

# MEDICAL PHYSIOLOGY

## CV Conference 2 - Quiz 4A

### October 16, 2000

#### **1. Why is cutaneous blood flow decreased during deep inspiration in a normal person?**

During inspiration, cardiac output is reduced because of the decreased intrathoracic pressure which increases compliance of cardiopulmonary vasculature, thus decreasing ventricular filling. The resulting decrease in stroke volume results in decreased stretch of the aortic and carotid sinus baroreceptor nerves. This leads to reduced impulse activity in the nucleus of the tractus solitarius and therefore reduced inhibition of C1, leading to increased discharge of sympathetic nerve fibers to the vasculature. The increased SNS discharge results in more norepinephrine being released in several vascular beds including the skin, where norepinephrine stimulates alpha 1 receptors on smooth muscle leading to increased resistance and therefore decreased flow.

#### **2. Phenylephrine, an alpha 1 agonist, is administered intravenously to a normal individual. What effect would this have on plasma levels of norepinephrine and why?**

Phenylephrine, an alpha 1 agonist, would decrease plasma norepinephrine. This is because it would cause vascular smooth muscle to contract, leading to increased TPR (arteriolar smooth muscle) and increased venous return (smooth muscle in veins and all venules except the post-capillary venules). This would increase blood pressure, leading to increased discharge in baroreceptor nerves, which would inhibit C1 and therefore reduce sympathetic nerve activity, which results in less norepinephrine release from sympathetic noradrenergic varicosities and therefore lower levels in plasma.

#### **3. Why were levels of antidiuretic hormone increased in this patient with pure autonomic failure?**

The patient had pure autonomic failure because her postganglionic sympathetic axons had deficient norepinephrine stores probably as a result of nerve degeneration. However, her sensory baroreceptor nerve pathways were intact, as were the projections from the nucleus of the tractus solitarius to the A1 region. Because her blood pressure was generally low, the lower levels of baroreceptor discharge resulted in less inhibition of A1, which results in increased release of ADH from the posterior pituitary. Because ADH causes vasoconstriction and increases plasma volume, this represents a potentially powerful (though incomplete) compensatory mechanism that may help to partially overcome the decreased cardiac output and blood pressure in patients with autonomic failure.

#### **4. Why is the increase in heart rate in response to the beta agonist isoproterenol greater than normal in this individual with pure autonomic failure?**

The pure autonomic failure is associated with degeneration of sympathetic nerves. The loss of innervation to the heart leads to receptor upregulation. Therefore the increased heart rate response is due to beta 1 receptor denervation supersensitivity. It should be noted that this is due entirely to changes in the receptor population (post-junctional supersensitivity) and not due to diminished catecholamine reuptake mechanisms (pre-junctional supersensitivity).

**5. How would total peripheral resistance measured 30 seconds after standing from a reclining position differ in a normal individual and in this patient with pure autonomic failure? Why?**

The TPR of the patient with pure autonomic failure would be lower than that of a normal individual 30 seconds after standing. This is because the patient's vasoconstrictor nerves have degenerated and she cannot elicit normal alpha 1-mediated contraction of her arteriolar smooth muscle.

**MEDICAL PHYSIOLOGY**  
**CV Conference 2 - Quiz 4B**  
**October 13, 2000**

**1. Why is cutaneous blood flow increased during deep expiration in a normal individual?**

During expiration, cardiac output is increased because of the increased intrathoracic pressure which decreases compliance of cardiopulmonary vasculature, which increases ventricular filling. The increased stroke volume results in increased stretch of the aortic and carotid sinus baroreceptor nerves. This leads to increased impulse activity in the nucleus of the tractus solitarius and therefore greater inhibition of C1, leading to decreased discharge of sympathetic nerve fibers to the vasculature. The lower SNS discharge results in less norepinephrine being released in several vascular beds including the skin, and less alpha 1 receptor-mediated smooth muscle contraction, resulting in decreased arteriolar resistance and increased flow.

**2. Why is the response to tyramine reduced in this patient with pure autonomic failure?**

Tyramine normally exerts a sympathomimetic (mimics sympathetic) effect by being taken up into varicosities and displacing the norepinephrine that resides in the vesicles. If the postganglionic sympathetic nerves which store norepinephrine have degenerated or cannot make or store norepinephrine, then tyramine will fail to elicit a normal response.

**3. Why might administration of the alpha 1 agonist phenylephrine produce an increase in blood pressure that is greater than normal in this patient with pure autonomic failure?**

Phenylephrine raises blood pressure by contracting arteriolar smooth muscle to increase TPR and venous smooth muscle to increase venous return. The patient with autonomic failure has a deficiency in postganglionic sympathetic innervation. This would be expected to result in, over time, an upregulation of vascular smooth muscle alpha 1 receptors. This postjunctional receptor denervation supersensitivity would result in a phenylephrine response that is greater than normal.

**4. What are the mechanisms by which the alpha blocker phentolamine leads to an increase in plasma norepinephrine in a normal individual?**

Phentolamine increases plasma norepinephrine by 2 mechanisms. By blocking alpha 1 receptors on venous and arteriolar smooth muscle, phentolamine elicits a decrease in blood pressure which is detected by the baroreceptors. In an attempt to correct the falling blood pressure, the sympathetic nervous system is activated via the baroreflex, leading to increased sympathetic

impulse activity and an increase in plasma norepinephrine. In addition, because phentolamine also blocks alpha 2 receptors, this drug will impair the feedback inhibition that normally occurs by way of the prejunctional alpha 2 autoreceptors on the sympathetic varicosity. In the absence of this feedback inhibition, more norepinephrine will be released per impulse.

**5. Why are plasma levels of the hormone aldosterone decreased in the patient with autonomic failure?**

The sympathetic nervous system is one of the primary mechanisms responsible for activating the renin-angiotensin system. It does so by stimulating beta 1 receptors on the juxtaglomerular apparatus in the kidney, thus leading to renin release. Renin acts on circulating angiotensinogen to cleave off angiotensin I, which is converted by angiotensin-converting enzyme to angiotensin II. Angiotensin II triggers the release of aldosterone from the adrenal cortex. In the patient with autonomic failure, the sympathetic nervous system fails to initiate the release of renin, with the net result that aldosterone (as well as renin, angiotensin I and angiotensin II) are below normal levels.