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Histological examination of the thyroid after experimental administration of Metizol

Metizol is a thyreostatic derived from thiourine, which inhibits the initial stages of thyroid hormone synthesis. The inhibition results from impaired formation of peroxidase–iodine complexes and thyrosine iodising in thyreoglobuline. Peripherally active Metizol blocks thyroxine conversion to triiodothyronine (2). That type of activity mechanism in used to treat hyperthyroidism.

In addition to basic activity, Metizol has many side effects. The most common include allergies such as rash, erythema (1) or changed blood picture: agranulocytosis, granulocytopenia (1).Thrombocytopenia and haemorrhagic diathesis occur rarely. Similarly rare is hepatic cholestasis (3, 4, 12). The administration of Metizol often causes side effects such as hypothyroidism and goitre development. Therefore, Metizol may be counted among goitre-forming substances, which, according to many authors, needs detailed investigation. The present experiment involved observation of the thyroid gland in white Wistar rats administered Metizol (Polfa).

MATERIAL AND METHODS

The investigations were carried out on white Wistar rats (adult males, weighing ca 300 g each). The animals were divided into four groups (three experimental groups and a control one). Experimental group 1: the animals were given Metizol for 3 days. Experimental group 2: the animals received Metizol for 21 days. Experimental group 3: the animals were given Metizol for 42 days. Control group: the animals were given distilled water by means of intragastric bougie.

Metizol dissolved in distilled water was administered intragastrically at the dose of 1 mg/kg b.m. After twenty-four hours following the last dose the animals were put to sleep by ether and the thyroid samples were taken for histological examination (stained with hematoxylin and eosin) and histochemical examination (stained by the PAS's and Feulgen's methods). The thyroid samples for the examinations under optic microscope were fixed in Baker's fluid (1% CaCl2 in 10% solution of neutralised formalin). 7μm thick paraffin sections were histologically and histochemically evaluated.

RESULTS

CONTROL GROUP

Standard staining, both with hematoxylin and eosine as well as by PAS method showed no deviation from the normal structure of the thyroid gland. The colloid in the thyroid follicle was acid-absorbent, of intense eosine colour. In the colloid there were quite numerous wall follicles located just at the epithelium. There were three epithelial types in the thyroid follicles observed: cubic, cylindrical,and flat. Most often the follicles were lined with cubic epithelium. The nuclei of the epithelial cells were round, located in the centre. The majority of the thyroid follicles were differentiated in size (Fig.1).

GROUP 1 (THREE DAYS OF METIZOL ADMINISTRATION)

In the lumen of the follicle no colloid was present or only small quantities were observed. The follicular epithelium was generally higher than in the controls. The cubic epithelium was the only type observed. The lumen shape was very regular. There was a bigger quantity of interfollicular tissue (Fig. 2).

GROUP 2 (THREE WEEKS OF METIZOL ADMINISTRATION)

Colloid was present in the follicular lumen. It was less intensely coloured in comparison to the controls. Part of the epithelium-forming cells was higher than the corresponding cells in the control group; some of them were of the same height. There were no follicles with flat epithelium. The lumen shape of the follicles was regular. There was a considerate congestion of the gland. Nearly every follicle was surrounded by a network of blood vessels. There was a bigger mass of interfollicular tissue (Fig. 3)

GROUP 3 (SIX WEEKS OF METIZOL ADMINISTRATION)

Colloid was present in the lumen of the follicle. It was of more intense colour compared to Group 2; it reminded that of the control group. The height of the follicular epithelium was comparable to the height observed in the controls. The lumen shape was irregular. In comparison to the control group bigger differentiation in the follicular size was observed. There was a bigger mass of the interfollicular tissue. Generally speaking, similarity to the control group was observed (Fig. 4).

DISCUSSION

Various factors, e.g. TRH, TSH and goitre-forming compounds influence iodothyronine formation (9). The latter include thiourine derivative – Metizol.

Three-day administration of Metizol at the dose 1 mg/kg b.m./24 h resulted in the changed appearance of the follicles and interfollicular tissue: the quantity of colloid decreased, the secretory epithelium was typically cubic, the quantity of the interfollicular tissue increased.

Longer administration of Metizol (for three weeks at the same dose 1 mg/kg b.m./24 h)

resulted in increased quantity of colloid in the follicles. Cubic epithelium became much more differentiated in terms of height, both cylindrical and cubic types were observed. The quantity of the interfollicular tissue was even much bigger and its congestion was considerate.

After six weeks of Metizol administration at the same dose the thyroid picture got similar to the control group. Other authors confirm our observations (7, 8, 9).

CONCLUSIONS

1. Three-day administration of Metizol results in decreased secretory function of the thyroid follicles.

2. Three-week administration of Metizol initiates reactions which result in increased secretory function of the thyroid follicles.

3. Six-week administration of Metizol results in comeback to the initial stage in the microscopic picture of the thyroid, which may be the evidence of adaptative mechanism in the body.

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EXPLANATION TO FIGURES

Fig. 1 The thyroid of the rat, control group. Hematoxylin and eosin. Magn. 400 x.

Fig. 2 The thyroid of the rat, experimental group 1. Hematoxylin and eosin. Magn. 400 x.

Fig. 3 The thyroid of the rat, experimental group 2. Hematoxylin and eosin. Magn. 400 x.

Fig. 4 The thyroid of the rat, experimental group 3. Hematoxylin and eosin. Magn. 400 x.

SUMMARY

The investigations were carried out on thyroids of white Wistar rats which were given Metizol for 3 days, 3 and 6 weeks at the dose of 1 mg/kg of b.m. for 24 hrs. The samples were stained with hematoxylin and eosin and by the PAS method. The following changes were observed:

1. Three-day administration of Metizol resulted in the decrease in the quantity of colloid; the secretory epithelium became uniform – i.e. cubic; the quantity of the interfollicular tissue increased.

2. Three-week administration of Metizol resulted in appearing of colloid stained differently than in the control group; secretory epithelium cells were of different height (cubic and cylindrical), a considerate congestion of the gland was visible, the quantity of the interfollicular tissue increased.

3. After 6 weeks of Metizol administration the morphological picture of the thyroid became similar to that of the control group.

Badania histologiczne tarczycy po doświadczalnych badaniach Metizolu

Badano tarczyce szczurów rasy Wistar, którym podawano Metizol przez 3 dni, 3 tygodnie, 6 tygodni w dawce 1 mg/kg m.c./24 h. Stosowano barwienie H+E i PAS. Zaobserwowano następujące zmiany:

1. Po 3 dniach podawania Metizolu w pęcherzykach tarczycy zmniejszyła się ilość koloidu, nabłonek wydzielniczy uległ ujednoliceniu – stał się sześcienny, wzrosła ilość tkanki międzypęcherzykowej.

2. Po 3 tygodniach podawania Metizolu w pęcherzykach tarczycy pojawił się koloid inaczej wybarwiony niż w grupie kontrolnej, komórki nabłonka wydzielniczego mają różną wysokość (sześcienne i walcowate), zaznacza się znaczne przekrwienie gruczołu, wzrasta ilość tkanki międzypęcherzykowej.

3. Po 6 tygodniach podawania Metizolu obserwuje się morfologiczne podobieństwo do grupy kontrolnej.

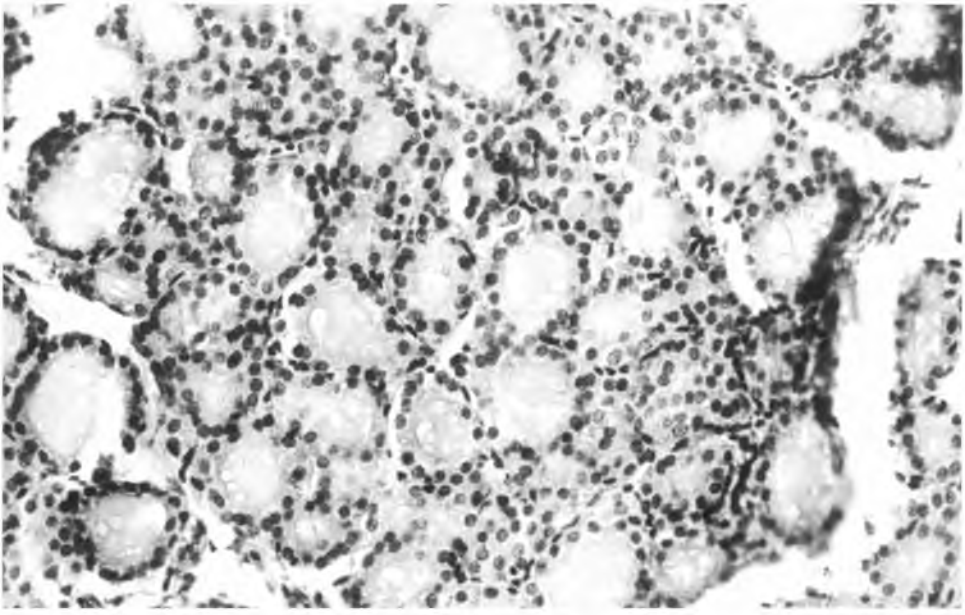

Fig. 1

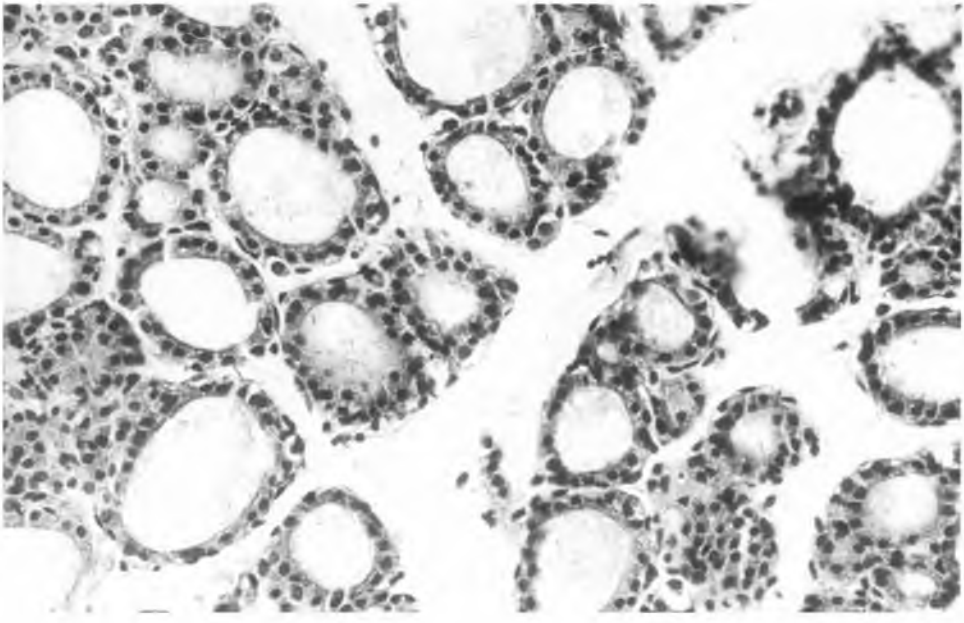

Fig. 2

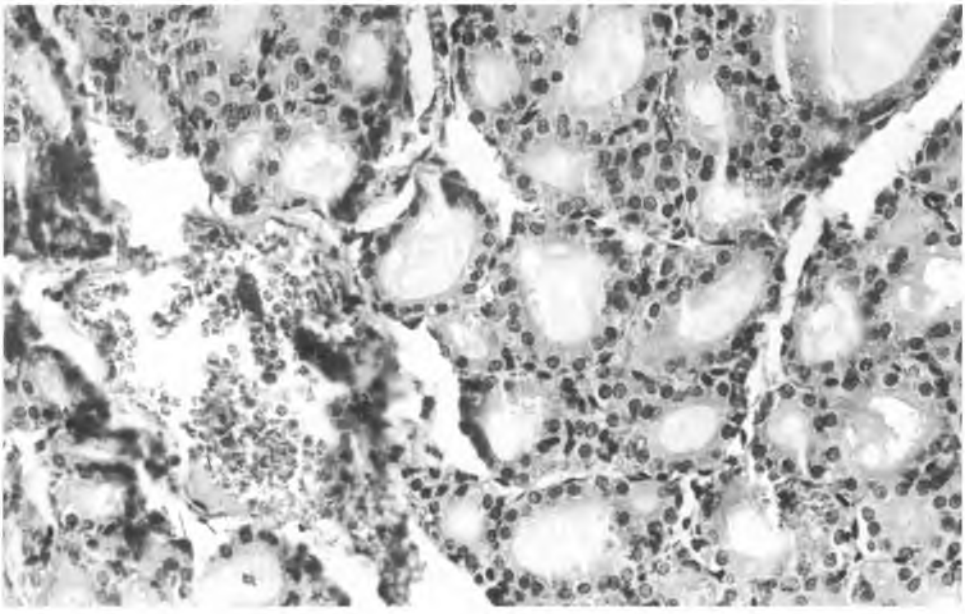

Fig. 3

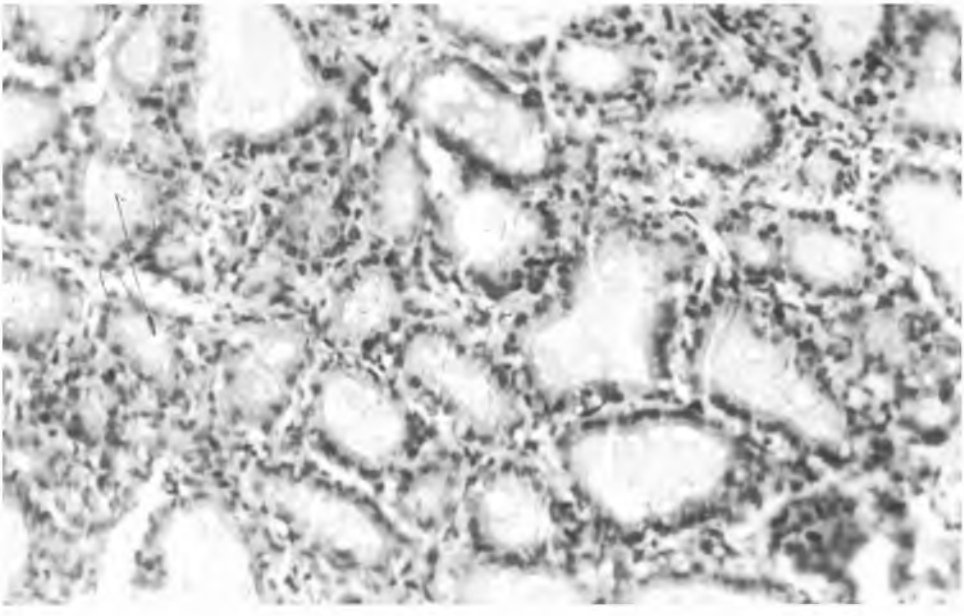

Fig. 4