Since the perinatal rat ovary is steroidogenically inactive[16,17] and is not required for feminine differentiation[3–5] it is possible that the rat fetal adrenal which does secrete hormone[3,18,19] and can affect feminine development[9] may organize the brain as female. As to the nature of the hormone, estradiol, like testosterone, prevents development of feminine sexual behavior in either sex of the rat[7,8] but, progesterone antagonizes the masculinizing action of testosterone[20], so that when administered to neonatal male rats it demasculinizes adult sexual behavior[21]. If progesterone is required for the development of a female brain, then the absence of feminine sexual behavior in the rat pseudohermaphrodite can be explained by our demonstration that the adult pseudohermaphrodite does not produce detectable quantities of progesterone[22], and the fact that the animal is also insensitive to progesterone[10]. Furthermore, elevated serum levels of progesterone in the female fetal monkey as compared to the male[23], suggests a possible role for this hormone in female development.

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Plasticity of the Hormone Receptors and Possibility of their Deformation in Neonatal Age

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Summary. Gonadotropin or TSH treated newborn animals reacted to TSH treatment in their adult age in a lesser degree than control ones. This suggests the plasticity of hormone receptors and the possibility of their deformation in neonatal age.

Membrane receptors reacting to vertebrate hormones were found in lower animals also[1–6]. These statements and the fact that in embryonic development, a single cell, the fertilized egg, delivers a great variety of specialized cells having different receptors leads to the conclusion that the receptors also have their own ontogenesis. In our experiments, we tried to elucidate the problem whether these receptors could be influenced or modified at such a critical period of development as the neonatal age.

Newborn Wistar CB rats were s.c. injected – strictly within 24 h after birth – with the following hormones: 1. thyrotropic hormone (TSH) – (Ambinon-Organon, Oss), 1 IU/animal; 2. gonadotropic hormone (Gestyl-Organon, Oss), 100 IU/animal. Animals of the control group were injected with the solvent only. After a lapse of 4 months, the animals were again treated with TSH (3 IU/animal) or, with gonadotropin (50 IU/animal) in a grouping given in the Table. Blood sampling was then made – 30 min after the treatments – by bleeding the animals to death. Concentration of thyroxine in the serum was determined by using radio-immunoassay (Amersham Thyopac-4 kit). Significance of the results was analyzed with the Student's *t*-test.

For examination of the hormone receptor's plasticity, we have chosen deliberately the TSH and the gonadotropin. Namely, these hormones provoke though different effects in adult organisms; they are only related in chemical structure – at least as regards their subunit[7]. Moreover, the gonadotropic hormones are produced only later. We might suppose, on this basis, that large doses of them injected into the newborn could deform the receptor of the chemically related TSH in such a way that its adult reactivity will be changed. For this reason, the change of the thyroxine level served as control of the reaction by determining it after TSH treatment in adult age.

As demonstrated by the results (Table), both the TSH and the gonadotropin treatment of the newborn rats resulted in the treated animals reacting – in adult age – much more weakly to the TSH stimulus than the control ones. The measured differences were significant in all cases. The gonadotropin given to the newborn produced a stronger inhibitory effect than the TSH. More precisely,

Thyroxine level of the serum in the treated and in the control groups

No. of animals	Newborn–adult	Thyroxine (μg/100 ml serum)	Related to the control (%)	Significance related to the control (*p*)
10	Control + TSH	13.54		
8	TSH + TSH	8.17	− 39	< 0.1
9	Gonadotropin + TSH	4.08	− 70	< 0.01
10	Control + gonadotropin	10.43		
9	TSH + gonadotropin	3.39	− 68	< 0.01
9	Gonadotropin + gonadotropin	4.63	− 55	< 0.05
10	Control + NaCl	9.50		
10	Control + TSH	13.54	+ 42	< 0.3
10	Control + gonadotropin	10.43	+ 9	< 0.7

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the gonadotropin caused a 70% decrease in the serum thyroxine level as compared with the controls, whilst the TSH's decreasing effect was as 'little' as 40%. At the same time, in adult age the gonadotropin did not influence the TSH-receptors; it was not able to modify them in neonatal age in such an adequate way that they would have become capable to respond to it by evoking iodine-hormone production.

As shown by the results, the adult control animals can perform a precise distinction between TSH and gonadotropin. This distinguishing capacity evolved, probably, in the course of the phylogenesis, since in bony fishes, for example, TSH and gonadotropin exert the same effect[8].

As it seems, in neonatal age this distinguishing capacity is not yet developed; therefore the gonadotropin can be bound and can deform the receptors, which are easy to shape.

We do not know why the TSH given in neonatal age decreased the receptor sensitivity. Based on literary data[9], we think it possible that the TSH would participate in the thyroid gland's regulation only later and also its too early appearing damages the receptor's structure, though in a lesser degree than the gonadotropin does. Elucidation of this problem needs further experiments.

These observations may have some importance for human pathology seeing that certain hormone analogues which occasionally found entrance into the foetus, could cause endocrine disturbances by changing the receptors.

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Time Function of Corticosteroid Levels in the Blood Plasma of Rats under the Influence of ^{222}Rn Inhalation

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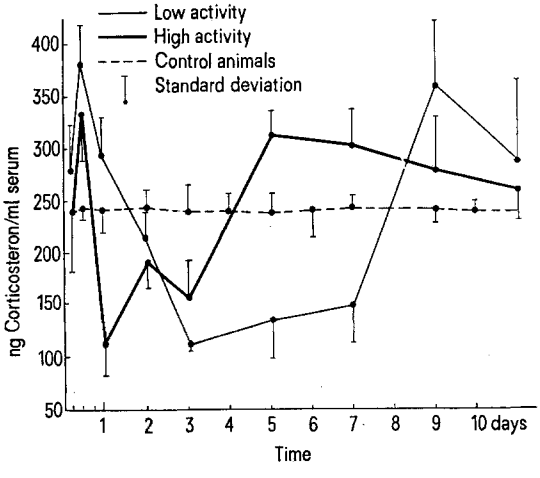
Summary. The time function of corticosteroid level in plasma of rats under two different ^{222}Rn concentrations was investigated. Both curves show a maximum after 8 h. Whereas the higher activity of ^{222}Rn produces a second maximum after 5 days, the lower activity reaches its second maximum not before 9 days. From both time functions, a two-step mechanism in the intracellular control can be concluded.

In some places the inhalation of ^{222}Rn (radon) and its decay products is used for therapeutical treatments. Especially in the treatment of all diseases of the rheumatic group, vascular diseases, disorder of endocrine organs and metabolic disorders, as well as gerontal complaints, success is being reported. However, there is no knowledge about the biochemical mechanisms which could explain such therapeutic effects. HENN[1] suggests a stimulated production of corticosteroids but no direct proof was possible. We have tried to detect this in in vivo experiments with rats.



Concentration of corticosteroid level in the plasma of rats during inhalation of ^{222}Rn.

Experimental techniques. Male Wistar-rats of 200 g body weight were kept on a standard diet. We have used a climatized inhalation chamber of 13.5 m^3 where the ^{222}Rn concentration and decay product ratio were kept constant. Two series of measurements with different ^{222}Rn concentrations were carried out with 45 animals each over a period of 12 days; Within the same period, control animals were kept under the same environmental conditions in a radon-free atmosphere.

The corticosteroid level in the blood was determined in groups of 5 rats each after defined periods of ^{222}Rn inhalation. Blood samples were taken from the veins of the tongue under weak halothan narcosis. The corticosteroid concentration was determined by the methods of FIORELLI et al.[2], using the kit for cortisol assay of CEA-IRE-SORIN, Centro Ricerche Nucleari, I-13040 Saluggia (Vercelli).

The dose resulting from the inhalation of ^{222}Rn and its decay products is very different for each organ. On the base of experimental techniques and calculations from POHL[3] and POHL and POHL-RÜHLING[4], the dose rate was determined for several organs (Table).

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