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Treatment of Paroxysmal Auricular or Nodal Tachycardia With the Vasopressor Drug, Neosynephrine.

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The cardio-inhibitory reflexes elicited by a rise in blood pressure are strikingly sensitive in unanesthetized animals.[1] Therefore, it was considered that a moderate, sudden, brief rise in blood pressure produced by intravenous injection of a vasoconstrictor drug might reflexly stop a paroxysmal auricular or nodal tachycardia.

Neosynephrine (laevo-α-hydroxy-β-methylamino-3-hydroxy-ethylbenzine hydrochloride) has a relatively high pressor potency as compared with its direct cardiac stimulating potency.[2,3] Following intravenous injection in normal human subjects, an amount which produces a moderate increase in blood pressure causes a striking bradycardia.[4,5] Therefore, neosynephrine was chosen as a favorable vasopressor compound to be given a trial in the treatment of paroxysmal tachycardia. Neosynephrine has been given to several patients having cardiac arrhythmias, including 2 with paroxysmal auricular tachycardia, and these 2 reverted to normal sinus rhythm.[4]

Results. Neosynephrine was given intravenously to each of 4 patients with idiopathic paroxysmal tachycardia of supraventricular origin. Each had a normal blood pressure between attacks and a somewhat lower blood pressure during attacks. Electrocardiographic records were taken and blood pressure was recorded repeatedly during and following the injections with the patient in the supine position. In each case the neosynephrine injection was completed within 30 seconds. The first patient had tachycardia which had persisted for several hours in spite of attempts to stop it with carotid sinus pressure, ocular pressure, amytal, and mecholyl. Her blood pressure was 100/70 during the attack. When she was given neosynephrine, the systolic pressure increased to 140 mm Hg within 60 seconds and the rhythm reverted to normal. The second patient had an attack that had persisted for 20 hours in spite of the usual mechanical methods of treatment and the administration of mecholyl. The patient was given 4 doses of neosynephrine intravenously, 0.15 mg, 0.30 mg, 0.50 mg and 0.80 mg respectively, with ample time for the blood pressure to return to the preinjection level after each dose. The first 3 doses were ineffective. When the dose of 0.8 mg was given, the blood pressure rose from 110 to 160 mm of Hg and the rhythm reverted to normal 45 seconds after the beginning of the injection. The third patient had had the tachycardia for several hours before she was seen. She was given 0.4 mg of neosynephrine; the systolic blood pressure rose from 110 to 140 mm of Hg and the rhythm reverted to normal within the first minute after the injection. The fourth patient was a man who had had frequent attacks which did not stop spontaneously but could be stopped by the Valsalva maneuver. A dose of 0.5 mg of neosynephrine failed to restore the normal rhythm. A dose of 0.80 mg increased his systolic blood pressure from 90 to 130 Hg in 50 seconds at which time the rhythm reverted to normal.

Over-dosage with neosynephrine must be avoided because of the danger of producing an excessively high blood pressure. Occasional ventricular beats were seen with the

1 Haney, H. F., Lindgren, A. J., Karstens, A. L., and Youmans, W. B., *Am. J. Physiol.*, 1943, **139**, 675.

2 Youmans, W. B., Haney, H. F., and Aumann, K. W., *Am. J. Physiol.*, 1940, **130**, 190.

3 Keys, A., and Violante, A., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 4.

4 Keys, A., and Violante, A., *J. Clin. Invest.*, 1942, **21**, 1.

5 Youmans, W. B., Gould, Jarvis, and Goodman, Morton J., experiments in progress.

larger doses used. However, experiments with animals have demonstrated that neosynephrine does not produce ventricular fibrillation even in relatively high doses in animals sensitized by cyclopropane anesthesia.[6] If a given dose is ineffective, a larger dose may be given after a 10-minute interval until the rhythm is reverted or until a rise of systolic pressure up to about 160 mm of Hg is produced. Doses between 0.5 mg and 1.0 mg should be effective in most cases.

Two of the 4 patients complained of mild precordial discomfort for a few minutes following the injection. This was the only unpleasant effect noted. Each patient described either a sensation of coolness of the skin or a tingling sensation evidently produced by the cutaneous vasoconstriction and piloerection.

Summary. Four nonhypertensive patients with idiopathic paroxysmal tachycardia of supraventricular origin were given neosynephrine intravenously in amounts sufficient to increase the systolic blood pressure 30 to 40 mm of Hg. In 2 of these the attacks had persisted for several hours in spite of all mechanical methods of treatment and administration of mecholyl. In all 4 cases the rhythm reverted to normal within one minute after the injection of neosynephrine. This is considered to be produced by reflexes from the carotid sinuses and aortic arch. Occasional ventricular beats occurred during the 2-minute period after the return to the normal sinus rhythm. Blood pressure returned to normal within 4 to 8 minutes after the injection.

Intravenous injection of neosynephrine or some other brief-acting vasopressor compound may prove to be the treatment of choice in selected cases of auricular or nodal paroxysmal tachycardia.

[6] Meek, W. J., *Harvey Lect.*, Ser. XXXVI, 1940-41, 188.

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Dark-field Observations on Lymphocytes Exposed to X-Rays and Other Injurious Agents.*

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By the method of unstained cell counts, it has been shown[1,2] that X-rays had a delayed cytocidal action on lymphocytes irradiated *in vitro* and incubated at 37°C. The death of the cells was preceded by irregularities in the shape and the refractivity of the cells. In the present study, these morphologic changes were studied by dark-field illumination with a cardioid condenser.

On dark-field examination of a fresh suspension of the thymus of a rabbit, most cells appeared filled with fine intranuclear granules and a few cytoplasmic mitochondria (Fig. 1). After irradiation of the suspension and incubation for 3.5 hours, about 32% of the cells developed one or a few small, dark, round structures which may be termed primary vacuoles (Fig. 2). On dark-field examination, it was not possible to determine whether these structures were in the nucleus or cytoplasm. The vacuoles occasionally increased in size during observation. Some of them were surrounded by thick, bright, circular walls. They caused the distortion of the shape of many cells. They were present in viable cells which resisted staining with

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[1] Schrek, R., *Radiology*, 1946, **46**, 395.

[2] Schrek, R., *J. Cell. and Comp. Physiol.*, 1946, **28**, 277.