Diabetes Mellitus and the individual with I/DD part 2

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Complications of Diabetes

- Adapted from: Baker DE. Management of type 2 diabetes. Clin Pharm Newswatch 2017;4:1-8
- ADA. Standards of medical care for patients with diabetes mellitus. Diabetes Care 2013;26:S33-S50

Complications	Comments
Cardiovascular Disease	Leading cause of diabetes related deaths
Stroke	Risk is increased by two to four times
Dyslipidemia	97% have lipid abnormalities contributing to higher rates of cardiovascular disease
High Blood Pressure	Incidence is 73%
Blindness	Retinopathy is the leading cause of new blindness in adults aged 20-74 years
Kidney Disease	Nephropathy is the leading cause of end stage renal disease (44% of new cases)
Nervous System Disease	60% to 70% have mild to severe form of damage
Amputations and Peripheral Neuropathy	Leading nontraumatic cause of lower limb amputations and foot ulcerations
Acute-Life Threatening Events	Diabetic ketoacidosis, hyperosmolar nonketonic coma, more susceptible to infections (e.g. pneumonia and influenza)

Outline

- Cardiovascular Disease
  - HTN
  - Dyslipidemia
- Kidney disease
- Neuropathy/amputation
- Eye problems
- Peridonal issues
- Immunizations

Cardiovascular Disease Risk Factors

- Hypertension*
- Cigarette smoking
- Obesity* (BMI ≥30 kg/m2)
- Physical inactivity*
- Dyslipidemia*
- Diabetes mellitus*
- Microalbuminuria or estimated GFR <60 mL/min
- Age (older than 55 for men, 65 for women)
- Family history of premature CVD (men under age 55 or women under age 65)

*Components of metabolic syndrome

Adapted from: US Pharmacist Continuing Education. Reducing cardiovascular complications in diabetes. 2019.

Cardiovascular Disease and Diabetes

- 52% of annual diabetes costs
- 65% of people with diabetes die from heart disease or stroke
- Risk of stroke increases 2 to 4 times
- Same risk for heart attack as people without diabetes and a history of heart attack
- Smoking doubles the risk
- 97% of those with diabetes have lipid abnormalities
- 70% of those with diabetes have high blood pressure

Prevention of Cardiovascular Disease

- Stop smoking
- Reduce blood pressure
- Cholesterol management
- Glucose control
- Weight management
- Antiplatelet agents
- Aspirin therapy

Antiplatelet Therapy and CVD

- Aspirin 81–162 mg/day
- Primary prevention for men/women with diabetes:
  - Age over 40 years
  - Additional risk factors for cardiovascular disease
    - Family history of cardiovascular disease (CVD)
    - Hypertension
    - Smoking
    - Dyslipidemia
    - Albuminuria
- Secondary prevention for men/women with diabetes with:
  - History of myocardial infarction
  - Vascular bypass procedure
  - Stroke or transient ischemic attack
  - Peripheral vascular disease
  - Claudication
  - Angina

Aspirin Therapy

Contraindications

- Aspirin allergy or intolerance
- Recent gastrointestinal bleeding or other hemorrhagic states

Precautions

- Bleeding tendency
- On anticoagulant therapy
- Clinically active hepatic disease
- Age under 21 years
  - Increased risk of Reye's syndrome

ADA. Aspirin therapy and diabetes. Diabetes Care 004;27:S72-3.
USP Drug Information for the Healthcare Professional. 2013.

Conditions Associated with Hypertension

Lifestyle Modifications to Lower Blood Pressure

Modification*	Recommendation	Approximate Reduction
Weight reduction	Maintain normal body weight (BMI 18.5-24.9 kg/m^2)	5-20 mmHg/ 10 kg weight loss
Physical activity	Regular aerobic physical activity such as brisk walking (at least 30 min/day, most days of the week)$^{\infty}$	4-9 mmHg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons	2-4 mmHg

*For overall cardiovascular risk reduction, stop smoking

JNC 7. Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 2003.

ADA. Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications. Diabetes Care 2002;25:202-12.

Nutritional Modifications to Lower Blood Pressure

Modification*	Recommendation	Approximate Reduction
Adopt dietary approaches to stop hypertension	Diet consisting of vegetables, lowfat dairy products, fruits, reduced saturated and total fat	8-14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to 2.4 g sodium per day (6 g sodium chloride)	2-8 mmHg

*For overall cardiovascular risk reduction, stop smoking

JNC 7. Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 2003.

ADA. Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications. Diabetes Care 2002;25:202-12.

Pharmacologic Management of Hypertension

- **Antihypertensive Drugs**
  - Angiotensin-converting enzyme inhibitors (ACEIs)
  - Angiotensin receptor blockers (ARBs)
  - Alpha-blockers
  - Beta-blockers
  - Diuretics
  - Calcium channel blockers
  - Combination therapies

ACE Inhibitors

- Slows progression of
  - Nephropathy
  - Cardiovascular events
  - Mortality
- Hypertensive patients with diabetes +/- microalbuminuria
- Blood pressure lowering effects seen by 4-6 weeks
- Evaluate protein lowering effects after 3 months
- Decrease mortality and morbidity in patients
  - With congestive heart failure
  - Post-myocardial infarction
- Reductions in cardiovascular end points
- Monitor serum potassium for development of hypoperkalemia; watch for drug interactions

ARBs

- Decrease proteinuria
- Prevent progression of nephropathy when microalbuminuria or more advanced stages of nephropathy present in patients with type 2 diabetes
- Cardiovascular data limited
- Not associated with a cough, like ACE inhibitors
- Combination of ACEIs and ARBs reduce blood pressure and urinary albumin levels more than either medication alone
- Monitor serum potassium for development of hyperkalemia; watch for drug interactions

ADA. Hypertension in diabetes. Diabetes and cardiovascular disease review 2022;2:1-4.

ACEIs or ARBs?

ACE Inhibitors

- drugs of choice over ARBs for prevention and treatment of proteinuria in patients with type 1 diabetes (Level 1 evidence)[1-3]
- drugs of choice for acute MI, congestive heart failure, hypertension (Level 1 evidence)

ARBs

- drugs of choice for first-line renoprotective therapy in hypertensive type 2 diabetic patients with microalbuminuria (Level 1 evidence)[4-6]
- recommended in patients who are candidates for renin-angiotensin blockade but demonstrate intolerance to ACEIs

References

1. Lewis EJ et al. The Collaborative Study Group. N Engl J Med 1993;329:1456-62.
2. Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000; 342;145-53.
3. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355:253-9.
4. Brenner BM et al. N Engl J Med 2001;345:861-9.
5. Lewis EJ et al. N Engl J Med 2001;345:851-60.
6. Parving HH et al. N Engl J Med 2001;345:870-8.

Beta-Blockers

- Atenolol
  - Reduces proteinuria and glomerular filtration rate
  - Equally effective as ACEI in decreasing risk of diabetes-related end points and microvascular events
- Demonstrated efficacy following myocardial infarction (with acebutalol, atenolol, metoprolol, propranolol, timolol)
- Reductions in mortality of ~25%
- May prolong or blunt hypoglycemia
  - Avoid use in insulin-using patients with history of severe hypoglycemia
  - In other patients with diabetes, especially those with recent myocardial infarction, benefits appear to outweigh potential risks related to hypoglycemia

ADA. Hypertension in diabetes. Diabetes and cardiovascular disease review 2022;2:1-4

Thiazide Diuretics

- May be considered first-line therapy in patients without additional cardiovascular risk factors or proteinuria
- Effect on the progression of diabetic nephropathy compared with other drugs is unknown
- Demonstrated efficacy in reducing the risk of stroke and heart failure in subjects with mild-to-severe hypertension
- In elderly patients with systolic hypertension:
  - A low-dose thiazide diuretic reduces cardiovascular event rate by 34% when compared with placebo
  - Absolute risk reduction twice as great for subjects with diabetes vs. subjects without diabetes
- Renal function issues (not useful when GFR<20ml/min)

American Diabetes Association. Diabetes Care 2004;27:S65-67.
Goodman & Gilman's The Pharmacological Basis of Therapeutics. 10th Edition. McGraw Hill. 2001

Second Line Antihypertensive Agents

- If target blood pressure goal not obtained with initial doses of 1st line drugs
  - Increase dose
  - Add second drug from different group
- Less effective in preventing complications
- Other classes of drugs without long-term data on efficacy in improving outcomes can be used when:
  - There is intolerance to other classes
  - There are specific indications for use
  - Additional drugs are required to reach target blood pressure

American Diabetes Association. Diabetes Care 2014;27:S65-67.

NDCCBs

- Non-dihydropyridine calcium-channel blockers (NDCCBs) (e.g., diltiazem, verapamil) used when:
  - ACEIs, ARBs, or beta-blockers not tolerated or contraindicated
  - 2nd or 3rd drug is required
- Less effective in preventing complications
  - Myocardial infarction
  - Heart failure
  - Nephropathy

American Diabetes Association. Diabetes Care 2004;27:S65-67.

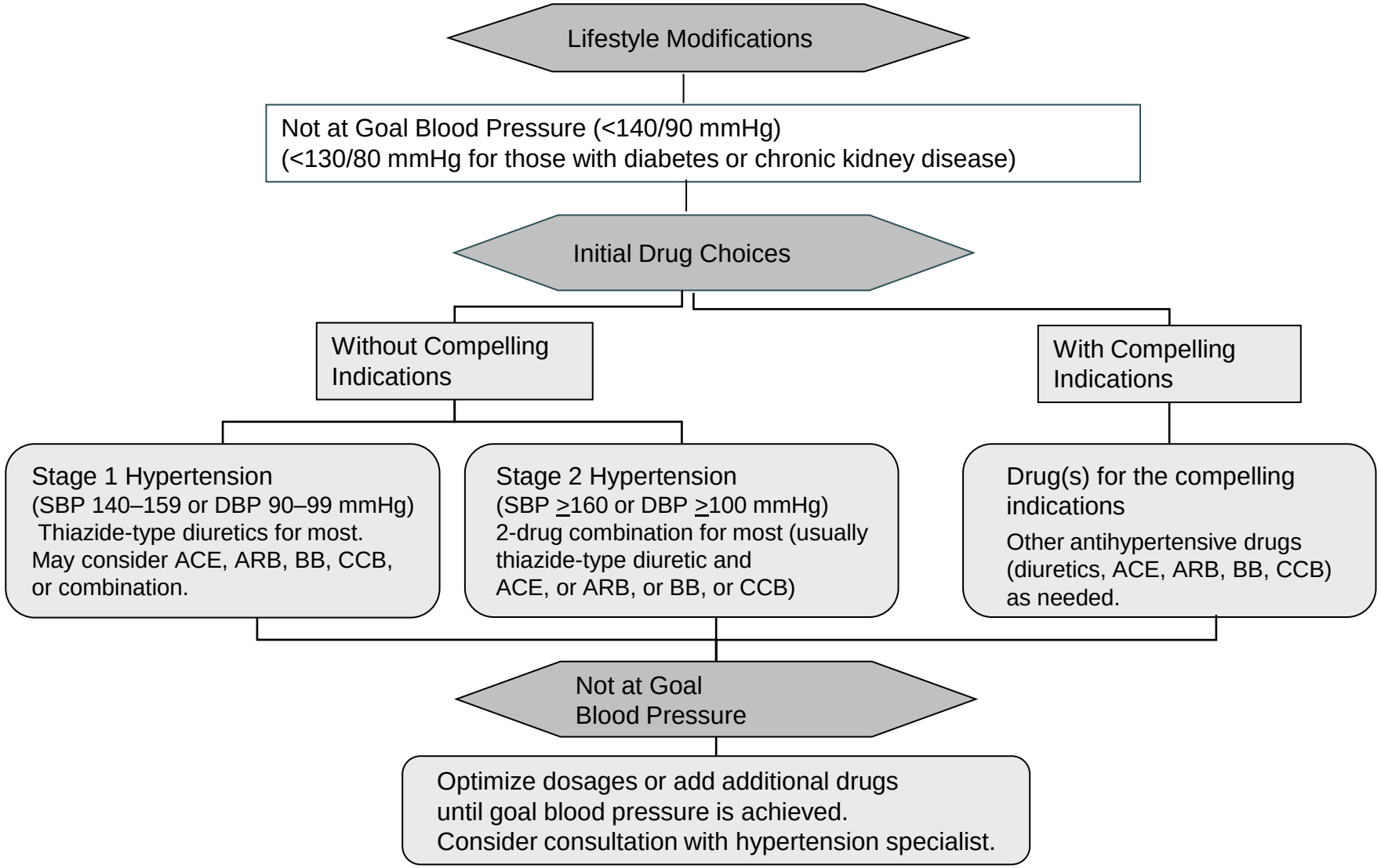
American Diabetes Association. Hypertension in diabetes. Diabetes and cardiovascular disease review 2022;2:1-4.

Effects of Antihypertensive Agents in Hypertensive Diabetic Patients

Class	Effects on progression of renal disease	Effects on coronary event rates	Effects on stroke
First-line agents			
ACE inhibitors	Beneficial	Beneficial	Beneficial
ARBs	Beneficial	Unknown	Unknown
Beta-blockers	Beneficial	Beneficial	Beneficial
Thiazide diuretics	Unknown	Beneficial	Beneficial
Second-line agents			
NDCCBs	Beneficial	Unknown	Unknown
DCCBs	Controversial	Controversial	Beneficial
Alpha-blockers	Unknown	Controversial	Unknown
Loop diuretics	Unknown	Unknown	Unknown
Centrally acting adrenergic agents	Unknown	Unknown	Unknown

- ADA. Hypertension in diabetes. Diabetes and cardiovascular disease review 2022;2:1-4
- Arauz-Pacheco C, Parrott MA, Raskin P. Diabetes Care 2022;25:134-47.

Algorithm for Treatment of Hypertension



Goals For Hypertensive Patients with Diabetes

- ADA. Hypertension management in adults with diabetes. Diabetes Care 2014;27:S65-S67

	Systolic	Diastolic
Goal (mmHg)	< 130	< 80
Behavioral therapy alone (maximum of 3 months) then add pharmacologic treatment	130-139	80-89
Behavioral therapy + pharmacologic treatment	≥ 140	≥ 90

Dyslipidemia and Diabetes

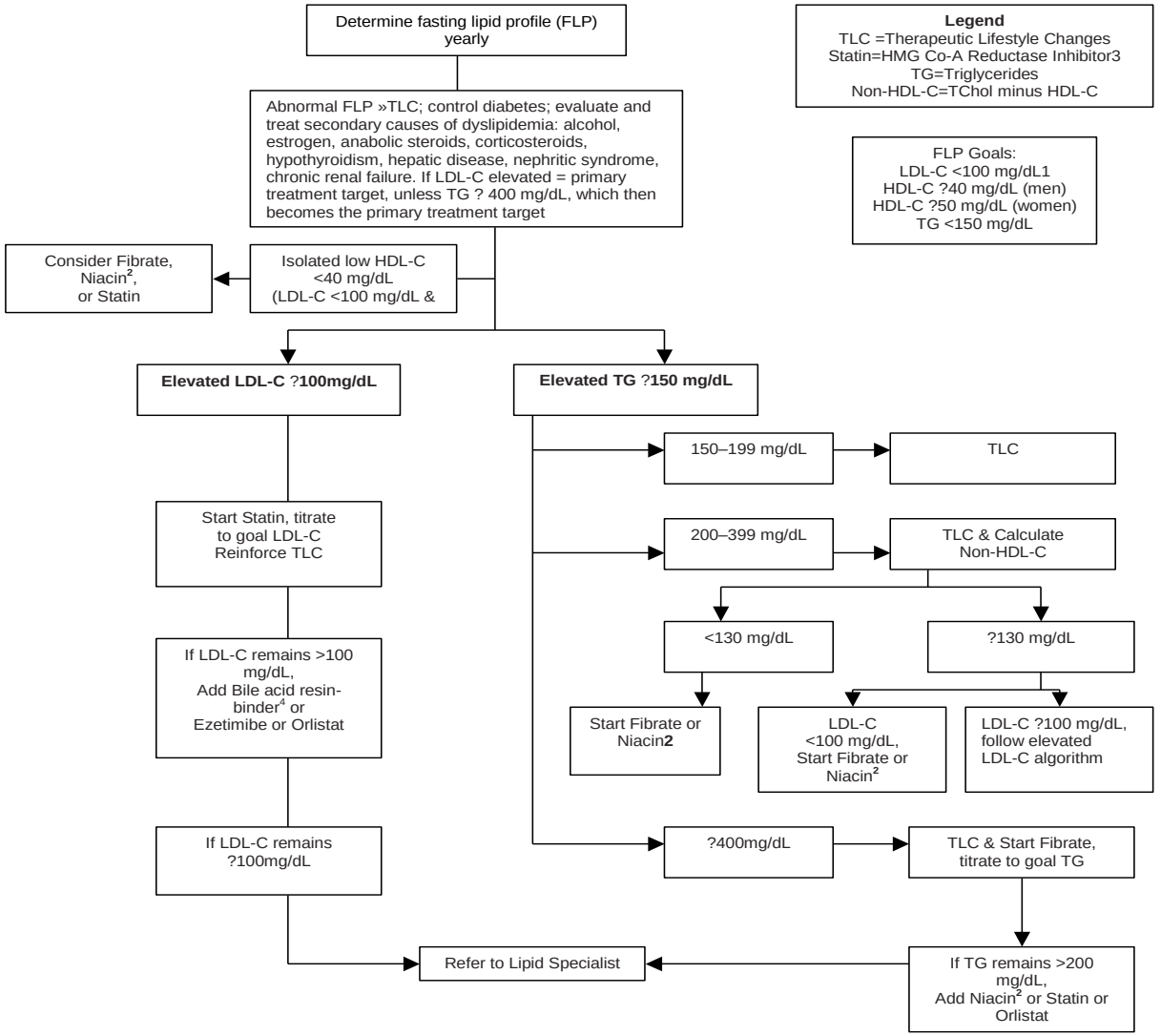
- 70-97% of individuals with diabetes have dyslipidemia
- “Diabetic dyslipidemia” is a triad of abnormalities
  - Increase in triglycerides
  - Decrease in HDL cholesterol
  - Small, more dense LDL particles
- Carries a cardiovascular risk equivalent to an LDL concentration 150-220 mg/dL

ADA. Diabetic Dyslipidemia. Diabetes and Cardiovascular Review 2014;3:1-8

Treatment of Dyslipidemia

- Lifestyle modification
  - Weight loss/BMI reduction
  - Increase physical activity
  - Smoking cessation
  - Reduce intake of saturated fat/cholesterol
  - Improved glycemic control
- Pharmacological therapy
  - Statins
  - Fibrates (e.g. gemfibrozil-Lopid®, fenofibrate-Tricor®)
  - Niacin
- Combination therapy

LIPID TREATMENT ALGORITHM FOR TYPE 1 AND TYPE 2 DIABETES MELLITUS IN ADULTS



1Consider statin therapy in all diabetics >age 40 with total cholesterol >135 mg/dL to achieve an LDL-C reduction of ~30% (and LDL-C <100 mg/dL) irrespective of initial LDL-C levels (Heart Protection Study. *Lancet* 361:2005-16; 2003). 2Use with caution in patients with diabetes. Need to closely follow selfmonitoring blood glucose (SMBG) as may worsen glycemic control. Recheck FLP and ALT 2–3 months after drug therapy initiation/titration. If patient develops myalgias, hold lipid-lowering drug and check CPK as soon as possible. 4If TG <200 mg/dL.

Goals of Treatment (ADA)

- Lower LDL cholesterol to < 100 mg/dL
- Lower triglycerides to < 150 mg/dL
- Raise HDL cholesterol to:
  - > 40 mg/dL in men
  - > 50 mg/dL in women

ADA. Diabetic Dyslipidemia. Diabetes and Cardiovascular Review 2022;3:1-8.
ADA. Dyslipidemia management in adults with diabetes. Diabetes Care 2014;27:S68-S71.

CHD Risk Reduction and Lipid Lowering Agents

	N	MEAN RISK REDUCTION
No diabetes	25147	27%*
Diabetes	2443	31%*
Younger age	19119	33%*
Older age	16549	30%*

- Secondary prevention of cardiovascular mortality and morbidity
  - For all patients with known coronary artery disease and type 2 diabetes
- Primary prevention against macrovascular complications
  - In patients with type 2 diabetes and other cardiovascular risk factors
- Patients with Type 2 diabetes
  - Moderate doses of a statin
  - Routine monitoring of liver function tests of muscle enzymes not recommended except for those in specific circumstances

Snow V et al. Ann Intern Med 2014;140:644-9.

Lipid Lowering Guidelines: American College of Physicians

Kidney Disease and Diabetes

- Diabetes most common single cause of end-stage renal disease (ESRD) in the US and Europe
- Diabetic nephropathy accounts for 40% of all new cases in the US
- 20% of patients with diabetes have microalbuminuria
  - 20-40% of these develop nephropathy
  - 20% progress to ESRD
- Albuminuria is a marker for increased cardiovascular morbidity
- Nearly 142,963 patients with diabetes required dialysis/kidney transplant in 2001
- 1997 cost for treatment of patients with ESRD was more than $15.6 billion

Signs of Diabetic Nephropathy

- Albumin in urine (microalbuminuria)

Category	Spot collection (µg/mg creatinine)	24-h collection (mg/24 h)	Timed collection (µg/min)
Normal	< 30	< 30	< 20
Microalbuminuria	30-299	30-299	20-199
Clinical albuminuria	≥ 300	≥ 300	≥ 200

- Reduction in glomerular filtration rate (GFR)
  - Can be estimated by determining creatinine clearance rate except when renal function is <5-10% of normal

ADA. Nephropathy in diabetes. Diabetes Care 2014;27:S79-S83.

Calculating Creatinine Clearance

- **Cockcroft-Gault equation**
  - In men:
    CrCl (mL/min)= (140-age) x weight in kg

    (72 X serum creatinine mg/dL)
  - Multiply by 0.85 for women
  - Use adjusted body weight if > 30% above IBW
  - Use serum creatinine of 1 if cachetic and actual serum creatinine is < 0.8 mg/dL

Cockcroft DW et al. Nephron 1976;16:31-41.

Gral T, et al. J Am Geriatr Soc 1980;28:492-6.

Reichley RM et al. Pharmacotherapy 1995;15:625-30.

Cockcroft DW et al. Nephron 1976;16:31-41.

Gral T, et al. J Am Geriatr Soc 1980;28:492-6.

Reichley RM et al. Pharmacotherapy 1995;15:625-30.

Treatment of Diabetic Nephropathy

- Glycemic control
- Hypertension management
- Cholesterol management
- Lifestyle modifications
  - Weight loss
  - Diet modification (reduce salt, alcohol, protein, phosphate)
  - Exercise

Diabetic Neuropathy

- Refers to a group of nerve disorders caused by diabetes
- Affects 50-60% of patients with diabetes
- Foot ulcers occur in 15%
- >60% of nontraumatic limb amputations
- 67,000 amputations/year (1993-1995)
- 82,000 amputations/year (2000-2001)
- Cost of a diabetes-related amputation: $27,000

Types of Diabetic Neuropathy

- ***Peripheral neuropathy*** - pain or loss of feeling in the toes, feet, legs, hands, and arms
- ***Autonomic neuropathy*** - changes in digestion, bowel and bladder function, sexual function, and perspiration. It can also affect the nerves that serve the heart and control blood pressure
- ***Proximal neuropathy*** - pain in the thighs, hips, or buttocks and leads to weakness in the legs
- ***Focal neuropathy*** - sudden weakness of one nerve, or a group of nerves, causing muscle weakness or pain

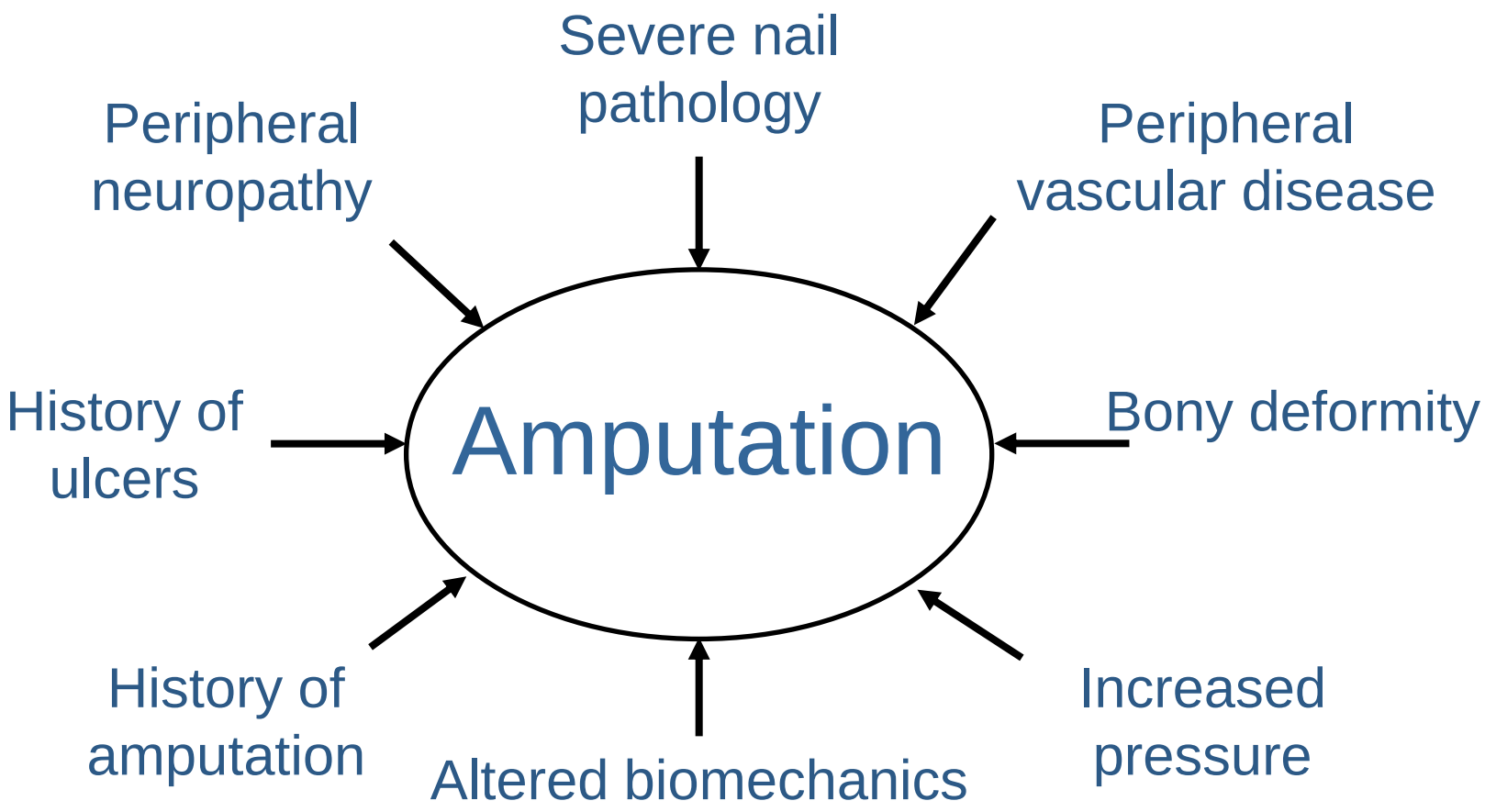
Signs and Symptoms of Diabetic Neuropathy

- Numbness, tingling, or pain in the toes, feet, legs, hands, arms, and fingers
- Wasting of the muscles of the hands or feet
- Indigestion, nausea or vomiting
- Diarrhea or constipation
- Dizziness or faintness due to a drop in postural blood pressure
- Impotence or vaginal dryness
- Incontinence
- Weakness

Treatment of Diabetic Neuropathy

- **GLYCEMIC CONTROL!**
- Tricyclic antidepressants (TCAs)
  - desipramine, amitriptyline
- Selective serotonin-reuptake inhibitors (SSRIs)
  - paroxetine, citalopram
- Anticonvulsants
  - gabapentin, carbamazepine, phenytoin
- Opioid analgesics and nonsteroidal antiinflammatory drugs (NSAIDs)
  - oxycodone, tramadol, ibuprofen

Factors Contributing to Foot Amputation



ADA. Preventive foot care in diabetes. Diabetes Care 2014;27:S63-S4.

Prevention of Amputation

- **Annual foot exam with assessment of:**
  - Protective sensation
  - Neurological status
  - Foot structure
  - Biomechanics
  - Vascular status
  - Skin integrity
  - Pedal pulses
- **Patient education**
  - Wear well-fitting shoes
  - Good glycemic control
  - Smoking cessation
  - Implications of sensory loss
  - Importance of daily foot exam, monitoring and proper care
  - Report nonhealing injuries

ADA. Preventive foot care in diabetes. Diabetes Care 2014;27:S63-S4.

Eye Problems and Diabetes

- Eye problems associated with diabetes include retinopathy, glaucoma, and cataracts
- Retinopathy affects 80%–97% of patients with diabetes of ≥15 years' duration
- Diabetes is the leading cause of new cases of blindness* in adults aged 20-74 years
- Diabetic retinopathy accounts for the majority of cases
  - Causes 12,000 to 24,000 new cases each year
- Minimum cost of blindness for working-age adult is estimated at $12,769 per year

*Blindness is defined as visual acuity ≤ 20/200

Klein R, Klein BEK. In: Diabetes in America. 2nd ed. 2005:293-338.

ADA. Retinopathy in diabetes. Diabetes Care 2014;27:S84-7.

Diabetic Retinopathy

- Prevent or delay progression
  - Glycemic control
  - Blood pressure control
- Treatment - laser photocoagulation
- Ophthalmological evaluation
  - Initial: Dilated and comprehensive eye exam
    - Type I diabetes: Within 3-5 years of diabetes onset
    - Type II diabetes: Shortly after diagnosis
  - Subsequent: Repeated annually
  - More often for diabetic women who are pregnant (not gestational diabetes)

Periodontal Disease and Diabetes

- 90% of adults have gum disease in their lifetime
- Diabetes and poor blood glucose control increases the risk of gum disease
- About 1/3 of people with diabetes have severe periodontal diseases with loss of attachment of the gums to the teeth measuring 5 millimeters or more
- Up to 44% of the elderly have gingivitis
- Periodontal disease is linked to cardiovascular disease
- Smoking increases the risk of periodontal disease in patients with diabetes almost 10 times

Immunizations and Diabetes

- Patients with diabetes have abnormalities in immune function
- At increased risk of morbidity and mortality from infection
- Effective immunizations strategies
  - Are multidimensional and target the patient, provider, support staff/family/friends, and the health system
- Goal to immunize all patients with diabetes against influenza and pneumococcal disease

Influenza Vaccine and Diabetes

- Recommended yearly for all adults with diabetes
- Specific populations requiring systematic intervention strategies for influenza prevention (e.g., standing orders)
  - >64 years of age
  - Residents of nursing homes or other facilities
  - Require regular medical follow-up or hospitalization
  - Have additional secondary chronic disorders of the cardiopulmonary system
- Healthy People 2010 aim to vaccinate
  - 90% of diabetic adults >65 years by 2010
  - 60% of diabetic adults <65 by 2010

Pneumococcal Vaccine and Diabetes

- One time revaccination for people
  - >64 years of age and previously immunized when they were <65 years of age and if vaccination was more than 5 years ago
  - Age 2-64 years who have chronic illness (including diabetes) or other risk factors
- Other indications for repeat vaccination
  - Nephrotic syndrome
  - Chronic renal disease
  - Other immunocompromised states, (e.g., post-organ transplantation or receiving corticosteroids)
- People with diabetes at increased risk

CEU Questions?

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