

Häggendal J. An improved method for fluorimetric determination of small amounts of adrenaline and noradrenaline in plasma and tissues.

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Several modifications of the trihydroxyindole method for the fluorimetric determination of adrenaline and noradrenaline were introduced. These included changes in the ion-exchange procedure for purification, stabilization of blank values, and reduction of the volumes of reagents. The result was an appreciable improvement in sensitivity and reproducibility. [The SCI® indicates that this paper has been cited in over 585 publications since 1963.]

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"After I had completed my medical studies at the end of the 1950s, I wanted to carry on with the thesis for my PhD degree within the area of mental illness, psychotropic drugs, and monoamines. Therefore I became interested in quantitative methods for estimation of small amounts of noradrenaline and adrenaline. A few years earlier, a sensitive method for estimation of catecholamines had been described by Bertler, Carlsson, and Rosengren.<sup>1</sup> Columns of strong cation exchange resin were used for the purification and concentration of catecholamines in the tissue extracts. The catecholamines were subsequently fluorimetrically determined after they had been converted to strongly fluorescent trihydroxyindoles by oxidation followed by stabilization.

"On the basis of these principles I started to adapt the method for increased sensitivity. A detailed investigation of different factors affecting the separation was performed. After that I tried to increase the sensitivity of the estimation procedure. This was achieved, e.g., by reducing the negative effect of too large volumes of reagents. Fur-

thermore, the different chemical steps in the procedure were stabilized and particular attention was paid to the question of various blanks. The method that finally came out permitted reproducible noradrenaline and adrenaline assays in rather small pieces of tissue and small blood plasma volumes. However, in order to be sensitive and reproducible the method demanded a large amount of carefulness and precision.

"The most important reason why this paper has been relatively frequently quoted is in all probability that the method was found to be useful in a field of research that rapidly expanded during the 1960s and 1970s. In this connection it should be noted that several different methods were available for catecholamine assay during that period of time. The other main methods were either based on fluorescence techniques or radiochemical methods.

"At present, however, the most sensitive and reproducible methods for quantitative catecholamine determinations are either radiochemical methods, or methods based on high-pressure liquid chromatography followed by electrochemical detection.<sup>2</sup> The role of procedures based on fluorescence appears now to be declining.

"I think that methodologic work can be of considerable importance for the student's training in science. Thus, the detailed knowledge about this method gave me self-confidence to use it as a tool for studies on basic mechanisms in the sympathetic noradrenergic neurons, where the results sometimes came out to be unexpected or even incompatible with what was earlier accepted.

"This may be illustrated by the studies on the axonal transport and life span of amine storage granules, together with A. Dahlström,<sup>3</sup> and also by the studies on the amount of noradrenaline released per nerve impulse from the varicosity of the adrenergic nerve ending, together with B. Folkow and B. Lisander.<sup>4</sup> In this connection the early suggestion of a local feedback mechanism for noradrenaline release<sup>5</sup> may be mentioned."

1. Bertler Å, Carlsson A & Rosengren E. A method for the fluorimetric determination of adrenaline and noradrenaline in tissues. *Acta Physiol. Scand.* 44:273-92, 1958.

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2. Hallman H, Farnbo L O, Hamberger B & Jonsson G. A sensitive method for determination of plasma catecholamines using liquid chromatography with electrochemical detection. *Life Sci.* 23:1049-52, 1978.

3. Dahlström A & Häggendal J. Studies on the transport and life-span of amine storage granules in a peripheral adrenergic neuron system. *Acta Physiol. Scand.* 67:278-88, 1966.

4. Folkow B, Häggendal J & Lisander B. Extent of release and elimination of noradrenaline at peripheral adrenergic nerve terminals. *Acta Physiol. Scand.* 307(Suppl.):1-38, 1967.

5. Häggendal J. Some further aspects on the release of the adrenergic transmitter. (Kroneberg G & Schümann H J, eds.) *New aspects of storage and release mechanisms of catecholamines.* Berlin: Springer-Verlag, 1970. p. 100-9.