Plasma Hemoglobin and Haptoglobin Levels in the Newborn Period

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The term «haptoglobin» was introduced by Polonovski and Jayle to describe a group of serum mucoproteins specifically capable of binding hemoglobin *in vitro* and *in vivo* by forming complexes with it. By starch-gel electrophoresis, different kinds of haptoglobin have been shown in the alpha two fraction of the serum which are inherited genetically.[1] The distribution of different haptoglobin types around the world shows certain racial characteristics.[2,3]

With the exception of the newborn period, haptoglobin concentration is independent of age in healthy children.[4] Besides the genetically determined ahaptoglobinemia,[5,6] there are several conditions in which plasma haptoglobins are decreased. In general, these are associated with some type of hemolytic anemia. In the newborn period also, a severely depressed haptoglobin level or ahaptoglobinemia is fairly well documented.[1,7–10] The haptoglobin levels in cord plasmas need not represent failure of production of this protein by the newborn infant, but might rather reflect exhaustion of haptoglobin by the chronically increased quantities of hemoglobin released into the plasma in the course of intravenous destruction of senescent erythrocytes. Our aim here is to show some correlation between the plasma hemoglobin concentration (p Hb c) and the presence of haptoglobin in the newborn. P Hb c and haptoglobin determinations in some babies were done up to two months of age.

Materials and Methods

Cord venous blood samples were collected from the placental site of 104 babies. With the exception of three, the birth weight was over

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2,500 grams. There were 57 males and 47 females. One premature was delivered by cesarean section and the rest were delivered normally. Blood samples were collected by gravity from the cord and p Hb c's were determined immediately. Only 70 of the samples were subjected to the horizontal starch-gel electrophoresis [1] at pH 8.6 (Tris-citric acid). Before electrophoresis, sufficient hemoglobin was added to the serum to saturate completely any haptoglobin present. One half of each resultant gel pattern was stained with amido-black for the detection of protein bands and the other half with a benzidine stain to indicate the haptoglobin-hemoglobin complexes.

Plasma hemoglobin concentration was determined using the method of Crosby and Furth.[11] Both plasma hemoglobin and serum haptoglobin levels could be determined in 21 (in two more only p Hb c was determined) and 13 out of 70 babies at two weeks and two months of age respectively.

Results

Haptoglobin was present in 28 out of 70 cord blood serum specimens. It was also present in 11 out of 21 and nine of 13 babies at two weeks and two months of age respectively. These results with the haptoglobin types are shown in Table 1.

TABLE 1

TYPE AND PERCENTAGE OF HAPTOGLOBIN FOUND IN CORD BLOOD AT TWO WEEKS AND TWO MONTHS OF AGE

	Hp 1-1	Hp 1-2	Hp 2-2	Total	Per cent of cases in which Hp is found.
Cord blood (70)*	5	9	14	28	40.0
At two weeks (21)	1	4	6	11	52.4
At two months (13)	–	4	5	9	69.2

* Numbers in parenthesis indicate the number of cases subjected to determination.

Cord plasma hemoglobin concentrations ranged from 0.1 to 44 mg and in only five of the cord blood samples were the plasma hemoglobin levels within the normal adult values used in our laboratory (up to 1 mg per cent). In five cases (13 per cent) p Hb c was more than 20 times the normal. P Hb c's were above the normal adult values in all cases at two weeks (3 to 25 mg per cent) and two months of age (2 to 18 mg per cent). Twenty times the normal

were found in two cases (10 per cent) at two weeks of age. P Hb c's on cord blood of 27 cases in whom haptoglobin was found [one was discarded since his cord plasma hemoglobin was exceptionally high (140 mg per cent) and was accepted as an error] and 42 cases in whom haptoglobin was not observed were compared statistically. In the first group, mean p Hb c was 8.98 ∓ 1.33 mg per cent with a standard deviation of 6.93 and, in the second group, it was 11.30 ∓ 1.64 mg per cent with a S. D. of 10.66. No statistically significant difference was found between these values ($p > 0.05$).

Discussion

Haptoglobin is synthesized by the liver and taken up by the reticuloendothelial cells when in combination with hemoglobin *in vivo*. This protein does not cross the placental barrier and the evidence of its synthesis by the newborn has been reported by Rausen, Gerald and Diamond.[8] Ahaptoglobinemia in the newborn period is known;[1 7–10] however, Rausen et al showed haptoglobin in 13 per cent of electrophoretically examined cord bloods and in three out of 14 premature cord blood specimens. We have found it in 40 per cent of our cord blood samples. If hemoglobin binding capacity were measured in the cord blood and in maternal sera, both would be found to be decreased to some extent. A much lower level of haptoglobin has been reported in the serum of a mother of a baby with hemolytic disease of the newborn.[12] Bilirubin also seems to influence the haptoglobin level.[9 13]

Strikingly elevated plasma hemoglobin concentrations similar to ours were reported in the cord blood [10] including a baby who was delivered by cesarean section. Umbilical arterial p Hb c was reported to be higher than umbilical venous p Hb c and was found to be related to whole cord blood hemoglobin values, but not to the mothers race, age, parity, length of pregnancy, duration of labor, or to the infant's sex or weight.[10]

Comparison of the whole blood hemoglobin, hematocrit and serum bilirubin values of the cord blood in ahaptoglobinemic newborns and those with detectable haptoglobin showed no significant relationship.[8] Comparison of the plasma hemoglobin in ahaptoglobinemia and haptoglobinemia has not been done in previous studies. In this study we made this comparison, but could not find any statistically significant difference between these groups. This substantiates Rausen et al's [8] suggestion that *in vivo* hemolysis is not the cause of hypohaptoglobinemia in the newborn. Therefore it is most

likely due to lack of synthesis by the liver in the fetus or in early neonatal life.

At two weeks and two months of age p Hb c's were found higher than cord blood in seven of 23 and three of 13 babies respectively. That one of these babies at two weeks and two others at two months of age showed haptoglobins in their serum when examined electrophoretically further supports the suggestion that the cause of hypohaptoglobinemia in the newborn period is not due mainly to increased *in vivo* hemolysis.

More than half of our babies' serum haptoglobin bands were shown at two weeks and almost 70 per cent at two months of age. Although the numbers of cases are not sufficent to consider the distribution of haptoglobin genotypes in this country, the results resemble those of Erdem et al.[3]

Summary

Plasmo hemoglobin and haptoglobin determinations were done simultaneously in 70 cord blood samples. No correlation was found between the plasma hemoglobin levels and the presence or absence of haptoglobin in this period of life. Plasma hemoglobin concentrations were also found to be increased at two weeks and two months of age. Hp 2-2 was more frequently observed in the babies on whom this study was conducted.

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