BIOCHEMISTRY

Origin of Norepinephrine in the Heart

NOREPINEPHRINE is present in various organs of the body and in the blood plasma[1]. The adrenal medulla is not necessary for the maintenance of tissue stores of this catecholamine[1], and it is likely that synthesis of norepinephrine occurs in the sympathetic nervous tissue throughout the body. Norepinephrine in the plasma originates from discharge of the neurohumour from the sympathetic nerve endings. The circulating catecholamine is excreted, metabolically inactivated (predominantly by *O*-methylation), or rebound in the tissues[2,3]. A portion of the norepinephrine present in each organ is derived from the circulating pool of catecholamine. The ability of the heart to take up, concentrate, and store intravenously administered norepinephrine has been amply demonstrated[4–6]. It has recently been shown that the isolated perfused heart is capable of synthesis of norepinephrine from tyrosine, at a sufficiently rapid rate to account for a considerable portion of the norepinephrine in this organ[7]. Thus norepinephrine stores in the heart could be maintained in part by extraction of the catecholamine from the circulation and in part by synthesis. We have used an isotope dilution technique to demonstrate that in the normal rat about 60 per cent of the norepinephrine present in the heart is synthesized in this organ, while the remainder is derived from the circulating pool of norepinephrine.

Male Sprague-Dawley rats, weighing 250–300 g, were placed in small restraining cages which allowed collection of urine during intravenous infusion through the tail vein. L-norepinephrine-8-^{14}C (130,000 c.p.m./μg) was infused slowly (0·896 μg/h) for 2, 6, 10, 24, 36, or 48 h. Groups of five to eight rats were used for each infusion period. Urine samples were collected during the 2-h interval before the end of the infusion. At the end of the infusion the animals were killed by a blow on the head and the hearts removed, weighed, and homogenized in 10 volumes of cold 0·4 N perchloric acid. The catecholamines were isolated from the clear supernatant of the tissue homogenates and from urine by absorption alumina and elution with 0·4 N perchloric acid[8]. Norepinephrine and epinephrine in the eluates were determined by a modification of the trihydroxyindole method[9]. Radioactivity present in 0·5 ml. of these eluates was estimated by liquid scintillation spectrometry[10]. The specific activity of the norepinephrine was calculated from the radioactivity and norepinephrine present in the alumina eluates. The ratio of the specific activity of norepinephrine isolated from the heart to that of the urinary catecholamine was determined.

Table 1. SPECIFIC ACTIVITY OF URINARY NOREPINEPHRINE-^{14}C

Time (h)	2	6	10	24	36	48
Specific activity (c.p.m./mμg)	32·0	60·0	62·0	63·6	52·6	59·4

L-Norepinephrine-8-^{14}C (130 c.p.m./mμg) was infused at a constant rate (0·896 μg/h). The specific activities shown are the means for the norepinephrine isolated from the urine of 5–8 animals at each time, collected during the 2-h interval prior to the indicated time.

After 6 h, the specific activity of the urinary norepinephrine was constant at about 60 c.p.m. ^{14}C/mμg norepinephrine (Table 1). This is considerably below the specific activity of the infused norepinephrine, indicating that the amount of norepinephrine being administered was largely diluted by endogenous norepinephrine and did not excessively increase the plasma catecholamine concentration. During the steady state that was established, the specific activity of the urinary norepinephrine may be assumed to be about the same as the plasma norepinephrine from which it is derived. If all the norepinephrine in the heart were derived from the plasma, then the specific activity of the catecholamine in this organ would be expected to increase until it became the same as the specific activity of the plasma (or urinary) norepinephrine.

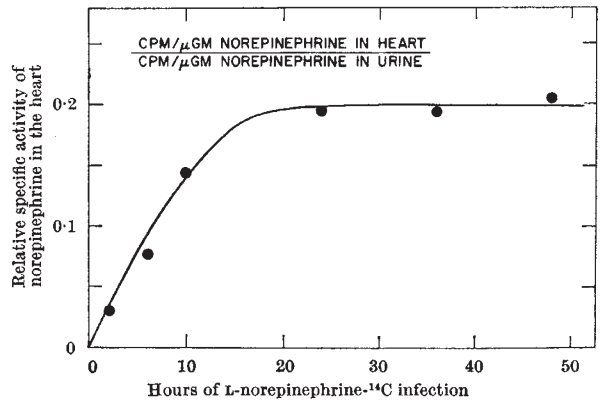

Fig. 1. Ratio of specific activity of norepinephrine in the heart and urine during a constant infusion of L-norepinephrine-8-^{14}C. Each point is the mean of this ratio for each of five to eight rats

If a portion of the norepinephrine in the heart were not derived from the plasma, but from synthesis, then the specific activity of the catecholamine in the heart would always be lower than the specific activity in the plasma (and urine). In the steady state, the ratio of the specific activity of the heart and plasma norepinephrine would be equal to the fraction of myocardial norepinephrine derived from the circulation. Fig. 1 shows the increase in the ratio of the specific activities of the myocardial and urinary norepinephrine. After one day of a constant slow infusion of L-norepinephrine-^{14}C the specific activity of the catecholamine in the heart remains at about 20 per cent of the specific activity of the urinary (and presumably plasma) norepinephrine. There was no increase in the myocardial norepinephrine concentration.

It can be concluded from these results that the myocardial stores of norepinephrine are maintained by both extraction of norepinephrine and by synthesis of catecholamine in the heart. About 80 per cent of the norepinephrine in the heart is synthesized in this organ (presumably within the sympathetic nervous tissue), while 20 per cent is derived from the circulating pool of norepinephrine.

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A Mucoid isolated from Bovine Red Cells exhibiting Strong *Pneumococcus* Type XIV Cross-reactivity

IT is well known that all human and some animal red cells are agglutinated by anti-Type XIV pneumococcus serum[1–3]. The chemical nature of this phenomenon has been elucidated by Watkins and Morgan[4] by means of hæmagglutination inhibition tests and has been interpreted as being due to the presence of *O*-β-D-galactopyranosyl-(1->4)-*N*-acetyl-D-glucosamine in terminal non-reducing position. This structure is considered to be