# OUTLINE: THE SYMPATHETIC INNERVATION OF THE HEART

1. Introduction
   1. Background
      1. Neurocardiac axis mediates connection between brain and heart
   2. Purpose
      1. Teach clinicians that sympathetic nervous system is important in normal function as well as pathophysiologic states
      2. Share how the heart and autonomic system was not built to respond to
      3. Explore the anatomy, physiology, and pathophysiology relevance of sympathetic outflow to the heart
   3. Objectives
      1. Understand how the sympathetic nervous system innervates the heart
      2. Understand how sympathetic tone effects the functions of the heart (such as chronotropy, inotropy, lusitropy, dromotropy)
      3. Review how sympathetic dysfunction occurs in pathological states, such as VT/VF, MI, and stress cardiomyopathy.
2. Anatomic and physiologic considerations
   1. Overview of section
      1. Sympathetic nervous system has three “distinct” levels, the brain and spinal cord, the thoracic/extracardiac ganglia, and the intrinsic cardiac nervous system
      2. Carry both afferent and efferent information, integrates that at multiple levels
   2. Spinal cord level
      1. Spinal cord anatomy of preganglionic neurons location, and both proximal and distal connections to brain and postganglionic neurons
         1. Automaticity and firing of these SNS neurons
      2. Effect of cerebral/nervous influences on these preganglionic cell bodies
         1. Examples include sympathetic storm from TBI, which leads to hyperactivation
         2. Nervous activity (e.g. panic attack) on the preganglionic bodies (what is the connection/mechanism of communicatin)
      3. Integration of systemic/peripheral reflex arcs into the spinal cord
         1. Examples include vasovagal syncope, mesenteric ganglia response to stress, etc (lumbosacral outflow)
   3. Thoracic, extracardiac level
      1. Anatomy of the thoracic ganglia
         1. Preganglionic fibers exit from DRG and enter white rami, then eventually form sympathetic chain and thoracic ganglia
         2. T1 to T6 specifically are responsible for cardiac outflow
      2. Stellate ganglia
         1. Historic examples include stellectomy/ganglion block to help decrease VT/VF burden
         2. Innervation of the heart is different between LSG and RSG, to some degree
   4. Intrinsic cardiac level
      1. Sympathetic nervous system is within GPs around epicardium of heart, particularly in epicardial fat pads.
      2. Innervation of the cardiac chambers and wall
         1. Epicardium is highest density of nerve fibers, which decrease as going into endocardium
         2. Atria have different right-to-left innervation of both adrenergic and cholinergic nerves
         3. Ventricles have a base-to-apex density gradient of adrenergic fibers, but barely any vagal fibers (except inferior wall)
      3. Coronary artery innervation goes from a plexus around major/large arteries, and decreases in size until it is only 1-2 nerves at level of arteriole
3. Ventricular fibrillatory threshold
   1. Pertinent history of SCD
      1. SCD occurs with increased sympathetic tone
         1. Historical studies about emotional and stress triggers
      2. Lown et al showed increased SNS leads to VT/VF in humans
      3. Increased PVC during times of stress and increased SNS activity in human recordings
      4. VF threshold is modulated by different factors (mainly SNS activity)
         1. Increased likelihood of ventricular dysrhythmias of the heart
   2. Normal effects of sympathetic tone through stellate ganglia stimulation
      1. Increased SNS (e.g. stellate stimulation) leads to increased inotropy/lusitropy
      2. RSG stimulation leads to increased SA firing, thus increased chronotropy/dromotropy
      3. Increased stimulation leads to increased episodes of VT/VF (excluding effects of ischemia)
4. Coronary perfusion
   1. Myocardial infarction/ischemia
      1. Advent of MI can change and increase VT/VF events
      2. Infarction leads to rewiring of the heart, including NE release
      3. Beta blockers, CCU “quiet and calm” can prevent sympathetic dysregulation
   2. Cardiac innervation heterogeneity
      1. Localized changes occur after infarct, included denervation
         1. FIGURE: myocardial ischemia leads to interdigitations of non-ischemic regions
      2. Scar tissue development becomes a nidus for VT/VF
         1. Benefit of epicardial ablation at times
      3. Adrenergic receptor dysregulation after ischemia
5. Catecholamine-based necrosis
   1. Malignant effects of catecholamines
      1. Takotsubo to discuss apical ballooning
         1. Mortality with Takotsubo is same with traditional AcS
      2. Wellen’s T waves occur in setting of significant apical NE levels
         1. Stress events
         2. Cerebral injury
      3. Effect of adrenergic receptor density on apex of the heart
   2. Important neurotransmitters that mediate sympathetic tone
      1. Sympathetic signals
         1. NE
            1. Alpha and beta adrenergic receptors have differential preference of location
         2. Galanin
         3. NPY
      2. Parasympathetic signals
         1. Ach
         2. NOS
      3. TABLE: Describe individual neurohormones and effect on heart
   3. Sympathetic dysregulation in heart failure
6. Conclusion
   1. Clinical importance of SNS
   2. Innervation and sympathetic outflow is modulated
   3. Has clinical effects on patients and leads to pathology