

scores (7) resulted in a *t*-ratio beyond the 0.001 level. If this procedure is not too unsound, the inference is that the highest and lowest I.Q. scores made by the same children are significantly different from each other.

Although the present experiment confounds the reliability of the examiners' test-administration with the reliability of the subjects' I.Q. scores, it is exactly from this kind of confounded situation that we are forced to draw practical conclusions about I.Q. test scores obtained in our clinics today. Therefore, it can be concluded that whereas group means on different tests of intelligence may not differ except by chance from one another, individual's I.Q.'s may differ widely and significantly from one another on different tests.

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## An Improved Method for the Determination of Blood Volume Using Radioactive Iodinated Human Serum Albumen<sup>1</sup>

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Improving techniques for the determination of blood volume have moved this procedure from that of an investigative tool to one of direct clinical value in the management of a wide variety of clinical problems. The earliest studies involved exsanguination of experimental animals. The introduction of essentially nondiffusible dyes, such as vital red and Evans blue, and the use of carbon monoxide permitted determination of blood volumes on living patients. Technical complexity and the inability to apply these methods repeatedly at short intervals in a given patient limits their clinical usefulness.

Tagging erythrocytes with P<sup>32</sup>, K<sup>42</sup>, and Fe<sup>58</sup> opened a new approach which, however, was still time-consuming.

In 1951, Aust *et al.* (1) devised a technique using 50–100  $\mu$ c of I<sup>131</sup> tagged human albumen.

The sensitivity of the recently available well-type scintillation counter<sup>2</sup> is such that 0.001  $\mu$ c of I<sup>131</sup> gives 895 ct/min.

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<sup>2</sup> Manufactured by Nancy Woods, Chicago, Ill.

I<sup>131</sup>-tagged human albumen as received from the supplier is diluted with sterile 0.85% saline solution so that 1 ml contains 3  $\mu$ c. It is essential that sterile technique be observed in making the dilutions and that both the stock and diluted reagent be refrigerated.

1. A volume of the diluted stock solution calculated to contain approximately 3  $\mu$ c of I<sup>131</sup> is accurately drawn up to the mark in a sterile syringe, and transferred quantitatively to an oxalate tube.

2. Using the same needle and syringe (to obviate error in standardization) an identical volume (drawn to the same mark as under 1) is injected into the subject's antecubital vein.

3. After 10 min (15–20 if patient is in shock) 10 cc of blood is withdrawn from the opposite antecubital vein and placed in an oxalate tube.

4. The control volume is diluted to 1000 ml in a volumetric flask with distilled water. This dilution gives approximately 10,000 ct/min/5 ml.

5. Background is determined for two 10-ml graduated test tubes. Average 200 ct/min.

6. Five milliliters diluted control solution is pipetted into one of the 10-ml tubes, and 5 ml of the oxalated blood (well mixed) is pipetted into the second 10-ml tube.

7. Each sample is counted in the well counter for 1 min.

8. Calculation:

$$\text{Total blood volume} = \frac{(\text{control count} - \text{background}) \times 1000}{\text{test count} - \text{background}}$$

9. Centrifuge blood at 2500 rpm 20 min and hematocrit determined.

10. Procedure for repeated determinations of blood volumes: a control blood specimen is drawn before the injection of the second dose of tagged albumen to determine residual radioactivity. Then repeat entire procedure.

$$\text{Total blood volume} = \frac{(\text{control count} - \text{background}) \times 1000}{(\text{blood \#2} - \text{background}) - (\text{blood \#1} - \text{background})}$$

The total time involved in this procedure is 45 min. The total dose of radiation is 3  $\mu$ c/determination.

The only serious disadvantage to this technique is the original cost of the equipment. Its advantages are speed, complete safety, and reproducibility (Table 1).

TABLE 1

BLEEDING DUODENAL ULCER WITH NO FLUID INTAKE DURING PERIOD OF STUDY

Date	Time	Hematocrit	T <sub>r</sub> V, cc	TBV, cc/kg	RCV, cc	RCV, cc/kg	PV, cc	PV, cc/kg
5/14	1:30 P.M.	24	3120	41.6	748	10	2372	31.6
5/14	4:30 P.M.	23	3250	43.3	747	10	2502	33.5
5/15	9:30 A.M.	19	3870	51.6	735	9.8	3145	41.8

Since there is no absolute measure of blood volume the important requirements in any clinical method are reproducibility and constancy of the normals. These requirements are fulfilled by the present method. In 42 determinations the normal range obtained corresponded closely to those reported by Storaasli and co-workers (2): total blood volume, 60–85 cc/kg; plasma volume, 34–60 cc/kg; and red cell volume, 26–40 cc/kg.

The method herein reported permits the rapid determination of blood volumes repeated at short intervals.

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## The Oxidative Deamination of Serotonin and Other 3-(beta-Aminoethyl)-indoles by Monamine Oxidase and the Effect of These Compounds on the Deamination of Tyramine

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Recent interest in the vasoconstrictor element of blood serum which had led to the elucidation of the structure of Serotonin (1–3) has resulted in the synthesis of this compound (4) and other derivatives of 3-(beta-aminoethyl)-indole (5) in these laboratories. Blaschko has reported that Serotonin itself is deaminated oxidatively by guinea pig tissue (6).

In an effort to assess the possible oral activity of the Serotonin derivatives reported herein, it was thought worth while to investigate their deamination by monamine oxidase.

The method was essentially that employed by Beyer (7) utilizing manometric determination of the increase in oxygen uptake by guinea pig liver homogenate in the presence of the amines above the blank oxygen utilization. Cyanide was used as aldehyde fixative. Tyramine was run as a standard in each manometric determination. All compounds were subjected to deamination in the amount of  $1.25 \times 10^{-5}$  mole. Thus the theoretical oxygen uptake/atom of oxygen used was 140 mm<sup>3</sup>.

It will be seen in Table 1 that similarly to the findings in the deamination of substituted phenyl ethylamines (8) substitution of a single methyl group in the side chain of these compounds does not impair deamination (see compounds II, IX). Dimethyl, isopropyl, benzyl, or diethyl substitution of the aminoethyl nitrogen, precludes deamination by this system as does ethyl substitution of the beta carbon of this

TABLE 1

Compound	Name	O <sub>2</sub> Uptake, mm <sup>3</sup>
I	3-(beta-Aminoethyl)-indole (acetate)	165
II	3-(beta-N-Methylaminoethyl)-indole (hydrochloride)	160
III	3-(beta-N-Benzyl-N-methylaminoethyl)-indole (hydrochloride)	-10
IV	3-(beta-N-Isopropylaminoethyl)-indole (hydrochloride)	0
V	3-(beta-N-Benzylaminoethyl)-indole (hydrochloride)	-10
VI	3-(beta-Aminobutyl)-indole (hydrochloride)	0
VII	3-(beta-N,N-Diethylamino)ethyl indole (hydrochloride)	0
VIII	5-Hydroxy-3-(beta aminoethyl)-indole (Serotonin) (creatinine sulfate monohydrate)	152
IX	5-Hydroxy-3-(beta-N-methylaminoethyl)-indole (creatinine sulfate monohydrate)	158
X	5-Hydroxy-3-(beta-N,N-dimethylaminoethyl)-indole (creatinine sulfate monohydrate)	28
	Tyramine	140
	Creatinine sulfate	0

chain (see compounds X, IV, V, VII, and VI, respectively). The small oxygen uptake seen with compound X (5-hydroxy ring-substituted) when compared with other compounds not ring-substituted and in which the aminoethyl nitrogen atom is blocked (III, IV, V, VI, VII) would suggest possible oxidation of the ring hydroxyl group.

This cannot be confirmed in the comparison of compounds VIII and IX with I and II, respectively, since all these compounds show a greater oxygen uptake than does tyramine. It is possible that this excess oxygen consumption could signify some ring oxidation other than that of the 5-hydroxy group.

Creatinine sulfate (complexed with compounds VIII, IX, and X) was not oxidized when examined separately. The rate of deamination of the compounds that were oxidized, although not illustrated, is uniformly more rapid than that of tyramine.

Since certain of these compounds showed slight depression of the basal oxygen uptake of the homogenate, it was thought of interest to investigate inhibition of tyramine oxidation by some of those compounds not deaminated. This was done by adding the compound to be tested for inhibition to both control and tyramine containing vessels. The percentage of in-

TABLE 2  
INHIBITION OF TYRAMINE OXIDATION  
(TYRAMINE 0.0066 M FINAL)

Compound	Final concentration	Inhibition, %
III	0.0066 M	37.2
IV	0.0066 M	83.8
V	0.0066 M	35.2
VI	0.0066 M	65.0
VII	0.0066 M	89.3