Hypertension and Dyslipidemia

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Objectives : Hypertension

Classify blood pressure measurement according to current definitions (e.g., Stage 1 or 2 hypertension).

- Compare home and in clinic blood pressure readings

Assess for social risk factors including tobacco, drug, and alcohol use

Assess past medical history for exacerbating factors or diseases associated with secondary hypertension including sleep apnea or renal disease

Identify characteristics and relevant review of systems that suggest uncontrolled hypertension including headaches and visual changes

Identify key physical exam findings that may suggest end organ effects of hypertension including extra heart sounds and reduced peripheral pauses

Describe a rational and evidence-based approach to treating a patient with hypertension

Describe possible complications of untreated hypertension including cerebrovascular and cardiovascular disease.

Objectives :Dyslipidemia

Identify relevant past medical history to determine associated risks of vascular disease including diabetes and causative med ications

Assess for social risk factors including tobacco use, diet, and exercise

Assess for familial risk factors, particularly inherited causes of dyslipidemias (including familial combined hyperlipidemia)

Identify key physical exam findings that determine associated systemic effects including xanthomas, decreased peripheral pulses, and arterial bruits

Identify and interpret key laboratory and imaging tests and list indications, benefits, test characteristics, risks, and cost s of testing that determine the extent of hyperlipidemia (including fasting lipid panel) and determine the secondary causes of lipid abnormalities (including fasting glucose and TSH level)

Describe a rational and evidence-based approach to treating a patient with dyslipidemia:

- Use risk calculators to decide on medical treatment including 10-year and lifetime ASCVD/mortality calculators
- Counsel patients on lifestyle modification including diet, exercise, and weight loss
- Describe treatment goals including LDL levels
- Describe frequency and type of lab monitoring including yearly LDL testing and liver enzyme monitoring

Describe a rational and evidence-based approach to screening and use patient characteristics to determine when to begin screening and frequency of screening

Definition and Diagnosis of HTN

≥ 130 mmHg systolic

AND/OR

≥ 80-89 mmHg diastolic

On 2 or more office visits

AND/OR

Current use of antihypertensive medications

Blood Pressure Categories

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120-129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130-139	or	80-89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

heart.org/bplevels

Hypertension

Covered in other lectures

Essential HTN = idiopathic

90 – 95%

"Multifactorial"
- Age
- Stress
- Weight
- Blood glucose
- Smoking
- Caffeine
- Cardiopulmonary fitness

Secondary HTN (~5%)

- Renal
  - Chronic Renal Failure (CRF)
  - Renin secreting tumors
  - Renal artery stenosis
- Endocrine
  - Adrenal
    - Adrenocortical hyperfunction
    - Pheochromocytoma
  - Thyroid
    - Hypothyroid
    - Hyperthyroid
- Cardiovascular
  - Coarctation of aorta
- Neuro
  - ↑ ICP

Diagnosis of Hypertension

- Basic Tests
  - Fasting blood glucose
  - Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
  - CBC
  - Lipid profile, after 8- to 12-hour fast
  - TSH
  - Urinalysis

- Optional Tests to Consider
  - EKG
  - Uric Acid
  - Microalbumin/Cr. ratio

Complications of Hypertension

- Direct relationship between BP and cardiovascular disease
  - Continuous
  - Consistent
  - Independent of other risk factors
- No evidence of a BP threshold for CVD risk
  - CV mortality increased progressively throughout range of BP
  - Risk of CVD beginning at 115/75 mmHg and doubles with each increment of 20/10 mmHg up to 185/115 mmHg

Sequelae of Hypertension

Untreated:

- 50% die of Ischemic Heart Disease (IHD)or Heart Failure
- 33% more die of stroke (CVA-cerebrovascular accident)

Cardiac hypertrophy

Heart failure

Multi-infarct dementia / Small vessel ischemia

Aortic dissection

End stage renal failure

Retinopathy

Hypertension: Clinical Manifestations

List of the classic symptoms of HTN …

NONE

HTN = “silent killer”

30% are unaware they have HTN

Often no symptoms until end organ damage

- Headaches, blurry vision (papilledema)

Hypertension: Exam findings

S3

- S3 gallop is an important and common early finding of HF associated with dilated cardiomyopathy and may also be heard in patients with ***diastolic HF*** (although less frequently than with systolic HF), aortic valve disease, and coronary artery disease (CAD)
- MR

S4

- S4 is most frequently observed in patients with decreased LV distensibility. Thus, S4 is common in ***hypertensive heart disease***, aortic stenosis, and HCM. LV hypertrophy, which is present in all these conditions

An aortic ejection sound is also heard in some patients with systemic hypertension, probably due to associated aortic root dilation

Papilledema on fundoscopic exam

Hypertensive Urgency

Severe elevation in BP ***WITHOUT*** acute end-organ damage

- >/= 180/120 mmHg, often with headache
- Most cases are inadequate treatment or nonadherent
- Can be sent home from office/ED with F/U
  - Confirm pressure is responsive (i.e. short acting meds, repeat reading)
  - Or if you are aware of the chronicity of the patient's pressures
  - Or, if you have an acute cause/explanation

Hypertensive Emergency

Severe elevation in BP ***WITH*** acute end-organ damage

- Hypertensive Encephalopathy
- Intracerebral / subarachnoid hemorrhage
- Acute MI / ACS
- Acute LV failure
- Acute aortic dissection
- Renal crisis (Collagen vascular disease)
- Acute glomerulonephritis
- Microangiopathic hemolytic anemia

Exceptions

Acute Ischemic Stroke - **not** lowered unless it is ≥185/110 mmHg in patients who are candidates for reperfusion therapy or ≥220/120

Acute Aortic Dissection – SBP should be **rapidly** lowered to a target of 100 to 120 mmHg (goal is within 20 minutes)

Requires hospitalization to lower BP

- IV medication : typically beta-blocker, calcium channel blocker
- given in ICU / Step-down unit
- Target: reduce by 10% in 1 hour, 5-15% in next 23 hours

Benefits of Lowering Blood Pressure

For each 10 mmHg decrease in systolic BP…

. . . 30% decrease risk of heart mortality

. . . 40% decrease risk of stroke mortality

Antihypertensive therapy reduces…..

- CVA 35-40%
- MI 20-25%
- CHF >50%

Stage 1 HTN (130-139/80-89 mmHg)

- Reduce systolic BP 12 mmHg over 10 yrs, prevents 1 death for every 11 treated

Hypertension Treatment

- Lifestyle modifications
- Medications
- Treat underlying condition / secondary cause

Hypertension : Lifestyle modifications

Diet

- Healthy choices
  - Low salt, increased vegetables (DASH)
- Healthy Portions
  - Calorie reduction
- Reduce Alcohol Consumption

Exercise

- Cardiopulmonary fitness vs “active”
- Heart rate to 120 bpm for at least 20 mins

Weight loss

- See above
- Set small goals – baby steps

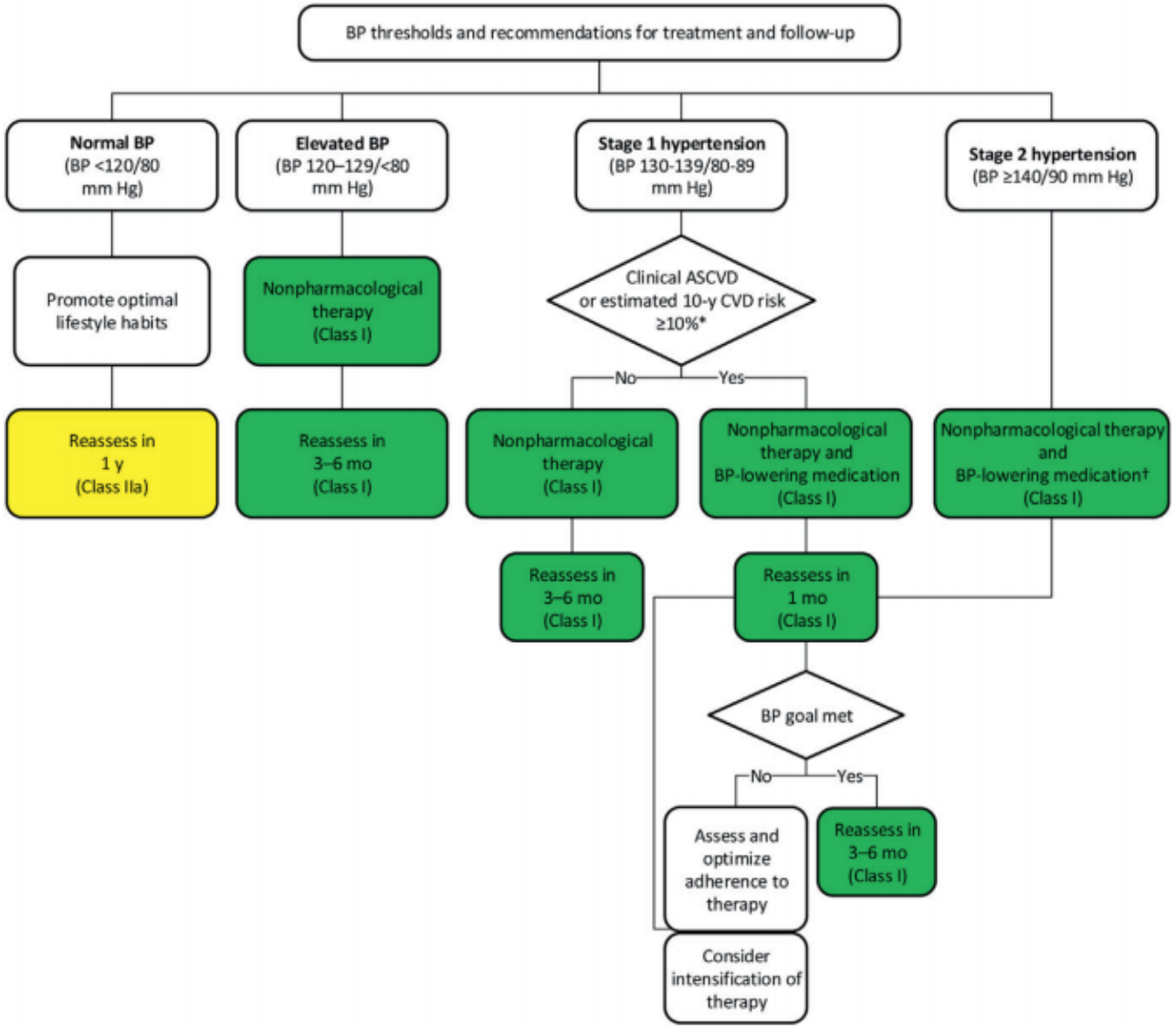
Smoking Cessation

Nonpharmacological Intervention		Dose	Approximate Impact on SBP		
			Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	−5 mm Hg	−2/3 mm Hg	(S6.2-1)
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	−11 mm Hg	−3 mm Hg	(S6.2-6,S6.2-7)
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	−5/6 mm Hg	−2/3 mm Hg	(S6.2-9,S6.2-10)
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	−4/5 mm Hg	−2 mm Hg	(S6.2-13)
Physical activity	Aerobic	■ 90–150 min/wk ■ 65%–75% heart rate reserve	−5/8 mm Hg	−2/4 mm Hg	(S6.2-18,S6.2-22)
	Dynamic resistance	■ 90–150 min/wk ■ 50%–80% 1 rep maximum ■ 6 exercises, 3 sets/exercise, 10 repetitions/set	−4 mm Hg	−2 mm Hg	(S6.2-18)
	Isometric resistance	■ 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ■ 8–10 wk	−5 mm Hg	−4 mm Hg	(S6.2-19,S6.2-31)
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: ■ Men: ≤2 drinks daily ■ Women: ≤1 drink daily	−4 mm Hg	−3 mm Hg	(S6.2-22–S6.2-24)

Resources: Your Guide to Lowering Your Blood Pressure With DASH—How Do I Make the DASH? Available at: https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to. Accessed September 15, 2017. (S6.2-72) Top 10 Dash Diet Tips. Available at: http://dashdiet.org/dash_diet_tips.asp. Accessed September 15, 2017. (S6.2-73) *Type, dose, and expected impact on BP in adults with a normal BP and with hypertension. †In the United States, one "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol) (S6.2-29).

DASH indicates Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

Modification	Approximate SBP reduction (range)
Weight reduction	5–20 mmHg/10 kg weight loss
Adopt DASH eating plan	8–14 mmHg
Dietary sodium reduction	2–8 mmHg
Physical activity	4–9 mmHg
Moderation of alcohol consumption	2–4 mmHg


BP thresholds and recommendations for treatment and follow-up
Normal BP (BP <120/80 mm Hg)
Elevated BP (BP 120–129/<80 mm Hg)
Stage 1 hypertension (BP 130-139/80-89 mm Hg)
Stage 2 hypertension (BP ≥140/90 mm Hg)
Promote optimal lifestyle habits
Nonpharmacological therapy (Class I)
Clinical ASCVD or estimated 10-y CVD risk ≥10%*
No
Yes
Reassess in 1 y (Class IIa)
Reassess in 3–6 mo (Class I)
Nonpharmacological therapy (Class I)
Nonpharmacological therapy and BP-lowering medication (Class I)
Nonpharmacological therapy and BP-lowering medication† (Class I)
Reassess in 3–6 mo (Class I)
Reassess in 1 mo (Class I)
BP goal met
No
Yes
Assess and optimize adherence to therapy
Reassess in 3–6 mo (Class I)
Consider intensification of therapy

Antihypertensive Agents

Thiazide Diuretic ***Avoid in Gout, BPH***

- Hydrochlorithiazide
- Chlorthalidone

ACE Inhibitors ***Diabetes***

- Lisinopril, Enalapril, Captopril, benazepril

ARB ***Diabetes***

- Losartan, valsartan, candesartan

Beta Blockers ***Heart Disease***

- Metoprolol, atenolol, carvedilol, labetalol, esmolol

Calcium Channel Blockers ***Advanced CKD***

- Diltiazem, verapamil , amlodipine, nifedipine,

Hypertension

Failure to reach goal BP in pts who are adhering to full doses or an appropriate three-drug regimen that includes a diuretic.

JNC 7, ACC/AHA 2017

- *….or when control is achieved but requires 4 or more medications.*

Should prompt a survey / consideration for secondary causes

ASSESS FOR IDENTIFIABLE CAUSES OF HYPERTENSION

- Sleep apnea
- Drug induced/related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushing's syndrome or steroid therapy
- Pheochromocytoma
- Coarctation of aorta
- Thyroid/parathyroid disease

Dyslipidemia: Definition

- Lipid disorders – Includes disorders of lipoprotein metabolism but also lipodystrophies and some lipid storage disorders
- Hyperlipidemia – Elevation of serum total or LDL cholesterol or triglyceride
- Hypercholesterolemia - Elevation of LDL or Total cholesterol, normal triglycerides
- Dyslipidemia - a large range of lipid abnormalities and may involve a combination of
  - increased total cholesterol (≥240 mg/dL [6.20 mmol/L])
  - LDL-C (>160 mg/dL [4.13 mmol/L]),
  - triglyceride levels (>200 mg/dL [2.25 mmol/L])
  - or *decreased* HDL-C (<40 mg/dL [1.03 mmol/L])

Optimal levels

Total Cholesterol : <150 mg/dL

Correlates to an LDL ~ 100 mg/dL

HDL: >39 mg/dL

Triglycerides: <150

Dyslipidemia: Scope

By World Health Organization (WHO) definitions, about 40 percent of people globally have elevated total cholesterol levels, while about 50 percent have elevated levels in Europe and the Americas

About 1 in 5 adolescents have an unhealthy cholesterol reading, and nearly 93 million U.S. adults age 20 or older have high cholesterol

But since high cholesterol doesn't have symptoms, many people don't know their levels are high

Dyslipidemia : Screening

Cholesterol should be checked starting early in life—even children and adolescents should have their cholesterol checked.

Cholesterol testing should be done very 5 years for people aged 20 or older who are at low risk for cardiovascular disease

The ACC/AHA recommends that all adults aged 20–78 years have a fasting lipid profile measured every 4–6 years if there is no atherosclerotic CVD and more often if this condition is present

Lipid testing is relatively quick, easy, and inexpensive

The tests are generally reliable

- should include baseline measurement of total cholesterol, LDL-C, HDL-C, and triglyceride levels
- For patients with a history of CVD or those with a very high level of risk, tests that may be considered in addition to the baseline lipid profile include measurement of lipoprotein(a), apolipoprotein B, and apolipoprotein A1

Dyslipidemia: Measurement

Fasting

- First time a lipid profile is obtained
- For the purpose of following known hypertriglyceridemia
  - Strongly affected by food consumption
- Ask the patient to fast for 8-10 hours
  - (before breakfast)

Non-fasting

- Ok in any other case

Serum total and HDL-C are measured directly and can be obtained in fasting or nonfasting individuals; there are only small, clinically insignificant differences in these values between measurements in the fasting or non-fasting state

Dyslipidemia: Risk factors

A family history of heart disease or high blood cholesterol: You are more at risk of having high cholesterol if other people in your family have it

Diabetes: Type 2 diabetes raises “bad” cholesterol and lowers high-density lipoprotein (HDL), or “good,” cholesterol, raising the risk for heart disease and stroke.

Older age: As you age, your body can’t clear cholesterol as well as it used to.

Being male. Men tend to have higher LDL and lower HDL cholesterol levels than women do. But after menopause (around age 55), LDL cholesterol levels in women increase.[4,5]

Overweight or obesity. Excess weight, unhealthy eating habits, and lack of physical activity can lead to high cholesterol

Dyslipidemia : Etiology

Primary

- Inheritable condition
- Overproduction or defective clearance of triglycerides and cholesterol
- Monogenic and polygenic – see table
  - Familial Combined Hypercholesterolemia

Secondary

- Accounts for 30-40%
- Unhealthy lifestyle factors
- Acquired medical conditions

Diabetes Mellitus
Cholestatic Liver disease
Hypothyroidism
Nephrotic Syndrome
Obesity
Excessive Alcohol intake
Cigarette Smoking
Medications

Disorder	Estimated prevalence	Characteristic lipid levels*	Clinical features		Confirmatory studies
			In adults	In children	
Heterozygous familial hypercholesterolemia	1/200 to 1/300	▪ Elevated TC and LDL-C ▪ LDL-C 190 to 450 mg/dL¶ ▪ TG usually normal	▪ Tendon or tuberous xanthomata ▪ Xanthelasmas ▪ Corneal arcus ▪ Premature CHD	▪ Subclinical atherosclerosis	▪ Exclusion of secondary disorders of cholesterol
Homozygous familial hypercholesterolemia	1/1,000,000	▪ Markedly elevated TC and LDL-C ▪ Untreated LDL-C >500 mg/dL ▪ TG usually normal	▪ Extensive xanthomata ▪ Severe and progressive atherosclerotic cardiovascular disease	▪ Cutaneous or tendon xanthomata often in the first year of life ▪ Premature CHD occurs in childhood if untreated	▪ Genetic testing for mutations in the LDLR, APOB, and PCSK9 genes
FCHL	1 to 2%	▪ Phenotypically heterogeneous ▪ Elevated TC and/or TG ▪ LDL-C/APOB ratio <1.2	▪ Xanthelasma ▪ Corneal arcus ▪ Premature CHD	▪ Clinical manifestations are typically not seen during childhood	▪ Similar lipid profile in one first- or two second-degree relatives
Familial hyperapobetalipoproteinemia	<1% Likely a variant of FCHL	▪ APOB >135 mg/dL ▪ LDL-C <160 mg/dL ▪ LDL-C/APOB ratio <1.2	▪ Xanthelasma ▪ Premature CHD ▪ Obesity	▪ Clinical manifestations other than obesity are typically not seen during childhood	▪ Similar lipid profile in at least two first- or second-degree relatives
Polygenic hypercholesterolemia	>25%	▪ Elevated TC and LDL-C ▪ TG usually normal ▪ LDL-C 130-250 mg/dL	▪ Premature CHD ▪ Tendon xanthomata are **not** seen	▪ Clinical manifestations are typically not seen during childhood	
Familial dysbetalipoproteinemia	1/5000	▪ Elevated TC and TG ▪ VLDL/TG ratio >0.3	▪ Tuboeruptive xanthomata ▪ Xanthomata of the palmar creases ▪ Premature CHD	▪ Clinical manifestations are typically not seen during childhood	▪ APOE isoform analysis

Summary of the clinical features of different lipid disorders.

TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; CHD: coronary heart disease; LDLR: LDL receptor; APOB: apolipoprotein B; PCSK9: proprotein convertase subtilisin kexin 9; FCHL: familial combined hyperlipidemia; VLDL: very low-density lipoprotein; APOE: apolipoprotein E.

* Lipid levels presented in this table represent the typical ranges seen in each disorder, primarily in affected adults. In most of these disorders, there is considerable variability in these values and lipid levels alone generally cannot be used to confirm or exclude the diagnosis.

¶ In pediatric patients, an LDL-C cutoff value of ≥190 mg/dL is generally used to establish a diagnosis of heterozygous FH. However, in patients with a concerning family history (ie, first-degree relatives with hypercholesterolemia and/or early cardiovascular disease), it may be appropriate to use a lower cutoff value (eg, LDL of ≥160 mg/dL).

Secondary Dyslipidemia

Items	Cholesterol	Triglyceride
1. Hypothyroidism	↑	
2. Nephrotic syndrome	↑	↑
3. Chronic kidney disease (CKD)		↑
4. Primary biliary cholangitis (PBC)	↑	
5. Obstructive jaundice	↑	
6. Diabetes	↑	↑
7. Obesity		↑
8. Cushing's syndrome	↑	↑
9. Pheochromocytoma	↑	↑
10. Drugs	Drug dependent	
11. Alcohol intake		↑
12. Smoking		↑

Dyslipidemia: Meditation Culprits

- **Atypical antipsychotic** agents:
  - ***clozapine*** and ***olanzapine***- associated with weight gain, obesity, hypertriglyceridemia, and development of diabetes mellitus
- ***Antiretroviral*** regimens HIV infection:
  - ***protease inhibitors***- lipodystrophy syndrome
- ***Thiazides, beta blockers, estrogen***

Causative drugs	LDL-C	TG	HDL-C
Diuretics (thiazide)	→	↑	→
β-blockers	→	↑	↓
Steroid	↑	↑	↑
Estrogen	↓	↑	↑
Progesterone	↑	↓	↓
Immunosuppressants	↑	↓	No available data
Anti-HIV drugs	↑	↑	↓
Atypical antipsychotics	→	↑	↓
Retinoids	↑	↑	↓

Dyslipidemia : Secondary

- **Smoking**: lowers HDL and impairs HDL function
- **Alcohol**: excessive intake (>1 drink /day for female, >2 drinks/day for male) raises triglycerides
- **CKD**: elevations in low-density lipoprotein (LDL) cholesterol and triglycerides, and low levels of high-density lipoprotein (HDL) cholesterol; hypertriglyceridemia (type IV hyperlipoproteinemia) occurs in 30 to 50 percent of cases of CKD
- **Nephrotic syndrome**: Increased hepatic production of lipoproteins (induced in part by the fall in plasma oncotic pressure) is the major abnormality, but also diminished lipid catabolism
- **Primary biliary cholangitis** and similar disorders may be accompanied by marked hypercholesterolemia that results from an accumulation of lipoprotein-X

Dyslipidemia : DMII

- Hyperlipidemia in association with insulin resistance is common in patients with type 2 diabetes mellitus
- Insulin resistance is associated with larger very low-density lipoprotein (VLDL) particle size, smaller LDL particle size, and smaller HDL particle size
- The number of VLDL, intermediate-density lipoprotein (IDL), and LDL particles increase with increasing insulin resistance, while HDL particle concentration decreases
- Hypertriglyceridemia results both from increased substrate availability (glucose and free fatty acids) and from decreased lipolysis of VLDL triglyceride

Type II Diabetes Mellitus : essentially a stand-alone reason to treat with statin therapy

Dyslipidemia : Hypothyroid

- 1- 5% of hypercholesterolemia have overt to sub-clinical hypothyroid
  - Thus, all patients with hypercholesterolemia (and hypertriglyceridemia) should be screened for hypothyroidism
- The primary mechanism for hypercholesterolemia in hypothyroidism is accumulation of LDL cholesterol due to a reduction in the number of cell-surface receptors for LDL, resulting in decreased catabolism of LDL. A decrease in LDL receptor activity has also been describe
- Treatment with T4 (levothyroxine) improves total and LDL cholesterol
  - Treating only with statin can induce myopathy

Dyslipidemia : Clinical Manifestations

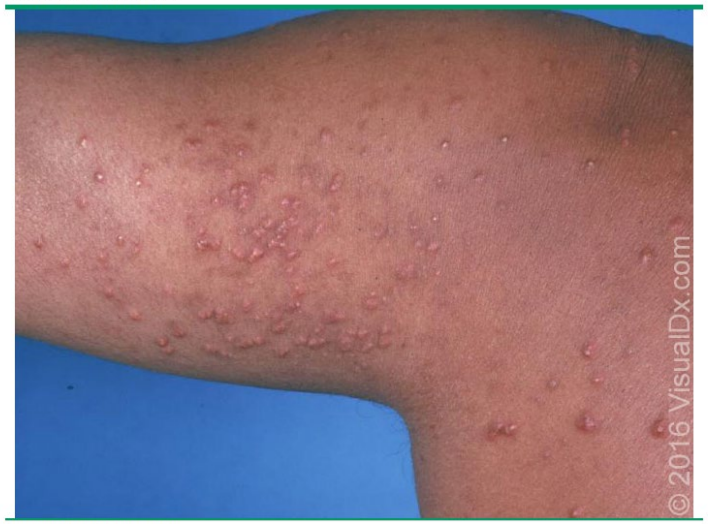
- Generally – none from just elevated levels

- Genetic Disease – some visible manifestations of excessive cholesterol
  - Xanthomas are **lesions on the skin containing cholesterol and fats**
    - may manifest as papules, plaques, or nodules in skin

  - Corneal Arcus or Arcus Senelis in geriatric patients
    - Always abnormal in <40
    - Cholesterol deposition around the cornea, visible when looking at the rim of the iris

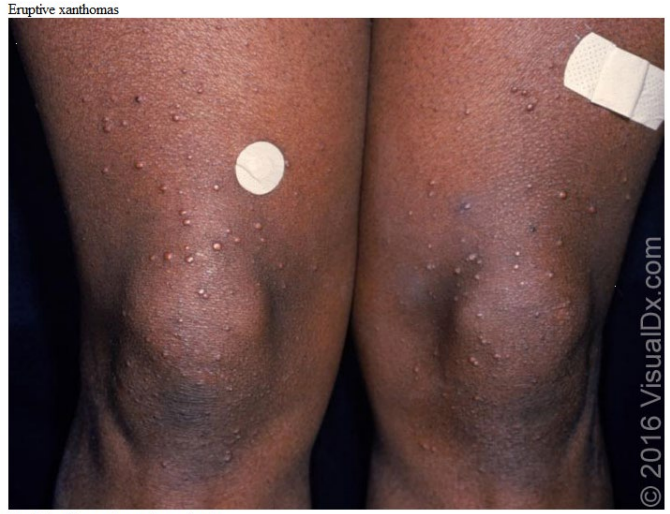
Often, the manifestation is vascular disease: Claudication, diminished pulses, bruits

Eruptive xanthomas



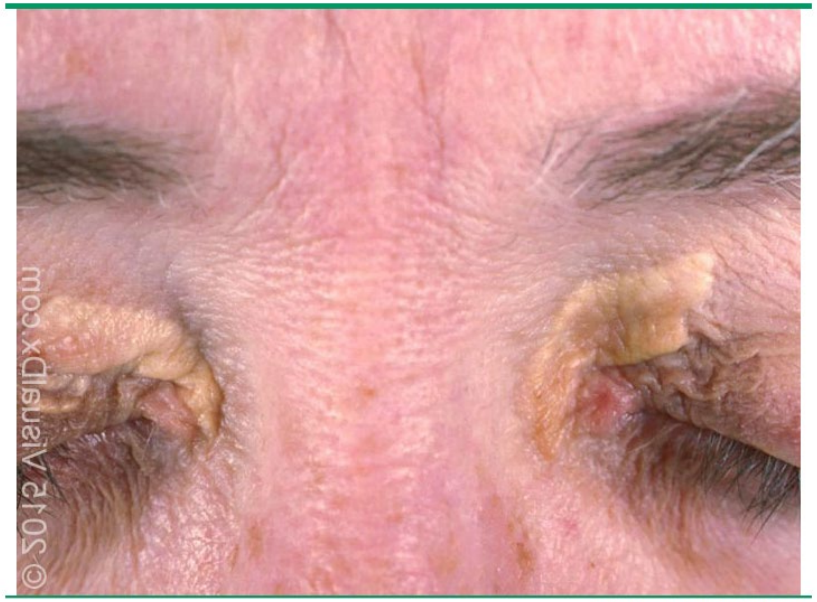
Multiple yellow-red papules.

Eruptive xanthomas



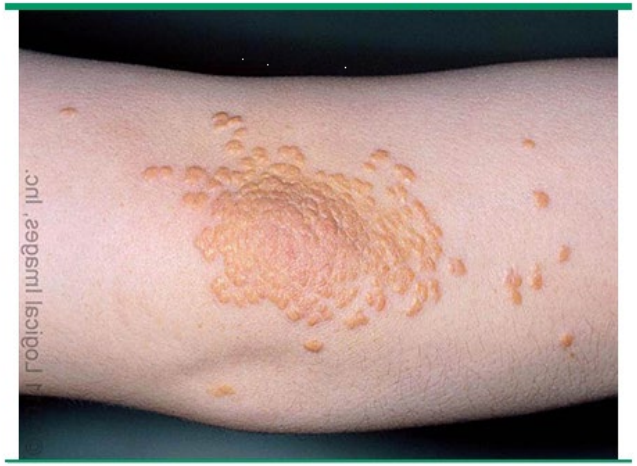
Multiple yellow-red papules on the legs.

Xanthelasma



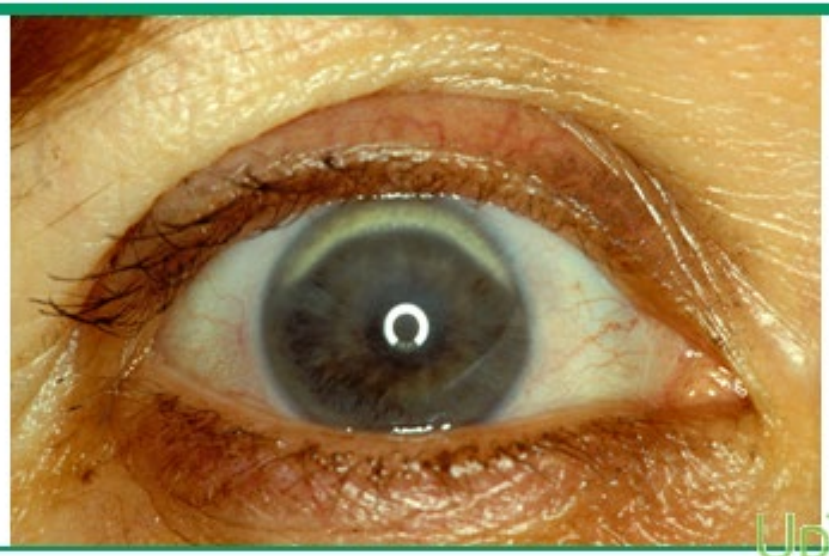
Yellow plaques on the eyelids.

Tuberous xanthoma

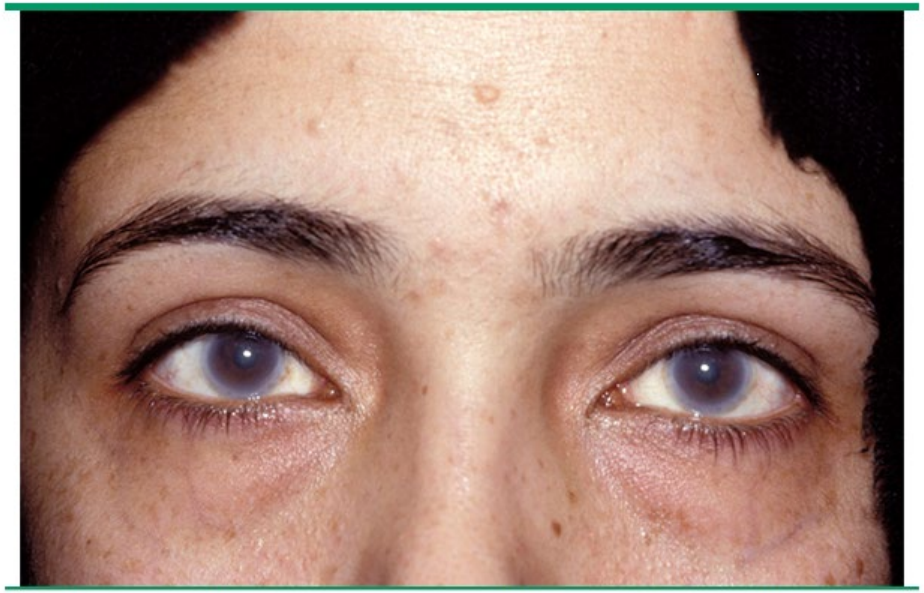


Yellow papules on the elbow in a case of tuberous xanthoma.

Early corneal arcus



Corneal arcus



Corneal arcus is a white or grey arc or ring around the cornea due to deposition of cholesterol. It is commonly seen in older adults (called arcus senelis), but is an abnormal finding in individuals under age 40.

Familial Combined hyperlipidemia

- (FCHL) is a common genetic lipid disorder (1 to 2 percent of the population)
- Patients present with elevated levels of plasma total cholesterol, low density lipoprotein cholesterol (LDL-C), triglycerides, and apolipoprotein (apo) B
- Premature atherosclerotic cardiovascular disease (ASCVD) is not uncommon
- There is an increased future likelihood of impaired glucose tolerance or type 2 diabetes

Familial Combined Hyperlipidemia

- FCHL is a complex, polygenic disorder in which gene variants causing elevations of VLDL and of LDL in the same families
- Screening relatives reveals variable dyslipidemia:
  - some with an increase in both cholesterol and triglycerides
  - some with increased cholesterol but normal triglyceridemia
  - some with principally hypertriglyceridemia (often mild, but occasionally type V)
  - and others there is little dyslipidemia.
- FCHL is caused by overproduction of hepatically-derived apoB-100 associated with very low density lipoprotein (VLDL)
  - an autosomal dominant pattern of inheritance
  - LDL phenotype A is associated with large buoyant LDL particles
  - LDL phenotype B is characterized by small, dense LDL particles, low HDL, and High triglycerides

Familial Combined Hyperlipidemia

Diagnosis :

- FCHL is diagnosed in patients with a family history of premature CHD and whose apoB concentration is >120 mg/dL in combination with either elevations in both LDL-C and triglycerides or either elevated LDL-Col or triglycerides

- The diagnosis of this disorder or the possible variant hyperapobetalipoproteinemia requires family data

- Is suggested by an LDL-to-apoB ratio of less than 1.2 (normal value >1.4).

familial combined hyperlipidemia

Treatment:

- The first-line treatment is a statin - which is effective therapy for lowering apoB levels
  - irrespective of whether or not triglyceride levels are elevated

- Goal - of achieving LDL-C <100 mg/dL in primary prevention and <70 mg/dL in secondary prevention

- Statins are used before fibrates in hypertriglyceridemic dyslipidemias
  - They are not better at lowering triglycerides, but randomized clinical trial evidence show that they are safe and that they decrease cardiovascular disease risk and mortality
  - High intensity statins (atorvastatin 80 mg and rosuvastatin 40 mg) lower triglycerides by 43 percent in patients with triglycerides as high as 800 to 850 mg/dL

Dyslipidemia: Treatment

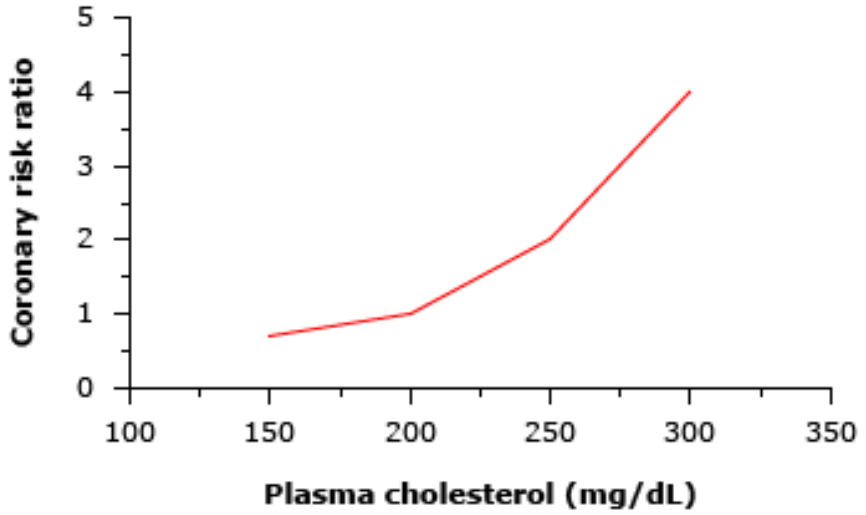
- Treatment of lipid disorders in patients at high risk of (or with established) CHD
- Large RCTs: LDL-C lowering has been consistently shown to reduce the risk of ASCVD
  - a lowering of LDL-C levels of 1% gives an approximate 1% reduction in the risk of ASCVD
- Statin therapy is divided into 3 categories
  - High-intensity statin therapy typically lowers LDL-C levels by ≥50%
  - Moderate-intensity statin therapy by 30% to 49%
  - Low-intensity statin therapy by <30%
- Other LDL-lowering drugs:
  - ezetimibe, bile acid sequestrants, and PCSK9 inhibitors

Triglyceride-lowering drugs : fibrates and niacin
They have a mild LDL-lowering action
RCTs do not support their use as add-on drugs to statin therapy

Table 3. High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg**§	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Association of increasing plasma cholesterol and coronary risk



Relation between plasma cholesterol concentration and six-year coronary heart disease risk in 361,662 men (ages 35 to 57) screened during the MRFIT study. There is a continuous, positive, graded correlation between the plasma cholesterol concentration and coronary risk. To convert plasma cholesterol to mmol/L, divide by 38.5.

Data from: Stamler J, Wentworth D, Neaton JD. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA 1986; 256:2823.

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Dyslipidemia: Treatment is Risk based

- Patients ages 20-75 years and LDL-C ≥190 mg/dl, use high-intensity statin without risk assessment
- T2DM and age 40-75 years, use moderate-intensity statin and risk estimate to consider high-intensity statins
- Age 40-75 years and LDL-C ≥70 mg/dl and <190 mg/dl without diabetes, use the risk calculator
  - Risk 5% to <7.5% Risk discussion: if risk-enhancing factors are present, discuss moderate-intensity statin
  - Risk ≥7.5-20% - use moderate-intensity statins and increase to high-intensity with risk enhancers
  - Risk ≥20% - initiate high-intensity statin to reduce LDL-C by ≥50%
- Age >75 years, clinical assessment and risk discussion

ASCVD Risk Estimate

ASCVD Risk Estimator Plus

https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/

App should be used for primary prevention patients (those without ASCVD) only.

Current Age ℹ *

Age must be between 20-79

Sex *

Male | Female

Race *

White | African American | Other

Systolic Blood Pressure (mm Hg) *

Value must be between 90-200

Diastolic Blood Pressure (mm Hg) ○

Value must be between 60-130

Total Cholesterol (mg/dL) *

Value must be between 130 - 320

HDL Cholesterol (mg/dL) *

Value must be between 20 - 100

LDL Cholesterol (mg/dL) ℹ ○

Value must be between 30-300

History of Diabetes? *

Yes | No

Smoker? ℹ *

Current ℹ | Former ℹ | Never ℹ

On Hypertension Treatment? *

Yes | No

On a Statin? ℹ ○

Yes | No

On Aspirin Therapy? ℹ ○

Yes | No

8.8% Intermediate — **Current 10-Year ASCVD Risk****

Lifetime ASCVD Risk: **50%** Optimal ASCVD Risk: **4.9%**

Current Age * : 55
Age must be between 20-79

Sex *: ✔ Male | Female

Race *: White | ✔ African American | Other

Systolic Blood Pressure (mm Hg) *: 138
Value must be between 90-200

Diastolic Blood Pressure (mm Hg): 82
Value must be between 60-130

Total Cholesterol (mg/dL) *: 242
Value must be between 130 - 320

HDL Cholesterol (mg/dL) *: 37
Value must be between 20 - 100

LDL Cholesterol (mg/dL): 150
Value must be between 30-300

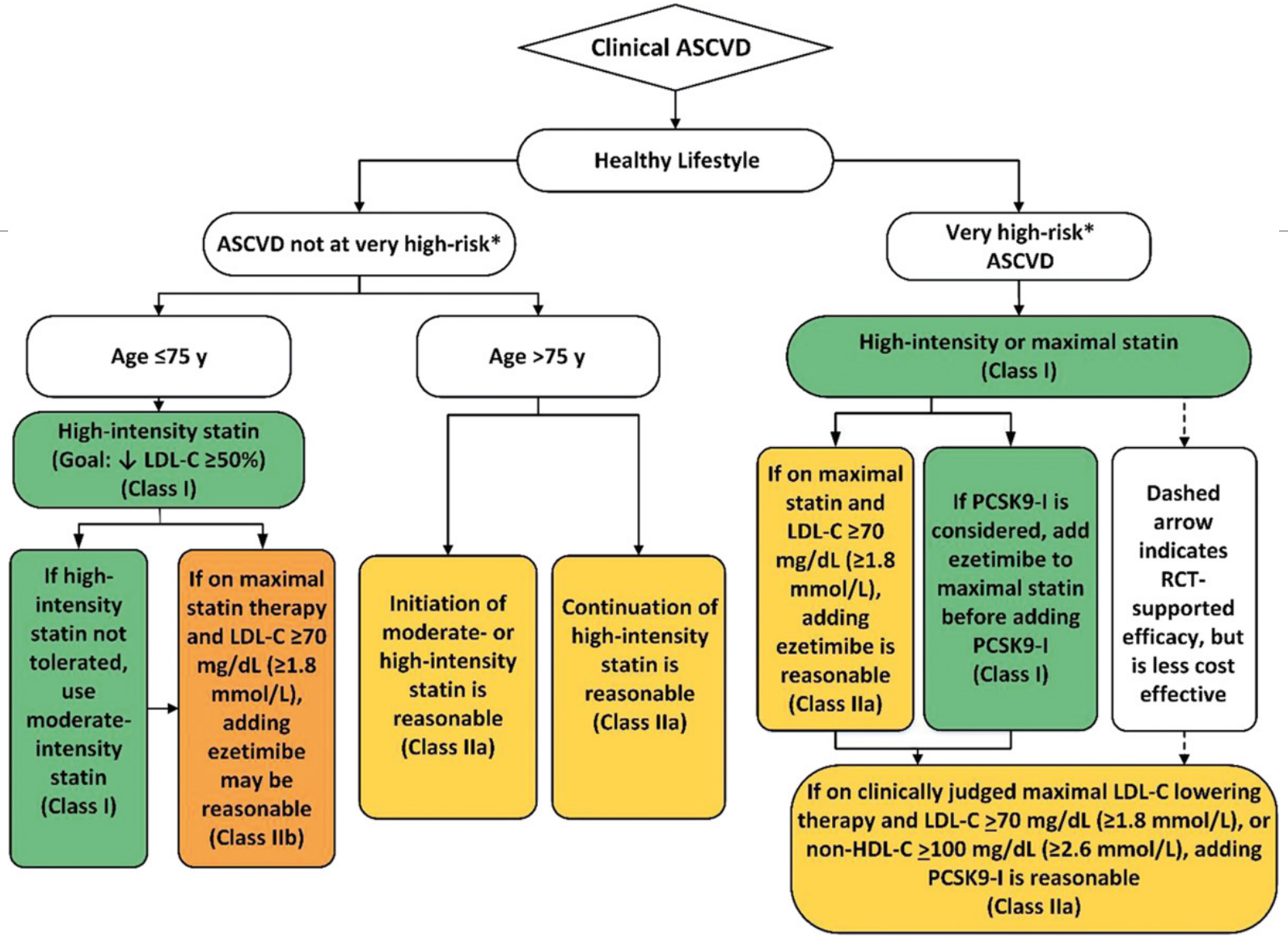
History of Diabetes? *: Yes | ✔ No

Smoker? *: Current | Former | ✔ Never

On Hypertension Treatment? *: Yes | ✔ No

On a Statin?: Yes | ✔ No

On Aspirin Therapy?: Yes | ✔ No


Clinical ASCVD
Healthy Lifestyle
ASCVD not at very high-risk*
Very high-risk* ASCVD
Age ≤75 y
Age >75 y
High-intensity or maximal statin (Class I)
High-intensity statin (Goal: ↓ LDL-C ≥50%) (Class I)
If high-intensity statin not tolerated, use moderate-intensity statin (Class I)
If on maximal statin therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe may be reasonable (Class IIb)
Initiation of moderate- or high-intensity statin is reasonable (Class IIa)
Continuation of high-intensity statin is reasonable (Class IIa)
If on maximal statin and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe is reasonable (Class IIa)
If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class I)
Dashed arrow indicates RCT-supported efficacy, but is less cost effective
If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L), adding PCSK9-I is reasonable (Class IIa)

Dyslipidemia: Management

Statin therapy

- Baseline liver transaminases
- No need for surveillance of ALT unless signs of hepatotoxicity

An asymptomatic increase in transaminases (>3 times upper limit of normal)

- is an infrequent statin-associated side effect
- often resolves with dose reduction
- or rechallenge with alternative statins

Severe statin-associated hepatotoxicity is rare

- not impacted by routine monitoring of transaminases.

Statins are not contraindicated in patients with increased ASCVD risk with chronic, stable liver disease (eg, nonalcoholic fatty liver)

Dyslipidemia : Lifestyle Changes

Emphasize intake of whole grains, legumes, healthy protein sources (low-fat dairy, low-fat poultry, fish/seafood, and nuts), and nontropical vegetable oils

Emphasize foods high in fiber, such as fresh fruits and vegetables, and in unsaturated fats, such as avocados and nuts

Limit intake of sweets, sugar-sweetened beverages, and red meats

Limit foods that are high in saturated or trans fats, sugar, and sodium (salt)

Physical Activity: same targets as for blood pressure

Smoking cessation or avoidance

Stroke: Quick Facts

In 2018, **1 in every 6 deaths** from cardiovascular disease was due to stroke

Every **40 seconds**, someone in the United States has a stroke

Every **4 minutes**, someone dies of stroke

Each year, **more than 795,000 people** in the United States has a stroke

Stroke is a leading cause of long-term disability

80% of strokes are preventable

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