

## Alkali Resistant Type of Hemoglobin in Women with Molar Pregnancy

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**A**LKALI resistant type of hemoglobin is normally found in the newborn (Fetal Hb) and at birth may constitute up to 90% of the total pigment.<sup>1</sup> This hemoglobin is replaced within the first few months of postnatal life by the adult type of hemoglobin. Small amounts of fetal Hb may continue to be produced by the healthy adult (up to 1% according to the immunologic technic<sup>2</sup> and up to 2% according to the alkali denaturation procedure<sup>3</sup>).

A high fetal Hb blood content has been demonstrated in adults in some genetically determined blood diseases such as sickle cell anemia, thalassemia and hereditary spherocytosis.<sup>4</sup> Although the manner of production of fetal Hb has been thought to be under genetic control, it may also be found in increased amounts in such acquired disorders as aplastic anemia, pernicious anemia, and multiple myeloma, and when the bone marrow is partly destroyed by cancerous metastatic lesions.<sup>4</sup>

In pregnant women significantly high blood levels of fetal Hb have been occasionally found in the second and third trimester of pregnancy. This finding, when observed in exceptional cases of late pregnancy, has been explained by transmission of fetal red blood cells through the placenta.<sup>5</sup>

In the second trimester of pregnancy it has been considered to be due to the excessive production of fetal Hb by the maternal embryonic hematopoietic system, reactivated by some hormonal or other factors present in pregnancy.<sup>6</sup> It has been suggested that acute changes in the concentration of chorionic gonadotropin occurring in early pregnancy may play a role in the stimulation of the embryonic maternal hematopoietic system and result in the production of fetal hemoglobin.<sup>6</sup>

An opportunity to study this hypothesis was presented in 4 cases of molar pregnancy characterized by the production of large amounts of chorionic gonadotropin.

### MATERIAL AND METHOD

In order to determine the variations of fetal Hb occurring in normal and disturbed early pregnancies, fetal Hb blood concentration was examined in a series of 40 pregnant women in the first three months of pregnancy and in 28 women suffering from bleeding due to imminent and incomplete abortion.

In the 4 patients with molar pregnancies, fetal Hb blood levels were determined at weekly intervals before and after evacuation of the hydatiform mole. Titrations of chorionic gonadotropin in the urine were repeatedly performed until negative results were obtained 3 to 6 months following the molar abortion.

The molar tissue was examined histologically by serial sections in all the 4 cases studied. Determinations of fetal Hb were made according to the alkali denaturation method as described by Singer et al.<sup>3</sup>

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## RESULTS

In the series of 40 healthy pregnant women in the first 3 months of pregnancy the fetal Hb blood concentration varied from 0.5% to 2.2% of the total Hb with an average of 1.49 and standard deviation of 0.45 (fig. 1). The 28 women with hemorrhagic complications of early pregnancy showed the fetal Hb as a percentage of total Hb to vary in ranges similar to those of the normal pregnant women (ranges from 0.8% up to 2.2% with an average of 1.72 and standard deviation 0.32) (fig. 1).

In all the 4 patients with molar pregnancy the percentage of fetal Hb was higher than the maximal values found in the control groups. Following the evacuation of the mole the fetal Hb blood content decreased gradually until normal values were reached within 2 to 5 months (fig. 1, table 1). Chorionic gonadotropin titrations showed very high titer in the 4 patients, the maximal values varying from 200,000 to 500,000 M.U. in 1 liter of urine. No chorionic gonado-

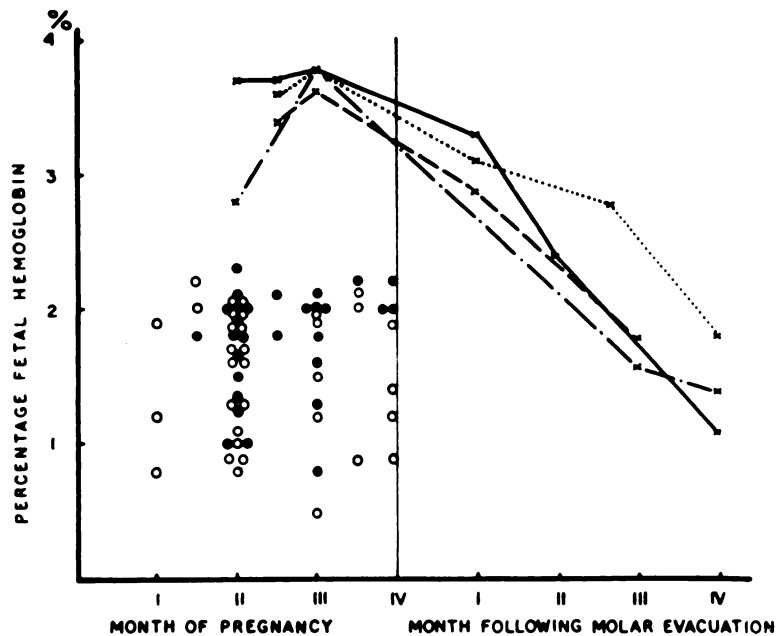


FIG. 1.—Percentage of fetal hemoglobin in molar pregnancies (X), normal early pregnancies (○), and abortions (●).

TABLE 1

*Percentage of Fetal Hemoglobin in Patients with Molar Pregnancies Before and After the Evacuation of the Mole*

Case No.	Weeks of Pregnancy			Weeks Following Molar Evacuation			
	8	10	12	4	8	12	20
1		3.4	3.6	2.9		1.8	
2	3.7	3.7	3.8	3.3	2.4		1.1
3	2.8		3.8			1.6	1.4
4		3.6	3.8	3.1		2.8	1.8

tropin could be detected in urine between 1 and 3 months following evacuation of the mole.

#### COMMENT

In the 4 cases of molar pregnancy no embryo was present and therefore the increased amounts of fetal Hb could not have resulted from the transplacental transmission of fetal blood. Thus it may be assumed that the fetal Hb found was produced by the patients' reactivated fetal erythropoietic mechanism.

Further investigations are required in order to establish whether excessive production of chorionic gonadotropin, stress due to a very rapidly growing tumor or some other factors are responsible for the reactivation of the erythropoietic activity in these patients.

#### SUMMARY

In 4 patients with molar pregnancy the fetal Hb blood concentration was found to be significantly higher than that found in control groups of normal early pregnancy and in imminent and incomplete abortions. Following the molar abortion the fetal Hb decreased gradually and reached normal values within three to five months.

It is assumed that the increased production of fetal Hb in these patients is due to the reactivation of fetal erythropoietic activity by either excessive amounts of chorionic gonadotropin, stress due to a rapidly growing tumor or to some other unknown factors.

#### SUMMARIO IN INTERLINGUA

In 4 patientes con pregnantias molari, significativemente plus alte concentrationes de fetal hemoglobina esseva constatate que in patientes de un gruppo de controllo con normal pregnantias non avantiante o con imminente e non-completate abortos. Post le aborto molari, le concentration del hemoglobina fetal descendeva e attingeva nivellos normal in le curso de inter tres e cinque menses.

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#### REFERENCES

- <sup>1</sup> ITANO, H. A.: Human hemoglobin. *Science* 117: 83, 1953.
- <sup>2</sup> CHERNOFF, A. I.: Immunologic studies of hemoglobins. II. Quantitative precipitin test using anti fetal hemoglobin sera. *Blood* 8: 413, 1953.
- <sup>3</sup> SINGER, K., CHERNOFF, A. I., AND SINGER, L.: Studies on abnormal hemoglobins; their demonstration in sickle cell anemia and other hematological disorders by means of alkali denaturation. *Blood* 6: 413, 1951.
- <sup>4</sup> —: Clinical significance of abnormal hemoglobins. *Yearbook of Pathology and Clinical Pathology, 1953-1954*, p. 393.
- <sup>5</sup> BROMBERG, Y. M., SALZBERGER, M., AND ABRAHAMOV, A.: Transplacental transmission of fetal erythrocytes with demonstration of fetal hemoglobin in maternal circulation. *Obst. & Gynec.* 7: 672, 1956.
- <sup>6</sup> RUCKNAGEL, D. L., AND CHERNOFF, A. I.: Immunological studies of hemoglobins. III. Fetal hemoglobin changes in the circulation of pregnant women. *Blood* 11: 1092, 1955.