Incorporation of Radioactive L-Cystine by Normal and Leukemic Leukocytes in Vivo

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Previous studies indicate that L-cysteine or related compounds may be important in the metabolism of leukocytes. Thus L-cysteine, and to a lesser extent homocysteine and glutathione, modify the leukopenia induced by nitrogen mustard. This protective effect appears to be specific in that many highly reactive compounds with structures closely related to L-cysteine fail to prevent the leukotoxic effect of nitrogen mustard. Only those compounds containing a sulfhydryl, amino, and carboxyl group in close apposition have been shown to be effective. Since the dextrosomer of cysteine is ineffective in preventing mustard induced leukopenia, a specific spatial configuration as well as the presence of certain structural components is required for this protective effect.

The requirement of such spatial and structural specificity for protection suggests that L-cysteine may have a unique role in the metabolism of leukocytes. The incorporation of radioactive L-cystine by normal and leukemic leukocytes in vivo was therefore studied. In addition to L-cystine, the incorporation of radioactive methionine, sodium sulfate, and sodium formate was also studied.

Methods

Tracer amounts of Sulfur-35 (35S) labeled L-cystine† were administered orally to twenty individuals. Ten patients had no hematologic abnormalities, five had acute leukemia, three had chronic myeloid leukemia and two had chronic lymphoid leukemia. The labeled L-cystine was suspended in water so as to contain 2 to 3 μc. per ml. Approximately 0.1 μM. of L-cystine by weight was present per μc. Each μc. of L-cystine was equivalent to approximately 1,250,000 counts per minute (c/min) as determined with a preflush flow counter. Three μc. per Kg. were administered orally to each patient. 10.0 ml. heparinized blood was withdrawn every 10 minutes for the first hour and hourly for 8 hours. Thereafter 10.0 ml. heparinized blood was withdrawn daily.

1. Determination of Radioactivity in Leukocytes

The heparinized blood was allowed to stand at room temperature, and plasma (containing leukocytes) was separated as erythrocyte sedimentation took place. The leuko...
cytes were separated from the plasma by centrifugation at 1500 rpm for 5 minutes and washed three times with 0.85 per cent saline. After the first saline wash the leukocytes were washed with 1 per cent acetic acid to remove trapped erythrocytes. The final saline wash contained negligible amounts of radioactivity.

Following the final saline wash, the leukocytes were resuspended in saline and an aliquot was taken for determination of the volume of packed leukocytes (hematocrit). The optimum leukocyte hematocrit for purposes of counting was approximately 5 per cent. Two drops of 1 normal sodium hydroxide were then added to dissolve the leukocytes. Of dissolved leukocyte suspension, 0.2 ml. were placed in a planchette, diluted with distilled water, and dried by infra red heat. An even, thin film was obtained in this manner.

Samples were counted for 15 minutes in a preflush flow counter* using helium gas with an absolute ethyl alcohol quench. The c/m per ml. packed leukocytes was then calculated.† The c/m per ml. packed leukocytes was chosen as the unit of reference instead of c/m per billion of leukocytes because of the difficulty in obtaining accurate counts from resuspended leukocytes. However, repeated determinations of the leukocyte count indicate that 1 ml. packed leukocytes contains approximately $2.5 \times 10^8$ leukocytes.

2. Determination of Radioactivity in Plasma

The radioactivity of the plasma was determined after the leukocytes were separated by centrifugation. Two-tenths ml. of plasma were placed in a planchette, diluted with distilled water, dried by infra red heat, and counted in the gas flow counter. The distribution of radioactivity between the protein and nonprotein fractions of plasma was determined by precipitating the proteins with 5 per cent trichloroacetic acid. The precipitate was removed by centrifugation and 0.2 ml. samples of the supernatant were counted.

3. Determination of Urinary Excretion of S\textsuperscript{35}

The radioactivity excreted in the urine during the first twenty-four hours was determined in twelve patients. The urine was diluted with distilled water and 0.2 ml. samples were placed in planchettes, dried, and counted in the gas flow counter. The total radioactivity excreted was then determined from the dilution factors and the twenty-four hour urine output.

4. Characterization of the Radioactive Material in Leukocytes

The radioactive material within the leukocytes was analyzed in one patient with acute monocytic leukemia. Twenty-five ml. of pooled leukocyte suspension (hematocrit 5 per cent) were precipitated with 5 per cent trichloroacetic acid and centrifuged at 4 C. for 15 minutes at 3000 rpm. The supernatant was extracted with 3 volumes of ether and then condensed to approximately 1 ml. by vacuum distillation. One-tenth ml. of the concentrated supernatant was placed on a strip of Whatman #1 filter paper and a chromatogram developed over a period of 12 hours using a butanol-acetic acid solvent system (1 vol. n-butanol and 1 vol. 50 per cent acetic acid). The trichloroacetic acid precipitate was washed three times with 5 per cent trichloroacetic acid and then hydrolyzed with 2N hydrochloric acid for 48 hours. The hydrolyzed material was then centrifuged and the supernatant condensed to approximately 1 ml. by vacuum distillation. One-tenth ml. of this concentrated material was placed on a strip of Whatman #1 filter paper and a chromatogram developed as above. Due to the acidity of the concentrate, it was necessary to expose this material to fumes from concentrated ammonium hydroxide at frequent intervals while it was being spotted on the filter paper.

On removal of the paper strips from the solvent system they were dried in room air, sprayed with ninhydrin solution and dried again at 60 C. to allow development of the color complex.

* Radiation Counter Laboratories, Mark 12, model 2.
† $c/m$ per ml. packed leukocytes = $\frac{1}{\text{hematocrit of sample}} \times c/m$ per ml. sample.
INCORPORATION OF RADIOACTIVE L-CYSTINE

Radioautographs of these chromatograms were obtained by placing them in direct contact with x-ray film for a period of two months. The areas of radioactivity were then compared with the migration of L-cystine, L-cysteine, glutathione, and methionine in the same solvent system.

5. Studies with $^{35}$S Sodium Sulfate, $^{35}$S Methionine and C¹⁴ Sodium Formate

The incorporation of equivalent amounts of orally administered $^{35}$S sodium sulfate (3 μc. per Kg.) was compared with that of $^{35}$S L-cystine in two normal individuals and in two patients with acute leukemia. The utilization of $^{35}$S methionine was studied in one patient with acute leukemia.

The utilization of parenterally administered C¹⁴ sodium formate (2 μc. per Kg.) was studied in one normal individual. This was compared to the utilization of $^{35}$S L-cystine and $^{35}$S inorganic sulfate which had previously been administered to the same individual at suitable intervals. The utilization of C¹⁴ sodium formate was compared with that of $^{35}$S L-cystine in one patient with chronic myeloid leukemia.

RESULTS

1. Incorporation of $^{35}$S L-Cystine by Normal Individuals

The results obtained in the ten normal individuals studied were remarkably similar in each instance. These results were averaged and the incorporation of $^{35}$S into plasma and leukocytes is compared in figure 1. Following oral administration of $^{35}$S L-cystine detectable amounts of radioactivity appeared in leukocytes of the peripheral blood and in the plasma within ten minutes. The plasma radioactivity was comparatively high during the first few hours and then gradually decreased over a period of several days, whereas the radioactivity in the leukocytes was low initially and then gradually increased as the plasma levels decreased. Maximum levels of radioactivity were present in the plasma in two hours, the average being approximately 4000 c/m per ml. plasma. Maximum

![Fig. 1](image-url)
levels of radioactivity were present in the leukocytes between the fifth and twelfth days. During this period an average of 5500 to 6500 c/rn were present per ml packed leukocytes.

The majority of the radioactivity in the plasma was present in the protein fraction precipitated by trichloroacetic acid. However, during the first twenty minutes more than half of the plasma radioactivity was present in the acid soluble fraction. Thereafter the radioactivity in this fraction decreased rapidly and after the first few hours almost all the radioactivity was present in the acid insoluble fraction. Between 5 per cent and 13 per cent of the orally administered \( ^{35}S \) was excreted in the urine during the first twenty-four hours. The average excretion was 9 per cent of the administered amount (table 1).

### Table 1. Urinary Excretion of \( ^{35}S \)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of cases</th>
<th>( ^{35}S ) compd administered</th>
<th>Av. % excreted in 24 hrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10</td>
<td>L-cystine</td>
<td>9</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>5</td>
<td>L-cystine</td>
<td>8.5</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>3</td>
<td>L-cystine</td>
<td>3</td>
</tr>
<tr>
<td>Chronic lymphoid leukemia</td>
<td>2</td>
<td>L-cystine</td>
<td>13</td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
<td>Sod. sulfate</td>
<td>25</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>2</td>
<td>Sod. sulfate</td>
<td>53</td>
</tr>
</tbody>
</table>

The incorporation of \( ^{35}S \) into the leukocytes of patients with acute leukemia was much more rapid than that occurring in normal leukocytes (fig. 2A). Within twenty minutes the amount of radioactivity found in acute leukemic leukocytes was greater than that found in normal leukocytes within forty-eight hours. Maximum levels of \( ^{35}S \) incorporation occurred within one hour in acute leukemia and lasted for two days before beginning to decrease. Although the rate of incorporation into leukocytes was more rapid in acute leukemia, higher levels of radioactivity were attained in normal leukocytes. Thus the maximum values in acute leukemia averaged between 4000 and 4500 c/rn per ml packed leukocytes compared to the maximum of 5500 to 6500 c/rn per ml packed leukocytes in normals. The pattern of incorporation was similar for all types of acute leukemia. The curve shown in figure 2A is an average of the results obtained in the five patients studied.

The appearance of radioactivity in the plasma of patients with acute leukemia closely paralleled that found in normal plasma (fig. 3A). However, the levels were at all times slightly lower than that in normal plasma. Unlike the normals, the level of radioactivity in the plasma was at all times comparatively less than that found in the acute leukemic leukocytes. Thus the c/rn per ml packed leukocytes always exceeded the c/rn per ml plasma. The majority of the radioactivity was present in the protein fraction and at no time were significant amounts of radioactivity found in the acid soluble fraction. The amount of radioactivity excreted in the twenty-four hour urine ranged from 3 per cent to 15 per cent of the orally administered \( ^{35}S \). The average excretion in twenty-four hours was 8.5 per cent of the radioactivity given (table 1).
Fig. 2.—Comparison of the incorporation of orally administered $^{35}$S-L-cystine into normal and leukemic leukocytes.

A. Comparison of normal leukocytes with acute leukemic leukocytes. The incorporation of $^{35}$S into acute leukemic leukocytes is much more rapid than in normal leukocytes. Although higher peak values are obtained in normal leukocytes than in acute leukemic leukocytes, the radioactivity disappears more rapidly from the circulating leukocytes in acute leukemia.

B. Comparison of normal leukocytes with chronic myeloid leukemic leukocytes. The incorporation of $^{35}$S into the leukocytes of chronic myeloid leukemia is much more rapid and peak values are higher than in normal leukocytes.

C. Comparison of normal leukocytes with chronic lymphoid leukocytes. A low, flat pattern of uptake is found in the leukocytes of chronic lymphatic leukemia.
Fig. 3.—Comparison of the radioactivity appearing in normal and leukemic plasma following oral administration of $^{38}$S L-cystine.

A. Comparison of normal plasma with acute leukemic plasma. The appearance of radioactivity in acute leukemic plasma closely parallels that found in normal plasma.

B. Comparison of normal plasma with chronic myeloid leukemia plasma. The appearance of radioactivity in chronic myeloid leukemia plasma parallels that found in normal plasma. The initial values are lower than those of normal plasma.

C. Comparison of normal plasma with chronic lymphoid leukemia plasma. A low, flat curve is found in chronic lymphoid leukemia compared to that found in normals.
3. Incorporation of $^{35}$S L-Cystine in Patients with Chronic Myeloid Leukemia

Initially the rate and amount of incorporation of $^{35}$S into the leukocytes of patients with chronic myeloid leukemia closely paralleled that found in acute leukemia (fig. 2B). Thus the incorporation during the first few hours was much more rapid and at a higher level than that in normals. As in acute leukemia, approximately 4000 c/min were present per ml. packed leukocytes during this period. Unlike acute leukemia, however, there was a progressive increase in utilization of $^{35}$S after this initial phase and the greatest concentration of radioactivity appeared in the leukocytes on the fourth day. An average of 8400 c/min was present per ml. packed leukocytes at this time. The radioactivity slowly decreased after the fourth day. In general, the level of radioactivity in the leukocytes of chronic myeloid leukemia at all times exceeded that found in normal leukocytes.

Plasma levels of radioactivity were less than those found in normal plasma but paralleled the normal curve (fig. 3B). The majority of the radioactivity was in the protein fraction precipitated by trichloracetic acid. Approximately 3 per
4. Incorporation of \( \text{S}^{35} \) L-Cystine in Patients with Chronic Lymphatic Leukemia

The incorporation of \( \text{S}^{35} \) into the leukocytes of chronic lymphatic leukemia was less rapid and of a lower magnitude than that found in the other types of leukemia. The initial values were only slightly greater than those found in normals and a low flat curve of incorporation was found throughout the period of study (fig. 2C). Thus there was a very slow rate of disappearance of radioactivity from the circulating leukocytes. The maximum concentration found at any time was 2500 c/m per ml. packed leukemic leukocytes compared with a maximum of 5500 to 6500 c/m per ml. packed normal leukocytes.

The plasma radioactivity was lower than that found either in the normals or in other types of leukemia. After the initial rise, a relatively low flat curve of incorporation was found (fig. 3C). Approximately 13 per cent of the administered \( \text{S}^{35} \) was excreted in the twenty-four hour urine (table 1).

5. Analysis of Radioactive Material Present in Acute Leukemic Leukocytes

Radioautographs of chromatograms obtained from trichloracetic acid fractions of pooled acute leukemic leukocytes are shown in figure 4. In the trichloracetic acid soluble fraction the radioactivity was present in spots conforming with the motility of L-cysteine (or L-cystine) and glutathione. Acid hydrolysis of the material precipitated with trichloracetic acid also resulted in chromatograms in which the radioactivity was present in spots conforming with the motility of L-cysteine (or L-cystine) and glutathione. The persistence of radioactivity at the point at which the material was spotted is presumably due to inorganic sulfate resulting from the acid hydrolysis.

6. Comparison of the Incorporation of Sodium Sulfate with the Incorporation of \( \text{S}^{35} \) L-Cystine

Incorporation of \( \text{S}^{35} \) from sodium sulfate into normal leukocytes was in general similar to the incorporation of \( \text{S}^{35} \) from L-cystine (fig. 5A). The amount of radioactivity incorporated was less with \( \text{S}^{35} \) sodium sulfate and the maximum incorporation shows a sharp peak on the ninth day compared to the earlier and longer period of maximum incorporation occurring with \( \text{S}^{35} \) L-cystine.

Plasma clearance of \( \text{S}^{35} \) sodium sulfate was much more rapid than with \( \text{S}^{35} \) L-cystine. Although the initial radioactivity was comparable to that obtained with \( \text{S}^{35} \) L-cystine, relatively insignificant amounts of radioactivity were present in the plasma after the first day. Approximately 25 per cent of the administered dose was excreted in the urine in twenty-four hours (table 1).

The incorporation of \( \text{S}^{35} \) from sodium sulfate into the leukocytes of acute leukemia differed markedly from that found in normal leukocytes. It also differed markedly from the pattern of incorporation of \( \text{S}^{35} \) L-cystine into acute leukemic leukocytes. Thus the \( \text{S}^{35} \) sodium sulfate was poorly utilized by the leukemic leukocytes and all traces of radioactivity rapidly disappeared (fig. 5A and B). Although the initial plasma radioactivity was comparable to that obtained with \( \text{S}^{35} \) L-cystine, plasma clearance was rapid and insignificant amounts were present.
in the plasma after the first day. Approximately 53 per cent of the administered $^{35}$S was excreted in the urine in twenty-four hours (table 1).

7. Incorporation of $^{35}$L-Methionine in Acute Leukemia

$^{35}$S from L-methionine was incorporated into acute leukemic leukocytes with great rapidity. Ten minutes after oral administration, 5000 c/m per ml. packed leukocytes were present, and maximum levels of incorporation were present within one hour, at which time 14,000 c/m were present per ml. packed leukocytes. Thereafter the radioactivity present in the leukocytes declined slowly and steadily so that at the end of twelve days there were 6000 c/m per ml. packed leukocytes.

Maximum plasma radioactivity was present within three hours and was comparable to that found following administration of $^{35}$L-cystine. The curve of

![Graph](image)

**Fig. 5.** A. The utilization of $^{35}$ sodium sulfate by normal leukocytes is comparable to that of $^{35}$L-cystine. There is marked reduction in the utilization of $^{35}$ sodium sulfate by leukocytes in acute leukemia.

B. There is marked reduction in the utilization of $^{35}$ sodium sulfate by acute leukemic leukocytes compared to the utilization of $^{35}$L-cystine.
disappearance also paralleled that with S\textsuperscript{35} L-cystine. The radioactivity in the leukocytes was at all times relatively greater than the radioactivity in the plasma. Thus the c/m per ml. packed leukocytes always exceeded the c/m per ml. plasma. These results are similar to those obtained with S\textsuperscript{35} L-cystine.

8. Incorporation of C\textsuperscript{14} Sodium Formate

The incorporation of C\textsuperscript{14} from parenterally administered C\textsuperscript{14} sodium formate into normal leukocytes was compared with the incorporation of S\textsuperscript{35} from orally administered S\textsuperscript{35} L-cystine and S\textsuperscript{35} inorganic sulfate in one individual. The utilization of C\textsuperscript{14} closely parallels that of S\textsuperscript{35} from inorganic sulfate. The chief differences in the utilization of these three compounds in this individual were noted during the period of maximum incorporation. With S\textsuperscript{35} L-cystine the peak is reached on the fifth day and maximum levels of incorporation are present through the ninth day. With S\textsuperscript{35} sulfate a sharp peak is reached on the ninth day and with C\textsuperscript{14} formate on the eighth day.

The pattern of utilization of C\textsuperscript{14} sodium formate by the leukocytes of chronic myeloid leukemia closely paralleled that of S\textsuperscript{35} L-cystine. There was no significant difference between the rate of incorporation nor in the levels of radioactivity attained.

DISCUSSION

It is apparent that L-cystine is rapidly absorbed and incorporated into the proteins of plasma and circulating leukocytes. Appreciable amounts of radioactivity were present in the leukocytes of the peripheral blood within ten minutes, even though only fifteen to twenty \( \mu \)M. of labeled L-cystine were administered orally. Incorporation of S\textsuperscript{35} L-cystine into protein is shown by the presence of radioactivity in the material precipitated by trichloracetic acid in both plasma and leukocytes. The presence of radioactivity in glutathione obtained from the leukocytes is further suggestive that S\textsuperscript{35} L-cystine participates in proteins metabolism within the cell.

The radioactivity incorporated into the leukocytes accounts for only a small fraction of the total radioactivity administered. However, distinctive differences were noted in rates and levels of utilization of S\textsuperscript{35} L-cystine by normal leukocytes and by the leukocytes of acute and chronic leukemia. Thus the S\textsuperscript{35} administered was most rapidly incorporated into the circulating immature leukocytes of acute leukemia and chronic myeloid leukemia. The avidity of these immature cells for L-cystine is not specific for this compound and is probably a manifestation of the rapid metabolic turnover which occurs in leukemia. Thus rapid utilization was also demonstrated in leukemia with S\textsuperscript{35} L-methionine and with C\textsuperscript{14} sodium formate. A rapid turnover of other compounds such as phosphorus is known to occur in leukemia. The rapid utilization of L-cystine may, however, have greater significance than the utilization of other metabolites. Disorders of sulfhydryl metabolism have frequently been implicated in leukemia\textsuperscript{a} and it is possible that the sulfhydryl amino acid L-cysteine (or L-cystine) may have a unique role in the metabolism of leukocytes. The observations on the specificity of L-cysteine and related compounds in modifying the leukotoxic effects of nitrogen mustard are further suggestive of the possible importance of L-cysteine (or L-cystine) in the metabolism of leukocytes.
L-cysteine is effective in modifying the neutropenia induced by nitrogen mustard but is less effective in preventing lymphopenia. This may be correlated with the observation that the greatest concentration of radioactivity was observed in the granulocytes of chronic myeloid leukemia whereas the lowest levels of radioactivity occurred in the lymphocytes of chronic lymphatic leukemia.

The appearance of appreciable amounts of radioactivity in normal circulating leukocytes within ten minutes suggests that mature leukocytes may metabolize L-cysteine (or L-cystine). However, the greatest concentration of radioactivity in normal leukocytes occurred between the fifth and twelfth days. It is probable that the immature cells of the marrow take up most of the radioactive L-cystine and that this radioactivity appears in circulating normal leukocytes as maturation occurs.

No accurate determination of the life span of leukocytes can be made from these data because of the possibilities of reutilization of S\textsuperscript{35} and of dilution in body pools. However, the curve obtained for the utilization of S\textsuperscript{35} L-cystine by normal leukocytes is almost identical with that obtained by Kline and Cliffton\textsuperscript{6} in studying the life span of normal leukocytes with radioactive phosphorus. These authors estimate the life span of normal leukocytes to be 13.2 days based on the incorporation of P\textsuperscript{32} into the desoxypentose nucleic acid (DNA) of leukocytes. Since the average life span of normal leukocytes estimated with S\textsuperscript{35} L-cystine is comparable to that obtained with DNA labelled P\textsuperscript{32}, it is possible that reutilization of S\textsuperscript{35} L-cystine by leukocytes is minimal.

In some instances the life span of normal leukocytes may be shorter than the average estimate of 13 days. Thus in one patient studied with S\textsuperscript{35} cystine, S\textsuperscript{34} sodium sulfate, and C\textsuperscript{14} sodium formate the life span of the leukocytes as estimated with each isotope was approximately 9 days. The data are also compatible with the suggestion of Kline and Cliffton that 4 days are required for cells to mature and appear in the peripheral circulation.

The comparatively rapid disappearance of radioactivity from maximum levels in acute leukemia indicates that the life span of acute leukemic leukocytes is considerably less than that of normal leukocytes. The life span of leukocytes in chronic myeloid leukemia appears to be slightly less than that of normal leukocytes. No estimate of the life span of leukocytes in chronic lymphoid leukemia can be made from the data. However, the slow degradation of radioactivity in chronic lymphoid leukemia is compatible with a lymphocytic life span of several months as estimated by others.\textsuperscript{7-9}

The differences observed in the incorporation of L-cystine by normal individuals and by patients with acute or chronic leukemia cannot be attributed to differences in the total number of leukocytes. Sufficient excess of S\textsuperscript{35} was given so that comparable levels of excretion were obtained. Comparable plasma levels were also obtained except in chronic lymphatic leukemia. Except for the latter, the minor differences noted in the plasma levels of radioactivity are not sufficient to account for the distinctive variations in pattern observed. The cause of the low levels of radioactivity observed in both the plasma and leukocytes of chronic lymphatic leukemia is not known. It is possible that this represents a fundamental defect in chronic lymphatic leukemia. It is also possible, however,
that a large sulfhydryl pool is present in chronic lymphatic leukemia and that
the differences noted are due to dilution of the $S^{35}$ in this body pool.

The utilization of $S^{35}$ sodium sulfate by normal leukocytes may be due to
direct incorporation of sodium sulfate. However, leukocytes are apparently
unable to utilize significant amounts of $S^{35}$ sodium sulfate directly in vitro. It
is therefore probable that $S^{35}$ sodium sulfate is first converted to some other com-
 pound, possibly L-cysteine, and that this compound is then incorporated by the
leukocytes. The comparatively rapid excretion of $S^{35}$ from sodium sulfate indi-
cates, however, that conversion of sodium sulfate to another compound is
limited.

The inability of acute leukemic leukocytes to utilize appreciable amounts of
$S^{35}$ sodium sulfate may be due to a rapid turnover and excretion of sulfur or
possibly to an intrinsic metabolic defect in acute leukemia.

**SUMMARY AND CONCLUSIONS**

Methods for studying the in vivo incorporation of radioactive amino acids by
leukocytes are described. The incorporation of $S^{35}$ L-cystine into normal and
leukemic leukocytes was studied and compared with the utilization of $S^{35}$ L-
methionine, $S^{35}$ sodium sulfate, and $C^{14}$ sodium formate.

Radioactive L-cystine is rapidly absorbed and rapidly incorporated into the
proteins of leukocytes. There are distinctive differences in rates and levels of
utilization of $S^{35}$ L-cystine by normal leukocytes and by leukocytes of acute and
chronic leukemia.

The leukocytes of acute leukemia and of chronic myeloid leukemia have a
greater avidity for L-cystine than normal leukocytes. This rapid utilization of an
amino acid by immature leukocytes is not limited to L-cystine and is probably
a manifestation of the rapid metabolic turnover characteristic of immature cells
in general. However, in view of the observations on the specificity of L-cysteine
and related compounds in modifying the leukotoxic effects of nitrogen mustard,
the avidity of immature leukocytes for L-cystine may have greater significance
than the utilization of other metabolites.

The data indicate that the life span of normal leukocytes is approximately 13
days. The life span of leukocytes in chronic myeloid leukemia is slightly less than
that of normal leukocytes whereas the life span of acute leukemic leukocytes is
much shorter than that of normal leukocytes. The life span of lymphocytes in
chronic lymphatic leukemia appears to be much longer than that of normal leuko-
cytes. Although L-cystine and L-methionine are readily utilized in acute leukemia,
there is marked impairment in the utilization of sodium sulfate in vivo. By
comparison, normal leukocytes readily utilize sodium sulfate in vivo. This dis-
crepancy may be due to the rapid turnover of sulfur in acute leukemia or to an
intrinsic metabolic defect of acute leukemic leukocytes.

**SUMMARIO E CONCLUSIONES IN INTERLINGUA**

Es describite methodos pro studiar in vivole incorporation de radioactive amino-
acidos per le leucocytos. Esseva investigate e comparete le incorporation in
leucocytos normal e leucemic de L-cystina etiquettate a sulfure-35 e de L-me-
thiouria etiquettata a sulphure-35, de sulfato de natrium etiquettate a sulphure-35, e de formato de natrium etiquettate a carbon-14.

Radioactive L-cystina es rapidemente absorbite e rapidemente incorporate in le proteinas leucocytic. Il existe characteristic differentias de rata e grado in le incorporation de L-cystina a sulphure-35 per leucocytes normal e per leucocytes de acute e chronic leucemia.

Le leucocytes de acute leucemia e de chronic leucemia myeloide ha un plus intense aviditate pro L-cystina que leucocytes normal. Iste rapide incorporation de un amino-acido per leucocytes immatur non es limitate a L-cystina e es probablemente un manifestation del rapide metabolismo que es characteristic de cellulas immatur in general. Nonobstante, si on considera lo que es cognoscite super le specificitate de L-cysteina e de compositos afin in modifier le effects leucotoxic de meclorothamino-hydrochlorido, on es tentate a suponer que le aviditate de immatur leucocytes pro L-cystina ha un plus profunde signification que le utilisation de altere substantias metabolic.

Le datos colligite indica que le duration del vita de leucocytes normal es circa 13 dies. Le vita de leucocytes in chronic leucemia myeloide es un pauc plus breve que le vita de leucocytes normal, sed le vita de leucocytes de acute leucemia es multo plus breve que le vita de leucocytes normal. Il pare que le vita de lymphocytes in chronic leucemia lymphatic es multo plus longe que le vita de leucocytes normal. Ben que L-cystina e L-metionina es promptemente utilizate in acute leucemia, le utilisation in vivo de sulfato de natrium es claramente defective. In comparation con isto, leucocytes normal es caracterisate per lor prompte utilisation in vivo de sulfate de natrium. Le differentia inter le duo es posiblemente debite al rapide metabolismo de sulphure in acute leucemia o a un intrinsec defecto metabolic in leucocytes de acute leucemia.

REFERENCES

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