# OUTLINE: THE SYMPATHETIC INNERVATION OF THE HEART

What are the key concepts of SNS in regulating the heart in physiological and pathophysiological states?

* The SNS gives the heart the ability to increase output to handle demands. It’s the mechanism for modifying the internal environment to match the needs of the external environment.
* ANS abnormalities are bidirectional, in that sympathetic nerve activity (SNA) leads to pathophysiology, but changes in cardiac function can lead to changes in SNA.

1. Introduction
   1. Purpose
      1. Sympathetic outflow to the heart regulates normal responses to stress. However, alterations in SNA can lead to pathophysiological changes of cardiac function, as well as alterations in cardiac function can lead to changes in SNA (bidirectional).
         1. High SNA can occur in trauma, psychological stress, brain-injury which then lead to cardiac changes (from arrhythmia, MSIMI, stress cardiomyopathy
         2. Cardiac disease (myocardial infarction/ischemia, heart failure) can lead to increased SNA subsequently
   2. Objectives / overview
      1. Review the relevant anatomy of the neurocardiac axis
      2. Understand the physiology of cardiac sympathetic innervation in normal circumstances (include cardiac reflexes that regulate SNA)
      3. Learn through examples of sympathetic toxicity in pathological states
      4. Identify treatment paradigms in place, and consideration of future directions targeting the ANS
2. Relevant cardiac anatomy
   1. Historical descriptions of sympathetic innervation
      1. Evolutionary perspective of development of sympathetic nervous system in vertebrates (“management of the internal environment of the organism”)
   2. Neurocardiac axis overview
      1. Pathways connecting the brain, spinal cord, and heart
      2. Respective anatomical innervations of the ventricles and atria, focusing on the conduction systems and relevant myocardium
      3. Imaging and anatomical evidence of how the heart is innervated (MIBG, clinically relevant imaging techniques)
3. Normal cardiovascular responses to sympathetic tone
   1. Sympathovagal interaction and local neurotransmitters
      1. Nor epinephrine, epinephrine, galanin, neuropeptide Y, acetylcholine
      2. Chronotropy, inotropy as physiological responses to innervation
   2. Coronary perfusion
      1. Coronary blood flow and vasoconstriction/vasodilation
      2. Coronary artery innervation
   3. Cardiac reflexes regulated by SNA
      1. Clinical relevance:
4. Pathological responses to sympathetic tone
   1. Ventricular fibrillation
      1. Psychological factors precipitating sudden cardiac death
      2. Change in ventricular fibrillatory threshold with psychological stress
   2. Myocardial ischemia and infarction
      1. Myocardial scars lead to a focus for VF/VT and SNS heterogeneity
      2. Myocardial infraction leads to asymmetrical effects based on location of injury
   3. Catecholamine excess
      1. Lead to heterogeneous, receptor-density-dependent changes in the myocardium (e.g. stress cardiomyopathy)
      2. Catecholamines lead to hypertrophy, neuronal edema, and vagal withdrawal (e.g. obesity and hypertension)
   4. Cardiac denervation (e.g. transplant, spinal injury)
      1. Heart transplant
      2. Spinal cord injury
5. Treatment methods
   1. Historical methods
      1. Stellate ganglion block and stellectomy lead to reduction in VT and VF events
   2. Neurohormonal blockade
      1. Beta blockers as protective in ischemia, VT, but mixed role in chronically elevated SNS states (e.g. hypertension, chronic heart failure)
      2. Discussion of nor epinephrine spill over in different disease states
      3. Angiotensin converting enzyme inhibitors
      4. Alpha-methyldopa
      5. Reserpine
6. Conclusion
   1. Review central purpose of paper: how cardiac disease are also manifestations of inappropriate SNS responses and vice versa
   2. Future directions including treatment with other sympatholytic techniques (e.g. ablations on cardiac ganglia, vagal nerve stimulation)