ROLE OF THYROID IN LABOUR & ABORTION

by

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Introduction

Litzenberg (1921) was one of the earliest clinicians to recognise the importance of the thyroid hormones in the reproductive processes. Delf and Jones (1948) reported that 63.5% of the cases in their investigation had an inadequate thyroid function and that in 35% of such subjects, the thyroid was the sole factor responsible for the failure of reproduction. The thyroid hormones circulate in the plasma as a complex with the globulin fraction and this complex has been designated as protein bound iodine (PBI) and one of the tests of thyroid function consists in the estimation of PBI. Peter *et al* (1948) have shown that the onset of pregnancy is associated with the elevation of PBI and that the increased level is maintained throughout the period of pregnancy. A similar observation was recorded by Heinemann *et al* (1948) who reported that the elevated value ranged from 6 to 10 micrograms per 100 ml of serum. Mann and his co-workers (1951) and Singh and Morton (1956) observed that the highest level of PBI was reached as early as in the second/third week of pregnancy (6 to 11 microgram/100 ml) and the increased level remained constant till a few days after delivery. Mann *et al* (1951) and Russell (1953) observed, in a small series of pregnancies, a correlation between the tendency to abort and the failure of PBI to rise above 6 microgram/100 ml.

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Dowling, *et al* (1956) and Robbins and Nelson (1958) have shown that the thyroxine binding capacity, probably the concentration of thyroxine binding globulin (TBG), was increased in pregnancy as early as the second month and persisted for some weeks after delivery. In some cases of habitual abortion, Dowling *et al* (1956) did not find any increase in TBG. A similar finding was also recorded by Russell and his co-workers who also postulated that the increase in TBG in pregnancy was probably due to the stimulation by the increased level of circulating oestrogens. As a proof of this hypothesis, it was shown that the administration of oestrogens to non-pregnant women caused a rise in the level of PBI in the serum. It is known that the oestrogen production gradually increases during pregnancy, although there are reports of a rather marked decrease about one week before term (Cantarow and Trumper, 1962) and this decrease in oestrogen production, in its turn, should cause a fall in the PBI level of the blood

before the onset of labour. The observations recorded earlier, however, do not indicate any fall in serum PBI level before delivery, and thus it was decided to reinvestigate the problem with a special reference to changes in the level of PBI near the end of the term.

Material and Method

Eighty pregnant cases were selected for this investigation. These cases were from the middle and low income group in the Armed Forces. Each case was examined thoroughly and only those cases who were thought clinically normal were selected for this study. Any case who was thought to have any organic disease was rejected. For every case a card was maintained in which monthly antenatal records were kept. The first blood sample for PBI was taken on their first visit after conception and they were asked to come every month for the subsequent estimations (records were maintained in their respective cards). When these patients were admitted to the hospital for delivery a blood sample for PBI was taken during the active stage of labour; a sample of cord blood was also taken in some cases after delivery of the foetus. The last blood sample was taken on or about the third postnatal week and this PBI level was taken to be her level of the non-pregnant state. It was ensured that a minimum of three PBI readings during pregnancy and one during active labour must be there before a case was submitted for observations.

A second group of 31 cases who came with bleeding during the early months of pregnancy was also investigated. This group was subdivided into (a) threatened abortion group-15 cases, (b) inevitable abortion group-2 cases, and (c) incomplete abortion group-14 cases, according to the clinical findings of each case. Here also, care was taken to see that the cases showed no other positive cause for abortion which could be detected either from history or from clinical examination.

The serum PBI was estimated by alkali incineration, according to Foss *et al* (1960).

The results are recorded in Tables I and II.

Observation: In normal pregnancy:

1. There is a tendency to a steady rise in the level of PBI as the pregnancy progresses.

2. There is a significant fall (1 mcgm% or more) in the level of PBI during the active stage of labour in 25 or 55.56% of cases; there is either a stationary level or a slight rise or fall (i.e. 0.5% mcgm%) in 12 or 26.7% of cases, and in 8 or 17.78% of cases there is a significant rise of 1 mcgm% or more.

3. The non-pregnant level in these cases ranges between 4 to 7 mcgm% with an average of 5.5 mcgm% and this level is more or less reached in 18 or 40% of cases.

4. Cord blood of 9 cases collected out of 11 showed that PBI level almost reached the pre-pregnant PBI level of the mother.

5. In 39 out of 45, the range of PBI in the last month of pregnancy ranged between 5.5 to 11 mcgm%.

6. But, during the active phase of labour this PBI level ranged between 5 to 8 mcgm% in 37 out of 45 cases

TABLE I

Showing monthly levels of PBI in McGm% in normal pregnancy during and after labour

S. No.	Name of the pt.	Months							During labour.	After labour.	Cord blood Mc Gm%
		3rd	4th	5th	6th	7th	8th	9th			
1.	MM	5	..	5.5	..	7	..	8	6	5.5	16
2.	SKC	..	..	..	..	8.5	9	9	7	6.5	..
3.	KP	..	..	..	5	6	..	5.8	6.3	6	6
4.	S	..	6	6.5	..	..	7	7.5	6	6	..
5.	NB	..	..	7.5	..	9	10	11	11.5	10	10
6.	SS	..	..	..	..	7.5	9	9	11	7.5	..
7.	M	5	..	5.7	..	..	..	6	5.5	5	5
8.	SD	5	6	5.8	..	7.5	..	..	5.5	5	..
9.	PMY	..	..	7.8	7	7.5	..	9.5	9	7	..
10.	L	..	..	..	7	7.5	..	8	6.8	6.8	20
11.	K	6.8	..	8	..	7.5	..	8	6	5.5	..
12.	T	5.3	..	..	7	..	..	8	7	5.5	5.
13.	SB	..	6	6.5	..	7.5	..	3	8	6.5	..
14.	DS	..	..	5.5	..	..	11	11	8.5	8.5	..
*15.	K	..	6.7	..	8.8	8.5	..	..	8	6	..
16.	S	4.8	..	4.5	..	8	..	7.5	6.3	6	..
17.	R	..	6	..	6.5	..	..	7	4.5	12	..
18.	V	..	..	7	..	9.5	..	7	8.7	6	..
19.	SK	..	..	..	..	7.5	8	6	7.5	7	..
20.	MN	5	..	6.5	..	7	..	15	4.4	5	4
21.	TB	..	..	..	7.5	..	10	8	12.5	8	..
22.	S	..	..	8	..	10	..	10.5	8.5	8	..
23.	S	..	4.5	..	6	..	6.5	7	2	4	5.5
24.	JB	..	..	7	7.5	..	10	..	7	6	..
25.	DB	..	..	5.8	..	6.3	6.5	7.5	7	6	..
26.	MD	..	..	5	..	5.5	5.3	..	5	5.5	..

* Still birth

S. No.	Name	3rd	4th	5th	6th	7th	8th	9th	10th	During labour.	After labour.	Cord blood.
27.	RB	..	5.8	..	7.5	..	7	..	10	4.5	6	..
28.	NBR	6	6.8	..	..	..	10	..	..	5.2	12.5	5.5
29.	P	..	..	..	..	..	7.5	9	9	11	7.5	..
30.	TD	..	5	..	6.5	..	7	..	..	6	5.6	..
*31.	SM	..	..	7	6.5	..	..	..	5	..	4.5	..
32.	SB	..	9	..	6	..	..	9	..	7.5	7	..
33.	U	..	..	..	6.8	..	7	..	7.8	8	6.5	..
34.	AB	..	..	..	8.8	..	9	..	10	9,5	7	..
35.	MM	..	..	..	6.5	9	..	10.5	10	9	7	..
36.	S	..	6	..	..	9.5	..	10	13.5	10	7	..
37.	NN	..	..	..	10	..	7	7.5	7.5	7	9.5	..
+38.	A	5.7	..	13.2	6	4	9	7	..	7.5	6	..
39.	MS	..	8	..	..	9	..	9.5	..	8.3	8	2.7
40.	S	6.8	..	7.3	..	7.5	..	10	11.5	8	7	..
41.	S	..	6.3	..	6	..	7	7.5	10	10	7.5	7.8
+42.	N	..	..	5	4	..	3.5	..	..	..	..	..
43.	T	..	7	..	11	..	11.5	..	11	10	10	..
44.	LB	..	..	..	6.3	..	7	11	..	10	6.5	..
45.	P	..	..	5.5	..	..	6	6.8	7.5	6.5	6.	..

* Still birth.
\+ Anencephalic monster delivered at full term.
\+ Anencephalic monster delivered at 8th month of pregancy.

TABLE II

Serum PBI Level in McGm% in different types of abortions, monthwise

S. No.	Patient	Threatened Month of pregnancy.						Inevitable Month of pregnancy.						Incomplete Month of pregnancy.					
		1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
1.	K	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	—	—
2.	AP	—	—	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
3.	SV	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	—	—
4.	ML	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6	—	—	—
5.	GM	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	—	—	—
6.	K	—	—	—	—	—	—	—	—	3.5	—	—	—	—	—	—	—	—	—
7.	K	—	—	6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
8.	T	—	—	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
9.	BRS	—	—	7.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10.	RDS	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7.5	—	—	—
11.	M	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	—	—	—
12.	P	—	—	6.3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
13.	SK	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6.5	—	—	—
14.	RK	—	—	8.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15.	P	—	—	—	—	—	—	—	—	—	—	—	—	—	—	17.5	—	—	—
16.	F	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5.5	—	—	—
17.	PS	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	—	—
18.	M	—	—	—	—	—	—	—	—	—	—	—	—	—	4	—	—	—	—
19.	MSDN	—	—	—	9.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20.	JS	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7.5	—	—	—
21.	P	—	—	—	—	—	—	—	—	—	—	—	—	—	—	9	—	—	—
22.	DVR	—	—	—	6.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—
23.	MRM	—	—	—	—	—	—	—	—	—	—	—	—	—	17	—	—	—	—
24	S	—	—	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25.	OP	—	—	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
26.	B	—	—	—	9	—	—	—	—	—	—	—	—	—	—	—	—	—	—
27.	L	—	—	—	—	—	—	—	—	4	—	—	—	—	—	—	—	—	—
28.	PS	—	—	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
29.	PKP	—	—	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30	JS	—	—	—	—	7.8	—	—	—	—	—	—	—	—	—	—	—	—	—
31.	N	—	—	—	—	—	10	—	—	—	—	—	—	—	—	—	—	—	—

This is almost equal to the level of non-pregnant euthyroid state, as found by us as well as other investigators.

7. There were two cases who gave birth to two anencephalic foetuses and the PBI levels in these two cases were low.

8. There were two cases of still born foetuses. In one case the PBI level at 5th month was 7 mcgm%, at 6th month 6.5 mcgm%, at 10th, 5 mcgm%, and during the active phase of labour no blood could be taken. In the other case the PBI level at 4th month was 6.7 mcgm%, at 6th month 8.8 mcgm%, at 7th month 8.5 mcgm%, in active phase of labour 8 mcgm% and her pre-pregnant level was 6 mcgm%. This gradual decrease in PBI level from 7 mcgm% to 5 mcgm% in one case and gradual increase in PBI level from 6.7 mcgm% to 8.8 mcgm% and then fall to 8 mcgm% during pregnancy may be due to withdrawal of oestrogens from the foeto-placental unit following intrauterine death of foetuses.

In Abortion Cases

1. In the inevitable abortion group, there were only two cases and both had low PBI level.

2. In the threatened abortion group there were 15 cases of which only one had a PBI level of 3 mcgm% and this case in spite of thyroid therapy aborted a week later.

3. In the incomplete abortion group there were 14 cases and nothing significant could be found in these cases as far as the PBI level was concerned (though in all the 31 abortions, the blood was drawn within the first 12 hours of the onset of bleeding).

Discussion

Peters *et al* (1948) have shown that the PBI level is elevated with the onset of pregnancy and this value remains high throughout pregnancy when compared with the non-pregnant level. Mann and his associates (1951) and Singh and Morton (1956) had a similar experience and state further that the high value was reached as early as the second or third week of pregnancy and remained so till a few days after delivery. The date recorded in this report, however, showed that the PBI level increases progressively till full term and there is a sudden fall with the onset of labour in 55.56% of cases; in the remaining cases, the level of PBI is either unchanged or has increased or decreased slightly. The non-pregnant levels of PBI in this series have been between 4 mcgm% to 7 mcgm%, with an average of 5.5 mcgm%, which is in agreement with that reported by other workers, Mann *et al* (1951), Singh and Morton (1960) and Russel *et al* (1960).

Russel and his co-workers (1960, 1964) thought that the increase in the thyroxine binding capacity of serum and hence the PBI level was the result of the stimulation of circulating oestrogens because they could produce a similar effect in non-pregnant women by administration of oestrogen. Diezfalusy and his colleagues (1961) have again shown that, although a large amount of oestrodiol-17 P and oestrone occur in the placenta, virtually all the oestrogens in the foetal tissue are in the form of oestriol and this is the reason for the predominence of oestriol in

the maternal urine.

From the above it can be concluded that the foetus and placenta form a separate autonomous unit in the mothers and may initiate many phenomena of pregnancy, such as onset of labour. Since it is presumed that oestrogen withdrawal from the maternal urine coincides with the initiation of labour, it can be postulated that the stoppage of production of oestrogen compound in the foeto-placental unit will ultimately reduce the level of oestrogens (total compound) which in turn will be reflected by a fall of PBI during labour if oestrogens are responsible for increase in level of PBI. In further support of this explanation it may be pointed out that Frandsen and Stokemann (1961) have found that mothers carrying anencephalic foetuses have a greatly reduced output of oestrogen in the urine, and in the present series there are two mothers whose PBI levels have been within pre-pregnant levels, who have given birth to two anencephalic babies. From the above it can also be concluded that the gradual reduction of PBI level in two cases of still births was due to the oestrogen withdrawal from the maternal blood due to the stoppage of production of oestrogen compounds by the foeto-placental unit of the mothers.

The level of PBI in the foetus during the intrauterine phase is lower than that of the pregnant maternal serum but greater than her non-pregnant state. But the work of Talalay and his colleagues (1958) prove that oestrogens exert tremendous effects on cellular metabolism and thus there may be a high level of PBI in the intra-uterine foetus. Withdrawal of oestrogens from the foeto-placental autonomous unit during the active phase of labour will naturally show low levels of PBI in the foetal blood during delivery. In 9 out of 11 specimens of cord blood estimation done by the present authors, it was shown that the PBI level of cord blood was more or less equal to the level of the mother in her non-pregnant state. However, no conclusion can be drawn from the above as we could not get the PBI estimation of foetal blood done during its intrauterine life before labour, nor in its post-natal stage.

In the 31 cases of abortions recorded in this series there are two cases in the inevitable abortion group characterised by a low level of PBI. In the thirteen cases of the threatened abortion group and fifteen in the incomplete abortion group, no correlation has been observed between the level of PBI and the tendency to abort.

Conclusion

1. There is a tendency to a steady rise of PBI level instead of reaching a peak in early months of pregnancy, as suggested by other workers.

2. In the majority of cases, there is a slight fall ranging from 0.5 mcgm% to 5 mcgm%, with an average of 2 mcgm%.

3. In the majority of cases it is noticed that the level almost reaches the pre-pregnant level just during labour which is contrary to the findings of other workers who found that the pre-pregnant level reached only during the first week of puerperium.

4. The foeto-placental unit oestrogen withdrawal before initiation of labour has an influence on the maintenance of PBI level.

5. Cord blood estimations show that PBI level is more or less similar to that of the pre-pregnant state.

6. Low levels of PBI in the maternal blood in relation to anencephalic and still born foetuses are of some significance.

7. There is no significant correlation between the PBI level and abortion.

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