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Total Iron-Binding Capacity in Normal Pregnancy[1]

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It is estimated that the human body normally contains 3 to 4 gm of iron, an essential component of hemoglobin, myoglobin, the cytochromes, and other enzyme systems. There are about 1.8 to 3.0 gm of iron in the circulating hemoglobin mass, 0.3 to 0.5 gm in myoglobin or cellular iron, with the remainder being stored in the liver, spleen and bone marrow.

Our current study involves the changes in the transport mechanism of iron surrounding normal pregnancy in white women. At any one time, approximately 3 mg of iron is bound to serum proteins. Studies using Fe^{59} have shown that this iron turns over five or six times per day, that is, approximately 30 mg is transferred to and from the plasmatic pool in any given 24-hour period.

Under normal nonpregnant conditions there is enough iron-binding protein to bind about 9 mg of iron; therefore only about one third of the iron-binding protein is saturated at any one time. The unsaturated iron-binding protein is referred to as the latent iron-binding capacity. The serum iron plus the latent iron-binding capacity constitute the total iron-binding capacity.

Though total iron-binding capacity has been studied in the past, we thought that the availability of a new sensitive rapid test warranted re-evaluation of this entity for establishment of its physiologic changes associated with normal pregnancy. We also thought that evaluation was indicated when these normal pregnant women were given maintenance doses (150 mg) of ferrous sulfate daily by mouth. With the establishment of this standard we would then be able to evaluate the changes in the total iron-binding capacity occurring with the anemias and the other complications of pregnancy such as the toxemias.

PROTOCOL

Serum iron and latent iron-binding capacities were determined on pregnant women whose hemoglobin concentrations were more than 10 gm per 100 ml of blood and whose pregnancies were considered normal in all other aspects. Four groups of patients were studied: (1) 121 who had received no iron therapy; (2)

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TABLE I

HEMOGLOBIN AND SERUM IRON IN PREGNANCY

Lunar month	*Nontreated*				*Treated*			
	Determinations	*Average hemoglobin, gm/100 ml*	*Serum iron, μg/100 ml*		*Determinations*	*Average hemoglobin, gm/100 ml*	*Serum iron, μg/100 ml*	
			Range	*Average*			*Range*	*Average*
2	15	12.5	55–176	111.3				
3	25	12.1	57–189	116.7				
4	22	11.6	69–215	124.4				
5	17	11.5	59–170	116.8				
6	5	11.9	43–150	108	3	11.8	69–122	100.6
7	7	11.4	56–220	141.7	5	12.3	40–174	111.0
8	6	10.7	61–107	82.8	5	13.1	56–128	87.2
9	6	11.7	95–180	119.6	6	11.2	44–209	124
10	15	10.9	56–152	107.7	27	12.1	31–244	110.2
11	3	12.6	92–107	98.0	8	11.7	30–241	108.8

54 who had received ferrous sulfate orally for 2 or more months prior to the tests; a single determination was made on each subject in groups 1 and 2 and tabulated for the lunar month of the pregnancy as estimated from the date of onset of the last menstrual period; (3) 32 who were in the postpartum period; and (4) 30 paired full-term infants and mothers on whom determinations were made on blood samples obtained at the time of delivery.

Serum iron was determined by a method described by Ramsay (1) utilizing the formation of the ferrous dipyridyl complex, a colorimetric method. The latent iron-binding capacity was determined by a method outlined by Tauxe (2) using a mixture of radioactive and nonradioactive iron, supersaturating the serum proteins, removing the excess iron with resin, and measuring the concentration of Fe^{59} remaining in the serum.

The standards established by these methods for normally menstruating nonpregnant women are 75 to 175 μg/100 ml of serum for serum iron and 275 to 400 μg/100 ml of serum for total iron-binding capacity.

TABLE II

SERUM IRON: COMPARISON BETWEEN PRIMIGRAVIDAS AND MULTIGRAVIDAS IN THE NONTREATED GROUP

Lunar month	*Primigravidas*			*Multigravidas*		
	Average hemoglobin, gm/100 ml	*Serum iron, μg/100 ml*		*Average hemoglobin, gm/100 ml*	*Serum iron, μg/100 ml*	
		Range	*Average*		*Range*	*Average*
2	11.9	68–127	110.7	12.8	55–176	111.7
3	12.6	98–144	116.4	12.1	57–189	120.7
4	11.8	69–167	120	11.6	70–215	126
5	12.2	59–142	98.3	11.1	79–170	127
6	11.9	111–150	135	11.9	43–92	77
7	11.1	56–126	91	11.5	84–220	162
8	11.2	75–107	91	10.5	61–92	78.7
9	11.8	117–180	148	11.7	95–110	105
10	10.6	78–107	95	12.7	56–152	110.9

RESULTS

Though the serum-iron levels fluctuated during pregnancy, neither the range nor the average showed any particular trend in either the treated or the nontreated group (Table I). In almost every category there were serum-iron levels below normal despite the normal hemoglobin levels. To evaluate the possibility that previous pregnancies might have influenced the serum-iron levels, primigravidas were compared with multigravidas in the nontreated group; there was no significant difference between the two groups (Table II).

The average total iron-binding capacity became increased in the nontreated group in the sixth lunar month and in the treated group in the seventh lunar month (Table III). The range of the total iron-binding capacities rose above the upper limit of normal in the eighth lunar month in the nontreated group and in the ninth month in the treated group. In the treated group the average total iron-binding capacity declined slightly as term approached.

The mean saturation of the iron-binding protein in the nontreated group declined from 32.8 per cent in the first trimester to 30.7 per cent in the second and to 26.3 per cent in the third. In the treated group the mean saturation of the iron-binding protein was 25.9 per cent in the second trimester and 29 per cent in the third.

In the postpartum period the serum-iron levels in both groups were lower in the first week than in the later weeks (Table IV). The total iron-binding capacities had returned to normal by the fourth postpartum week in both groups.

The data for the two groups during pregnancy and the postpartum period are summarized in the illustration.

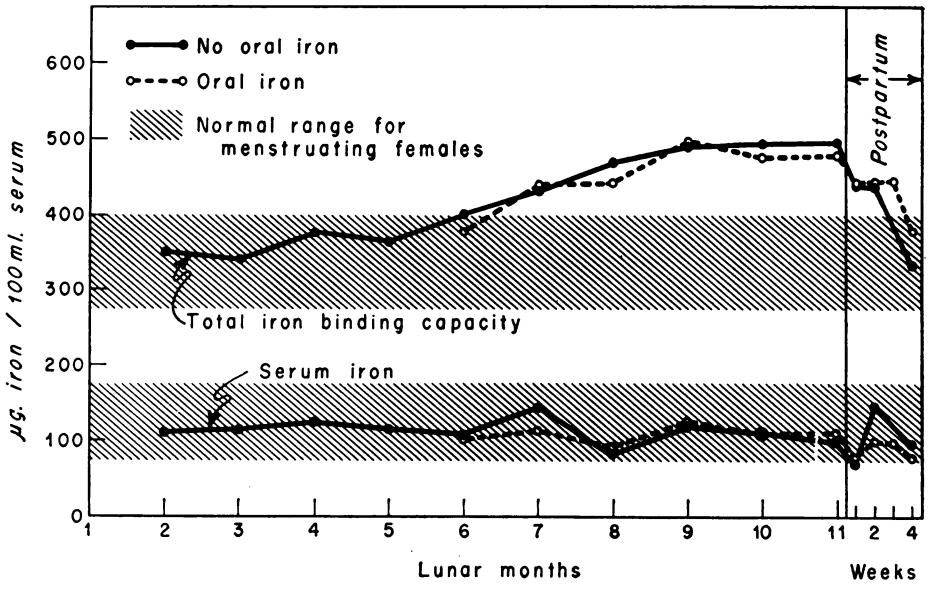

Fig. 1. Total iron-binding capacity and serum iron during pregnancy and the postpartum period in treated and untreated women.

The serum-iron level in the mothers was consistently lower than in the cord blood of the infants at term, and the total iron-binding capacity in the mothers was consistently higher than in the infants (Table V). The mean saturation of the iron-binding protein was 23.2 per cent in the mothers at term and 61.5 per cent in the infants. In 37 per cent of the infants the iron-binding protein was 80 per cent or more saturated.

DISCUSSION

The method used to determine latent iron-binding capacity has an error of less than 1 per cent. The Ramsay chemical method of serum-iron determination has an error of 2 per cent. Bowie and co-workers (3) have shown that there is no significant diurnal variation in total iron-binding capacity.

TABLE III

TOTAL IRON-BINDING CAPACITY IN PREGNANCY

Lunar month	*Nontreated*			*Treated*		
	Determinations	*Total iron-binding capacity, μg/100 ml*		*Determinations*	*Total iron-binding capacity, μg/100 ml*	
		Range	*Average*		*Range*	*Average*
2	15	252–472	350.8			
3	25	246–442	342.8			
4	22	261–559	375.5			
5	17	214–442	365.0			
6	5	347–514	401.0	3	358–406	378.6
7	7	335–525	426.7	5	393–479	437.2
8	6	463–504	473.8	5	354–518	438.0
9	6	456–529	489.3	6	461–565	496
10	15	381–661	491.5	27	317–655	475.4
11	3	472–579	496.3	8	418–515	479.5

TABLE IV

POSTPARTUM VALUES FOR HEMOGLOBIN, SERUM IRON, AND TOTAL IRON-BINDING CAPACITY

Week	*Nontreated*						*Treated*					
	Determinations	*Average hemoglobin, mg/100 ml*	*Serum iron, μg/100 ml*		*Total iron-binding capacity, μg/100 ml*		*Determinations*	*Average hemoglobin, mg/100 ml*	*Serum iron μg/100 ml*		*Total iron-binding capacity, μg/100 ml*	
			Range	*Average*	*Range*	*Average*			*Range*	*Average*	*Range*	*Average*
1	5	11.4	56–76	69.8	352–531	441.6	10	10.6	42–141	76.3	401–516	443.1
2	3	12.6	140–160	149	360–490	436	5	12.3	53–197	100.2	387–515	446.4
3							4	11.8	61–131	97.7	376–523	448.5
4	3	10.8	71–115	96	324–348	333	2	11.0	72–84	78	368–384	376

It is frequently stated that in normal women the serum-iron levels decline progressively during pregnancy (4-8), but other authors (9, 10) state that they remain constant. Gerritsen and Walker (10) in their study of Bantu women hypothesized that the unchanged serum-iron levels in pregnancy are due to the high iron intake of their subjects. It has been shown (7, 11) that iron uptake from the intestinal tract is increased in the later part of pregnancy. In this light it is of particular interest that the serum-iron levels in both the treated and the nontreated group in our series did not change during pregnancy. Parity did not account for any difference in serum-iron levels.

Our finding that the total iron-binding capacity rose during pregnancy is consistent with that reported by others (4-7, 9). This suggests that the deviation in iron-binding capacity is part of the mechanism aiding in the increased absorption of iron from the gastrointestinal tract (12). This increased absorption is known to occur late in pregnancy. The constant serum-iron levels are consistent with an increased rate of iron turnover from the plasmatic pool either to maternal storage or to the fetus whose need for iron is increasing.

SUMMARY

Using a chemical method of determining serum iron described by Ramsay and a method utilizing Fe^{59} for determining total iron-binding capacity as described by Tauxe, we found that (1) serum-iron levels remained within normal limits with or without supplemental iron therapy during pregnancy; (2) the total iron-binding capacity exceeded normal starting in the sixth lunar month in the nontreated group and in the seventh lunar month in the treated group, and it decreased slightly in the latter toward term and had returned to normal in both groups by the fourth postpartum week; and (3) the fetal serum-iron levels were consistently higher than the maternal levels despite a consistently lower total iron-binding capacity in the fetus.

TABLE V

VALUES FOR SERUM IRON AND TOTAL IRON-BINDING CAPACITY IN MOTHERS COMPARED WITH VALUES IN INFANTS

	Serum iron, μg/100 ml		*Total iron-binding capacity, μg/100 ml*	
	Range	*Average*	*Range*	*Average*
Maternal	80–244	117.6	339–601	508.0
Infant	125–333	176.8	202–393	287.0

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