

<sup>131</sup>I-19-iodocholesterol followed by rectilinear scanning appears to be a reliable method of

differentiating bilateral adrenocortical hyperplasia from unilateral adrenocortical adenoma.

### **Clinical Studies on the Metabolism and Plasma Protein Binding of Fluocortolone**

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Twenty  $\mu$ Ci (5 mg) of 1, 2, 4-<sup>3</sup>H-fluocortolone (6 $\alpha$ -fluoro-16 $\alpha$ -methyl-1-dehydrocorticosterone) was administered orally to three normal male volunteers and radioactive substances in the blood plasma, urine and feces were analyzed for 72 hours. Total <sup>3</sup>H and ethyl acetate extractable free <sup>3</sup>H in the plasma reached maximum values 2 hours after the administration. <sup>3</sup>H-fluocortolone itself in the plasma reached maximum value 2 or 3 hours after the administration, and the radioactive concentration at that time was equivalent to about 2 or 3  $\mu$ g of non-radioactive fluocortolone per 100 ml plasma. Of the administered <sup>3</sup>H, 45-61% was excreted into urine in 24 hours, 53-64% in 48 hours, and 55-76% in 72 hours. Of the total <sup>3</sup>H in 24 hour urine, 3-18% was in free fraction, 66-75% was in glucuronide, 2-3% was in sulfate and 9-13% was in the remainder. In one case 5% of the administered <sup>3</sup>H was excreted into feces in 72 hours. In this feces, 61, 17, 9 and 13% of total

<sup>3</sup>H were found in free fraction, glucuronide, sulfate and remainder, respectively. Radioactive fractions or hydrolyzed fractions in 24 hour or 6 hour urine were analyzed using thin-layer or paper chromatography and radiochromatogram scanner. In the free fraction, at least 5 radioactive peaks with corresponding UV-absorbing spots were found on the chromatogram. None of them corresponded to fluocortolone itself. In the glucuronide fraction, at least 6 radioactive peaks with corresponding UV-absorbing spots were found. Two of them were considered to be fluocortolone and 11-dehydrofluocortolone. In the sulfate fraction, at least 4 radioactive peaks, three of which had corresponding UV-absorbing spots, were found. One of them was thought to be fluocortolone. One to 100 ng of non-radioactive fluocortolone reduced % binding of <sup>3</sup>H-cortisol to CBG to a small extent, indicating slight binding of fluocortolone to CBG.

### **Evaluation of Portopulmonary Shunt Based on the Measurement of Aldosterone in Peripheral Plasma by a Double Isotope Dilution Method**

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Splenopneumopexy was devised as a surgical treatment for portal hypertension, especially for Budd-Chiari syndrome. And this splenopneumopexy has been proved to be an effective

procedure for portal hypertension by extensive experimental and clinical investigations.

In this paper, the effect of splenopneumopexy on the hyperaldosteronism caused by constrict-

tion of the supradiaphragmatic inferior vena cava is studied based on the measurement of aldosterone in peripheral plasma using a double isotope dilution derivative method by Brodie and Shimizu et al.

Dogs were divided into three groups as follows.

1. Normal dogs (group I).
2. Dogs with constriction of the supradiaphragmatic inferior vena cava (group II).
3. Dogs with splenopneumopexy and constriction of the supradiaphragmatic inferior vena cava (group III).

The values of plasma aldosterone and electrolytes and liver function were evaluated in each group.

Results were summarized as follows.

#### 1. Specificity

Water blanks:

$$0.116 \pm 0.007 \text{ (SD) } \mu\text{g}/20 \text{ ml (N = 7)}$$

Plasma from adrenalectomized dogs:

$$0.155 \pm 0.001 \text{ (SD) } \mu\text{g}/20 \text{ ml (N = 3)}$$

-H/--C: 2.8-9.9

#### 2. Recovery:

$$19.730 \pm 0.770 \text{ (SD) } \% \text{ (N = 54)}$$

#### 3. Precision:

$$2.031 \pm 0.094 \text{ (SD) } \mu\text{g}/20 \text{ ml (N = 4)}$$

$$5.042 \pm 0.339 \text{ (SD) } \mu\text{g}/20 \text{ ml (N = 4)}$$

#### 4. Accuracy:

$$Y = 0.225 + 0.926 \times$$

In group I plasma aldosterone was  $0.842 \pm 0.207 \mu\text{g}/100 \text{ ml}$ . It was  $20.217 \pm 1.469 \mu\text{g}/100 \text{ ml}$  postoperative 10 days and increased to  $25.308 \pm 3.118 \mu\text{g}/100 \text{ ml}$  postoperative 20 days following constriction of the supradiaphragmatic inferior vena cava in group II.

On the other hand, it was  $10.0246 \pm 2.195 \mu\text{g}/100 \text{ ml}$  postoperative 10 days and decreased to  $5.885 \pm 2.887 \mu\text{g}/100 \text{ ml}$  postoperative 20 days following constriction of the supradiaphragmatic inferior vena cava, and ascites was well controlled in group III.

It is concluded that this measurement of plasma aldosterone is warranted to be reliable one and hyperaldosteronism caused by constriction of the supradiaphragmatic inferior vena cava is alleviated remarkably by portoplumunary shunt.

## Analysis of Calcium Metabolism in Humans

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Curve fitting methods were examined to define the optimum parameters of the calcium metabolism in humans.

The iterative Newton-Raphson method was used to solve the simultaneous non-linear least squares equations, and was tested its ability of convergence from arbitrary initial parameter guess.

To the parameters once converged, random error was added and the curve fitting was repeated with artificial parameters.

Convergence was always obtained and was

not influenced by the addition of 5 percent parameter error, but three different least squares minima were found when the parameter error was 50 percent. Parameters with 100 percent error were converged once out of ten trials and were entirely unsatisfactory.

These results show that Newton-Raphson method was greatly influenced by the initial parameter guess, which, therefore, should be close to the true solution. Other search methods were being tested for better curve fitting procedure.