Good Morning!
We are going to have a really good day today!

Opening Remarks

- Objectives
  - Professional Practice
  - Risk Factors
  - A/P, Assessment, Physiology
  - Pharmacology
- Schedule for the day
  - Break 10:00 am
  - Lunch 12:15 to 1:00 pm
  - Break 2:30 pm
  - Conclusion 4:30 pm
- Turning Point Questions
- FUN!
Cardiovascular Nurse – Board Certified
175 Questions / 150 Scored

– I Assessment and Diagnosis 16%
– II Planning and Implementation 22%
– III Evaluation 18%
– IV Cardiac/Vascular Education 17%
– V Professional Role Performance 27%

American Nurses Credentialing Center
Updated test plan 4-6-2012

Cardiovascular Nurse – Board Certified
175 Questions / 150 Scored

– I Assessment and Diagnosis 22%
– II Planning / Implementation / Evaluation 35%
– III Education and Health Promotion 17%
– IV Professional Role Performance 26%

American Nurses Credentialing Center
Updated test plan effective February 6th 2015
Opening Thought

Link your roots deeply into whatever task you are doing, for commitment and enthusiasm transform monotony into freshness; and routine into joy and discovery.
Definitions

- Morality: social consensus regarding norms of right and wrong

- Ethics
  - Study of moral conduct

- Bioethics
  - Focus on ethical dilemmas within healthcare
  - Symphonology (agreement): Husted & Husted – A Practice Based Theory
  - Ethical decision making is contextual

Moral Virtues for Health Care

- Compassion
- Trustworthiness
- Conscientiousness
- Integrity
- Discernment
Ethical Principles

• Beneficence
• Nonmalficence
• Autonomy
• Justice
• Veracity
• Privacy / Confidentiality
• Fidelity

ANA Code of Ethics for Nurses

HIPPA:
The Health Insurance Portability and Accountability Act of 1996

Informed Consent

• Decision making capacity
  – Must be evaluated at each decision point
  – Surrogate decision makers
    • Substitute judgment
    • Best interest standard
    • Order (court appointed, DPA for health care, spouse, adult children, parents, adult siblings)
      – Issue of consensus

• Disclosure
• Understanding
• Voluntariness
• Consent
## Special Issues

- **Advanced Directives**
  - Living Wills
  - DPAHC
  - Patient self determination act of 1990

- **Withdrawal or withholding of treatment**
  - Quantitatively (<1% chance of effectiveness) versus qualitatively futile
  - Ordinary versus extraordinary interventions
  - Double effect (intended versus unintended)

- **Access to Care**
  - Major ethical issue
  - Based on principle of justice

- **Patient rights**
  - Ethical theory of Liberal Individualism
  - 1990, American Hospital Association “Patient’s Bill of Rights”

---

## Ethical Reasoning

- Review both facts and assumptions
- Define specific dilemma
- List options in course of action

- Consider the context
- Choose the course
- Evaluate the course
Professional Standards of Practice

• Standards of care versus standards of professional performance
  – Competent level of nursing care
  – Competent level of behavior in the professional role

• 1980 Social Policy Statement defining nursing
  – The diagnosis and treatment of human responses to actual or potential health problems
    • Full range of human responses and experiences related to health and illness
    • Integration of objective data with patient subjective perception
    • Use of scientific knowledge
    • Use of caring relationships to facilitate healing

Professional Standards of Practice

• Professional licensure (legal recognition)
  – Advanced practice

• Professional certification
  – Private rather than governmental organizations

• Nurse Practice Acts
  – Law
    • State level
    • Creates boards of nursing
  – Interpretation
  – Rules / regulations
Legal Aspects

**Accountability**
- Personal accountability
  - Duty to communicate

- Employer accountability
  - Issue of scope of practice
  - Does not eliminate personal accountability
  - Employer assurance of competency and credentialing

**Torts**
- Unintentional (negligence)
  - Duty
  - Breach of duty
  - Injury
  - Causation

- Intentional
  - Assault and battery
  - Defamation
  - Invasion of privacy

CVN Review Course

THEORY TO GUIDE PRACTICE
The Importance of Theory

• The relationship between theory – practice – and research

• What is theory?
  – Set of concepts, definitions, and propositions that provide a view (explanation for understanding) of a specific phenomena.

More on Theory

<table>
<thead>
<tr>
<th>Concept</th>
<th>Propositions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear description of an abstract concept</td>
<td>Statements about relationships between concepts</td>
</tr>
<tr>
<td>Building blocks for theory</td>
<td></td>
</tr>
<tr>
<td>Concept analysis sample components</td>
<td>Example: Resiliency improves health.</td>
</tr>
<tr>
<td>– Attributes</td>
<td></td>
</tr>
<tr>
<td>– Prerequisites</td>
<td></td>
</tr>
</tbody>
</table>
Grand Theories (Conceptual Models)

- **Patient**
  - Dorthea Orem: Self Care
  - Sister Callisata Roy: Adaptation

- **Nursing**
  - Betty Neuman: Systems Model
    - Nurse assists patient to develop defenses against stressors
  - Martha Rogers: Unitary Man
    - People are open energy systems — nurse assist people to evolve to full potential

- **Environment**
  - Betty Neuman: Systems Model

- **Health**
  - Jean Watson: Caring
  - Margaret Newman: Expanding Consciousness
    - People are energy fields that can expand consciousness

Mid Range Theories (Resiliency Theory) and Nursing Practice Theory

Health as Primary Focus of Nursing

- Difference between focus on health and illness
  - Health moves beyond the absence of illness

- Difference between illness and disease
  - Illness is a subjective experience
  - Disease is a specific entity

- Definitions of health within nursing theory
  - Clinical health
  - Role health
  - Adaptive health
  - Eudaimonistic
    - Maximum potential
    - WHO definition: State of complete physical, mental, and social well being.
Theories Related to Human Behavior

Maslow’s Hierarchy of Needs
– Physiological
– Safety
– Belonging
– Self actualization

Erickson’s Stages of Human Development
• Trust versus mistrust
• Autonomy versus shame and doubt
• Initiative versus guilt
• Industry versus inferiority
• Identity versus role confusion
• Intimacy versus isolation
• Generosity versus absorption
• Integrity versus despair

Social Cognitive Theory and the Importance of Self Efficacy:
- mastery experience, vicarious experience, physiological cues, verbal / social persuasion

Theories Related to Human Behavior

Health Belief Model
• Individual perceptions
  – Perceived barriers play important role

• Modifying factors
  – Demographics
  – Psychosocial characteristics

• Cues to action
  – Media campaign
  – Advice from others

Health Promotion Model
• Individual characteristics, expectations, and experiences

• Behavior specific thoughts and feelings
  – Perceived benefits of an action
  – Perceived barriers

Focus is more on health seeking rather than disease prevention behaviors.
Summary of Transtheoretical Model

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precontemplation (Not Ready)</td>
<td>No commitment to make a change within the next six months.</td>
</tr>
<tr>
<td>Contemplation (Getting Ready)</td>
<td>Desire and willingness to make a healthy change in the next six months.</td>
</tr>
<tr>
<td>Preparation (Ready)</td>
<td>Plan to make a change in the next 30 days.</td>
</tr>
<tr>
<td>Action</td>
<td>Behavior change has been recently made (within last six months).</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Behavior change was made greater than six months ago.</td>
</tr>
</tbody>
</table>

Theory Related to Community Change

- Social Ecology Theory
  - Responsibility for health is shared between individual and the community
  - Health promotion goes beyond individual to include community action and public policy.
Theories Related to Organizational Change

• **Lewin’s Planned Change**
  - Unfreezing existing structures
  - Introducing change
  - Moving to a new level
  - Refreezing structures
  - Strengthen driving forces
  - Reduce restraining forces

• **Roger’s Theory of Adoption of Innovation**
  - Process of diffusion
  - Innovators
  - Early adopters
  - Early majority
  - Late majority
  - Laggards

• **Strategies**
  - Empirical rationale
    • Theory of reasoned action
    • People are rationale
    • Show the benefit and people will change
  - Normative re-educative (Social Cognitive Theory)
    • Replication of actions of others
  - Power-coercive strategies
    • Motivational theory
    • Change to reduce pain

• **Barriers**

• **Drivers**

Theory Related to Family Dynamics

• **Family Systems Theory**
  - Functional whole
  - Contact with environment
  - Transmission of culture
  - Roles and functions
  - Social support
  - Problems reflect adaptation
  - On time events create less strain than off time events

• **Family Life Cycle**
  - Unattached young adult
  - Newly married
  - Family with young children
  - Family with adolescent children
  - Family launching
  - Later life family
Crisis Theory

• Loss and threat can precipitate situational crisis
• Developmental crisis can occur at predictable points
• Usual coping is insufficient
• All energy and resources are directed at crisis
• Crisis is self limited (4 to 10 weeks)
• Those in crisis more open to help
  – Minimal help may yield meaningful results

Crisis Intervention

• Goals:
  – Safety
  – Restore to previous level of function or higher
  – Enhance coping / self esteem

• Strategies
  – Reassurance
  – Suggestion
  – Support
  – Environmental manipulation
  – Pharmacotherapy
LEADERSHIP

Leadership Styles

• Autocratic
• Participative
• Laissez-faire
• Situational
• Transactional
  – Focus on daily activities
• **Transformational**
  – Articulates vision
  – Empowers
Team Building Models

Traditional Model of Team Effectiveness
- Examines the symptoms of team effectiveness rather than causes
- Assumes team is passive and stable
- Team processes include communication, social integration, role clarification, and goal setting
- Team effectiveness is measured by process and perception indicators

Cognitive Motivational Model of Team Effectiveness
- Assumes team is active, dynamic, and cognitively motivated
- Team purpose includes self evaluation and ability to redesign interventions
- Team effectiveness is measured by results
- Team building: Redesigning cognitive functioning by analyzing team effectiveness

Case Management

- Case Management Society of America: Process
- ANCC: Defines nursing case management
- Nursing case management models
  - Coordination of care
  - Transitions of care
  - Interdisciplinary
- Community based case management
- Long term healthcare models
- Rehabilitation models
- Insurance based models
- Managed care and HMO models
- Private models
Quality

Total Quality Management
• Emphasizes empowerment of employees
  – Person at point of service as most information
• Customers are internal and external
• Quality problems more related to systems problems rather than people problems
• Quality is cost effective

Continuous Quality Improvement
• Focus is more on processes than people
• Complex processes require an interdisciplinary team
• Also empowers workers to reduce cost and improve quality
• Data driven
• Synonymous with Performance Improvement

Shewhart Cycle
• Also known as Deming Cycle
• Used in Continuous Quality Improvement
• 4 Steps in the Cycle (PDCA)
  – Plan (based on assessment and measurements)
  – Do (trial)
  – Check (assesses results)
  – Act (full implementation)
  – Back to Plan
Outcomes Evaluation

• Process Indicators versus Outcome Indicators
  – Compliance with VAP protocol (versus)
  – Infection rates

• Patient Outcomes
• Provider Outcomes
• System Outcomes
  – Often includes financial outcomes

Benchmark Data and Recognition

• Magnet Designation
  – NDNQI (nurse sensitive indicators)

• Joint Commission

• Specialty Organizations
  – ACC
  – AHA

• ProgramCertifications
  – JC Disease Specific
    • Heart Failure

  – Chest Pain Center Accreditation

  – Cardiopulmonary Rehab
    • AACVPR
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PATIENT EDUCATION AND COUNSELING

Therapeutic Communication

- Empathy
- Unconditional acceptance
- Acknowledging patient worth
- Listen thoroughly before concluding

- Non verbal skills
  - Mindful approach
  - Same level
  - No interruptions / distractions
Therapeutic Communication: Techniques

- Offering leads
- Restating
- Reflecting
- Focusing
- Clarifying
- Sequencing

- Encourage participation
- Encourage evaluation
- Make observations
- Summarize

Communication No Nos!

- Use Clichés
- False Reassurance
- Why Questions
- Use Leading Questions
- Use Jargon
- Defensive Response
- Give Advice
Barriers

• Language
• Vision
• Hearing
• Culture

Healthcare Literacy

Learning

<table>
<thead>
<tr>
<th>Adult Learners</th>
<th>Domains of Learning</th>
<th>Conditions for Learning</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Self directed</td>
<td>• Cognitive</td>
<td>• Motivation to learn</td>
</tr>
<tr>
<td>• Need to know</td>
<td>• Affective</td>
<td>• Ability to learn</td>
</tr>
<tr>
<td>• Life Experiences</td>
<td>• Psychomotor</td>
<td>• Learning environment</td>
</tr>
</tbody>
</table>

More on Healthcare Literacy

- REALM tool (11 items, 3 not scored)
- National Institute for Literacy
  - Be informed
  - Be caring
  - Be realistic
  - Be there
- Signs of low literacy???
- Interventions
  - Simple language
  - Teach back
  - Open ended questions
  - Repeat information

Patient Education Process

- Assessment
- Diagnostic Statement and Objectives
- Teaching / Learning Interventions
- Education and Reteaching
- Documentation
Strategies for Patient Education

- Include expected effects of interventions
- Small changes rather than large changes
- Be specific!
- Focus on addition of positive behaviors
- Link new behavior to existing behavior
- Power of the profession
- Interdisciplinary / multifaceted
- Ask patient for a commitment

Teach Back
Health and Self Management

Health Maintenance/Improvement
- Perception of health, Motivation to Change, Adherence to Prescribed Interventions
- Maintenance or improvement

Population Based Initiatives
- Disease Prevention: Primary, Secondary, Tertiary
- Health Promotion Macro Level Initiatives

Self Care
- Maintenance
- Management

Discharge Planning

Levels
- Basic
  - Patient Education
- Simple
  - Referral to community resources
- Complex
  - Interdisciplinary
  - Sub-acute
  - Long term

Transitions of Care
- Hand offs
- Medication reconciliation
- Coordination / facilitation of care
- Negotiation
- High risk populations
  - Elderly
  - Chronic disease states
- Models for transitions of Care
  - Dr. Eric Coleman
Problem Identification

Clinical Inquiry
- All research starts here!
- Questions stem from observation

Review the Evidence
- Has the question been answered?
- To what degree?

Does the question warrant a research initiative?
- Frequency and magnitude of problem?
- Would answers change practice?
- Can interest sustain the effort?

What research method will answer the question?
- Qualitative
- Quantitative
Qualitative

- Inductive
- Broad research question
- Used when little is known about subject
- To generate hypothesis for further testing
- Can be used with quantitative research – Triangulation

- Discover meaning
- Explore complexities
- Data collection and analysis occur concurrently
- Purposeful sampling is used
- Trustworthiness is key issue with qualitative studies

Qualitative Research Methods

Phenomenology
Grounded theory
Ethnography
Historiography
Content Analysis

Theory is the outcome for Phenomenology and Grounded Theory.

Social processes
Uses numbers to describe frequency of words.
Quantitative Research

- **Variables**
  - Independent
    - Manipulated
  - Dependent
    - Response
  - Demographic

- **Causality versus correlation**

- **Validity**
  - Internal
    - Study actual measures what it intends to
  - External
    - Generalizable
  - Construct
  - Type 1 Error
    - State difference when no difference
    - Multiple analyses
  - Type 2 Error
    - State no difference when there is a difference

Quantitative Design

- **Descriptive**

- **Correlational**
  - Cross sectional
  - Longitudinal

- **Experimental**
  - Control
  - Randomization

- **Quasi-experimental**
  - Control
Concepts in Quantitative Research

**Sampling**
- Population / accessible population
- Sampling criteria
  - Inclusion
  - Exclusion
- Representativeness
- Sampling error
  - Systematic variation
- Adequacy of size
  - Effect size (strength of relationship between variables)
  - Power (minimum is .80)
  - Statistical significance

**Measurement**
- Process of assigning numbers according to a rule
  - Interval scale
  - Ratio scale
- Error
  - Random error
  - Systematic error
- Reliability
  - Reproducible
- Validity
  - Measures what is intended
- Sensitivity

Concepts in Quantitative Research

**Data Collection**
- Observation
- Self Report
- Existing Data
- Physiological Measures

**Data Analysis**
- Descriptive statistics
  - Measures of central tendency
  - Shape of distribution
  - Measures of dispersion
  - Measures of association
- Inferential statistics (non parametric when sample is small)
  - Tests of difference
    - t-test, ANOVA (parametric)
    - Mann-Whitney U test, sign test (non parametric)
  - Tests of association
    - Pearson correlation coefficients (parametric)
    - Spearman and Kendall correlation coefficients (nonparametric )
- Meta-analysis
  - Pooled statistics from multiple studies
  - Helpful when study outcomes varied
Evaluation of Research

<table>
<thead>
<tr>
<th>Qualitative</th>
<th>Quantitative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Credibility (truth value)</td>
<td>Internal validity</td>
</tr>
<tr>
<td>Transferability</td>
<td>External validity</td>
</tr>
<tr>
<td>Dependability</td>
<td>Reliability</td>
</tr>
<tr>
<td>Confirmability</td>
<td>Objectivity</td>
</tr>
</tbody>
</table>

Additional Research Concepts

**Epidemiology**
- Population based research
- **Prevalence**: total number of cases in given period
- **Incidence**: number of new cases in a given period
- Relative risk
- Framingham Study

**Protection of Human Rights**
- **Historical abuses**
- **Role of IRB / HRRB**
- **Informed consent**
- **Vulnerable populations**
Application to Practice

**Evidence Based Practice**

- Sources
  - Agency for Healthcare Research and Quality
  - ACC
  - AHA

- Grading of Evidence
  - Class
  - Level

**Outcome Evaluation**

- Scientific and statistical
- Differs from research

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**RISK FACTORS**
Disease Paradigm

Atherosclerosis is a diffuse inflammatory process. We need to treat the systemic disease and not just the symptomatic stenosis.

Class Summary: Hyperlipidemia, hypertension, and diabetes impair endothelial function.

Risk Factor

Characteristic found in a healthy person that independently increases the risk of CAD.

Can be lifestyle habit, environmental factor, or inherited characteristic.
Non Modifiable Risk Factors

- Age
  - Increases risk, hospitalization and death
- Gender
- Family History
- Previous CHD event

- Socioeconomic Status
- Ethnicity

Family History

- Presence of CAD in a first-degree relative.
  - Mother, father, brother, or sister.

- Premature is considered the development of CAD in men < age 55 and in women < age 65.

- Family history of a premature coronary event in a parent has double the risk for CAD (Roger et al., 2012; Lloyd-Jones et al., 2004).
Gender

- Women: Incidence for CAD lags behind men by approximately 10 years and the incidence for myocardial infarction and sudden death lags behind by approximately 20 years.

- Before the age of 75 years more CAD events are attributed to men than to women

- (Roger et al., 2012).

Women

- Effectiveness based guidelines for cardiovascular disease prevention in women state:
  
  – Hormone therapy and selective estrogen-receptor modulators should not be used for the primary or secondary prevention of cardiovascular disease in women.

  – Aspirin is not indicated for primary prevention in healthy women age < 65 years.

  (Mosca et al., 2011).
Socioeconomic Status

• Most specifically associated with the risk factors of tobacco use and diabetes mellitus type 2 (Kanjilal, 2006).

• Men age 30 to 59 years with a low socioeconomic status have a 55% increased risk of death from CAD compared to those with a higher socioeconomic status (Fihn et al., 2012).

Ethnicity

• Prevalence of hypertension in non-Hispanic blacks in the United States is among the highest prevalence rate for hypertension in the world.

• Compared to non-Hispanic whites, the risk for diagnosis of diabetes mellitus type 2 is 66% higher for Hispanics and Latinos, and 77% higher for non-Hispanic blacks. (Roger et al., 2012).

Risk Equivalents

• **There are 4 CHD Risk Equivalent Groups:**
  - Patients with other forms of atherosclerotic vascular disease (peripheral vascular disease, abdominal aortic aneurysm, or symptomatic carotid disease)
  - Patients with type II diabetes mellitus
  - Patients with chronic kidney disease
  - Patients with two or more CAD risk factors who score at the equivalent risk on the Framingham risk tool.
Modifiable Risk Factors

- Optimization of nine potentially modifiable risk factors could result in a 90% reduction in the risk of first acute myocardial infarction. These nine risk factors are: cigarette smoking, dyslipidemia, hypertension, diabetes mellitus, abdominal obesity, lack of adequate physical activity, low consumption of fruits and vegetables, overconsumption of alcohol, and psychosocial stressors (Roger et al., 2012).
### Diagnostic Criteria for Diabetes Mellitus

<table>
<thead>
<tr>
<th>Test</th>
<th>Criteria for Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>&gt; 6.5%</td>
</tr>
<tr>
<td>Fasting glucose (no caloric intake for 8 hours or more).</td>
<td>&gt; 126 mg/dL</td>
</tr>
<tr>
<td>2 hour plasma glucose with glucose tolerance test</td>
<td>&gt; 200 mg/dL</td>
</tr>
<tr>
<td>Classic symptoms and random glucose</td>
<td>&gt; 200 mg/dL</td>
</tr>
</tbody>
</table>

Source:  ADA, 2013

### Pre-Diabetes

- A1C 5.7 to 6.4%
- Fasting glucose of 100 to 125 mg/dL
- 2 hour plasma glucose with glucose tolerance test of 140 to 199 mg/dL

(ADA, 2013)
Complications / Treatment Goals

- Macrovascular complications include CAD and stroke.

- Microvascular complications include retinopathy, nephropathy, and peripheral neuropathy.

- Lowering of the A1C to < 7% is associated with a reduction in microvascular complications and also in macrovascular complications when the target is implemented soon after the diagnosis of diabetes.
  - This is the A1C goal for most patients.

  - A stricter target of < 6.5% may be a treatment goal in patients recently diagnosed and who have no existing cardiovascular disease and a long life expectancy.
  - Tighter glycemic control should only be an option if the goal is able to be achieved without inducing hypoglycemia.

Diabetes Mellitus

- Diabetes is a major cause of heart disease and stroke.

- Approximately 70% of persons over the age of 65 years with diabetes die from some form of heart disease and another 16% die of stroke.

- The death rate from heart disease among persons with diabetes mellitus is two to four times higher than in those without diabetes mellitus. Longer durations of diabetes mellitus are associated with greater cardiovascular risk (Go et al., 2013).
Diabetes Mellitus Type II

- 75 to 85% have co-existing hypertension.
- 70 to 80% have an elevated LDL-C.
- 60 to 70% have obesity.

(Go et al., 2013)

Blood Pressure Control more important than glycemic control in reducing risk of death / macrovascular risk.

Metabolic Syndrome: 3 or More

- Waist circumference > 40 inches for men and > 35 inches for women in the European and American population
  - The criterion for waist circumference depends on the specific population and country specific definitions.
- Triglyceride level > 150 mg/dL or drug treatment for high triglycerides
- HDL-C level < 40 mg/dL for men and < 50 mg/dL for women, or drug treatment for low HDL-C levels
- Blood pressure > 130 mm Hg systolic or > 85 mm Hg diastolic or drug treatment for hypertension
- Elevated fasting glucose level > 100mg/dL or drug treatment for elevated glucose levels.

(Miller et al., 2011; Alberti et al., 2009)
Metabolic Syndrome

- Metabolic syndrome abnormalities
  - Defective glucose uptake by skeletal muscle
  - Increased release of free fatty acids by adipose tissue
  - Over production of glucose by the liver
  - Hyper-secretion of insulin by beta cells in pancreas

- Implications:
  - Dyslipidemia
  - Elevated triglycerides
  - Elevated apoprotein B
  - Small LDL particles
  - Low HDL-C
  - Elevated blood pressure
  - Elevated glucose
  - Proinflammatory state
  - Prothrombotic state

Obesity

- Obesity adversely affects most other risk factors
- Obesity and LVH
- Abdominal obesity (determined by waist / hip ratio) is an independent risk factor for vascular disease in women and older men.
- BMI independently predicts coronary atherosclerosis in whites
Body Mass Index Formula

\[
\frac{\text{Weight (in pounds)}}{\text{Height (in inches)}^2} \times 704.5
\]

Body Mass Index Values

- **Underweight**: < 18.5 kg/m²
- **Healthy**: 18.5 to 24.9 kg/m²
- **Overweight**: 25.0 to 29.99 kg/m²
- **Obesity**: > 30 kg/m²
- **Morbid Obesity**: > 40 kg/m²

Waist to Hip Ratio

- Waist circumference < 35 inches for women and < 40 inches for men
- Waist to hip ratio < 0.8 for women and ≤ 1.0 for men
Obesity and CABG

• Independent risk factor for:
  – Perioperative respiratory failure
  – Sternal and leg wound complications
  – Perioperative MI
  – Arrhythmias

Obesity and Prevention

• Weight loss:
  – Improves lipid levels
  – Improves insulin resistance
  – Lowers blood pressure
  – Weight loss is especially important for those with high lipids, HTN and elevated blood glucose levels

• Prevention of obesity is high priority to reduce CVD risk

• Heredity and environmental factors play a role in obesity

• Obesity is associated with many co-morbidities

Caution with weight loss in heart failure.
ACC / AHA Secondary Prevention Guidelines

• BMI 18.5 to 24.9 kg/m²

• Waist circumference
  – Men < 40 inches
  – Women < 35 inches

Initial goal: Decrease 10% from baseline

Barriers to Effectiveness of Dietary Counseling

• Lack of assessment of the patient’s interest in making dietary change,
• Primary care providers have low estimate of self efficacy with regard to nutrition counseling,
• Providers are unwilling to confront patients on weight issues, and
• Time restrictions on reimbursement impose limitations on traditional medical office visits.
Validated Tools

- Eating Pattern Questionnaire
- Starting the Conversation tool
- WAVE (Weight, Activity, Variety, Excess) tool
- REAP (Rapid Eating and Activity Assessment for Patients) tool

Nutrition Guidelines

- Providers should deliver simple positive messages
  - Eat breakfast
  - Eat fruits, vegetables, and whole grains
  - Limit snacks to once a day
  - Eat smaller portions
  - Limit intake of sugar containing beverages to less than 12 oz./day
  - Weigh yourself regularly and adjust dietary intake based on your weight.
Tobacco Use

– Tobacco use should be approached as a chronic disease itself as opposed to a mere risk factor

– Approximately 21% of adult Americans smoke resulting in approximately 45 million adult American smokers (Fiore, et al., 2008).
Tobacco Use

• Most important modifiable risk factor
  – > 20 cigarettes per day results in a 2 to 3 fold increase in CHD risk
  – Increased cardiovascular risk exists even in persons who smoke less than five cigarettes per day (U.S. Department of Health and Human Services, 2010).

Effects of Tobacco

• The components of cigarette smoke with the greatest cardiovascular effects are nicotine, carbon monoxide, and oxidant gases.
  – Nicotine is a sympathomimetic drug that releases catecholamines.
  – Carbon monoxide increases the percent of carboxyhemoglobin.
  – Exposure to oxidative chemicals in smoke results in a depletion of endogenous antioxidants.
### Cardiovascular Effects of Cigarette Smoking

<table>
<thead>
<tr>
<th>Effects of tobacco smoking:</th>
<th>Downstream physiological consequences:</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Stimulation of sympathetic nervous system and release of epinephrine and norepinephrine</td>
<td>♦ Increased heart rate and blood pressure</td>
</tr>
<tr>
<td>♦ Increased carboxyhemoglobin</td>
<td>♦ Endothelial and vasomotor dysfunction</td>
</tr>
<tr>
<td>♦ Release of free radicals directly from components of cigarette smoke and activation of</td>
<td>♦ Functional anemia</td>
</tr>
<tr>
<td>endogenous free radicals</td>
<td>♦ Increased blood viscosity</td>
</tr>
<tr>
<td>♦ Activation of neutrophils, monocytes, and T cells</td>
<td>♦ Increased prothrombotic and decreased fibrinolytic factors</td>
</tr>
<tr>
<td>♦ Activation of platelets</td>
<td>♦ Increased oxidative stress and lipid peroxidation</td>
</tr>
<tr>
<td>Source: US Department of Health and Human Services, 2010.</td>
<td>♦ Increased cytokines, inflammatory molecules, and adhesion</td>
</tr>
<tr>
<td></td>
<td>♦ Smooth muscle proliferation</td>
</tr>
</tbody>
</table>

### Cessation Benefits

- No evidence that simply decreasing the number of cigarettes smoked will decrease the risk of a future cardiovascular event (Roger et al., 2012).
- 10-15 years after quitting: Risk of CAD is that of a non-smoker.
- Cessation after a MI reduces the risk of mortality and morbidity by 36% to 50%.
- The cardiovascular benefit of cessation does not decrease with advancing age. (American Cancer Society, 2012; U.S. Department of Health and Human Services, 2010.).
Cessation Pitfalls

• Only 5% will achieve long term abstinence (US Department of Health and Human Services, 2010).
  – Filtered, low tar, and light cigarettes do not reduce the risk of disease related to smoking.
  – Electronic cigarettes are not recommended for cessation efforts.

Nicotine Addiction

• Nicotine is most important chemical in cigarette smoke in terms of addiction.
• Smoking creates physiological and psychological addiction.
• Withdrawal
  – Several effects including physical, emotional, behavioral, and cognitive.
  – Withdrawal syndrome lasts for one to four weeks -can persist for months.
  – Symptoms are the most intense during the first week (U.S. Department of Health and Human Services, 2010).
Understanding Addiction

**Physical**
- Withdrawal cravings lessen over time and are less severe than situational cravings

**Behavioral**
- Situational cravings – levels remain high but become more sporadic

Evidence Based Recommendations

- Smoking cessation counseling, including minimal interventions of less than 3 minutes has been proven effective in reducing tobacco use.
- Physician advice to stop smoking adds to the success of cessation efforts.
- Intensive interventions are more effective than minimal interventions.
  - Interventions including 4 or more sessions are especially effective
- Therapies with the highest success include those that offer both practical and supportive strategies.
- Both counseling strategies and pharmacotherapy are effective when used alone. However, the two strategies are more effective when combined. (Fiore et al., 2008).
Cessation Counseling

• Cessation techniques
  – Pharmacologic agents
  – Behavior modification

  – Important point: ASK PERMISSION !!

Cessation Counseling

• Ask the patient if he or she uses tobacco.
• Assess the patient’s interest in quitting.
• Advise (Inform) the patient about the importance of quitting.
• Assist the patient by helping him or her pick to resources that can provide counseling and pharmacotherapy.
• Arrange a follow-up phone call with the patient and referral to a smoking cessation resources
Pharmacological Agents: Nicotine Replacement

• Patch (OTC), gum (OTC), inhaler, and nasal spray

• Caution with very recent MI, worsening angina, and serious arrhythmias – not contraindicated in CAD

• Cardiovascular effects no worse than smoking

• The use of nicotine-replacement therapy can substantially improve smoking cessation success rates (Fiore et al., 2008).

Pharmacological Agents: Nicotine Replacement

Benefits of maintenance and bolus dosing
  – Two combinations very effective
    • Patch with the use of either gum or nasal spray
    • Patch with the inhaler (Fiore et al., 2008).
    • Patch and lozenges

• NRT is not recommended
  – People who smoke less than 10 cigarettes per day
  – Those who use smokeless tobacco
  – Pregnant women, and adolescents.
Pharmacological Agents: Bupropion (Zyban and Wellbutrin)

• Can double rate of cessation compared to placebo
  – Started while smoking; quit date set for during 2nd week of therapy (1 week till therapeutic level).
  – Therapy continued for 7 to 12 weeks
    • May be continued for up to six months
  – Bupropion may also be used in conjunction with a nicotine patch (Fiore et al., 2008).

Pharmacological Agents: Bupropion (Zyban and Wellbutrin)

• Neuronal blockade of the re-uptake of norepinephrine and dopamine
• Blockade of the nicotinic acetylcholinergic receptors.
Pharmacological Agents: Varenicline (Chantix)

• Selectively binds to nicotine acetylcholine receptors in the brain
  – Binds to and partially stimulates the receptors without full nicotine effect on release of dopamine
  – Blocks ability of nicotine to stimulate the central nervous mesolimbic dopamine system (system that reinforces smoking)
• Superior to Bupropion and placebo in achieving smoking cessation
  – FDA recommends that patients disclose any psychiatric history to their provider before the starting the medication, and that providers monitor for any behavior or mood changes after starting a patient on the medication (Fiore, et al., 2008).

Pharmacological Therapy: Varenicline (Chantix)

• 5 days to achieve steady state; set quit date 1 week from starting
• Started with low dose to prevent nausea
• 12 weeks of initial therapy (starting month pack x 1 and continuing month pack x 2)
• Additional benefit with an additional 12 weeks of therapy
• Not used with nicotine replacement therapy
Tips for Effectiveness

• Ask Permission – worth saying twice

• Congratulations on committing to QUIT

• A failed attempt at cessation should be viewed as practice for future successful cessation

Tips for Effectiveness

• Preparing patients for post discharge triggers

• Develop strategies for cravings

• Action plan for any slips or relapses

• Involving significant others

• Address depression and weight gain

• Quit dates for women
Referrals and Resources

• Inform patient of available quit line support 1-800-QUITNOW for access to all state quit lines. (Fiore et al., 2008).
• Additional on-line resources available for patients can be found at http://smokefree.gov/

Motivational Interviewing

• Accept ambivalence
  — The Importance Ruler
  — The Confidence Ruler
• Ask patient to elaborate
• Use open ended questions
  — Ask – don’t tell
  — The patient must own the idea to change
Motivational Interviewing

- Focus on priorities
- Listen reflectively
- Support and encourage
- Be a barrier remover
- If committed – guide the patient in formulating a plan
## Lipid Levels

<table>
<thead>
<tr>
<th>Total</th>
<th>LDL</th>
<th>HDL</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 200 desirable</td>
<td>&lt; 100 (≤70) optimal</td>
<td>&lt; 40 low</td>
<td>&lt; 150 Normal</td>
</tr>
<tr>
<td>200-239 borderline</td>
<td>100-129 above optimal</td>
<td>≥ 60 desirable</td>
<td></td>
</tr>
<tr>
<td>≥ 240 High</td>
<td>130-159 borderline high</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>160-189 high</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 190 very high</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### More on Lipids

- The size of LDL-C particles is also important (small dense particles)
  - VLDL: Very low density lipoprotein
  - Combination of low LDL-C and normal systolic BP very important to optimal outcomes!
Cholesterol

• The cholesterol content of the liver is derived predominantly from three sources.
  – Synthesis of cholesterol by the liver
  – Uptake of cholesterol from the blood from circulating lipoproteins
  – Uptake of cholesterol absorbed by the small intestine.

Effect of Drugs on LDL-C Levels

<table>
<thead>
<tr>
<th>Drug</th>
<th>% Reduction</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG CoA RI (statins)</td>
<td>20-50%</td>
<td></td>
</tr>
<tr>
<td>Bile acid resins</td>
<td>15-25%</td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid</td>
<td>15-30%</td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>10-15%</td>
<td></td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>10-25%</td>
<td></td>
</tr>
<tr>
<td>Intestinal Absorption Inhibitors</td>
<td>18%</td>
<td></td>
</tr>
</tbody>
</table>
## Effect of Drugs on Triglyceride and HDL-C Levels

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>HDL-C Change</th>
<th>Triglyceride Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotinic acid</td>
<td>↑ 10-25%</td>
<td>↓ 20-50%</td>
</tr>
<tr>
<td>Fibrates</td>
<td>↑ 10-25%</td>
<td>↓ 20-50%</td>
</tr>
<tr>
<td>HMG CoA RI</td>
<td>↑ 5-10%</td>
<td>↓ 10-25%</td>
</tr>
<tr>
<td>Bile acid resins</td>
<td>↑ 3-5%</td>
<td>↑ 0-20%</td>
</tr>
<tr>
<td>Intestinal Absorption Inhibitors</td>
<td>↑ 1%</td>
<td>↓ 8%</td>
</tr>
</tbody>
</table>
Relationship to ATP III-IV

• The 2013 ACC/AHA Expert Panel included all 16 members of the National Heart, Lung, and Blood Institute Adult Treatment Panel (ATP) IV.

• Commissioned by NHLBI in June 2013

• Guidelines replace ATP III

Transition from Treating Numbers to Treating Patients and Their Risk

• Focus is no longer on targeting the LDL-C
  – Treat to level of risk not to target LDL-C

• New guidelines focus on 4 groups of patients who can benefit from statin therapy with a good safety margin

• Benefit includes reduction in atherosclerotic cardiovascular disease events (ASCVD)
Patient Group 1

• Individuals with clinical ASCVD (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.

Patient Group 2

• Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dl.
Patient Group 3

- Individuals 40-75 years of age with diabetes, and LDL-C 70-189 mg/dl without clinical ASCVD.

Patient Group 4

- Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dl, and have an estimated 10-year ASCVD risk of 7.5% or higher.

- **Pooled Cohort Equations for ASCVD risk prediction.**
  
  - Men and women; black and non-Hispanic white
    - May use non Hispanic White calculator for other populations (may under estimate risk in certain populations)
  
  - Ages 40 to 79
  
  - Identifies cohorts most likely to benefit from statin therapy
Pooled Cohort Equations for ASCVD Risk Prediction.

• Required information to estimate ASCVD risk includes age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure lowering medication use, diabetes status, and smoking status.

• Source: Based on the Pooled Cohort Equations\(^2\) and the work of Lloyd-Jones, et al., *Circulation*, 2006.

Non Recommendations

• No recommendations for treatment outside the 4 groups.

• No recommendation to start or stop statins in NYHA Class II-IV systolic HF that is ischemic in etiology

• In patients with a 10-year risk < 7.5%, other factors can be considered:
  – Family history
  – LDL-C > 160mg/dL
  – HS C-reactive protein > 2mg/dL
  – Coronary calcium score ≥ 300
  – ABI < 0.9
  – Etc.
HMG CoA Reductase Inhibitors (Statins)

**Agents**
- Atorvastatin (Lipitor)
- Provastatin (Pravachol)
- Fluvostatin (Lescol)
- Simvastatin (Zocor)
- Lovastatin (Mevacor)
- Rosuvastatin (Crestor)

**Mechanism of Action**
- Inhibition of HMG-CoA reductase
- HMG-CoA reductase catalyzes an early step in cholesterol biosynthesis

✓ Decrease mortality
✓ Reduce risk of major coronary events by 30%
✓ Stimulate plaque regression

Statin Therapy: Greatest LDL-C Lowering Effect:

**atorvastatin**
- 80 mg: 55-60% reduction
- 40 mg: 50% reduction
- 20 mg: 43% reduction
- 10 mg: 35-39% reduction

**rosuvastatin**
- 40 mg: 55-63% reduction
- 20 mg: 47-55% reduction
- 10 mg: 46-52% reduction
- 5 mg: 45% reduction
Statin Dosing

<table>
<thead>
<tr>
<th>High Intensity</th>
<th>Moderate Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients &lt;75 years with ASCVD</td>
<td>Patients with diabetes with a 10 year ASCVD &lt;7.5%</td>
</tr>
<tr>
<td>All patients &gt; 75 years?</td>
<td>Patients with indication for high intensity but who are not able to take high intensity</td>
</tr>
<tr>
<td>Patients with LDL-C ≥ 190 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Patients with diabetes with a 10 year ASCVD ≥7.5%</td>
<td></td>
</tr>
<tr>
<td>Persons 40-75 years with a ≥7.5% 10-year ASCVD risk</td>
<td>should receive moderate- to high-intensity statin therapy.</td>
</tr>
</tbody>
</table>

Statin Dosing

- High intensity: daily dose that lowers LDL-C by > 50%

- Moderate intensity: daily dose that lowers LDL-C by 30% to 50%
Statin Therapy

• Short or unknown half life: administration in evening for maximum efficacy
  – Simvastatin, lovastatin, and immediate release fluvastatin

• Hydrophilic (fluvastatin, pravastatin, and rosuvastatin)
  – Minimally metabolized by the cytochrome P450 (CYP450) enzyme system
  – Lowest rates of myopathy *

• The lipid soluble statins are associated with insulin resistance and an increased Hemoglobin A1C.
  – Use cautiously with medications with strong CYP3A4 inhibition
  – Benefit of cardiovascular risk reduction is felt to outweigh the downside of elevated glucose levels.

Statin Therapy: Myopathy

CPK Levels

• Total CPK levels prior to initiation and repeated for suspected myopathy.
• Asymptomatic CPK elevations are common.
• Discontinue if CPK levels are > 10x the upper limit of normal.

Risk Factors

• Advanced age (> 80 years)
• Frailty
• Small body size
• Renal insufficiency
• Under treated hypothyroidism
• Co-administration of other drugs such as colchicine

Interactions

• No > 1 quart per day of grapefruit juice – particularly with simvastatin and atorvastatin.
• Combined with gemfibrozil (a fibrate), increase the risk of rhabdomyolysis.
Statin Therapy and Liver Enzymes

• Liver enzymes should be assessed at baseline and as clinically indicated.

• **Routine monitoring of liver enzymes is not necessary.**

• Statin therapy can result in an elevation of liver enzymes not associated with liver toxicity.
  – Association with higher dose statins.

• Contraindicated in active liver disease or in persistently and unexplained elevated liver enzymes.
  – AST and ALT > 3x the upper limit of normal.

• **Considered safe in patients with mild to moderately elevated liver enzymes attributable to chronic conditions such as nonalcoholic fatty liver and hepatitis C.**

Lifestyle and Other Lipid Lowering Agents

• Lifestyle: Important prior to and during statin therapy

• Non-statin therapies, whether alone or in addition to statins, do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.
  – Addition of these other agents can be considered in patients with LDL-C > 190 mg/dL.
  – **Information included on negative trials for niacin and fenofibrates.**
Niacin and AIM High Study

• The purpose of the AIM-HIGH trial was to test whether adding Niaspan to patients at LDL-C goal but with continued low HDL-C levels, would improve cardiovascular outcomes.
• Despite an improvement in lipid levels the study was stopped early due to lack of effectiveness in achieving the primary endpoint which was a composite of cardiovascular death, non-fatal myocardial infarction, acute coronary syndrome, ischemic stroke, or symptom driven cardiac or cerebral revascularization (Boden et al., 2011).

Niacin ER and THRIVE STUDY

• TREDAPTIVE: Niacin ER plus laropiprant
  – No US approval
  – No longer marketed outside US
• Failure to improve cardiovascular outcomes

• Increased adverse events
  – Diabetic complications
  – New onset diabetes
  – GI problems
  – Musculoskeletal complaints
  – Heart failure
  – Bleeding
  – Skin complaints
Fibric Acids

- Indicated for hyperlipidemia with **Hypertriglyceridemia**.

- Agents
  - Clofibrate (Atromid-S)
  - Fenofibrate (Tricor)
  - Gemfibrozil (Lopid)

- Mechanism of Action
  - Unclear
  - Decreases VLDL-C synthesis
  - Reduces triglycerides by stimulating lipoprotein lipase activity
  - Decreases hepatic TG production

Fibric Acids

- SE: dyspepsia, rash, alopecia, fatigue, HA, impotence, anemia; myositis flu like syndrome, cholelithiasis, abnormal liver function studies

- Contraindicated in severe renal (renally excreted) and hepatic disease, pre-existing gall bladder disease

- ACCORD Study
  - No reduction in cardiovascular mortality or non-fatal myocardial infarction or stroke when a fenofibrate was added to simvastatin in patients with type 2 diabetes mellitus (Ginsberg et al., 2010).

- The FIELD study
  - Effects of long-term fenofibrate therapy on cardiovascular events in people with type 2 diabetes did not show a statistically significant reduction in major coronary events in persons treated with fenofibrate therapy compared to placebo (Keech et al., 2005).
Statin plus Fibrate Combination Therapy

- May be associated with a greater risk of myopathy and rhabdomyolysis
- The myopathy risk is enhanced under these situations:
  - High doses of statins
  - Renal insufficiency (Cr > 2.0)
  - Concomitant medications: Itraconazole, Ketoconazole, Cyclosporin A, Erythromycin
  - Age > 70 years

Other Agents

- Bile Acid Sequestrants

- Agents
  - Cholestyramine (Questran)
  - Colestipol (Colestid)
  - Covesevelam (Welchol)

- Intestinal Absorption Inhibitors

- Ezetimibe (Zetia)
Joint National Committee

- Joint National committee on the prevention, detection, evaluation and treatment of high blood pressure

- JNC 8 Guidelines released December 2013

- Rigorous examination of evidence to make recommendations

- Three questions were asked in the review of evidence
  - Smaller scope than JNC 7 Guidelines
Questions Addressed

• In adults with hypertension – does initiating antihypertensive pharmacological therapy at specific BP thresholds improve health outcomes?
• In adults with hypertension, does treatment with antihypertensive pharmacology to a specified BP goal lead to improvements in health outcomes?
• In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes.

Key Features of JNC 8

• Age < 60 years general population (strongest recommendation ages 30 to 59 years)
  – Initiate at DBP > 90 mmHg and treat to < 90 mmHg
  – Initiate at SBP > 140 mmHg and treat to < 140 mmHg

• Age > 18 years, diabetes, chronic kidney disease (CKD)
  – BP goal < 140/90 mmHg

• Age > 60 years without diabetes or CKD
  – Treat > 150/90
  – BP goal < 150/90 mmHg
  – * if treatment achieves goal of < 140/90 with no adverse effects
  – this is acceptable
Key Features of JNC 8

• For CKD: ACE-I or ARB as first line agent

• Without CKD
  – Nonblack: Thiazide diuretic or ACE-I/ARB or calcium channel blocker
  – Black: Thiazide diuretic or calcium channel blocker

However!

• AHA / ACC November 2013 statement recommend < 140/90 mmHg as goal for all patients.

• AHA / ACC Guidelines for HTN to be published?
American Society of Hypertension: Position Papers

Evaluation and Treatment of Orthostatic Hypotension
Obesity-Related Hypertension: Pathogenesis, Cardiovascular Risk, and Treatment
Blood Pressure and Treatment of Persons with Hypertension as it Relates to Cognitive Outcomes Including Executive Function
ASH Compendium of Antihypertensive Pharmacology
Management of Hypertension in the Transplant Patient
Adherence and Persistence With Taking Medication to Control High Blood Pressure
Combination Therapy in Hypertension
Dietary Approaches to Lower Blood Pressure
Hypertension in Pregnancy
When and How to Use Self (Home) and Ambulatory Blood Pressure Monitoring
Treatment of Hypertension in Patients with Diabetes

JNC 7: CLASSIFICATION OF BLOOD PRESSURE

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mm Hg)</th>
<th>Diastolic (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>less than 120</td>
<td>and less than 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>or 80-90</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140-159</td>
<td>or 90-99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160 or higher</td>
<td>or 100 or higher</td>
</tr>
</tbody>
</table>

Unusually low readings should be evaluated for clinical significance.
*(From the Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure)
Hypertension

• Primary (essential) hypertension
  – Without known cause
  – 90 to 95% of hypertension in adults

• Secondary hypertension
  – Identifiable cause that can be corrected
  – More than 80% of hypertension in children

Pathophysiology Primary Hypertension

– Excessive salt and water retention
– *Increased SNS activity*
– Increased vasoconstrictive response to circulating catecholamines
– At any age HTN impairs endothelial function
  • Decreased production of nitric oxide
– Co-existing Risk Factors
  • Vascular dysfunction predicts diabetes in patients with HTN
  • HTN and diabetes incrementally worsen endothelial function
– Complications:
  • Structural and functional changes
    – Impaired coronary vasodilation
    – Impaired endothelial function
    – Inward remodeling and hypertrophy of vessels
    » Increased risk cerebral bleed
Systolic Hypertension

- Isolated systolic hypertension accounts for 70% in the elderly
- Systolic hypertension correlates with cardiovascular disorders more than diastolic hypertension
- Pulse pressure as predictor or coronary events
- Clinical Application: The coronary arteries are perfused during diastole so it is important to maintain an adequate diastolic blood pressure.

Hypertension Management

**Lifestyle Interventions**

- **Weight reduction**
  - 5 – 20 mmHg / 10 kg

- **Physical Activity**
  - 4-9 mmHg

- **Sodium restriction**
  - 2-8 mmHg

- **Alcohol intake reduction**
  - 2-4 mmHg

- **DASH Diet**
  - 8-14 mmHg
Pharmacological Management

• Diuretics (Thiazide)
  – Thiazide diuretics cost effective with relatively low risk of side effects
    • Concern: impact of thiazide induced hyperglycemia and diabetes mellitus on long term CHD risk (Rosendorff, et al., 2007).
• ACE Inhibitors
• Angiotensin II receptor blockers
• Calcium Channel Blockers
• Beta Blockers
• Alpha Blockers
• Centrally Acting Drugs
• Direct Vasodilators
• Many combination medications available for dual therapy

✓ Obtaining BP goal is most important objective.
✓ Use what works.
✓ Let co-morbid conditions (if present) impact choices.
Stage II Hypertension = 2 Drug Therapy

Thiazide diuretic plus another agent based on specific disease process or other risks.

Resistant Hypertension

• **Definition:** A patient is considered to have resistant hypertension if he or she is on 3 or more medications at full-dose therapy, including a diuretic and still unable to achieve target blood pressure.

• A patient is also considered to have resistant hypertension if it takes 4 medications to achieve goal (Calhoun et al., 2008).

Consultation with hypertension specialist
Resistant Hypertension

• Before the diagnosis of resistant hypertension is made, pseudo resistance must be ruled out.

• Common causes of pseudo resistance include:
  – White coat effect
  – Poor technique
  – Poor adherence

Blood Pressure Measurement

Proper technique for blood assessment includes using a proper sized cuff that encircles 80% of the patient’s arm. Use of a cuff that is too small is one of the most causes of inaccurate readings, resulting a recorded measurement that is falsely high.
Resistant Hypertension Causes

- **Lifestyle related**
  - High dietary sodium
  - Obesity
  - Heavy alcohol intake

- **Medication related**
  - Non narcotic analgesics especially NSAIDs
  - Sympathomimetics (decongestants / diet pills)
  - Stimulants
  - Oral contraceptives
  - Glucocorticoids and mineralcorticoids
  - Herbals (ephedra / ma huang)
  - Natural licorice (found in smokeless tobacco)

Resistant Hypertension Causes

**Secondary Diagnoses (Most Common)**

- Obstructive sleep apnea
- Chronic kidney disease
- Primary aldosteronism
- Renal artery stenosis

**Secondary Diagnoses (Less Common)**

- Pheochromocytoma
- Cushing’s disease
- Hyperparathyroidism
- Coarctation of the aorta
- Intracranial tumor
  (Calhoun et al., 2008)
Pharmacological Strategies for Resistant Hypertension

- Maximize diuretic therapy with long acting thiazide diuretic.
  - Chlorthalidone is preferred agent in resistance.
- Consider addition of mineral corticoid antagonist such as spironolactone or eplerenone.
- Use loop diuretic if chronic kidney disease is present.
- Combine medications that have different modes of actions.
  - Recent research has shown favorable results when an ACE inhibitor or angiotensin receptor blocker is combined with a calcium channel blocker.
- Consider giving at least one antihypertensive at bedtime to achieve better overall control.

Nursing Considerations for Hypertension

- Dose reduction should be attempted after one year of controlled therapy
- Adherence
  - Cost
  - Side Effects
- Self Monitoring of BP
- OTC Medications may increase BP
- Aggressive Risk Factor Modification / Lifestyle Interventions
CVN Review Course

SLEEP APNEA AND CARDIOVASCULAR DISEASE

Sleep Apnea

Obstructive
- Repetitive interruption of ventilation during sleep caused by collapse of pharyngeal airway.
- > 10 second pause in respiration associated with ongoing ventilatory effort

Central
- Repetitive cessation of ventilation during sleep resulting from loss of ventilatory drive
- > 10 second pause with no associated ventilatory effort
- > 5 events per hour considered abnormal

ACC / AHA 2008 Scientific Statement
Sleep Apnea Syndromes

**Obstructive**
- Apnea / hypoapnea index (Number per hour of sleep)
  - > 5 and
  - Symptoms of excessive daytime sleepiness

**Central**
- > 5 central apneas per hour of sleep and
  - Associated symptoms of disruption of sleep (frequent arousals) and / or
  - Hypersomnolence during the day

**Hypoapnea**
- Decrease in but not complete cessation
- Fall in oxygen saturation or arousal from sleep
  - Fall in ≥ 4% might be clinically significant
Obstructive Sleep Apnea

- Higher prevalence of following with OSA
  - HTN (resistant)
  - Type 2 diabetes
  - CV disease (nocturnal angina)
  - Atrial fib
  - Stroke

- Difficult to tease out causative effect of these overlapping disorders
  - Overlapping risk factors for CV disease and OSA

- Male gender and obesity are risk factors
  - Not uncommon in women and non obese
  - Age is more associated than obesity with women

Obstructive Sleep Apnea

- Approximately 1 in 5 adults: mild
- Approximately 1 in 15 adults: moderate / severe
- 15 million Americans
- > 85% have not been diagnosed
- Adverse consequences may be greater in those < 50 years.
- High prevalence of pathological daytime sleepiness in OSA
- Almost all with OSA snore but not all snorers have OSA
OSA

- Pharyngeal airway from posterior nasal septum to epiglottis dependent on muscle activity for patency
- Collapse usually occurs posterior to tongue, uvula, or soft palate (or some combination)
- Etiology: anatomically small pharyngeal airway
  - Obesity
  - Bone and soft tissue structure
  - Tonsils / adenoids in children
Compensation when Awake

- Increase airway resistance
- Increase negative pressure during inspiration
- Mechanoreceptors in larynx respond:
  - Increase activity of pharyngeal dilator muscles

During Sleep

- Reflex muscle activity is reduced / lost
  - Airway narrowing or collapse
- Apnea or hypoapnea occurs
  - Hypoxia and hypercapnea stimulate ventilatory effort and arousal occurs
Obstructive Sleep Apnea

Severe intermittent hypoxemia

- Saturations ≤ 60%

CO₂ retention

- Both interfere with normal autonomic and hemodynamic response to sleep

Physiological Impact of Obstruction

- Increased negative intrathoracic pressure
- Increased transmural gradient
- Hemodynamic instability
- Ventricular dysfunction
- Increased afterload
- Increased atrial size
- Diastolic dysfunction
- Aortic dilation
Physiological Consequences of Apnea

- Systemic Inflammation
- Pressor Surges
- Endothelial Dysfunction
- SNS Activation
- Oxidative stress

Other Possible Physiological Consequences

- Insulin Resistance
- Platelet Activation
- Increased Fibrinogen
Central Sleep Apnea

Associated with Cheyne Stokes
- Crescendo – decrescendo pattern with central apnea or hypoapnea at the nadir

In Heart Failure: Unstable Ventilatory Control
- Thought to be due to increased hypercapnic responsiveness combined with prolonged circulatory time

Idiopathic central sleep apnea: Due to very steep ventilatory response
- Idiopathic CSA can lead to obstructive events

Central Sleep Apnea
- May not be clinically recognized
- Requires full night polysomnogram
Treatment for OSA

General
- Weight loss
- Avoid alcohol and sedatives
- Behavior techniques if apnea is positional
- Oral appliance (2nd line)
- Uvulopalatopharyngealplasty
  - Limited efficacy
- CPAP as primary therapy
  - Pneumatic splint for pharyngeal airway
  - Adherence to therapy is problem
    - Humidification
    - Appropriate mask
    - Addition of pressure ramp

Special Circumstances
- Aggressively treat HF
  - Fluid retention can exacerbate obstruction
- Manage ischemia
- Nocturnal diuresis or more aggressive dialysis in ESRD
Treatment for CSA

• Optimize management of heart failure
  – Diuresis
  – Beta blockers may help modulate ventilatory response in HF
  – ACE inhibitors potentially helpful
    • Caution side effect can exacerbate obstruction

• Nocturnal $O_2$
• Potential other medications
• CRT Therapy ?
• Role of CPAP Unclear
• Adaptive Servo Ventilation

CVN Review Course

STROKE AND PAD RISK
Stroke Risk Factors

- Hypertension
- Cigarette smoking
- Diabetes
- Hyperlipidemia
- Physical inactivity
- Increased body weight / abdominal fat
- Excessive alcohol use
- Oral contraceptive use
- Age
- Gender
- Race ethnicity
- Heredity

Conditions with Increased Risk for Stroke

- Previous TIA
- Vascular bed disease
- Migraine HA
- Sleep apnea
- Hypercoagulability
- Sickle cell disease
- Atrial fibrillation
- Dilated myopathy
- Extensive MI
- Valvular heart disease (endocarditis)
- Cardiac surgical procedures
- Congenital heart defects

Risk factors for CVA similar for those for CAD: Hypertension most important risk factor!
Prevention of Stroke

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Estimated Percent Exposed</th>
<th>Estimated Relative Risk</th>
<th>Estimated Population-attributable Risk, %</th>
<th>Projected No. of Strokes Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>56.2</td>
<td>2.73</td>
<td>49.3</td>
<td>~246,500</td>
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<tr>
<td>Cigarette smoking</td>
<td>27.0</td>
<td>1.52</td>
<td>12.3</td>
<td>~61,500</td>
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<tr>
<td>Atrial fibrillation</td>
<td>3.98</td>
<td>3.60</td>
<td>9.4</td>
<td>~47,000</td>
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<tr>
<td>Heavy alcohol consumption</td>
<td>7.2</td>
<td>1.68</td>
<td>4.7</td>
<td>~23,500</td>
</tr>
</tbody>
</table>


Risk Factors for PAD

- Cigarette smoking
  - 80% of PAD patients
- Diabetes
- Dyslipidemia
- Hypertension
- Hyperhomocysteinemia
  - 30-40% PAD patients
- Increased C reactive protein
- Age
CVN Review Course

HISTORY / ASSESSMENT

ACS Symptoms

<table>
<thead>
<tr>
<th>Classic Symptoms</th>
<th>Symptom Variations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable angina</td>
<td>MI</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>Women</td>
</tr>
<tr>
<td></td>
<td>Elderly</td>
</tr>
<tr>
<td></td>
<td>Diabetics</td>
</tr>
</tbody>
</table>

2014
Stable Angina

- **Typical angina** is defined as angina that meets all three of the following characteristics:
  - Substernal chest discomfort with a characteristic quality and duration
  - Provoked by exertion or emotional stress
  - Relieved by rest or nitroglycerin.

- **Atypical angina** is defined as angina meeting two of the characteristics of typical angina:
  - Non cardiac chest pain is defined as chest pain with none or only one of the characteristics of typical angina.

Unstable Angina

- Occurs with minimal exertion
- OR increased dose of nitroglycerin is required to achieve relief.
- Prolonged rest angina is also considered unstable angina.
- Angina that increases in severity or is very severe on first presentation
- Caused by unstable or ruptured plaque that causes abrupt closure of a coronary artery which may spontaneously reperfuse.
Assessment of Angina

- **Quality:**
  - Use the word “discomfort” or “symptoms” when assessing.
  - Many patients with dyspnea or chest pressure deny the presence of pain.
- **Location:**
  - Assessment of location includes radiation of symptoms.
- **Time:**
  - Both the time of onset and duration of symptoms.
- **Aggravating and alleviating factors:**
  - Key in differentiating stable from unstable angina.
- **Reproducibility:**
  - Reproducibility of chest pain by applying pressure to the chest wall suggests a musculoskeletal etiology.
  - Does not completely rule out the presence of angina.

Characteristics of Angina

**Sensation of pressure, tightness, heaviness, burning, or squeezing.**

- Rarely described as a sharp or stabbing pain.
- Should not worsen with changes in position or respiration.

**Location behind the sternum and in the upper back, shoulder, arm, jaw, or epigastric area.**

- Not usually located in the middle to lower abdomen and does usually not radiate to the lower extremities.

**Associated symptoms (or stand alone symptoms) of dyspnea, nausea, palpitations, or diaphoresis.**

**Duration typically defined in minutes.**

- Not typically defined in seconds or hours.

**CAUTION WHEN ASKING THE PATIENT ABOUT “PAIN”!**
Angina in Women

• Delay presenting with symptoms
• Attribute symptoms to other non-cardiac causes

• Most common presentation:
  – Middle or upper back pain
  – Neck or jaw pain
  – Shortness of breath, paroxysmal nocturnal dyspnea, or cough
  – Indigestion, nausea or vomiting, or loss of appetite
  – Fatigue or weakness
  – Palpitations
  – Dizziness.
  (Canto et al., 2007).

• Less documented stenotic disease of major epicardial coronary arteries
  – Altered microvascular and endothelial function
  – Downstream microembolization

• 25% of men presenting with ACS will not experience chest pain or discomfort.

More on Women and Heart Disease

• Stable angina is often initial presentation
• Women with Non-STEMI and unstable angina are older than men and have more co-morbid conditions (diabetes and HTN)
• The average age for first MI is 64.7 years for men and 72.2 years for women (Go et al., 2013)
• Female sex is a risk factor for mortality in STEMI
• Women receive less evidence based therapies including reperfusion
**Angina in the Elderly**

- Generalized symptoms
  - Dyspnea, diaphoresis, N&V, and syncope
  - Confusion
- Symptoms often attributed to the aging process
  - Importance of assessment with activity tolerance
- Don’t complain about chest pain
  - 37% of patients > 65
  - 42% of patients > 75 years
  - 75% of those > 85 years
- Silent MI s account for 60% of MI s in those > 85 years of age
  - STEMI
    - < 65 years = 90% pain
    - > 85 years = 57% pain

**PAD: Claudication**

- Definition
  - Ischemic pain during exercise
  - Specific leg muscle groups
  - Relieved in 2 to 3 minutes
  - Reproducible, stable
- Prevalence
  - Most common symptom
  - Symptoms only in 20% of patients with PAD
- Location
  - Gastrocnemius muscle
  - Relation of pain to location of disease
Key Signs and Symptoms of Stroke

- Numbness
- Confusion
- Slurred speech / difficulty speaking
- Sudden visual problems
- Loss of balance / coordination
- Severe dizziness
- Sudden severe HA

FAST

Sample Face Arm Speech Test

F - Facial palsy affected side
A - Arm weakness affected side
S - Speech impairment
T - Time of onset
Symptoms: Left (dominant hemisphere)

- Left gaze preference
- Right visual field deficit
- Right hemiparesis
- Right hemisensory loss

Symptoms: Right (nondominant hemisphere)

- Right gaze preference
- Left visual field deficit
- Left hemiparesis
- Left hemisensory loss neglect (left hemi-inattention)
Symptoms: Brainstem

- Nausea and/or vomiting
- Diplopia, dysconjugate gaze, gaze palsy
- Dysarthria, dysphagia
- Vertigo, tinnitus
- Hemiparesis or quadriplegia
- Sensory loss in hemibody or all 4 limbs
- Decreased consciousness
- Hiccups, abnormal respirations

Symptoms: Cerebellum

- Truncal/gait ataxia
- Limb ataxia, neck stiffness
Symptoms: Hemorrhage

- Focal neurological deficits as in AIS
- Headache (especially in SAH)
- Neck pain
- Light intolerance
- Nausea, vomiting
- Decreased level of consciousness

Questions in Expected Stroke

- Time patient last known well (will be used as presumed time of onset)
- Time symptoms were first observed (if different from time last known well)
- Was anyone with patient when symptoms began? If so, who?
- History of diabetes?
- History of hypertension?
- History of seizures?
- History of trauma related to current event?
- History of myocardial infarction or angina?
- History of cardiac arrhythmias? Atrial fibrillation?
- History of prior stroke or TIA?
- What medications is patient currently taking? Is patient receiving anticoagulation therapy with warfarin?
ANATOMY AND PHYSIOLOGY

Neuro Anatomy

- Cerebral hemispheres
- Diencephalon
  - Thalamus
  - Hypothalamus
  - Limbic system
- Brainstem
  - Midbrain
  - Pons
  - Medulla
- Cerebellum
Cerebral Hemisphere Key Functions

- **Left**
  - Analysis
  - Problem solving
  - Language
  - Mathematics
  - Abstract reasoning

- **Right**
  - Spatial relationships
  - Non verbal communication
  - Music
  - Artistic ability

Corpus Callosum
Cerebral Lobes: Key Functions

- Frontal: Voluntary motor function, intellectual function, personality
- Temporal: Memory function and emotion
- Parietal: Sensory function, object recognition and position sense, body awareness and image
- Occipital: Visual reception

Cerebral Circulation

- Two internal common carotid arteries anteriorly
  - Provide the major blood supply to the brain
  - Arise from the common carotids
  - Supply optic nerves, retina, and the majority of the cerebral hemispheres
  - Divides into: Anterior cerebral artery and middle cerebral artery
- Two vertebral arteries posteriorly
  - Arise from right and left subclavian arteries.
  - Merge to form basilar artery; basilar artery divides into two posterior cerebral arteries.
  - Supplies the cervical cord, brainstem, medulla, cerebellum, caudal part of diencephalons, medial and posterior temporal lobes, and the occipital lobes
Cerebral Circulation

- Circle of Willis - an anatomical ring of vessels joining the carotid artery system and the vertebrobasilar system.
  - Posterior communicating artery.
  - Posterior cerebral artery.
  - Anterior communicating artery.
  - Anterior cerebral artery.

Anatomy Application

Middle Cerebral Artery

Most common intracerebral vessel affected by stroke

<table>
<thead>
<tr>
<th>Symptoms of TIA</th>
<th>Carotid</th>
<th>Vertebrobasilar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of vision</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Weakness</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Numbness or tingling</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Slurred speech</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Language difficulty</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vertigo</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ataxia, imbalance</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Double vision</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Heart Anatomy

- Muscular organ
- 4 Chambers
- Blunt Cone-shaped
- Located between the sternum and spine
  - Mediastinum

Heart Anatomy

- Base
  - 2nd intercostal space
  - Behind Sternum
- Apex
  - 5th intercostal space
  - mid-clavicular line.

Figure 2-1  Location and orientation of the heart within the thorax. (From Price SA, Wilson LM. Pathophysiology—clinical concepts of disease processes, ed 5, St Louis, 1995, Mosby.)
Chambers Of The Heart

- 4 chambers
- Atria
  - Right Atria
  - Left Atria
- Ventricles
  - Right ventricle
  - Left Ventricle
- Divided by:
  - Interatrial septum
  - Interventricular septum

Ventricles Of The Heart

Right ventricle
- thin-walled
  - 3-5 mm
- Low pressure pump
- Pumps blood to the lungs

Left ventricle
- thick-walled
  - 8-15 mm
- High pressure pump
- Pumps blood to all other parts of the body
Cardiac Anatomy – Structure

Layers Of The Heart Wall

- Pericardium
  - Layered sac
  - Surrounds and protects the heart
  - Serous Pericardium
    - Visceral layer
    - Parietal layer
  - Fibrous Pericardium
Layers Of The Heart Wall

- **Pericardial Space**
  - **Pericardial Fluid**
    - Serous fluid
    - 10-30 ml
    - Reduces friction as the heart moves
    - Sac in which to move during contraction

![Layers of the cardiac wall](image)

**Figure 2-2** Layers of the cardiac wall. (From Copstead L: *Perspectives on pathophysiology*, Philadelphia, 1995, WB Saunders.)

Blood Flow Through the Heart

![Blood flow through the heart](image)

**Figure 4-5** Normal blood flow through the heart and intrachamber pressures; arrows indicate normal direction of blood flow. This schematic representation of the heart shows all four chambers and valves visible in the anterior view to facilitate conceptualization of blood flow. (For the correct anatomic position of the heart within the thorax, see Figure 4-6.)
The Coronary Arteries

- Layers of Arteries
  - Intima
  - Media
  - Adventitia

Plaque forms between the intima and media (donut analogy)

Veins

- Layers of Veins
  - Intima
  - Media
  - Adventitia
  - Valves
The Coronary Arteries

- Left Main Coronary Artery (LM)
  - Left Anterior Descending Artery (LAD)
    - Diagonal Branch
    - Septal Perforator
    - Ramus
  - Left Circumflex Artery (LCA)
    - Obtuse Marginal (OM)

- Right Coronary Artery
  - Marginal Branch
  - Posterior Descending Artery
  - Concept of dominance

The Coronary Arteries

- LAD
  - Anterior LV
  - Septum (anterior 2/3)
  - Apex of LV

- LCA
  - Lateral LV (OM)
  - Posterior LV (OM)

- RCA
  - Inferior LV (marginal)
  - Septum (posterior 1/3)
  - Right Ventricle (marginal)
  - Posterior LV (PDA)
The Coronary Arteries
Conduction System Supply

- **SA node** ➔ RCA in 55% (LCA in 45%)
- **AV node** ➔ RCA in 90% (LCA in 10%)
- **Bundle Branches** ➔ Predominately LAD

Pathophysiology of Coronary Ischemia

- Ischemia starts in the endocardium, moves outward, then laterally
The Electronics

**Action Potential of Cardiac Cells**

- **Phase 0**: Rapid depolarization
- **Phase 1**: Brief, rapid initiation of repolarization

---

The Electronics

**Action Potential of Cardiac Cells**

- **Phase 2**: Slowing of the repolarization
- **Phase 3**: Sudden acceleration in the rate of repolarization
- **Phase 4**: Resting membrane potential

---
The Electronics Conduction System

- Sinoatrial Node (SA)
- Internodal atrial conduction tracts
- Interatrial conduction tract
- Atrioventricular node (AV)
- Bundle of His
- Atrioventricular (AV) junction

The Electronics Conduction System

- Left Bundle Branch
- Right Bundle Branch
- Purkinje Network
- Purkinje Fibers
The Valves

• Purpose
  – Permit Antegrade Flow
  – Prevent Retrograde Flow

Heart Valves

• 4 Valves in the heart.
• AV Valves
  – Tricuspid
  – Mitral (bicuspid)
• Semilunar Valves
  – Pulmonic
  – Aortic
AV (Atrioventricular) Valves

- **Tricuspid**
  - Between right atrium and right ventricle
  - Larger, but thinner
  - 3 cusps

- **Mitral**
  - Smaller
  - 2 cusps
  - Between left atrium and left ventricle

- Both have fibrous rings
- Both have Cordae Tendineae
- Both have papillary muscles

**AV Valves**

- **Chordae Tendineae**
  - Tendon like fibrous cords that connect the pointed ends of the valves to the papillary muscles that are located on the inner surface of the ventricles.
Semilunar Valves

Semilunar valves:
- Pulmonic
  - Between the right ventricle and pulmonary trunk
- Aortic
  - Between the left ventricle and aorta

- Three cusps
- Leaflets are smaller and thicker than the AV valves
- Openings are smaller than the AV valves
- The velocity of ejected blood is higher than AV valves.
The Heart as a Pump

**Goal:** Forward propulsion of blood to perfuse the body.

Flow is determined by:
- √ Pressure
- √ Resistance
- √ Volume
Right Sided versus Left Sided System

Key Principles in Understanding Hemodynamic Assessment

- **Pulse pressure** tells us about arterial compliance
- **Variation of up to 15mm Hg** between arms is normal
- **MAP = Calculated**

- **Systolic BP**
  - Very dynamic
  - Arterial pulse waveform proportional to SV - SBP can be used to reflect stroke volume

- **Diastolic BP**
  - Continuous / less dynamic pressure
  - Reflects state of arterioles
  - Drives capillary opening pressure
Key Principles in Understanding Hemodynamic Assessment

- Vascular tone is affected by:
  - Large vessel compliance
  - Peripheral vascular resistance (smaller vessels)

- Vessel resistance changes more quickly than large vessel compliance

- Increased resistance = increased DBP and narrowing pulse pressure

Key Principles in Understanding Hemodynamic Assessment

- **Pressure** does not always = **Flow**

  - “We measure BP because we can” – Barbara Mclean
Definitions

- **Cardiac Output**: Volume of blood ejected by the ventricle each minute
  - Normal: 4-8 liters/minute
- **Cardiac Index**: Adjustment made for body size
  - Normal cardiac index: 2.5-4 liters/minute/m²
- **Stroke Volume**: Volume of blood ejected with each beat.
  - Normal 60-120 ml / beat
  - Systolic BP as non invasive indicator
- **Ejection Fraction**: Percent of blood ejected from the ventricle
  - Normal: 55% to 60%

Basic Hemodynamic Formula

Cardiac Output = Heart Rate X Stroke Volume

Preload | Afterload | Contractility

Same four components also determine myocardial oxygen demand
## Preload

- The ventricle is **preloaded with blood at the end of diastole**: Creates stretch on myocardial muscles fibers
  
  - Greater the volume the greater the stretch (muscle fiber length)
  
  - Greater the stretch the greater the contraction
  
  - Greater the contraction the greater cardiac output

### Factors Influencing Preload

- Body Position
- Venous Tone
- Intrathoracic pressure
- Intrapericardial pressure
- Dysrhythmias
- Atrial Kick
- LV Function

- Circulating blood volume
  - Hypervolemia
  - Hypovolemia
  - Third spacing

- Distribution of blood volume
  - Sepsis
  - Anaphylaxis
  - Venous vasodilators
Preload Assessment: Indirect

Right ventricular preload

- **Noninvasive assessment**
  - JVD
  - Hepatojugular reflux
  - Peripheral edema
  - Weight

Left ventricular preload

- **Noninvasive Assessment**
  - Orthopnea
  - CXR
  - BNP
  - Lungs sounds
  - S₃
  - Blood Pressure
  - Urine Output
  - Weight

Also assess skin turgor, mucous membranes, and orthostatic blood pressures.

Right Side and Left Side are Related

Afterload

- **After the ventricle is loaded: It must work!**

- **Pressure ventricle needs to overcome to eject blood volume**
  - SVR for left ventricle
  - PVR for right ventricle

- **Smaller vessel resistance is major component of LV afterload**

- **Other components of LV afterload**
  - Valve compliance
  - Viscosity of blood
  - Arterial wall (aortic) compliance
Afterload Assessment

• Left ventricle:
  – Noninvasive assessment: Diastolic blood pressure and pulse pressure

• Right ventricle:
  – Pulmonary HTN increases RV afterload
  – Hypoxemia / Positive Pressure Ventilation / PEEP increase RV afterload

Contractility

• Ability of myocardium to contract independent of preload or afterload
  – Velocity and extent of myocardial fiber shortening
  – Inotropic state

• Related to degree of myocardial fiber stretch (preload) and wall tension (afterload).

• Influences myocardial oxygen consumption

• ↑ contractility
  ⇒ ↑ myocardial workload
  ⇒ ↑ myocardial oxygen consumption
Contraction of the Myocardium
(Ability to shorten and to develop force)

Important Points about Contractility

- No accurate way to measure contractility

**Noninvasive Assessment: Ejection Fraction**

- Low cardiac output does not necessarily mean diminished contractility (i.e. hypovolemia)

- Correct preload and afterload problems first in a patient with a low ejection fraction.

- Increasing contractility with medications will also increase myocardial oxygen demand.
Heart Rate

• Mathematically heart rate increases cardiac output

• Physiological limit where increased heart rate will decrease cardiac output due to decreased filling time (decreased preload)

Neurologic Control of the Heart

• Autonomic Nervous System
  – SNS
  – PNS
• Chemoreceptors
• Baroreceptors
Autonomic Nervous System

- Both divisions of the autonomic nervous system extend into the heart
- The atria are innervated by both parasympathetic and sympathetic fibers
- The ventricles are almost entirely innervated by sympathetic fibers only
Sympathetic Nervous System

• Fight or Flight

**Alpha₁ Receptors**
- Vasoconstriction of vessels

**Beta₁ Receptors** (Heart)
- Increased heart rate
- Chronotropic response
- Increased conductivity
- Dromotropic response
- Increased contractility
- Inotropic response
- Increased automaticity

**Beta₂ Receptors** (Vessels, Lungs)
- Bronchodilation
- Peripheral vasodilatation

*Cause renin release and activation of the RAAS*

**Dopaminergic Receptors**
- Renal and mesenteric vasodilation

Parasympathetic (Vagal) Nervous System

• Maintains a steady state
• Causes – chronotropic, dromotropic effects
• Causes minimal decrease in inotropic effects
• Primarily slow heart rate and conduction
• Cardiovascular effects of PNS generally undesirable
Chemoreceptors

- Located in carotid and aortic bodies
- Sensitive to changes in PaO$_2$, PaCO$_2$, and pH.
- $\downarrow$ in pH or O$_2$ or $\uparrow$ in CO$_2$
  $\Rightarrow$ SNS response
- $\uparrow$ in pH or $\downarrow$ in CO$_2$
  $\Rightarrow$ PNS response

Baroreceptors

- Located in the carotid sinus and aortic arch
- Sensitive to arterial wall tension
- Cause reflex response in either SNS or PNS

- Decrease BP $\Rightarrow$ SNS (adrenergic) response
- Increase BP $\Rightarrow$ PNS (cholinergic) response
Systolic vs Diastolic Dysfunction

A

B
Left and Right Sided Heart Failure

- Two sides of the heart form a circuit, neither side can pump significantly more blood than the other for long
- Signs/symptoms of failure reflect each respective ventricle
The Real Culprit: Neurohormonal Response

Ventricular Remodeling

• Process of pathological growth
• Can occur from prolonged activation of SNS/RAAS
• Involves
  □ Hypertrophy of myocytes
  □ Pressure – thicken (concentric)
  □ Volume – elongate (eccentric)
  □ Genetically abnormal – inefficient contraction
  □ Increased ventricular muscle mass, change in ventricular shape
  □ Collagen matrix becomes fibrotic
Apoptosis
(a component of remodeling)

- Preprogrammed cell death without inflammation/scarring (necrosis)
- Process is accelerated in HF in a random pattern
- Cell slippage
  - Bricks – myocytes
  - Morter – collagen
    - Degredation (slippage) or
    - Fibrotic

Non Invasive and Invasive

DIAGNOSTIC TESTING
Transthoracic Echo (TTE)

- Obtained in 4 views
  - Parasternal (long and short axis), apical, subcostal, suprasternal notch
- Valve function
  - Regurgitant volumes
  - Valve gradients
- Atrial size
- Right and left ventricular function
- Systolic and diastolic abnormalities
- Regional wall motion abnormalities
- Pulmonary artery pressures
- Pericardial abnormalities

Limitations of TTE

- Body habitus
- COPD
- Critical condition / supine acquisition
- Post operative condition

**Solutions:**
- LV contrast
- Off axis imaging
- Transesophageal echo
Transesophageal Echocardiogram (TEE)

- More invasive
- Imaging at shallower depths / higher frequency transducer
- Mid esophageal view (most information)
- Transgastric view (long and short axis)
  - Aortic valve gradients
  - Pericardial effusions
  - LV function (intraoperative)
- High esophageal view
  - Visualization of ascending aorta and great vessels
TEE: Vegetation on Mitral Valve

TEE: Perioperative Wall Motion
Ankle Brachial Index

• Most objective measure of lower extremity PAD
• Does not correlate strongly with walking impairment
• Systolic in brachial arteries, posterior tibial, and dorsalis pedis arteries
  – Supine resting position for 10 minutes
• Ankle pressure should be 10 to 15mmHg higher than brachial pressure
• Normal ABI> 1.0

Indications for Resting ABI

• Exertional leg symptoms
• Non healing wounds
• > 70 years
• ≥ 50 years with history of smoking or diabetes
### ABI Values

<table>
<thead>
<tr>
<th>ABI Values</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>&gt; 1.4</td>
<td>Non compressible</td>
</tr>
<tr>
<td>1.0-1.4</td>
<td>Normal</td>
</tr>
<tr>
<td>0.91-0.99</td>
<td>Borderline</td>
</tr>
<tr>
<td>&lt; 0.90</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

Source: Anderson et al., 2013; Rooke et al., 2011

### Stress Testing in Patients Presenting with Chest Pain

- Indicated when ECG and biomarkers are not diagnostic
- Should be done before discharge or within 72 hours as outpatient
- Precautionary pharmacotherapy for low risk patients being done on outpatient basis
  - ASA
  - SL NTG
  - Beta blockers
Contraindications to Stress Testing

- Acute MI ≤ 2 days old
- Acute myocarditis or pericarditis
- Acute pulmonary embolism
- Acute aortic dissection
- Symptomatic heart failure
- Severe aortic stenosis
- Symptomatic arrhythmias
- High-risk unstable angina

(Gibbons et al., 2003)

Sensitivity and Specificity of Stress Tests

- The sensitivity and specificity for exercise stress testing without myocardial imaging is lower in women than in men.

- Exercise only stress testing also has lower sensitivity and specificity than stress testing that includes myocardial imaging
Stress Testing

• Exercise Stress Test with or without myocardial imaging
  – Nuclear Scanning
  – Echocardiogram
  – MR

• Patient conditions requiring myocardial imaging with stress testing due to lack of reliable ECG interpretation include:
  – Left bundle branch block
  – > 1 mm ST-segment depression at rest
  – Paced ventricular rhythm
  – Significant left ventricular hypertrophy
  – Wolf-Parkinson-White syndrome

Additional Challenges in ECG Stress Test Interpretation

• Right bundle branch block (RBBB):
  – Exercise induced ST depression in leads V1-V3 not associated with ischemia
  – Exercise-induced ST depression significant when it occurs in the low lateral or inferior leads

• Digoxin can produce false positive ST segment depression

• Low serum potassium may cause false positive ST segment depression

• Anti-ischemic medications can prevent ischemic changes from showing on the ECG and result in a false negative stress test
Goals of Exercise Stress Test

• Exclude obstructive CAD by demonstrating no ECG changes during maximal exertion
• Assess the extent and severity of ECG changes and symptoms at a given workload to predict the presence and severity of obstructive CAD
• Note: Submaximal exercise or coronary artery stenosis of < 70% may fail to show ECG signs of ischemia
  – * ECG changes are late in the ischemic cascade

Exercise Stress Testing Logistics and Candidates

• Standard treadmill protocols begin at 3.2 to 4.7 metabolic equivalents (METs) of work
• Workload is increased by several METs every 2 to 3 minutes during the stress test
• The majority of activities of daily living require 4 to 5 METs of work

• Thus patients who have limitations in activities of daily living will have a difficult time exerting enough work to perform an optional stress test
• Exercise stress testing is preferred to chemical stress testing when the patient has the functional capacity to perform regular activities of daily living / 6 to 12 minutes during stress test
Exercise Stress Test

- NPO 2 hours prior for plain exercise
- Light breakfast (dry toast & juice) to be given 2 hrs prior! NO CAFFEINE for 12 hours prior! – if done in conjunction with imaging

- No HR lowering medications unless specifically ordered (beta blockers / diltiazem or verapamil)
- No smoking (risk for spasm)

- Comfortable and safe foot ware

Exercise Capacity

- Strong prognostic indicator for risk, including the risk of death
- Maximum exertion rather than achievement of 85% of age-predicted maximum heart rate is the goal
- Heart rate criterion alone may not indicate a sufficient enough work for an optimal stress test
- Submaximal exercise can interfere with the accuracy of results
Diagnostic ECG Changes During Stress Test

- ST segment depression ≥ 1 mm (80 msec after the J point) during peak exercise.
  - Horizontal or down-sloping
- ST segment depression with exertional symptoms at suboptimal exercise or persists into the recovery period is associated with a higher risk of cardiovascular mortality (Fihn et al., 2012).

- ST elevation not common - could represent an unstable plaque and acute coronary syndrome.

High Risk Features During Exercise Stress Test

- Short exercise duration
- Anginal symptoms
- Chronotropic incompetence
- Complex ventricular arrhythmias during stress or recovery
- Low heart rate recovery score *
  - Peak minus 1 minute post recovery
  - Normal > 12; Low < 8
- Inappropriate hemodynamic response to exercise *
  - Failure to raise SBP to > 120 mmHg
  - Sustained decrease in SBP of 10 mmHg or >
Chemical Stress Tests

• Only indicated for patients who are incapable of moderate physical functioning or who have one or more disabling comorbid conditions.

• Four pharmacological agents are used in chemical stress testing:
  – Dobutamine
  – Dipyridamole
  – Adenosine
  – Regadenoson.

• All pharmacological stress testing is done in conjunction with myocardial imaging.
  – Nuclear myocardial perfusion imaging
  – Or – echocardiography with dobutamine

Chemical Stress Testing

• Dipyridamole and adenosine
  – Non specific adenosine receptor agonists
  – Stimulation of these other receptors is what causes the unwanted side effective of atrioventricular (AV) block (A1 receptor) and bronchospasm (A2b and A3 receptors).
  – Contraindications:
    • Severe lung disease or if wheezing
  
• All 3 agents: Stimulation of Adenosine A2a receptor causes coronary vasodilation
  • Causes coronary microvascular dilatation similar to the coronary artery vasodilatation that occurs with exercise

• Regadenoson is A2a selective
• Another advantage over other two agents:
  – Rapid dosing
  – Non weight based

  – Antidote: Aminophylline for all 3 agents
  – Patients should be off aminophylline or related products prior to testing with these chemical agents
Regadenoson (Lexiscan)

- Single-use pre-filled syringe: Injection solution containing Regadenoson 0.4 mg/5 mL (0.08 mg/mL).
- Given over 10-15 seconds
- Half life 2 to 3 minutes
- Most common side effects – feeling flushed and slight shortness of breath; abdominal and leg cramping may occur.
- Do not administer to patients with: second or third degree AV block or sinus node dysfunction, considered safer in patients with risk for bronchospasm

Chemical Stress Testing

- Dobutamine
  - High-dose dobutamine increases contractility and heart rate
  - Increasing myocardial oxygen demand
  - More closely mimics exercise stress testing
  - May be done with Echo instead of nuclear scan
  - Side effect: Tachyarrhythmias
  - Antidote: Beta blocker
Dobutamine Stress Echo

- Echo done first
- Dobutamine given starting at 10mcg & increasing to 40mcg ceiling until target HR achieved (85% of PMHR)
- Echos obtained at each level & in recovery
- NPO 4 hours before test
- Hold beta blockers

Imaging with Stress Testing

- Exercise can be done with or without imaging
- Imaging is required during exercise if ECG is not interpretable
- Imaging is required for chemical stress testing
- Imaging can be done with nuclear or echocardiography
- Imaging includes pre and post stress images
Nuclear Imaging

• Both types of imaging use radionuclide tracers.

• SPECT (single-photon emission computerized tomography)
  – A common tracer in SPECT imaging is technetium-99m (Tc-99m).

• PET (positron emission tomography) imaging.
  – PET imaging uses physiological substrates prepared with positron-emitting isotopes and these agents have shorter half-lives than those used for SPECT imaging.

Nuclear Imaging

• Information about the extent, severity, and location of ischemia.

• Differentiate areas of necrosis from ischemia but cannot differentiate viable tissue.

• Provide information about high risk features including: stress induced wall motion abnormalities, post stress reduction in ejection fraction, transient ischemic left ventricular dilation, or globally reduced ejection fraction.
Nuclear Imaging

- Results reflect perfusion at the time of injection
- Patients can be injected during an episode of pain and scanning can be delayed for several hours
- Accuracy is impacted by obesity and large amounts of breast tissue. When SPECT imaging is used, global reductions in perfusion, such as that seen with triple vessel disease or left main disease, can result in an underestimation of the degree of ischemia (Fihn et al., 2012).

Stress Echocardiography

- Used to evaluate for regional wall motion abnormalities or for global changes in left ventricular function during or immediately after stress.
  - Intravenous contrast agents can be used with echocardiography imaging to improve the diagnostic accuracy.
- Used with both exercise and chemical stress testing.
  - When used with chemical stress testing, dobutamine is the most common agent.
Cardiac Magnetic Resonance (CMR)

• Can also be used as an imaging modality
  – If used with dobutamine stress testing, ischemia is detected by a new wall motion abnormality
  – If used with dipyridamole, adenosine, or regadenoson, ischemia is detected by a new perfusion abnormality

Cardiac Computed Tomography (CT) for Coronary Artery Calcium Scoring

• Cardiac CT calcium scoring has been used for two different purposes:
  – As a risk assessment tool in an asymptomatic patient
  – For prediction of significant coronary stenosis as the etiology of chest pain in a symptomatic patient

• Current evidence based guidelines state there is insufficient evidence for the use of CT for coronary artery calcium scoring in symptomatic patients to rule in or rule out significant coronary stenosis as the etiology of the symptoms
Calcium Scoring

Cardiac/Coronary Computed Tomography Angiography (CCTA)

- CCTA is an anatomic test
- More sensitive in detecting obstructive coronary artery disease compared to myocardial perfusion imaging
- Sensitivity and specificity appear to be similar between men and women.
- Very high negative predictive value for obstructive CAD.
- Can evaluate arterial remodeling and detect plaque that is not obstructive.
- Can also classify plaque at calcified, noncalcified, or mixed.
- An option in
  - (a) patients who continue to have symptoms in the presence of normal stress test findings,
  - (b) patients who have indeterminate results from the stress test, or
  - (c) patients who cannot undergo stress testing with nuclear MPI or echocardiography
Coronary Angiography: Indications

- Patients with disabling angina despite medical treatment
- Patients with high-risk criteria for coronary heart disease (CHD) on noninvasive testing
- Patients who have survived sudden cardiac death
- Patients with angina and clinical signs of CHD
- Patients with low ejection fraction and ischemia on noninvasive testing
- Patients with inadequate information obtained from noninvasive testing
**Right Heart Catheterization**

- Right atrial and right ventricular pressures
- Pulmonary artery pressure
- \( O_2 \) content of right heart chambers and pulmonary artery
- Determine cardiac output
- Evaluate tricuspid and pulmonic valves
- Detect and evaluate intracardiac shunts

**Left Heart Catheterization**

- LV function / wall motion abnormalities
- LV pressures
- Aortic and mitral valve assessment

![Images of Right heart catheterization, Coronary arteriography, and Left ventriculography](https://www.cardionursing.com)
Cardiac Biomarkers

- Released into the blood when necrosis occurs as a result of membrane rupture of the myocytes
- Used in the evaluation of ACS
- Myoglobin
  - Rises the earliest
  - Within 2 hours after damage
  - Very sensitive, not specific
- CK (creatine kinase)
  - Enzyme present in the heart, brain, and skeletal muscle
  - Elevations are not specific to myocardial damage.
- CK-MB
  - More specific to the heart
  - Helpful in identifying more than minor amounts of myocardial damage
  - Rapidly rises in the presence of myocardial damage.
Troponin I and I (cardiac troponins)

- Found only in cardiac muscle
- Most sensitive indicator of myocardial damage
  - Capable of diagnosing small amounts of myocardial necrosis not measured by rises in CK-MB levels
- Approximately 30% of patients with Non-STEMI and normal CKMB levels will have a positive Troponin
- Of equal sensitivity and specificity
- Troponin remains elevated for a long period
  - Beneficial for late presentation
  - Challenging for re-infarction
- Positive troponin + ECG changes of injury / ischemia or ACS symptoms = infarct

More on Troponin

- Non infarct cardiac causes of elevated troponin: heart failure, left ventricular hypertrophy, tachyarrhythmias, pericarditis, cardiac trauma
- Non CAD causes of troponin elevation (sepsis, pulmonary emboli, chronic kidney disease, chemotherapy, respiratory failure, burns, neurological disease)
- Troponin I more specific in renal dysfunction
  - Patients with ESRD commonly have elevated troponin T
  - < 10% of patients with ESRD have elevated troponin I in absence of ACS
- Elevated troponin levels are marker of risk – even when diagnosis is not myocardial infarction
## Cardiac Biomarker Summary

<table>
<thead>
<tr>
<th>Cardiac Biomarker</th>
<th>Specificity / Sensitivity</th>
<th>Rise</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myoglobin</td>
<td>Sensitive but not specific</td>
<td>Within 2 hours</td>
<td>4 to 10 hours</td>
<td>&lt; 24 hours</td>
</tr>
<tr>
<td>CK-MB</td>
<td>Highly specific</td>
<td>4 to 6 hours</td>
<td>18 to 24 hours</td>
<td>2 to 3 days</td>
</tr>
<tr>
<td>Troponin I or T</td>
<td>Highly specific and sensitive</td>
<td>4 to 6 hours</td>
<td>18 to 24 hours</td>
<td>10 or more days</td>
</tr>
</tbody>
</table>

### Timing of Release of Various Biomarkers After Acute Myocardial Infarction

![Graph showing the timing of release of various biomarkers after acute myocardial infarction](image)


Anderson JL, et al. J Am Coll Cardiol 2007;50:e1–e157, Figure 5.
HIGH SENSITIVITY TROPONIN T

Diagnosis of Heart Failure

- Based on signs and symptoms
- B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP)
  - Good to assess in patients with dyspnea being evaluated for HF
  - Should not be used as the sole tool to diagnose HF
  - Must be used in concert with signs and symptoms
  - Special consideration with renal insufficiency and obesity.
  - Low values rule out HF
# Causes of Elevated Natriuretic Peptide Levels

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Non-cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heart failure, including RV syndromes</td>
<td>• Advancing age</td>
</tr>
<tr>
<td>• Acute coronary syndrome</td>
<td>• Anemia</td>
</tr>
<tr>
<td>• Heart muscle disease, including LVH</td>
<td>• Renal failure</td>
</tr>
<tr>
<td>• Valvular heart disease</td>
<td>• Pulmonary: obstructive sleep apnea, severe pneumonia, pulmonary</td>
</tr>
<tr>
<td>• Pericardial disease</td>
<td>• Hypertension</td>
</tr>
<tr>
<td>• Atrial fibrillation</td>
<td>• Critical illness</td>
</tr>
<tr>
<td>• Myocarditis</td>
<td>• Bacterial sepsis</td>
</tr>
<tr>
<td>• Cardiac surgery</td>
<td>• Severe burns</td>
</tr>
<tr>
<td></td>
<td>• Toxic-metabolic insults, including cancer chemotherapy and envenomation</td>
</tr>
</tbody>
</table>
Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th>1. Little interest or pleasure in doing things</th>
<th>Lot at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td></td>
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<td></td>
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<tr>
<td>4. Feeling tired or having little energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>5. Poor appetite or overeating</td>
<td></td>
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<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

| 6 | Very, very light | How you feel when lying in bed or sitting in a chair relaxed. Little or no effort. |
| 7 | Very light       |                                            |
| 8 | Fairly light     |                                            |
| 9 | Somewhat hard    | Target range: How you should feel with exercise or activity. |
| 10| Hard             |                                            |
| 11| Maximum exertion | How you felt with the hardest work you have ever done. |
| 12| Very hard        |                                            |
| 13| Very, very hard  | Don’t work this hard!                    |
| 14|                  |                                            |
| 15|                  |                                            |
| 16|                  |                                            |
| 17|                  |                                            |
| 18|                  |                                            |
| 19|                  |                                            |
| 20|                  |                                            |
### National Institutes of Health Stroke Scale

<table>
<thead>
<tr>
<th>Score = 0</th>
<th>No stroke</th>
<th>Score = 1-4</th>
<th>Minor stroke</th>
<th>Score = 5-15</th>
<th>Moderate stroke</th>
<th>Score = 16-20</th>
<th>Moderate to severe stroke</th>
<th>Score = 21-42</th>
<th>Severe stroke</th>
</tr>
</thead>
</table>

#### Physical Exam

<table>
<thead>
<tr>
<th>Item</th>
<th>Scoring Criteria</th>
</tr>
</thead>
</table>
| 1. Level of consciousness | 0 = Alert, seems responsive
1 = Not alert, but awake by minor stimulation
2 = Not alert, requires repeated stimulation
3 = Unresponsive or responds only with reflexes |
| 2. Level of consciousness: What is your name? | 0 = Answers two questions correctly
1 = Answers one question correctly
2 = Answers neither question correctly |
| 3. Level of consciousness: How are you feeling? | 0 = Performs both tasks correctly
1 = Performs one task correctly
2 = Performs neither task correctly |
| 4. Level of consciousness: Open and close your eyes. Grip and release your hand. | 0 = Normal
1 = Partial gaze palsy
2 = Focal deviation |
| 5. Level of consciousness: Motor arm | 0 = No drift
1 = Drift
2 = Some effort against gravity
3 = No effort against gravity; limb falls |
| 6. Level of consciousness: Motor leg | 0 = No drift
1 = Drift
2 = Some effort against gravity
3 = No effort against gravity
4 = No movement |
| 7. Level of consciousness: Limb ataxia | 0 = Absent
1 = Present in one limb
2 = Present in two limbs |
| 8. Level of consciousness: Sensory | 0 = Normal, no sensory loss
1 = Mild/moderate sensory loss
2 = Severe to total sensory loss |
| 9. Level of consciousness: Speech | 0 = Normal speech
1 = Mild to moderate aphasia
2 = Severe aphasia
3 = Motor aphasia |
| 10. Level of consciousness: Dysarthria | 0 = Normal
1 = Mild to moderate dysarthria
2 = Severe dysarthria |
| 11. Level of consciousness: Inattention | 0 = No inattention
1 = Visual, tactile, auditory, spatial, or personal inattention
2 = Profound hemi-inattention or extinction |

Total score = 0–42.

---

**CVN Review Course**

**PHYSICAL EXAM**
The Key to Understanding Heart Sounds

Begins With The Cardiac Cycle

Ventricular Diastole: 2 Phases
Ventricular Systole: 2 Phases

Cardiac Diastole (Atrial & Ventricular):
Early Passive Ventricular Filling

Phase I of Ventricular Diastole
Atrial Systole & Ventricular Diastole:

**Late Active Ventricular Filling**

**Phase 2 of Ventricular Diastole**

Atrial Kick

---

Beginning Ventricular Systole:

**Isovolumic Contraction**

**Phase 1 of Ventricular Systole**
Ventricular Systole: 

**Ejection**

Phase 2 of Ventricular Systole

---

**The Basis for the Sounds**

- **Diastole**
  - Passive Ventricular Filling
    - S3
  - Active Ventricular Filling
    - Atrial Kick – S4
  - Valves Open
    - Mitral
    - Tricuspid
    - Don’t open well
      - Stenosis
  - Valves Closed
    - Aortic
    - Pulmonic
    - Don’t close well
      - Regurgitation

- **Systole**
  - Isovolumic contraction
  - Ejection of LV Contents
  - Valves Open:
    - Aortic
    - Pulmonic
    - Don’t open well
      - Stenosis
  - Valves Closed
    - Mitral
    - Tricuspid
    - Don’t close well
      - Regurgitation
“The most important part of the stethoscope is the part between the ear pieces”

Dr. Terry Tegtmeier 1999

Auscultatory Areas
**Basic Heart Sounds**

### S₁

- **Closure of the Mitral (M₁) valve and the Tricuspid (T₁) valve**
- **Beginning of Ventricular Systole and Atrial Diastole**
- **Location:** Mitral area
- **Intensity:** Directly related to force of contraction
- **Duration:** Short
- **Quality:** Dull
- **Pitch:** High

![Diagram of heart valves and sounds](image)

### S₂

- **Closure of Aortic (A₂) and Pulmonic (P₂) Valve**
- **End of Ventricular Systole**
- **Location:** Pulmonic area
- **Intensity:** Directly related to closing pressure in the aorta and pulmonary artery
- **Duration:** Shorter than S₁
- **Quality:** Booming
- **Pitch:** High

![Diagram of heart valves and sounds](image)
**Diastolic Filling Sounds**  
**S3 - Ventricular Gallop**

- **Early diastolic filling sound**
- Caused by increased pressure and resistance to filling
- Most frequently associated with systolic dysfunction
- Associated with:
  - Fluid overload state
  - Right or left ventricular failure
  - Ischemia
  - Aortic regurgitation
  - Mitral regurgitation
- May be normal in children, young adults (up to 35-40) and in the 3rd trimester of pregnancy.

---

**Diastolic Filling Sounds**  
**S₃**

- **Patient position:** left lateral decubitus position
- **Location:**
  - Left-sided S₃ – mitral area
  - Right-sided S₃ – tricuspid area
- **Intensity**
  - Left-sided heard best during expiration
  - Right-sided heard best during inspiration
- **Duration:** short
- **Quality:** dull, thud like
- **Pitch:** low (Bell of stethoscope)
Diastolic Filling Sounds
S₄ - Atrial Gallop

- **Late diastolic filling sound**
- Caused by atrial contraction and the propulsion of blood into a noncompliant (stiff) ventricle.
- Most frequently associated with diastolic dysfunction
- Associated with:
  - Fluid overload state
  - Systemic hypertension
  - Restrictive cardiomyopathy
  - Ischemia
  - Aortic stenosis
  - Hypertrophic cardiomyopathy
- May be normal in athletes

Diastolic Filling Sounds
S₄

- Patient position: left lateral decubitus position
- Location
  - Left-sided S₄ – mitral area
  - Right-sided S₄ – tricuspid area
- Intensity
  - Left-sided louder on expiration
  - Right-sided louder on inspiration
- Duration: Short
- Quality: Thud like
- Pitch: Low (Bell of stethoscope)
Extra heart sounds add to an advanced assessment and to the total clinical picture. This is in comparison to a new murmur that may represent an acute change in condition and an emergency.

**KEY POINT**
Murmurs

- High blood flow through a normal or abnormal valve
- Forward flow through a narrowed or irregular orifice into a dilated chamber or vessel
- Backward or regurgitant flow through an incompetent valve

Murmur Fundamentals

- **Timing**
  - Systolic
    - Holosystolic
    - Ejection (mid systolic)
    - Late
  - Diastolic
    - Early
    - Mid diastolic
    - Late

- **Location**
  - Place heard the loudest

- **Radiation**
  - Direction in which murmur radiates
Murmur Fundamentals

- **Configuration**
  - Crescendo
    - Gets louder
  - Decrescendo
    - Gets softer
  - Crescendo – Decrescendo
    - Louder then softer
  - Plateau
    - Even intensity throughout

- **Pitch**
  - High Pitched - diaphragm
  - Low Pitched – bell

- **Quality**
  - Soft
  - Harsh
  - Blowing
  - Musical
  - Rumbling
  - Rough

Grading Murmurs

- **Grade 1**
  - Barely audible in a quiet room

- **Grade 2**
  - Quiet, but readily heard immediately after placing stethoscope on chest

- **Grade 3**
  - Moderate intensity, readily audible

- **Grade 4**
  - Loud with palpable thrill

- **Grade 5**
  - Very loud, usually with a thrill. Audible with stethoscope titled slightly off the chest

- **Grade 6**
  - Very loud, usually with a thrill. Audible with stethoscope lifted off the chest.
### Murmur Fundamentals

<table>
<thead>
<tr>
<th>STENOTIC MURMURS</th>
<th>REGURGITANT MURMURS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve does not open properly</td>
<td>Valve does not close properly</td>
</tr>
<tr>
<td>Heard during the part of the cardiac cycle when the valve is open</td>
<td>Heard during the part of the cardiac cycle when the valve is closed</td>
</tr>
</tbody>
</table>

### Systolic Murmurs

#### Systolic Filling Murmurs
- Forward flow across stenotic or obstructed valve
- **Pulmonic and Aortic valve open**
  - Pulmonic Stenosis
  - Aortic Stenosis

#### Systolic Regurgitant Murmurs
- Retrograde flow across an incompetent valve
- **Tricuspid and Mitral valve closed**
  - Tricuspid Regurgitation
  - Mitral Regurgitation

#### INNOCENT SYSTOLIC MURMURS
AORTIC Stenosis
Systolic Ejection Murmur

- May be present before any significant hemodynamic changes occur
- More severe AS ➔ longer murmur
- Timing: Midsystolic
- Location: Best heard over aortic area
- Radiation: Toward neck and shoulders
  - May radiate to apex
- Configuration: Crescendo-decrescendo
- Pitch: Medium to high
- Quality: Harsh

Mitral Regurgitation

- Timing: Holosystolic
- Location: Mitral area
- Radiation: To the left axilla
- Configuration: Plateau
- Pitch: High
- Quality: Blowing, harsh or musical
Diastolic Murmurs

Diastolic Regurgitant Murmurs
- Retrograde flow across an incompetent semilunar valve
- Pulmonic and Aortic Valves Close
  - Pulmonic Regurgitation
  - Aortic Regurgitation

Diastolic Filling Murmurs
- Forward flow across stenotic or obstructed AV valves
- Tricuspid and Mitral Valves Open
  - Tricuspid Stenosis
  - Mitral Stenosis

NO SUCH THING AS AN INNOCENT DIASTOLIC MURMUR

Chronic Aortic Regurgitation

Physical Examination
- Diastolic Murmur of AR
  - Length of murmur correlates severity of AR
  - **Timing**: Early diastole
  - **Location**: left sternal boarder
    - 3rd, 4th ICS
  - **Radiation**: Towards apex
  - **Configuration**: Decrescendo
  - **Pitch**: High
  - **Quality**: Blowing
  - **Patient Position**: Sitting and learning forward at end expiration
  - **Intensity**: Increases with increased peripheral vascular resistance: Squatting, exercising, hand gripping

www.cardionursing.com
Systolic Flow Murmur with Chronic AR

- Result of turbulent flow across valve during systolic
- Large volumes of blood from hyperdynamic perfusion causes turbulence
- Timing: Mid systolic
- Location: Along left sternal boarder
- Configuration: Crescendo-decrescendo
- Pitch: Medium (best with diaphragm)
- Quality: Soft
- Intensity: May increase after coughing or when elevating legs while in lying position

Measuring JV Pulsation / Pressure

- Raise HOB 30 – 45 degrees
- Internal preferred
- May use external
- Use tangential light
- Use centimeter ruler
- Difficult to assess if HR>100
- Normal JVP level is < 3 cm above the sternal angle
- Sternal angle is 5cm above right atrium
- JVP of 3 cm + 5cm = estimated CVP of 8cm H₂O

www.cardionursing.com
Estimated CVP > 8 cmH₂O
• Increased blood volume
• Usually RV failure
• Tricuspid valve regurgitation
• Pulmonary hypertension

JVD (Jugular Venous Distension)

May be present in cardiac tamponade.

Additional assessment tips:
Lying flat to verify location of jugular
Sitting or standing patient up to see top of column
<table>
<thead>
<tr>
<th>Jugular Vein</th>
<th>Carotid Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pulsations palpable.</td>
<td>Palpable pulsations.</td>
</tr>
<tr>
<td>Pulsations obliterated by pressure above the clavicle.</td>
<td>Pulsations not obliterated by pressure above the clavicle.</td>
</tr>
<tr>
<td>Level of pulse wave decreased on inspiration; increased on expiration.</td>
<td>No effects of respiration on pulse.</td>
</tr>
<tr>
<td>Usually two pulsations per systole (x and y descents).</td>
<td>One pulsation per systole.</td>
</tr>
<tr>
<td>Prominent descents.</td>
<td>Descents not prominent.</td>
</tr>
<tr>
<td>Pulsations sometimes more prominent with abdominal pressure.</td>
<td>No effect of abdominal pressure on pulsations.</td>
</tr>
</tbody>
</table>

**Clinical Differentiation of Venous and Arterial Disease**

<table>
<thead>
<tr>
<th></th>
<th>Arterial</th>
<th>Venous</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td>Ruddy when dependent</td>
<td>Cyanotic when dependent</td>
</tr>
<tr>
<td></td>
<td>Pale when elevated</td>
<td></td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>Cool</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Diminished to absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>Acute Occlusion: Severe to excruciating</td>
<td>Aching</td>
</tr>
<tr>
<td></td>
<td>Chronic Occlusion: Intermittent claudication</td>
<td></td>
</tr>
<tr>
<td><strong>Edema</strong></td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Skin Variations</strong></td>
<td>Thin and shiny</td>
<td>Brown pigmentation at the ankles</td>
</tr>
<tr>
<td></td>
<td>Loss of hair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thick toes</td>
<td></td>
</tr>
<tr>
<td><strong>Ulcerations</strong></td>
<td>Toes</td>
<td>Side of ankles</td>
</tr>
<tr>
<td></td>
<td>At the site of traumatic injury</td>
<td></td>
</tr>
</tbody>
</table>
A Closer Look at Beta Blockers
Decreases Myocardial Oxygen Demand

- Decrease HR
  - $\beta_1$ blockade

- Decrease Contractility
  - $\beta_1$ blockade

Blood pressure = CO x SVR
Beta Blockers

- **Nonselective: Block both Beta \(_1\) and Beta \(_2\)**
  - Propranolol (Inderal)
  - Timolol (Blocadren)
  - Nandolol (Corgard)
  - Sotolol (Betapace)
  - Labetolol (Normodyne, Trandate) (also alpha blockade)
  - Carvedilol (Coreg) (also alpha blockade)

- **Cardio selective: Block Beta 1**
  - Acebutolol (Sectral)
  - Metoprolol tartrate (Lopressor)
  - Metoprolol succinate (Toprol XL)
  - Atenolol (Tenormin)
  - Esmolol (Breviblock)
  - Bisoprolol (Z Beta)
  - Nebivolol (Bystol) (also nitric oxide vasodilatory properties)

Beta Blockers in a STEMI

- **DO NOT** administer in acute presentation IF:
  - STEMI precipitated by cocaine
    - Risk of exacerbating coronary spasm
  - Heart blocks
    - 1\(^{st}\) degree AV block with PR \(\geq 0.24\) sec
    - 2\(^{nd}\) or 3\(^{rd}\) degree AV block
  - Heart rate < 60 BPM
  - SBP < 100 mm Hg
  - Moderate LV failure is present (signs of HF or shock)
  - Active asthma or reactive airway disease
Beta Blockers

Recommended by Disease State: Mortality Reduction

- **Post MI**
  - Atenolol
  - Carvedilol
  - Metoprolol
  - Propanolol
  - Timololol

- **Heart Failure**
  - Bisoprolol
  - Carvedilol
  - Metoprolol Succinate (XL)

Renin-Angiotensin System

\[
\downarrow \text{Renal Flood Flow} \\
\downarrow \\
\text{Renin release} \\
\beta \text{ blockers} \\
\text{Angiotensinogen} \rightarrow \text{Angiotensin I} \quad \text{(converting enzyme)} \\
\text{Angiotensin II} \quad \text{Angiotensin Receptor Blockers} \\
\text{Vasoconstriction} \rightarrow \text{Aldosterone release} \quad \text{Aldosterone Blockers} \\
\uparrow \text{Na}^+ \& H_2O \text{ retention} \\
\uparrow \text{BP}
\]
A Closer Look at ACE Inhibitors and Angiotensin II Receptor Blockers

- Angiotensin-converting enzyme inhibitors ("pril" medications)
  - Captopril, Enalapril, Lisinopril, Quinapril, Ramipril, Benazepril, Fosinopril

- Angiotensin II Receptor Blockers ("sartan" medications)
  - Losartan, Irbesartan, Candesartan, Telmisartan, Valsartan, Eprosartan

A Closer Look at ACE Inhibitors

- ACE Inhibitors impact afterload and preload because they block the vasoconstrictive effects of angiotensin II
  - Very important in reducing workload of left ventricle in systolic dysfunction
  - Decrease systemic vascular resistance without reflex stimulation of heart rate and contractility

- ACE Inhibitors additionally assist with preload reduction by blocking the effects of aldosterone release
A Closer Look at ACE Inhibitors

• Reduce mortality in patients with systolic heart failure

• Reduction of left ventricular mass in LV hypertrophy

• Slows progression of renal disease in diabetes and hypertensive nephrosclerosis

ACE Inhibitors and Renal Function

• Can cause acute renal failure in patients with bilateral renal artery stenosis
  – Dilation of efferent glomerular arterioles with no ability to dilate afferent arterioles which results in decreased glomerular filtration

• Can cause bump in creatinine when initiated in patients with heart failure due to prevention of compensatory efferent vasoconstriction
  – Creatinine can be allowed to be 35% above baseline without stopping the drug.
ACE Inhibitors and GFR

Cough in ACE-I

- Influences bradykinin and can produce cough
- Cough is side effect in 10-20% of patients
- Need to assure cough is not sign of worsening heart failure
- Patient may need changed to ARB

Absolute Contraindication: Oral Angioedema!
ACE Inhibitor

- Assess renal function and potassium within 1 to 2 weeks of initiation if outpatient
  - High risk features: diabetes, hyponatremia, hypotension, azotemia, potassium supplementation, combination with aldosterone antagonist.

- Cautions/Contraindications
  - Bilateral renal artery stenosis
  - Creatinine > 3 mg/dL
  - Potassium > 5.0 mEq/L
  - Systolic BP < 80 mmHg

Note * difference between AKI (hold regardless of creatinine) and CKD may give until creatinine of > 3.0)

ESRD: ACE Inhibition ok. SBP most often limiting factor. Need reasonable SBP for dialysis.

Clinical Effects of Aldosterone

- Promotes retention of sodium
- Promoted loss of potassium and magnesium
- Potentiates catecholamines
- Inhibits the parasympathetic nervous system
- Decreases arterial compliance
- Promotes direct remodeling
- Has prothrombotic properties
- Causes vascular inflammation and injury
**Spironolactone (Aldactone)**

- Non selective aldosterone blocker
  - Blocks aldosterone and androgen; stimulates progesterone
  
  Major side effect: gynecomastia, sexual dysfunction and menstrual problems due to non selectivity

- Hyperkalemia – especially when used with ACE Inhibitor or ARB

- Hold: Creatinine of 2.5 in men / 2.0 in women

- Mortality reduction

**Eplerenone (Inspra)**

- Selective aldosterone receptor antagonist

  Eliminates most gynecomastia and sexual side effects associated with aldactone

- Side effect of hyperkalemia when used with ACE Inhibitor or ARB

- Indicated in MI with LV Dysfunction
  - Prevent progression of heart failure
  - Prevent sudden cardiac death
  - Prevent recurrent MI
A Closer Look at Calcium Channel Blockers

**Note:** Not all calcium channel blockers are created equal: therefore not all calcium channel blockers have the same actions.

<table>
<thead>
<tr>
<th></th>
<th>Verapamil</th>
<th>Dihydropyridines</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart Rate</strong></td>
<td>▼▼</td>
<td>▲</td>
<td>▼</td>
</tr>
<tr>
<td><strong>AV Nodal Conduction</strong></td>
<td>▼▼</td>
<td>======</td>
<td>▼</td>
</tr>
<tr>
<td><strong>Contractility</strong></td>
<td>▼▼</td>
<td>▼</td>
<td>▼</td>
</tr>
<tr>
<td><strong>Arterial Vasodilatation</strong></td>
<td>▲▲</td>
<td>▲▲▲▲</td>
<td>▲</td>
</tr>
</tbody>
</table>
Amlodipine (Norvasc)

- Effects vascular smooth muscle with minimal to no effect on heart rate or conductivity
- Good decrease in total peripheral vascular resistance
- Directly dilates coronary arteries (nitric oxide release)

Alpha1 Adrenergic Blockers

- Terazosin (Hytrin) and Prazosin (Minipress) have the potential for a significant first dose hypotension and syncope, particularly in the elderly
  - Hyponatremia worsens hypotensive episodes
  - * First dose should be taken at bedtime and patient warned to use extreme caution if getting out of bed
  - These are not first choice medications and are reserved for refractory hypertension
- Alpha blockers (Prazosin, Terazosin, Doxazosin) are not recommended as first line antihypertensive therapy in the elderly
Central Anti-Adrenergics

- Clonidine, moxonidine
- Not a first line agent
- Sedation (particular concern in elderly)
- Bradycardia
- Abrupt discontinuation leads to hypertension and tachycardia

Direct Smooth Muscle Relaxers

- Hydralazine, minoxidil
- 4th line anti hypertensive agents
- Only used as part of combination therapy
- Concerns:
  - Tachycardia
  - Fluid accumulation (Minoxidil)
  - Atrial arrhythmias (Minoxidil)
Direct Renin Inhibitors

**Aliskiren (Tekturna)**
- FDA approved as antihypertensive
- Angioedema is potential serious adverse reaction
- Monitor potassium and renal function
- May increase uric acid levels
- Not studied in significant renal impairment
  - Creatinine > 1.7 in women or 2.0 in men and/or estimated GFR < 30 mL/min

Loop Diuretics

- Work in ascending loop of Henle
- Loss of H2O, K+, Na+, Cl-, H+
- More loss of H2O and less K+ and Na+ than thiazides
- Promotes venous vasodilatation
- Rapid onset and short duration
- Can be effective in presence of renal failure
- High ceiling diuretic
Loop Diuretics

<table>
<thead>
<tr>
<th>Bumetanide (Bumex)</th>
<th>Furosemide (Lasix)</th>
<th>Torsemide (Demadex)</th>
</tr>
</thead>
</table>

- Equivalents
  - Furosemide 40 mg
  - Torsemide 20 mg
  - Bumetanide 1 mg

- Dosing
  - Adequate to relieve symptoms
  - Start equal or greater than home maintenance dose
Differences in Loop Diuretics

<table>
<thead>
<tr>
<th>Bumetanide</th>
<th>Furosemide</th>
<th>Torsemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of randomized control data with comparison to furosemide.</td>
<td>BID Dosing when GFR is low</td>
<td>2 randomized trials comparing Torsemide and Furosemide N=471</td>
</tr>
<tr>
<td>Better pharmacokinetic profile (oral bioavailability) than furosemide but turosemide has evidence of more efficacy and more safety. (Wargo &amp; Banta, 2009)</td>
<td></td>
<td>Torsemide associated with reduction in HF and CV readmission in systolic HF with a trend towards reduction of all cause mortality. (DiNicolantonio, 2012)</td>
</tr>
</tbody>
</table>

More on Loop Diuretics

DOSE Trial

- NEJM: Felker et al., 2011

- No significant difference in symptoms or renal function between continuous drip versus intermittent dosing

- Non significant trend toward improvement in symptoms with high dose (IV at 2.5 x PO dose) versus low dose; (IV at same as PO dose) no change in renal function
Thiazide Diuretics

- Inhibit reabsorption of Na+ and Cl–
  - In the distal tubule.
- Delayed onset but longer duration of action than loop diuretics
- Low ceiling diuretics
- Less potent diuretic than loop diuretics
- Diminished effectiveness in presence of renal failure

<table>
<thead>
<tr>
<th>Thiazide Diuretics</th>
<th>Side effects:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bendrofluazide (Naturetin)</td>
<td>Blood Chemistry changes:</td>
</tr>
<tr>
<td>Benthiazide (Aquatag, Exna)</td>
<td>Hyponatremia (↓ Na+)</td>
</tr>
<tr>
<td>Chlorothiazide (Diyuril)</td>
<td>Hypokalemia (↓ K+)</td>
</tr>
<tr>
<td>Chlorthalidone (Hygroton)</td>
<td>Hypomagnesemia (↓ Mg++)</td>
</tr>
<tr>
<td>Cyclothiazide (Anhydron)</td>
<td>Hyperglycemia (↑ blood sugar)</td>
</tr>
<tr>
<td>Hydrochlorothiazide (HCTZ) (HydroDiuril, Esidrix)</td>
<td>Hyperuricemia (↑ uric acid)</td>
</tr>
<tr>
<td>Hydroflumethazide (Saturon, Diucardin)</td>
<td>Hypercalcemia (↑ Ca++)</td>
</tr>
<tr>
<td>Indapamide (Lozol)</td>
<td>Decreased glomerular filtration in kidneys (↑ BUN, creatinine)</td>
</tr>
<tr>
<td>Metolazone (Zaroxolyn)</td>
<td>↑ cholesterol</td>
</tr>
<tr>
<td>Polythiazide (Renese)</td>
<td>↑ triglycerides</td>
</tr>
<tr>
<td>Trichlormethazide (Metahydrin, Naqua)</td>
<td>↓ HDL cholesterol</td>
</tr>
<tr>
<td>Other side effects:</td>
<td></td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td></td>
</tr>
<tr>
<td>Gout</td>
<td></td>
</tr>
<tr>
<td>Impotence</td>
<td></td>
</tr>
<tr>
<td>Ventricular arrhythmias (↓ K+)</td>
<td></td>
</tr>
<tr>
<td>Nausea, dizziness, headache</td>
<td></td>
</tr>
</tbody>
</table>
The Clotting Cascade

- **The Common Pathway**
  - Prothrombin is converted to thrombin
  - Thrombin permits fibrinogen to be converted to fibrin
  - Result is fibrin stable clot (red clot)
A Closer Look at Heparin

- Antithrombin activator that inhibits factors Xa and IIa
- **Prevents conversion of prothrombin to thrombin by binding to antithrombin III**
- Antithrombin III naturally inhibits Xa and thrombin; when heparin binds with it the inhibition is increased 1000 times
- Neutralizes the clotting capabilities of thrombin
- Works in the intrinsic and common pathway
- Also inhibits platelets (thrombin is most potent platelet stimulator)
- Anticoagulation is almost instant
- ½ life relatively short
- Antidote: Protamine 1 mg per 100 units

More About Heparin

- Must monitor safety and efficacy
  - aPTT (activated partial thromboplastin time): Goal is aPTT 1.5 Xs the control
  - Unfractionated heparin levels by anti-Xa activity: 0.3 to 0.7 IU/mL
- Weight based heparin dosing reaches goal 90% of time compared to 77% with standard therapy
- Baseline aPTT, PT/INR, platelets and CBC
- Increased bleeding can occur with renal failure
  - Heparin has dual clearance mechanism but
Complications of Heparin

- **Bleeding**

- **Mild thrombocytopenia**
  - Mild thrombocytopenia occurs in 10-20% of patients

- **Severe thrombocytopenia occurs in 1-2% of patients**
  - Heparin Induced Thrombocytopenia (HIT) or Heparin Induced Thrombocytopenia with Thrombosis (HITT)
  - Platelet aggregation resulting in venous or arterial thrombosis
  - Determining patients at risk is unpredictable
  - Generally occurs 5 to 10 days after initiation of heparin
    - Could be sooner if recent exposure to heparin
  - Severe thrombocytopenia is due to an immune response

**More on HIT / HITT**

- **Immune system forms antibodies against heparin when heparin is bound to the protein platelet factor 4 [PF4]**
  - PF4 antibodies formed in many people receiving heparin
    - Not necessarily associated with thrombocytopenia or thrombotic risk
    - Can disappear 3 months after exposure - antibody does not persist for longer than 3 months
  - First test ELISA
    - All PF4 antibodies detected in ELISA testing – not just those associated with HIT/HITT
  - Confirmatory test is washed platelet assay test

- **HIT antibodies are usually IgG class**
  - Take 5 days to form
  - Antibodies form a complex with heparin and PF4, tail of antibody binds to a protein on the platelet – this results platelet activation and increased thrombin generation

- Called HITT (heparin induced thrombocytopenia and thrombosis)
- Called HIT (heparin induced thrombocytopenia) when there is not associated thrombosis
Treatment of HIT / HITT

1. Discontinue and avoid all heparin.
2. Give a non-heparin alternative anticoagulant: Direct thrombin inhibitors (argatroban).
3. Postpone warfarin pending substantial platelet count recovery (give vitamin K if warfarin has already been started). Warfarin is associated with protein C deficiency and increased risk for microthrombosis – warfarin necrosis.
4. Avoid platelet transfusions – leads to platelet activation.
5. Test for HIT antibodies (ELISA and washed assay)

Low Molecular Weight Heparin

- Enoxaparin, dalteparin, tinzaparin, and nadroparin
- Smaller in size
- Antithrombin by inhibiting factor Xa
- Causes less inactivation of thrombin and less inhibition of platelets and less bleeding than standard heparin
- Does not significantly influence bleeding time
- Anti Xa levels can be drawn 4 hours after SQ dose
- Renal failure results in increased risk of bleeding because LMWH is renally cleared
  - Special dosing for chronic renal insufficiency with enoxaparin
Benefit of Low Molecular Weight Heparin over Unfractionated Heparin

- More predictable anticoagulant response
- Lower incidence of heparin induced thrombocytopenia
- No need to monitor APTT
- Less platelet activation
- Can be self administered with Sub – Q administration
- ½ life 4-6 hours
- Protamine reverses 60% of drug effect

Administration of Enoxaparin

- Full length of 27 gauge ½ needle (prepackaged) should be injected
- Skin fold held until needle withdrawn
- Use anterolateral or posterorlateral walls of abdomen
- Rotate sites frequently
- Do not massage site
- Prevention of DVT
  - 40 mg daily in most situations
  - 30 mg daily for renal adjustment (CR Clearance < 30 ml/min)
- Venous thrombosis / DVT
  - 1mg/kg BID or 1.5 mg/kg daily depending of specific circumstances
- Unstable Angina / NSTEMI (or as adjunct in STEMI)
  - 1 mg/kg BID
  - IV dosing can be used in STEMI
- Embolism with Atrial Fib
  - 1 mg/kg BID

Dosing adjustments are required in several renal impairment
Direct Thrombin Inhibitor

- Indicated for patients with HIT
- **Approved in Non STEMI guidelines and for PCI**
- Ability to inactivate fibrin bound thrombin
- Less binding to plasma proteins, therefore more reliable anticoagulation effect
- Examples
  - Lipirudin and desirudin (hirudin)
  - Argatroban
  - Bivalirudin* (Angiomax)

Synthetic Factor Xa Inhibitor

- Fondaparinux (Arixtra)
  - Used for venous thromboembolism and PE
  - Approved for DVT prophylaxis in certain surgical patients
  - Approved and added to NonSTEMI Guidelines
    - **Cannot be used as sole anticoagulant during PCI**
- Neutralizes Factor Xa and interrupts the clotting cascade
- Does not inhibit thrombin
- No reported HIT
- Sub Q injection (initial dose IV)
- Once daily dosing (fixed dose can cover a range of body weights – lower dose for low body weight)
- Contraindicated in severe renal dysfunction
- No laboratory monitoring
- No antidote (Recombinant factor VIIa can help reverse anticoagulation effect)
Oral Antiplatelet Therapy

- ASA
- Clopidogrel (Plavix)
  - 600 mg initial dose
  - 75 mg daily
- Prasugrel (Effient)
  - 60 mg initial dose
  - 10 mg daily
- Ticagrelor (Brilinta)
  - 180 mg initial dose
  - 90 mg twice daily

P2Y$_{12}$ Receptor Inhibitors

- Thienopyridines
  - Clopidogrel
  - Prasugrel

- Non thienopyridine
  - Ticagrelor
Thienopyridines

- Thienopyridines are a class of adenosine diphosphate (ADP) / P2Y\textsubscript{12} receptor blockers
  - Clopidogrel (Plavix)
  - Prasugrel (Effient)
- Thienopyridines
  - ADP Receptor blockers
    - Adenosine Diphosphate (ADP) - Stored in platelets and released upon platelet activation.
    - ADP interacts with P2Y\textsubscript{12} chemoreceptors to enhance adhesiveness and aggregation of platelets through the activation of the GP IIb/IIIa pathway
    - Irreversibly inhibits P2Y\textsubscript{12} receptor
    - Referred to as platelet inhibitors

Clopidogrel and Non Responders

- ACCF/AHA Clopidogrel Clinical Alert
- FDA Boxed Warning March 2010
- Role of genotype testing or routine platelet function testing
  - Class II b recommendation pending results of randomized controlled clinical trials.
- Prodrug
  - 2 step process
  - Involves several CYP450 isoenzymes
    - CYP2C19 isoenzyme responsible for almost half of the first step formation
    - 3 major genetic polymorphisms are associated with loss of function
    - Observational studies have shown an association between an increased risk of adverse cardiovascular events and the presence of one nonfunctioning allele
Clopidogrel and PPIs

- Using proton pump inhibitors (PPIs) and antiplatelet drugs (thienopyridines) together is an appropriate way of treating patients with cardiovascular (CV) disease who are at high risk of upper gastrointestinal (GI) bleeds, despite recent concerns about an adverse interaction between these two types of drugs, according to an *Expert Consensus Document released jointly today by the American College of Cardiology (ACC), the American College of Gastroenterology (ACG), and the American Heart Association (AHA)*.

Clopidogrel and PPIs
2012: World Journal of Gastroenterology

- Because PPI induced risk reduction clearly overweighs the possible adverse cardiovascular risk in patients with high risk of gastrointestinal bleeding, combination of clopidogrel with the less CYP2C19 inhibiting pantoprazole should be recommended.

- Several pharmacodynamic studies found a significant decrease of the clopidogrel platelet antiaggregation effect for omeprazole, but not for pantoprazole.
- More recent RCT and retrospective co-hort studies have not resulted in same concerns with PPIs as observational studies suggested.
Take Away Prasugrel Points

- Greater anti-ischemic protection
- Less concern with PPI administration
- Less concern regarding non responders
  - Prodrug but not as dependent on CYP2C19 isoenzyme
- Only used in patients with planned PCI
- Increased bleeding risk
- Cannot be used:
  - ≥ 75 years old
  - ≤60 KG
  - Previous CVA / TIA

Take Away Ticagrelor Points

- PLATO trial
  - Better anti-ischemic effect compared to clopidogrel
  - No significant increase in major bleeding
  - Faster onset and shorter duration than clopidogrel (known as reversible mode of action)
  - BID dosing is a potential concern for compliance
  - North American effect – thought to be due to higher dose ASA
  - Although shorter ½ life – recommendation to be held 5 days before surgery.

Anticoagulants in Atrial Fibrillation: Warfarin

- Target INR of 2.0-3.0 in most patients
- Target INR adjusted in those with mechanical heart valve – at least 2.5
- It takes 4-5 days to reach a therapeutic level.
  - Can have initial transient hypercoagulable state
  - Must be overlapped with heparin
- Chronic conditions require lifelong therapy
- **Bridging**: Mechanical valve, recent stroke / TIA/ CHADS₂ 5 or 6
- Acute conditions (PE, DVT) usually require at least six months of therapy

A Closer Look at Warfarin

- Inhibits the synthesis of prothrombin

- Acts indirectly through the liver by altering the synthesis of vitamin K dependent factors in the extrinsic pathway. The vitamin K dependent factors are left biologically inactive
More About Warfarin

- PT (prothrombin time monitored to evaluate effectiveness and safety)
- PT – problems with standardization of anticoagulation intensity
- INR (International Normalized Ratio) – relates the patients PT to the intensity of actual coagulation.

- **Dosing**
  - Start with 5mg per day
  - Loading doses not recommended
  - PT / INR daily until therapeutic level reached
  - Dosage may need adjusted after 4-6 days due to individual sensitivity
  - PT / INR twice weekly for 2 weeks and weekly for two months
  - PT / INR every 4-6 weeks after dose stable

Nursing Considerations with Warfarin

- Many many drugs interact with coumadin to alter PT
- Consistency in diet is important especially with known high vitamin K foods (green vegetables)
- Patient compliance is critical

- Antidote: Vitamin K
- Fresh frozen plasma if severe hemorrhage
- Recombinant factor VIIa is also an option for life threatening bleeding
Dabigatran (Pradaxa)

- Oral direct thrombin inhibitor
  - Is a prodrug (dabigatran etexilate) that is converted in liver to active form
  - Eliminated mostly by kidneys (reduced dose for moderate renal failure, not recommended in severe renal failure)
- Approved for reduction of stroke in patients with AF at intermediate or high risk of stroke.
- RE-LY trial (Connolly et al, 2009)
- Predictable dose-response relationship so no lab monitoring of coagulation status needed
- Drug to drug interactions still exist
- No antidote
- GI bleeding risk of concern
- Dose:
  - 150 mg PO BID
  - 75 mg PO BID with creatinine clearance 15 to 30 mL/minute
    • These patients and this dose not tested in clinical trials

Rivaroxaban (Xarelto)

- Oral direct factor Xa inhibitor
  - Dose 20 mg PO daily
  - Should be taken with food
  - Hepatic and renal excretion
    • Contraindicated in severe renal failure
- Predictable dose-response relationship so no lab monitoring needed
- ROCKET AF (Patel et al., 2011)
- Tested in nonvalvular atrial fibrillation with increased stroke risk
- No difference in major bleeding but less intracranial and fatal bleeding
Apixaban (Eliquis)

• Oral factor Xa inhibitor
• 25% renal excretion
• Dose: 5 mg BID
• Dose: 2.5 mg BID
  – Creatinine > 1.5 mg/dL and either
  – Age > 80 years
  – Weight ≤ 60 kg
• ARISTOTLE (Granger et al., 2011.)
• Less major bleeding than warfarin

Nitroglycerin

• Minimal mortality benefit
  – Nitrates may be more helpful in patients > 70 years in reduction of death and heart failure @ 6 month follow up
• Symptom benefit
  
Mortality reducing agents should always take precedence over non mortality reducing agents: I.E. Beta blockers precede nitrate use

• Mixed venous and arterial vasodilator
  – Dosage < 1mcg/kg/min = venous vasodilator
    • Decrease preload
  – Dosage > 1mcg/kg/min = arterial and venous vasodilator
    • Decrease preload and afterload
  – Sublingual tablets provide high enough dosage to dilate arteries and veins
    • Decrease preload and afterload
Nitrate Contraindications

- Systolic BP < 90 mm Hg or ≤ 30 mm Hg below baseline
- Bradycardia < 50 BPM
- Tachycardia > 100 BPM (in absence of clinical HF)
- Right ventricular infarct
- Within 24 hours of sildenafil
- Within 48 hours of tadalafil

Question female patients: Pulmonary HTN

Nitroglycerin

- **Side Effects:** H/A, Hypotension, flushing
  
  Treat H/A with pain meds and decrease dose
  - Pain activates the SNS

- **Caution:** Severe diastolic dysfunction
  - Hypertrophic cardiomyopathy
  - Severe aortic stenosis
SL NTG Instruction Post Discharge

- No more than 1 dose of SL NTG
  - If chest discomfort is unimproved or is worsening 5 min after 1 NTG call 9-1-1 immediately before taking additional NTG.
  - May take additional NTG while waiting for EMS.
  - Chew ASA while waiting for EMS.

- In chronic stable angina if symptoms are significantly improved by 1 dose of NTG may repeat NTG every 5 min for a maximum of 3 doses and call 9-1-1 if symptoms have not resolved completely.

Digoxin

- Inhibits the NA+ and K+ membrane pump
- Increase in intracellular Na+
- Enhances the Na+ and Ca++ exchange
- Leads to ▲ in intracellular Ca++
- ▲ inotropic activity
Digoxin

- Increases vagal activity
- Digoxin decreases conduction velocity through the AV node (sympathetic stimulation easily overrides the inhibitory effects of digoxin on AV node conduction)
- The conduction velocity increases in the atria, but decreases in the AV node.
- Automaticity is also increased, in the atria, AV node, Purkinje fibers and ventricles.
  - Calcium channel blockers are replacing digoxin as agent for rate control in atrial arrhythmias
  - Digoxin no better than placebo in converting atrial fibrillation to SR
- Digoxin decreases sympathetic outflow and decreases renin production
  - Beneficial in heart failure

Digoxin

- Has a narrow therapeutic range
- Toxicity may occur at therapeutic levels
- Lower doses now routinely used 0.125 mg daily
- Amiodarone increases serum digoxin concentration (digoxin doses must be reduced if starting amiodarone)
- Multiple other medication interactions
- Dialysis is not effective with digoxin toxicity because of high tissue binding of digoxin
More About Digoxin Toxicity

- **EKG Changes with Toxicity**
  - Increased automaticity with impaired conduction is common (example: PAT with AV Block)

- **Other Signs and Symptoms of Toxicity**
  - N & V, HA, Confusion
  - Visual disturbances: halos, change in color perception

### Antiarrhythmics in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Class</th>
<th>Specific Medications</th>
<th>Purpose of Medication</th>
<th>Major Cardiac Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I A</td>
<td>Disopyramide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes, HF Torse de pointes</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quinidine</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not used in atrial fibrillation</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td>Class I B</td>
<td>Floxainide</td>
<td>Rhythm Control</td>
<td>Ventricular tachycardia, HF, Atrial Flutter</td>
</tr>
<tr>
<td>Class I C</td>
<td>Flecainide</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Propafenone</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>Beta Blockers</td>
<td>Rate Control</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>Amiodarone</td>
<td>Rhythm / Rate Control</td>
<td>Torsade de pointes (rare) * Organ toxicity</td>
</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dofetilide</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ibutilide</td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sotalol (Also contains beta blocker)</td>
<td>Rhythm Control (also controls rate)</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>Calcium Channel Blockers</td>
<td>Rate Control</td>
<td></td>
</tr>
</tbody>
</table>
Class I: Na⁺ Channel Blockers

Class III: K⁺ Channel Blockers

Class IV: Calcium Channel Blockers

ECG complex

QRS complex

T wave

Marked prolongation of refractory period (prolong QT interval).

Slow conduction (widen QRS).

Some prolongation of refractory period (prolong QT interval).
Antiarrhythmic Medications Effecting the Action Potential

- **Class I** – Fast sodium channel blockers
  - IA: Quinidine, Procainamide, Disopyramide
  - IB: Lidocaine, Mexiletine, Tocainide
  - IC: Flecainide, Propafenone
- **Class III** – Potassium channel blockers
  - Amiodarone, Ibutilide, Dofetilide, Sotalol
- **Class IV** – Calcium channel blockers
  - Verapamil, Diltiazem

**Class I C Antiarrhythmics**

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Potent inhibition of fast sodium channel; decrease in maximal rate of phase 0 depolarization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Slow His-Purkinge conduction and cause QRS widening; QT intervals are also usually prolonged</td>
</tr>
<tr>
<td></td>
<td>No effect on refractory period</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic effects</td>
</tr>
<tr>
<td>Uses</td>
<td>Life threatening ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Conversion to SR (Flecainide)</td>
</tr>
<tr>
<td>Drugs</td>
<td>Flecainide (Tambocor)</td>
</tr>
<tr>
<td></td>
<td>Moricizine (Ethmozine)</td>
</tr>
<tr>
<td></td>
<td>Propafenone (Rhythmol)</td>
</tr>
</tbody>
</table>

422
### Class I C Antiarrhythmics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
</table>
| Flecaïnide (Tambocor) | Not a first line agent for ventricular arrhythmias  
Will slow conduction over accessory pathways in WPW tachycardias  
Used in atrial fibrillation (pill in the pocket)  
CAST Trial: propensity for fatal proarrhythmic effects  
Not used post MI or with depressed LV function |
| Moricizine (Ethmozine) | CAST studies: Reserved for life threatening ventricular arrhythmias  
Has properties of class I B also |
| Propafenone (Rhythmol) | Used in supraventricular arrhythmias and life threatening ventricular arrhythmias  
Also has small beta blocking actions and calcium channel blocking effects that can worsen HF  
Must be initiated in hospital setting to monitor ECG |

### Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Inhibits potassium ion fluxes during phase II and III of the action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Directly on myocardium to delay repolarization (prolongs QT); prolongs effective refractory period in all cardiac tissue; By definition act only on repolarization phase and should not impact conduction</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic Effects (amiodarone less)</td>
</tr>
<tr>
<td>Uses</td>
<td>Drug dependent</td>
</tr>
</tbody>
</table>
| Drugs            | Amiodarone (Pacerone, Cordorone)  
Dronedarone (Multaq)  
Ibutilide (Corvert) – pure class III  
Dofetilide (Tikosyn) – pure class III  
Sotalol (Betapace) |
Class III Antiarrhythmics

| Amiodarone (ARREST Trial) | Approved for life threatening refractory ventricular arrhythmias; considered before lidocaine in pulseless VT or V fib; considered ahead of lidocaine for stable VT with impaired cardiac function; expanded to atrial and ventricular arrhythmias, conversion and maintenance of atrial fib
| Use in atrial fibrillation is off label |
| Slows conduction in accessory pathways |
| Originally marketed as anti-anginal (potent vasodilator) |
| Relaxes smooth and cardiac muscle, reduces afterload and preload (well tolerated in heart failure and cardiomyopathy) |
| Proarrhythmias less frequent |
| Is also a weak sodium channel blocker, also has effects similar to class II and IV, also has anticholinergic properties |

More on Amiodarone

- Peripheral IV concentration not to exceed 2mg/ml

- Oral administration = GI symptoms
Potential Extra Cardiac Effects

<table>
<thead>
<tr>
<th>Pulmonary toxicity without initial symptoms / Potentially lethal interstitial pneumonitis /</th>
<th>Photosensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity</td>
<td>Corneal micro deposits</td>
</tr>
<tr>
<td></td>
<td>Optic neuropathy / neuritis</td>
</tr>
<tr>
<td></td>
<td>Thyroid dysfunction</td>
</tr>
</tbody>
</table>

Toxic side effects increase with length of use and increased dose

Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Ibutilide (Corvert)</th>
<th>Indicated for rapid conversion of atrial fib or flutter to sinus rhythm; IV use only; also facilitated cardioversion (Don’t convert atrial fib or flutter of duration without anticoagulation) Rather than blocking outward potassium currents – promotes influx of sodium through slow inward sodium channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dofetilide (Tykosin)</td>
<td>More “pure” class III agent Conversion to and maintenance of SR in A fib and flutter Reserved for very symptomatic patients, monitored 3 days in hospital Widens the QT; cannot be given with many other drugs (prolong QT or inhibit metabolism or elimination); no negative inotropic effects, neutral effect on mortality from arrhythmias post MI and in in HF, can be used in this population to prevent worsening HF from atrial fib</td>
</tr>
</tbody>
</table>
Simultaneous 2-lead ECG (leads II and V1) showing initiation and termination of torsade de pointes in patient in AF after ibutilide infusion.


Class III Antiarrhythmics

| Sotalol (Betapace<sup>R</sup>) (Betapace<sup>AF</sup>) | Used in atrial arrhythmias and life threatening ventricular arrhythmias  
Indicated for stable monomorphic VT or Polymorphic VT with normal QT in ACLS protocol  
Non selective beta blocking agent with class III properties  
Significant class III effects are only seen at doses > 160 mg  
Proarrhythmic potential (prolonged QT)  
More effective in preventing reoccurring arrhythmias than several other drugs |

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Dronedarone

• Similar to amiodarone without iodine component and less fat soluble
• Class III antiarrhythmic (K⁺ channel blocker) with effects from all four classes
• **Less effective than amiodarone at maintaining sinus rhythm but also less toxic**
• Elimination half-life 13-19 hours
• Has both rate and rhythm control effects but is primarily indicated for rhythm control
• May reduce incidence of stroke (mechanism uncertain)

Dronedarone (ATHENA)

• Approved for maintenance of sinus rhythm in patients with history of paroxysmal or persistent AF or flutter with EF > 35% who are in sinus rhythm or will be cardioverted
• Dose: 400 mg PO bid with meals
  – Avoid grapefruit juice
  – Multiple drug interactions
• **Contraindicated in patients with NYHA Class IV HF or NYHA Class II-III HF with recent decompensation requiring hospitalization or referral to a specialized HF clinic**
  – > twofold increase in mortality in HF patients
• Side Effects
  – GI, skin disorders
  – Can prolong QTc but low risk of Torsades
  – Interferes with digoxin metabolism

Concern: LIVER Dysfunction: 1/2011
CVN Review Course

**QT MONITORING AND TORSADES**

Expected QTc Intervals

<table>
<thead>
<tr>
<th></th>
<th>1 to 15 Years</th>
<th>Adult Males</th>
<th>Adult Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; .44 seconds</td>
<td>&lt; .43 seconds</td>
<td>&lt; .45 seconds</td>
</tr>
<tr>
<td>Borderline</td>
<td>.44 to .46 seconds</td>
<td>.43 to .45 seconds</td>
<td>.45 to .47 seconds</td>
</tr>
<tr>
<td>Prolonged</td>
<td>&gt; .46 seconds</td>
<td>&gt; .45 seconds</td>
<td>&gt; .47 seconds</td>
</tr>
</tbody>
</table>


QTc .50 sec (500 msec or more is dangerous and should be considered an ominous sign of impending Torsade's de Pointes.
U Waves and Biphasic T waves.

Measurements are using seconds.

$$QTc = \frac{QT \text{ Interval}}{\sqrt{R-R \text{ Interval}}}$$

- Bazett Formula
  - Formula not reliable at slow rates (under estimates); over estimates QT interval at fast HRs

- QT Dynamics
  - Linear regression analysis
Practicing the Bazett Formula

- **HR 70**
  - QT = .43 sec
  - R to R = .84 sec
  - .43 / .9165 = QTc .469

- **HR 38**
  - QT = .80 sec
  - R to R = 1.56 sec
  - .80 / 1.28 = QTc .641
Torsade's De Pointes

- Recognition of this life-threatening arrhythmia is important because it is not treated like other VTs
- Two groups: Acquired and congenital
- Acquired
  - Drugs prolonging repolarization
    - Most often as a result of blocking the potassium channel
  - Electrolyte abnormalities
    - Low potassium
    - Low magnesium
  - Severe bradycardias / pauses

More on Drugs that Prolong Repolarization (blocking of potassium channel efflux)

- www.QTdrugs.org
- www.torsades.org

- Class Ia and Class III antiarrhythmics
- Antihistamines
- Antibiotics
- Antipsychotics
- Antidepressants
- Sedatives
- Gastric motility agents
- Anticancer agents
- Opiate agonists

✔ Risk
✔ Possible Risk
✔ Conditional
Other Risk Factors for Torsade's de Pointes

- Rapid (IV) administration of QT prolonging agent
- Renal or hepatic dysfunction
- Female gender (particularly for drug induced)
- Advanced age
- Anorexia
- Heart disease
- Poly pharmacy
Warning signs for Torsades de Pointes

- Increase QTc from predrug baseline of 60 ms,
- Marked QTc interval prolongation .500 ms
- T-U wave distortion that becomes more exaggerated in the beat after a pause
- Visible (macroscopic) T-wave alternans
- New-onset ventricular ectopy, couplets
- Nonsustained polymorphic ventricular tachycardia initiated in the beat after a pause.
Torsade's de Pointes

- **Class I**
  - Discontinue offending drugs
    - Note: Class IA drug induced TdP usually appears soon after the initial administration of the drug
  - Correct electrolytes
    - Magnesium
    - Potassium
  - Increase HR
    - Isoproterenol
      - 2 mcg/min then titrate to HR of 100 beats per minute
    - Temporary pacing at rate of 100 to 110
    - Permanent pacing if bradycardia or CHB cannot be resolved.

- Defibrillation if sustained
  - However, continue to assess for and treat cause

More on Magnesium in Torsade's de Pointes

- 2 Gm IV bolus over 1-2 minutes
  - Followed in 15 minutes by another bolus if necessary
  - May start continuous infusion at rate of 3-20 mg/min
- Benefit occurs without shortening of QT interval and in presence of normal Magnesium level

Magnesium is considered treatment of choice.
Pulling It All Together

Q & A

A FINAL THOUGHT
MY PERSONAL VISION FOR PRACTICE

Impact every patient and family on their journey and provide safe passage by meeting them where they are, connecting with them in a meaningful way, and delivering care with wisdom and intention.

- Karen
Reflection and Gratitude