

THYROIDECTOMY AND PARATHYROIDECTOMY IN PROGENY ENCUMBERED WITH AN INSUFFICIENCY OF THESE GLANDS IN THE ANCESTORS

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L. I. Gromov and G. I. Plakutina

Thanatological Department (Head-Prof. L. I. Gromov) Institute of Forensic Medicine
(Dir.-Prof. V. I. Prozorovskii) Ministry of Sanitation SSSR, Moscow

(Presented by Active Member N. N. Zhukov-Verezhnikov AMN SSSR)

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The effects of thyroparathyroidectomy on the development of the progeny and also the immediate and delayed after-effects following the extirpation of the thyroid and parathyroid glands have not been adequately studied [5].

The effects of thyroparathyroidectomy on the development of the progeny in the embryonic or early postembryonic period of development have been investigated [4, 6, 7, 9]. Following partial parathyroidectomy in rabbits, rats and guinea pigs, Z. P. Ignat'eva [2] observed an increase in the functional activity of the parathyroid glands in the embryo. Gerloczy and Farkas [3] gave an account of a clinical case in which a deficit of parathormone in the mother during pregnancy gave rise to hypertrophy of the parathyroid glands in the fetus.

It has been demonstrated earlier that the fetus protects itself from a functional incompetence of the maternal organism. This process has been called the premature functioning of the fetus. In response to thyroparathyroidectomy in the mother, the thyroid and parathyroid glands in the progeny begin to function at an increased rate. The raised functional background of these glands, which develops in the progeny of the first generation, is carried over into the second and third generations and becomes linked with various constitutional defects.

Described in the present work are experiments which show that the premature functioning of the fetus leads to a premature exhaustion of the parathyroid glands. The aim of the experiments was to elucidate the reactions of animals, suffering from the effects of thyroid and parathyroid incompetence in the ancestry, to thyroparathyroidectomy.

EXPERIMENTAL METHODS

The first series of experiments was made on 616 white rats. Their progeny (130 young rats) served as controls. The second series comprised rats, 3-4 months old and 195-210 g in weight, from which the thyroid and parathyroid glands had been removed under ether narcosis (parental generation). The progeny of these rats was followed up over three generations ($P_1 = 139$, $P_2 = 103$, $P_3 = 67$ rats). Having reached sexual maturity the rats were used in a third series of experiments. This group of rats consisted of daughters, granddaughters and great-granddaughters suffering from the effects of thyroparathyroidectomy in their ancestry.

The thyroid and parathyroid incompetence acquired from the ancestry, which had undergone thyroparathyroidectomy, was made apparent in the progeny by the "provocative" method. This required that the female rats in the third series of experiments were operated on during pregnancy in the same way as the rats in the second series. One hundred and thirty-four rats, operated on in the second series of experiments, served as controls for the third series.

EXPERIMENTAL RESULTS

The thyroparathyroidectomized, pregnant rats of the second series of experiments were sluggish, lifeless and very thirsty directly after operation (1-2 days). A little swelling of the eyelids, a running at the nose and occasional convulsive movements of the head and extremities were observed. The second half of pregnancy elapsed without

Weight of Newborn Rats from Operated Mothers

Animal group	Condition of animals	Progeny				
		No. of observations (n)	Wt. of young rats (g)		Ratios between wts. of progeny (%)	
			$M \pm m$	Fluctuations in weight	Parental generation to control	Progeny to parental generation
Control	Unoperated	90	5,094 \pm 0,089	3,700—5,900	100	—
Parental generation	Operated	69	4,215 \pm 0,074	3,360—5,700	82,74	100
Daughters	"	35	2,908 \pm 0,075	2,050—3,810	—	68,99
Granddaughters	"	49	3,500 \pm 0,004	2,700—4,070	—	83,03
Great-granddaughters	"	50	3,755 \pm 0,137	2,400—5,800	—	89,08

complications. For one or two days before parturition the animals were restless and began to show frequent spasmodic movements of the head and extremities. Parturition lasted from two or three to 12 h and was difficult. Symptoms of a condition very frequently developed in the rats which had undergone total extirpation of thyroid and parathyroid glands. The duration of parturition in the controls was from 30 min to 1½ h. Out of ten rats, operated on during pregnancy, nine gave birth to young and only one died without delivering. After parturition many females (12.9%) devoured their young; in the controls this behavior was registered to an extent of only 3.8%.

With the lapse of time following operation an increasing emaciation and a considerable thinning of the woolly coat were observed in the majority of the rats, also disturbances in the dentine of the teeth (caries) including fractures of the teeth and irregularities in their growth. Every now and then strong spasms developed, including spasms of a clonic and tonic nature with symptoms of tetany. The losses in weight among the operated rats amounted to 25-30%.

Unlike the rats in the second series of experiments, the animals in the third series had difficulty in withstanding narcosis at the time of operation; the coagulability of the blood was altered and spasms arose. Tremors were observed after operation. When pregnancy terminated, the rats were sluggish, passive and enfeebled. They left their food untouched, the tremors increased considerably and spasms developed. The rats were dropsical and the abdomen was bulky and flabby. Eight out of 14 rats were unable to deliver by themselves. Consequently, we were obliged to resort to Caesarean section in order to preserve the mothers.

When comparing the viability indices of the progeny in the different generations we took into account only those instances of pregnancy and parturition in which operative intervention had taken place.

An analysis of these data showed that, among the rats (parental generation) which had had their thyroid and parathyroid glands removed during pregnancy, 65.2% of the young had died while among the controls there was only 1.1% of stillbirths (one instance among 90 rats).

In the third series of experiments the maximum percentage of losses (91.4) was observed in the progeny of operated daughters. Out of 35 young rats, eight were stillborn, 11 died in miscarriages and only three were born alive; the 13 live fetuses released by Caesarean section proved to be premature and were not viable.

In the succeeding generations, that is among the granddaughters and great-granddaughters, the percentage of stillborn rats remained high (87.8 and 80 respectively) and exceeded the percentage loss in the progeny of the parental generation by a considerable amount. The qualitative composition of the progeny from the operated mothers was variable. The percentage of abortions in each generation was most stable (34.3-46.5).

The weight of the live and stillborn rats from the mothers of the parental generation amounted, on an average, to 4.215 g (3.360-5.700 g) while in the controls the neonates weighed 5.094 g (3.700-5.900 g).

The young rats from the operated daughters, granddaughters and great-granddaughters were small and did not attain the weight characteristic of those from the parental generation. All the progeny in the experimental and control groups are listed in the table.

A study of the thyroid and parathyroid glands in the fetuses and neonates of the mothers in the third series of experiments brought to light a decided difference when the progeny suffering from the effects of an insufficiency of the glands in the ancestry, were compared with the controls. Particularly large changes were seen in the parathyroid glands. Macroscopically, the parathyroids were already so characteristic that it was possible to affirm that they belonged to young rats from operated mothers suffering from the effects of thyroparathyroidectomy in the ancestry.

Both parathyroid glands were easily detected since they were three of four times larger than normal. Such changes were more often met with in the right gland. Macroscopically, they were big and turgid. A similar macroscopic picture was observed by Rezza in a 2 months old infant who had died from tetany [8].

In the third series of experiments 109 young rats from a total of 134 were examined. In the progeny from animals suffering a twofold operative intervention, hyperemia and enlarged parathyroid glands were observed to an extent of 50-60%. The changes in the parathyroid glands were more often seen in young rats born of operated great-granddaughters.

Histological examination disclosed a marked atrophy of the parenchyma of the glands and its replacement by paretically dilated vessels. The thyroid glands attained various degrees of maturity against the background of which changes of a destructive nature were seen. In the majority of instances the atrophy of the parathyroid glands with acute plethora of the vessels led to the loss of the fetus and neonate. We found no descriptions of similar cases of hypothyroidism in the literature.

The thyroid and parathyroid glands, modified as a result of thyroparathyroidectomy in the ancestry, quickly react to one or other functional load and, by virtue of the close connection between mother and fetus, lead to considerable pathological changes both in the mother and in the fetus. The parathyroid and thyroid glands in such progeny undergo peculiar destructive and dystrophic changes indicating the exhaustion of their functions and their premature decay.

SUMMARY

Thyroid and parathyroid glands were studied in 134 fetuses and neonates born of thyroparathyroidectomized rats.

Parathyroid and thyroid glands in such progeny were subject to destructive and dystrophic changes indicating their functional exhaustion and premature waste. In 50-60% of the progeny presenting an aggravated history of a two-fold surgical intervention in the ancestry, microscopy demonstrated the presence of hyperemia and enlargement of the parathyroid glands. Histological examination showed a marked atrophy of the parathyroid gland parenchyma and its replacement by paretically dilated vessels.

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