





Learning Objectives

- Brief Definition of Metabolic Syndrome
- Why Diagnosis is Important
- Prevention of Metabolic Syndrome in Adults & Children
- Treatment of Metabolic Syndrome in Adults & Children



Definition of Metabolic Syndrome

Several definitions

 The National Cholesterol Education
 Program Adult Treatment Panel III is the most widely used.



5 Definitions for Metabolic Syndrome.

- NCEP ATP3 2005
- International Diabetes Foundation 2006
- Group for the Study of Insulin Resistance 1999
- World Health Organization 1999
- American Association of Clinical Endocrinologists 2003
- There is a graph in Up-To-Date that compares all 5

The National Cholesterol Education Program Adult Treatment Panel III

MUST HAVE 3 OF 5 COMPONENTS FOR DIAGNOSIS

Must have: Abdominal Obesity – measured by waist circumference women > or equal to 88cm (35in) men > or equal to 102cm (40in)
 ***Need to use specific ethnic based guidelines

•Plus 2 of these:

- Blood Sugar greater than 100 mg/dL or on medication
- BP 130/85 mmHg or higher or on medication
- HDL less than 50 mg/dL in women or 40 mg/dL in men or on medication
- Triglycerides greater than or equal to 150 mg/dL or on medication



- According to the International Diabetes Federation, <u>waist</u> <u>circumference</u> is the #1 element that needs to be considered when diagnosing metabolic syndrome
- Measurements need to be done according to ethnic group (not country of residence)
- In the US, continue to use the guidelines, in the future may be more specific to better estimate risk

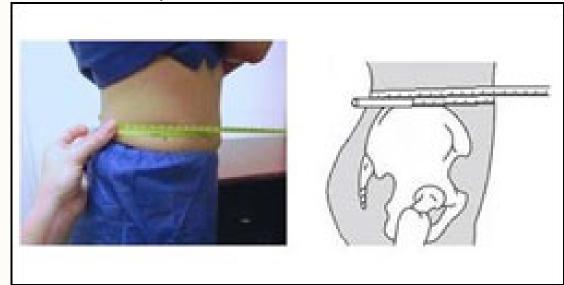


- Sub-Saharan Africans & Eastern Mediterranean and Middle East populations use European parameters
- Ethnic South & Central Americans use South Asian parameters

Ethnicity	Female	Male
White People of Europeon Origin	>80 cm	>94cm
South Asians	>80 cm	>90 cm
Chinese	>80 cm	>90 cm
Japanese	>80 cm	>90 cm

How to Measure Waist Circumference₂₆

- Measure while patient is standing
- Place measuring tape above iliac crests
- Do not pull snuggly
- Measure after patient exhales





Other Possible Markers

- Elevated C-reactive Protein
- Elevated Interleukin (IL) 61
- Plasminogen Activator Inhibitor (PAI) 1.
- Interleukin 1, 6, and 18, Resistin, TNF Alpha
- Elevated Uric Acid,
- Prothrombotic Factors,
- Elevated WBC's,
- Elevated Dimethylarginine,
- Urine Microalbumin,



Why is Metabolic Syndrome a BIG DEAL?

- IT IS A WARNING OF WHAT IS TO COME!
- The #1 killer in the US is heart disease.
- Coronary Heart Disease is inversely related to levels of HDL-C₃₃
- The risk for MI increases by 5% for every 5mg/dL below recommended values of HDL-C₃₃
- Obesity is widespread:
 - 1/3 of American adults & 1/6 of adolescents are obese₅
 - ¼ of adults in the world are obeses

Disorders Associated with Metabolic Syndrome

- Sleeping Disorders
- PCOS
- Chronic Renal Disease
- Fatty Liver Disease
- Hepatocellular/Intrahepatic Choleangiocarcinoma
- Elevated Uric Acid/Gout
- Dementia
- Inflammatory States?

Metabolic Syndrome,

- Increases with age
- Native Americans affects 60% of women and 45% of men
- Very common in Mexican American women
- Global Industrialization is associated with obesity increasing
- >4 hours of TV/day = 2 fold increase risk
- Over age 50, 50% of people have it
- In CVD patients, they are 3x more likely to have MI or CVA if they have Metabolic Syndrome & 50% of CAD patients have it



Start diagnosing obesity!

 We have no problem diagnosing diabetes, hypertension, hypothyroidism. Obesity should not be any different.



Diagnosing Obesity₂₉

- If there is a diagnosis, then there is an obligation to treat
- Medicare Obesity Benefit
- It provides reimbursement in primary care setting for intensive behavioral therapy with face to face counseling

- Billing Code = G0447
- 22 visits are covered per year
- Need obesity dx with associated BMI for it to pay





Prevention

- Screen every patient you see
- BMI done at most every visit anyway
- Review medications
- Review family history
- Review vital signs
- Physical exam



Amitryptyline, Doxepin, Imipramine,
Mirtazapine, Nortriptyline, Paroxetine,
Phenelzine, Chlorpromazine, Clozapine,
Olanzapine, Paliperidone, Quetiapine,
Risperidone, Amlodipine, Atenlolol, Felodipine,
Metoprolol, Nifedipine, Propranolol, Insulin,
Meglitinides, Sulfonylureas, TZDs, Estrogen,
Steroids, Benadryl, Lithium, Carbamazepine,
Gabapentin, Pregabalin, Valproate



Medications that Cause Hypertriglyceridema₃

Estrogen (not transdermal)
Oral Contraceptives
Tamoxifen
Beta Blockers
Glucocorticoids
Cyclosporine
HIV antiretroviral regimens
Retinoids



Medications that cause <u>low</u> HDL-C₃₃

Anabolic Steroids

Benzodiazepines

Beta-blockers



Medications that cause Hyperglycemia₃

Fluoroquinolones HIV antiretrovirals Antipsychotics (1st and 2nd generation) Beta-Blockers Niacin ER Statins (low risk) Thiazide diuretics Vasopressors Vasodilators (diazoxide) Systemic Glucocorticoids **Oral Contraceptives** Progestin **Growth Hormones** Immunosuppressants



Acanthosis Nigricans

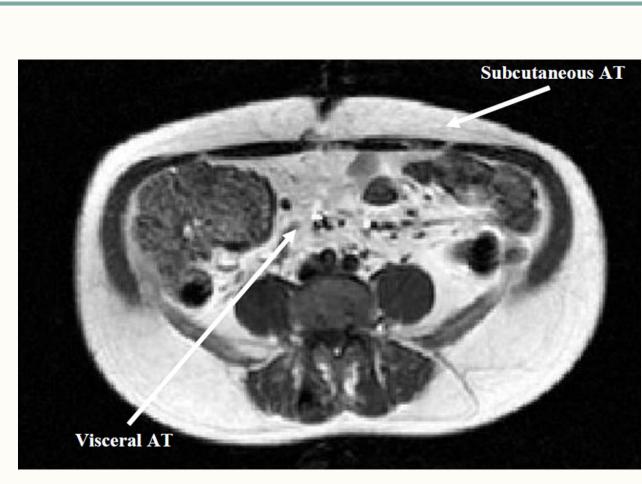


Acanthosis Nigricans 10





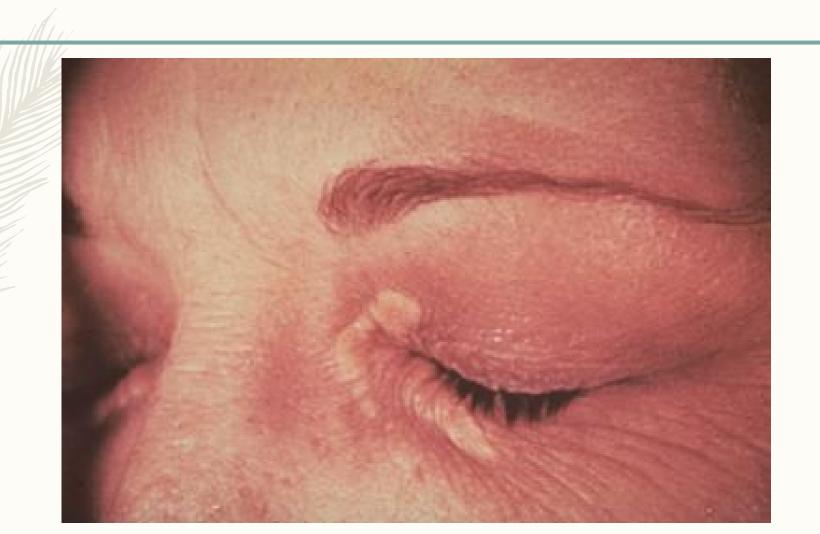
Visceral Obesity₁₇



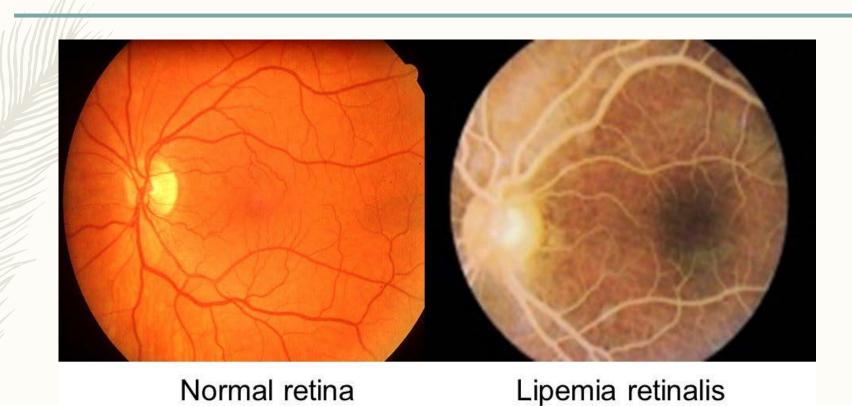




Eruptive Exanthomas₁₃







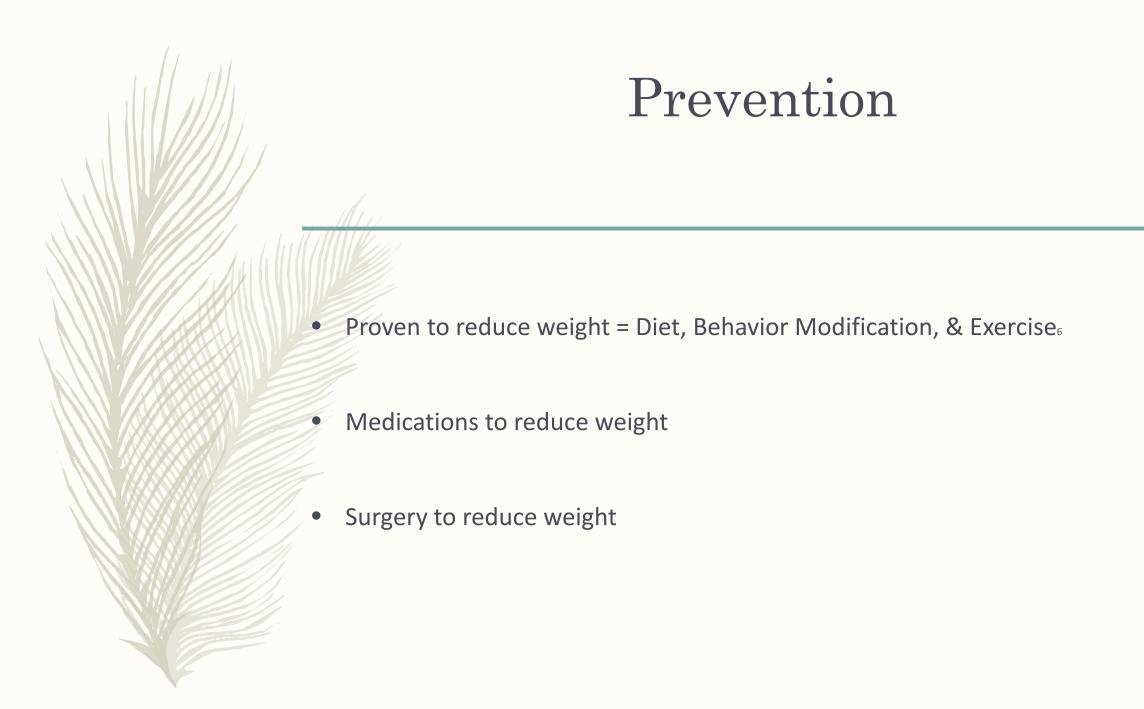
Elevated triglycerides





Key to Prevention = Weight Loss

 Focus on weight management and the other parameters like blood pressure, lipids, and glucose will also improve





One diet does not fit all!

Many diets are out there, we need to find one that best fits our patient.

Mediterranean Diet,27

- Fruit, veggies, nuts, whole grain, olive oil
- Most wt loss seen
- BP, lipids improve
- Insulin resistance decreases
- Inflammation decreases
- Proven to reduce cardiovascular mortality



- 20 year anniversary in 2017
- Low sodium, high fruit/veggie/fiber/protein, low dairy, lean meat
- Drop Systolic by 10 & Diastolic by 4.7
- Triglycerides & glucose drops
- Proven to reduce risk of CAD



Low Glycemic Index Diet

Reduces glucose and lipid levels



American Heart Association Diet

High fiber (30g/day)

• Low sugar, moderate ETOH to none, lean meat, whole grain, fruits, & veggies

Causes wt loss and drop in BP

Weight Watchers Diet.

- Weight Loss
- Decreases waist circumference
- Decreases C-Reactive Protein
- Decreases A1C
- No change in blood pressure or lipids



Calorie Restriction

- This is the most important₂₂
- 500 kcal restriction per day = 1 lb/week,
- Recommendation for women 1200-1500 kcal₂₂
- Recommendation for men 1500 –1800 kcal₂₂
- Severely obese need to restrict calories to 800-1000 kcal/day with regular physician supervision⁶
- Rather than restrict foods, suggest that they add more fruits and veggies, etc₂₂

Behavior Modification Motivational interviewing Encourage meal planning Food journaling (there is an app for that) Exercise planning Problem solving Recognize eating cues Self monitoring weight Counseling

The A's of Obesity Counseling 15

- Ask Permission to discuss weight & explore readiness
- Assess Obesity related risks & root causes
- Advise Health risk & treatment options
- Agree Health outcomes & behavioral goals
- Assist Accessing appropriate resources & providers

TABLE 1

THE FOUR PROCESSES OF MOTIVATIONAL INTERVIEWING

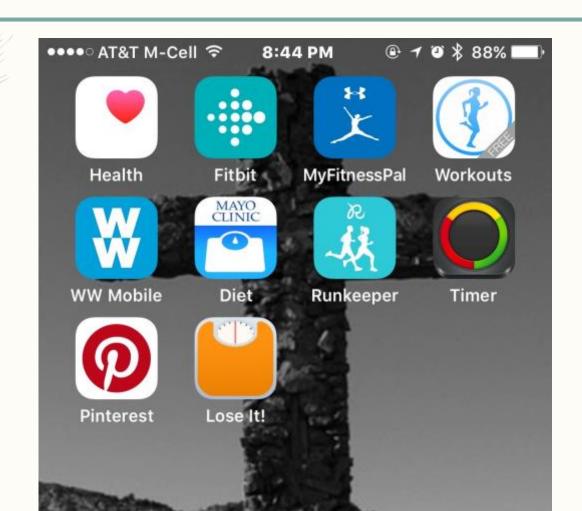
Phase	Description
Engaging	The provider and patient establish a working relation- ship. The provider makes it clear that he or she is not there to tell the client what to do.
Focusing	The patient-provider dyad settles on an agenda. The provider maintains patient autonomy by focusing on the patient's most pressing concern.
Evoking	The provider elicits the patient's personal reasons for change. When done successfully, the patient will be voicing the arguments for change.
Planning	This phase is marked by the shift from the "why" of change, to the "when" and "how." The provider guides the patient to come up with the best options for himor herself.



Smart Phone Applications 31,38

- Apps have been shown to help with short term weight loss
- More weight loss is seen with face to face interactions
- 77% of US adults have smartphones

Examples of Smart Phone Applications





- Sedentary life style = Increased mortality and abnormal glucose metabolism₃₉
- More exercise = more weight loss₆
- Exercise alone is not enough₂₂
- Inactivity costs \$24 billon a year in health care expenses.
- Exercise costs nothing
- 30-40% risk reduction of myocardial infarction with brisk walking daily for only 20 minutes₃



Exercise Recommendations

Moderate Intensity Cardio - 30 min 5 days a week

Or

Vigorous - 20 min 3 days a week

Or

• Combo to achieve total energy expenditure of greater than 500-1000 metabolic equivalent



Exercise in the Elderly.

- Osteoarthritis Aquatic based exercises
- Diabetes Aerobic + Resistance Training = lower A1C, If they have autonomic neuropathy, need stress test
- Osteoporosis Resistance Exercises
- Cognitive Impairment exercise decreases risk for dementia, improves cognitive function, and improves ADL's
- CVD need stress test
- Falls Exercising reduces falls, Tai Chi, gait training
- Pulm Dz Match time of exercise to bronchodilator med peak, use oxygen PRN



Weight Loss Meds: When and Who₂₂

• Start them when weight loss goals have not been achieved and risks & benefits have been discussed

When BMI is > 30kg/m2

Or when BMI is > 27kg/m2 with co-morbid condition (DM,HTN,CH)

Optimal duration is not clear due to inadequate studies

Weight Loss Medications

- Catecholaminergic Medications
- Absorption Inhibitors
- Selective Serotonin Receptor Agonist
- Combo Drugs
- Glucagon-Like Peptide-1 Receptor Agonist



Catecholaminergic Medications.

• Examples: Phentermine, Diethylpropion, Benzphetamine, Phendimetrazine

• Appetite suppressants

Stimulates CNS activity

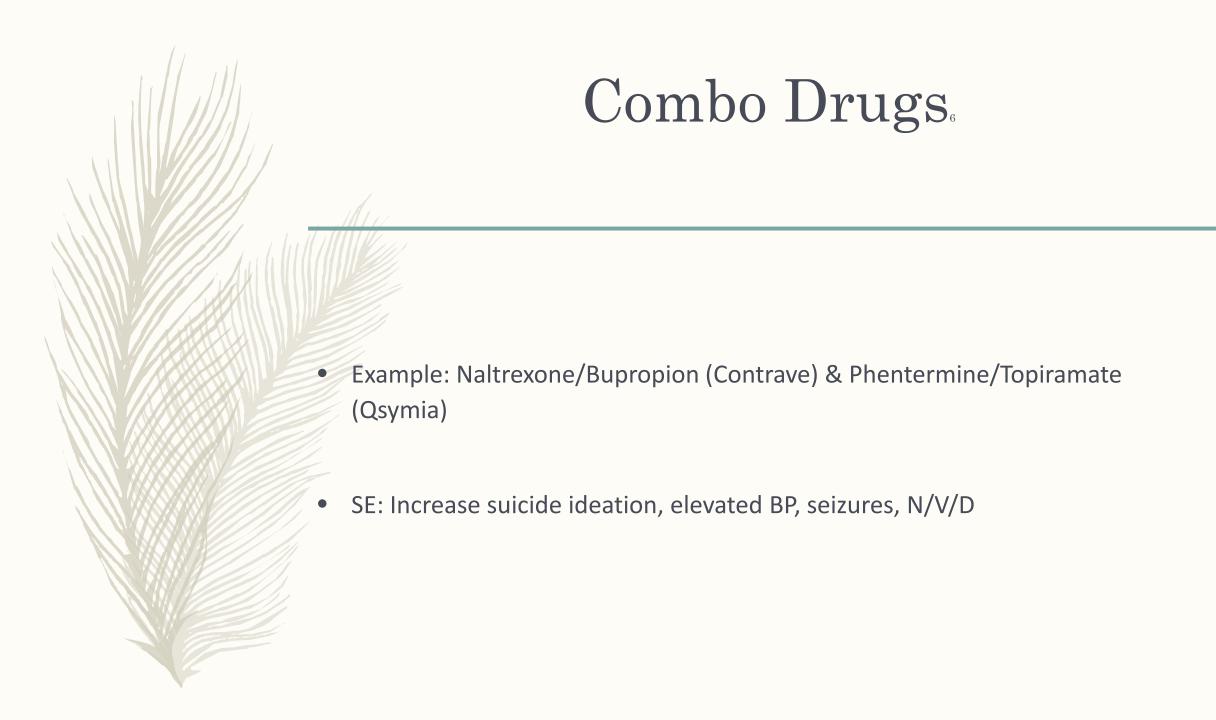
Short term only

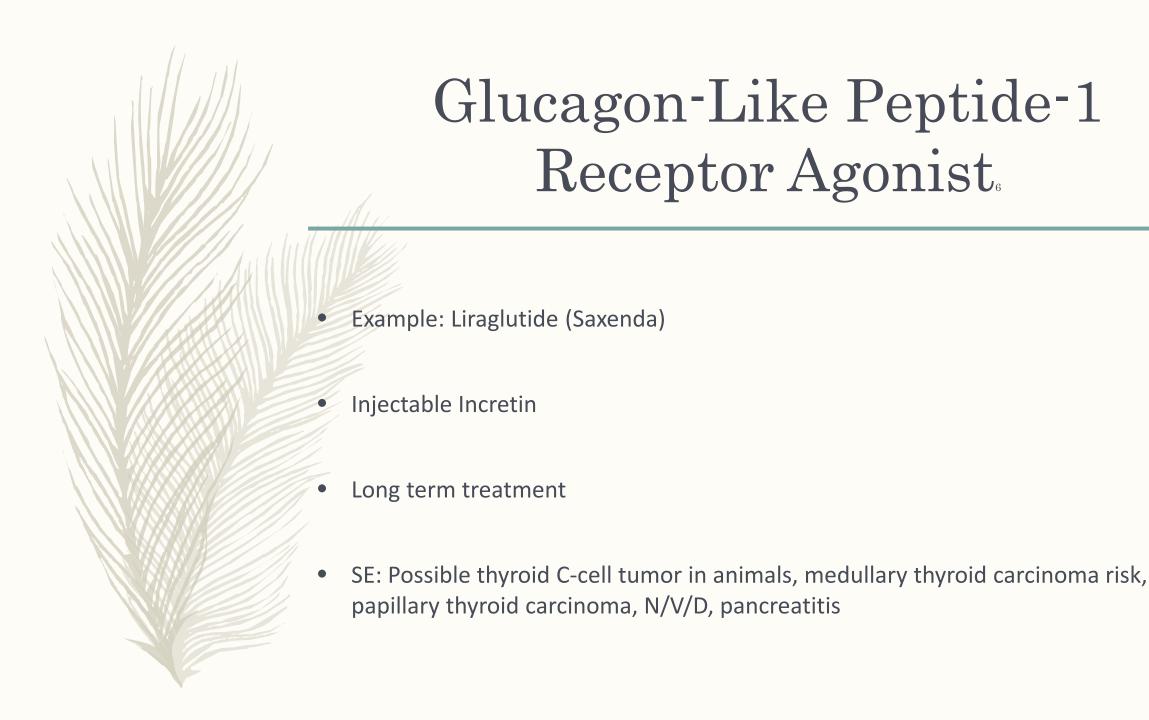
Absorption Inhibitors

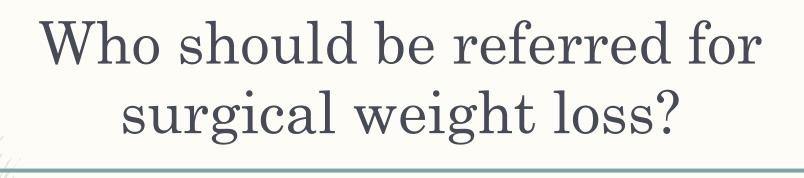
- Example: Orlistat (both OTC in low dose, and prescription in higher dose)
- Common first choice due to lack of systemic side effects and long history
- Inhibits intestinal lipase
- SE: gas, diarrhea, decrease absorption of vitamins, anal leakage
- Lowers BP, lipids & sugar₂₂

Selective Serotonin Receptor Agonist

- Example: Lorcaserin (Belviq)
- Causes modest weight loss
- Expensive
- SE: possible breast tumors in animals, possible valve issues, psych effects
- DC if no more than 5% wt loss seen in 12 weeks22







 BMI > 40 kg/m2 OR BMI > 30kg/m2 who have DM, HTN, CH, OSA, NASH, arthritis, or impaired quality of life₆

• Patients that have a lower BMI have overall better success rates – therefore refer sooner₂₈



Success of Wt Loss Compared to Adjustable Lap Band₂₈

Roux-en-Y 19x more weight loss than lap band

Sleeve Gastrectomy 7.2x more weight loss than lap band

Duodenal Switch Procedure 72x more weight loss than lap band



Surgical Weight Loss₂₈

• 1/3 of patients post-op have a BMI of <30 at 1 year follow up

• BMI > 30 are at 50-100% higher risk for premature death, but surgery decreases risk by 30-40%



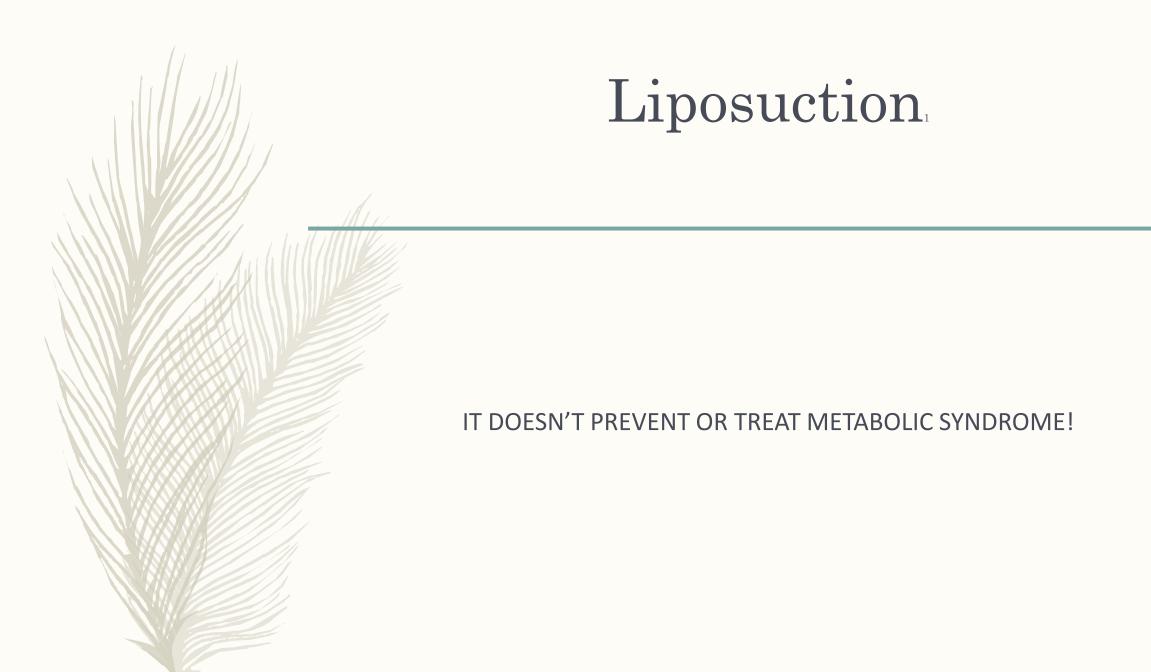
Surgical Weight Loss

Roux-en-Y Gastric Bypass

Complications in 40% of patients

Gastric Band

60% need reoperation





Prevention

- Best screening tool for obesity is BMI₄
- Age 6+ should be screened₄
- Of children ages 2-19, 1/3 are obese
- Perform risk assessment family history, ROS, VS, PE
- If risk present perform fasting lipids and CMP₄
- If risk not present perform fasting lipids₄
- Age 2-11 no more than 1 pound of wt loss in a month₄
- No more than 2 pounds/week if older than 11₄

Diet₄

- No particular diet recommended
- Cut sugar drinks
- Increase fruits and veggies
- Breakfast Daily
- Try to eat most meals at home with family









Obesity Behavioral Modification

- Ask about eating habits & activity level
- Assess motivation to change
- Cultural & socioeconomic status affects how weight is perceived
- Scare tactics don't typically work because they only see short-term effects of obesity
- Stage an intervention with family



Exercise

- Nothing recommended below age 63
- Age 6-17 need 60 minutes daily₃
- No TV/screen time less than 2 years of age4
- No more than 2 hours of TV/screen time per day₄
- Activities included are the following: play, games, sports, work, transportation, recreation, PE, planned exercise
- Appropriate exercise: jump rope, running, sit-ups, weight lifting, resistance bands₃₅
- Included in the 60 minutes per day, also need muscle-strengthening 3 days per week











Already discussed weight loss Insulin Resistance/Elevated Blood Sugar Hypertension Hypertriglyceridemia/Low HDL

Treatment of Metabolic Syndrome

Increased Waist Circumference/Obesity





Treatment: Insulin Resistance/Elevated Glucose

1. Lifestyle Modification: Diet, Exercise

2. Biguanides: Enhance insulin action in liver & suppresses endogenous glucose production

3. Thiazolidinediones: Improve insulin uptake in muscles & adipose tissue and reduce inflammatory markers



Treatment: Hypertension

- #1 Lifestyle modification₁₈
- If the patient has diabetes ACE/ARB recommended,
- Non-African American thiazide diuretic, calcium-channel blocker, ACE inhibitor or ARB₁₈
- African American thiazide or calcium-channel blocker₁₈



Treatment of Hyperlipidemia.

- New recommendation: Use calculators to estimate cardiac risk and then determine type of treatment
- Framingham Risk Calculator
- Pooled Cohort Equations http://www.cvriskcalculator.com
- QRISK 2 Calculator http://www.qrisk.org
- This focused more on risk rather than numbers







Treatment of Low HDL_{7,32}

- Lifestyle modification #1 treatment
- Most pronounced increase with estrogen in postmenopausal women, fibrates, and niacin
- However, adding niacin may not provide cardiovascular benefit, adding niacin to statins are found to be harmful, niacin may also make glucose tolerance worse



Treatment of Hypertriglyceridemia

- Lifestyle modification need weight loss of >10% to affect,
- Aerobic exercise!34
- Current guidelines no tx unless level >886mg/dL treatment aimed at preventing pancreatitis₃₄
- "Dietary fat is not a primary source of liver triglycerides and higher fat diets do not raise plasma triglyceride levels in most people." 34

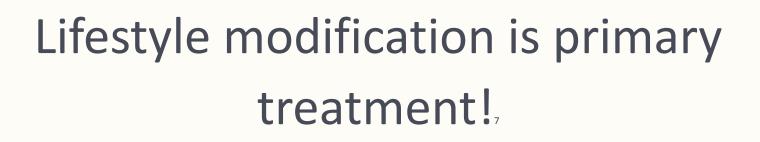


Treatment of Hypertriglyceridemia₃₄

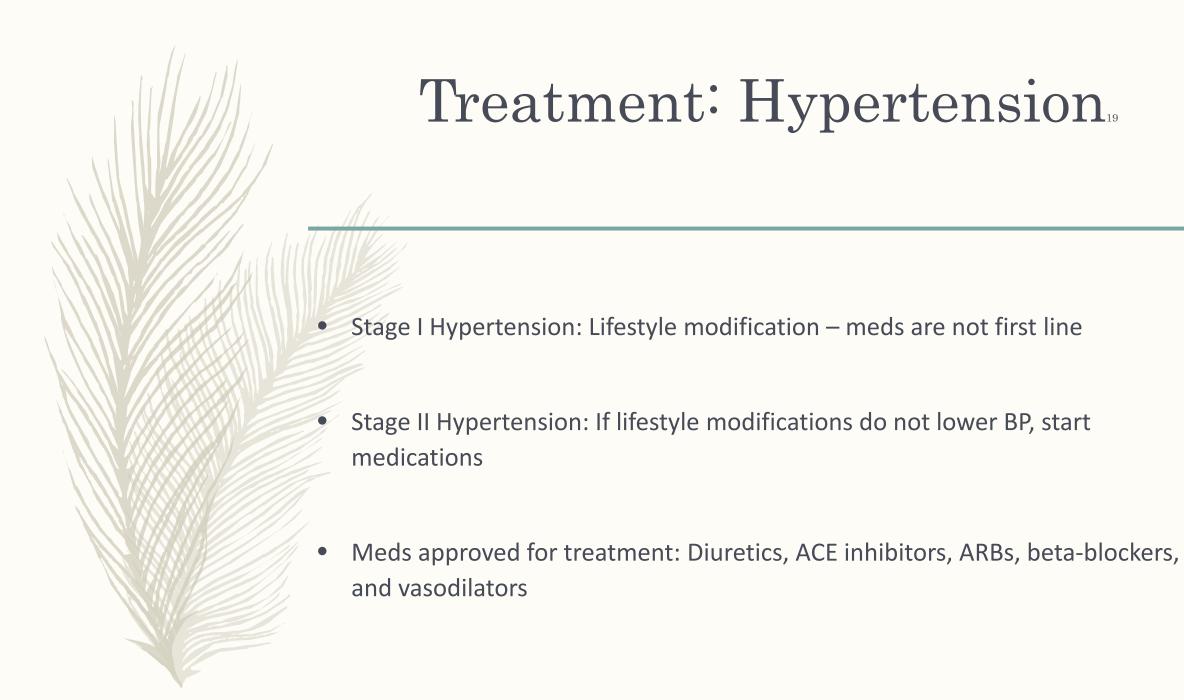
- Unsure if there is a CV risk reduction and mortality reduction with fibrates but will decrease level by 50%
- High dose statins reduce by 44% (Atorvastatin 80mg/Rosuvastatin 20mg)
- Combo therapy of Fenofibrate + Fluvastatin or Pravastatin are safe as they are not extensively metabolized by CYP3A4
- Fish Oil
- Nicotinic Acid can reduce by 25% but can cause glucose tolerance issues and combo w/ statin is harmful















High Blood Pressure in Children and Adolescents

MEDICATION	INITIAL DAILY DOSAGE	MAXIMUM DAILY DOSAGE	DOSING FREQUENCY
Angiotensin-converting en	zyme inhibitors		
Benazepril (Lotensin), ≥ six years of age	0.2 mg per kg, up to 10 mg	0.6 mg per kg ar 40 mg	Once daily
Enalapril (Vasotec)	0.08 mg per kg, up to 5 mg	0.6 mg per kg or 40 mg	Once or twice dally
Fosinopril (Monopril), ≥ six years of age and weighing > 111 lb (50 kg)	5 to 10 mg	40 mg	Once daily
Lisinopril (Zestril), ≥ six years of age	0.07 mg per kg, up to 5 mg	0.6 mg per kg ar 40 mg	Once daily
Angiotensin II receptor bloc	ckers		
Losartan (Cozaar), ≥ six years of age	0.7 mg per kg, up to 50 mg	1.4 mg per kg or 100 mg	Once daily
Valsartan (Diovan), ≥ six years of age	1.3 mg per kg, up to 40 mg	2.7 mg per kg or 160 mg	Once daily
Beta blockers			
Metoprolol, extended release, ≥ six years of age	1 mg per kg, up to 50 mg	2 mg per kg or 200 mg	Once daily
Propranolol	1 to 2 mg per kg	4 mg per kg or 640 mg	Two or three times daily
Vasodilator			
Hydralazine	0.75 mg per kg		



		7.5 mg per kg or 200 mg	Four times daily
Minoxidil	0.2 mg per kg, up to 5 mg (< 12 years of age), 5 mg (≥ 12 years of age)	50 mg (< 12 years of age), 100 mg (≥ 12 years of age)	Once or twice daily
Other			
Calcium channel blocker: amlodipine (Norvasc), ≥ six years of age	2.5 mg	5 mg	Once daily
Central alpha agonist: clonidine (Catapres), 12 years of age	0.2 mg	2.4 mg	Twice daily
Diuretic: hydrochlorothiazide	1 mg per kg	3 mg per kg, up to 50 mg	Once daily

NOTE: Other medications within these classes are considered safe but are not approved by the U.S. Food and Drug Administration for treating hypertension in children and adolescents.

Information from references 9, 10, and 29.

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Treatment of Children with Dyslipidemia

- Lifestyle modification #1₃₇
- Long term use of statins in children unknown₂₀
- Data is limited, most information came from studies of children with familial hypercholesterolemia₃₇
- Medications should be initiated and managed by a Pediatric Lipid Specialist₃₇
- Unlike adults you don't use calculators to determine criteria: Based on lipid levels and CVD risk



Considerations for Treatment₃₇

- Age
- Severity of dyslipidemia
- Risk Factors
- Family preference



Treatment is RARE₃₇

- According to the National Heart, Lung, and Blood Institute those that meet criteria for treatment are:
 - 0.8% of children less than age 17
 - 2.5% of adolescents & young adults age 17-21

Children Age 10+ Years

- LDL>130 mg/dL (goal is <110 mg/dL or 100 mg/dL if high risk)
- Should be started on medications after failing 6 months of life style changes
- Based on risk (High Risk: DM, CRF, Kawasaki, Heart Transplant, CAD)

Children < 10 years of Age₃₇

- In general don't do it!
- Unless: VERY high risk, LDL >400 mg/dL, TG>500mg/dL



Hyperlipidemia Medications in Children₃₇

- Statins: Lovastatin, Simvastatin, Pravastatin, Rosuvastatin,
 Atorvastatin use lowest dose
- Ezetimibe
- Bile Acid Sequestrants: not as effective as statin, but very safe because it isn't absorbed, but causes bloating and constipation
- Niacin: no proof that decrease CVD risk, but raises HDL
- Fish Oil: Can lower Triglycerides but can raise LDL
- Fibric Acid Derivatives: Raises HDL, Lowers triglycerides, but limited data, monotherapy only, used rarely, use when at increased risk for pancreatitis due to elevated triglycerides



Monitoring Labs in Children on Medications₃₇

- Pregnancy test before starting statin
- Every 4-6 weeks need: hepatic enzymes, fasting lipid, CK, preg
- If stable, then monitor every 6 months



OK, so this is what I do...

- I express genuine concern, and explain what being overweight means.
- I have them keep a food journal of everything they put in their mouth for one week. I have them return to discuss what they have eaten and I help them substitute the things they like with healthier options.
- Diet: Shop on perimeter of store, stay away from anything that comes through a window or in a bag or can, eat at home.
- Diet: I do not tell my patients to eat low fat, I want them to eat a diet high in healthy fats.
- Diet: I encourage the Paleo Diet. Read this book! The Paleo
 Answer by Loren Cordain & Eat Fat Lose Weight by Ann Louise
 Gittleman

More of what I do...

- Exercise: Do the things your enjoy. I show the patient in the room simple exercises
- Exercise is only 20% of losing weight, but is paramount to be fit.
- Some movement is better than none
- I schedule a follow up appointment to discuss more.
- I read up on the new fads so that I can give an educated opinion
- I refer to Oklahoma Healthy Aging Initiative provides education and instruction for the elderly regarding diet and exercise. Locations: OKC, Tulsa, Enid, Durant, Lawton
- For 65 and below I do the teaching Durant has very little resources but search your community



Resources that I recommend to Patient

- WebMD food/exercise journal
- www.takebackyourtemple.com
- Various smart phone applications
- Various books:

The Quest for Wellness by Mark Sherwood, N.D. with Michele Neil-Sherwood, D.O.

Overeating Freedom from Food Fixation by June Hunt



WebMD Food and Fitness Journal

Studies show (and successful losers have proven) that keeping track of what you eat and your activity level is **one** of the most powerful tools to help you shed unwanted pounds and keep them off for good.

Use this printable Food & Fitness Journal or check out the personalized WebMD Food & Fitness Planner to help keep you working toward your goals.

MY FOOD JOURNAL	Date		
MY FOOD JOURNAL			
Breakfast	SERVING	CALORIES	
		SUBTOTAL	
Mid-Morning Snack		GUBTOTAL	
The manning street			
		SUBTOTAL	
Lunch			
		1200	
	611	SUBTOTAL	
Mid-Afternoon Snack			
Dinner			
		-	
		SUBTOTAL	
Evening Snack			
		SUBTOTAL	
	TOTAL CALORIES FROM FOOD		
MY FITNESS JOURNAL			
Activity	DURATION	CALORIES	
THE TOTAL OF THE T	DORATION	UNLUNIES	
	TOTAL CALORIES FROM FITNESS		





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