FURTHER STUDIES OF CHORIONIC GONADOTROPHIN IN TOXAEMIA OF PREGNANCY

by

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The main source of the gonadotrophic principle which floods the body during pregnancy is the placenta and not the pituitary. The placenta is also the source of oestrogen and progestin. It is also believed that the cytotrophoblast or the Langhan's cells take the place of the anterior lobe and liberate the chorionic gonadotrophin whereas the syncytiotrophoblast takes up the functions of the ovary and liberates oestrogen and progestin.

The methods and materials have already ben discussed in our preliminary report published in Jour. Obst. and Gynae. of India, September 1953. It may not be out of place to mention that Loraine's Prostatic Weight Technique was followed all throughout the investigation.

Altogether 155 rats were dissected during the period of the enquiry. Of these 11 rats were untreated, 30 rats treated with normal pregnancy urine and 75 rats were treated with urine of cases of toxaemia of pregnancy. 39 rats were dissected for the preparation of the Standard Curve which was essential for the interpretation of the results in International Units. The Standard preparation used was 'Antuitrin S'. All the cases for this study were between 36 to 40 weeks of pregnancy. Only the cases whose kidney function tests were found normal were taken up in this series.

Table I.

Detailed data of 30 rats treated with urine of 10 cases of normal pregnancy.

Serial No.	B.Wt. in gms.*	P.Wt in mgms.*	Op.Wt/100 gms. of B.Wt.	Mean P.Wt. per 100 gm. of B.Wt.	P.Wt. in I.U.	Total Quantity of urine in c.c./24 hours.	24 hrs. excretion of C.G. in urine in I.U.
1	16.5	11.7	71				
2	20.5	10.2	49.8	66.6	0.02	2927	117.8
3	24.1	19.0	79				
4	28.0	19.3	69.2				
5	23.5	11.0	81	71.4	0.04	3443	275.4
6	20	12.8	64				

Serial No.	B.Wt. in gms.*	P.Wt. in mgms.*	Op.Wt/100 gms. of B.Wt.	Mean P.Wt. per 100 gm. of B.Wt.	P.Wt. in I.U.	Total Quantity of urine in c.c./24 hours.	24 hrs. excretion of C.G. in urine in I.U.
7	25	22.5	90				
8	30	30.3	101	82.9	0.12	1558	373.9
9	40	23.0	57.7				
10	23	19.0	87				
11	25	17.6	70.5	77.5	0.09	1727	310.8
12	25	18.7	75.0				
13	25	17.8	71.3				
14	32	25.6	80.0	85.1	0.15	2700	810.0
15	33	21.0	64.0				
16	19	15.3	80.7				
17	25	22.7	91.0	87.9	0.16	2872	919.0
18	29	32.5	112.0				
19	20	18.4	92				
20	30	21	70.3	80.1	0.1	1211	142 2
21	27	22.4	78				
22	28	18.7	80				
23	25	23.3	75	76.7	0.05	2660	266.0
24	31	20	75.1				
25	25	20	80				
26	30	21.0	70	80	0.1	1058	211.6
27	28	25.2	90				
28	21	21	100				
29	27	21.3	79	83	0.11	2000	440 0
30	35	24.5	70				

* P.Wt Prostatic weight.
* B.Wt Body weight.

Table II.

Detailed data of 75 rats treated with urine of 25 cases of toxaemia pregnancy.

Serial No.	B.Wt. in gms.*	P.Wt. in mgms.*	P.Wt./100 gms. of B.Wt.	Mean P.Wt. per 100 gm. of B.Wt.	P.Wt. in I.U.	Total Quantity of urine in C.C. per 24 hrs.	24 hrs. excretion of C.G. in Urine
1	20	22.4	112				
2	18	18	100	112	0.42	595	495.8
3	22	27.2	124				
4	23	28.7	125				
5	23	27.5	119	108.6	0.38	1331	1011.5
6	21	22.7	90.8				
7	16	20.8	130.6				
8	20	30	150	143.9	1.1	523	1150.6
9	24	36.2	151.1				

Serial No.	B.Wt. in gms.*	P.Wt. in mgms *	P.Wt./100 gms. of B.Wt.	Mean P.Wt. per 100 gm of B.Wt.	P.Wt. in I.U.	Total Quantity of urine in C.C. per 24 hrs.	24 hrs. excretion of C.G. in Prine.
10	22.5	25.2	112				
11	20	20.2	101.3	108.3	0.36	2020	1454 4
12	21.3	23.7	111.6				
13	19.5	31.2	160				
14	20	30	150	154	1.65	1100	363.0
15	23	34.9	152				
16	27	40	148				
17	24	36.2	151.1	148	1.3	2708	7040.8
18	20	28.9	144				
19	23	23	100				
20	28.5	25.5	90	39.2	0.2	2873	1149
21	21	16.3	77.6				
22	23	56.2	168				
23	24	36.1	151	170	2.8	1738	9732.8
24	30.5	58.2	191				
25	32	54.5	170.4				
26	25	45	180.2	170.3	2.8	2043	11440.5
27	21.5	34.4	160.3				
28	38	33.2	87.4				
29	28	28.8	103	86.4	0.15	3000	450
30	25.5	17.8	70				
31	24	33.6	140				
32	31	37.2	120	137	0.9	1500	2700
33	33	49.8	151				
34	33	29	126				
35	42	73	174	150	1.4	1527	4275.6
36	35	52.5	150				
37	27	28	102.1				
38	34	36.7	108	103.7	0.35	626	438.2
39	26.5	26	101				
40	22.5	37	164				
41	27	48	177.7	185.3	3.85	816	3973.2
42	26	56	215.3				
43	28	31.3	111.8				
44	35	41.7	119.1	115.5	.45	2156	1940.4
45	23.5	27.2	115.7				
46	32.5	46.4	142.7				
47	30.7	51.6	168.0	152	1.5	1216	3648
48	29.5	42.9	145.4				
49	30	42.4	140.6				
50	25	36.7	146.8	133.5	.85	1490	2533
51	22.5	25.5	113.3				

Serial No.	B.Wt. in gms.*	P.Wt. in mgms.*	P.Wt./100 gms. of B.Wt.	Mean P.Wt. per 100 gm. of B.Wt.	P.Wt. in I.U.	Total Quantity of urine in C.C. per 24 hrs.	24 hrs. excretion of C.G. in Prine.
52	26.6	22.9	86				
53	31.4	33.2	105.7	93.9	.225	2150	967.5
54	28.5	25.7	90.1				
55	19.0	24.3	127.9				
56	20.0	30.1	107.5	119.7	.50	1370	1370
57	26.5	32.8	123.8				
58	23.0	25.0	108.7				
59	21.0		119.0	118	.475	1010	959.5
60	23.7	30.2	127.4				
61	28.5	30	105				
62	20.5	25	122	118.0	.45	956	908.2
63	25	31.8	127.2				
64	23.5	30	106.3				
65	25	25	120	115	.475	472	448.4
66	19	22.6	118.9				
67	25.5	20	117.6				
68	27.0	34	126	131.5	.75	555	832.5
69	26.5	40	150.9				
70	24	25	104				
71	21.5	24	111.5	117.5	.475	970	9215
72	25.5	35	137.2				
73	17.5	19.5	111				
74	20.5	30	146	127.8	.65		1287
75	22.5	28	126.6				

* P.Wt - Prostatic weight.
* B.Wt - Body weight.

TABLE III

Mean prostatic weight ratio and the excretion of C. G. per 24 hours in 10 normal and 25 cases of toxaemia of pregnancy.

Cases Nature of Treatment		No. of rats dissected	Average B.Wt. in gms.*	P.Wt/100 gms. of B.Wt.*	24 hrs. excretion of C.G. in I.U.
Untreated		15	21	65.7	
Treated with normal pregnancy urine	10	30	26.3	79.12	396.6
Treated with Toxaemia of Pregnancy urine	25	75	25.53	127.92	2554.09

* B.Wt - Body weight.
* P.Wt - Prostatic weight.

Comments:

Smith and Smith postulate that in addition to the independant production of oestrogen and progestin from the placenta during pregnancy, the chorionic gonadotrophin is also converted into the folliculoid and leuteoid fractions, when there is a demand, to maintain constant supply in the body. As it is well known that the Langhan's cells in the later months of pregnancy are few and far between, if they are present at all, the declining chorionic gonadotrophin levels in serum and urine, as the pregnancy advances, are a natural consequence.

The normal level during the later months of pregnancy varies from 4,000 to 11,000 I.U. A value beyond this range is abnormal and some sort of obstetrical accident may be apprehended.

White and Hunt in 1943, got high level of chorionic gonadotrophin in the urine of pregnant diabetics. Smith and Smith in 1944, obtained high level of chorionic gonadotrophin with low blood oestrogen and low yield of urinary pregnanediol in pre-eclamptics.

This hormonal aberration in abnormal pregnancy is difficult to understand. The renal clearance of chorionic gonadotrophin in toxaemia has been found by Loraine to be within normal limits. It is 1.00ml./min. or less. This figure is typical of protein clearance.

There are two schools of thought amongst those who believe in the endocrinological theories of the etiology of pre-eclampsia. Some believe that this rise in chorionic gonadotrophin with the fall of placental steroids is compensatory, similar to the reciprocal behaviour of the anterior pituitary and the gonads.

Others believe that the rise is not due to an actual increased production but is due to the deficient utilisation of chorionic gonadotrophin resulting in decreased production of oestrogen and progestin.

Necessarily chorionic gonadotrophin is incompletely utilised resulting in its accumulation in the system and hence the rise in blood and urine level.

A bio-assay is a long drawn-out process. One has to depend on the supply of suitable materials. The colony, the climate, the feeding and particularly the breeding are very difficult problems.

Dr. Loraine's observations were based on 45 cases. Our results on 10 normal cases and 25 toxaemia cases do not compare favourably with Dr. Loraine's results.

Our range in 10 normal cases is between 117 to 919 I.U. (average 396.6 I.U.) and in 25 cases of toxaemia between 438 to 11,440 I.U. (average 2,554 I.U.)

In our series of 35 cases it was not possible to find out a line of demarcation between the high normal and low toxaemic values.

We consulted Dr. Loraine in Edinburgh about our results. He advised that constancy in the weight of the rats was more important than the constancy in the age of the rats. Since then we were trying to keep the weight of the rats more or less constant, irrespective of the age of the rats, but at the same time keeping in mind that the importance of

the investigation lies in the immaturity of the rats. But unfortunately the results did not change appreciably.

Another factor seemed significant about this discrepancy. One of us saw in Edinburgh that in Dr. Loraine's series the average body weight of the immature rats was between 40 to 50 gms., and sometimes more when they were 20 to 23 days old. For the same age, the average weight in our series was 25 gms. Whether this retardation of the growth was due to climate, in spite of the balanced diet and air conditioned room allotted for them, is not clear. This retardation in the general growth might affect the growth of the prostate even when the rat was treated with a growth stimulus like chorionic gonadotrophin.

However, the results shown in the tables are based on the animals locally bred in our animal house. We have observed, as Dr. Loraine has also observed, that there is often a significant rise in chorionic gonadotrophin content of urine of some of the cases of toxaemia of pregnancy, although the lower limit is definitely within the range of higher limits of normal cases.

Conclusion:

Compared to our 10 normal cases, the urine of 25 cases of toxaemia in our series did not show an increase in the C.G. titre beyond the normal range.

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