Instructions
Please prepare for the class sessions by reading the learning objectives and reviewing the required self-study work listed below. I have also included a folder containing supplemental information for those who would like additional resources on the topic.

Required Self-Study Work:
- Watch the “Introduction to Atrial Fibrillation” video (~10 min.)
- Review relevant sections of the Anatomy, Physiology, and Assessment text as well as the pharmacology videos, as needed
- Read the below outline, including the accompanying algorithms and tables
- Read Contemporary Review of Antiarrhythmic Drugs (6 pages) with focus on the following sections:
  - Introduction & Management of AF
  - Indications for Rhythm Control
  - Drugs for Maintenance of Sinus Rhythm
    - Bullet points a, b, and c
    - Flecainide, propafenone, amiodarone, dofetilide, sotalol, dronedarone

Learning Objectives
1. Explain the normal electrical conduction of the heart and correlate it with an electrocardiogram (ECG) tracing (e.g., P-wave, QRS complex, QT interval) (Anatomy, Physiology, and Assessment material)
2. Explain the most common mechanisms of arrhythmias (i.e., altered automaticity and reentry) (video 2 of pharmacology videos)
3. Recognize common causes and contributing factors to the development of atrial fibrillation (specifically those factors that have been previously taught in the course)
4. Describe common symptoms and complications of atrial fibrillation
5. Define the therapeutic objectives in treating atrial fibrillation
6. Compare and contrast rate and rhythm control strategies for the management of atrial fibrillation, including advantages and disadvantages of each
7. Identify the appropriate heart rate goal for patients with atrial fibrillation being rate controlled
8. Differentiate management of atrial fibrillation in patients with and without heart failure with reduced ejection fraction
9. Given a patient with atrial fibrillation, create a pharmacotherapy plan for rate and/or rhythm control including appropriate monitoring and follow-up
10. List non-pharmacologic interventions that can prevent/reduce the incidence atrial fibrillation
11. Explain the role of electrical cardioversion for the management of atrial fibrillation
12. Identify contraindications and major adverse effects of antiarrhythmic drugs used for the management of atrial fibrillation

Outline
- Atrial Fibrillation Overview
  - Atrial fibrillation is the result of one or more reentry circuits within the atria. This causes dyssynchronous atrial depolarization and uncoordinated myocyte contraction. It also causes variable conduction through the AV node to the ventricles.
    - Atrial rate 600+ “beats” per minute
    - Ventricular rate varies widely and is dependent on the refractoriness of the AV node
      - If the ventricular rate is >~120 beats per minute we term this “atrial fibrillation with rapid ventricular rate”
  - Prevalence
    - 1 in 3 adults over age 55 have atrial fibrillation
    - Greatest incidence among older adults and in patients with CAD, valvular heart disease, obesity, diabetes, and chronic kidney disease
  - Electrocardiogram findings
    - “Irregularly irregular” rhythm on ECG due to the erratic transmission of action potentials from the AV node to the ventricles
    - Indiscernible p-waves
Classifying atrial fibrillation

- Paroxysmal vs persistent vs permanent atrial fibrillation
  - In many instances, atrial fibrillation is **paroxysmal** (meaning that it comes and goes based on various circumstances and triggering factors)
  - In some instances, atrial fibrillation is longstanding (ie, lasting 7 days or more). This is termed persistent atrial fibrillation
  - In some instances, atrial fibrillation is permanent (ie, return and maintenance of normal sinus rhythm is not possible with rhythm control strategies)

Symptoms of atrial fibrillation:

- **40% of patients are entirely asymptomatic**
- The most common symptom is palpitations (sensation that the heart is beating rapidly or abnormally), or sometimes referred to as “fluttering”
- Dizziness, lightheadedness, dyspnea, fatigue, worsening heart failure, and hypotension may also occur

Risk factors for the development of atrial fibrillation

- Obesity
- Smoking
- Alcohol consumption
- Obstructive sleep apnea
- Chronic obstructive lung disease
- Inflammatory diseases (e.g., rheumatoid arthritis)
- Diabetes mellitus
- Hypertension
- Coronary artery disease
- Heart failure
- Valvular heart disease
- Acute illness or surgery
- Hyperthyroidism
- Physical inactivity
- Electrolyte abnormalities (e.g., hypokalemia)

Complications and health burden of atrial fibrillation

- 5-fold increase in stroke (a focus of Dr. Ives’ material)
- 2-fold increase in the risk of mortality
- Impaired quality of life
- Increased risk of hospitalization

Atrial Fibrillation Management

- ABC's of atrial fibrillation management
  - A = anticoagulation for stroke prevention (Dr. Ives’s material)
  - B = better symptom control
  - C = control comorbidities

- Focusing on “B”etter symptom control
  - Common symptoms of patients in atrial fibrillation include palpitation (“heart fluttering”), dizziness, syncope, dyspnea, or fatigue. In severe cases, it can cause hemodynamic instability.
  - **Up to 40% of patients are entirely asymptomatic**
  - Symptoms can be controlled in atrial fibrillation by one of two ways: 1) **controlling the ventricular rate** or 2) **restoring a normal sinus rhythm**

- Rate control involves controlling ventricular rate, typically by giving drugs that slow impulse conduction & refractoriness at the level of the AV node, without attempting to restore a normal rhythm (in other words, you accept that they’re in atrial fibrillation and just try to control their ventricular rate to reduce symptoms and long term complications)
  - Beta-blockers and non-dihydropyridine calcium channel blockers are first-line therapies
  - Digoxin may be considered as an *add-on therapy* for rate control, particularly in patients with heart failure with reduced ejection fraction
  - Defining a goal heart rate
    - When rate controlling patients with atrial fibrillation, a goal HR is typically specified:
      - **Lenient rate control** – resting heart rate <110 bpm
      - **Strict rate control** – resting heart rate <80 bpm
      - Lenient vs Strict rate control
        - Lenient rate control requires *fewer drugs and has less adverse drug effects* compared to strict rate control. Lenient rate control
is the preferred first-line approach. If the patient remains symptomatic, strict rate control can be pursued.

- Heart rate "goals" in patients with heart failure with reduced ejection fraction
  - Patients with HFrEF should be on a beta-blocker at baseline. Achieving a goal heart rate does not trump achieving a goal dose of a beta-blocker (i.e., continue to strive for goal doses of beta-blockers even if the heart rate is below 80-110)

- Rhythm control involves attempting to restore normal sinus rhythm through antiarrhythmic drugs, electrical cardioversion, or catheter ablation
  - Rhythm control can provide improved symptom control in patients who are persistently symptomatic in spite of adequate rate control
  - Antiarrhythmic drugs are associated with more adverse drug effects than rate controlling medications
  - Safety should be the primary guide for selection of AAD

- Non-pharmacologic rhythm controlling strategies
  - Direct current cardioversion ("electrical cardioversion")
    - Fastest and most reliable way to restore normal sinus rhythm
      - 90% success rate of restoring normal sinus rhythm, but this does not guarantee the patient will stay in a normal sinus rhythm long term

- Treatment of choice in hemodynamically unstable patients
  - Catheter ablation
    - Involves burning (or freezing) an area of the atria to break the reentry circuit(s) (beyond the scope of AST 5)

- Selecting rate vs rhythm control (Algorithm 1)
  - Rate control is generally the preferred first-line approach because it is associated with fewer adverse drug effects
    - Lenient rate control may be sufficient, but if symptoms persist strict rate control (or rhythm control) can be pursued. This is often a patient-specific decision (i.e., shared decision making with the patient based on their preferences)
  - Rhythm control can be pursued in patients who are persistently symptomatic

- Hemodynamically unstable patients
  - Some patients will experience hemodynamic instability from atrial fibrillation (e.g., shock, hypotension with altered mental status)
  - Instances where patients are hemodynamically unstable require immediate electrical cardioversion to quickly restore normal sinus rhythm

- "C"ontrolling comorbidities
  - Controlling comorbidities is one of the best ways to reduce atrial fibrillation "burden" (i.e., time in atrial fibrillation)
  - Strategies to reduce atrial fibrillation burden
    - Lifestyle changes
      - Increase physical activity
      - Weight loss
      - Reduce (or eliminate) alcohol consumption
    - Cardiovascular and other comorbidity management
      - Blood pressure control
      - Blood glucose control
- Lipid control
- Heart failure management (optimize goal-directed medical therapy)
- Treatment of obstructive sleep apnea
Algorithm 1: Initial Treatment for Symptom Management of Atrial Fibrillation in Hemodynamically Stable Patients

Atrial Fibrillation

Target Lenient Goal (HR < 110 bpm)

Persistently symptomatic?

Yes

Target Strict Goal (HR < 80 bpm)

No (continue lenient rate control)

Rhythm control
Table 1: Rate Control Medications in Patients with Atrial Fibrillation

<table>
<thead>
<tr>
<th>First Line</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers (metoprolol tartrate or succinate, carvedilol, bisoprolol, others)</td>
<td>Preferred in patients with HFrEF (metoprolol succinate, carvedilol, bisoprolol) Avoid new initiation in acute decompensated heart failure or aggressive up-titration in patients with HFrEF Optimize dose before adding non-DHP or digoxin</td>
</tr>
<tr>
<td>Non-dihydropyridine calcium channel blockers (e.g., verapamil, diltiazem)</td>
<td>Contraindicated in HFrEF May be preferred in severe COPD or asthma Optimize dose before adding beta-blocker or digoxin</td>
</tr>
<tr>
<td><strong>Second Line</strong></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>Add-on therapy to beta-blocker or non-DHP CCB In patients with HFrEF, goal digoxin level remains &lt;1 ng/ml Drug-drug interaction with amiodarone secondary to P-gp inhibition (generally requires 25-50% dose reduction of digoxin)</td>
</tr>
</tbody>
</table>

Table 2: Antiarrhythmic Drugs for Maintenance of Sinus Rhythm in Atrial Fibrillation*

<table>
<thead>
<tr>
<th>Class IC</th>
<th>Preferred in….</th>
<th>Contraindicated in….</th>
<th>Clinical Considerations</th>
<th>Adverse Effects/Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flecainide</strong></td>
<td>Structurally normal hearts (e.g., no heart failure or coronary artery disease)</td>
<td>X</td>
<td>X</td>
<td>Interpatient variability due to differences in CYP 2D6 genotype Differences in bioavailability between immediate and extended release formulation (due to CYP 2D6 saturation)</td>
</tr>
<tr>
<td><strong>Propafenone</strong></td>
<td>Structurally normal hearts (e.g., no heart failure or coronary artery disease)</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>Sotalol</strong></td>
<td>Structurally normal hearts or CAD</td>
<td>X</td>
<td></td>
<td>Dose reduce in renal dysfunction Pharmacodynamic interactions (e.g., with other QT prolonging medications)</td>
</tr>
<tr>
<td><strong>Dofetilide</strong></td>
<td>Patients with CAD or HFrEF</td>
<td></td>
<td>Dose reduce in renal dysfunction Pharmacokinetic drug interaction with hydrochlorothiazide, sulfamethoxazole/trimethoprim, and verapamil Pharmacodynamic interactions (e.g., other QT prolonging medications)</td>
<td>QTc interval Renal function</td>
</tr>
<tr>
<td><strong>Amiodarone</strong></td>
<td>Heart failure with reduced ejection fraction OR patients who have failed other antiarrhythmic drugs</td>
<td></td>
<td>One of the most effective at maintaining normal sinus rhythm Drug interactions (e.g., digoxin, warfarin)</td>
<td>See table of adverse effects in pharmacology lectures</td>
</tr>
<tr>
<td><strong>Dronedarone</strong></td>
<td>Structurally normal hearts or CAD</td>
<td>X</td>
<td></td>
<td>Less effective than amiodarone, but fewer toxicities Drug-drug interaction with dabigatran (avoid use)</td>
</tr>
</tbody>
</table>

*Note that Class IA and IB medications are not used for long-term maintenance of sinus rhythm for atrial fibrillation
Algorithm 2: Strategies for Rhythm Control in Patients with AF

**No Structural Heart Disease**

- Dofetilide
- Dronedarone
- Flecaainide
- Propafenone
- Sotalol
- Catheter ablation
- Amiodarone

**Structural Heart Disease**

- CAD
  - Dofetilide
  - Dronedarone
  - Sotalol
  - Catheter ablation
  - Amiodarone
- HF
  - Dofetilide

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**FIGURE 2** Strategies for rhythm control in patients with paroxysmal* and persistent AF.†

*Catheter ablation is only recommended as first-line therapy for patients with paroxysmal AF (Class IIa recommendation).
†Drugs are listed alphabetically.
‡Depending on patient preference when performed in experienced centers.
§Not recommended with severe LVH (wall thickness >1.5 cm).
||Should be used with caution in patients at risk for torsades de pointes ventricular tachycardia.
¶Should be combined with AV nodal blocking agents.
AF indicates atrial fibrillation; AV, atrioventricular; CAD, coronary artery disease; HF, heart failure; and LVH, left ventricular hypertrophy.