Inhomogeneity of Hemoglobin. VI. The Minor Hemoglobin Components of Cord Blood

By BENNETT F. HORTON, ROBERT B. THOMPSON, ANDREE M. DOZY, CARL M. NECHTMAN, EVAN NICHOLS, AND TITUS H. J. HUISMAN

During the past few years, some human hemoglobins have been found composed of one single type of polypeptide chain in contrast to the more common hemoglobins, composed of two types of polypeptide chains. The most important of these are Hb-Bart's, composed of four of the \(\gamma\) chains of Hb-F,\(^{17}\) and Hb-H, composed of four of the \(\beta\) chains of Hb-A.\(^{18}\) It would appear, therefore, that Hb-Bart's is related to Hb-F in the same way as Hb-H is to Hb-A. Small amounts of Hb-Bart's have been observed primarily in cord bloods and in the blood of Hb-H carriers,\(^{24}\) while Hb-H has been reported to occur principally in the presence of a gene of thalassemia.\(^{22}\) Ramot et al.\(^{23}\) recently reported two cases in which both Hb-Bart's and Hb-H were present; evidence has been presented that similar combinations should occur more often.\(^{9}\)

During routine electrophoretic studies of the hemoglobin of umbilical cord blood of Negro babies, varying amounts of Hb-Bart's-like and Hb-H-like components were noticed in many of these blood samples. The present study reports the results of a more extensive investigation dealing with the characterization of these minor hemoglobin components.

**Materials and Methods**

Over 300 cord blood samples of Negro babies were used for electrophoretic studies. Fifty-four cases, selected at random, were studied more intensively along with blood samples of the respective mothers. The gestational age of the newborns was estimated in weeks, on the basis of body weight, date of expected confinement and date of last menstrual period.

Seven babies, who showed specific abnormalities, were investigated five months after birth. When possible, both parents were included in these special investigations.

Routine hematologic studies, which included the determinations of total hemoglobin, red blood cell counts, hematocrit and osmotic fragility, were performed using standard procedures.\(^{29}\)

Hemoglobin solutions were prepared by mixing the triply washed erythrocytes with an equal volume of distilled water and 0.5 volume of toluene. After 20 hours the hemolysates were centrifuged at high speed to remove the debris. Starch gel electrophoresis\(^{13,26}\) was performed using a 0.03 M Tris-EDTA-Boric acid buffer pH 8.1 for the preparation of the starch gel ("Connaught" starch) and a 0.1 Boric acid-Sodium hydroxide buffer pH 9.0 as the bridge solution. Amido black 10B was used as a protein stain and an 0-dianisidine reagent (100 mg. 0-dianisidine dissolved in 200 ml. absolute alcohol, 100 ml. 0.25 M sodium phosphate buffer pH 4.7 and 0.5 ml. 30 per cent hydrogen peroxide) for the
Fig. 1.—The chromatographic behaviour of the $V_1$ and $V_2$ fractions on CMC-cellulose and of Hb-A$_2$ on DEAE-cellulose.

demonstration of the different hemoglobin zones. The percentages of alkali resistant hemoglobin were determined by the method of Jonxis and Visser.¹⁹

Quantitative analyses of the fast moving hemoglobin fractions were performed with carboxymethylcellulose (CMC) chromatography. The technic used was a modification of that described earlier.¹¹,²¹ Columns of 25 x 0.9 cm. were filled to a final height of 20 cm. with CM-Cellulose, which was equilibrated with an 0.01 M phosphate buffer of pH 6.5. Amounts varying from 35 to 40 mg of Hb (dissolved in 1 ml.) were chromatographed. Prior to chromatography, the Hb solutions were dialyzed overnight at 4 C. versus the same buffer as used for the equilibration of the cation exchanger. Elution was performed with the equilibration buffer at a flow rate of approximately 10 ml/hour. After collecting 40–45 ml. of the effluent, the elution was continued with an 0.01 M phosphate buffer of pH 8.4. During the first elution period, two fractions were obtained; one ($V_1$) was a large number of non-hemoglobin proteins, and the second ($V_2$) a column artifact. The remaining hemoglobin (Hb-A + Hb-F + Hb-A$_2$) was recovered during the second elution period allowing a calculation of the percentages of the $V_1$ and $V_2$ fractions.

When no fast moving Hb components were detectable by starch gel electrophoresis, the amount of the $V_1$ fraction was found to be about 0.2 per cent and that of $V_2$ 0.38 per cent, both being calculated as hemoglobin. In cases with notable amounts of fast moving hemoglobin fractions (designated as Hb-Bart's and Hb-H) an increase in the percentages of the $V_1$ and $V_2$ fractions was noted (fig. 1), allowing a reasonably accurate method for the quantitative determination of the amounts of fast Hb-fractions present in such samples. The isolated fractions were studied by starch gel electrophoresis, denaturation towards alkali,¹¹ UV spectral analyses and hybridization experiments.²⁶,²⁵ The hemoglobin present in the $V_1$ fraction showed the characteristic properties of Hb-H, such as the electrophoretic mobility of Hb-H, and UV spectrum similar to that of Hb-A and a high rate of denaturation by alkali. Hb-A was produced as hybrid hemoglobin when the hemoglobin of the $V_1$ fraction was hybridized with the $\beta$ chain abnormality Hb-S. The hemoglobin of the $V_2$ fraction, isolated from cases with notable quantities of the fraction designated as "Hb-Bart’s," possessed an electrophoretic mobility similar to that of Hb-Bart’s, while small
amounts (5–10 per cent) of Hb-A were also detectable. The fraction showed a moderate rate of denaturation by alkaline reagents, while its UV spectral adsorption curve was identical to that of Hb-F. Fetal hemoglobin was produced as hybrid hemoglobin when the component was hybridized with β chain abnormalities or with Hb-A or with Hb-A2. No fast hemoglobin components were detectable by starch gel electrophoresis in the bulk of the hemoglobin collected in the second phase of the elution. Considering these results, we feel confident in stating that V1 is composed of non-hemoglobin proteins and Hb-H, and that V2 is composed of small but constant amounts of Hb-A and varying quantities of Bart’s hemoglobin.

The percentages of Hb-A2 were determined by DEAE-cellulose chromatography following the simplified method described before. Since only very small amounts of Hb-A2 were present in cord blood samples, reasonable quantities (35–40 mg) of Hb were chromatographed (fig. 1). The results were expressed as per cent of total hemoglobin; the range of consistency of the method was found to be 20 per cent in cases with Hb-A2 below 0.15 per cent, 10 per cent for cord blood samples with Hb-A2 varying from 0.15 to 0.5 per cent, and 5 per cent for the adult blood samples with higher percentages of Hb-A2.

Large amounts of pure Bart’s hemoglobin were also isolated by CM-cellulose chromatography. Freshly prepared hemoglobin solutions, obtained from cord blood samples with larger quantities of the abnormal Hb fraction, were carefully dialyzed against the 0.01 M phosphate buffer pH 6.5. Three to five Gm. of Hb (dissolved in 20–30 ml.) were applied to a 40 x 2.0 cm. column of CM-cellulose which was equilibrated with the same phosphate buffer. Elution was carried out with the 0.01 M phosphate buffer pH 6.5 at a flow rate of about 100 ml./hour. The Bart’s Hb, which was almost completely separated from the faster moving V1 fraction and from the slow moving Hb-A and Hb-F components, was collected and the combined elution fractions concentrated by the use of short CM-cellulose columns. Starch gel electrophoresis revealed less than 5 per cent of Hb-A to be present.

Small quantities (4 ml.) of a 1 per cent solution of Hb-Bart’s were dialyzed against 0.1 M phosphate buffers with pH values ranging from 6.5 to 7.8. Oxygen equilibrium curves of these solutions were determined following the method of Brinkman and Dirken, which was also used in earlier studies. Since dilute Hb solutions were studied, per cent oxygenation was measured at the wavelength of 470 and 508 mμ using a Beckman DU spectrophotometer. Spectrophotometric analysis with the Beckman DK-2 automatic recording spectrophotometer revealed the presence of less than 3 per cent of methemoglobin. Mixtures of Hb-A and Hb-F, pure Hb-A and pure Hb-F, all isolated by the same procedure, served as controls.

**Results**

Over 300 cord blood samples were studied by starch gel electrophoresis. The hemoglobin patterns fell into three groups, namely, with no detectable Hb-Bart’s or Hb-H, with small amounts of Hb-Bart’s and Hb-H, and with moderate quantities of Hb-Bart’s and Hb-H. Examples are shown in figure 2. Hb-Bart’s and Hb-H were detectable in over 30 per cent of all the samples studied.

Fifty-four cord blood samples, selected at random, were arbitrarily divided on the basis of the starch gel electrophoretic pattern into the three groups: 1) 31 cases with no visible amounts of Hb-Bart’s and Hb-H; 2) 16 cases with small quantities of Hb-Bart’s and Hb-H; and 3) 7 cases with moderate amounts of Hb-Bart’s and Hb-H.

Results of the quantitative studies for the isolated fractions A2, V1 and V2 are shown in figure 3. All three groups show a similar tendency for an increase in the percentage of Hb-A2 with a proportional decrease in per cent
of fetal hemoglobin. When the percentage of $V_1$ was compared with the percentage of Hb-F, a reasonably constant value for $V_1$ of about 0.2 per cent was found in group 1, while a slight but definite increase in the percentage of $V_1$ with a decrease in Hb-F was noted for group 2. In group 3 a definite relationship could not be established, although there was a suggestion of an increase in $V_1$ with decrease of Hb-F. Larger amounts of $V_1$, namely, 0.5 to 1.5 per cent, were found to be present in this group.

The per cent $V_2$ in group 1 remained constant when compared with the per cent of Hb-F. Under our experimental conditions, about 0.4 per cent of Hb was eluted as the $V_2$ fraction, which, as has been pointed out before, is considered to be an artifact. In group 2, however, the $V_2$ percentages were found to be higher, 0.5–1.0 per cent, and decreased with decreasing levels of Hb-F, while in group 3 no definite relationship was apparent. The amounts of $V_2$ in this group ranged from 1.1 to 5.5 per cent.

In group 1, the sum of the isolated fractions $V_1$ and $V_2$ remained constant, whereas in group 2 a decrease with decreasing levels of Hb-F was noted. The ratio of $V_2/V_1$ in group 1 remained constant at about two. In group 2 the ratio of $V_2/V_1$ decreased with a decrease in the amount of fetal hemoglobin, indicating a relatively larger production of Hb-Bart's when the percentage of fetal hemoglobin was high. The ratio of $V_2/V_1$ in group 3 seemed to be constant at about 3.9. No definite relationship was evident between total Hb levels of cord blood and amounts of fetal hemoglobin.

Blood samples from the mothers of the 54 babies involved were studied for
the total Hb concentration, the levels of Hb-A2 and the possible presence of hemoglobin abnormalities. The total Hb values ranged from 7.5 to 15.6 Gm. per cent. The Hb abnormalities consisted of four sickle cell trait carriers, three Hb-C trait carriers and two heterozygous Hb-B2 carriers. The levels of Hb-A2 (1.6 to 2.9 per cent) varied within the normal range. Two cases exhibited an increased amount of Hb-A2 of 3.9 and 5.0 per cent, respectively. The babies from these two cases fell within the normal group (No. 1). At this time, the fathers were not available for study.

The quantities of the various hemoglobin fractions, Hb-A2, Hb-H present in V1, and Hb-Bart's present in V2 and Hb-F, were plotted against the estimated fetal age. It became apparent that no close relationship existed between fetal hemoglobin and fetal age. Hemoglobin A2 levels increased and Hb-Bart's and Hb-H percentages decreased as the fetal age increased.

Because of the large amounts of Hb-Bart's and Hb-H in group 3, these seven cases were studied more intensively. Blood samples were obtained from the babies five months after birth and from their respective parents when possible. Analytical data pertaining to the babies is shown in table 1. Using starch gel electrophoresis and the CMC-chromatographic procedure, no appreciable amounts of Hb-Bart's and Hb-H were detectable at this time. Small amounts of fetal hemoglobin, from 6.5 to 16 per cent, were still present. Hb-A2 levels were increased and fell within the normal range of 1.7 to 2.4 per cent.

Results of the studies pertaining to the parents of these seven children are presented in table 2. Absence of Hb-Bart's and Hb-H was demonstrated on starch gel electrophoresis and by column chromatography. The percentages of V1 and V2 were below the established upper limit of the normal range. The hematologic data, including the values obtained in the osmotic fragility
tests, were within the normal range with the exception of those of the mother of case 2 who exhibited a sickle cell trait anomaly. Her low hemoglobin of 8 Gm. per cent was probably due to her hemoglobin abnormality and a nutritional or iron deficiency anemia. One other mother, the mother of case 3, was a heterozygous Hb-B2 carrier.

In a cord blood sample from one member of premature white twins of about 7½ months (fig. 2) a slow moving minor hemoglobin fraction was found to be present with a mobility comparable to that of the Hb-B2. This minor Hb-fraction was isolated by DEAE cellulose chromatography and was found to be present for 0.3 per cent. Analysis of another sample collected two weeks after birth yielded approximately the same result. The ultraviolet absorption spectrum of this component was similar to that of fetal hemoglobin, while that of Hb-B2 is similar to that of Hb-A. Unfortunately, there was inadequate material for further study. Because of the ultraviolet absorption spectrum, the electrophoretic mobility and the absence of Hb-B2 in the mother, we, at present, feel that this component is probably identical with Hb-Gower II. The baby subsequently died of encephalitis at the age of five weeks. The other twin, as well as the mother, appeared to be normal.

Examples of the oxygen dissociation curves of the isolated Hb-Bart’s and the remaining mixture of Hb-F and Hb-A are shown in figure 4. It should be stressed that both components were always isolated from the same cord blood sample. Three major differences were found to be apparent: a) an enormous increase in the oxygen affinity of Hb-Bart’s as compared to that of the Hb-A and Hb-F mixture (approximately eight-fold); b) the oxygen dissociation curve of Hb-Bart’s showed a greatly reduced heme-heme interaction. The interaction constant n, as calculated from Hill’s equation \( y = \frac{K_o^n}{1 + K_o^n} \), was found to be 1.08 for Hb-Bart’s and 2.1 for the Hb’s AF mixture; c) when the oxygen affinity of Hb-Bart’s was studied over a wide range of pH values, no notable difference was found indicating the absence of a Bohr effect.

**Discussion**

The data presented have demonstrated the presence of small amounts of Hb-Bart’s and Hb-H in many cord blood samples of Negro babies. The quantities of these abnormal components varied to some extent with the age of the fetus; larger amounts of α chains lacking hemoglobin types were present in the cord blood of the premature born babies. Formation of Bart’s hemoglobin (γ4) was found to be decreased and the production of Hb-H (β4) increased in cases with lowered Hb-F formation, indicating the existence of a single deficiency in the production of normal Hb-F (α2γ2) and Hb-A (α2β2). The study of the blood samples of the mothers failed to disclose a genetic basis for this phenomenon. Apart from two cases with “classical” thalassemia trait, four cases heterozygous for Hb-S, three cases heterozygous for Hb-C, and two cases heterozygous for Hb-B2, no abnormalities were encountered. These findings, therefore, support the idea that a slight “α chain deficiency” is a common feature in the human fetus, resulting in the temporary forma-
Table 2.—Hematologic Data Pertaining to Parents of Some of Cases in Group 3

<table>
<thead>
<tr>
<th></th>
<th>Hb Pheno-type</th>
<th>Hb Gm.%</th>
<th>RBC 10^12/mm.³</th>
<th>PCV %</th>
<th>MCV cu.µ</th>
<th>MCH γ</th>
<th>MCHC %</th>
<th>Osmotic* Resistance</th>
<th>A₁ %</th>
<th>V₁ %</th>
<th>V₂ %</th>
<th>HbF %</th>
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<tr>
<td>Mother, case 1</td>
<td>A</td>
<td>13.2</td>
<td>4.55</td>
<td>43</td>
<td>94</td>
<td>29</td>
<td>31</td>
<td>0.43</td>
<td>2.5</td>
<td>0.05</td>
<td>0.05</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Mother, case 2</td>
<td>AS</td>
<td>8.0</td>
<td>3.88</td>
<td>31</td>
<td>80</td>
<td>20.5</td>
<td>26</td>
<td>0.34</td>
<td>—</td>
<td>0.13</td>
<td>0.11</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Father, case 2</td>
<td>A</td>
<td>14.2</td>
<td>4.99</td>
<td>43</td>
<td>85.5</td>
<td>28.5</td>
<td>33</td>
<td>0.47</td>
<td>2.8</td>
<td>0.13</td>
<td>0.08</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Mother, case 3</td>
<td>A B₂ A₂</td>
<td>10.9</td>
<td>4.89</td>
<td>38</td>
<td>78</td>
<td>22.5</td>
<td>28.5</td>
<td>0.45</td>
<td>2.1</td>
<td>—</td>
<td>—</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Father, case 3</td>
<td>A</td>
<td>14.9</td>
<td>4.77</td>
<td>43</td>
<td>90</td>
<td>31</td>
<td>35</td>
<td>0.41</td>
<td>2.8</td>
<td>0.05</td>
<td>0.05</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Mother, case 4</td>
<td>A</td>
<td>13.2</td>
<td>4.48</td>
<td>41</td>
<td>91</td>
<td>29.5</td>
<td>32</td>
<td>0.45</td>
<td>2.4</td>
<td>0.10</td>
<td>0.11</td>
<td>&lt; 2</td>
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<tr>
<td>Father, case 4</td>
<td>A</td>
<td>13.8</td>
<td>5.03</td>
<td>36</td>
<td>91</td>
<td>26.5</td>
<td>30</td>
<td>0.39</td>
<td>1.9</td>
<td>0.10</td>
<td>0.05</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Normals: females</td>
<td>A</td>
<td>12.0</td>
<td>4.64</td>
<td>38</td>
<td>82</td>
<td>26</td>
<td>31.5</td>
<td>0.43</td>
<td>2.1 ± 0.2</td>
<td>&lt; 0.2</td>
<td>&lt; 0.4</td>
<td>&lt; 2</td>
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<tr>
<td></td>
<td>males</td>
<td>13.5</td>
<td>4.93</td>
<td>40</td>
<td>82</td>
<td>27.5</td>
<td>34</td>
<td>0.46</td>
<td>2.1 ± 0.2</td>
<td>&lt; 0.2</td>
<td>&lt; 0.4</td>
<td>&lt; 2</td>
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*Per cent NaCl necessary for 50 per cent hemolysis.
†Total per cent of A₂ + B₂.
INHOMOGENEITY OF HEMOGLOBIN VI

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**Fig. 3.**—Relationship of the percentages of the isolated fractions Hb-A₂, V₁, V₂ versus Hb-F.

Of particular interest is the relatively high incidence of Negro babies with larger amounts of Bart's hemoglobin (up to 5.5 per cent) and of Hb-H (up to 1.7 per cent). Different authors have described newborn babies with similar abnormalities, the infants being the offspring of parents of primarily mongoloid origin. Our results are similar to those obtained by Hendrickse et al. who have found Bart's hemoglobin in about 10 per cent of all cord bloods of Nigerian Negro babies. In some studies a relationship between the occurrence of Bart's Hb and the presence of Hb-H disease or thalassemia is detectable in the parents; in most instances, however, no connection between the hemoglobin abnormality of the newborn and the hematologic picture of the parents could be established. The results of the continued studies of the seven cases with larger production of Bart's hemoglobin also failed to offer evidence for the existence of a definite hemoglobinopathy in either the
parents or the five-month old infants. This finding suggests the absence of expression beyond infancy of an abnormality, which could be responsible for the larger production of $\alpha$ chains lacking hemoglobin types. Our studies also failed to demonstrate any definite basis for distinguishing between group 2 with low amounts of Hb-Bart's and Hb-H, and group 3 with moderate quantities of these abnormal Hb fractions.

One of us$^{14}$ recently offered evidence for the existence of a quantitative difference in cases with "$\alpha$ chain deficiencies" which has led to the hypothesis of an independent control of the production of $\alpha$ chains by two $\alpha$ chain genes, one regulating the production of the $\alpha$ chains of Hb-F, and a second, that of the $\alpha$ chains of adult hemoglobin. This hypothesis was based on: a) the failure to detect any alteration in the pattern of the hemoglobins of the parents of babies with a large production of Hb-Bart's; b) the absence of Hb-H in cord blood samples with increased amounts of Hb-Bart's; and c) the presence of small amounts of a Hb-H-like component in both the cord blood samples showing the abnormal $\beta_4^*$ (Augusta 1) fraction and in the blood of some family members of one of these babies. The data obtained in the present investigations, which were carried out with more refined technics, indicate that the occurrence of Bart's Hb is always accompanied by definite production of Hb-H. This finding, together with the noted decrease in formation of Hb-Bart's and a corresponding increase in the amount of Hb-H when the per cent of Hb-F was lowered, supports the existence of one single deficiency in the production of $\alpha$ chains of Hb-A and Hb-F in many newborn babies and makes the above mentioned hypothesis no longer tenable.

Abnormalities other than Hb-Bart's and Hb-H were encountered in cord
bodings in our studies, namely, Hb-S in four cases, Hb-C in two cases, while
the discovery of a Hb-Gower-II-like component in one (white) baby was
of interest because this component is considered to be present in very young
fetuses only. Unfortunately, lack of material prevented an extensive study
of this abnormal component. It is worth noting that abnormalities such as
the \( \beta^* \) and \( \beta^+ \) which have been demonstrated in cord blood samples of
a few Negro babies, were not present in the presented material.

The results of the oxygen equilibrium determinations of the isolated Hb-
Bart's bear some underlying physiologic and theoretical aspects. The results
obtained for Hb-Bart's are comparable to those recently described for the
Hb-H. Both \( \alpha \)-chain-lacking Hb-types showed an enormous increase in oxygen
affinity, a decreased heme-heme interaction and the absence of any Bohr
effect.

It, therefore, becomes apparent that a hemoglobin with such gross func-
tional abnormalities could not occur as the major component, since under
physiologic oxygen tensions, its oxygen would be unavailable to the tissues.
This might explain the cause of death of the newborn children described by
Lie-Injo Luan Eng in whom Hb-Bart's formed the major hemoglobin fraction.

The absence of the Bohr effect in hemoglobin types composed of only \( \gamma \)
chains or \( \beta \) chains suggests that an interaction between \( \alpha \) and \( \gamma \) or \( \alpha \) and \( \beta \)
chains is essential for the change in the conformation of the protein respon-
sible for the Bohr effect.

The absence of heme-heme interactions in Hb-Bart's likewise indicates that
an \( \alpha-\gamma \) chain interaction, rather than a direct interaction between the hemes,
plays an important role in determining the sigmoid shape of the oxygen dis-
sociation curves of Hb-F and Hb-A.

**Summary**

In a survey of over 300 cord bloods of Negro babies, some 54 cases were
selected at random to study the occurrence of the minor hemoglobin com-
ponents Hb-Bart's, Hb-H, and Hb-A$_2$. The relationship of these components
to Hb-F is discussed. Seven cases with moderate amounts of Hb-Bart's and
Hb-H were studied more intensively, along with the respective parents when
possible. The findings suggest the absence of expression beyond infancy of
any abnormality responsible for \( \alpha \)-chain-lacking hemoglobin types of cord
blood.

The physiology of Hb-Bart's reveals its high oxygen affinity to be approxi-
mately 8–10 times that of Hb-A, its lack of a Bohr effect and an oxygen dis-
sociation curve showing no heme-heme interaction.

The discovery of a minute amount of a Hb-Gower II-like component in a
cord blood sample of a prematurely born white baby of 7.5 months is also
presented.

**Summario in Interlingua**

In un studio de plus que 300 specimens de sanguine de cordon ab neonatos
negre, 54 cases eseva seligite aleatorimente pro determinar le occurrentia
del minor componentes hemoglobina Bart's, hemoglobina H, e hemoglobina A$_2$. 
Es discutite le relationes inter iste componentes e hemoglobina F. Esseva executate plus intense studios de 7 sanguines con moderate quantitates de hemoglobina Bart's e de hemoglobina H, insimul con studios del parentes del donatores in tanto que isto esseva possibile. Le resultatos pare indicar le absentia—post le infantia—de omne expression del anormalitates responsabile pro le presentia in le sanguine de cordon de typus de hemoglobina sin le catena a.

Studios del physiologia de hemoglobina Bart's revela in illo (1) un alte affinitate pro oxygeno—approximativemente 8 a 10 vices illo de hemoglobina A, (2) absentia del effecto Bohr, e (3) un curva de dissociation de oxygeno que non monstra ulle interaction inter hem e hem.

Es etiam presentate le discoperta de un minute quantitate de hemoglobina Gower-II-like in un specimen de sanguine de cordon ab un infante blanc a nascentia prematur post 7,5 menses de gestation.

ACKNOWLEDGMENTS

The authors are grateful to Dr. C. S. Wright, Department of Medicine, Medical College of Georgia, for assistance in reviewing hematologic data, and to the Department of Medical Illustration for preparation of the figures.

REFERENCES

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