TAYROID STIMULATING HORMONE EXTRACTED FROM HUMAN PLACENTA

FUMIO AKASU, SETSU KAWAHARA, HIROSHI OHKI,
MICHIKO HARANO AND YOKO TEJIMA

(Director Prof. F. Akasu)

*Department of Obstetrics & Gynecology, School of
Medicine, Toho University*

SEVEN FIGURES

In spite of many investigations, it has not yet been settled whether the activity of the adenohipophysis is increased or decreased during pregnancy. Gonadotrophin in human pregnancy urine is believed to be secreted from the placenta and not from the adenohipophysis. Since the steroid hormones increase in the circulating blood with the progress of pregnancy, it seems not unlikely that the activity of the adenohipophysis is depressed during pregnancy.

It seems likely that the placenta produces many trophic hormones just like the adenohipophysis. Besides gonadotrophin, ACTH has already been extracted from the placenta (Opsahl, Long and Fry, 1951; Akasu and Miyakawa, 1953; Akasu, Takeuchi and Miyakawa, 1954).

There have been various reports which suggest that the function of the thyroid gland is increased during pregnancy. For examples, it has been reported that during pregnancy the thyroid gland is hypertrophied (Mussey, 1938), B. M. R. is increased (Javert, 1940), I^{131} uptake is increased (Hertz, 1946) and protein bound iodide (PBI) level is elevated (Peters, Man and Heineman, 1948; Heineman, Johnson and Man, 1948; Danowski, Gow, Mateer *et al.*, 1950).

In this paper the extraction of TSH-like substance from the human placenta will be reported.

MATERIAL AND METHOD

Fresh human placentae which were obtained by cesarean section in the late stage of pregnancy without toxemia symptom were used.

Extraction of TSH from the placenta was carried out at first by a modified Loeser's method (1932; Akasu, 1955). As this method was found to be not very efficient, later on Ciereszko's method was used for the extraction.

Bioassay was carried out by Junkmann-Schoeller's method (1922) using young guinea-pig. Proper dose of the extract was injected subcutaneously daily for three days. On the fourth day test animals were killed, blood specimens were taken for PBI determination, and the thyroid glands were extirpated and examined histologically by the Haematoxylin-eosin technic.

Determination of PBI was carried out by Baker's method (1951). Serum cholesterol was measured by Bloor's method (1922, 1928).

RESULTS

I) Results using the TSH-like substance extracted by Loeser's method

Three-hundred and fifteen mg. of slightly brown coloured, fine homogenous and water soluble powder was obtained from 350 g. of human placenta.

The change of PBI level and the histological finding of the thyroid gland in guinea-pigs administered proper doses of this extract are shown in Table 1 and Figs. 1, 2 and 3.

Table 1. Effect of administration of placental TSH on the PBI level and thyroid histology in guinea-pigs (Loeser's method).

Daily dose (mg.)	Body weight (g.)	PBI (γ /dl.)	Histological findings of thyroid glands		
			Epithelium of follicles	Content of colloid	Dilatation of capillary nets
0.5	199	3.4	low cuboidal	rich	—
	197	3.3	//	//	//
1.0	210	3.5	//	//	//
	197				
1.5	182	3.3	low cuboidal	rich	—
	200	3.6	//	//	//
2.0	181				
	215	3.5			
3.0	160	3.6	*columnar, folded, hypertrophied	small amount	++
	162	4.1	//	//	//
5.0	172	3.9	* //	//	+
	176	3.6	//	//	//
control	151	3.3	*low cuboidal	rich	—
	225	3.1	//	rich	//
	217	3.4	//	//	//
Pregnant	760	4.7	columnar, folded, hypertrophied	small amount	++
	600	4.0	//	//	//

* Histological pictures of these cases were shown in Figs. 1, 2 and 3.

The PBI levels of all guinea-pigs administered the TSH-like substance were elevated compared with that of control animals.

Thyroid glands of the guinea-pigs administered less than 2.0 mg. of the TSH-like material daily showed no hyperfunctioning figures, but those receiving more than 3.0 mg. showed the histological pictures of hyperfunction. The epithelium of follicles was thickened, folded and hypertrophied. Colloid was decreased in amount, and the capillary nets were dilated.

Fig. 1. Thyroid of control guinea-pig

Fig. 2. Thyroid of guinea-pig which received P-TSH (daily dose 3.0 mg.)

Fig. 3. Thyroid of guinea-pig which received P-TSH (daily dose 5.0 mg.)

II) Results using the TSH-like substance extracted by Ciereszko's method

Sixty-one mg. of white, transparent and water soluble lyophilized substance was obtained from 900 g. of human placenta by this method.

Histological findings of the thyroid glands and the cholesterol level of the serum of test animals receiving the extract are shown in Table 2 and Figs. 4~7.

As shown in the table, the serum cholesterol level in the injected groups fell significantly compared with the control group, except in the groups which received 0.1 mg. and 0.25 mg. of the material. The thyroid glands in the injected groups showed distinctly hyperfunctioning pictures.

Table 2. Effect of administration of placental TSH on the cholesterol level and thyroid histology in guinea-pigs. (Ciereszko's method).

Daily dose (mg.)	Body weight (g.)	Total cholesterol (mg./dl.)	Histological finding of thyroid gland		
			Epithelium of follicles	Content of colloid	Dilatation of capill. nets
0.1	103	75.5	low cuboidal	rich	—
	88	110	//	//	//
0.25	97	87.5	columnar, hypertrophied	//	—
	*119	95.5	//	//	//
0.5	*146	67.5	columnar, hypertrophied	decreased	+
	143	62.5	//	//	//
	131	72.0	//	rich	±
	113	62.5	columnar, hypertrophied folded	decreased	++
1.0	*121	27.5	//	//	//
	113	45.0	//	//	//
	107	55.5	//	//	//
3.0	142	65	//	//	//
	*142	57.5	//	//	//
	123	62.5	//	//	//
	121	67.5	//	//	+
control	150	100	low cuboidal	rich	—
	149	85	//	//	//
	134	80	//	//	//

* Fig. cases

DISCUSSION

The function of adenohypophysis during pregnancy has not yet been understood clearly but there are many evidences which show that the activity of the adenohypophysis is decreased during pregnancy.

On the other hand, increase of thyroid activity during pregnancy has been confirmed by many experimental studies. As there is no evidence that the adenohypophysis secretes more TSH during pregnancy than usual, these facts suggest that the origin of TSH during pregnancy is extraadenohypophyseal.

Fig. 4. Thyroid of control guinea-pig

Fig. 5. Thyroid of guinea-pig which received P-TSH (daily dose 0.25 mg.)

Fig. 6. Thyroid of guinea-pig which received P-TSH (daily dose 1.0 mg.)

Fig. 7. Thyroid of guinea-pig which received P-TSH (daily dose 3.0 mg.)

It is well known that the placental extract has a luteinizing hormone (LH) like activity. Moreover, we have demonstrated the placental follicle stimulating hormone (FSH). ACTH has also been extracted from the placenta (Opsahl, Long and Fry, 1951; Akasu and Miyakawa, 1953; Akasu, Takeuchi and Miyakawa, 1954). In this paper, the placental TSH has been demonstrated. We presume that growth hormone and prolactin will be extracted from the placenta in the near future. In our opinion, the placenta is the second adenohypophysis and it functions in stead of adenohypophysis during pregnancy.

SUMMARY

1) Three hundred and fifteen mg. of TSH-like substance has been obtained from 350 g. of human placenta by Loeser's method. Sixty-one mg. of the similar substance has been extracted from 900 g. of placenta by Ciereszko's method.

2) By the administration of this TSH-like substance to guineapigs, an elevation of the PBI level and a decrease in serum cholesterol were caused.

3) Distinctly hypertrophied and columnar cells of the epithelium of follicles, small amount of colloid in the follicles, dilatation of capillary nets in the guinea-pigs thyroid glands were observed histologically after administration of the TSH-like substance.

4) We propose the name P-TSH (placental thyroid stimulating hormone) for this substance.

REFERENCES

- Akasu, F.: N. S-F. GK. Z. (Jap. J. Obst. & Gynec.) **7**: 655, 1955.
Akasu, F. and K. Miyakawa: N. S-F. GK. Z. (Jap. J. Obst. & Gynec. **5**: 953, 1953.
Akasu, F., M. Takeuchi and K. Miyakawa: Hormon to Rinsho **2**: 1082, 1954.
Baker, S. B. and M. J. Humphrey: J. Clin Endocrinol. **10**: 1136, 1950.
Bloor, W. R.: J. Biol. Chem. **24**: 227, 1916.
Bloor, W. R.: *ibid.* **77**: 53, 1928.
Bloor, W. R., K. F. Pelkan and D. M. Allen: J. Biol. Chem. **52**: 191, 1922.
Ciereszko, L. S.: J. Biol. Chem. **160**: 585, 1945.
Danowski, T. S., R. C. Gow, F. M. Mateer, W. C. Everhart, S. Y. Johnston and J.H. Greenman: Proc. Soc. Exp. Biol. and Med. **74**: 323, 1950.
Heineman, M., C. E. Johnson and E. B. Man: J. Clin. Investig. **27**: 91, 1948.
Hertz, S.: Am. J. Physiol. **128**: 565, 1946.
Javert, C. T.: Am. J. Obst. and Gynec. **39**: 954, 1940.
Junkmann, K. and W. Schoeller: Klin. Wschr. **11**: 1176, 1932.
Loeser, A.: Klin. Wschr. **11**: 1271, 1932.
Mussey, R. O.: Am. J. Obst. and Gyne. **36**: 529, 1938.
Opsahl, J. C., C. N. H. Long and E. G. Fry: Yale J. Biol. Med. **23**: 399, 1951.
Peters, J. P., E. B. Man and M. Heineman: *ibid.* **20**: 449, 1948.
Philipp, E.: Zbl. Gynaek. **8**: 450, 1930.
Philipp, E.: *ibid.* **30**: 1858, 1930.