MITERM- NR566

1 Know what meds you would give for asthma and COPD (LABA and intermittent use)

- LABA- indacaterol (Arcapta). Indacaterol is a once-daily long-acting bronchodilator that has an onset of 5 minutes and a duration of 24 hours
- FORMOTEROL/ SALMETEROL/ INDACATEROL

3 What to do when a patient calls you with hypoglycemia

4 How many gms of carb is needed during hypoglycemic episode- **15** what to tell patient to do for low blood sugar

5 how many mcg of dietary intake of iodine

- Dietary iodine of about 100 to 150 mcg/d is required for normal thyroid hormone production.

6 alendronate (Fosamax) patient education- osteoporosis

- PO meds should be taken first thing in the morning, at least 30 mins prior to medications.
- Take it with 8oz plain water
- Mineral water, coffee, OJ, and other beverages greatly reduce absorption.
- Remain upright for least 30 mins after taking meds, which allows for passage out of the stomach and minimizes the risk for esophageal irritation.
- GI distress and dyspepsia are the most common s/e's. if needed take aluminum and magnesium containing anatacids may be taken more than 2 hours fosomax.
- Patients should eat a diet that has calcium and vitamin D

7 what medication decreases the T4 and the answer was Carbamazepime/ drug increases t4 (carbamazepine)

8 First choice for hypertension – which diuretic

- thiazide-type diuretic has been typically chosen because in the landmark

Chlorothiazide (Diuril)
Chlorthalidone.
Hydrochlorothiazide (Microzide)
Indapamide.
Metolazone.

9 Besides hypertension, BB are indicated for (I selected MI)

Angina/ HTN/ MI prophylaxis/ glaucoma / migraine prophylaxis

10 Mechanism of action of Theophylline

- Treats asthma (bronchodilator)
- Work directly by an unknown mechanism believed to be mediated by selective inhibition of specific phosphodiesterases. This, in turn, produces an increase in cAMP, which then leads to bronchial smooth muscle and pulmonary vessel relaxation.
- Theophylline and caffeine have an impact on most of the major body systems. They are powerful CNS stimulants, often causing insomnia and excitability. Although both drugs have cardiovascular effects, theophylline has a greater effect on the cardiovascular system. Theophylline directly stimulates the myocardium and increases myocardial contractility and heart rate. By relaxing vascular smooth muscle, theophylline dilates the coronary, pulmonary, and systemic blood vessels.

11 What should you test a patient c/o muscle pain, on atorvastatin

- For all reductase inhibitors, muscle tenderness or pain may indicate a serious problem that may require discontinuance of the drug.
- patient C/O muscle pain on atorvastin: check cK level.

12- 7 yo with pneumonia, what to give if already on amoxicillin

- high-dose amoxicillin (90 mg/kg daily, divided in two doses) is the drug of choice for 7 to 10 days of outpatient treatment (Bradley et al, 2011)). I**f highly resistant pneumococci are in the community, the practitioner may choose between IV or IM ceftriaxone (50 mg/kg in one daily dose) or cefotaxime** (150 mg/kg/d every 8 hours) followed by appropriate oral therapy after 1 or 2 doses

13 What to give for high cholesterol if cannot take statins – name of medication

- Nicotinic acid (niacin) was always touted as effective in lowering total cholesterol and triglyceride levels and raising HDL levels

14 Which inhaler to give on asthma exacerbation

- Ipratropium is an inhaled anticholinergic that may be used in combination with **albuterol** to treat asthma exacerbation in the emergency department (NAEPP, 2007). Hospital admission may be avoided by the addition of ipratropium to the treatment regimen in cases of exacerbation seen in the clinic or emergency department

15 Nicotine replacement drugs– bupropion should be avoided with what?

- Bupropion is contraindicated in patients with seizure disorders, bulimia, and anorexia nervosa and within 14 days of the use o**f monoamine oxidase inhibitors (MAOIs).**
- Bupropion should not be used in patients with a history of stroke, brain tumor, brain surgery, or history of closed head injury.
- Bupropion should be used with caution in patients with hepatic cirrhosis, with the dose decreased to 150 mg every other day.
- *The concurrent use o**f bupropion (Zyban) and Wellbutrin** is contraindicated. Risk of suicide ideation and suicidality in children, adolescents, and young adults. Zyban is not approved for smoking cessation in children under 18 years of age. Patients prescribed Zyban should be monitored closely for signs of suicide ideation when treatment is started.*

16 INH - risk for liver toxicity

- INH has a Black-Box Warning regarding the development of severe and sometimes fatal hepatitis, even after many months of treatment.
- .Increased risk for hepatitis is associated with daily alcohol use, chronic liver disease, and IV drug use. Black and Hispanic women, as well as any woman during the postpartum period who takes INH, may have increased risk of developing fatal hepatitis. nitro sublingual
- All patients taking INH should have monthly symptom reviews to screen for hepatitis. Symptoms to screen for include unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, persistent paresthesias of hands or feet, fatigue, weakness, fever longer than 3 days, or abdominal tenderness especially in the right upper quadrant.
- Liver enzymes should be measured in patients over age 35 years prior to starting INH and then periodically throughout treatment.
- They should report all flu-like illness immediately and see their health-care provider at least monthly during treatment.

17 Angina patient should be on ASA- **aspirin**

- Atenolol, metoprolol, nadolol, and propranolol are indicated for long-term management of angina

18 Angina and diabetic should be on what

19 Which medication to take for SVT

- **Verapamil** might be chosen for patients with supraventricular tachycardia who also have angina.
- Type 1 CCBs (calcium channel blockers) are useful in treating selected supraventricular tachycardias because they slow AV nodal conduction. Verapamil (80 to 120 mg orally) can be used to terminate the rhythm. Conversion usually occurs in about 1 hour. Diltiazem (40 to 80 mg orally) can also be tried. Prophylaxis with verapamil (240 to 480 mg/d) is effective for patients with paroxysmal supraventricular tachycardia (PSVT)

20 MOA of nitroglycerine sublingual

- Nitroglycerin (NTG) and its analogues act largely by providing more nitric oxide (NO) to vascular endothelium and arterial smooth muscle, resulting in vasodilation (Fig. 16-5). All parts of the vascular system, from larger arteries to large veins, relax in response to nitrates.
- Sublingual absorption is dependent on salivary secretion. Dry mouth (including drug-induced) decreases absorption.
- The sublingual route avoids hepatic first-pass effect and is preferred for achieving a rapid blood level.

21 Goal for HgA1C when on tx; **7mg/dL**

22 Glucagon route; How glucagon is given

- Glucagon is well absorbed after parenteral administration. (IM)

23 MOA of insulin

- once insulin arrives to the receptors, it creates changes within the cell membrane that result in translocation of certain proteins, such as glucose transporters from sequestered sites within the cell to the cell surface.
- Insulin promotes the storage of fat as well as glucose and influences cell growth and metabolic functions in a wide variety of tissues.
- Insulin acts on the liver to increase storage of glucose as glycogen and resets the liver after food intake by reversing the amt of catabolic activity.
- Insulin reduces the circulation of free fatty acids and promotes storage of triglycerides in adipose tissue, done by the suppression of cAMP production and dephospherylation of the lipases in fat cells.

24 stages of asthma adults (>12yrs)

1. **Mild intermittent asthma:** Symptoms occur less often than twice a week and the patient is asymptomatic between exacerbations; nighttime symptoms occur less than twice a month; and peak expiratory flow (PEF) is greater than 80% predicted. The use of short-acting beta2 agonists (SABA) should be less than twice a week, unless used for exercise-induced bronchospasm (EIB).
2. **Mild persistent asthma:** Symptoms occur more often than twice a week but less often than once a day and exacerbations may affect activity; nighttime symptoms occur 3 to 4 times a month; and PEF is greater than 80% predicted. Patients with mild persistent asthma may use their short-acting beta2 agonists more than twice a week but not daily, and not more than once daily.
3. **Moderate persistent asthma:** The patient is having daily symptoms; requires daily use of a beta2 agonist; exacerbations affect normal activity; nighttime symptoms occur more often than once a week; and PEF is greater than 60% to less than 80%.
4. **Severe persistent asthma:** The patient has some degree of symptoms all the time; extremely limited physical activity and frequent exacerbations; frequent nighttime

symptoms, often 7 days a week; and decreased lung function (PEF less than 60% predicted). Table 30-1 outlines the classifications of asthma severity in patients aged 12 years or older.

stages of asthma children (<12 yrs)

1. **Mild intermittent asthma:** Symptoms occur less often than twice a week and the patient is asymptomatic between exacerbations. Children aged 0 to 4 years have no nighttime symptoms, and children aged 5 to 11 years have nighttime symptoms less than twice a month and PEF is greater than 80% predicted. The use of short-acting beta2 agonists should be less than twice a week, unless using for EIB. Exacerbations requiring oral systemic corticosteroids occur no more than once a year.

2. Mild persistent asthma: Symptoms occur more often than twice a week but less often than once a day and exacerbations may affect activity. In children aged 0 to 4 years, nighttime symptoms occur 1 to 2 times a month, and in children aged 5 to 11 years, nighttime symptoms occur 3 to 4 times a month; PEF is greater than 80% predicted. Patients with mild persistent asthma may use their short-acting beta2 agonists more than twice a week but not daily, and not more than once daily. Children younger than age 4 years with mild persistent asthma have more than two exacerbations in 6 months requiring systemic steroids or four episodes of wheezing in a year lasting more than a day and risk factors for persistent asthma. Children aged 5 to 11 with mild persistent asthma have exacerbations 2 or more times a year.

3. Moderate persistent asthma: The child is having daily symptoms; requires daily use of a beta2 agonist; and exacerbations affect normal activity. In children aged 4 years or younger, nighttime symptoms occur 3 or 4 times a month, and in children aged 5 to 11 years nighttime symptoms occur more than once a week but not nightly; PEF is greater than 60% to less than 80%. Children with moderate persistent asthma have exacerbations 2 or more times a year.

4. Severe persistent asthma: The patient has some degree of symptoms all the time; extremely limited physical activity; frequent nighttime symptoms (more than once a week in children younger than age 4 years and in older children often occurring 7 days a week); and decreased lung function (PEF less than 60% predicted). Children aged 5 to 11 with severe persistent asthma have exacerbations 2 or more times a year.

25 what to give pregnant pt with TB **(niacin)**

26 know what hgA1c percent is equal to blood sugar/ levels

-

Hemoglobin A1c Levels	Mean Plasma Glucose (mg/dL)
6	126
7	154
8	183
9	212
10	240
11	269
12	290

- which diabetic meds are contraindicated in what diseases

27 aspirin is given to all patients with cardiovascular disease

28 which drug to give peds pt with chlamydial pneumonia **(erthryomicin)**50 mg/kg daily for 14 days or oral azithromycin (Zithromax) 20 mg/kg/d for 3 days

29 teaching for pancreatic enzymes

- all doses are taken immediately before or with meals or snacks with a fatty component.
- Fruit, hard candy, fruit juice-like drinks, tea or coffee or popsicles do not require enzymes.

- PANCRELIPASE is destroyed by acid. PPIs, sodium bicarb, or aluminum-Based antacids may be used w/ preparations w/o enteric coating to neutralize gastric pH.
- Ca+ and Mg based antacids should not be used for this purpose because they interfere with drug action.
- Dietary recommendations depend on the reason enzyme replacement is needed, but generally the diet is **high calorie, high protein, and low fat.** For children with CF, the diet is high calorie, high protein, and high fat. The dosage of the enzyme replacement is based on fat content of the diet, so the amount of fat in each meal should be fairly consistent.
- Small, frequent meals are often better tolerated than three large meals, especially when the reason for the enzyme replacement is CF, post-operative gastrectomy, or bariatric procedure. Use the same brand consistently. Enzymes should not be refrigerated, nor stored in hot places, and must be checked for expiration dates.

30 pt has pneumonia, on doxycycline, and comes back 3 days later says he feels better but cxr is worse **(I chose do nothing because this is normal in pneumonia: this is what I read on PP)**

31 what to do about angina and SL nitro- if CP is not relieved by 2nd dose take 3rd dose and call 911

32 Fibric acid

- There are four general classes of lipid-lowering drugs: niacin, **fibric-acid derivative**s, bile-acid sequestrants, and competitive inhibitors of HMG
- Fibric acid derivatives (gemfibrozil [Lopid] and fenofibrate [Tricor]) increase lipolysis of triglycerides via lipoprotein lipase, resulting in a decrease of 50% or more in triglyceride levels. A decrease in VLDL is also related to decreased secretion by the liver.
- Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has occurred with reductase inhibitors and fibric-acid derivatives.
- Combining reductase inhibitors and fibric-acid derivatives also increases the risk for rhabdomyolysis.

34 most common pathogen for CAP

Streptococcus pneumoniae

- Dietary intake for iodine: 100-150 mcg/Day
- Alendronate patient education:
- oral medications should be taken first thin in the morning at least 30 mins before other medication, beverages or food (60 min for IBANDRONATE). Mineral water, coffee, OJ greatly reduce absorption. If supplemental antacids are tkaen, it should be given at least 1 hr before these other drugs.
    - Supplemental vitamin D are typically needed, and behaviours such as smoking and alcohol intake increase the risk for osetoporosis.

33 stages of angina

Class	New York Heart Association	Canadian Cardiovascular Society
Class I	Proven coronary artery disease without symptoms	Ordinary physical activity, such as walking or climbing stairs, does not cause angina.
Class II	Mild symptoms: angina and slight limitation during ordinary activity	Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold wind, under emotional stress, or only during the few hours after awakening.
Class III	Marked limitations: angina during less-than-routine physical activity (walking short distances)	Marked limitations of ordinary activity.
Class IV	Severe limitations: angina during minimal activity or rest	Inability to carry on any physical activity without discomfort. Angina may occur at rest.

- ACE and DM meds MOA,

TYPE 2 DIABETES

- Treatment is based on the disfunction on insulin secretion
    - Some medications are given to increase insulin secretion
    - Others rx are given to help overcome the insulin resistance
- TX:
    - Lifestyle modification (nutrition, physical activity, and weight loss)
    - Biguanides - METFORMIN (first line of action!!)
        - DO NOT give to pts who have LIVER FAILURE (lactic acidosis)
    - Thiazolididiones (TZDs)
    - Sulfonylureas
    - Incretins (GLP-1 or DPP-4)

Biphosphonates

- Drugs: etidronate (Didronel) / Pamidronate (Aredia) /risedronate (Actonel)/ Alendronate (Fosamax) / Tiludronate (Skelid)
- MOA: most commonly used rx for bone remodeling, adhere tightly to bone and inhibit osteoclastic activity, are potent inhibitors for both normal and abnormal bone resorption.
- Metabolism/ Secretion: have the potential for esophagitis and bone irritation. The bioavailability is significantly reduce in the presence of food. Therefore these rx should only be taken with water and in an empty stomach, and pt should remain upright for at least one hour.
- Indications: osteoporosis/ bone loss related to smoking/ calcium deficiency. Providers should consider the prophylactic use of bisphosphonates in pts w/ early osteopenia r/t the use of long term md of thyroid hormones, aromatase inhibitors, and glucocorticoids.
- Precautions/ contraindications: caution use with pts who have GI issues. Pts taking ETIDRONATE should be monitored w/ xrays to assess for fractures w/ Paget's disease when high doses are given. Forcing fluids after IV formulations is recommended to avoid renal toxicity.
    - It is recommended that adults taking more than 7.5 mg PREDNISONE for more than 3 weeks, ALENDRONATE or RISEDRONATE should be given. Initial dosing for this starts at 5mg/day or 35mg/week
- ADRs: musculoskeletal pain. Rarely jaw osteonecrosis occur usually with dental issues. Potential for atrial fibrillation.

- Drug Interactions: Histamine2 blocking agents (antiacidic rx such as RANITIDINE) impact the bioavailability of ALENDRONATE. Calcium supplements and anatacids should be taken within one hour. The risk for GI bleeding is increased w/ aspirin and NSAIDs.
- Monitoring: before beginning tx, other diseases should be r/o which might be helpful to know the cause of bone mass loss. Tests should include, TSH, serum creatinine levels, vit D, serum calcium.
    - Measurement of bone mineral density is the most accurate predictor of fracture risk and the efficacy of these drugs.
- Patient Education: oral medications should be taken first thin in the morning at least 30 mins before other medication, beverages or food (60 min for IBANDRONATE). Mineral water, coffee, OJ greatly reduce absorption. If supplemental antacids are tkaen, it should be given at least 1 hr before these other drugs.
    - Supplemental vitamin D are typically needed, and behaviours such as smoking and alcohol intake increase the risk for osetoporosis.

Aromatase inhibitors

- Drugs: also known as estrogen synthetase or synthase. Anastrazole (Arimidex) and letrozole (Femara)/ Exemestane (Aromasin)
- MOA:
- Metabolism/ Secretion:
- Indications: breast cancer, usually used as adjuvant therapy in estrogen receptor positive postmenopausal breast cancer pts.
    - First line of tx for advanced or metastatic cancer
- ADRs: vertigo, insomnia, sleepiness, confusion, increased risk for blood clots and hair loss. Bone loss can be significant when considering post-menopausal or osteoporotic risks. A life threatening increase in blood clotting can result in MI, stroke, and PE.
- Drug Interactions: none should be taken with tamoxifen or an estrogen product. Anastrazole cannot be taken with pimozide. Both anastrazole and letrazole will decrease the effect of digoxin and vitamin K antagonists. Exemestane should not be taken with axtinib or simeprevir. It will decrease the effect of aripiprazole and saxagliptin and increase the effect of methadone and vitamin K antagonists. Letrozole cannot be taken with tegafur.
- Patient Education: advise patients on how to recognize DVT, stroke, and MI, due to the potential for clot formation.

Growth hormones

- Drugs:
- MOA:
- Metabolism/ Secretion:
- Indications:
- ADRs:
- Drug Interactions:
- Patient Education:

Pancreatic enzymes

- Drugs: PANCRELIPASE
- MOA: the enzymes secreted by the exocrine pancreas are trypsinogen (protein digestion), chymotrypsin (protein digestion), amylase (carbohydrate digestion), and lipase (fat digestion). Pancrelipase contains principally lipase with some amylase and protease. This drug family substitutes for pancreatic enzymes and hydrolyzes fats to glycerol and fatty

acids, changes proteins into peptides and amino acids, and converts starch into dextrins and sugars.

- Metabolism/ Secretion/ absorption: these rx exert most of their effects in the duodenum and upper jejunum with limited if any systemic distribution.
    - Because they are inactivated by gastric acid pH of 4 or less and pepsin secretion, problems in drug delivery by the oral route may occur. Enteric coating may prevent destruction or inactivation by gastric acid but inhibits enzyme delivery to the duodenum. For this reason, it is important to synchronize the delivery of the drug with gastric emptying; therefore, the drug is taken immediately before or with a meal.
- Precautions and contraindications: PANCRELIPASE is derived from porcine source. Pancreatic enzymes are contraindicated during the acute exacerbation of chronic pancreatitis. During this time patients receive nothing by mouth in order to rest the GI tract and have no need for these enzymes. The presence of these enzymes would exacerbate the pancreatic disorder.
- Indications: deficient exocrine pancreatic secretions, cystic fibrosis, chronic pancreatitis, pancreatic insufficiency, steatorrhea of malabsorption syndromes, and post gastrectomy.
- ADRs: high doses have been r/t to GI symptoms such as nausea, cramping, abdominal pain, diarrhea, and colonic strictures. One brand- VIOKASE must be admin. With a proton pump inhibitor to help protect the gastric lining.
- Drug Interactions: calcium and magnesium based antacids will decrease the effectiveness of the enzymes. The ability of oral iron to increase serum iron levels may be reduced by concomitant administration.
- Monitoring: stools are monitored for fat content (steatorrhea) and pt is told to report foul-smelling and frothy stools.
    - Because these rx may produce elevated uric acid levels, serum and urine are tested for uric acid at regular intervals.
    - CF patients are originally diagnosed using fecal elastase test to determine the need for pancreatic enzyme replacement.
    - Because fat malabsorption pathologies can render patients at risk for deficiencies in the fat soluble vitamines (A,C,E,K), suspicion of hypovitaminosis and osteopenia should trigger monitoring of these key factors.
- Patient Education: all doses are taken immediately before or with meals or snacks with a fatty component.
    - Fruit, hard candy, fruit juicelike drinks, tea or coffee or popsicles do not require enzymes.
        - PANCRELIPASE is destroyed by acid. PPIs, sodium bicarb, or aluminum-Based antacids may be used w/ preparations w/o enteric coating to neutralize gastric pH.
        - Ca+ and Mg based antacids should not be used for this purpose because they interfere with drug action.
        - Dietary recommendations depend on the reason enzyme replacement is needed, but generally the diet is high calorie, high protein, and low fat. For children with CF, the diet is high calorie, high protein, and high fat. The dosage of the enzyme replacement is based on fat content of the diet, so the amount of fat in each meal should be fairly consistent.

- Small, frequent meals are often better tolerated than three large meals, especially when the reason for the enzyme replacement is CF, post-operative gastrectomy, or bariatric procedure. Use the same brand consistently. Enzymes should not be refrigerated, nor stored in hot places, and must be checked for expiration dates.

Insulin

- MOA: once insulin arrives to the receptors, it creates changes within the cell membrane that result in translocation of certain proteins, such as glucose transporters from sequestered sites within the cell to the cell surface.
  - Insulin promotes the storage of fat as well as glucose and influences cell growth and metabolic functions in a wide variety of tissues.
  - Insulin acts on the liver to increase storage of glucose as glycogen and resets the liver after food intake by reversing the amt of catabolic activity.
  - Insulin reduces the circulation of free fatty acids and promotes storage of triglycerides in adipose tissue, done by the suppression of cAMP production and dephospherylation of the lipases in fat cells.
- Types of Insulin- Short acting, Intermediate, Long acting
  - Lispro, Glusine, NPH, insulin glagine, detemir, inhaled human insulin

	Onset (m)	Peak (h)	Duration (h)*	Elimination	Compatibility
			Rapid-Acting		
Insulin aspart	0–15	0.5–2	3–5	Urine	NPH
Insulin glulisine	0–15	0.5–2	3–5	Urine	NPH
Lispro	0–15	0.5-1.5	3–5	Urine	NPH
Short-Acting					
Regular	30–60	2–3	3–7	Very little unchanged insulin is excreted in the urine	NPH
Regular U-500	30-45	2-4	8–24 hr*	Same	Not recommended
Intermediate-Acting					
NPH	30–60	4–10	10–16	Very little unchanged insulin is excreted in the urine	Regular, Glulisine, Lipro, Aspart
Long-Acting					
Insulin glargine	60	—	24	Urine	No other insulin
Insulin detemir	60	—	Up to 24	Urine	No other insulin
Inhaled					
Inhaled Human Insulin (Afrezza)	0-12**	1	2-3	Urine	N/A

- Metabolism/ Secretion- metabolized by the liver, kidney, and muscle cells
- Precautions and contraindications: the only contraindications to insulin are hypoglycemia and hypersensitivity to the ingredients in the product.
  - Pregnancy requires careful diabetes management. Human insulin does not cross the placenta and is the drug of choice for pregnant women.
  - Hypothyroidism may delay insulin turnover, requiring less insulin to tx
  - Hyperthyroidism may cause an increase in the renal clearance of insulin.

        - Patients with either issue require more frequent monitoring of glucose levels than other patients with diabetes when insulin management in needed.
    - ADRs: two main life-threatening adverse reactions are central to patient management with insulin- HYPOGLYCEMIA and DIABETIC KETOACIDOSIS.
        - Hypoglycemia- less than 70 mg/dL. Use the tx of RULE OF 15- consume 15 gr of fast cabs, wait 15 mins, and check BG.
    - Drug Interactions- beta blockers are especially problematic because they can increase insulin resistance, produces hyperglycemia, but it can also mask most of the signs and symptoms of hypoglycemia.
    - Patient Education-

Oral hypoglycemic agents

- Drugs: METFORMIN (GLUCOPHAGE)- Biguanide
- MOA: metformin increases peripheral glucose uptake and utilization (insulin sensitivity), decreases hepatic glucose production, and decreases intestinal absorption of glucose.
    - Metformin does not stimulate insulin release from the pancreatic beta cells, nor does it produce hypoglycemia except in specific circumstances. Metformin does not cause hyperinsulinemia. Metformin also does not cause weight gain; often patients lose weight.
- Metabolism/ Secretion/ Absorption:

Drug	Onset*	Peak*	Duration*	Protein Binding	Bioavailability	Half-Life	Excretion
Metformin IR and solution	Days	1–8 h	UK	Minimal	50%–60% if taken fasting; nonlinear; reduced by food intake	6.2 h (plasma) 17.6 h (blood)	100% excreted unchanged in urine
Metformin ER (Fortamet, Glumetza)	Days	3–10 h	UK	Minimal	Increased by 60% with food for Fortamet and Glumetza	UK	In urine
Acarbose (Precose)	0.5–1 h	1 h	2–3 h		Less than 2% in plasma	2 h	51% in feces as unabsorbed drug; 34% in urine
Miglitol (Glyset)	0.5–1 h	2 h	3h		100% in extracellular fluids at 25 mg; 50%–70% at higher doses	Normal renal function: 2 h; renal impairment: CCr <25: 4 h	95% in urine as unchanged drug
Nateglinide (Starlix)	20 min	1 h	4 h	98%	73%	1.5 h	83% in urine; 10% in feces

- Precautions and contraindications: the two major contraindications to metformin are: renal disease and metabolic acidosis. ADA recommends using eGFR above 30 mL/min as the cut point, which is moderate kidney disease.
    - Latic acidosis is rate but serious complications which is fatal 50% of the time. The risk of lactic acidosis increases in the presence of renal and hepatic dysfunction, making the interaction of these two contraindications more serious than one alone.
    - Metformin should also be temporarily withheld 48 hours before to 48 hours after undergoing radiological studies that involve an iodine-based contrast medium because such material may result in altered renal function and have been associated with lactic acidosis.
    - Patients who are at risk of anemia due to B12 deficiency, should get this treated first before beginning therapy with metformin.

    - There is a risk that metformin increases the risk of developing low TSH levels. This occurs in persons with normal thyroid function, but is increased 55% for those with hypothyroid issues.
- ADRs: most common s/e's involve GI disturbances such as abdominal bloating, diarrhea, nausea, vomiting, and an unpleasant metallic taste. These effects are usually transient and resolve in about 2 weeks without a chance in dose. They may be reduced by inhibiting therapy with a low dose and titrating the dose slowly.
- Drug Interactions

Interacting Drug	Possible Effects	Implications
Alcohol	Potentiates the effect of metformin on lactate metabolism	Warn patients against excessive alcohol intake while taking metformin
Amiloride, digoxin, morphine, procainamide, quinidine, ranitidine, triamterene, trimethoprim, vancomycin	May compete for elimination pathway	Dosage adjustments may be needed for metformin or interacting drug
Beta-adrenergic blockers	May mask signs and symptoms of hypoglycemia	Does not affect diaphoresis as indicator of hypoglycemia; teach patient to check blood glucose level if experiencing diaphoresis
Cimetidine, furosemide	Increases plasma levels of metformin without concurrent increase in renal excretion	Dosage adjustments of metformin may be needed
Iodine-based contrast media	May affect renal function and increase the risk for lactic acidosis	Withhold metformin for 48 h before and after procedure in which contrast is used
Nifedipine	Enhances absorption of metformin and may increase effects	Dosage adjustments of metformin may be needed

- Monitoring: before starting therapy, at least annually thereafter, assess renal function. Assessment is by serum creatinine and CCr initially and then by serum creatinine annually.
    - Assessment for risk for lactic or metabolic acidosis should include: serum electrolytes and ketones, BG, and blood pH if indicated.
- Patient Education: If a patient is not responsive to metformin monotherapy after 3 months, addition of another drug, including insulin, should be considered (see Table 33-3). There are combination formulations that include metformin plus glipizide (Metaglip) and metformin plus glyburide (Glucovance).
    - When metformin is added to a sulfonylurea, the increased sensitivity to insulin caused by metformin results in less need for the insulin

secretion generated by the sulfonylurea. If the BG level drops too much, the dose of the sulfonylurea should be reduced.
    - Patients are taught to take the drug at the same time each day exactly as prescribed.
    - If the GI disturbances include vomiting or diarrhea or the patient develops a fever, the drug is stopped. Dehydration may result and presents a risk for the patient to develop lactic acidosis and decreased renal function. Patients are taught the **signs and symptoms of lactic acidosis** (e.g., chills, dizziness, low blood pressure, muscle pain, sleepiness, trouble breathing, slow heart rate, and weakness) and to report them immediately.

Sulfonylureas

- Drugs: DiaBeta, Glynase, or Micronase (glyburide or glibenclamide)/ Amaryl (glimepiride) /Diabinese (chlorpropamide) / Glucotrol (glipizide) / Tolinase (tolazamide) / Tolbutamide.
    - first class of oral rx for DM, and are truly oral hypoglycemics, and are useful for pts with some endogenous insulin secretion.
- MOA: sulfonylureas cause an increase in endogenous insulin secretion by the beta cells of the panaceas related to increased cAMP generation.
    - Hypoglycemic effects appear to be due to increased endogenous insulin production and to improved beta cell sensitivity to BG levels or suppression of glucose release by the liver. Sulfonylureas also potentiate the effect of antidiuretic hormone and may produce a mild diuresis.
    - Tolbutamide, glyburide, and glipizide are more effective when taken 30 minutes prior to a meal. Tolazamide (Tolinase) is absorbed more slowly than the other sulfonylureas.
- Metabolism/ Secretion: all sulfonylureas are metabolized in the liver to active or inactive metabolities. The hypoglycemic effects of these drugs may be prolonged by severe liver disease because of reduced metabolism.

Drug	Onset (h)	Peak (h)	Duration (h)	Protein Binding	Half-Life (h)	Metabolism	Elimination
First-Generation							
Chlorpropamide	1	3–6	25–60	99%	36 (prolonged by renal disease)	80% metabolized in liver; activity unknown	Excreted 100% in urine; renal elimination may be hastened by increased urine pH
Tolazamide	4–6	1–6	12–24	99%	7	Metabolized in liver to several mildly active metabolites	Excreted 100% in urine
Tolbutamide	1	4–6	6–12	99%	4.5–6.5	Oxidized in liver to inactive metabolites	Excreted 100% in urine
Second-Generation							
Glipizide	1–1.5	1–2	10–16	99%	2–4	Metabolized in liver to inactive metabolites	Excreted 80%–85% in urine
Glyburide				99%		Metabolized in liver to weakly active metabolites	Excreted as metabolites in bile and urine, approximately 50% by each route
Nonmicronized	2–4		24		10		
Micronized	1	1.5–3	24		4		
Glimepiride	2	2–3	24	99.5%	5	Completely metabolized by liver	Excreted 60% in urine and 40% in feces

- Precautions and contraindications: sulfonylureas are contraindicated for patients with hypersensitivity to the drugs or the compounds in which they are mixed.
    - Other conditions in which sulfonylureas should not be used include type 1 diabetes; DKA or diabetic coma; and uncontrolled infection, burns, or trauma.
    - Patients with adrenal or pituitary insufficiency are especially susceptible to hypoglycemia, and sulfonylureas should be used cautiously and patients monitored more frequently if they have these comorbid conditions. Severe hepatic impairment may cause inadequate hepatic release of glucose in response to hypoglycemia.
- ADRs: all sulfonylureas may produce severe hypoglycemia. Hypoglycemia may be difficult to recognize in patients who are concurrently taking beta blockers because drugs mask the signs and symptoms of hypoglycemia, with the exception of diaphoresis.
    - Hypoglycemia is also more likely when caloric intake is reduced , after severe or prolonged exercise, when alcohol is consumed.
    - GI disturbances s/e's tend to disappear once the dosage is reduced.
    - Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) has occurred after administration of sulfonylureas, especially with patients who also have congestive heart failure or hepatic cirrhosis.
- Drug Interactions

Drug	Interacting Drug	Possible Effect	Implications
All sulfonylureas	Androgens, anticoagulants,* chloramphenicol, fluconazole, gemfibrozil, histamine2 blockers, magnesium salts, methyldopa, MAO inhibitors,	Enhance the hypoglycemic effect of the sulfonylurea	Avoid concurrent administration or monitor blood

	NSAIDs (except diclofenac), phenylbutazone, probenecid, salicylates, sulfonamides, tricyclic antidepressants, urinary acidifiers		glucose levels closely if drug must be given
All sulfonylureas	Beta-adrenergic blockers, cholestyramine, diazoxide, hydantoins, rifampin, thiazide diuretics, urinary alkalinizers	Decrease the hypoglycemic effect of the sulfonylurea	Avoid concurrent administration or monitor blood glucose levels closely
Glimepiride*	In addition to drugs with all sulfonylureas: corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, nicotinic acid, sympathomimetics, and isoniazid	May cause loss of glucose control because these drugs can cause hyperglycemia	If concurrently administered, monitor closely for loss of glucose control; when they are withdrawn, monitor closely for hypoglycemia

- Patient Education: both first and second generation sulfonylureas are used to tx type 2 DM. They are effective as second-line- therapy w/ patients who have previously used diet, exercise, weight control, and metformin.
    - Take medication at the same time each day, preferably before or w/ morning meal.
    - GLIPIZIDE must be taken 30 mins before a meal to prevent a reduction in absorption if a dose is missed, instruct the patient to take it as soon as remembered.
    - If pt experiences GI upset, pt can divide dose to twice daily to minimize s/e's
    - ALCOHOL produces hypoglycemia, and masks the indication of adverse reactions.

Thiazolidinediones (TZD) are oral antihyperglycemic drugs that are best classified as insulin sensitizers. .

- Drugs: Pioglitazone (Actos) and rosiglitazone (Avandia) are the only FDA-approved agents
- MOA: Thiazolidinediones activate a nuclear receptor that regulates gene transcription, resulting in increased utilization of available insulin by the liver and muscle cells and adipose tissue.
- Metabolism/ Secretion:
- Precautions and contraindications: These drugs, especially rosiglitazone, should be used cautiously because of the potential for cardiovascular problems.
- ADRs:
- Drug Interactions:
- Patient Education:

MEGLITINIDES

- Drugs: repaglinide (Prandin) and nateglinide (Starlix)
    - They are most useful in patients whose primary glucose alteration is postprandial hyperglycemia.
- MOA: They work by closing the adenosine triphosphate (ATP)–dependent potassium channels in the beta cell membrane by binding at specific receptor sites. This

potassium channel blockade depolarizes the beta cell and leads to an opening of calcium channels. The resultant influx of calcium increases the secretion of insulin.

- Metabolism/ Secretion:
- Precautions and contraindications: Because their time in the plasma is less than 2 hours, the effect is very short. Plasma insulin levels fall to baseline by 4 hours after dosing. The end result of their stimulation of insulin secretion is a lowering in postprandial blood glucose levels. To achieve this effect, they are dosed 3 times daily no more than 20 minutes before meals.
- ADRs:
- Drug Interactions:
- Patient Education: These drugs are not commonly used because adherence is difficult, GI side effects can be distressing, and they are expensive. They can reduce Hb A1c by 0.5% to 1%.

Selective Sodium Glucose Co-transporter 2 (SGLT-2)

- Drugs: Canagliflozin (Invokana), dapglifoxin (Farxiga), and empagliflozin (Jardiance)
- MOA: inhibit renal SGLT-2 action, thereby blocking about 90% of the reabsorption of glucose in the kidneys and promoting excretion of excess glucose in the urine. This translates to nearly 250 calories a day.
- Metabolism/ Secretion:
- Precautions and contraindications:
- ADRs: Major side effects are genital yeast infections in both genders related to the continuous presence of glucose in the urine.
- Drug Interactions:
- Patient Education: They can be used with some renal insufficiency which helps cover patients previously on medications that must be stopped when GFR begins to decline. They are combined with many other agents to help reduce glycemic levels.

Dipeptidyl Peptidase-4 inhibitors

- In the older population, DPP-4 inhibitors may be the best choice due to their glucose-lowering effect, the neutral effect on caloric intake, and therefore less negative effect on muscle and total body protein mass.
- Drugs: sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina)
- MOA: The action of DPP-4 inhibitors is different from all other oral agents because they act on the incretin hormone system to have an indirect effect to increase insulin production. They improve glycemic control by increasing insulin synthesis and secretion, reducing glucagon, slowing gastric emptying by prolonging the action of the remaining GLP-1 hormones, and suppressing the appetite. One main advantage is the oral preparation
- Metabolism/ Secretion:
- Precautions and contraindications: sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina).
- ADRs:
- Drug Interactions:
- Patient Education:

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1s)

- Drugs: Liraglutide (Victoza), albigutide (Tanzeum), and dulaglutide (Trulicity)

- MOA: activate GLP-1 receptors, which decreases fasting and postprandial glucose levels. They increase insulin synthesis and secretion in the presence of elevated glucose levels and improve first-phase insulin release, lowering glucagon, slowing gastric emptying, and reducing food intake.
    - They have been noted to produce lower Hb A1c levels of 0.5% to 1.5% and weight loss. Liraglutide has been given formal FDA indication for obesity therapy; the others in the class may soon follow suit

Cardiac glycosides and antiarrhythmics

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Acetaminophen (Tylenol), although not an anti-inflammatory drug by chemistry, is often used to treat pain and fever and so is included in this section.
- MOA: Although the exact mode of action of NSAIDs is not known, the major mechanism is thought to be inhibition of cyclo-oxygenase activity and prostaglandin synthesis. Inhibition of lipo-oxygenase, leukotriene synthesis, lysosomal enzyme release, neutrophil aggregation, and various cell membrane functions may also occur. These agents may also suppress rheumatoid factor.
    - Three COX-2 selective drugs (e.g., celecoxib [Celebrex], rofecoxib [Vioxx], valdecoxib [Bextra]) have been developed that appear not to inhibit COX-1
- Metabolism/ Secretion/ Absorption: NAPROXEN SODIUM (NAPROSYN) is more rapidly absorbed than NAPROXEN and it is used when rapid analgesia is desired.
    - DICLOFENAC POTASSIUM (CATAFLAM) is formulated to release the drug in the stomach, where as sodium formation VOLTAREN is released in the higher pH environment of the duodenum.
    - In general food delays absoprtion of all NSAIDs but does not affect the total amt. absorbed.
    - Administration w/ food will reduce GI s/e's
    - KETOROLAC (TORADOL) is the only drug in the class w/ an IM route
- Indications: the NSAIDs are primarily used for anti-inflammatory activity, but are effective analgesics useful for the relief for mild to moderate pain. They also have antipyretic properties.
    - ACETAMINOPHEN- is an analgesic and anitypyretic with limited anti-inflammatory activity. Though its MOA is not understood, it is thought that it acts by inhibiting central and peripheral prostaglandin synthesis. It has the advantages of minimal GI irritation and of not affecting bleeding times, uric acid levels, or respiration.
- Precautions of contraindications: *The only relative contraindications are for* ***ketorolac, mefenamic acid (Ponstel), flurbiprofen, and nabumetone*** *in the presence of preexisting renal impairment. Because NSAID metabolites are excreted primarily by the kidneys, all others should be used with caution in the presence of renal function impairment. Renal function should be assessed prior to initiation of therapy and during therapy.*
    - Naproxen may exhibit an increase in unbound fraction and reduced clearance of free drug in cirrhotic patients. A reduced dose may be necessary.

    - GI s/e's are the most common reasons for cautious use, serious GI bleeding, ulceration and perforation can occur at any time w/o warning signs.
    - Indomethacin may aggravate depression or other psychiatric disturbances. A different NSAID should be chosen in this situation.
    - Mefenamic acid and meclofenamate are not recommended for children under age 14 years. Children under age 14 should not take indomethacin except in circumstances that clearly warrant the risk. Closely monitor the liver function of children between ages 2 and 14 who take it. C
- ADRs: the most common adverse reactions w/ NSAIDs are GI disturbances, nausea, vomiting, constipation, and diarrhea. Taking the rx w/ food may help to reduce these reactions.
    - Acute renal insufficiency has occurred in patients w/ preexisting renal disease or compromised renal perfusion. Patients at greatest risk are older adults, premature babies, diuretic use, HF, lupus, chronic glomerulonephritis.
    - NSAIDs inhibit platelet aggregation and may increase bleeding time.
    - Fluid retention and peripheral edema are not severe but can be problematic for patients with compromised cardiovascular function.
    - **ACETAMINOPHEN POISONING:** single dose in children of 150mg/kg or 7.5 g to 10 g in adults may be toxic.
        - .5 to 24 hours- nausea, vomiting, pallor, anorexia, diaphoresis
        - 24-72 hours= clinically improved, AST, ALT, bilirubin and prothrombin levels begin to rise
        - 72-96 hours= peak hepatotoxicity, jaundice, confusion, AST of 10,000 not unusual.
        - 4-14 days= death or recovery. Patients who survive enter a recovery phase.
        - TREATMENT: gastric lavage in all cases, preferably within 4 hours of ingestion. ORAL N-ACETYLCYSTEINE is a specific antidote for acetaminophen toxicity.
- Drug Interactions

All NSAIDs	Anticoagulants	May prolong prothrombin time (PT)	Avoid coadministration; monitor PT and patients closely; instruct patients to watch for indications of bleeding
	Beta adrenergic blockers	Antihypertensive effect impaired; sulindac and naproxen do not affect atenolol	Select appropriate drug match If they must be used together, monitor serum levels and adjust dose accordingly
	Hydantoins	Serum levels of phenytoin increased, resulting in increased	Avoid concurrent use or select sulindac; monitor serum levels Avoid concurrent use for long-term therapy or select different

	Lithium	pharmacological and toxic effects of phenytoin	diuretic Avoid concurrent use
	Loop diuretics	Serum lithium levels increased; sulindac has no effect or decreases levels	Avoid concurrent use; offers no therapeutic advantage and significantly increases incidence of GI adverse reactions
		Decreased effects of loop diuretics	
	Probenecid	Probenecid may increase concentrations and toxicity risk of NSAIDs	
	Salicylates	Decreased plasma concentrations of NSAIDs	

- Patient Education: if a dose is missed, ideally it should be taken as soon as the patient remembers unless it is almost time for the next dose.
    - Taking the drug w/ food or a full glass of water and remaining in an upright position for 15-30 mins may reduce GI discomfort and adverse reactions.
    - Remind patients to avoid taking aspirin, alcohol, and other GI irritants while taking these drugs.

Aspirin (ASA)

- MOA: salicylates have analgesic, anti-inflammatory, antipyretic, and antiplatelet actions.
    - Salicylates lower body temperature through their effect on the hypothalamic thermostat and vasodilation of peripheral vessels, thus enhancing dissipation of heat.
    - The anti-inflammatory and analgesic activities are mediates through inhibition of prostaglandin synthesis in the same manner as NSAIDs.
- Metabolism/ Secretion: the presence of food may slow down the absorption, resulting in lower salicylate levels.
    - Aspirin has a half-life of 15-20 mins.
- Indications: in addition to analgesic, anti-inflammatory, and antipyretic properties, common to the NSAIDs, the salicylates also possess antiplatelet properties to varying degrees.
- Precautions and contraindications: **taking aspiring by children/teens with influenza or chicken pox has been associated w/ the development of Reye syndrome, a rare but life-threatening condition characterized by vomiting, lethargy, and eventually coma.**
    - Aspirin should be avoided 1 wk before sx due to increased risk of post-op bleeding due to antiplatelet effects.
    - Due to the same reasons, salicylates are contraindicated with pts who have active peptic ulcer disease or GI bleeding.

        - Aspirin ingestion during pregnancy may lead to anemia in mother and increased risk of postpartum hemorrhage.
- ADRs: the most common s/e is GI irritation and bleeding. Fecal blood may occur. In that case H2 blockers, antaciads and PP inhibitors.
    - **Toxicity:** acute lethal doses of salicylates in adults is 10-30g and in children is 3 g.
        - Chronic salicylate toxicity can occur when more than 100 mg/kg is ingested more than 2 or more days.
        - S/E: respiratory alkalosis, hyperpnea, increased CO2 production. Nausea, vomiting, hypokalemia, tinnitus, disorientation, hyperthermia, thrombocytopenia.
        - Tx: induction of emesis or gastric lavage to remove any unabsorbed drug from the stomach. Activated charcoal diminishes salicylate absorption if its given within 2 hours of ingestions.
- Drug Interactions: Aspirin may potentiate the anticoagulant action of heparin, warfarin, or thrombolytic agents (Table 25-11). It may increase the risk for bleeding with cefamandole, cefoperazone, cefotetan, valproic acid, or plicamycin.
    - All salicylates may enhance the activity of penicillins, phenytoin, methotrexate, valproic acid, sulfonylureas, and sulfonamides
    - There is an increased risk for GI bleeding when aspirin is taken with any other drug with any other GI irritant, such as ethanol. The risk for ototoxicity is increased when it is taken with any other drug that causes ototoxicity (e.g., aminoglycosides, loop diuretics).
    - Some foods contain salicylate. Foods and spices high in salicylate include curry, paprika, licorice, Benedictine liqueur, prunes, raisins, tea, and gherkins. Foods that acidify the urine may increase serum salicylate levels, and those that alkalinize the urine may have the opposite effect.
- Monitoring: because these drugs are eliminated by the kidneys and sodage adjustments may be requires based on renal function, serum creatinine levels should be assessed before therapy is begun.
    - Urinary Ph should be checked regularly to check for toxicity
    - CBC should be drawn prior to starting therapy and at least annually for long term therapy.
    - Fecal occult blood studies should be done as well for any indication of GI bleeding.
- Patient Education: tell pts to take with food or full glass of water and remaining in an upright position for 15-30 mins to reduce GI irritation.
    - Remind pts not to crush or chew enteric-coated tablets or take antacids within 1 hr.
    - Most common s/e are ototoxicity and GI irritation and bleeding. Pts should report tinnitus, unusual bleeding from the gums, bruising, black tarry stools, fever lasting longer than 3 days.

Gout medications

- Drugs: allopurinol (Zyloprim), colchicine, and febuxostat (Uloric), and the two uricosuric agents, probenecid (Benemid) and sulfinpyrazone (Anturane)

- MOA: ALLOPURINOL and FEBUXOSTAT inhibit xanthine oxidase, the enzyme responsible for the conversation of hypoxanthine and xanthine to uric acid.
- Metabolism/ Secretion: Both probenecid and sulfinpyrazone are highly protein bound and tend to displace other drugs that have a high affinity for the same binding sites.
    - However, colchicine is not effective in the presence of renal failure. The other two drugs are excreted primarily in urine, and the dose of probenecid may need to be reduced in the presence of renal impairment.
- Indications: antigout rx act to reduce the inflammatory process or to prevent the synthesis of uric acid. In order to reach the therapeutic range, a week or more may be needed before the full effects of the drugs can be seen.
    - The goal is to have a serum acid level of less than 6mg /dL, it may take 2 or more weeks to see the effect of febuxostat.
    - PROBENECID and SULFINPYRAZONE inhibit renal tubular reabsorption or urate and thus increase the renal excretion of uric acid and decrease serum uric acid levels. Both drugs lack anti-inflammatory activity, therefore they are most useful with for patients w/ reduced urinary excretion of uric acid.
- Precautions and Contraindications: *ALLOPURINOL, COLCHICINE, PROBENECID, AND SULFINPYRAZONE are r/t poor urate clearance in the presence of renal impairment. The should be used cautiously, and renal function tests should be performed regularly to determine appropriate dosage of the drug.*
    - ALLOPURINOL and COLCHICINE are r/t hepatotoxicity. They're not recommended for patients with severe haptic dysfunction.
    - Pts are taking these rx and develop anorexia, weight loss, pruritus, evaluation of liver function should be part of the diagnostic work-up.
    - PROBENECID & SULFINPYRAZONE are sulfa based drugs and pts w/ known suspected sulfa allergies should not use them. The appearance of a hypersensitivity reaction requires immediate discontinuance of the drug.
- ADRs: COLCHICINE, PROBENECID and SULFINPYRAZONE r/t to adverse reactions affecting the GI tract. s/e include: nausea, vomiting, diarrhea, and abdominal pain. These symptoms are particularly troublesome for pts w/ a hx of peptic ulcer disease or active peptic ulcer disease.
    - ALLOPURINOL is r/t a maculopapular skin rash that can be fatal. Therefore rx should be d/c at the first sign of rash. Most severe reactions include fever, chills, arthralgia, cholestatic, jaundice, eosinophilia, mild leukocytosis, or leukopenia.
    - COLCHICINE- some pts may develop elevated plasma levels due to renal function have developed myopathy and neuropathy that results in weakness. This problem is often unrecognized and misdiagnosed as polymyositis or uremic neuropathy.
- Drug Interactions: Probenecid inhibits the tubular secretion of most penicillins and cephalosporins and increases plasma levels by any route these antibiotics are given.
- Monitoring: uric acid levels should be normal after 1-3 week of therapy, and serum levels should be drawn again periodically throughout therapy.

        - ALLOPURINOL: renal and liver function must be assessed prior to initiation of therapy and periodically during the first few months of therapy.
        - Probenecid and sulfinpyrazone both have blood dyscrasias (anemia, hemolytic anemia) as adverse reactions. Patients taking these drugs should have periodic complete blood counts (CBCs).
    - Patient Education: in the even of a acute attack during maintenance therapy, allopurinol, febuxostart, probenecid, and sulfinpyrazone should be continued while COLCHICINE is added to the regimen to tx acute attack.
        - ALLOPURINOL can be crushed and given w/ fluid and mixed with food for pts who have difficulty in swallowing.
        - The main s/e is GI distress, pts may take rx w/ food or milk to minimize GI irritation.
        - Probenecid and sulfinpyrazone are sulfa-based drugs that have been associated with hypersensitivity. A hypersensitivity reaction requires immediate discontinuance of the drug. Other symptoms to report with these drugs include sore throat, fatigue, yellowing of the skin or eyes, and unusual bleeding or bruising. These drugs have been associated with blood dyscrasias and hepatotoxicity.

o Drug of choice for treatment of gout and most common adverse effects

Allopurinol, the drug of choice for patients with a history of urinary calculi, renal insufficiency, chronic tophaceous gout, or high levels of serum urate, is given in doses of 200 to 300 mg/d for mild gout and 400 to 600 mg/d for moderately severe tophaceous gout.

o Role of NSAID use in treatment of gout

There is a risk of gout flare-up when febuxostat is started. Patients should be concurrently treated with an NSAID or colchicine for up to 6 months.

o Gout medications that require renal or hepatic dose adjustments

-probenecid may need to be reduced in the presence of renal impairment.

-In the presence of renal impairment, a once-daily dose of 1 g probenecid may be used. The daily dose may be increased in 500 mg increments every 4 weeks (usually to less than 2 mg/d) if symptoms are not controlled or the 24-hour urate excretion is less than 700 mg. Probenecid is not effective in chronic renal failure if the glomerular filtration rate is 30 mL/min or less. Patients must maintain hydration and adequate sodium bicarbonate (2 to 7.5 g daily) or potassium citrate (7.5 mg daily) to maintain an alkaline urine while on probenecid to prevent formation of uric acid crystals. Alkalization of the urine is recommended until the uric acid level is in the normal range.

o Allopurinol drug interactions and medications to avoid

Drug	Interacting Drug	Possible Effect	Implications
Allopurinol	Angiotensin-converting enzyme inhibitors	Higher risk of hypersensitivity reaction	Avoid concurrent use
	Aluminum salts	Decreased effects of allopurinol	Separate administration
	Ampicillin	Rate of ampicillin-induced rash much higher	Warn patients
	Anticoagulants	Anticoagulant effect of some drugs enhanced; not warfarin	Use warfarin for anticoagulation; conflicting data
	Cyclophosphamide	Myelosuppressive effects enhanced; increased risk for bleeding	If must be used together, monitor for bleeding risk
	Theophylline	Theophylline clearance decreased with large doses of allopurinol; increased toxicity risk	Select different respiratory drug
	Thiazide diuretics	Increased incidence of hypersensitivity reactions	Avoid concurrent use or monitor for hypersensitivity
	Thiopurines	Clinically significant increases in pharmacological and toxic effect of thiopurines	Avoid concurrent use
	Uricosuric agents	Uricosuric agents that increase excretion of urate also likely to increase excretion of oxypurinol and lower degree of inhibition of xanthine oxidase; avoid concurrent use	Dosage adjustments may be needed if uricosuric added to treatment regimen

DIABETES MELLITUS

- Clinical signs & symptoms

• Risk factors & associated complications

- Prevalence of type 2 varies in the United States by ethnic group, with a higher frequency in Native Americans, Asian Americans, Latinos, Pacific Islanders, and African Americans (ADA, 2015). Other risk factors include obesity, sedentary lifestyle, hypertension, dyslipidemias, family history, gestational history, and age. Genetics have a strong influence, and a locus has been found on chromosome arm 7q that may be related to insulin resistance, one underlying alteration in type 2 diabetes.
- Insulin resistance has also been linked to three other important disorders: hyperlipidemia, hypertension, and coronary artery disease.
- Microvascular involvement affects the eyes, heart, kidneys, and nervous system. Complications such as retinopathy with potential loss of vision, nephropathy leading to renal failure, peripheral neuropathy with risk of foot ulcers, amputation, and Charcot's joint and autonomic neuropathy with gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction may occur.

• Diagnostic criteria

- DM diagnosis: acute symptoms of diabetes plus plasma glucose concentration > 200 mg/dL
    - Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes are polyuria, polydipsia, and unexplained weight loss.
    - Fasting plasma glucose ≥126 mg/dL. * Fasting is defined as no caloric intake for at least 8 h.
    - 2-h postload plasma glucose in an oral glucose tolerance test ≥200 mg/dL. The test uses a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
    - Hb A1c ≥6.5%

• Criteria for screening asymptomatic adults

- Individuals ≥45 yr and who have a BMI ≥25 kg/m2 should be tested. If normal, the test should be repeated at 3 yr intervals.

- Individuals <45 yr and who have a BMI ≥25 kg/m2 and have additional risk factors should have more frequent testing.
- Additional risk factors are the following:

• Physically inactive
• First-degree relative with diabetes
• Members of high-risk ethnic group (African American, Hispanic, Native American, Asian American, Pacific Islander)
• Delivered a baby weighing >9 lb or previously diagnosed with GDM
• Hypertensive (B/P ≥140/90 mm Hg)
• HDL cholesterol ≤35 mg/dL and/or triglyceride level ≥250 mg/dL
• Have polycystic ovary syndrome (PCOS)
• IGT or IFG on previous testing
• Have other clinical conditions associated with insulin resistance (PCOS or acanthosis nigricans)
• History of CVD
• Differentiate between onset, peak and duration of insulin and oral hypoglycemic agents (table 33-4)

Type	Insulin	Onset	Peak	Duration
Rapid-Acting	Humalog (Lispro) Novalog (Aspart) Apidra (Glulisine)	5–30 min	0.5 h–3 h	3–4 h
Short-Acting	Regular (Humulin R, Novalin R)	30–60 min	2–4 h	3–7 h
Intermediate-Acting	Isophane(NPH, Humulin N)	1–2 h	4–10 h	10–16 h
Long-Acting	Lantus (Glargine) Levimir (Detemir)	1–2 h 1–2 h	None	20–24 h 20–24 h
Fixed Combination	70/30 (NPH/regular ratio) 50/50 (NPH/regular ratio) 75/25 (NPH/lispro) 70/30 (NPH/aspart)	30–60 min 30–60 min 5–15 min 5–15 min	Dual	10–16 h

• Know treatment algorithms
• A1C treatment goal

- (1) near normalization of blood glucose, (2) prevention of acute complications such as hypoglycemia, (3) prevention of progression of the disease to target organ damage, and (4) appropriate patient-oriented self-management.
- Association of Clinical Endocrinologists/American College of Endocrinology [AACE/ACE] (2009) is a primary glycemic goal of an A1c of 6.5%, which must be individualized for the patient.
- Many studies have shown that treatment regimens that reduce average Hb A1c <7% are associated with fewer long-term microvascular and neuropathic complications (ADA, 2015). For selected patients, a lower goal of 6.5% can be suggested if it can be achieved without significant hypoglycemia or other adverse effects of treatment. Such patients might include those with short-term duration of diabetes, long life expectancy, and no significant CVD

• Calculate an appropriate daily dose of insulin for initiation of insulin therapy

- Concentrated insulin is given twice daily before breakfast and dinner if the standard daily dose is around 200 units/day. For patients who require 300 to 750 units daily, the U-500 can be dosed three times daily. Dose requirement between 750 and 2,000 units can be divided into 4 injections. U-500 can be used in insulin pumps for patients requiring 2,000 plus units a day.

• Insulin treatment algorithm for Type 1 DM

- The total daily insulin requirement is 0.3 to 0.5 units/kg body weight/d with titration to glycemic targets. Higher doses may be indicated during an acute illness.

• A1C monitoring during oral or insulin diabetes management
• Correlate mean plasma glucose level according to A1C (table 33-6)
• Clinical manifestations of diabetic autonomic neuropathy

- Symptoms, including resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, sweat gland dysfunction, impaired neurovascular function, and the potential for autonomic failure in response to hypoglycemia. Cardiovascular autonomic dysfunction (CAN) is a CVD risk factor and is the most clinically important form of DAN.