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From the Department of Obstetrics and Gynecology and the Pediatric Clinic, Karolinska Sjukhuset, Stockholm

Concentration of Fibrinogen in the Plasma of Healthy and of Erythroblastotic and Hyperbilirubinemic Newborn Infants

by LARS ENGSTRÖM and LARS KAGER

Taylor (5) presented the data from the literature on the concentration of fibrinogen in the plasma of newborn infants. The mean values reported in the various studies range from 140 to 350 mg/100 ml, with individual observations from 50 to 800 mg/100 ml. The discrepancies are thus considerable. Taylor also made observations of the concentration of fibrinogen in the plasma during the first week of life of 45 healthy infants. He used the clot density technique of Losner *et al.* (2) and found a slight increase in mean concentration of fibrinogen during the first three days of life. (First day mean 231 and range 182–398, third day mean 264 and range 196–399.) Neither sex, birth weight, nor concentration of fibrinogen in the mother's plasma had any influence on the infant's initial concentration of fibrinogen. Taylor discussed the possibility of fibrinogen concentration being used as a measure of an infant's liver function.

Rice (4) reported an immature infant (birth weight 1900 g) with erythroblastosis and petechiae on the abdomen and face and with blood-tinged sputum. The clotting time was two hours. Addition of thrombin in excess resulted in the formation of a fine fibrinous network. After exchange transfusion of 25–35 % of the blood, the plasma fibrinogen was 120 mg/100 ml. Rice concluded that the quantity of fibrinogen *before* the transfusion had either been appreciably lower, or that the blood had been initially free of fibrinogen.

Proceeding from Taylor's and Rice's results we have investigated whether there is any difference between the concentrations of fibrinogen in the plasma of healthy newborn infants and in infants with erythroblastosis or hyperbilirubinemia without blood-group incompatibility.

Material and Methods

Samples for fibrinogen study were drawn from 39 infants by means of a polyethylene catheter introduced into the umbilical vein. Twenty of the subjects were healthy full-term infants; the samples from fourteen of these infants were collected within two hours after birth, while in the other six the study extended over the first three to six days of life.

Ten infants had erythroblastosis due to Rh or ABO immunization of the mother. In these cases the samples were collected within two hours of birth and *before* an exchange transfusion.

TABLE 1. *Fibrinogen concentration in plasma of erythroblastotic infants at birth (mg/100 ml).*

Degree of severity	No. of cases	Fibrinogen
Group 1		
Coombs(+); 0 exchange transfusion	1	270
Group 2		
1 exchange transfusion	4	190, 230, 240, 310
Group 3		
2 exchange transfusions	2	240, 300
Group 4		
3 or more exchange transfusions	3	285, 290, 350

Groups 1–4

No. of cases	Range	Mean	SE	SD
10	190–350	271	14.7	46.3

Nine infants had exchange transfusions performed because of hyperbilirubinemia without blood-group incompatibility. Samples for fibrinogen determination were drawn before the first transfusion, which was between the third and sixth day of life.

The fibrinogen was determined by Morrison's syneresis method (3) as modified by Blombäck (1), a method not previously used in determination of fibrinogen in the plasma of newborn infants. The anticoagulant used in the collection of the samples consisted of 3.8% trisodium citrate (2 H_2O) in a dilution of one part to nine parts of blood. To every ml of trisodium citrate 40 mg of lysin ethyl ester dihydrochloride were added, so that any fibrinolytic activity present in the sample was eliminated (1, 6).

In 33 infants hematocrit values were determined concurrently with collection of the sample for fibrinogen determination (centrifugation for 5 minutes at 10,000 r.p.m.).

Results

A. *Healthy full-term infants examined within two hours of birth*

Individual observations ranged from 175 to 285 mg/100 ml, giving a mean value of 225. (Standard error ± 10.0, standard deviation ± 37.3, number of cases 14.) No difference was found between boys and girls.

One infant, who was excluded from the normal material because of mongolism, had the lowest fibrinogen concentration in plasma of any infant studied, i.e., 120 mg/100 ml.

B. *Healthy full-term infants examined during third to sixth day of life*

The mean was 322, lowest 240 and highest 380 mg/100 ml. (Standard error 21.2, standard deviation 51.9, number of cases 6.)

C. *Erythroblastotic infants*

These infants are classified in four groups in Table I according to the severity of the condition. Group 1 comprises the mildest cases whose Coombs test was directly positive but who did not require an exchange transfusion. The infants in Group 2 received one exchange transfu-

TABLE 2. *Fibrinogen concentration in plasma of infants with hyperbilirubinemia without blood-group incompatibility.*

Case no.	Non-conjugated bilirubin, mg/100 ml	Fibrinogen mg/100 ml
1	24.0	195
2	17.1	200
3	21.9	225
4	20.2	270
5	20.8	285
6	24.3	290
7	23.1	350
8	19.5	415
9	21.3	445

Case 1–9

No. of cases	Range	Mean	SE	SD
9	195–445	297	30.0	89.8

sion, in Group 3 two, and in Group 4 at least three. The most seriously affected children are thus those in Groups 3 and 4. The table also shows the fibrinogen concentration at the time of the first transfusion. The individual values ranged from 190 to 350 mg/100 ml with mean 271. (Standard error 14.7, standard deviation 46.3, number of cases 10.)

D. *Hyperbilirubinemic infants without blood-group incompatibility*

The severity in terms of the non-conjugated serum bilirubin concentration at the time of the first exchange transfusion, which immediately followed the drawing of the sample for fibrinogen study, is shown in Table 2. The fibrinogen concentrations ranged from 195 to 445 mg/100 ml, mean 297. (Standard error 30.0, standard deviation 89.8, number of cases 9.)

In 33 cases the plasma fibrinogen concentration was correlated to the hematocrit value at the time of drawing the sample, without regard to the above classification (Table 3).

Discussion

The results show that the concentration of fibrinogen in plasma was not lower in erythroblastotic than in healthy full-term infants. Indeed, the most severely affected infants proved to have fairly high fibrinogen levels.

Statistical analysis revealed that there was no correlation between hematocrit value and fibrinogen concentration as shown in Table 3. Thus a low hematocrit value in conjunction with erythroblastosis did not affect the fibrinogen concentration.

Samples for fibrinogen determination were drawn within two hours of birth. No account has been taken in this study of the possibility that the fibrinogenolytic activity in erythroblastic infants might become elevated after birth. Hemorrhagic tendencies were not observed clinically in any case.

Proceeding from Taylor's postulate that the plasma fibrinogen may be an index of the liver function at birth, we determined the concentration of fibrinogen in

TABLE 3. *Relationship between haematocrit value and plasma fibrinogen concentration.*

Case no.	Hematocrit, %	Fibrinogen, mg/100 ml	Case no.	Hematocrit, %	Fibrinogen, mg/100 ml
1	32	300	18	55	195
2	35	350	19	56	285
3	35	310	20	56	340
4	35	290	21	56	325
5	43	285	22	57	200
6	43	380	23	57	270
7	46	240	24	57	270
8	46	445	25	58	190
9	46	290	26	59	290
10	47	240	27	59	415
11	49	210	28	59	250
12	50	325	29	60	175
13	50	350	30	60	370
14	52	230	31	61	180
15	54	215	32	62	275
16	55	230	33	70	120
17	55	240			

the plasma of a group of infants with neonatal hyperbilirubinemia without blood-group incompatibility. The indication for exchange transfusion was here an elevated, non-conjugated bilirubin level in serum (Table 2), i.e. an expression of inadequate hepatic capacity. Since the transfusions and determinations of fibrinogen concentration were not done in these infants until the third to sixth day of life, the fibrinogen concentration was also studied in a group of infants of the same age but without icterus. No change was observed in plasma fibrinogen as a result of elevated, non-conjugated serum bilirubin. Nor was there any correlation between fibrinogen concentration and the quantity of non-conjugated bilirubin.

Apart from the fibrinogen value of the mongoloid infant, all fibrinogen levels fell within the limits found by Taylor for healthy children during the first week of life.

Our results, therefore, do not support Rice's hypothesis that Rh-immunization is accompanied by a low concentration of fibrinogen in the plasma of the affected infant—nor that the fibrinogen concentration changes as a result of hyperbilirubinemia not caused by blood-group incompatibility. This does not exclude the possibility, of course, that severe cases of erythroblastosis or hyperbilirubinemia may be complicated by afibrinogenemia due, for example, to intravasal clotting or fibrinogenolysis without direct association with the basic disease. In erythroblastosis and hyperbilirubinemia in general, however, the fibrinogen concentration in plasma is not a test of functional value, though this does not preclude the necessity of complete investigation of coagulation, including determination of fibrinogen concentration in the plasma, in all cases of clinically observed hemorrhagic diathesis in infants. But, as already stated, we had no case of hemorrhagic diathesis in our material.

Summary

The concentration of fibrinogen in the plasma of 39 infants during the neonatal period was determined by Morrison's syneresis method as modified by Blombäck. The samples were drawn from the umbilical vein by catheterization. The results, expressed in mean and standard error of the mean, were as follows:

A. Healthy full-term infants at birth: 225 ± 10.0 mg/100 ml.
B. Healthy full-term infants during third to sixth day of life: 322 ± 21.2 mg/100 ml.
C. Erythroblastotic infants at birth: 271 ± 14.7 mg/100 ml.
D. Hyperbilirubinemic infants without blood-group incompatibility during third to sixth day of life: 297 ± 30.0 mg/100 ml.

No statistically significant difference was found between healthy and erythroblastotic or hyperbilirubinemic infants as regards concentration of fibrinogen in the plasma.

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Department of Obstetrics and Gynecology
Karolinska sjukhuset
Stockholm 60
Sweden