Chapter 19

Vasopressors, Inotropes, and Antiarrhythmic Agents

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Cardiovascular System

- Factors affecting blood pressure
  - Systolic blood pressure (SBP)
  - Diastolic blood pressure (DBP)
  - Mean arterial pressure (MAP)
    - Drives blood into tissues over entire cardiac cycle
    - CO x SVR, where CO is cardiac output and SVR is systemic vascular resistance
  - CO
    - Blood leaving heart with each contraction
    - HR x SV, where HR is heart rate and SV is stroke volume
  - Summary equation
    - MAP = HR x SV x SVR

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Cardiovascular System (cont'd)

- Pulmonary artery catheter
  - Used to monitor patient response to vasoactive therapy
  - Used to determine cause of hypotension
- ***Fluids*** are first-line therapy for hypotensive episodes

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Agents Used in the Management of Shock

- Catecholamines
  - Norepinephrine (Levophed) and epinephrine (Adrenalin)
    - Endogenous catecholamines secreted by adrenal medulla
    - Net response is vasoconstriction and tachycardia

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Agents Used in the Management of Shock (cont'd)

- Isoproterenol (Isuprel)
  - Synthetic catecholamine
  - Treat symptomatic bradycardia and torsades de pointes
  - β-Receptor agonist
  - Pronounced inotropic and chronotropic effects

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Agents Used in the Management of Shock (cont'd)

- Dopamine (Inotropin)
  - Endogenous catecholamine
  - Precursor to norepinephrine
  - Vasopressor dose: 5 to 20 μg/kg/min
  - Stimulates β receptors
  - Chronotropic and inotropic effects
  - Careful: Increases afterload and myocardial O_2 demand

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Agents Used in the Management of Shock (cont'd)

- Phenylephrine (Neo-Synephrine)
  - Purely an α agonist
  - Induces vasoconstriction
  - Elevates SBP and DBP
  - Aortic vasoconstriction may produce a reflex bradycardia

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Agents Used in the Management of Shock (cont'd)

- Vasopressin (Pitressin)
  - Vasopressive and water retention effects
  - a.k.a. antidiuretic hormone
  - Dose: 0.04 unit/min
  - May decrease splanchnic blood flow
    - Not good first choice
    - Not to be used as a lone agent

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Agents Used in the Management of Shock (cont'd)

- Inotropic agents
  - Dobutamine (Dobutrex)
    - For short-term treatment of heart failure secondary to depressed contractility
    - Adverse effects: tachyphylaxis, tachycardia, hypotension, increased O_2 demand
    - (R)-Isomer
    - (S)-Isomer

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Agents Used in the Management of Shock (cont'd)

- Phosphodiesterase inhibitors: inamrinone (Inocor) and milrinone (Primacor)
  - Inotropic vasodilator agents
  - Inhibit intracellular phosphodiesterase
  - Milrinone has shorter half-life
    - Initial bolus 50 µg/kg over 10 minutes
    - Infusion: 0.375 to 0.75 µg/kg/min

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Agents Used in the Management of Shock (cont'd)

- Cardiac glycosides: digoxin (Lanoxin)
  - Management of chronic heart failure
  - Inotropic effect on myocardium
  - Inhibits vagus nerve
  - Generally no hypotensive effects
  - Narrow therapeutic margin

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Electrophysiology of the Myocardium

- Sinoatrial (SA) node initiates electrical activity
  - Generates action potential
  - Depolarized atria
- Atrioventricular (AV) node links activity of atria and ventricle
  - Potential travels to bundle of His, bundle branches, Purkinje fibers

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Electrophysiology of the Myocardium (cont'd)

- Ablation with radiofrequency current
  - Application of radiofrequency current to part of heart causing arrhythmia via catheter
  - Effective when atrial fibrillation (AF) is due to single circuit
  - 30-90% success rate of normal sinus rhythm (NSR) over next year

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Electrophysiology of the Myocardium (cont'd)

- Internal cardioverter-defibrillator
  - Used to cardiovert, terminate ventricular tachycardia (VT), and pace bradycardia
  - Indicated for cardiac arrest secondary to:
    - VT or ventricular fibrillation (VF) that is not reversible/transient
    - Syncope due to VT/VF with no drug tolerance
    - Nonsustained VT in coronary artery disease (CAD), myocardial infarction (MI), left ventricular (LV) dysfunction
    - Generally used if drug therapy will not suffice

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Pharmacology of Antiarrhythmics

- Class IA
  - Block fast Na channels in atrium and block repolarizing K currents
  - Quinidine (Quinaglute)
    - Efficacious in atrial fibrillation/flutter (AF/AFL)
    - Initiate rate-controlling agent first
    - Caution in: asthma, muscle weakness, fever
    - Overdose: respiratory depression, vomiting, diarrhea, seizures, hypotension, syncope, EKG changes

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Pharmacology of Antiarrhythmics (cont'd)

- Procainamide (Pronestyl)
  - Indicated for treatment of VT and torsades de pointes
  - Has proarrhythmic effects
  - May produce leukopenia and agranulocytosis
  - Adverse effects: lupus erythematosus-like syndrome

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Pharmacology of Antiarrhythmics (cont'd)

- Disopyramide (Norpace)
  - Indicated for life-threatening VT and paroxysmal supraventricular tachycardia (PSVT)
  - Should be initiated at hospital
    - Has negative inotropic properties
    - Anticholinergic side effects

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Pharmacology of Antiarrhythmics (cont'd)

- Class IB
  - Lidocaine (Xylocaine)
    - Frequently used to treat ventricular arrhythmia (VA) during cardiac surgery or after MI
    - IV bolus followed by infusion
    - Metabolites formed in liver are seizurogenic
    - Side effects

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Pharmacology of Antiarrhythmics (cont'd)

- Mexiletine (Mexitil)
  - Available in oral formulation
  - Treatment of life-threatening VA
  - Also has anesthetic properties
  - Adverse effects

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Pharmacology of Antiarrhythmics (cont'd)

- Tocainide (Tonocard)
  - Oral congener of lidocaine
  - Used to treat VA, myotonic dystrophy, and trigeminal neuralgia
  - May cause:
    - Pulmonary edema
    - Fibrosing alveolitis
    - Pneumonitis
    - Respiratory arrest
    - Blood dyscrasias

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Pharmacology of Antiarrhythmics (cont'd)

- Class IC
  - Generally not used due to high proarrhythmic potential
  - May be used for supraventricular or ventricular arrhythmias

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Pharmacology of Antiarrhythmics (cont'd)

- Flecainide (Tambocor)
  - Indicated for prevention of paroxysmal AF/AFL, PSVT, and sustained VT
  - Long half-life
  - Shown to contribute to excessive mortality and nonfatal cardiac arrest
  - Clearance affected by urinary pH
    - Acidic pH increases clearance
    - Alkaline pH decreases clearance
  - "Pill in the pocket" approach shown successful

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Pharmacology of Antiarrhythmics (cont'd)

- Propafenone (Rythmol)
  - Prevents PSVT and maintains NSR postcardioversion
  - First-line agent for recent onset AF
  - Nonselective β blocker
    - Use caution with bronchospastic patients

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Pharmacology of Antiarrhythmics (cont'd)

- Class II
  - β Blockers
    - Control AF/AFL and SVT
    - Caution in bronchospastic patients
    - IV and oral
      - Propranolol (Inderal)
      - Metoprolol (Lopressor)
      - Atenolol (Tenormin)
      - Nadolol (Corgard)
    - IV only
      - Esmolol (Brevibloc)

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Pharmacology of Antiarrhythmics (cont'd)

- Class III
  - Amiodarone (Cordarone)
    - Used for ventricular and supraventricular arrhythmias
    - May induce pulmonary toxicity
    - May also cause life-threatening interactions with other prescription, herbal, or OTC medications

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Pharmacology of Antiarrhythmics (cont'd)

- Dofetilide (Tikosyn)
  - Oral formulation
  - Maintenance of NSR after conversion
  - Ineffective in paroxysmal AF
  - Significant risk of VA
  - Treatment must begin with inpatient monitoring
  - Prescriber and pharmacy must be TIPS (Tikosyn in Pharmacy System) participants

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Pharmacology of Antiarrhythmics (cont'd)

- Sotalol (Betapace/Betapace AF)
  - Oral medication
  - Prolongs action potential and relative refractory period
  - Used for ventricular and supraventricular arrhythmias
  - Required 3-day inpatient monitoring

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Pharmacology of Antiarrhythmics (cont'd)

- Ibutilide (Corvert)
  - IV formulation
  - Alternative to cardioversion
  - Indicated for rapid conversion of recent-onset AF/AFL
  - No other class I or III medications within 4 hours!
  - Patients should be adequately anticoagulated before administration

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Pharmacology of Antiarrhythmics (cont'd)

- Class IV
  - Calcium channel blockers (CCBs)
    - Verapamil (Isoptin) and diltiazem (Cardizem)
    - Used in management of supraventricular arrhythmias and ventricular rate control
    - Block Ca channels in AV node
    - Good alternative to β blockers
    - Not favorable in chronic heart failure

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Pharmacology of Antiarrhythmics (cont'd)

- Miscellaneous
  - Digoxin (Lanoxin)
    - AV-blocking and vagotonic properties
    - Prolongs relative refractory period
    - Not a first-line agent for AF
      - 2 hours to maximal effect
      - Less effective than β blockers

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Pharmacology of Antiarrhythmics (cont'd)

- Adenosine (Adenocard)
  - Used to terminate SVT
  - 12-second half-life
  - Use central or brachial line (hold arm up)
  - Flush immediately!
  - Side effects:
    - Bronchospasm
    - Dyspnea
    - Hyperpnea
    - Cough

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Management and Pharmacotherapy of Advanced Cardiac Life Support

- Sudden cardiac death (SCD)
  - Leading cause of death in United States
  - VF, pulseless ventricular tachycardia (pVT), pulseless electrical activity (PEA), or asystole
  - Goals:
    - Restore sinus rhythm
    - Prevent further SCD episodes
    - Prevent neurological damage
    - How?
      - CPR
      - Minimize time to defibrillation

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Management and Pharmacotherapy of Advanced Cardiac Life Support (cont'd)

- Epinephrine
  - Endogenous neurotransmitter
  - 1-mg dose of 10-ml solution
  - Stimulates α_1 receptors
    - Coronary and cerebral vasoconstriction
  - Also has β-adrenergic activity
    - Increases HR and impairs delivery of O_2 to myocardium and CNS
  - Decreased affinity with metabolic acidosis

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Management and Pharmacotherapy of Advanced Cardiac Life Support (cont'd)

- Vasopressin (Pitressin)
  - Endogenous antidiuretic hormone and potent vasoconstrictor
  - One-time dose of 40 units IV
    - May substitute for first or second dose of epinephrine
  - Nonadrenergic
    - Affinity not compromised in face of metabolic acidosis

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Management and Pharmacotherapy of Advanced Cardiac Life Support (cont'd)

- Atropine (AtroPen)
  - 1-mg IV push for asystole or PEA
  - Given along with epinephrine or vasopressin
  - Blocks action of acetylcholine
    - Short-lived chronotropic effect
  - Maximum daily dose: 0.04 mg/kg
  - Adverse effects:
    - Miosis
    - Dry mouth
    - Urinary retention
    - Constipation

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Management and Pharmacotherapy of Advanced Cardiac Life Support (cont'd)

- Sodium bicarbonate
  - Dose: 1 mEq/kg
  - Limited use:
    - Patient fails to respond to adequate ventilation, defibrillation, and compressions or is refractory to vasopressors
    - Use to keep pH > 7.2
  - Will increase CO_2 levels
    - Patient must be well ventilated

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Management and Pharmacotherapy of Advanced Cardiac Life Support (cont'd)

- Magnesium sulfate
  - Used for torsades de pointes
  - Dose: 1 to 2 g (may repeat after several minutes)
  - Caution with renally impaired patients
  - Magnesium toxicity:
    - Sweating, hypotension, hypothermia, reflex depression, CNS depression
    - Respiratory paralysis, circulatory collapse, flaccid paralysis

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Alternative Routes of Medication Administration

- Intraosseous route
  - Used if IV access is too difficult to gain
    - Infants
    - Children
    - Elderly
    - IV drug abusers
  - Needle should not remain for >3 or 4 hours

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Alternative Routes of Medication Administration (cont'd)

- Endotracheal route
  - ***LEAN (lidocaine, epinephrine, atropine, and naloxone***)
  - Double the dose and dilute with 10 ml of normal saline (NS) or sterile H_2O
    - Insert with catheter down endotracheal tube (ETT)
    - Follow with 5 to 10 rapid ventilations

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