EMSP 2348

PHARMACOLOGY

LECTURE NOTES

INSTRUCTOR

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CONTENTS

DRUG ADMINISTRATION

Giving your patient the correct drug dosage is essential to proper pre-hospital care. The medications used in EMS come from various manufacturers and vary in concentration, volume and packaging. You need to be able to prepare the correct drug at the correct concentration and volume and give it by the correct route. Once you have given a medication it cannot be taken back.

So, you must get it right the first time!

Systems of Measurement

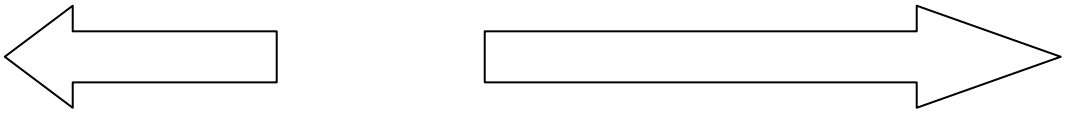
There are 3 systems of measurement used in medication dosage and administration: Metric, Apothecary and Household systems.

Metric System:

- A decimal system of weights and measure based on units of ten.
- The Gram is the unit of weight – abbreviated as g or gm.
- The Liter is the unit of volume – abbreviated as L.
- The Meter is the unit of length – abbreviated as m.

Multiples, Submultiples and Prefixes of the Metric System

1000	100	10	1	1/10	1/100	1/1000	1/1000,000
Kilo	Hecto	Deka	BASE UNIT	deci	centi	milli	micro



Each conversion is 10 times LARGER than the preceding unit.

Each conversion is 10 times SMALLER than the preceding unit.

The Base Units we will use are the gram, Liter or meter.

Apothecary System:

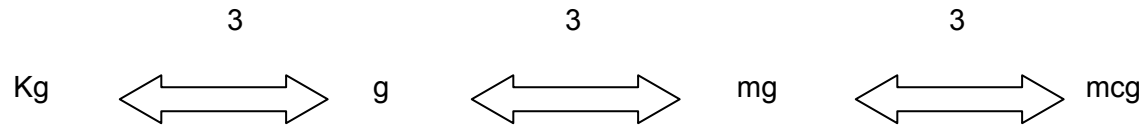
Uses fractions to measure and weigh drugs and solutions.

Household System:

Very inaccurate due to the varying size of utensils.

Conversions Between Multiples

FROM:	TO:	TO CONVERT:
Kilograms	grams	Multiply by 1000 or move decimal point three Places to the right
Grams	milligrams	Multiply by 1000 or move decimal point three Places to the right
Milligrams	micrograms	Multiply by 1000 or move decimal point three Places to the right
Kilograms	milligrams	Multiply by 1 000 000 or move decimal point Six places to the right
Grams	micrograms	Multiply by 1 000 000 or move decimal point Six places to the right
Micrograms	milligrams	Divide by 1000 or move decimal point three Places to the left
Milligrams	grams	Divide by 1000 or move decimal point three Places to the left
Grams	kilograms	Divide by 1000 or move decimal point three Places to the left
Micrograms	grams	Divide by 1 000 000 or move decimal point Six places to the left
Milligrams	kilograms	Divide by 1 000 000 or move decimal point Six places to the left



To convert from one multiple to the other, move the decimal point 3 places in the direction indicated. For example, if you are converting grams to milligrams, move the decimal point three places to the right.

Example: How many milligrams are there in 1 Kilogram?

Answer: 1 Kg can be written as 1.0 Kg.

Looking at the chart above you will see that we need to move the decimal point a total of 6 places to the right.

1 Kg = 1000 000 mg.
To be really accurate you could say 1Kg = 1 000 000.0 mg

NOTE:
We do not place commas to separate the thousands. 1,000,000 would be incorrect.

PHARMACOLOGY MATH

There are many different ways to perform drug calculations. I am going to show you just one.

In order to perform drug calculations there are 2 pieces of information we must have:

1. We need to find the **REQUESTED DRUG AMOUNT**– what you have been asked to give the patient. Most times this is clearly stated; occasionally it is based on the patient's weight.

2. We need to find out how much of the drug is present in 1ml of the solution – this is the **DRUG CONCENTRATION.**

$$\text{Drug Concentration} = \frac{\text{AMOUNT OF DRUG (in g/mg/mcg)}}{\text{VOLUME OF SOLUTION (in ml)}} = \text{\_\_\_g/mg/mcg/mL}$$

For example, a common preparation of Furosemide is a pre-filled 4 milliliter (4 ml) syringe containing 40 milligrams (40 mg) of Furosemide.

$$\text{Drug Concentration} = \frac{\text{40 mg (Total mg)}}{\text{4 mL (Total mL)}} = \text{10mg/mL}$$

Once you know the drug concentration, you know how much drug is in one milliliter of solution. From that, you can determine how much of the solution is required to deliver the amount of drug ordered.

Divide the amount of drug ordered by the drug concentration.

$$\text{REQUIRED VOLUME (mL) OF SOLUTION} = \frac{\text{REQUESTED DRUG AMOUNT (mg)}}{\text{DRUG CONCENTRATION (mg/ml)}} = \text{\_\_\_\_ml}$$

The Required Volume of Solution is the amount of medication you will give to your patient in order to give them the correct amount of the drug. In EMS this is usually a liquid, which is given via injection or the IV route.

INFUSION RATE CALCULATION

Now, what if you have been ordered to start an IV infusion on your patient? This is the formula you will use to calculate the infusion rate.

$$\text{Infusion Rate (gtts/min)} = \frac{\text{Required Volume (ml)} \times \text{Set Size (gtts/min)}}{\text{Infusion Time (min)}} = \_\_\_ \text{ gtts/min}$$

Sometimes the Required Volume will have been stated in the order. Occasionally you will have to calculate the Required Volume using steps 1 and 2 outlined previously.

NOTE:

- gtts is the abbreviation for drops. Infusions are always run at # gtts/min.
- Set Size – this tells you how many drops are needed to give 1ml of the Infusion.

  Maxi Drip = 10 drops/ml. This means that it takes 10 drops to deliver 1ml.

  Micro/Mini Drip = 60 drops/ml. This means that it takes 60 drops to deliver 1ml.

USEFUL CONVERSIONS

1 Kilogram = 1000 Grams (g)	1 Liter = 1000 Milliliters
1 Gram = 1000 Milligram (mg)	1 Liter = 1000 Cubic Centimeters
1 Milligram = 1000 Microgram (mcg)	1 Milliliter = 1000 Micro liters
1 Kilogram = 2.2 pounds	1 pound = 0.454 Kilograms
1 Grain = 65 mg or 0.065 g	1 milligram - 0.015 grains
1 Teaspoon = 5 cubic centimeters	1 Tablespoon = 3 Teaspoon.

NOTE: The terms cubic centimeter (cc) and milliliter (mL) are interchangeable.

Temperature Conversion:

To convert between °Fahrenheit and °Celsius:

°F = 9/5 °C + 32
°C = 5/9 (°F – 32)

METRIC SYSTEM - PRACTICE PROBLEMS

Conversions:

1. 50 kg = _____lb
.
2. 180 lb = _____kg
3. 0.2 mg = _____mcg
4. 3.0 L = _____ml
5. 0.3 g = _____mg
6. 10 ml = _____cc
7. 3.0 g = _____mg
8. 0.06 g = _____mg
9. 200 lb = _____kg
10. 4.0 g = _____mg
11. 0.03 g = _____mg
12. 8000 mg = _____g
13. 200 ml = _____cc
14. 2.0 mg = _____mcg
15. 0.1 L = _____ml
16. 4000 000mcg = _____mg
17. 1000ml = _____L
18. 1 mcg = _____mg
19. 0.8 mg = _____mcg
20. 250 mL = _____L
21. 10 kg = _____lbs
22. 0.000 5 g = _____mg
23. 10 kg = _____mg
24. 0.0016 kg = _____mcg
25. 0.03 L = _____mL
26. 1000 g = _____kg
27. 600 mcg = _____mg
28. 10 000 mg = _____g
29. 4 mg = _____g
30. 1500 mL = _____L
31. 0.25 L = _____mL
32. 0.715 g = _____mg
33. 0.1 g = _____mg
34. 1.6 mg = _____mcg
35. 186 lbs = _____kg
36. 146 kg = _____lbs

PHARMACOLOGY MATH #1

1. Perform the following conversions:

a. 150 ml = _____L
b. 2.63 L = _____ml
c. 1376 ml = _____L
d. 0.671 L = _____ml
e. 26.7 ml = _____L
f. 762 mg = _____g
g. 0.76 g = _____mg
h. 2729 mg = _____g
i. 3.7641 g = _____mg
j. 23 mg = _____g

2. Calculate the volume of medication required to deliver the given dosages:

	Drug Conc/1ml.		Volume to give
a.	Conc. = 500mg/10mL	_____ Desired dose = 125mg	Vol. = _____ml
b.	Conc. = 40mg/4ml	_____ Des dose = 200 mg	Vol. = _____ml
c.	Conc. = 10mg/2ml	_____ Des dose = 2.5mg	Vol. = _____ml
d.	Conc. = 100mg/10ml	_____ Des dose = 12.5 mg	Vol. = _____ml
e.	Conc. = 2g/50ml	_____ Des dose = 500mg	Vol. = _____ml
f.	Conc. = 1mg/10ml	_____ Des dose = 0.6 mg	Vol. = _____ml
g.	Conc. = 1g/10ml	_____ Des dose = 250 mg	Vol. = _____ml
h.	Conc. = 1mg/1ml	_____ Des dose = 0.2mg	Vol. = _____ml
i.	Conc. = 50mg/1ml	_____ Des dose = 35mg	Vol. = _____ml
j.	Conc. = 1mg/5ml	_____ Des dose = 0.25mg	Vol. = _____ml

3. Your patient is a 5 y.o. white male who weighs 44 lbs. The physician orders IM Benadryl @ 1mg/1kg of body weight. The drug is supplied as 50mg/1ml. How many mg should the patient receive & how many ml's is this dosage?

4. Your patient is a 9 y.o. black female who weighs 88 lbs. The physician orders IV Valium @ 0.3mg/kg of body weight for status epilepticus. The valium is supplied as10mg/2ml. How many mg should the patient receive and how many ml's is this dosage?

5. You give 5 ml of a drug to a patient. The ampule you took the drug from is labeled 15mg/10ml. How many mg did you give the patient?

6. A 68 y.o. female weighing 132 lbs. requires a bolus of sodium bicarbonate. The bicarbonate should be administered in a 1 mEq/kg of body weight bolus.
   How many mEq need to be administered?

7. You receive an order to administer 4mg/minute Lidocaine to a patient following a 100 mg bolus to abolish premature ventricular ectopy. This is accomplished by mixing 2g of Lidocaine in 500ml of D5W. At what rate in gtts/min must you administer the Lidocaine to deliver the proper dose, using a 60gtt/mml administration set ?

8. You arrive on the scene of a MVA to find a 22 y.o. female patient with signs and symptoms of internal bleeding. Medical control orders you to start an IV with a large bore catheter and administer fluid at a rate of 200cc/hr. Use an administration set of 15gtts/cc, how many gtts/min should the patient receive?

9. You get an order for 1mEq/kg of sodium bicarbonate. You give the patient 98 ml. Assuming that the bicarbonate was supplied as 44.6mEq/50ml, how much does the patient weigh, <u>IN POUNDS</u>?

PHARMACOLOGY MATH #2

1. You are ordered to administer 125cc/hr of Lactated Ringer's solution. Your set delivers 15gtts/ml. How many drops per minute must you run your IV?

2. You are ordered to administer 1500 ml of Normal Saline over 4 hours to your patient via IV. Your solution set delivers 20gtts/cc. How many drops per minute must you run your IV?

3. The physician orders you to start a D5W IV on your patient and run it a 200cc/hr. Your administration set delivers 60gtts/ml. How many gtts. per minute must you set your IV?

4. Your patient is a 23 y.o. male who has suffered blunt trauma to the left upper quadrant of his abdomen. The patient's pulse is 130 and thready, his blood pressure is 98/74, his respirations are 30 and shallow and his skin is pale and diaphoretic. Your orders are to start a large bore IV and infuse Lactated Ringer's at 2000ml/hr. Your solution set delivers 15gtts/ml. How fast must you flow your IV?

5. The physician orders you to administer 1mg/kg of Lidocaine to your 48 y.o. patient who is experiencing multi-focal PVC's. Your patient weighs approx. 180 pounds. The pre-loaded syringe of Lidocaine is 100mg/10cc. How many ml's of Lidocaine must you administer?

6. Your standing orders state you must administer a 2mg/min Lidocaine infusion to your post resuscitation V-Fib patient. The orders also state you must mix 2g of Lidocaine in a 500ml bag of D5W for this infusion. Your solution set of choice for infusions is the mini-drop set, which delivers 60gtts/cc. How many gtts/min must you flow the infusion?

7. You call in to the hospital with a report on the patient in #6 and tell the physician the patient is in 1st degree AV block with multi-focal PVC's. The doctor orders you to increase the infusion to 4mg/min. How many drops per minute must you now flow the infusion?

8. The doctor orders you to administer a dopamine infusion to you patient in cardiogenic shock. Your protocols state you must mix 800mg of dopamine in 500ml of D5W and use a minidrip set for administration. The doctor wants you to start the infusion @ 10mcg/kg/min and titrate on blood pressure thereafter. How many gtts/min must you run your infusion? (your patient weighs 188 pounds.)

PHARMACOLOGY MATH #3

Work the following problems on your own paper. Please show your work so that you might receive partial credit for wrong answers. Circle your final answer.

Compute the following weights:

1. 250 lbs = _____Kg
2. 175 lbs = _____Kg
3. 200 lbs = _____Kg
4. 110 lbs = _____Kg
5. 54 lbs = _____Kg
6. 90 lbs = _____Kg
7. 186 lbs = _____Kg
8. 160 lbs = _____Kg
9. 125 lbs = _____Kg
10. 320 lbs = _____Kg

Convert the following concentrations:

11. 100mg/2ml Drug concentration = _____ Give 75mg = _____ml
12. 0.4mg/1ml Drug concentration = _____ Give 1.0 mg = _____ml
13. 40mg/4ml Drug concentration = _____ Give 60mg = _____ml
14. 25g/50ml Drug concentration = _____ Give 25,000mg = _____ml
15. 10mg/1ml Drug concentration = _____ Give 1/8 grain = _____ml

Compute the following doses:

Drug Conc.

16. 500mg/10ml Patient weighs 200# _____ Give 5mg/kg = _____ml
17. 100mg/5ml Patient weighs 105# _____ Give 1.5mg/kg = _____ml
18. 10mg/5ml Patient weighs 170# _____ Give 0.1 mg/kg = _____ml
19. 200mg/10ml Patient weighs 220# _____ Give 0.5mg/kg = _____ml
20. Nitrostat is 1/150 of a grain, how many mg is this?

21. 250mg/ml Give 1.5 ml. How many mg is that?

For the following calculations assume use of a mini-drip set unless stated.

22. Mix 1.0mg in 250cc of D5W.

    i) What is the concentration in

    a) mg/ml _____

b) mcg/ml _____

ii) How many ml must you give to achieve 4 mcg/min.

23. You have a 4 mg/ml premix infusion, give 3 mg/min.

24. a) Administer 500 ml of 20% Osmitrol over 20 minutes using a mini drip set.

b) How many mg did you just give?

Use the following concentration for questions 25 – 28
Dopamine 400 mg in a 250 ml solution.

25. a) What is the concentration in mg per ml?

b) What is the concentration in mcg per ml?

26. 225# patient, give 2 mcg/kg/min

27. 150# patient, give 3 mg/kg/min

28. 90# patient, give 4 mg/kg/min

PHARMACOLOGY MATH #4

1. You arrive at an MVA and find one male in urgent condition. The base hospital orders LR at 200 cc/hr. Your drip set gives 15 gtts/ml. What drip rate do you set?

2. You are on an air transfer of a multiple shooting patient now in stable condition. Bilateral IV's are in place using 14g and 16g angiocaths with 15 gtts/ml Blood Y-Type drip sets. Your ER physician orders 1000 cc/hr. What drip rates do you set?

3. Per protocol you are to give 1.0 mg/kg of Lidocaine IVP. Your patient weighs 180#. Lidocaine is supplied in 100 mg/10ml. How many ml's do you give?

4. You are to follow this directive with a maintenance infusion of 2 mg/min of Lidocaine. You have a 1.0 g vial of Lidocaine, a 0.25 L bag of D5W, and a minidrip set at your disposal. Assume an IV is in place. What drip rate will you select to administer the proper dose of Lidocaine?

5. You are ordered to give 5 mg Diazepam slow IVP. You have Valium 10 mg/ml. How many ml should you administer?

6. Epinephrine 1:10,000 come 1mg in 10 ml. The pediatric dose is 0.01 mg/kg. The baby weighs 38#. How much do you give?

7. You are treating a patient in severe pain. The ER physician orders ¼ grain of Morphine Sulfate IV over five minutes. You have two syringes with 10 mg in 1.0 ml each. How many ml's do you give?

8. Hospital records show that your patient weighs 225# and is in Cardiogenic shock secondary to an AMI. You are transferring him to another facility. The receiving physician orders Dopamine 5 mcg/kg/min. As luck would have it, the infusion pump malfunctions enroute. Considering the use of a minidrip set, how many gtts/min must you give? (the concentration of Dopamine is 400 mg/500 ml D5W)

9. An overdose patient states he took 32 tablets of 0.750 g of Drug X. How many mg did he take?

10. In the Emergency Room, you are told to add 150 mg of Aminophylline to D5W for a total volume of 100 ml. Aminophylline is available in 0.5 g in 0.02 L vials. How many ml of the drug do you add to the IV solution?

11. You are ordered to give 60 mg of a drug that comes in a 2 ml vial, 40 mg/ml concentration. How many ml do you give?

Use the following information to answer questions 12 – 18.

You have a pediatric cardiac arrest in progress. The patient weighs approximately 25lbs. You have standard pre-filled syringes of

Epinephrine 1:10,000 - 1 mg in 10 ml
Atropine - 1 mg in 10 ml
Lidocaine - 100 mg in 10 ml

You receive these orders: (answer in ml when appropriate)

12. Epi 0.01 mg/kg IVP

13. Atropine 0.02 mg/kg

14. Lidocaine 1.0 mg/kg

15. Defibrillate @ 2 J/kg – how many Joules?

16. D50W 0.5 g/kg

17. Narcan 0.1 mg/kg

18. Fluid challenge 20 cc/kg

19. You add 2 g of Lidocaine to 250 cc of D5W. What concentration (mg/ml) did you create?

Convert:

20. 5 mg _____g
21. 30 cc _____L
22. 45 Kg _____lbs
23. 15 cc _____ml
24. 250 g _____mg
25. 500mcg _____g
26. 1/8 grain _____mg
27. ¼ gram _____mg
28. 258 lbs _____Kg
29. 0.750L _____ml
30. 0.45 g _____mcg
31. 1 tbsp _____cc

GENERAL PRINCIPLES of PHARMACOLOGY

Refer to pages 275 – 286 in main text.

FEDERAL DRUG LEGISLATION

Purpose: to protect the public from adulterated or mislabeled drugs.

1906 Pure Food and Drug Act

- To improve the quality and labeling of drugs
- Named the United States Pharmacopoeia (USP) as the official source for information.

1914 Harrison Narcotic Act

- To regulate the import, manufacture and sales of narcotics and their derivatives.

1938 Federal Food Drug and Cosmetic Act

- Empowered the FDA to set and enforce safety standards. (In 1937 Elixir of Sulfanilamide was marketed – everyone died. It is the main ingredient in anti-freeze!)

1951 Durham-Humphrey Amendment to 1938 FDA

- Aka the prescription drug amendment
- Required pharmacists to have a written or verbal Rx (prescription.)
- Also created the category of OTC drugs

1970 Comprehensive drug Abuse Prevention and Control Act

- Most recent review
- Repealed and replaced the Harrison Narcotic Act
- Created 5 schedules each with its own level of control and record keeping
- EMS – use a few controlled substances, narcotics and anticonvulsants ex. Morphine and Benzodiazepines. The majority of EMS drugs are Rx drugs - given under the Medical Directors License.
- See **Table 9-1 page 279** in Brady text. You **NEED TO KNOW** this table!

PHARMACOKINETICS and PHARMACODYNAMICS

PHARMACOKINETICS

The study of how drugs move through the body (how they enter, move around and then exit.)

Physiology of transport mechanisms:

How substances are moved between the various body compartments.

- Intracellular
- Extra cellular – which is further divided into
    - Interstitial
    - Intra vascular

MEMBRANE TRANSPORT HANDOUT -

Understanding membrane transport mechanisms will help you to understand how drugs work. The handout is very detailed – look at the big picture!

There are two broad mechanical categories.

ALL of which takes place ACROSS A SEMI-PERMEABLE MEMBRANE i.e. the CELL MEMBRANE.

1 - Requires Energy:

- (i) Active transport:
  Moving substances AGAINST their concentration gradient. Like pushing a car uphill.

- (ii) Carrier-mediated/facilitated diffusion:
  PROBLEM - large molecules do not readily pass through the cell membrane, they are too big!
  SOLUTION – large molecules bind with a carrier protein and are transported into the cell.
  Example – Insulin and glucose.

2 – Passive Mechanisms (No Energy Required.)

- Most drugs move by passive transport mechanisms.

- Needs a concentration gradient in a solution, (like rolling a car downhill.)

Two terms to know:

1.SOLUTE = molecules or ions (the solid stuff, like the sugar in your coffee.)

2. SOLVENT = the solution (the liquid part, usually water, like the water in your coffee.)

Three processes to know:

- 1. Diffusion – the movement of a SOLUTE down the concentration gradient.

  HIGH $\rightarrow$ LOW

- 2. Osmosis – the movement of the SOLVENT (water) down its concentration gradient.

  HIGH $\rightarrow$ LOW

- 3. Filtration – movement down a pressure gradient.
  Example?

Pharmacokinetic Processes:

There are 4 distinct stages:

1. Absorption
2. Distribution
3. Bio-transformation
4. Elimination

1. Absorption:

For a drug to be absorbed:

- Drug must get to site.
  The first step is to enter the bloodstream unless given IV.

Factors affecting absorption:

- Absorption is directly related to tissue blood supply.
- Consider IM vs. SQ?
- Slow blood flow = slow absorption, example?
- Increased blood flow = increased absorption, example?
- Oral meds $\rightarrow$ digestive chemicals $\rightarrow$ gut wall $\rightarrow$ bloodstream.

- Need to be water soluble for good absorption.

- Need to be fat (lipid) soluble to cross cell membrane.

- Drugs that have an enteric coating = slow release.
  Allows the drug time to exit the stomach and pass to the duodenum for absorption.
  Causes less stomach irritation and less drug destruction.

- Many drugs ionize (dissociate/break down)
  Ions do not readily cross the cell membrane.
  Most drugs do not fully ionize.

- pH affects ionization:

  Weak acidic drug + alkaline environment → ionized drug

  Alkaline drug + acidic environment → ionized drug.

  Aspirin (Acetyl Salicylic Acid/ASA) in the stomach.
  (Very acidic environment) = little ionization = readily absorbed.

- Surface area and blood flow play an important part.

- Drug concentration – remember Diffusion and the concentration gradient?

- Loading dose – a bolus given to get the drug concentration to its therapeutic level in the bloodstream.

- Maintenance infusion – to maintain the therapeutic level consistently.

- Bio-availability - is a measure of the amount of drug that is still active after it reaches its target tissue.

2. Distribution

- Most drugs pass easily through
  Bloodstream → interstitial spaces → cells.

- Drug + protein (ex. Albumin, a blood protein) → sustained release = (↑ period of action.)

- The therapeutic effects come mainly from the unbound portion of the drug.
  The bound drug is too large.

- PH affects protein binding.

Tri Cyclic Antidepressants (TCA's) bind strongly with proteins.
If you ↑pH = ↑ protein binding.

Sodium Bicarbonate is an alkali and will ↑ pH
↑ Protein binding = ↓ free drug.

Sodium Bicarbonate is the drug of choice in **KNOWN TCA overdoses**.

- The presence of other serum protein binding drugs can affect the drug-protein binding mechanism.

Examples – Aspirin and Warfarin.

What is ASA used for? _____

What is Coumadin? _____

You know that albumin is a blood protein.
What effect will low albumin levels have on drug availability?

_____

Which patient populations have low blood proteins?

_____

Why is this important to us?

_____

- Blood Brain Barrier:

  A protective mechanism - occurs in the CNS, allows only non-protein bound, highly lipid soluble substances to pass.

- Placental Barrier:

  Restricts – drugs must be lipid soluble, non-ionized and non-protein bound.

- Drug Reservoirs:

Fatty tissue – highly stable, cannot absorb or release large amounts of stored drugs in a short time. There is the potential for these drugs to be released when fat stores are utilized. Bad news if the patient used PCP previously and then diets at some time in their life!

Bones and Teeth – especially tetracycline antibiotics, these cross the placental barrier and cause the teeth to be discolored – ORANGE!

3. Bio-transformation

This is the metabolism (breaking down) of drugs.

Has one of two effects:

EITHER

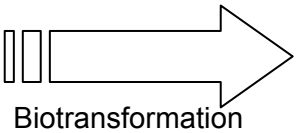
The drug is transformed into a more or less active metabolite.

OR

The drug is made either more water-soluble or less lipid soluble to aid elimination.

- **NOTE** - Protein bound drugs **CANNOT** be eliminated.

Prodrug (parent drug)

- Inactive form  Active metabolites

Biotransformation

First-pass Effect:

- All enteral route drugs $\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow$ LIVER $\rightarrow\rightarrow\rightarrow\rightarrow$ $\rightarrow\rightarrow\rightarrow$bloodstream.
  (Partial or complete inactivation)

- Liver enzymes react with drugs in one of two ways:

  1. Phase I reactions or non-synthetic reactions:
     Increases water solubility = easier to excrete.

  2. Phase II reactions or conjugate reactions:
     Drug binds with an endogenous chemical = increased polarity = easier to excrete.

4. Elimination

Via

- Urine (renal)
- Expired air
- Feces, sweat, saliva and breast milk.

Renal Excretion:

- Affected by renal blood flow and BP.
- Affected by pH (remember giving Sodium Bicarbonate in TCA OD?)
- Specialized transport "pumps" secrete drugs into the urine. Some are highly specific while others transport a range of similar chemicals. Competition for these "pumps" can lead to drug toxicity or can be used to delay the excretion of a specific drug thus prolonging its effect.

  Example: Probenecid blocks renal pumps and competes with many antibiotics.

  Benefit? _____

Expired Air:

- Basis of breath test-
  Ethanol released = blood alcohol level.

DRUG ROUTES/FORMS/STORAGE:

- See text pages 290-292.

PHARMACODYNAMICS

The study of drug Mechanisms of Action (how they work.)
Why would this be of use to us? _____

Drugs can act in 4 different ways:

1. Binding to a Receptor:

- Drug receptors are protein molecules on the surfaces of cells. They have specific shape/s. Each cell may have hundreds of receptors and the numbers change constantly.

- Receptors can have sub-types. The Adrenergic receptors have 5 sub-types and are of special interest to paramedic practice.

- The binding can be either stimulatory, (causes an action) or inhibitory, (blocks an action.)

- Receptors are named for the drug that causes the action.

  Example - Opiate receptors are stimulated by opiates.

Affinity:

- The force of attraction between a drug and a receptor.

- The greater the affinity = the greater the bond.

Efficacy:

- A drugs ability to cause the expected response.

- Affinity and efficacy are NOT directly related.

- Drug + receptor→→→→→drug effect

  Stimulates } **A Drug CAN NOT Create A New Cell Function**

  OR

  Inhibits } **A Drug CAN NOT Create A New Cell Function**

Sometimes……

- Drug + receptor →→→→→ second →→→→→→→→→ AMPLIFIED
  Messenger EFFECT
  (Ex. Cyclic AMP)

- Thus a small amount of drug initiates a powerful force.
  This is of special importance in the endocrine system - hormones.

Down-Regulation:

Receptor numbers change constantly.

- Drug + receptor →→→→ ↓ receptor formation = ↓ responsiveness to drugs.

Up-Regulation:

- Drug + receptor →→→→ ↑ receptor formation = ↑responsiveness

Agonist:

- Drug + receptor $\rightarrow\rightarrow\rightarrow$ expected response

Antagonist:

- Drug + receptor $\rightarrow\rightarrow\rightarrow$ no response.

Agonist-Antagonist (Partial Agonist):

- Drug + receptor $\rightarrow\rightarrow\rightarrow\rightarrow$ produces some of the drugs effects and blocks others.
  Example – Nubain, which stimulates the opiod agonists' analgesic properties but partially blocks others - like respiratory depression.

Competitive Antagonism:

- Drug "A" + receptor$\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow$ $\rightarrow$expected effect.
  Drug "A" + another drug + receptor $\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow$ effect blocked.

Non-Competitive Antagonism:

- Antagonist + receptor $\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow$ changes binding site = blocked.

Irreversible Antagonism:

- Antagonist + receptor $\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow$ PERMANENT bond.
  Cell must create new receptors.

<u>2. Drugs That Act by Changing Physical Properties</u>

- Osmitrol – an osmotic diuretic.
  Increases blood's osmotic "pull".
  When would this be useful?

  _____

<u>3. Drugs That Act by Chemically Combining with Other Substances.</u>

- Change the chemical nature of the substance on which it acts.

  Examples – cleaning of skin with alcohol prior to starting an IV.
  – Antacids neutralize acid in the stomach.

<u>4. Drugs That Act by Altering a Normal Metabolic Pathway</u>

- Drugs used to treat cancers and viruses.
  These drugs are "fake" building blocks, which get incorporated into the cell wall. The cell dies because the anticipated product is either faulty or missing.

Responses to Drug Administration – Page 295/6

Drug-Response Relationship – Page 296

Factors Altering Drug Response – Page 297

Drug Interactions – Page 298

DRUG CLASSIFICATION

In order to study drugs we need to break them down into manageable groups. This can be done in many ways:

- Body system affected
- MOA
- Indications
- Source/chemical class
- Common properties and principles shared by a class of drugs.
- Prototype – a drug that demonstrates the class's common properties and illustrates its particular characteristics.

It is important to know how medications work so you will have an idea as to their possible effect on your patient.

We will study drugs based on body systems.

DRUGS USED TO AFFECT THE NERVOUS SYSTEM

See Figure 9-3 page 299 for an overview.

You MUST be able to reproduce this diagram.

- CNS = Brain and Spinal cord.
- PNS = Peripheral Nervous System.

CENTRAL NERVOUS SYSTEM MEDICATIONS

- Analgesics
- Anesthetics
- Anti-anxiety and sedative/hypnotics.
- Anti-seizure or anti-epileptic agents.

- Psychotherapeutic agents
- Anti-psychotic agents.
- Anti-depressant agents.

Analgesics and Anesthetics:

- Analgesic – drug that relieves the sensation of pain.

- Anesthetic – drug that prevents all sensation often impairs consciousness.
  2 sub-classes:
  Opiod derivative
  Non-opiod derivative

Opiod Agonists:

- An opiod is chemically similar to opium (poppy plant)

- They treat pain in a similar way to endogenous Endorphins.

- Both opiods and endorphins work by decreasing sensory nerve signals to the brain.
  Prototype – Morphine Sulfate (MS)
  Therapeutic levels = analgesia
  Sedation
  Euphoria
  Miosis
  Decreased cardiac preload and afterload, good for the treatment of MI and pulmonary edema.
  Higher doses = respiratory depression and hypotension.

Non-opiod Analgesics:

3 broad types that have analgesic and anti-pyretic properties:

- Salicylates, Ex. Aspirin (ASA)

- Non-steroidal anti-inflammatory drugs (NSAIDS), Ex. Ibuprofen.

- Para-aminophenols, Ex. Acetaminophen.

Non-opiod Antagonists
Prototype: Narcan (Naloxone) – short half-life.
Used to treat respiratory depression from opiod drugs.

Adjunct Medications

- These drugs have little analgesic effect on their own

- When given with an analgesic enhances or intensifies the effect.

- Examples – Benzodiazepines (Valium.)

Antihistamines – Promethazine (Phenergan.)

Opiod Agonist-Antagonist

Prototype: Pentazocine (Talwin)

EMS: Nalbuphine (Nubain) – decreases pain with fewer respiratory and addictive S/Es.

Hospital: Butophoranol (Stadol.)

Anesthetics:

Cause loss of sensation to touch or pain.

Neuroleptanesthesia – anesthesia that combines decreased sensation of pain while the patient remains conscious. Used when the patient needs to remain alert and conscious.

- Anesthetics as a group cause respiratory, CNS and CV depression.
- Rarely used singly, given in combination for a balanced anesthetic result.
- Given by injection or inhaled.
- Act by slowing nerve impulse propagation.

Prototype inhaled – Halothane.

EMS inhaled – Nitrous Oxide (Nitronox.)

- Inhaled drugs are cleared mostly through the lungs so respiratory rate and depth affect the duration of their effect.

IV Anesthetics:

- Faster onset and shorter duration.
  EMS use – primarily to assist with intubations in RSI.

Local Anesthetics:

- Used as nerve blocks – suturing, prototype is Xylocaine.

Antianxiety and Sedative-Hypnotic Drugs

Sedation – a state of decreased anxiety and inhibition.

Hypnosis – instigation of sleep.

There are 2 main classes of these drugs:

- 1. Benzodiazepines – relatively safe and effective, may be given orally.
- 2. Barbiturates – much broader general depressants with higher potential for abuse. Prior to 1960 Barbiturates were frequently prescribed but since the discovery of Benzodiazepines they are not in common use.
- Note – Alcohol is in this class too!

GABA

- Gamma-amino butyric acid is the chief inhibitory neurotransmitter in the CNS.
- Think of it as slowing down everything in the brain. Then, if you give a drug that increases this effect, you can see how Barbs and Benzos work.

How do they work?

- Benzodiazepines increase the effectiveness of GABA; therefore the amount of GABA present limits their effects.
- Barbiturates at high doses can actually mimic GABA's effects and thus can have unlimited effects.

Antagonist for Benzodiazepines?

- flumazenil (Romazicon) – competitively binds with the benzodiazepine receptors.
- Benzodiazepines are commonly prescribed for seizures, alcohol withdrawal, or given in combination with TCA's. The use of flumazenil may cause the patient to suffer a seizure – this would be an untoward effect.

Anti-seizure or Anti-epileptic Drugs

Seizures are a state of hyperactivity of either a section of the brain (partial) or all of the brain (generalized.)

Goal: Balance seizure elimination : medication S/E's.

Life-long process.

1 reason for a patient with a seizure history to have a seizure?

Review different types of seizures;

Partial

Simple Complex

Generalized

Petit Mal

Status Epilepticus

Treatment for each type of seizure varies

Several general mechanisms, generally act upon the sodium and calcium channels in nerve cells.

- See table 9-3 page 304

CNS Stimulants

2 techniques are involved:

Either:

↑ The release or effectiveness of excitatory neurotransmitters.

Or:

↓ The release or effectiveness of inhibitory neurotransmitters.

Three Pharmacological Classes:

- 1. Amphetamines – stimulate excitatory neurotransmitters= Foot on gas.

  Increases wakefulness and awareness, decreases appetite.

  Most S/E's are from over stimulation = tachycardia, dysrythmias, HTN, convulsions and insomnia
  .
  Example - Dexedrine and amphetamine sulfate (the prototype.)

  2. **Methylphenidate – Ritalin**, a schedule II drug (high abuse potential.)

  Commonly prescribed for **ADHD**.

  Its **STIMULANT** action allows the person to focus and concentrate.

  3. Methylxanthines – mechanism is unclear, appear to block adenosine receptors.

Adenosine occurs naturally in the body (endogenous)
It can be used in the treatment of certain tachycardias.

Patients taking a methylxanthine will need a larger dose of Adenosine.

Caffeine (prototype drug in this class) has few clinical uses.

Theophylline is another and is used to relax smooth muscle in asthma.

Psychotherapeutic Drugs

The Pathophysiology of mental dysfunction is not well understood.

Medications are given on the basis that they work without us fully understanding their mechanism. They are used as adjunctive therapy.

The mental disorders are believed to involve the monoamine neurotransmitters in the CNS.

Neurotransmitters act as chemical messengers carrying information from one neuron (nerve) to another neuron, muscle, gland or organ.

These neurotransmitters (norepinephrine, epinephrine, dopamine and serotonin) are involved in the regulation and control of emotions.

Imbalances in these chemicals, especially dopamine, appear to be responsible for most mental disease.

- Schizophrenia is related to increased dopamine levels.
- Depression is related to decreased dopamine levels.

Schizophrenia drugs:

- Anti-psychotic + anti-anxiety + anti-depressant. A cocktail!
- Common side effects: EPS (Extra Pyramidal Symptoms) - including muscle tremors and orthostatic hypotension.

Anti – Psychotic Drugs

Major classes: Phenothiazines e.g. Chlorpromazine (Thorazine)
Butyrophenones e.g. Haloperidol (Haldol)

EMS Concern: A patient new to these medications may experience EPS.

These are acute dystonic reactions – muscle spasms often involving the face and neck. Very disabling and embarrassing.

Treatment: Diphenhydramine, (Benadryl)

Dose: _____ Routes _____

Anti – Depressant Drugs

Depression is linked to the monoamine neurotransmitters, norepinephrine and serotonin.

Treated by regulation of these neurotransmitters.

3 ways to regulate:

1. Increase production

2. Increase the release.

3. Decrease the uptake.

3 Classes:

(i) TCA's - Tricyclic Antidepressants

- Effective, safe, few S/E's.
- Work by blocking uptake of the neurotransmitter, thus extending action.
- O.D. (Overdose) causes cardiac toxicity

Tx. Sodium Bicarbonate – changes pH and aids renal clearance.

Prototype TCA – Tofranil

Others – Elavil, Norpramin and Pamelor.

(ii) SSRI - Selective Seratonin Reuptake Inhibitors.

Prototype SSRI – Prozac, most widely prescribed antidepressant in the US.

- Avoids many of the S/E's of TCA's.
- Primary S/E's – sexual dysfunction, HA and nausea.
  Other SSRI's – Zoloft and Paxil.

(iii) MAOI's - Mono Amine Oxidase Inhibitors

Block the breakdown of neurotransmitters

- MAOI's are not in common use – used to treat conditions refractory to TCA's and SSRI's.

Prototype MAOI – Nardil

CAUTION: eating foods rich in Tyramine e.g. Red wine and cheese can cause a hypertensive crisis.
Why? _____

Bipolar Disorder

Drug of choice is Lithium – low therapeutic index.

Mechanism of action – decreases mania without causing sedation.

Recently two anti-seizure medications have been successful in the treatment of bipolar disorders:

Carbamazapine (Tegretol)

Valproic Acid (Depakote)

AUTONOMIC NERVOUS SYSTEM

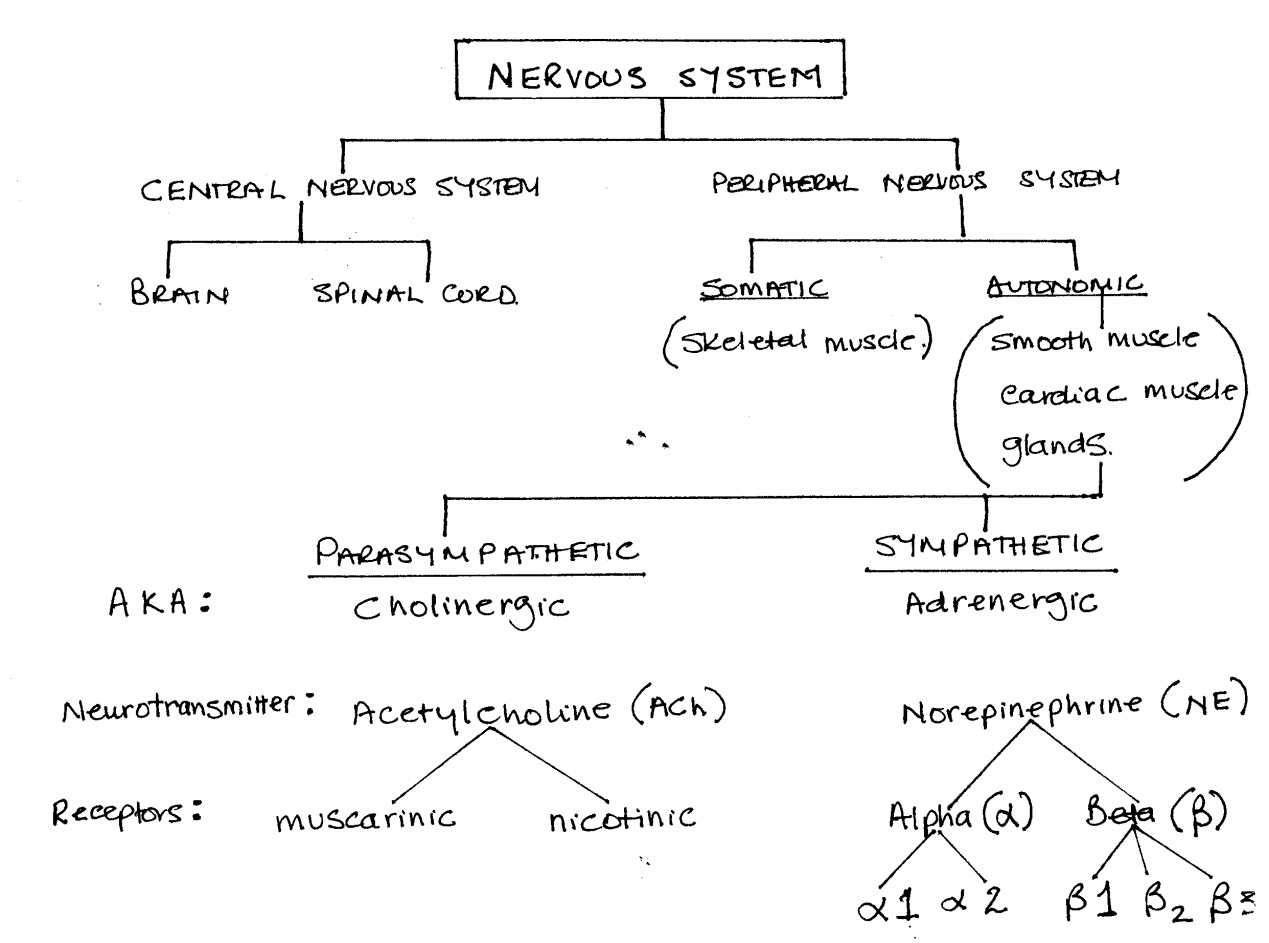
The ANS is primarily regulatory and controls involuntary actions.

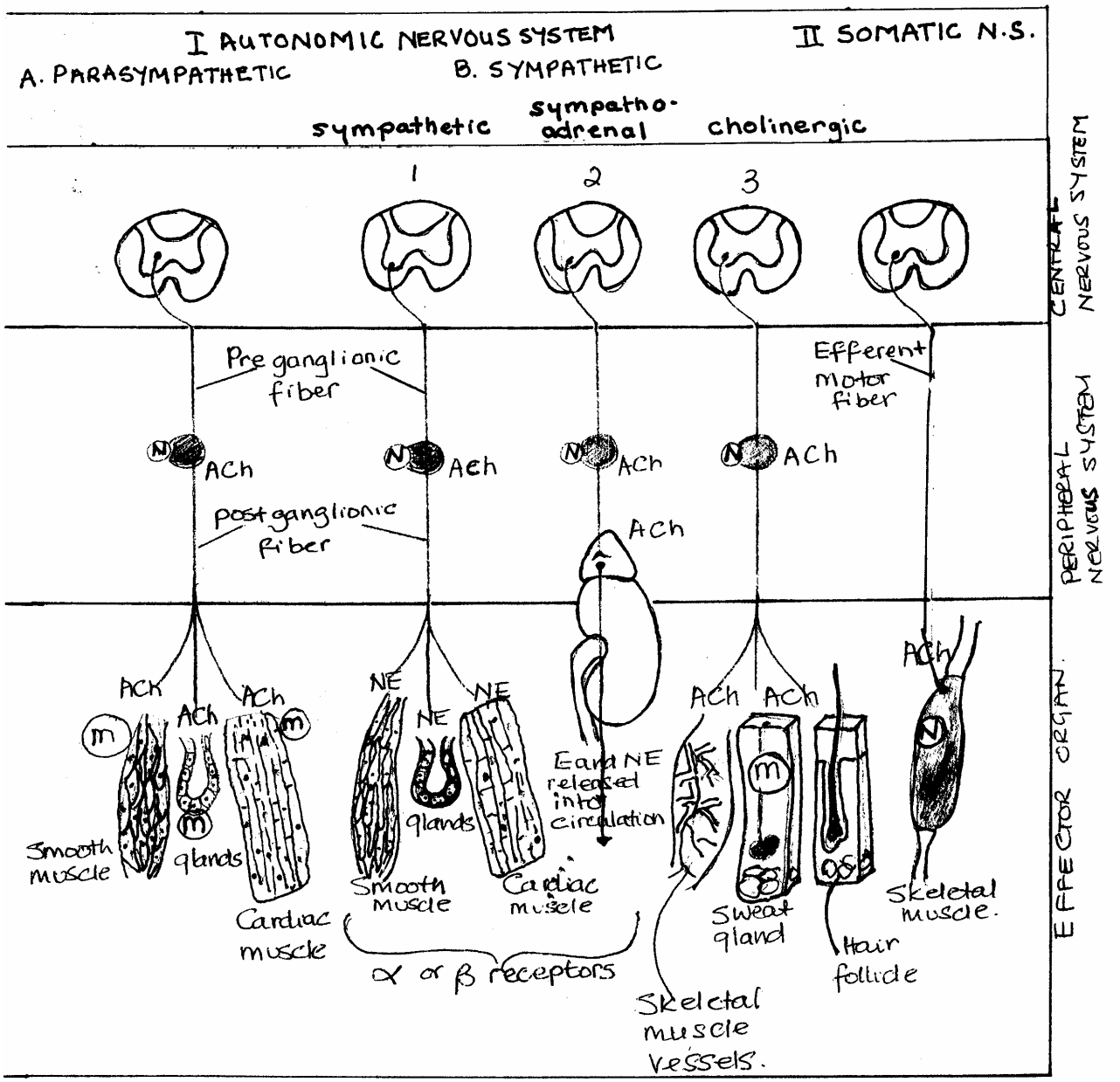
It has two functional divisions:

- Sympathetic – allows the body to function under stress, aka. The flight or fight system.
- Parasympathetic – regulates vegetative functions, aka. Feeding and breeding or resting and digesting system.

These two systems work in constant opposition to control organ responses –their opposite actions balance one another.
Many organs have dual innervations, this allows for remarkable precision.

Nervous System Classification





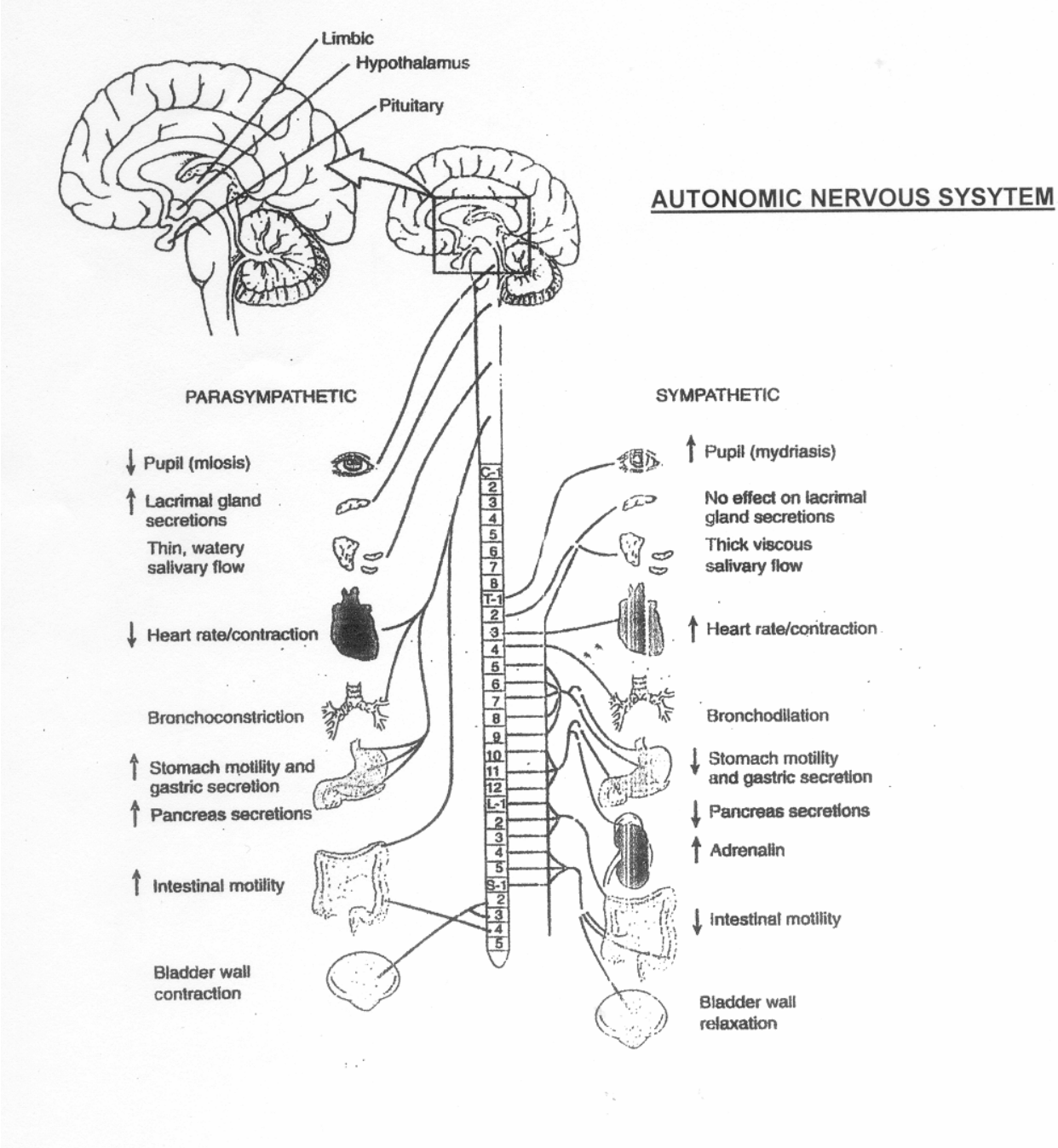
- I- Autonomic nervous system where preganglionic fibers of both sympathetic and parasympathetic nerves synapse in the ganglia. (ganglia are a group of nerve cell bodies in the PNS.)
- II - Somatic nervous system.
- N = nicotinic sites. • M = muscarinic sites.

Physiological Differences

As previously stated - the sympathetic and parasympathetic systems both innervate many of the same organs; their opposing actions balance one another**.**

- Sympathetic NS – flight or fight.
- Parasympathetic NS – feeding and breeding or resting and digesting.

Anatomical Differences



Sympathetic (aka Adrenergic and Thoracolumbar)

- Originates from thoracic nerves 1 through 12 and lumbar nerves 1 and 2. (T1 – L2)

Parasympathetic (aka Cholinergic and Cranio-sacral)

- Originates from Cranial nerves III, VII, IX and X, plus sacral nerves 2 - 4.

Neuro-humoral transmission:

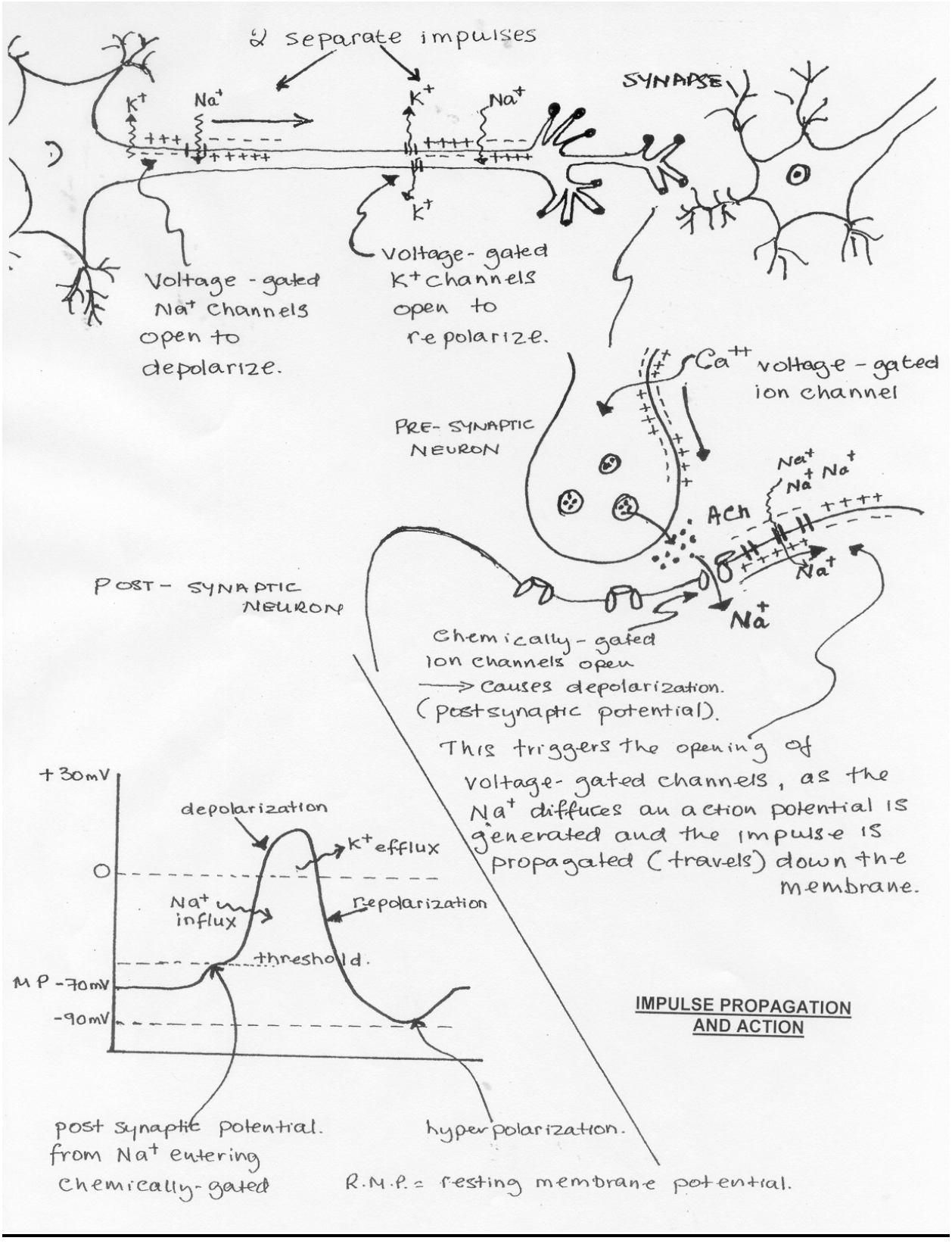
Neuron = nerve
Humor = a body fluid.

Information in the nervous system is transmitted electrically and chemically due to two special characteristics:

1. Nerves can conduct electrical signals (action potentials) along the length of the nerve. The impulse travels on one direction.

2. Nerves have intercellular connections with other nerve cells, muscles and glands. The presence of a specific chemical (neurotransmitter) at these connections determines its actions. The passage of a nerve impulse with the use of a chemical is called neuro-humoral transmission.

In this mechanism, the arrival of an action potential (signal), at a nerve terminal starts the release of the neurotransmitter – which acts as a chemical messenger.


2 separate impulses
SYNAPSE
K+
Na+
K+
Na+
K+
Voltage - gated Na+ channels open to depolarize.
Voltage - gated K+ channels open to repolarize.
Ca++ voltage - gated ion channel
PRE- SYNAPTIC NEURON
Na+ Na+ Na+
ACh
Na+
Na+
POST - SYNAPTIC NEURON
Chemically - gated ion channels open
→ causes depolarization. (postsynaptic potential).
This triggers the opening of voltage- gated channels, as the Na+ diffuces an action potential is generated and the impulse is propagated (travels) down the membrane.
+30mV
depolarization
K+ efflux
0
Na+ influx
repolarization
threshold.
MP -70mV
-90mV
post synaptic potential. from Na+ entering Chemically- gated
hyperpolarization.
R.M.P. = resting membrane potential.
IMPULSE PROPAGATION AND ACTION

Types of Neurohumoral Transmission:

Using the neurotransmitter acetylcholine:

Sequence of events:

1. Biosynthesis
2. Storage
3. Release
4. Action
5. Inactivation of the neurotransmitter.

Cholinergic Receptors:

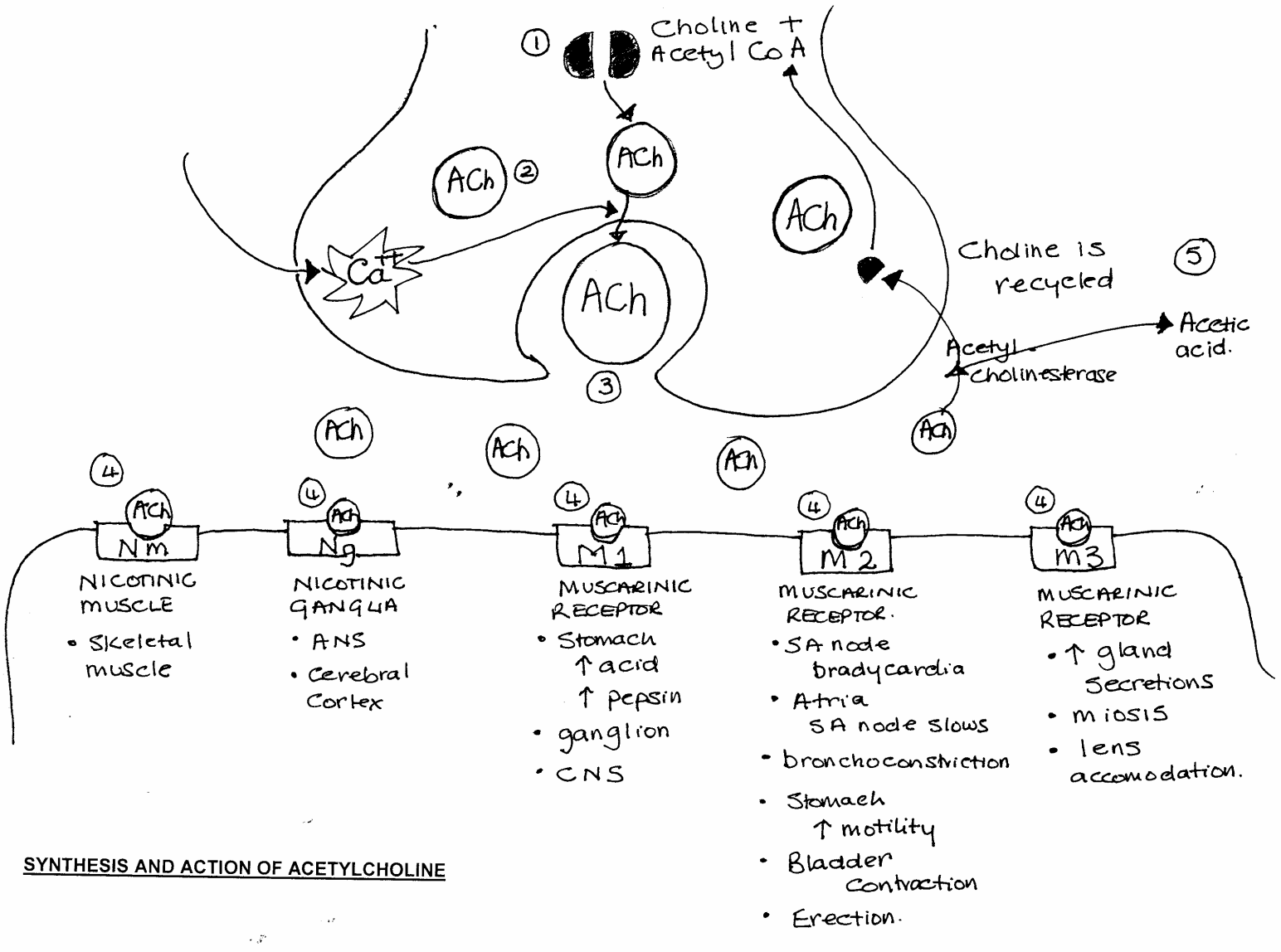
These receptors are found in the sympathetic and parasympathetic systems.

Receptors that are stimulated by Acetylcholine are either:

- Nicotinic (N) receptors – in the ganglia of both sympathetic and parasympathetic nerves, adrenal medulla and skeletal muscle.

- Muscarinic (M) receptors – in smooth muscle, cardiac muscle and glands, and the effector organs of the cholinergic sympathetic fibers.

SEE DIAGRAM ON FOLLOWING PAGE.



SYNTHESIS AND ACTION OF ACETYLCHOLINE

Adrenergic Transmission:

These neurotransmitters are a group of chemically related compounds called CATECHOLAMINES.

- Norepinephrine (noradrenalin)
- Epinephrine (adrenalin)
- Dopamine

Adrenergic Receptors:

These receptors are only found in the sympathetic system.
2 types: Alpha and Beta.

Alpha receptors by neuron location:

Alpha 1 – EXCITATORY, located on postsynaptic target cell membranes, vascular smooth muscle, GI, bladder sphincters and the radial muscle of the eye.

Alpha 2 – INHIBITORY, located on pre synaptic nerve terminals, platelets, fat cells and walls of the gut.

Beta receptors by organ location:

Beta 1 – EXCITATORY, found mostly in cardiac muscle cells. Cause an increase in HR and SV.

Beta 2 – INHIBITORY, they produce relaxation of smooth muscles (eg, dilation of bronchioles) and decrease secretions.

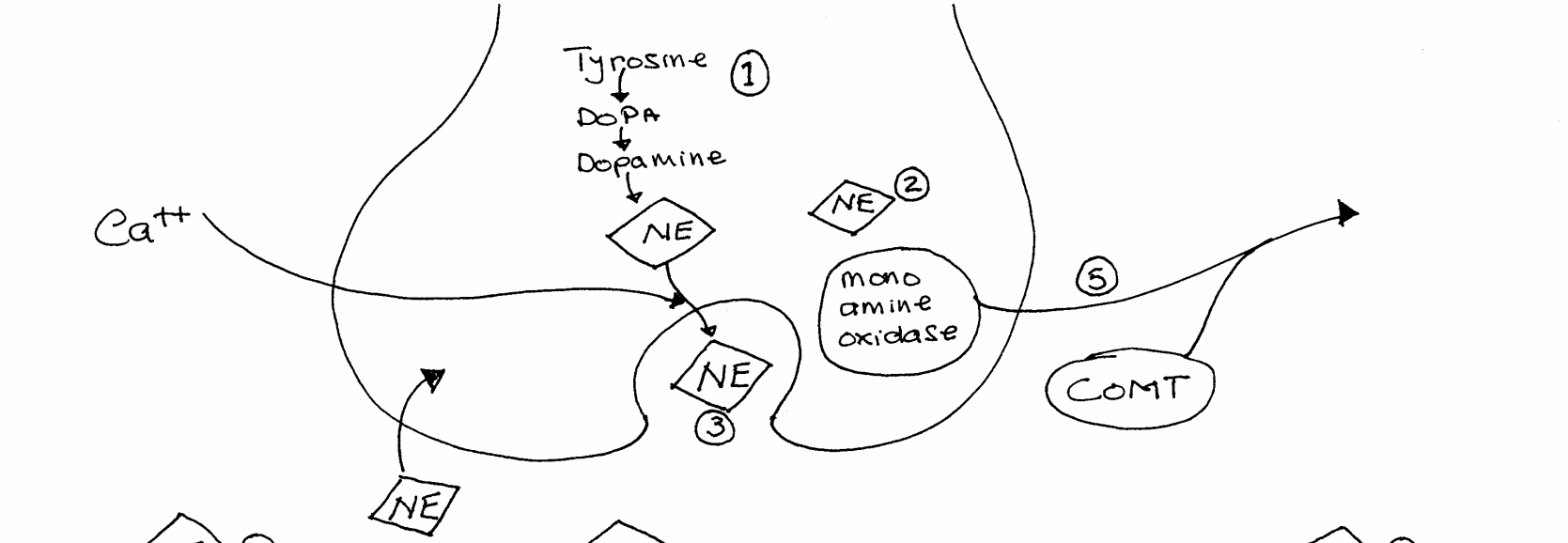
Beta 3 – EXCITATORY, limited distribution, low levels in adipose (fat) tissue and GI tract.

Adrenergic Neurotransmitter Inactivation

Must be rapidly stopped to prevent prolonged effects, inactivated by:

- 1. Enzymatic action: MAO – Mono Amine Oxidase and COMT.
- 2. Re-uptake: important role, maintains supplies.
- 3. Diffusion: a small amount of NE enters circulation and is metabolized.

SEE DIAGRAM ON FOLLOWING PAGE.



SYNTHESIS AND ACTION OF NOREPINEPHRINE

PARASYMPATHETIC NERVOUS SYSTEM

Review:
Cranial nerves carrying parasympathetic fibers:

III	Occulomotor	- intrinsic eye muscles, pupil and lens shape.
VII	Facial	- facial muscles
IX	Glossopharyngeal	– salivary glands
X	Vagus	- heart, lungs and most abdominal organs

Sacral nerves carrying parasympathetic fibers:

S2	kidneys
S3	bladder, sex organs
S4	terminal portions of the large intestine.

Stimulation causes:

- Pupillary constriction.
- ↑Secretion by digestive glands.
- ↓ HR and ↓ SV (cardiac contractile force) = ↓ BP.
- ↑ Smooth muscle activity in GI tract.

Neurotransmitter – Acetylcholine (Ach)

Ach is very short-lived, deactivated (broken down) by the enzyme Acetylcholinesterase (Achase.)

Receptors:

- Nicotinic N – neuron, located in all pre-synaptic ganglia of the Peripheral NS.
- Nicotinic M – muscle, located at the neuromuscular junction of the Somatic NS and in many organs.

PARASYMPATHOMIMETICS:

A drug or other substance that causes the same effect as the parasympathetic nervous system, aka. A cholinergic drug.

ACTION - LIKE PUTTING YOUR FOOT ON THE BRAKE.

PARASYMPATHOLYTICS:

A drug or other substance that blocks the actions of the parasympathetic nervous system, aka. An anti-cholinergic drug.

LIKE TAKING YOUR FOOT OFF THE BRAKE.

Drugs Used to Affect the Parasympathetic NS

Cholinergic (parasympathomimetic)

- Drugs act either directly or indirectly.

Direct acting drugs:

- Simulate effects by binding directly with Ach receptors.

Causes:

- ↓ HR — Hypotension
- ↓ PVR — Hypotension
- ↑ Salivation
- ↑ Urination
- ↑ Defecation
- ↑ Sweating
- ↑ Vomiting and abdominal cramps

SLUDGE These are adverse effects.

Prototype:

Bethanechol (Urecholine.)
Not broken down by acetylcholinesterase = longer duration of action.

- most effects on muscarinic receptors in bladder
- given PO or SQ
- primary use is increased micturition (urination) and increased peristalsis (gets food through the gut faster.)

Indirect acting drugs:

Work by inhibiting the actions of acetyl cholinesterase = prolonged cholinergic response.
These drugs affect both Nicotinic and Muscarinic receptors.

- Used to treat:
  Myasthenia gravis
  Some types of poisonings
  Glaucoma and reversal of neuro-muscular blockade

Indirect Acting Cholinergic Drugs:

There are two basic types - both bind with Acetlycholinesterase, which disables it.

1. Reversible Inhibitors:
   Prototype:
   Neostigmine (Prostigmin) – used to treat myasthenia gravis.
   S/E's: SLUDGE responses (treat with a cholinergic blocker.)

   Phyostigmine (Antilirium) - used to treat an Atropine OD. Atropine is an anti-cholinergic drug. What would the patient look like who took an OD of Atropine? _____

2. Irreversible inhibitors:
   Only one drug:
   Echothiophate (Phospholine iodide) – used in the treatment of glaucoma.

Cholinesterase Inhibitors:

Are very useful as -

- Insecticides (organophosphates)

- Chemical weapons (nerve gases VX and Sarin)

TOXIC exposure results in MASSIVE SLUDGE effects
Treated with – atropine } cholinergic
pralidoxime } blockers

Anticholinergic (Parasympatholytic)

There are multiple types of cholinergic receptor antagonists.
Remember the parasympathetic nervous system receptors?

- Muscarinic
- Nicotinic:
  Nicotinic N (neuron)
  Nicotinic M (muscle.)

Muscarinic Cholinergic Antagonists

These drugs are anti-cholinergic, aka parasympatholytic.

- Bind with receptor and blocks acetylcholinesterase binding
- PARASYMPATHOLYTIC = FOOT OFF BRAKE

Prototype:

Atropine Sulfate – from the plant Atropa Belladonna (beautiful lady)

- Low doses = drying effect
- Moderate doses = ↑HR, mydriasis (dilated pupils) and blurry vision
- Higher doses = ↑GI motility and ↑stomach acid secretion
- Used to treat cholinergic or cholinesterase inhibitor OD. Which effects would this cause?

- S/E's of treatment:

Dry mouth	
Blurred vision	hot as hell
Photophobia	blind as a bat
Urine retention	dry as a bone
Increased intraocular pressure	red as a beet
Tachycardia	mad as a hatter
Constipation	
Anhidrosis (decreased sweating)	

Ipratropium Bromide (Atrovent) An inhaled anti-cholinergic.

- Used to treat _____
- Effect _____

Ganglionic Blocking Agents:

Blocks Acetylcholine at the presynaptic neuron

- Effect - _____

- Mecamylamine (Inversine) } treatment of
- Trimethaphan (Arfonad) } hypertensive crisis

NOT IN COMMON USE – NON-SELECTIVE !!

Neuromuscular Blocking Agents:

Affect Nicotinic M receptors = paralysis without affecting consciousness.

The name is based on their mechanism of action:

EITHER
- Depolarizing

OR
- Non-depolarizing, Ex. Succinylcholine – EMS preferred paralytic.

Ganglionic Stimulating Agents:

Nicotinic N receptors are at the presynaptic ganglia of both the parasympathetic and sympathetic nervous system.

Nicotine responses are dose related, affects both nervous systems.

Parasympathetic effects:
↑Salivation ↑ peristalsis ↑ gastric acid

Sympathetic effects:
↑HR ↑ SV ↑ PVR ↑ awareness
↓Fatigue ↓ appetite

Drug example: Nicotine!

Effects of long-term Nicotine use?

_____

Sympathetic Nervous System

Stimulation of sympathetic fibers causes:

- ____sweating
- _____ Peripheral (cutaneous) vasoconstriction (the patient looks pale.)
- ____blood flow to skeletal muscles
- _____ HR and ____SV (cardiac contractile force) = ____BP.
- ____Bronchodilation
- ____Blood flow to GI tract
- ____Digestive activity
- Relaxes smooth muscle in the urinary bladder wall (don't need to pee!)
- Release of glucose stores from the liver. Why is this important?

THIS IS EXACTLY WHAT HAPPENS TO YOUR PATIENT IN SHOCK

They are pale, cool and clammy, with rapid heart rate and an increased respiratory rate. How does this affect the BP? _____

What else can cause these signs and symptoms? _____

Sympathetic fibers also innervate the adrenal medulla, when stimulated:

- Release a mix of 80% Epinephrine (E)
- And 20 % Norepinephrine (NE)

These travel in the bloodstream to tissues not innervated by sympathetic nerve fibers thereby causing a widespread effect.

Also prolongs the effects of direct sympathetic stimulation.

The body is able to deal with stressful and dangerous situations.

<u>Types of Sympathetic Receptors</u>

These are adrenergic receptors:

- alpha 1 stimulation causes _____
- alpha 2 stimulation causes _____
- beta 1 stimulation causes _____
- beta 2 stimulation causes _____
- beta 3 stimulation causes _____
- dopaminergic stimulation causes _____

<u>Sympathomimetics Aka. Adrenergic:</u>

Cause the same effects as stimulation of the sympathetic NS.
LIKE PUTTING YOUR FOOT ON THE GAS.

Sympatholytics Aka Anti-Adrenergic:

Cause the same effects as blocking the sympathetic NS.
LIKE TAKING YOUR FOOT OFF THE GAS.

Medications Affecting Alpha 1 Receptors:

Alpha 1 stimulation:

- Primary clinical use is peripheral vasoconstriction

  by constricting arterioles = _____

  by constricting venules = _____

- Also used with local anesthetics to decrease systemic absorption.
  Example: Lidocaine with Epinephrine.

- Used in nasal decongestants.

S/E's:

- Primarily HTN and local tissue necrosis (death)

- Reflex bradycardia – because you have made your vascular container smaller by stimulation of Alpha 1 receptors = ↑ BP; this is detected in the cardiac center in the CNS which ↓ the BP by slowing the HR.

Alpha 1 antagonism:

- Primary clinical use - control HTN.

- Tx. local tissue necrosis by increasing blood flow.

- Tx. Pheochromocytoma (tumor of the adrenal gland.) What S&S would your patient exhibit with this condition? _____

Common S/E's:

- Orthostatic hypotension.
- Reflex tachycardia, because your BP would_____.
- Nasal congestion.
- Inhibition of ejaculation.
- Increased blood volume, this is treated with a with a diuretic.

Medications Affecting Beta Receptors:

Beta 1 stimulation:

Affect on the heart:

- Increases **H**eart **R**ate = positive chronotropic effect.
- Increases **S**troke **V**olume (contractile force) = positive inotropic effect.
- Increases rate of conduction = positive dromotropic effect.

Note – conduction refers to the rate at which the impulse is generated from the SA node.

Primary indications:

- Cardiac arrest.
- Hypotension from inadequate pumping, as in _____ _____.

S/E's:

- Tachycardia.
- Dysrhythmias (abnormal heart rhythms.)
- Chest pain from increased workload, (increased myocardial O2 demand.)

Beta 1 antagonism:

Beta 1 antagonists are among the most frequently prescribed medications in the world.
Called Beta–Blockers:

- Decrease HR = negative chronotropic effect
.
- Decrease SV = negative inotropic effect.
.
- Decrease conductance = negative dromotropic effect.

Used to treat:

- SVT's. – A rapid heart rhythm that originates in the atria.
- Angina pectoris.
- Reduces the risk of MI

Major S/E's:

- Symptomatic bradycardia. What does this mean? _____
- Hypotension, Why? _____
- AV block (an abnormal slow heart rhythm caused by blocking conduction.) What type of negative effect would this be? _____

Beta 2 Agonists:

Relax smooth muscle.

Used in the treatment of:

- Diseases causing bronchoconstriction. _____
- Pre-term labor (the uterus is smooth muscle.)

S/E's:

- Muscle tremors.
- Unintended beta 1 stimulation, this would cause _____

Beta 2 blockers:

No clinical purpose**.**

Non-selective beta blockers have the same side effects as beta 2 blockade:

- Bronchoconstriction.
- Inhibits glycogenolysis – the breaking down of glycogen (stored in the liver) to increase blood glucose levels. This would be bad for diabetics.

Drugs Affecting The Sympathetic NS

Adrenergic agonists aka Sympathomimetics:

These drugs can act either directly, indirectly, or in combination.

Direct:

- Binds with receptor, has same response as normal neurotransmitter.
- Most drugs in this category are synthetic (man made) versions of the normal neurotransmitter.

Indirect:

- Stimulate the release of epinephrine from the adrenal medulla and Norepinephrine from the pre-synaptic terminals.

Combination:

- Combines both mechanisms.

Catecholamines (Aka Adrenergic Agents):

These are drugs that are chemically and functionally similar to the endogenous (naturally occurring) neurotransmitters.

Natural:
- Epinephrine
- Norepinephrine
- Dopamine

Synthetic:
- Isoproterenol
- Dobutamine

Non-Catecholamine Adrenergic Agents:

- Ephedrine
- Phenlyephrine
- Terbutaline (Brethine) – common EMS medication.

Adrenergic Antagonists aka Sympatholytics:

Highly selective at therapeutic doses. At higher doses affect other receptors.

2 basic sub-groups:
1. Non-competitive, long acting.
2. Competitive, short acting.

Differ in stability of their bond with the receptors.

Beta Adrenergic Antagonists aka BETA-BLOCKERS.

Prototype: Propranolol (Inderal) the first clinically used.

- Non-selective i.e. blocks beta 1 and beta 2.

Used to treat:
- Tachycardia
- HTN
- Angina pectoris

S/E's:
- Bronchoconstriction, which patient population would this be bad for?
  _____
- Inhibits glycogenolysis which patient population would this be bad for?
  _____

More beta 1 selective antagonists:
- Metoprolol (Lopressor)
- Atenolol (Tenormin)

What would be the effect of these medications on your patient's heart? _____

Note: The suffix OLOL = Beta Blocker

Skeletal Muscle Relaxants:

Used to treat muscle spasm from injury and muscle spasticity from diseases and CNS injuries.

Uses either centrally acting agents or direct acting agents:

Central acting:

Causes general sedation, MOA not well understood.

Prototype:

- Baclofen (Lioresal)

Treatment of:

- Muscle spasticity (Flexaril and Soma)

Direct acting:

Decreases the release of calcium in response to action potentials generated across the neuro-muscular junction. (You need calcium for the muscle to contract.)

Prototype:

- Dantrolene

Treatment:

- Spasticity associated with multiple sclerosis (MS) and cerebral palsy.
- Malignant hyperthermia (a rare complication of anesthesia and of succinylcholine administration.)

CARDIOVASCULAR SYSTEM

To understand the drug therapies used to treat cardiovascular disease you need an understanding of the anatomy, physiology and electrical properties of the heart.

Electrical conduction (measured by an ECG tracing) and mechanical contraction (measured by vital signs) combine for an organized and efficient pumping action.

Heart:

- 2- sided pump.
- Right side is low pressure – pulmonary circulation.
- Left side is high pressure – systemic circulation, much thicker wall.
- 4 chambers – 2 atria and 2 ventricles.
- Atria accept blood, which pours passively into the ventricles.
- Just before ventricles contract the atria contract to "top off" ventricles; accounts for 25% of the ventricular load. Termed the "Atrial kick".
- Ventricles contract - forces blood out of the heart.
- Atria contract downward and ventricles contract upwards – designed for efficient pumping.

<u>Myocardial contraction is dependant upon 3 factors:</u>

1 Electrical stimulation from the conduction system

2 Enough **A**denosine **T**ri **P**hosphate (energy)

3 Enough Calcium ions.

<u>Impulse generation and conduction:</u>

The key to a precise cardiac cycle (0.8 seconds) is the electrical conduction system.

See diagram page 325 in text.

- Sinoatrial Node (SA) is the dominant pacemaker, fires at a rate of 60-100 bpm.

- Impulse travels across the atria via the intra-atrial pathways.

- Arrives at the Atrio-ventricular Node (AV), slight delay here that allows for ventricular filling.
  Can fire between 40-60 bpm. If SA node fails.

- Impulse the travels down the Bundle of His and Purkinje fibers
  The Purkinje fibers have a firing rate of 20-40 bpm.

All heart tissue, both contractile and conductive, has automaticity, (the ability to generate) and the ability to propagate (send) due to:

1. The movement of ions across a semi-permeable membrane.

2. The Resting Membrane Potential (RMP) is slightly negative on the inside of the cell. This polarization occurs due to the separation of ions by the cell membrane.

3. The cell membrane is said to depolarize when the charge is eliminated or reversed.

4. Calcium ions are present in storage packets (vesicles) surrounding the cell. Ca++ is responsible for muscle contraction.

5. See diagrams on page 326 of text.

Fast Potentials

Occur in myocardial tissue (muscle) and the ventricular conduction (electrical) system.
Has 5 phases:

i. Phase O: Rapid depolarization due to rapid sodium channels opening (Na++ influx), inside of cell becomes more positive.

ii. Phase 1: Slow potassium channels open (K+ efflux), this marks the start of repolarization

iii. Phase 2: Calcium ions enter the cell and cause a plateau, (maintaining the positive charge.)
This delays repolarization – important for muscle contraction.

iv. Phase 3: Calcium stops influx and Potassium rapidly exits cell.
This returns the cell membrane to its normal electrical charge.

v. Phase 4 – represents the RMP.

IMPORTANT POINT

Phase 2 is called the absolute refractory period – if a stimulus occurred at this point it would not have any effect. This is because the ions are all in the "wrong place."

Phase 3 is called the relative refractory period – if an **unusually strong** stimulus occurred at this point enough ions are back in the "right place" for an action potential to be propagated. What does this mean?

Slow Potentials

These are similar to the fast potentials but have several important distinctions:

- Located in the two dominant pacemaker cells of the heart, the SA and AV nodes.

- Depolarize gradually by slow influx of Ca++, (slow Ca++ channels.) This is where Calcium Channel Blocker medications take effect.

- Mechanism is unknown but is responsible for the spontaneous generation of impulses in the SA and AV nodes.

Remember the firing rates for the SA and AV nodes? Well, since the SA rate is faster it over-rides the AV node's rate.

Dysrhythmia Generation

Abnormal heart rhythms arise from:

Either
Abnormal impulse formation (automaticity.)
Or
Abnormal conductivity (re-entry.)

Most common Dysrhythmias are the tachys (fast) and the bradys (slow.)

- Often caused by an imbalance between the sympathetic and parasympathetic systems.

- What would excessive parasympathetic stimulation do to the heart rate?_____

  Treat with an anti-cholinergic, which is the drug of choice? _____

- Tachydysrhythmias have a variety of causes.

Abnormal impulse formation:

- Fast potential depolarization dominates most of the heart, where does this occur? _____

- In pathological conditions (MI, ischemia and increased sympathetic stimulation) phase 4 depolarization develops (instead of phase 0.)

  This is termed an ectopic focus (impulse from some place other than normal)

Abnormal Conduction

See Figure 9-15 page 328.

Caused by:

- Reactivation of myocardial tissue for second or more time by the same impulse.
- Occurs when normal impulse transmission is delayed, blocked or both.
- Reentry mechanism is a “short circuit” and uses tissue that is no longer absolutely refractory, i.e. can be stimulated (phase iii)

Classes of Cardiovascular Drugs

2 broad classes, anti-dysrhythmic and anti-hypertensive:

Anti-Dysrhythmia drugs classification:

Routinely classified in the Vaughn-Williams and Singh Classification System. See Text page 329.

- Used to treat and prevent abnormal rhythms.
- Can cause dysrhythmias when used inappropriately.

Sodium Channel Blockers (Class I):

- Affect Na++ influx in phases 0-4 of fast potentials.
- Slows impulse propagation, i.e. negative? _____
- Does not affect SA or AV node (these are slow potentials which use Ca++ to depolarize.)

Class 1A:

- Slows conduction.
- Decreases repolarization rate = wide QRS, long QT interval.

Prototype: Procainamide.

- Used in the treatment of atrial fibrillation with rapid ventricular response (RVR) and ventricular dysrhythmias.

Class 1B:

- Increases the rate of repolarization.

- Decreases automaticity in ventricular cells.
- Used in the treatment of V.tach and V.fib.

Prototype: Lidocaine.

- CAUTION – Lidocaine toxicity has CNS effects.
  tinnitus, confusion and seizures.

To avoid Lidocaine toxicity in the elderly halve the dose.

Class 1C:

- ↓ Conduction = a negative? _____
- ↓ Ventricular repolarization.
- Used when class 1A and 1B have failed.

Beta Blockers (Class II):

Propranolol (Inderal) – non-selective. What does this mean? _____

Esmolol (Brevibloc) - β1 selective.

- Treatment of tachycardia from ↑ sympathetic stimulation.
- β1 receptors in the heart are linked to Ca++ channels, blocks these slow Ca++ channels.

Potassium (K) Channel Blocker (ClassIII)

Anti-adrenergic properties.

- Amiodarone (Cordarone) used as an alternative to Lidocaine.

Blocks efflux of K+ → prolonged repolarization and ↑ effective refractory period.

Calcium Channel Blockers (Class IV)
Effect is identical to Beta- blockers.

- Decrease SA and especially AV node automaticity.
- Verapamil (Calan) and diltiazem (Cardizem) are the only 2 CCB's that affect the heart.

S/E's:

- Hypotension.

- Bradycardia.

Miscellaneous Anti-dysrhythmics:

Adenosine:

- Endogenous (naturally occurring) nucleoside, brief half-life of 10 seconds.
- Effects K+ and Ca++ channels.
- ↑ K+ efflux, this causes hyper polarization = **slowed conduction**
- ↓ Ca++ influx in slow potentials. Where do slow potentials occur? _____

S/E's.

Short lived but ALARMING for both you and your patient!!!

- Brief period of Asystole
- Facial flushing.
- Bradycardia.
- Chest pain.
- GIVEN FAST!

Which type of tachycardic Dysrhythmia would Adenosine be used to treat – Atrial or ventricular? _____.

Digoxin (Lanoxin)

Paradoxical drug because it has a very narrow Therapeutic Index.

It is both an effective anti-Dysrhythmia and potential pro-dysrhythmic agent.

- ↓ Firing rate of SA node (negative chronotropy) = parasympathetic effect.
- ↓ Conduction speed of AV node (negative dromotropy) = parasympathetic effect.
- In the purkinje and ventricular cells:
  ↓ Refractory period - this increases ventricular dysrhythmias
  ↑ Automaticity - this increases ventricular dysrhythmias

Magnesium

Mechanism of action is unknown.

- It is the treatment of choice in torsades des pointes, a type of ventricular tachycardia (caused by a re-entry mechanism.)

BLOOD PRESSURE

BP = CARDIAC OUTPUT (**STROKE VOLUME**: **PRELOAD**, **CONTRACTILITY**, **AFTERLOAD**) × **HEART RATE**

PERIPHERAL VASCULAR RESISTANCE

CO: Cardiac Output

The amount of blood discharged from the ventricles/minute.

PVR: Peripheral Vascular Resistance

The diameter of the blood vessels.

SV: Stroke Volume

The amount of blood discharged from the ventricles/minute.

HR: Heart Rate

The number of contractions/minute.

Preload:

The degree of stretch exerted on cardiac muscle fibers at the end of diastole.

After load:

The degree of stretch exerted on cardiac muscle fibers at the end of systole.

Contractility:

The force with which left ventricular ejection occurs. It is independent of the effects of preload and after load.

Anti-hypertensive Medications:

You know that BP = CO x PVR and CO = HR x SV.

Medications used to treat HTN manipulate all or some of these factors.

.

- Primary regulation of PVR is by the peripheral arterioles.
- HR regulated by sympathetic and parasympathetic nervous systems.
- SV controlled by contractility and volume.
- Blood volume control of HTN manipulates pre-load.

Medication Classification

Diuretics Beta-blockers and anti-adrenergics. ACE inhibitors. CCB's. Direct vasodilation.	Patient is usually on a combination of these drugs.

Diuretics:

- Reduce circulating blood volume by increasing urine production.
- ↓ Pre-load → ↓ CO.
- Main categories include loop diuretics, thiazides and potassium-sparing diuretics.
- All affect the reabsorption of sodium and chloride and create an osmotic gradient that decreases the reabsorption of water.
- Classes differ according to which area of the nephron they affect.
- In general, the earlier in the nephron the drug works, the more sodium and water will be affected.
- Earlier effect = increased diuretic effect.

In order to better understand these medications you need a basic knowledge of kidney physiology.

Kidney function

Urine is formed by 3 processes that occur in the kidneys:

1. Filtration:
   - Blood is filtered in the glomerulus and produces a substance called filtrate – this is chemically similar to blood plasma.
   - Blood flow to the kidneys is 1200ml/min = 20 -25% of the cardiac output.
   - Rate of glomerular filtrate is 125ml/minute, 99% is ultimately reabsorbed.
   - The kidneys filter 60 times the total blood volume every 24 hours!
   - You can see how important BP is to urine production.
2. Re-absorption:
   Many of the substances are returned to the bloodstream.
   - Occurs in the tubules due to an osmotic gradient and an ion gradient.
   - There is a tubular transport maximum for almost every substance that is transported across the membrane.
   - Once this maximum is exceeded the substance will not be reabsorbed but appears in the urine. Example – the TTM (tubular transport maximum) of glucose is 320mg/min, higher levels will overflow into the urine.
3. Secretion:
   Substances once again exit the bloodstream and enter the urine.
   - Affects urine composition by allowing compounds to enter tubule fluid from the capillaries.

<u>Loop Diuretics</u>

Used in the treatment of CHF and acute pulmonary edema.

Prototype: Lasix (Furosemide)

- Blocks re-absorption of Na+. Remember, water follows sodium so, lose more sodium = lose more water = lower BP.

S/E's:

Hyponatremia (low sodium)
Hypovolemia
Hypokalemia (low potassium) treat by↑ dietary K+
Dehydration
Reflex tachycardia, treat with a β1 blocker
Unexplained ototoxicity – tinnitus (ringing in ears) and deafness.

<u>Thiazides:</u>

Mechanism of action is similar to diuretics.

- Affects distal part of tubule ∴ cannot block as much Na+ from reabsorption.

.

Prototype: Hydrochlorothiazide (HCTZ)

- Thiazides depend upon GFR (glomerular filtration rate) this is affected by blood flow.

- Loop diuretics do not depend upon GFR – preferred in renal disease states where the blood flow may be affected.

Potassium sparing diuretics:

- Act late in the nephritic loop = not very potent diuretics.

- Generally used with another diuretic.

Mechanisms of action:

Either

- Inhibits Aldosterone's effect on distal tubules. Aldosterone regulates the secretion/resorption of Na+ and K+. (Spironolactone,)

Or

- Inhibits the Na+/K+ exchange mechanism (Triamterene.)

Osmotic diuretics:

Not used in the treatment of HTN.

- Osmotically large sugar molecule pulls water after it.

Prototype: Mannitol (Osmitrol)

- Treatment of ↑ ICP. What would cause an increase in ICP? _____

- Treatment of ↑ intra- ocular pressure. Which disease causes an increase in IOP? _____

Adrenergic Inhibiting Agents

These drugs work by inhibiting the CNS stimulation of adrenergic receptors – they act like α 2 agonists.

Remember α 2 stimulation? = inhibits the release of NE.

This causes vasodilation which in turn lowers BP.

There are several broad mechanisms:

1. Beta Adrenergic Antagonists:

- Most β1 receptors are in the heart, also in some specialized cells of the kidney.
- Selective β blockade:

  ↓ Contractility = ____ CO = ____ BP

  ↓ Reflex tachycardia.

  ↓ Rennin release from kidneys = ↓ vasoconstriction = ___ PVR = __ BP

Prototype: Metoprolol (Lopressor)

2. Centrally Acting Adrenergic Inhibitors:

   These are CNS α2 agonists.

   - ↓ Sympathetic stimulation of α 1 and β1 receptors = _____?

   Prototype: Clonidine (Catapres) – Relatively safe, frequently prescribed.

   S/E's = drowsiness and dry mouth.

3. Peripheral Adrenergic Neuron Blocking Agents:

   These drugs work indirectly to decrease the stimulation of adrenergic receptors.

   - ↓ NE release from sympathetic pre-synaptic terminals.
   - No longer in common use.
   - Works by ↓ synthesis of NE and exposing it to MAO.
   - Causes ↓ stimulation of α1 receptors = _____?
   - Causes ↓ stimulation of β 1 receptors = _____?
   - Also decreases release of several CNS neurotransmitters, causes primary S/E of? _____

   Prototype:Reserpine (Serpalan)

4. Alpha 1 Antagonists:

   These drugs competitively block α 1 receptors.

- Dilates venules – what is the effect on preload? _____

- Dilates arterioles – what is the effect on afterload? _____

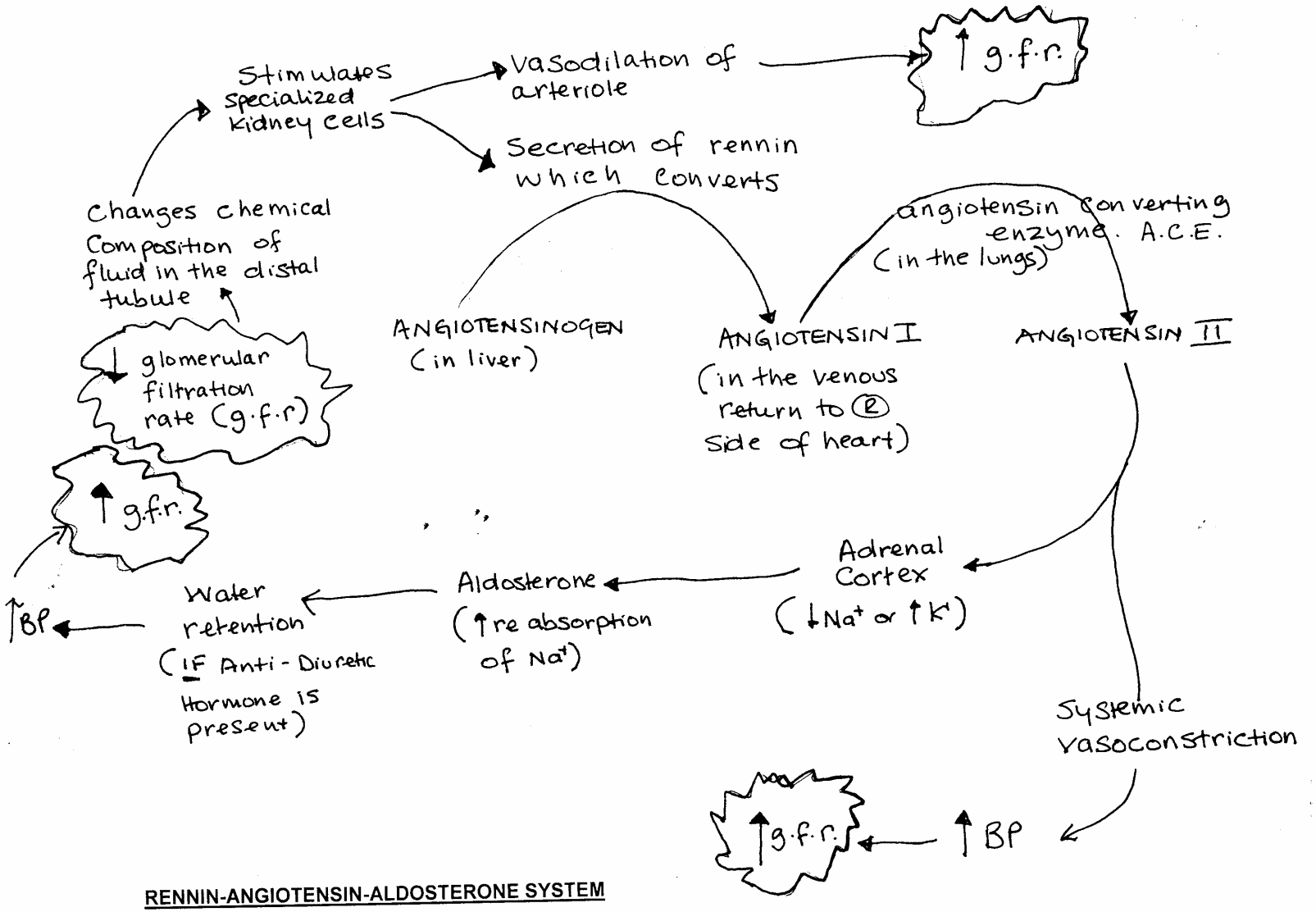
Prototype:Prazosin (Minipress)

5. Combined Alpha/Beta Antagonists:

   - Competitively bind with both α1 and β1 receptors, ↓ PVR ↓ HR ↓ SV ↓ rennin release from the kidneys, all these factors = _____?

   - Prototype: Labetolol (Normodyne) – common use in EMS.

   - What does the suffix OLOL denote? _____



RENNIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

Angiotensin Converting Enzyme (ACE) Inhibitors:

Drugs in this class interrupt the **R**ennin-**A**ngiotensin-**A**ldosterone **S**ystem (**RAAS**) by preventing the conversion of Angiotensin I to Angiotensin II.

- ACE is found mainly in the lungs and also in the lumen of all blood vessels.
- ACE inhibitors ↓ arteriole constriction = _____ PVR and ____ after-load.
- Little venous dilation = no _____ preload.
- No drop in pre-load means no orthostatic hypotension.

Prototype:Catopril (Catapres)

- Main advantage is the absence of S/E's common to other anti-hypertensive drugs.
  - No beta effects.
  - No K+ loss.
  - No depression or drowsiness.
  - No effect on sexual desire or performance.
  - Main S/E's are persistent cough and angioedema.

Other Ace inhibitors:
Enlapril (Vasotec)
Lisinopril (Zestril)

Angiotensin II Receptor Antagonists:

New class of drug that has the same effect as ACE inhibitors without the S/E's.

Prototype: Losartan (Cozaar)

Calcium Channel Blocking Agents:

Verapamil and Cardizem have already been discussed.

Subclass- Dihydropyridines:

Prototype: Nifedipine (Procardia, Adalat)

- At therapeutic doses does not affect Ca++ channels of the heart.
- Acts on smooth muscles of the arterioles = _____ afterload and dilates coronary arteries and arterioles.
- Used to treat angina pectoris and chronic HTN.

S/E's: reflex tachycardia, facial flushing, HA and peripheral edema.

- It was a commonly used EMS drug but is being widely replaced by Labetolol since it often had a precipitous effect on HTN.

Direct Vasodilators
2 specific classes:

1. Dilate arterioles.

   Prototype: Hydralizine (Apresoline)

   S/E's:
   Reflex tachycardia - to compensate for a ↓BP,
   Increased blood volume - treated with beta blocker

   - Used to treat PIH. _____

   - Another drug in this class is Minoxidil. S/E is hypertrichosis. _____

2. Dilate Arterioles and Veins.

   Prototype: Sodium nitroprusside (Nipride)

   - This is the fastest acting antihypertensive drug – only used in ICU setting.

Ganglionic Blocking Agents:

These are nicotinic antagonists – effect? _____

Prototype: trimethaphan (Arfonad.)

Cardiac Glycosides:

A glycoside is a substance derived from plants that yields a sugar and other substances.

Occurs naturally in the foxglove plant, used to treat CHF.

Prototype: Digoxin (see page 53.)

- One of the 10 most frequently prescribed drugs in the US.

- Complex mechanism of action:

  1. Blocks the action of the Na/K pump, allows Na to build up intracellularly. Ca++ follows Na into the cell and increases the strength of muscle contraction = ↑ SV. Also called? _____

  2.↑ Renal blood flow → ↑ g.f.r. causes ↓ blood volume → ↓ preload.

- S/E's:
  Narrow TI
  Dysrhythmia
  Fatigue
  Anorexia and vomiting
  Blurred vision with a yellow haze and halos around dark objects.

Other Vasodilators and Anti-Anginals:

Commonly used to treat angina.

There are 3 Types of angina pectoris (chest pain.)

1. Stable (exertional) - due to a build up of plaque (atherosclerosis)

2. Unstable (at rest) – which ↓vessel diameter.

3. Variant or Prinzmetal's – vasospasm.

All cause an imbalance between myocardial oxygen demand and supply.

Calcium Channel Blockers:

Used to treat angina:

- Verapamil (Calan, Isoptin)
- Diltiazem (Cardizem)
- Nifedipine (Procardia, Adalat)
- All dilate arterioles thus causing?_____
- Primary S/E is hypotension.

Organic Nitrates:

The prototype, since 1879, is nitroglycerine (Nitrostat)

- Others include isosorbide (Isordil, Sorbitrate) and amyl nitrate.
- MOA: Primarily dilates venules = _____ preload.
- In Prinzmetal's angina it reverses coronary artery spasm.

S/E's:

- Orthostatic hypotension – treat with fluid infusions.
- Head ache –due to? _____
- Reflex tachycardia.

Haemostatic Agents

Hemostasis = stoppage of bleeding.

EXTRINSIC FACTORS	**INTRINSIC FACTORS**
(Blood vessel damage)	(Contact with a damaged blood vessel – plaque rupture)

Release of Thromboxane A2 (TXA2)
(Stimulates platelet aggregation (clumping) and vasoconstriction

⇩

TEMPORARY PLUG

⇩

Prothrombin

⇩

Thrombin

⇩

PERMANENT REPAIR
(fibrin mesh)

Plasminogen ⇨ (tPA and other substances) Plasmin ⇨ **FIBRINOLYSIS** (breaks down fibrin mesh)

Note: t-PA = tissue Plasminogen Activator

- Thrombi are the primary pathology in MI, CVA and PE.
- Drugs used to treat these conditions are either antiplatelet, anticoagulant or thrombolytics.

Antiplatelet:

Decreases the formation of platelet plugs.

Prototype: Aspirin (ASA)

- Has no effect on existing thrombi
.
- Used to treat acute MI and CVA.

S/E's:

Bleeding and the formation of gastric ulcers.

Other anti-platelet drugs:
Dipyridamole (Persantine)
Abcixamab (Reopro)
Ticlopidine (Ticlid)

Anticoagulants
Interrupt the clotting cascade.

2 main types – parenteral and oral.

Parenteral anticoagulants:

Prototype: Heparin

- Derived from the lungs of cattle and the intestines of pigs.
- MOA – enhances antithrombin III's ability to inhibit the clotting cascade.
- Used to treat:
  DVT _____
  PE _____
  Some CVA's _____
  MI _____

S/E's:
Bleeding

↓ Platelet count

Note – Heparin is measured in units.

- A unit is the amount of heparin needed to keep 1ml. of sheep plasma from clotting for 1 hour.

Antagonist – Protamine sulfate, used to treat severe bleeding from heparin use.

Oral anticoagulants:

Prototype: Warfarin (Coumadin) – rat poison.

- Antagonizes the effect of vitamin K.
- Used to treat "high risk" patients:
  Post hip replacement
  Atrial fibrillation.
  Artificial heart valve recipients.

What is the common risk for all these patients? _____

- Overdose is treated with vitamin K.

Thrombolytics

Break down thrombi.

Prototype: Streptokinase – breaks down fibrinogen, converts plasminogen to plasmin.

Alteplase (tPA) – recombinant i.e. same as naturally occurring tPA.

What does tPA stand for? _____

Reteplase (Retavase)

Anistrepelase (Eminase)

Differ in how administered.

Anti-hyperlipidemic Agents

Remember lipid = fat.
Lipoproteins are transport mechanisms for lipids (triglycerides and cholesterol.)

- Low density lipoproteins deposit cholesterol from the liver into the circulation thus forming plaque, which leads to Coronary Artery Disease (CAD)
  LDL = BAD cholesterol.

- High density lipoproteins (HDL's) deposit cholesterol from the circulation to the liver.
  HDL = GOOD cholesterol

Goal of anti-hyperlipidemic agents is to prevent atherosclerosis and subsequent CAD.

- MOA: inhibits an enzyme needed by the liver to produce LDL.

- There are 5 types, all end in "statin."

  - lovastatin (Mevacor)

  - simvastatin (Zocor)

S/E's:
HA, rash, flushing and liver disease (rare.)

DRUGS USED TO AFFECT THE RESPIRATORY SYSTEM

1. Anti-asthmatics
2. Cough suppressants
3. Nasal decongestants
4. Antihistamines

Anti-asthmatics

Asthma is a common disease characterized by shortness of breath, wheezing and coughing.
The basic Pathophysiology has 2 components: -

Bronchoconstriction } as a response to
Wheezing } an allergen

1

Allergen binds with antibody (on mast cell membrane) → Mast cell membrane ruptures → Release of inflammatory chemicals (Histamines, prostaglandins and leukotrienes) → **IMMEDIATE** Broncho-constriction

2

SLOWER Inflammatory Response → Formation of mucus plugs → Further decrease in airway diameter

Inflammation may cause an increased reactivity to the stimuli = ACUTE ATTACK

Drug treatment is twofold:

- Relieve bronchospasm
- Decrease inflammation

Specific approaches: see table 9-8 page 341

a. Beta 2 selective agents.
b. Non-selective Sympathomimetics
c. Methylxanthines
d. Anticholinergics
e. Glucocorticoids
f. Leukotriene antagonists
g. Cromolyn

a. Beta 2 Specific Agents

Treatment of asthma-induced SOB.

Prototype; Albuterol (Proventil, Ventolin)

- Relaxes bronchial smooth muscle
- May be use daily for prophylaxis (protection).
- Given via MDI or SVN.
- Albuterol and terbutaline (brethine) are given orally.
- Terbutaline may be given SQ.

S/E's:

- Beta 2 specificity not absolute.
- Tachycardia, dysrythmias and tremors.

b. Nonselective Sympathomimetics
Stimulate alpha and beta-receptors.

- Rarely used to treat asthma.
- Include epinephrine, ephedrine and isoproterenol.
- Epi is the only one in common use today. Given for intractable asthma.

c. Methlyxanthines
CNS stimulants that have additional bronchodilatory properties.
Their specific action is unknown.

Prototype: Theophylline – oral medication.

- Aminophylline is given IV and is rapidly metabolized into theophylline.

S/E's:

- Nausea and vomiting
- Restlessness
- Dysrhythmia
- Occasionally used to treat acute asthma attacks.

d, Anticholinergics

Prototype: Ipratropium (Atrovent) – an atropine derivative.

- A muscarinic antagonist –causes bronchodilation
- Inhaled – no beta effects
- Given in conjunction with beta 2 agonists, they act along different pathways to increase the effect of either given separately.
  What would this be termed? _____

S/E: - dry mouth.

e. Glucocorticoids.
Have anti-inflammatory properties.

- Decrease inflammatory substances
- Reduce mucus plugs and edema secondary to vascular permeability.
- Route – oral, inhaled or IV.

Prototype oral - prednisone } primarily preventive, taken on
Prototype inhaled - beclomethasone } a regular basis – very safe.
Prototype injectable: methylprednisolone (Solu-Medrol) - emergent use.

S/E's occur when given long-term:

- Adrenal suppression
- Hyperglycemia

f.Cromolyn – Anti-inflammatory inhaled powder.

- Not a glucocorticoid
- Very safe, taken prophylactically before activities known to cause SOB.

g.Leukotriene Antagonists
Leukotrienes are mediators, (chemicals that make something happen) released from mast cells upon their contact with allergens.

- Can block either its synthesis or receptors.
- Prototype synthesis blocker – Zileuton (Zyflo)
- Prototype receptor blocker – Zafirlukast (Accolate)

Drugs Used for Rhinitis and Cough

Rhinitis – inflammation of nasal lining } cause by allergic reaction or viral
Rhinorrhea – runny nose } infections – common cold.

Nasal Decongestants

Constrict dilated and engorged nasal capillaries.
Treat with an alpha 1 agonist.

- Topically or orally.
- Phenylephrine, pseudoephedrine, phenylpropanolamine.
- Topical use for more than 7 days continuously causes rebound congestion.

Antihistamines
Histamine is an endogenous substance that affects a wide variety of organ systems.

Vasculature – H1 receptors

Binding causes increased capillary permeability.

What will be the local effect? _____

What will be the systemic effect? _____

Lungs – H1 receptors

Binding results in bronchoconstriction.

Gut – H2 receptors

Binding results in increased gastric acid secretion.

CNS

In the CNS histamine acts as a neurotransmitter.

Histamine is synthesized and stored in 2 types of granulocytes (white blood cells.)

- Tissue- bound in mast cells
- Plasma- bound in basophils

Some antihistamines stabilize the cell membrane.

Traditional antihistamines antagonize histamine receptors.

Chief S/E is drowsiness.
Now 2nd generation antihistamines are available – no sedation.
First Generation Antihistamines contain several subclasses:

- Alkylamines (Chlorpheniramine[chlor-Trimeton])
- Ethanolamines (Diphenhydramine [Benadryl])
- Clemastine (Tavist)
- Phenothiazines (Promethazine [Phenergan])

Several also have anticholinergic effects – treatment of motion sickness.

Second Generation Antihistamines:

- Loratadine (Claritin)
- Cetirazine (Zyrtec)
- Fexofenadine (Allegra)

They do not cross the blood-brain barrier, so no sedation.

Cough Suppressants
Coughing is a complex reflex that aids in the elimination of foreign particles.

Antitussives
Suppress stimulation in the CNS.

- Opiods – codeine and hydrocodone.
- S/E is euphoria.
- Non-opiod – dextromethorpan
  Diphenhydramine

Expectorants
Increase productivity of cough.
Little supporting data.

Mucolytics
Intended to make mucus more watery.
Little supporting data.

Drugs Used To Affect the GI System

Peptic Ulcer Disease (PUD)

Characterized by an imbalance between factors of the GI system that increase acidity and those that protect against acidity.

Most common cause of PUD:

Helicobacter Pylori – a bacterium, which infests the space between the endothelial cells and the mucus lining of the stomach.

- May be present and inert for years.
- Predisposing and contributing factors, (smoking and the long-term use of NSAID's) combine with H.Pylori to cause ulceration.

Treatment:

- Antibiotics plus drugs to block or decrease gastric acid.
- Typically 3 antibiotics;
  Metronidazole (flagyl)
  Amoxicillin (Amoxil)
  Tetracycline (Achromycin V)
- Drugs – H2 receptor antagonists (H2RA's)
- Proton pump inhibitor
- Anticholinergic agents.

Histamine + H2 receptor = increased production of H K ATPase (an enzyme that exchanges K for H) = **Increased gastric acid secretion**

Histamine + Ach receptor ========== Increased gastric acid secretion.

Histamine + PG receptor ========== Decreased gastric acid secretion.

H2 Receptor Antagonists (H2RA'S)

4 in use.

Prototype: cimetadine (Tagamet). S/E's – decreased libido and impotence, CNS effects.

Ranitidine (Zantac)
Famotidine (Pepcid)
Nizatidine (Axid pulvules)

Treatment of:

- Ulcers

- GERD
- Heartburn
- Acid indigestion
- Given routinely for the prevention of aspiration pneumonia during anesthesia.

Proton Pump Inhibitor

Acts directly on K+ H+ ATPase enzyme.

Prototype: omeprazole (Prilosec)
Lansoprazole (Prevacid)
Irreversibly blocks enzyme.

Antacids
Alkalotic compound used to increase pH.

- aluminum
- Magnesium calcium
- Sodium

Anticholinergics.

Most have too many unwanted S/E's.
One exception – pirenzipine (Gastrozepine.)

Drugs Used To Treat Constipation
Laxatives – decrease stool firmness and increase water content.
This may be desirable in certain patients, recent episiotomy, hemorrhoids, colostomies and cardiovascular disease. Why would this be beneficial?

Bulk Forming

- Methylcellulose (Citrucel)
- Psyllium (Metamucil)

Surfactant Laxatives

- Docusate sodium (Colace)

Stimulant Laxatives
Prototype: phenolpthalein (Ex-Lax, Correctol)

Osmotic
Prototype: magnesium hydroxide (Milk of Magnesia)
Drugs Used To Treat Diarrhea
Diarrhea – abnormally frequent passage of soft, liquid stool.

Symptomatic of underlying disease – usually bacterial infection.
Caused by

- Increased gastric motility
- Increased water secretion
- Decreased water absorption

Usually beneficial and self-correcting.
Treated with an antibiotic.

Drugs Used To Treat Emesis

Vomiting is a complex process that involves 2 areas of the brain.

1. Vomiting center of medulla by direct stimulus of H1 and ACh receptors and by sensory input (sights and smells) and in response to anxiety or fear.

2. Chemoreceptor Trigger Zone (CTZ) by indirect stimulation from serotonin receptors in the stomach and blood-borne substances (opiods, ipecac)

Emesis can be useful in certain OD's and poisonings.
Ipecac is the drug of choice – stimulates CTZ.

Anti-emetics

- Indicated in conjunction with chemotherapy.
- Indicated in prophylactic treatment of motion sickness.

Multiple transmitters are involved in vomiting reflex

- Serotonin
- Dopamine
- Acetylcholine
- Histamine

Serotonin Antagonists

Prototype: ondansetron (Zofran)

- Blocks serotonin receptors in CTZ, stomach and small intestine.
- Good in NV associated with chemotherapy.

S/E's

- HA
- Diarrhea

Dopamine Antagonists

- Phenothiazines – prochlorperazine (Compazine)
  Promethazine (Phenergan)
- Butyrophenones – haloperidol (Haldol)
  Droperidol (Inapsine)

S/E's

- EPS – treat with?_____

- Sedation

Another dopamine antagonist is metaclopramide (Reglan)
- Unique action – bocks both serotonin and dopamine receptors in CTZ.

Cannabinoids

These are derivatives of tetrahydrocannabinol (THC) – the active ingredient in marijuana.
- Used to treat chemotherapy induced N&V.

2 agents:
- Dronabinol (Marinol)
- Nabilone (Cessant)

Drugs Used to Aid Digestion

These are similar to endogenous digestive enzymes.
Treatment of patients, whose vagal stimulation has been surgically removed, as in duodenal bypass.

- Pacreatin (Entozyme)
- Pancrelipase (Viokase)

S/E's – N&V, abdominal cramping.

Drugs Used To Affect The Eyes

Primarily used to treat glaucoma and trauma, some are diagnostics.

Glaucoma – degenerative disease that affects the optic nerve and causes increased intraocular pressure (IOP.) Drugs aim to decrease IOP.

Beta-blockers – unknown mechanism of action.
- Timolol (Timoptic) and Betaxolol (Betoptic)

Cholinergic – stimulate muscarinic receptors in eye.
- Cause miosis and ciliary muscle contraction (Affects vision and focus.)
- Decreases IOP
- Pilocarpine (Isopto Carpine) a topical preparation.

S/E's – blurred vision and local irritation.

Diagnostics.
- Anticholinergics – mydriasis (pupil dilation.)
- Adrenergic agonists – cyclopegia (paralyze ciliary muscles.)
- Tetracaine (Pontocaine) – local anesthetic, decreases pain, sedation.

Drugs Used To Affect The Ears

Elimination of underlying bacterial or fungal infection or breaking up impacted earwax.
- Antibiotics – chloramphenicol

Gentamicin sulfate

- Treat ear wax – carbamide peroxide
  Carbamide peroxide with glycerin
- Treat swimmer's ear – isopropyl alcohol
  Isopropyl alcohol with boric acid.

Ototoxicty – occurs when drugs are taken too quickly or in an OD.

- ASA
- Erythromycin and vancomycin
- Furosemide (Lasix)

Drugs Used To Affect The Endocrine System

The endocrine and nervous systems work in conjunction to regulate homeostasis.

Nervous system is "wired" directly to organs for a fast, short-lived response.

The endocrine system is "wireless" - relies on the bloodstream to carry its signals, makes for a slow, sustained response.

See table 9-9 page 349.

Pituitary Gland

Has 2 lobes, the anterior and posterior – physically connected to the hypothalamus.

Anterior hormones are synthesized in the anterior lobe and are released upon stimulation from the hypothalamus.
There are 6 main anterior pituitary hormones.

Posterior hormones are synthesized in the hypothalamus then migrate to the posterior pituitary lobe. They are released upon stimulation from the hypothalamus.

Anterior Pituitary Drugs

- Treatment of abnormal growth

- Dwarfism – somatrens (Protropin)
  Somatropin (Humatrope)

- Acromegaly and Gigantism – which usually arises from a tumor.

  The treatment of choice is surgical removal
  - Octreotide (Sandostatin)

Posterior Pituitary Drugs

The 2 posterior pituitary hormones are oxytocin and ADH (Vasopressin.)

- ADH increases water reabsorption in the kidneys.

- ADH is a key component in regulation of BP blood volume and electrolyte balance.

- ADH analogues used to treat Diabetes Insipidus – caused by decreased ADH.

- High doses of ADH cause ↑ PVR and ↑ BP, hence its other name - Vasopressin.

Desmopressin – an intranasal spray for nocturnal enuresis.

Drugs Affecting The Parathyroid and Thyroid Glands

Parathyroid Gland

Regulates blood calcium levels.

Hypoparathroidism

- Causes ↓ Ca++ levels and ↓ Vitamin D levels – treat with a supplement

Hyperparathyroidism

- Causes ↑ Ca++ levels - usually due to a tumor – treatment is surgical removal.

Thyroid Gland

Regulates growth, maturation and metabolism.

Hypothyroidism:

- Child – Cretinism = dwarfism and mental retardation

- Adult - ↓ BMR, weight gain, bradycardia and fatigue.

Prototype – levothyroxine (Synthroid)
OD – thyrotoxicosis/thyroid storm, tachycardia, hyperthermia, angina HTN.

Goiter – an enlarged thyroid gland due to ↓ dietary iodine.

Hyperthyroidism

- Usually as a result of tumors.

- Causes Grave's disease – tachycardia, HTN, ↑BMR, weight loss, hyperthermia, nervousness. Severe cases exhibit exopthalmous.

Treatment – surgical removal.

Drugs Affecting The Adrenal Cortex

Synthesizes and secretes 3 classes of hormones.

1. Glucocorticoids - ↑ production of glucose. Most important - Cortisol.

2. Mineralcorticoids – regulate sodium and water balance. Most important - Aldosterone.

3. Androgens – regulation of sexual maturation and development.

Cushing's Disease

Hyper-secretion of adrenocorticotropic hormone (ACTH.)
Causes ↑ synthesis of corticoids → ↑ glucocorticoids = LOTS of GLUCOSE.

S&S
- Hyperglycemia
- Obesity
- HTN
- Electrolyte imbalance

Treatment
- Usually surgical
- K+ sparing diuretics
- ACE inhibitors
- Antiadrenals – ketoconazole (Nizoral) at high doses.

Addison's disease:

Hypo-secretion of ACTH.

Treatment
- Replacement therapy –
  Cortisone (Cortistan)
  Hydrocortisone (SoluCortef)

Drugs Affecting The Pancreas

Diabetes Mellitus (DM) – inappropriate carbohydrate metabolism.
Diabetes Insipidus (DI) – inadequate ADH secretion.

Type I DM –Insulin Dependant Diabetes Mellitus (IDDM)

- Inadequate insulin production.
- Usually occurs before the age of 30, aka. Juvenile Onset.
- Requires insulin injections for life.

Type II DM – Non-Insulin Dependant Diabetes Mellitus (NIDDM)

- Accounts for 90% of diabetics
- Adult onset – typically aged 40+
- Usually due to obesity
- Usually treated with oral hypoglycemic.

Gestational Diabetes

- Occurs during pregnancy
- Stress- induced type (physical, not mental!)
- Resolves post delivery, generally within 2 –14 days.

<u>Pancreas</u>

Secretes the two main glucose-regulating substances:

INSULIN – a HYPOGLYCEMIC agent.

- Synthesized in the beta cells of the Islet of Langerhans.
- Produced in response to ↑ glucose levels.
- ↑ Transport of glucose, K+ and amino acids into the cells.
- Converts glucose into glycogen = gluconeogenesis (glycogen is stored in the liver and skeletal muscle)
- Promotes cell growth and division

GLUCAGON – a HYPERGLYCEMIC agent.

- Synthesized in the alpha cells of the Islet of Langerhans.
- ↑ glycogenolysis i.e. converts glycogen → glucose.

INSULIN

3 sources – cow intestines (bovine)
- Pig intestines (porcine)
- Human (using recombinant DNA)

All are given SQ except regular insulin, which may be given IV.

Treatment of

- IDDM
- Emergency treatment of hyperglycemia
- Emergency treatment of hyperkalemia in non-diabetics.

NOTE

- Beta-blockers can mask the effects of hypoglycemia, plus their action ↓ glucagon release – aggravates condition.

Oral Hypoglycemic Agents

Stimulate insulin secretion from the pancreas in patients with NIDDM.
4 classes:

1. Sulfoylureas

Also known as first or second-generation hypoglycemics.

- Tolbutamide (Orinase)
- Chlorpromide (Diabinese)
- Glipizide (Glucotrol)
- Glyburide (Micronase)

S/E's

- Hypoglycemia

2. Biguanides

↓ Glucose synthesis and ↑ glucose uptake.

- Metformin (Glucophage)

S/E's

- N&V
- ↓ appetite

3. Alpa-Glucosidase Inhibitors.

Delay carbohydrate metabolism.

- Acarbose (Precose)

S/E's

- Flatulence
- Cramps
- Diarrhea
- Abdominal distension

ALL DUE TO COLONIC BACTERIA FEEDING ON THE INCREASED CARBS IN THE FECAL MATTER

4. Thiazolidinediones

New class - ↑ tissue response to insulin.

- Troglitazone (Rezulin)

S/E's

- None?????

UPDATE – OFF THE MARKET DUE TO LIVER DAMAGE!

Hyperglycemic Agents

Increase blood glucose levels.

- Glucagon – emergency treatment of hypoglycemia, given IM.
- D50 in DW – treatment of acute hypoglycemia. Primary S/E is tissue necrosis if infiltrated
- Diazoxide (Proglycem) – treatment of hyper-insulin secretion, usually as a result of pancreatic tumors. Inhibits insulin release.

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DRUGS AFFECTING THE FEMALE REPRODUCTIVE SYSTEM

Estrogens and Progestins.

Estrogens:

- Produced by the ovaries and ovarian follicles.
- Produced by the placenta during pregnancy.

- Primary ovarian estrogen is estradiol.
- Primarily indicated for HRT in post- menopausal women.
- Decreased estrogen levels lead to osteoporosis and CAD.
- HRT has been linked to an increased risk for breast cancer - the information is conflicting.

Progestins:

- Counteract the effects of estrogen in HRT.
- Used in the treatment of amenorrhea, endometriosis and dysfunctional uterine bleeding.

Oral Contraceptives:

- Primary MOA is to inhibit ovulation.
- Combination of estrogen and progestin.
- Second most popular means of birth control after surgical sterilization.

S/E's

- Unintentional pregnancy – less than 3%.
- Thrombo-embolism (the risk is less with low estrogen pills.)
- HTN
- Abnormal uterine bleeding.

Uterine Stimulants and Relaxants:

Oxytocin means rapid birth.

Oxytocics

- Drugs that increase uterine contraction (stimulant.)
- Used to induce labor and treat severe PPH. _____
- Oxytocin is available as Pitocin and Syntocinon.
- The uterus becomes increasingly sensitive to Oxytocin during the pregnancy.
- Oxytocin also affects cartilage – has the effect of "loosening" joints.
- Ergonovine (Ergotrate) is only used in PPH – it increases both the strength and duration of contractions.

Tocolytics

- Drugs that decrease uterine contractions (relaxants.)
- Stimulate Beta 2 receptors in the uterus. _____

- Terbutaline (Brethine) – not approved by the FDA for this purpose. In EMS Brethine is used for respiratory emergencies.

S/E's

- Tremors
- Tachycardia
- Glycogenolysis

Infertility Agents

- Infertility has many possible causes.

DRUGS AFFECTING THE MALE REPRODUCTIVE SYSTEM

Testosterone replacement therapy:

- Treatment of cryptorchidism. Greek crypt = hidden and orchis = testis.
- Treatment of orchitis.
- HRT post orchidectomy

Benign Prostate Hypertrophy:

- Enlarged prostate.
- Common age-related disease.
- By the age of 70 treatment is sought by 75% of men.
- Cause urinary frequency and retention.

Treatment:

- Surgery
- Finasteride (Proscar

S/E's

- Rash, breast tenderness. HA, impotence and decreased libido.

Drugs Affecting Sexual Behavior

Many classes of drugs decrease libido, inhibit erection and ejaculation.
Examples

- Anti –hypertensive.
- Anti- anxiety/psychotics.

Many substances claim to improve libido but have no proven physiologic effects. Examples:

- Cantharis (Spanish fly.)
- Hallucinogens – LSD, alcohol and marijuana.

Levodopa (L-Dopa)

- Treatment of Parkinson's disease.
- Increases libido and erectile ability as a side effect.

Sildenafil Citrate (Viagra)

- Approved in 1998 for the pharmacological treatment of erectile dysfunction.
- Relaxes vascular smooth muscle.
- Increases blood flow to the corpus cavernosum.
- Unique in that it has no effect in the absence of sexual stimulation.

S/E's:

- When used in conjunction with nitrates – hypotension.
- EMS concerns – not in conjunction with NTG or any nitrate.
- How would you treat this patient in the event that both drugs were taken and you have a severely hypotensive patient? _____

DRUGS USED TO TREAT CANCER

- Anti-neoplastic agents are drugs used to treat cancer.
- Cancer – an abnormal growth of tissues. aka a neoplasm.

- Surgery is the most effective treatment; only a few cancers are successfully treated with chemotherapy.
- The more lethal cancers do not involve a compact growth – they are widely dispersed, therefore surgery is not an option.
- Have to develop drugs that only target cancer cells

.

- Chemotherapy is a balancing act between killing cancerous and non-cancerous cells.
- Cancer cells divide and replicate rapidly.

Drugs are grouped according to their MOA:

Antimetabolite

- Mimic enzymes and proteins needed for DNA replication
- Inhibit cell reproduction.
- Prototype – fluorouacil (Adrucil)

Alkylating agents

- Interfere with DNA splitting.
- Cyclophosphamide (Cytotoxan)
- Mechlorethamine (Mustargen)

Mitotic inhibitors

- Stop cell division.
- Vinblastine (Velban)
- Vincristine (Oncovin)

S/E's

- N&V
- G I disturbances
- Hair loss
- Weakness

DRUGS USED TO TREAT INFECTIOUS DISEASES AND INFLAMMATION

Bacterial cells have hypertonic cytoplasm and a rigid impermeable cell membrane

When cell wall synthesis is inhibited water enters and ruptures the cell.

Bactericidal – kills bacteria.

Bacteriostatic – inhibits bacterial growth.

Antibiotic side-effects:

- GI problems due to a decrease in the number of bacteria in the colon.

NOTE: THE SUFFIX "CIDE" = DEATH

Anti-fungal agents:

- Fungi are parasitic microorganisms
- Azole anti-fungals inhibit fungal growth.
- Prototype – Ketoconazole (Nizoral)

Anti-viral agents:

- Acyclovir (Zovirax)
- Zidovudine (Retrovir) – AZT (used in Tx. AIDS)

Malaria

- Parasitic infection common to the tropics.
- Transmitted by mosquito or less commonly blood borne.
- Treat with schizonticides
  Chloroquine (Avalem)
  Mefloquine (Lariam)
  Quinine – Gin and Tonic!

Tuberculosis:

- Bacterial infection via airborne droplets.
- Pockets of disease can become "walled off" in the lungs and may remain dormant for years.

Treated with:

- Isoniazid (Nydrazid, INH)
- Rifampin (Rifadin)

Amebiasis:

- Parasitic infection of the intestines.
- Spread by the oral-fecal route, by poorly cooked food and poor hygiene.

Treated with:

- Pyromyacon (Humatin)
- Metronidazole (flagyl)

Helminthiasis:

- Caused by parasitic worms.
- Causes malnutrition, bowel obstruction and the worms produce toxins.
- Need to kill directly or detach and flush out.

Treated with:

- Mebendazole (Vermox.)
- Niclosamide (Niclocide.)

Leprosy:

- Bacterial disease treated with –
  Dapsone (DDS, Avlosulfon)
  Clofezamine (Lamprene)

NSAID:

Non-Steroidal Anti-Inflammatory Drugs.

- Used as analgesics and anti-pyretics.
- OTC – ibuprofen and acetaminophen.

- Block the production of prostaglandins – this interrupts the inflammatory process.

- Used to treat –
  HA
  Arthritis
  Dysmenorrhea
  Orthopedic injuries.
  Pain post trauma and surgery.

Other NSAID's:

- Ketorolac (Toradol)
- Piroxicam (Feldane)
- Naproxen (Naprosyn)

Uricosuric Drugs

Used in the treatment of gout.

- Gout is an inflammatory disease caused by altered metabolism of uric acid and increased uric acid blood levels.

- Acute episodes cause pain and swelling of joints.

- If left untreated can lead to – kidney stones
  Nephritis
  Atherosclerosis.

Drugs:

- Colchicine

- Allopurinol (Zyloprim.)

Serums, Vaccines and other Immunizing Agents

The body has a complex series of systems to prevent disease:

- Anatomical barriers – skin and mucus membranes.

- Pathogen – a disease-causing organism.

- If a pathogen breaches the anatomical barriers then the immune system is activated.

- The immune system comprises:
  Spleen
  Lymph nodes
  Thymus gland
  Leukocytes
  Antibodies (in the plasma)

Passive and Active Immunity:

Passive – antibodies pass directly into the plasma. Example: maternal fetal.

Active – a new pathogen is introduced to the body which manufactures antibodies to the new pathogen.

Serums and vaccines may augment the immune system:

Serum – a solution containing antibodies for a specific pathogen. The serum may confer temporary or passive immunity.

Vaccine – a solution containing a modified pathogen tha does not actually cause the disease but stimulates the development of antibodies specific to it.

Immune suppressing and Enhancing Agents:

Immunosuppressants:

- Used to prevent the rejection of transplanted organ sand grafted skin.

Example: Azothiaprine (Imuran)

Immunomodulators:

- Enhance the natural immune reaction

- Used in immunosuppressed patients

Example: Zidovudine (Retrovir) AZT

Dietary Supplements

Vitamins:

- Vitamins are essential for many physiologic processes.
- Must be obtained from the diet. Usually adequate in developed areas.
- Several populations may need vitamin supplements –
  Pregnant and nursing mothers
  Alcoholics

Absorption disorders
Malnourishment
See table page 362.

Minerals

- Iron is essential for the transport of oxygen.

Drugs Used To Treat Poisonings and Overdoses

Treatment is dependant upon the substance involved.

General

- Emptying of gastric contents – Syrup of Ipecac.
- Increasing gastric motility (decreases time available for absorption)
- Alkalinizing the blood (and ultimately the urine) with Sodium Bicarbonate in TCA and Salicylate overdoses.

How does this help? _____

- Filtering the blood – dialysis.
- CCB overdose – treated with? _____

- Beta blocker overdose – treated with? _____

Antidotes – very few.

- Receptor site antagonism.
- Blocking metabolic enzymes.
- Chelation – the binding with a stable substance, renders the poison inert.
- Acetylcysteine (Mucomyst) - treatment of acetaminophen overdose.
- Deferoxamine is used to chelate iron.
- Organophosphate poisoning – these chemicals are common in herbicides, insecticides and chemical weapons.

What would your patient look like who had been exposed to an organophosphate? _____

Which is the drug of choice to treat them? _____