when the liver and muscle glycogen supplies have been exhausted.

Summary. The time function of free fatty acids and of corticosterone in plasma in fed and fasted rats was investigated. Also a study of the influence of hypoxia on the concentration of plasma free fatty acids was carried out. Whereas fasting does not seem to stimulate lipolysis markedly before 12 h, 2 h of hypoxia elevate the free fatty acid level to its maximum. In the fasted condition, all values are significantly higher than corticosterone in the fed animal.

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Evidence for Purine Biosynthesis in Human Leukocytes

Previous studies have shown that isolated human leukocytes are able to incorporate ^{14}C-labelled formate and adenine into their nucleic acid bases[1]. Diamond et al.[2] observed also an increased ^{14}C-glycine incorporation into adenine and guanine of RNA and DNA of leukocytes from gouty patients. However, adenine and guanine are not metabolic end products of purine metabolism and their concentration cannot give adequate information on the behaviour of purine metabolism; moreover, the glycine incorporation rate determined in leukocytes in vitro does not necessarily reflect the actual importance of de novo purine biosynthesis. Recently, Reem[3] found that Burkitt lymphoma and human spleen cells could synthetize the first and second intermediate compounds of the purine biosynthetic pathway, and Wood and Seegmiller[4] assayed and determined some properties of 5-phosphoribosyl-1-pyrophosphate amidotransferase, the enzyme that catalyzes the first step involved in de novo purine biosynthesis, in human lymphoblasts maintained in tissue culture. The purpose of the present study was to investigate whether human leukocytes and lymphocytes are capable of de novo purine biosynthesis. We assayed the activity of 5-phosphoribosyl-1-pyrophosphate amidotransferase in leukocytes and lymphocytes isolated by the usual procedures from 11 healthy volunteer subjects according to the method of Wyngaarden and Ashton[5]. The assays were performed on leukocytes and lymphocytes extracts dialyzed 24 h against distilled water in order to remove heparin and other molecules interfering or inhibiting the enzyme. Enzyme activity was expressed as units/10^6 cells, where one unit of enzyme activity is the amount that produces an increase of 0.001 absorbance unit/min at 363 nm at pH 8 and room temperature (25 °C). Enzyme activity has been detected in both kinds of cells examined. The mean values resulted 1.34 $\pm$ 0.58 units/10^6 cells in leukocytes and 0.86 $\pm$ 0.66 units/10^6 cells in lymphocytes (Table).

Preformed purines converted by cellular metabolism to ribonucleotides have been considered the only source of purine nucleotides for many human cells[3,6]. Most of the conclusions on this dependence are, however, based on indirect or negative evidence. Study of the early steps of de novo purine biosynthesis in human cells, such as fibroblasts, leukocytes and platelets, has been limited to evaluating the accumulation of formylglycinamide ribonucleotide [3,6] or observing the failure to incorporate glycine or formate into purine nucleotides in vitro[6], while the presence and the properties of 5-phosphoribosyl-1-pyrophosphate amidotransferase have not been extensively examined[4]. However, the interpretation of isotope-incorporation studies involving purine synthesis reactions requires some care concerning the concentration of precursors and intermediate compounds[1,6], and the possibility that some substrate necessary for de novo synthesis may been lacking[6]. Our results provide evidende that human leukocytes and lymphocytes possess the enzyme activity that catalyzes the formation of the first intermediate compound of the purine biosynthetic pathway. The finding of the presence of 5-phosphoribosyl-1-pyrophosphate amidotransferase in human leukocytes and lymphocytes suggests, therefore, that these cells have the capacity for de novo purine biosynthesis and are not solely dependent on the liver for their supply of purines. De novo purine synthesis may therefore be more widespread than previously reported, and human leukocytes and lymphocytes may be an important extrahepatic site for de nove purine biosynthesis in man. The study of the purine biosynthetic pathway in human leukocytes and lymphocytes seems of particular interest since it could provide a valuable experimental model to investigate the factors involved in the regulation of de novo purine biosynthesis and clarify purine metabolism alterations in patients with hyperuricemia, gout, or leukemia and other myeloproliferative diseases.

5-Phosphoribosyl-1-pyrophosphate amidotransferase activity in leukocytes and lymphocytes of healthy human subjects

Cell type	Enzyme activity (units/10^6 cells)
Leukocytes	1.34 $\pm$ 0.58
Lymphocytes	0.86 $\pm$ 0.66

Summary. Human leukocytes and lymphocytes have shown to be equipped with 5-phosphoribosyl-1-pyrophosphate amidotransrease, the enzyme which catalyzes the synthesis of the first intermediate of the purine pathway, thus providing evidence that these cells have the capacity for de novo purine biosynthesis.

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