FACTITIOUS HYPOGLYCEMIA IN PATIENTS WITH LEUKEMIA

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In 1927, Falcon-Lesses3 reported on the rapid disappearance in vitro of glucose in blood removed from patients with leukemic leukocytosis. He demonstrated complete disappearance of glucose from the blood of patients with both myelogenous and lymphocytic leukemia within 1½ to 4 hr. after the blood was drawn. He took great care not to inhibit glycolysis in the blood samples removed from his patients, using heparin as an anticoagulant and incubating the blood at 37 C. during the experiments.

Although extensive work has been done on glycolysis in leukemic leukocytes since then,1 2 we have not found a report of patients with leukemic leukocytoses demonstrating factitious hypoglycemic values when blood glucose determinations were made under routine laboratory conditions.

This paper deals with some observations on values for blood glucose, as determined under usual laboratory conditions in 2 patients with leukemia who had unusually high white blood counts (ranging between 300,000 and 600,000 cells per cu. mm.). Glucose was so rapidly metabolized in whole blood removed from these patients that, when routine blood glucose determinations were made, the amount of glucose detected was virtually nil.

All bloods were anticoagulated with 20 mg. of lithium oxalate. Glucose determinations were made by means of either the Nelson-Somogyi or the AutoAnalyzer-ferri-
ferricyanide methods, which yielded nearly identical results. Inasmuch as different experiments were performed on each patient, they will be described separately.

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STUDIES OF CASES

Patient 1 (G. M.). This 21-year-old white man was admitted to the hospital on December 27, 1961, complaining of fever, weakness, and upper abdominal pain for 6 months, and dyspnea for 3 months. The patient was very pale. His liver and spleen were greatly enlarged. Admission hemogram was: white blood cells, 600,000 cells per cu. mm.; hematocrit value, 31 per cent; hemoglobin, 10.0 Gm. The peripheral smear revealed: neutrophils, 23 per cent; meta-myelocytes, 28 per cent; myelocytes, 28 per cent; promyelocytes, 12 per cent; myeloblasts, 3 per cent; lymphocytes, 2 per cent; monocytes, 1 per cent; eosinophils, 3 per cent. The diagnosis was chronic myelocytic leukemia in leukemic phase. On December 27, 1961, therapy with 6-mercaptopurine was begun.

His total white count and differential remained approximately the same while the tests were being performed.

The first blood glucose determination made on this patient, 90 min. after phlebotomy, was 4 mg. per 100 ml. A quick check of the patient's chart and hematology laboratory report revealed the previously described findings. A repeat blood glucose value determination made 15 min. after drawing was 97 mg. per 100 ml. It was thought that the low value was factitious and probably resulted from rapid aerobic glycolysis in vitro by the large number of leukemic cells present. Following is a description with comments of 2 experiments performed on this patient's blood.

We attempted to inhibit the glycolysis, using sodium fluoride. A concentration of 2 mg. of NaF per ml. of whole blood only partially inhibited the glycolysis at 90 min. From a starting value of 97 mg. per 100 ml. (done immediately after drawing), the value in the fluoridinated tube at 90 min. was 65 mg. per 100 ml. In the nonfluoridi-
TABLE 1
VALUES FOR BLOOD GLUCOSE IN 2 LEUKEMIC PATIENTS (G. M. AND P. R.) WITH LEUKOCYTOSIS

<table>
<thead>
<tr>
<th></th>
<th>Blood Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg./100 ml.</td>
</tr>
<tr>
<td></td>
<td>15 min.</td>
</tr>
<tr>
<td>Normal patient*</td>
<td></td>
</tr>
<tr>
<td>G. M.—oxalate only</td>
<td>80</td>
</tr>
<tr>
<td>G. M.—with NaF</td>
<td>97</td>
</tr>
<tr>
<td>B. R.—oxalate only</td>
<td>98</td>
</tr>
<tr>
<td>B. R.—with NaF</td>
<td>98</td>
</tr>
</tbody>
</table>

* Normal patient was 1 of several non-diabetic 20-year-old white women.

Another sample of whole blood was incubated at room temperature for 70 min. At this time the cells were removed from the tube by means of centrifugation. From a second sample, drawn at the same time, the cells were removed immediately and the cell-free plasma was incubated at room temperature for 70 min. The glucose value in the sample of whole blood incubated at room temperature was 15 mg. per 100 ml. The value in the cell-free plasma also incubated at room temperature was 133 mg. per 100 ml. In this instance immediate removal of the cells prevented rapid glycolysis, indicating that the enzymes responsible for this glycolysis resided in the leukocytes.

Patient 2 (B. R.). This 43-year-old white woman was admitted to the hospital on March 29, 1962, complaining of headaches, weakness, and a weight loss of 5 lb. since January 1962. Physical examination revealed hepatosplenomegaly and generalized lymphadenopathy. The hemogram on admission was: white blood cells, 636,000 cells per cu. mm.; hematocrit, 24 per cent; hemoglobin, 7.0 Gm. Her peripheral smear revealed: stem cells, 99 per cent; neutrophils, 1 per cent. The bone marrow aspiration revealed the marrow to be packed with the same immature cells seen on her peripheral smear. The diagnosis of stem cell leukemia in leukemic phase was made on the basis of these findings. A routine blood glucose determination made 2 hr. after phlebotomy was 30 mg. per 100 ml. A repeat blood glucose determination made 15 min. after drawing was 98 mg. per 100 ml.

This time higher concentrations of sodium fluoride were used, in an attempt to inhibit glycolysis by the leukocytes. Serial glucose determinations were made on samples of blood standing at room temperature for 4 hr., containing concentrations of 1 mg., 4 mg., and 8 mg. of NaF per ml. of whole blood. From a starting value of 98 mg. per 100 ml., all of the fluoridinated tubes had concentrations of 65 mg. per 100 ml. at the end of 4 hr. The value in the control tube at the end of 4 hr. was 50 mg. per 100 ml. (Table 1). Once again sodium fluoride only partially inhibited glycolysis.

Even with an 8-fold increase in the amount of sodium fluoride used there was no appreciable increase in the inhibition of glycolysis. Possibly sufficient glycolytic enzymes were present to compete successfully with sodium fluoride for available magnesium. If this mechanism pertains, higher concentrations of sodium fluoride than those tried would be required in order to effect complete inhibition.

SUMMARY
Factitiously low values for blood glucose in 2 patients with leukemic leukocytoses are reported. These abnormal values are most likely the result of the presence of large numbers of leukocytes in the whole blood, inasmuch as the glycolysis can be prevented by means of rapid removal of these cells. Sodium fluoride used in the usual concentrations recommended for inhibition of glycolysis did not effectively prevent the glycolysis.

SUMMARIO IN INTERLINGUA
Es reportate facticiamente basse valores pro le glucosa sanguinee in 2 patientes con leucocytosis leucemic. Iste anormalitate resulta probabilissimemente ab le presentia de grande numeros de leucocytes in le sanguine total, proque le glycolyse pote esser prevenite per medio del rapido elimination de iste cellulas. Fluoruro de natrium, usate in le
concentrations usually recommended for the prevention of glycolysis, non resulted in an efficace inhibition of glycolysis.

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REFERENCES