On the Regulation of 2,3-Diphosphoglycerate Concentration in the Erythrocytes of Newborns with Transitory Hyperbilirubinemia

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ATP concentration and diphosphoglycerate mutase activity did not show any differences in icteric and non-icteric children.

Glucose consumption, however, is significantly lowered in icteric newborns. This explains the reduced 2,3-diphosphoglycerate concentration in these children and must be explained as a peculiarity of erythrocyte metabolism.

Key words: 2,3-Diphosphoglycerate — Hyperbilirubinemia — Glucose consumption — Diphosphoglycerate mutase — Adenosine triphosphate.

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Die ATP-Konzentration und die Aktivität der Diphosphoglyceratmutase zeigen keine Unterschiede bei ikterischen und nichtikterischen Kindern.

Der Glucoseverbrauch der Erythrocyten ist jedoch bei Neugeborenen mit transitorischer Hyperbilirubinämie signifikant niedriger. Dieser Befund erklärt den verminderten 2,3-Diphosphoglycerat-Gehalt der Erythrocyten und muß als Besonderheit des Erythrocytenstoffwechsels gedeutet werden.

The concentration of 2,3-diphosphoglycerate (2,3-DPG) is very high in red cells as compared to other tissues [2, 7, 19]. This appeared remarkable because the formation of 2,3-DPG avoids the phosphoglyceratekinase reaction and therefore one molecule of adenosinetriphosphate (ATP) is lost per molecule of glyceraldehyde-3-phosphate.
In 1967, however, it was found that 2,3-DPG influences the oxygen-dissociation curve of hemoglobin [3, 4]. High levels of 2,3-DPG decrease the oxygen affinity and cause a shift of the oxygen-dissociation curve to the right. In this way the organism can regulate the oxygen affinity of blood not only by changing the carbon-dioxide tension and pH, but by varying the amount of 2,3-DPG in the red cell, too.

Since that time several disorders have been found in which the oxygen dissociation curve is influenced by a change of the intra-erythrocyte 2,3-DPG level, e.g. anemia, heart failure, and the respiratory distress syndrome [6, 20, 21]. In 1973 we found that 2,3-DPG is significantly lowered in the erythrocytes of newborns with transitory hyperbilirubinemia [16]. In our present study we want to show how 2,3-DPG concentration might be regulated in the erythrocytes of these children. There are two possibilities:

1. There may be reduced activity of diphosphoglycerate mutase, the enzyme which produces 2,3-DPG from 1,3-DPG.

2. The whole glycolysis is reduced. This is indicated by the investigations of Cheung [5], who found in vitro a reduced red-cell glycolysis, when the red cells were preincubated with high concentrations of unconjugated bilirubin.

To answer these questions, the activity of diphosphoglycerate mutase, the ATP concentration of the red cell, and the glucose consumption were determined and all results were compared to the serum bilirubin concentration of the same child.

Material and Methods

Term born, healthy infants with an uncomplicated obstetric history were investigated. Blood groups of mothers and children revealed no incompatibility in the Rh and AB0 systems. Even when direct or indirect antiglobulin test was negative, no child of a pregnancy with Rh or AB0 constellation was included. All newborns were investigated at ages of 48—72 hrs.

The activity of diphosphoglycerate mutase was determined after hemolyzing the blood [10] according to Schröter [18] in 19 newborns. ATP and glucose concentration were measured enzymatically with the Boehringer Biochemica pack of reagents (phosphoglycerate kinase, respectively the hexokinase method). 18 infants were investigated for intra-erythrocyte ATP concentration and 22 for glucose consumption.

For the incubation studies one part of blood was mixed with one part of Ringer-phosphate buffer, 0.1 m, pH 7.4. Glucose concentration was approximately 200 mg/100 ml of incubation medium. Consumption of glucose was determined by estimating glucose before and after incubating the cells for 90 min. Leucocytes were removed in all studies by taking off the buffy coat layer after centrifuging the blood at 1000 g for 15 min. The results of all investigations were evaluated by regression analysis and determination of the p value.