Determination of Trace Elements in Human Thyroid Glands by Activation Analysis

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Estimations of iodine, bromine, copper and manganese were made in a series of diseased and normal thyroid glands removed surgically and also in sera from the same patients.

A irradiation was performed in TRIGA-II reactor for 1 hour at a neutron flux of about $4 \times 10^{12}$ n cm$^{-2}$ sec$^{-1}$. For the determination of I and Br in samples, induced $^{128}$I and $^{82}$Br were extracted with organic solvents and precipitated as Ag$^{128}$I or Ag$^{82}$Br with AgNO$_3$ solution. A new organic solvent extraction method for rapid radiochemical separation of $^{64}$Cu and $^{56}$Mn was proposed. Assay of $^{128}$I, $^{82}$Br, $^{56}$Mn and $^{64}$Cu was made by $\gamma$-ray spectrometry.

The contents of I and Br in thyroid adenomas were lower than in normal thyroid tissue. The content of Mn in thyroid adenomas did not differ from that of the normal tissue, while Cu content was in a lower level.

The Mn content in adenocarcinomas was raised, while the Cu content slightly decreased.

The content of Mn in thyrotoxicosis increased, but the Cu content appeared to decrease.

For the interpretation of these data, further studies are necessary including nucleic acids determination, protein determination and histopathological observations in various thyroid diseases.

Double antibody method of radioimmunoassay for HTSH and its clinical applications

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Plasma TSH concentration was determined by radioimmunoassay using a highly purified HTSH for labelling with radioiodine ($^{125}$I or $^{131}$I), a potent anti-HTSH serum and Human Thyrotrophin Research Standard A. The antibody-bound $^{125}$I or $^{131}$I-HTSH was separated from the “free” by double antibody method with the addition of EDTA. The method was sensitive to detect as little as 0.2 $\mu$U (1.0 $\mu$U/ml) HTSH. The sensitivity was 250 times higher than that of the McKenzie bioassay. No significant effect was observed when HCG, HGH, FSH, ACTH and bovine TSH were assayed. Some effects were observed when more than 100 mg/ml of human $\gamma$-globulin was present in the double antibody system, but it was negligible for clinical application. The between assay reproducibility of serum HTSH assays was $\pm 3.5\%$ (S.D. of variation). Recovery of HTSH-R-STD-A added to the
serum in vitro was 99.6 ± 9.5%. Multiple doses of the purified or crude HTSH, and dilutions of the hypothyroid serum resulted in parallel curves to that obtained for the HTSH-R-STD-A. Serum TSH concentration ranged <1.0-2.5 μU/ml in normal subjects and pregnant women; 2.5-7.5 μU/ml in patients with simple goiter; 2.5-20 μU/ml in patients with Hashimoto’s thyroiditis in euthyroid state; 22-800 μU/ml in primary hypothyroid patients; 200-700 μU/ml in cases of cretinism; and undetectable in untreated patients with Graves’ disease, and cases of panhypopituitarism. There were in good agreements between immunological and biological potencies of HTSH which were determined by radioimmunoassay and McKenzie’s bioassay in sera from hypothyroid patients and pituitary preparations.

Studies of radioimmunoassay of Arginine Vasopressin (AVP)

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The studies on the radioimmunoassay of arginine vasopressin and comparison to bioassay were performed as follows.

Synthetic lysine vasopressin (LVP) was coupled to bovine serum albumin by ethyl CDI after the method of Permutt et al. The complex was emulsified in normal saline and complete Freund’s adjuvant and injected into the foot pad or subcutaneous tissue of rabbits, 3 or 5 times at two weeks interval. The I-125 labelled LVP was prepared by the method of Hunter and Greenwood at Dainabotts Laboratory and its specific activity was from 100 to 200 mCi/mg.

The standard curves for LVP and arginine vasopressin (AVP) were made by two antibody assay system using anti-rabbit γ-globulin goat serum, in the range from 5 μU to 3000 μU and from 10 μU to 5000 μU respectively. On the other hand oxytocin showed competitive binding affinity to the antibody at the rate less than 0.1% of LVP.

The radioimmunoassay of AVP in tumor and neurohypophysial tissues were performed in a case of bronchogenic carcinoma of oat cell type that caused syndrome of inappropriate secretion of ADH. The dose response curve of the tissue extracts showed good correspondence with the standard curve. The concentrations of AVP in the tissues measured by this standard curve of radioimmunoassay were 138 μU/mg in tumor and 138 mU/mg in neurohypophysial tissue, while the values measured by bioassay using water loaded and alcohol anesthetised rats were 41.5 μU/mg and 98.5 mU/mg respectively.