ADRENALINE AND NORADRENALINE IN BLOOD AND URINE

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Adrenaline and noradrenaline, when infused intravenously into man in small amounts (at a rate of 0.2 micrograms per kilogram of body weight per minute), produce their typical cardiovascular effects; the chemical changes in the composition of the blood are considerably greater with adrenaline than with noradrenaline (8, 10, 16). In patients with shock noradrenaline often increases the blood pressure very effectively (7, 15). The adrenaline content in the human adrenal glands decreases during surgical shock, indicating the increased secretion of adrenaline into the circulation (20).

In the peripheral blood the content of adrenaline and noradrenaline is small not only under normal conditions, but also during increased secretion, as with phaeochromocytoma (12, 13, 21), because these substances disappear from the circulation rapidly (11, 14). Adrenaline and noradrenaline can be more easily determined by biological or chemical methods in the urine than in the blood (1, 2, 3, 5, 12, 17, 18).

To determine the noradrenaline and adrenaline content of the urine and tissues (17, 19), a 200 ml. aliquot of the 24-hour specimen of acid urine (pH 4) or 200 ml. of protein-free filtrate of minced tissue, from which trichloracetic acid has been removed by ether, is first brought to pH 8.5 with 1 N sodium hydroxide. Precipitated phosphates are centrifuged or filtered off. Noradrenaline and adrenaline are adsorbed by the addition of 8 gms. of aluminum oxide (designed for chromatographic analysis), mixed with a blendor and centrifuged. For the elimination of other fluorescing and inhibiting substances, the aluminum oxide is washed 5 times with 100 ml. portions of distilled water and centrifuged. Noradrenaline and adrenaline are eluted from the aluminum oxide with 1 N oxalic acid (2 times with 20 ml. of acid), which precipitates calcium oxalate; otherwise, calcium will cause later interference.

The pH of the eluate is increased to 6.3 with sodium hydroxide and sodium acetate buffer, and noradrenaline, adrenaline, and suitable standards in the eluate are oxidized by small amounts of manganese dioxide (10 mg. per 6 ml. of eluate) for 30 seconds. Since substances may be present which inhibit the fluorescence reaction, oxidation is usually carried out after 5-fold dilution. A state of equilibrium, where maximum fluorescence is obtained, must be maintained by the careful adjustment of conditions in the solutions during oxidation. The mixture is then centrifuged or filtered. Noradrenochrome and adrenochrome in 2 ml. of filtrate are converted to the fluorescent substances by the addition of 0.4 ml. of 5 N sodium hydroxide containing 200 mg. per cent ascorbic acid. A blank is simultaneously prepared without ascorbic acid. If a precipitate is still present after addition of alkali, it should be centrifuged, as it can disturb the estimation of the fluorescence reaction. The total fluorescence of adrenaline and noradrenaline is measured as the noradrenaline equivalent.

For the differentiation of the amount of noradrenaline from that of adrenaline in the eluate, the fluorescence reaction is simultaneously performed without manganese dioxide oxidation by the direct addition of alkali without ascorbic acid. The slowly developing noradrenaline fluorescence is then very weak at the time of maximal adrenaline fluorescence, the former being only 1 to 2 per cent of the amount observed after complete oxidation, and the latter 25 per cent.

The average daily urinary excretion in 17 medical students was 81 micrograms of noradrenaline equivalent, ranging from 31 to 185 micrograms (18). In 26 patients, mainly cases of hypertension, and a few with neuroses, the level was definitely elevated in 3 cases. In one of these, an operated case of paraganglioma, the daily urinary noradrenaline excretion ranged from 430 to 2400 micrograms during a period of two weeks, the mean excretion being 1354 micrograms per day (18). In the other 23 patients, the excretion was from 25 to 200 micrograms per day.

After a continuous intravenous infusion of noradrenaline (2500 to 15000 micrograms) in a man being treated for shock, the mean excretion in the urine was for the first day 319 micrograms, during the second day 178 micrograms and during the third day 206 micrograms (18). Thus, only a small percentage of the total amount intravenously infused was recovered in the urine, the largest part having been metabolized, as has also been observed by biological methods (6).

The concentration of noradrenaline and adrenaline found in the urine of normal individuals has been from 3 to 17 micrograms per cent, and during an increased excretion in the urine in the patient with paraganglioma was as much as 150 micrograms per cent, with a mean of 80 micrograms per cent (18) during a two weeks' period. After intravenous infusions of noradrenaline in patients with surgical shock the concentrations in the urine were from 5 to 85 micrograms per cent (18).

In considering the determination of noradrenaline and adrenaline in the urine as a picture of the activity of the sympathico-adrenal system, we must remember that the secretion of these substances in the urine indicates that part which has not been metabolized in the organism. Goldenberg and Rapport (9) have stated that the noradrenaline in the urine originates chiefly from secretion by the peripheral sympathetic nerve endings and to a lesser extent from secretion by the adrenal medulla in normal conditions. If this is correct, the normal excretion of noradrenaline and adrenaline in the urine may give a better picture of sympathetic function than determination of the blood levels.

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