomarker for carcinoma of the pancreas in the presence of normal renal function (31). A proper assessment of this enzyme as a potential biomarker for neoplastic disease cannot be carried out in the absence of careful evaluation of rates of glomerular filtration. In this connection, studies that follow disease status, glomerular filtration rate (as CCr), and RNase levels over periods of time are useful and in most cases give a clear indication of the parameters that correlate with RNase levels. As such, this type of analysis serves as an adjunct to the statistical sampling of a variety of patient populations and, in addition, demonstrates graphically whether or not levels of enzyme may be utilized as a diagnostic tool either for the detection of neoplasia or as an indicator of response to therapy.

Although normal values of the concentration of creatinine in serum are often cited as indicators of normal rates of glomerular filtration, this type of measurement may not accurately reflect renal insufficiency in certain cases. Decreased daily urinary creatinine excretion, for example, has been noted in patients with several types of renal failure (6, 10, 14, 19). The etiology of this change is not known (19), although it has been shown that, in some cases, creatinine is metabolized, presumably by the microflora of the gut (14). If creatinine is disposed of by means other than urinary excretion, it is quite possible that significant reductions in the rate of glomerular filtration may occur with very little elevation in the concentration of serum creatinine (2, 4, 6). The problems with obtaining routine, accurate CCr values are well known and have been described (35). In this respect, if it is suspected that serum creatinine does not give an accurate reflection of glomerular filtration rate, examination of concentrations of a medium-molecular-weight serum protein that correlates with CCr, such as RNase, may be of utility. We are not suggesting RNase levels as a replacement for CCr, but rather as a serum test giving a more accurate reflection of the glomerular filtration rate than do serum creatinine concentrations in those cases where creatinine is disposed of by routes other than urinary excretion. In view of the fact that the measurement of RNase activity is a simple, reproducible, highly accurate spectrophotometric procedure, levels of RNase deserve further examination as an indicator of glomerular filtration. Further

Charts 3 to 6. The correspondence over time between serum creatinine (△–△) and RNase (●–●) is illustrated for 11 leukemic patients. The creatinine scale varies from panel to panel. •, date of patient death.

Chart 3. E. B. (BCH 68-32-01) was a 34-year-old white male with acute myelogenous leukemia who received therapy with cytosine arabinoside and daunorubicin, which completely cleared leukemic cells from blood and bone marrow. He died during aplasia on Day 19 following initiation of therapy with advancing pneumonitis and progressive renal failure, the latter believed secondary to amphotericin.

D. G. (BCH 63-85-28) is a 28-year-old white male with acute myelogenous leukemia who presented in bone marrow relapse after a prior complete remission of 30 months duration. He received therapy with cytosine arabinoside and daunorubicin and early during aplasia was treated with several antibiotics plus amphotericin for fever, pneumonitis, and pleuritic pain. Renal insufficiency developed, and amphotericin was replaced with WBC transfusions. 5-fluorocytosine, and miconazole. Renal insufficiency resolved, and another complete remission was achieved.

J. M. (BCH 67-57-75) was a 13-year-old white female who failed prior chemotherapy and was referred with florid peripheral and marrow relapse (including leukemia cutis) for bone marrow transplantation. This was performed following busulfan and cyclophosphamide preparation with complete disappearance of the disease by 6 months. The patient did not receive post-transplant conditioning and was not given evidence of graft-versus-host disease. During the middle of her course, she developed a number of infectious complications and was treated with a number of antibiotics including amphotericin. Mild renal insufficiency developed which recovered when amphotericin was stopped. Cardiac arrest and death occurred unexpectedly just before a planned discharge.

Chart 4. N. S. (BCH 68-04-44) was a 37-year-old white female with acute myelogenous leukemia which proved to be unresponsive to therapy with cytosine arabinoside and daunorubicin. Terminal events included progressive renal failure attributed to amphotericin complicated by acute tubular necrosis.

A. B. (BCH 60-98-48) was a 55-year-old black female with acute myelogenous leukemia whose tumor cleared completely with cytosine arabinoside and daunorubicin therapy. Death occurred during aplasia due to sepsis unresponsive to multiple antibiotics, including amphotericin. Fluctuations in creatinine were closely paralleled by RNase levels throughout her course.

A. S. (BCH 68-07-17) was a 40-year-old white male with acute myelogenous leukemia refractory to prior chemotherapy who received a bone marrow transplant after busulfan and cytoxan pretreatment. Tumor was eradicated but death, due to diffuse interstitial pulmonary infiltration and progressive hypoxia, occurred before status of engraftment could be determined. Renal insufficiency, as judged by steeply rising creatinine, was a preterminal event, although RNase was observed to gradually rise over the preceding week.

Chart 5. B. R. (BCH 68-30-56) was an 11-year-old white female with acute lymphocytic leukemia refractory to prior chemotherapy. She was treated with a bone marrow transplantation following a combination of chemotherapy and total-body irradiation. Complete disappearance of the leukemia was observed with good evidence of marrow engraftment. Preterminal events included progressive hepatic failure and rapidly progressive renal failure.

Y. C. (BCH 61-26-36) is an 18-year-old black female with acute lymphocytic leukemia who achieved a complete remission on sequential therapy with vincristine and prednisone followed by cyclophosphamide, cytosine arabinoside, and vincristine. The induction course was not complicated by any periods of renal insufficiency.

Chart 6. J. D. (BCH 58-12-83) was a 45-year-old white male with a 5-year history of chronic myelogenous leukemia who was referred for evaluation of blastic crisis associated with anemia and thrombocytopenia. Many of his cells contained 2 Philadelphia chromosomes. Treatment was initiated with hydroxyurea, followed by busulfan and cyclophosphamide, cytosine arabinoside, and vincristine. Good tumor response was achieved, but infectious complications during aplasia required treatment with multiple antibiotics and amphotericin. Renal function gradually deteriorated, and death occurred during aplasia due to this complication and persistent sepsis.

M. S. (BCH 67-97-37) was a 16-year-old white male with chronic myelogenous leukemia in blastic crisis. He was treated with bone marrow transplantation following busulfan and cyclophosphamide preparation. Aplasia resolved and was complicated by pulmonary Aspergillus infection. Control of the tumor and marrow engraftment did not occur. Several spikes of increased RNase activity were seen during his course, which were coincident with attempts to increase his amphotericin dosage. However, renal function remained good until terminal events were precipitated by progressive pulmonary failure.

M. L. (BCH 68-01-95) was a 16-year-old white female with chronic myelogenous leukemia in blastic crisis with a double Philadelphia chromosome abnormality. She received therapy with cyclophosphamide, cytosine arabinoside, and vincristine. A good partial response was achieved, and the patient was discharged improved. Over her course, fever during aplasia was treated with several antibiotics, including amphotericin, but no episodes of renal insufficiency occurred.
The binding of the RNases present in the crude human plasma samples to either anti-liver-spleen- or anti-plasma-type RNase postimmunization sera conjugated to Sepharose 4B was carried out as described in "Materials and Methods." Control mixtures, containing preimmunization serum conjugated to Sepharose 4B, were also prepared. Enzyme that did not bind was then measured under 2 sets of conditions designed to detect liver-spleen-type activity and plasma-type activity (see "Materials and Methods"). The volume of each plasma sample used was chosen so as to give an activity of approximately 1.0 absorbance unit in the control tubes containing the immobilized preimmunization serum. For comparative purposes, purified plasma and liver RNases were also evaluated. The values listed below are the ranges of enzyme activity removed by antibody binding (expressed as a percentage of the total activity obtained using the conjugated preimmunization serum) followed by the mean ± S.E.

### Enzyme activity removed by antibody binding (% of total)

<table>
<thead>
<tr>
<th>Origin of serum</th>
<th>Anti-liver-spleen RNase serum</th>
<th>Anti-plasma RNase serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control group (10)*</td>
<td>3.8-23.9 (14.9 ± 2.1)</td>
<td>95.5-100 (99.0 ± 0.5)</td>
</tr>
<tr>
<td>Leukemia (5 samples from patients)</td>
<td>9.3-24.9 (14.3 ± 2.8)</td>
<td>86.6-100 (96.1 ± 2.7)</td>
</tr>
<tr>
<td>Multiple myeloma (10)</td>
<td>0.0-10.5 (3.3 ± 1.4)</td>
<td>74.5-100 (94.9 ± 2.6)</td>
</tr>
<tr>
<td>Leukemia and renal failure (12 samples from 5 patients)</td>
<td>0.0-22.7 (6.9 ± 2.2)</td>
<td>92.5-100 (98.4 ± 0.8)</td>
</tr>
<tr>
<td>Multiple myeloma and renal failure (10)</td>
<td>0.0- 6.6 (1.9 ± 1.0)</td>
<td>95.0-100 (98.0 ± 0.9)</td>
</tr>
<tr>
<td>Renal failure (5)</td>
<td>0.0-17.9 (5.8 ± 3.2)</td>
<td>93.7-100 (97.8 ± 1.1)</td>
</tr>
<tr>
<td>Hepatocellular damage (4)</td>
<td>0.0-22.7 (6.1 ± 5.6)</td>
<td>93.3-99.9 (9.7 ± 1.5)</td>
</tr>
<tr>
<td>Purified enzymes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen-type RNase</td>
<td>62.3-91.3 (77.6 ± 6.1)</td>
<td>0.0-13.7 (3.2 ± 2.7)*</td>
</tr>
<tr>
<td>Plasma-type RNase</td>
<td>0.0- 7.8 (2.7 ± 1.7)</td>
<td>85.4-100 (93.8 ± 3.3)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses, number of samples.

These values were obtained using the assay procedure for the human plasma-type enzyme, except that yeast RNA was utilized as the substrate since purified liver RNase hydrolyzes potassium polycytidylate so poorly (9).

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