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Welcome to Everything Gut or "Gut to the Butt" or Let's give our Second Brain Some Cred

2023

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President, Diabetes Education Services

Diabetes Education SERVICES

Handouts and Resources

Diabetes and the Gut – ADCES Hawaii 2023 Conference with Coach Beverly | Handout & Resource Page

ADCES Hawaii Coordinating Body

ADCES Hawaii Chapter & Coach Bev invite you to join this class that covers gastrointestinal health from top to bottom. Topics include: fatty liver disease diagnosis and treatment, intestinal complications associated with diabetes, keeping the microbiome healthy, and more. Join us to explore the magnificent wonders of diabetes and the gut.

Handouts (PDFs)

Note-Taking Handouts

Full Slide Handouts

Coupon Code Aloha23 (Save $200).
CDCES Deluxe Preparation Bundle on our Diabetes Education Online University for **discounted rate of $299 (usual rate is $499).**
The coupon code **Aloha23** and will be active for 1 year.
Expires October 28, 2024.

Diabetes and the Gut – ADCES Hawaii 2023 Conference with Coach Beverly | Handout & Resource Page - Diabetes Education Services

Go to DiabetesEd.Net and type in Hawaii in search

Proposed Agenda

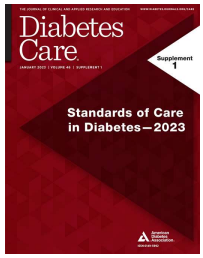
08:00 to 9:00 am	Prediabetes and Diabetes in the Lean Asian Population and Impact on Fatty Liver | Dr. Richard Arakaki, Endocrinologist
09:00 to 9:45 am	From the Mouth to the Stomach
10:15 to 11:45 pm	Complications connected to the Alimentary Canal
11:45am to 1:00pm	Lunch
1:00 pm – 2:15 pm	Fatty Liver Disease – Scope, Screening, Stages NASH Treatment Options, from MNT to Exercise
2:30 pm – 3:30 pm	Intestines as an Endocrine Organ & Bacterial Host
3:30 pm – 4:30 pm	Medication Modifications in Liver Disease – Dr. Alan Parsa

Objectives:

- Explore the co-relationship between hyperglycemia and the gastrointestinal system.
- Discuss the relationship between glucose and fatty liver disease in the Lean Asian Population
- Explain the links between diabetes and oral disease and intestinal disruption and discuss treatment approaches.
- Describe the pancreatic exocrine dysfunction in diabetes, pancreatitis and cystic fibrosis.
- List the scope, stages, and screening guidelines for Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH).
- Discuss the endocrine function of the intestine and the importance of a healthy microbiome.
- Describe medication modifications that improve outcomes in those with liver disease.

Coach Bev has no conflicts of interest

- Not on any speaker's bureau
- Does not invest in pharmaceutical or device companies
- Gathers information from reading package inserts, research and standards



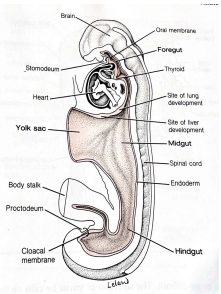
Content from ADA Standards
www.Diabetes.org

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023* FREE

Books

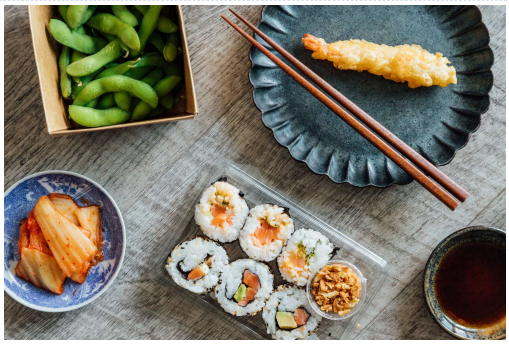
Gut Tube -Embryonic Starting Point

- Embryonic endoderm develops into the interior linings of two tubes in the body, respiratory *and*
- **Digestive Tube**
  - Salivary glands
  - Esophagus
  - Stomach
  - Small and Large Intestine
  - Liver
  - Gallbladder
  - Pancreas
- Thyroid gland
- Parathyroid glands
  - Lose connection with gut before birth to become endocrine organs



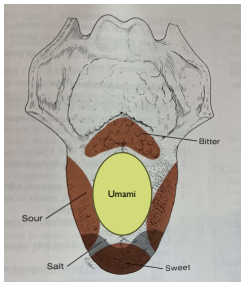
Basic Human Anatomy, A. Pense, 1982

Eating Starts with the Eyes



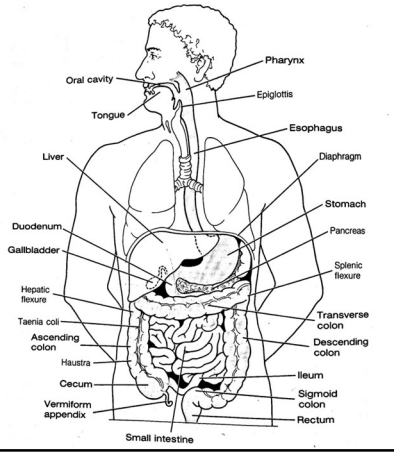
5 or 6 types of Flavor Detection

- Sweet
- Sour
- Bitter
- Salty
- Umami (savory)
- Tongue might also detect ammonium chloride (USC recent discovery) to avoid harmful substances?



Digestion Gets Started

- Eyes see food and make an appraisal of how to best prepare for incoming load.
- Glands secrete saliva to prepare for chewing.
- Salivary enzymes (amylase) help with initial digestion
- Creates bolus.
- Upper pharynx and esophagus under conscious control, the rest involuntary.
- Esophagus smooth muscle, controlled by brain.
- Lower esophageal sphincter gateway from esophagus to stomach.
  - Prevents reflux of gastric contents



Alimentary Canal

Buckle up!

Quick Question

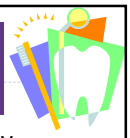
- Diabetes is associated with an increased risk of oral disease. Which of the following statements is true?

a. People with diabetes benefit from vinegar gargles to decrease bacterial load
b. People with diabetes are at greater risk for tongue cancer.
c. 1 in 5 cases of tooth loss is linked to diabetes
d. Diabetes is associated with increased tonsillitis.

Salivary Dysfunction and Xerostomia (dry mouth) in DM

- Less saliva uptake and excretion = less protection against bacteria
- Hyperglycemia increases glucose levels in saliva, providing medium for bacterial growth- also promotes dry mouth
- Dry mouth increases risk o infection and can alter nutritional intake (due to chewing, swallowing difficulties)

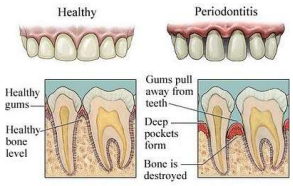
Diabetes and Oral Health – It's all the RAGE



- People with diabetes 2-3x's more likely to have periodontal disease (gingivitis and periodontitis)
- People with periodontal disease are more likely to be hyperglycemic
- Both groups may have excess RAGE
- (receptors for Advanced Glycation Endproducts = inflammation)

Periodontal Disease

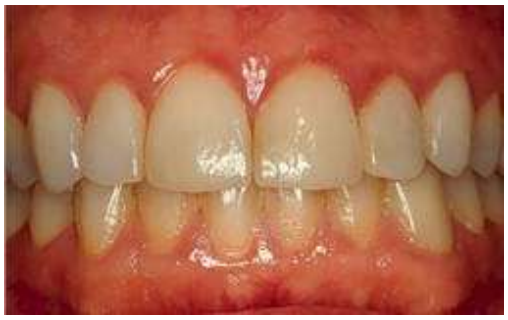
- More severe and prevalent with diabetes and elevated A1c levels.
  - periodontal treatment associated with better glycemic control
    (A1C 8.3% vs. 7.8%)
  - Benefits lasted for 12 mo's
- People with periodontal disease have higher rates of diabetes.
- Bidirectional



Oral Care Matters

- See dentist at least yearly
- Dental hygienist twice yearly
- Brush twice daily
- Floss daily

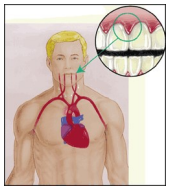
Gingivitis



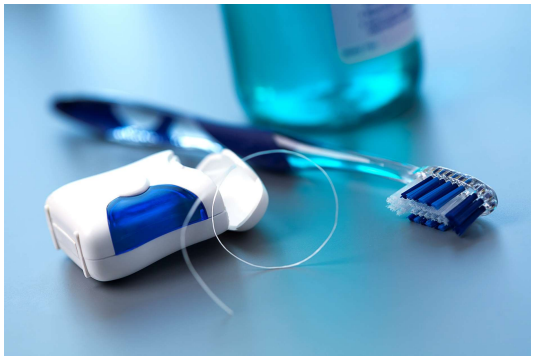
Mild to Severe Periodontitis

Periodontal disease and Heart Disease

- Heart disease link:
  - oral bacteria enter the blood stream, attach to fatty plaques in coronary arteries increasing clot formation
  - inflammation increases plaque build up, which may contribute to arterial inflammation
- Hyperglycemia = Gingivitis = Heart Disease



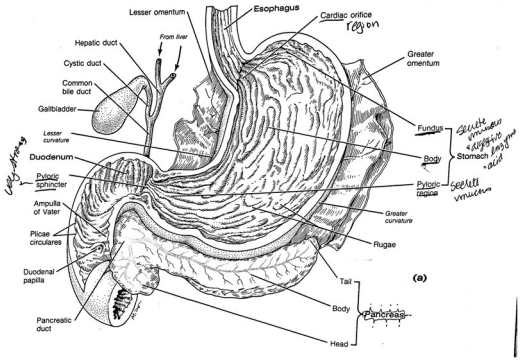
Best $10 You Will Ever Spend



Keeping Oral Healthy

- Oral disease linked with heart disease
- Dental exams (every 6 mo's)
- Brush Twice Daily, Floss at least once daily.
- Quit smoking
- Treat infections with ATB'x
  - Lowers A1C by 1-2%.
  - Lowering BG shortens infection.
- Cost a barrier to getting care

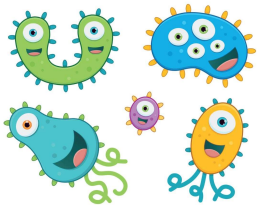
Stomach, gallbladder, pancreas



What Happens in Stomach?

- Food in fundus – serves as a holding and mixing area
- Gastric juice start breaking down larger particles.
- Bolus moved to lower regions and broken into smaller particles through stomach acid and motility.
- Gurgling and stomach rumbling (borborygmi) is audible reflection of movement.
- Usual meal takes about 4 hours to pass through or 1-4 kcals per minute.
- Carbs take a few hours to pass through.
- Protein/fatty meals can take up to 6 hours.

Stomach Issues



- H. Pylori infection
- Gastroparesis
  - G-POEM
  - Gastric Pacer
- Disordered Eating
- Vomiting syndrome
- Metabolic surgery

H. Pylori Quick Question

JR is 50, has type 2 diabetes. Referred to G.I. due to six months of stomach pain, intestinal, bloating, and generalized G.I. discomfort. Since they were due for their colonoscopy, provider also ordered an upper endoscopy to biopsy the esophagus, stomach and duodenum.

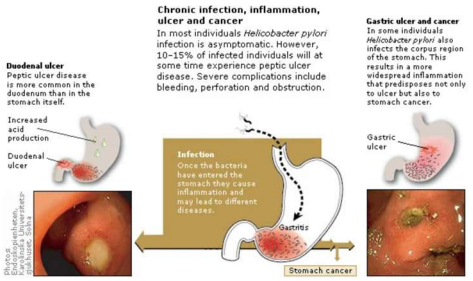
The biopsy revealed that JR had moderate chronic gastritis and an H. pylori infection. JR wants to learn more about H. pylori infection.

- **Which of the following statements are accurate?**

1. Since H. pylori is found in about half the population, it is a normal finding, and there is no need for treatment.
2. Treatment includes double antibiotic therapy and a medication to decrease gastric acidity.
3. The preferred treatment is the consumption of prebiotics and probiotics to increase bacterial diversity.
4. Most people with H. pylori infection experience stomach cancer within the next 20 years.

Nobel Prize for Link Between H. Pylori and Gastric Ulcers

The Nobel Prize in Physiology or Medicine 2005 | The Nobel Prize In Physiology Or Medicine



H. Pylori Infection Symptoms

- 50% of world's population co-exist with H. Pylori
  - Causes inflammation in a small percentage of people
- Main Symptom - An aching or burning pain in abdomen which may be worse with an empty stomach.
- H. pylori infection symptoms include:
  - Feeling of fullness or bloating with fluid and solid food
  - Hunger and empty feeling in the stomach, often 1 to 3 hours after meal
  - Mild nausea that may go away with vomiting
  - Loss of appetite
  - Weight loss without trying
  - Burping
  - Bloody or dark, tarry stools or bloody vomit
- About 10% to 15% of people infected with *H pylori* develop peptic ulcer disease.
- About 1-3% develop stomach cancer

H. Pylori Good or Bad?

Drawbacks

- Infection caused by this curved rod bacteria with flagella that burrows through your stomach mucus to infect the mucus & cells of your stomach lining.
- Uses stomach mucous lining for fuel.
- Locally neutralizes stomach acid so that it is not digested (produces a urease that makes ammonia).

Benefits

- 50% of the world's population is infected with H. pylori
  - it is a human-associated disease, we co-evolved with it in OUR stomachs!
  - Different strains in different human groups
- Instructs immune system not to overreact
- People with H. pylori seem to have less asthma and autoimmune conditions, like celiac and less risk of TB
- More research is needed

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6064966/

H. Pylori Infection – Test & Treat

Testing Options

- **Breath test** -- urea breath test (Carbon Isotope-urea Breath Test, or UBT).
- Swallow liquid with urea. If *H pylori* are present, the bacteria turn the urea into carbon dioxide. This is detected and recorded in your exhaled breath after 10 minutes.
- **Blood test** -- measures antibodies to *H pylori* in your blood.
- **Stool test** -- detects the presence of bacteria in the stool.
- **Biopsy** -- tests a tissue sample taken from the stomach lining using endoscopy. The sample is checked for bacterial infection.

Treatment

Combination of antibiotics and proton pump inhibitor for 14 days.

- **Antibiotics:** Usually two of these antibiotics choices: amoxicillin, clarithromycin (Biaxin®), metronidazole (Flagyl®) and tetracycline.
- **Proton pump inhibitor:** include lansoprazole (Prevacid®), omeprazole (Prilosec®), pantoprazole (Protonix®), rabeprazole (Aciphex®) or esomeprazole (Nexium®).
- **Bismuth subsalicylate:** Sometimes added to proton pump inhibitor to protect stomach lining.
- Newer medication, Talicia®, combines two antibiotics (rifabutin and amoxicillin) with a proton pump inhibitor (omeprazole) into a single capsule.

Quick Question: Bloating & Post Meal Hypo

- JR has lived with type 1 diabetes for over 30 years and has been complaining that they feel full and bloated after eating and experiencing more post-meal hypoglycemia.
- **Based on this information, what is the most appropriate recommendation for JR?**

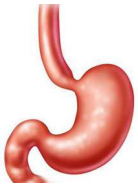
a. Evaluate transglutaminase levels.
b. Encourage small, frequent, low fiber meals.
c. Suggest a consult for a gastric pacemaker.
d. Recommend they try avoiding foods with gluten for a few weeks to see if they feel better.

Gastroparesis

- Gastroparesis: affects 20 – 30% of individuals with longstanding diabetes
- Delayed emptying of stomach contents due to nerve damage
- S/S include early satiety, fullness, postprandial hypo, vomiting
- Diagnosis: gastric emptying studies, post-prandial hypoglycemia
- Tx: improve BG, small, low fat & fiber meals & meds

Nutrition for Gastroparesis

- Dietary changes are a high priority in treatment
- Consider the following dietary modifications:
  - Decrease fiber (may lead to bezoar formation)
  - Evaluate fat intake
    - Fat is a good/high source of calories so limit only after other measures are exhausted
    - Liquid fats may be tolerated better



Nutrition for Gastroparesis

- Consider dietary modifications:
  - Multi supplement if intake is insufficient
  - Small and frequent meals
  - Liquid/pureed calories
    - May need to try liquid calories later in the day
  - Chew foods well
  - Sit up for 1-2 hours after eating

Meds & Glucose Improvement to treat Gastroparesis

- Metoclopramide (Reglan)
  - Causes tightening, or contraction, of the muscles in the wall of the stomach and may improve gastric emptying.
  - Metoclopramide may also help relieve nausea and vomiting.
  - Can cause tardive dyskinesia
- Erythromycin
  - increases stomach muscle contraction and may improve gastric emptying.
- Antiemetics:
  - Prescribed may include ondansetron, prochlorperazine, and promethazine.
  - Over-the-counter antiemetics include bismuth subsalicylate and diphenhydramine. Antiemetics do not improve gastric emptying.
- Antidepressants - such as mirtazapine may help relieve nausea and vomiting. Does not improve gastric emptying.
- Pain medicines - Pain medicines may reduce abdominal pain due to gastroparesis.

https://www.niddk.nih.gov/health-information/digestive-diseases/gastroparesis/treatment

Gastric Electrical Stimulator

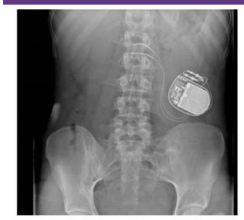


FIGURE 1. Radio of gastric electrical stimulator after implantation.

https://www.frontiersin.org/articles/10.3389/fnins.2022.909149/full

Bielefeldt (2017) analyzed the adverse events recorded in the manufacturer registry from 2001 to 2015. Perioperative complications are quite rare, with mainly hematoma after surgery. The complications related to the device mostly occur during the first 2 years after surgery. The most commonly reported adverse event is abdominal pain after implantation. Pain can either be reported as pain at the pocket or as an electrical shock sensation, with rarely muscle contractions. This sensation could be due to the leads, with also a role of visceral hypersensitivity. In the study of Ducrotte et al. (2020), pain was reported in 16% of patients and was always medically managed. Serious adverse events are rare. Site infection must be suspected in case of fever after surgery (6–10%), and it rarely leads to device explantation (1.5%; Abell et al., 2003b; Ducrotte et al., 2020). Intestinal occlusion has been reported and might be due to the position of the lead and the device. Thus, it is important to minimize the intraabdominal length of the leads during surgery, positioning the device in the left upper quadrant if possible (Zoll et al., 2019). Rare perforation of the leads has been reported and also requires explantation, but is very uncommon. GES safety during pregnancy has never been assessed. One case report in a female with type 1 diabetes reported a favorable outcome (Fuglsang and Ovesen, 2015).

Quick Question - G-POEM

JR lives with type 1 diabetes and severe gastroparesis, despite maintaining an A1C of less than 7% for the past few years. The endocrinologist referred JR to a GI specialist, who recommended a surgical procedure called a Gastric Peroral Endoscopic Myotomy, G-POEM, to address JR's longstanding gastroparesis.

- **JR asks what you think about this intervention. What is the best response?**

1. It sounds like you are worried about the effectiveness and risks of this procedure. Is that right?
2. Tell me more about what your GI doctor told you about this procedure.
3. I know you are frustrated, but the primary treatment for gastroparesis is low fiber meals.
4. Usually, gastroparesis improves as your A1C reaches target so I would wait and see if things improve

Gastric peroral endoscopic myotomy or G-POEM

- The gateway from the small intestine to the duodenum is the pylorus.
- Food knocks of the pyloric sphincter for admission to duodenum
- Doors usually easily open, with limited resistance.
- With gastroparesis, pyloric sphincter is stiff and closed shut.

- This endoscopic G-POEM procedure cuts the muscles near the pyloric sphincter (a myotomy).
- Helps to permanently relax the sphincter, so food can empty freely.

Quick Question: Gastric Emptying Rates

Glucose fluctuations can impact gastric emptying rates. Which of the following the MOST accurate statement that describes the impact of glucose levels on gastric emptying rates?

A. Chronic hyperglycemia is associated with delayed gastric emptying.
B. Hypoglycemia is associated with delayed gastric emptying and increased glucagon secretion.
C. Hyperglycemia can lead to delayed or rapid gastric emptying.
D. Gastric emptying rates are usually about 10-40 kcals per minute regardless of glucose levels.

Cannabinoid Hyperemesis Syndrome (CHS)

CHS is defined as recurrent nausea, vomiting and cramping abdominal pain that is associated with at least weekly cannabis use.

- A common treatment for this syndrome is hot bath or shower.
- Heavier marijuana use increases risk for Cyclic Vomiting Syndrome (CVS) with unrelenting nausea and vomiting.
- Treatment includes abstaining from cannabis for at least a few weeks.
- People with type 1 diabetes and gastroparesis are especially at risk for both CHS and CVS.
- A person with type 1 and gastroparesis is also more at risk for other neuropathies and the associated chronic, often debilitating pain.

"Hyperglycemic ketosis due to cannabis hyperemesis syndrome" or HK-CHS.

- Ask about cannabis for those admitted with type 1 with severe vomiting in hyperglycemic crisis, especially if the person presents with an elevated pH and bicarbonate.
- Vomiting leads to hyperglycemia and is often associated with alkalosis.

https://diabetesjournals.org/care/article/45/2/481/139018/Differentiating-Diabetic-Ketoacidosis-and

Disordered Eating Patterns

- Anorexia nervosa: restricted energy intake relative to need
  - Marked by low body weight, fear of weight gain, and disturbance in the way in which one's body weight or shape is experienced
- Bulimia nervosa: recurring binge eating and compensatory behavior
  - Binging characterized by a sense of a lack in control.
  - Compensatory behaviors vary
- Diabulimia (unofficial diagnostic term): reduction/omission of insulin doses
  - This causes hyperglycemia and loss of glucose calories through the urine.

Disordered Eating

- For people with type 1
  - insulin omission causing glycosuria in order to lose weight is the most reported disordered eating behavior
  - Have high rates of diabetes distress and fear of hypoglycemia.

- For people with type 2
  - bingeing excessive food intake with an accompanying sense of loss of control most reported.
  - If treated with insulin, intentional omission is also frequently reported.
- People with diabetes and diagnosable eating disorders have high rates of other psychiatric disorders

STANDARDS OF CARE | DECEMBER 12 2022
5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes—2023*

Disordered Eating

- People with diabetes give themselves less insulin than needed to lose weight
- Tends to start in adolescence, more likely to occur in women than men.
- Signs: unexplainable spikes, A1c, weight loss, lack of marks from fingerpricks, lack of prescription refills for diabetes meds, records that don't match A1C.
- Treatment – Mental health specialist and team knowledgeable about disordered eating.

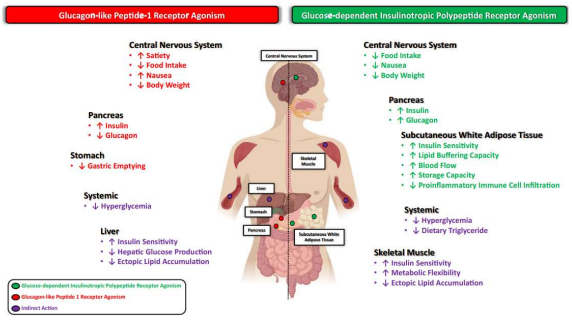
Treatment options for BMI 25+

Treatment options for overweight and obesity in type 2 diabetes

Treatment	BMI category (kg/m²) 25.0–26.9 (or 23.0–24.9[a])	27.0–29.9 (or 25.0–27.4[a])	≥30.0 (or ≥27.5[a])
Diet, physical activity, and behavioral therapy	+	+	+
Pharmacotherapy		+	+
Metabolic surgery			+

Consider using diabetes medications that contribute to weight loss, including GLP-1 RAs and SGLT-2 inhibitors.

GLP-1 & GIP Hormones



Samms RJ, Coghlan MP, Sloop KW. How May GIP Enhance the Therapeutic Efficacy of GLP-1? Trends Endocrinol Metab. 2020 Jun;31(6):410-421.

GLP-1 & GIP Receptor Agonists

Class/Main Action	Name	Dose Range	Considerations
GLP-1 RA - Glucagon Like Peptide Receptor Agonist **"Incretin Mimetic"** • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	**Side effects:** nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis or intestinal blockage (ileus) and stop med. Increase dose monthly to achieve targets. **Black box warning:** Thyroid C-cell tumor warning (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. †Approved for pediatrics 10-17 yrs Lowers A1C 0.5 – 1.6% Weight loss: 4-6% body weight loss.
	exenatide XR† (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*†	0.6, 1.2 and 1.8 mg daily	
	dulaglutide* (Trulicity)†	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	semaglutide* (Ozempic) (Rybelsus) Oral tablet	0.25, 0.5, 1.0 and 2.0 mg 1x a week pen injector 3, 7, and 14 mg daily in a.m. Take on empty stomach with sip of water	
GLP-1 & GIP Receptor Agonist Activates receptors for GLP-1 (see above) & Glucose-dependent Insulinotropic Polypeptide (GIP).	Tirzepatide (Mounjaro)	2.5, 5.0, 7.5, 10, 12.5 and 15 mg 1x a week prefilled single dose pen Increase dose by 2.5 mg once monthly to reach targets.	**Side effects:** nausea, diarrhea, injection site reaction. Report pancreatitis, signs of intestinal blockage. **Black box warning:** Avoid if family history of medullary thyroid tumor. Lowers A1C ~ 1.8 - 2.4% Weight loss: 7-13% body weight loss at max dose.

DiabetesEd.net © 10/2023

Gut Hormones

- Gut hormones secreted by the L-cell of the intestine. Some in the small intestine, but more the larger intestine.
- People with type 2 make about 50% less of gut hormones, but new study shows that people with type 1 may benefit from GLP-1 therapy early in diagnosis.
- Can slow peristalsis down too much, and lead to an intestinal blockage – Ozempic warning.

GLP-1 RA's as Adjunctive Therapy for Newly Diagnosed Type 1

- NEJM study looked at the effects of semaglutide on new-onset type 1 diabetes.
- Study evaluated blood glucose of 10 adults, ages 21-39, who had started taking semaglutide within three months of diagnosis.
- At diagnosis, all the participants were taking basal and mealtime insulin.
- Participants started with 0.125 mg semaglutide per week, with a maximum of 0.5 mg semaglutide per week, while mealtime insulin dose was lowered.
- Basal insulin dose was reduced based on CGM readings.

https://www.nejm.org/doi/full/10.1056/NEJMc2302677

GLP-1 RA's as Adjunctive Therapy for Newly Diagnosed Type 1

What were the key findings?

- Within 3 months, participants no longer needed mealtime insulin.
- At six months, 7 out of 10 no longer needed basal insulin.
- Most of the people in the study were able to stop taking any insulin after six months of treatment with semaglutide.
- A1C levels fell from an average of 11.7% at diagnosis to 5.9% at six months and 5.7% at one year,
- Participants also achieved time in range (70-180) of 89%.
- **Side effects:**
  - Some participants experienced mild hypo while the semaglutide dose was increased. Once the semaglutide dose stabilized, there were no problems with hypoglycemia.
  - There were no reports of diabetic ketoacidosis or other serious side effects.

GLPs & Intestinal Blockage

- More than a dozen reports of intestinal blockage or ileus among people using semaglutide (Ozempic).
- New warning to report any signs of intestinal blockage including:
  - Bloating, abdominal cramps, constipation, nausea, vomiting, and constipation that doesn't subside within a few days.
- Encourage individuals to report these signs and consult with a healthcare provider.

Enteric Nervous System or Brain in our Gut

Enteric Nervous System communicates with the brain via the vagus nerve when necessary and vice versa

2nd Brain of the body

Produces 80% of serotonin and contains most of the immune system

"I have a gut feeling"

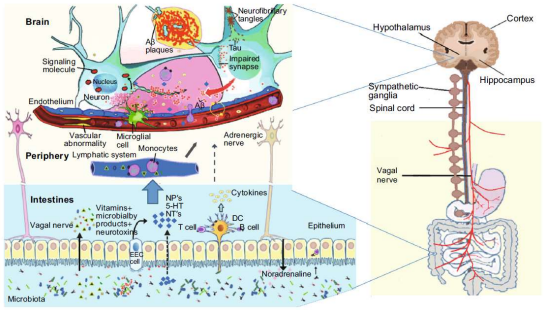
"That was hard to swallow"

"That was a gut punch"

"Follow your gut"

Plus, strong emotions propel gut content forward, so the gut can help the brain with problem solving.

Link Between Gut and Brain



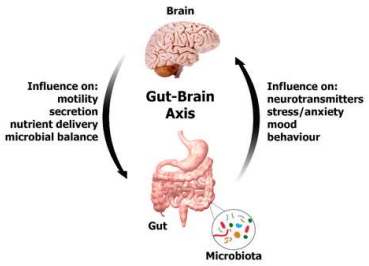
Benoit Chassaing, Shreya M. Raja, James D. Lewis, Shanthi Srinivasan, Andrew T. Gewirtz
Cellular and Molecular Gastroenterology and Hepatology (September 2017)

Gut's Messaging Brain

- Gut has its very own nervous system
- Functions independently of brain or spinal cord
- Neurons in gut wall can activate spinal cord neurons
- Powerful mechanism to transmit info from gut to brain
- Viscerofugal neurons relay info from gut to sympathetic nervous system
- Brain can "sense" what is going in gut.
- Influences our decision, mood, general well being.
- Most serotonin, a chemical mood messenger, is found in gut
- Understanding how gut messaging controls other organs can lead to treatment breakthroughs

New way for gut neurons to communicate with brain. Medical News Today Aug 2020

Gut Neurons Direct Messaging



- Enteric Nervous System = Nervous System of Gut
- Sometimes referred to as "second brain".
- Critical part of Gut-Brain Axis

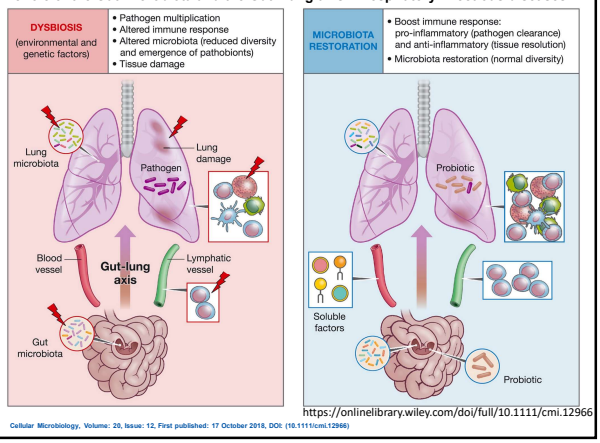
New way for gut neurons to communicate with brain. Medical News Today Aug 2020

Quick embryonic review

- It all starts in the embryonic tube
- Oral cavity - Tonsils
- Esophagus
- Pancreas
- Liver
- Gall bladder
- Stomach
- Duodenum
- Small intestine
- Appendix
- Large intestine

- Endoderm gives rise to:
- Epithelium of digestive track
- Lungs
- Liver
- Pancreas
- Thyroid

The role of the Gut Microbiota and the Gut–Lung axis in respiratory infectious diseases



https://onlinelibrary.wiley.com/doi/full/10.1111/cmi.12966

Cellular Microbiology, Volume: 20, Issue: 12, First published: 17 October 2018, DOI: (10.1111/cmi.12966)

Emerging new theory Gut – Lung Axis

- Gut microbiota potentially affects pulmonary health
- Gut-Lung cross talk between 2 mucosal sites in body
- Bi-Directional conversation
- Significant GUT-LUNG Axis dysfunction in the elderly population with COVID infections?
- Elderly population have less diverse gut microbiota
  - Most vulnerable for COVID
  - Loss of Gut bacterial diversity (dysbiosis)

Metabolic Surgery for Weight Loss

- *Considered* as an option to treat T2DM for screened surgical candidates with:
  - BMI 30 – 34.9 kg/m^2 for those who don't achieve wt. loss w/ nonsurgical methods
- *Recommended* as an option to treat T2DM for screened surgical candidates with:
  - BMI ≥ 40 kg/m^2
  - BMI 35 - 39.9 kg/m^2 for those who don't achieve wt. loss w/ nonsurgical methods

*All BMI thresholds need to be reduced by 2.5 kg/m2 for Asian Americans

Metabolic Surgery for Weight Loss

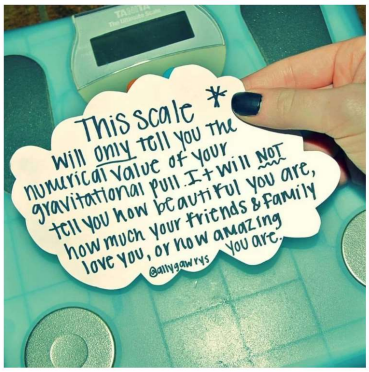
Advantages in T2DM

- Diabetes remission in 30-63% of those with RYGB.
  - 35-50% of those who go into remission experience recurrence, but median disease-free period is 8.3 years.
- Many with diabetes will sustain glycemic improvement for 5-15 years.
- Additional health benefits

Disadvantages

- Costly (but likely cost effective)
- Long-term concerns: dumping syndrome, anemia, osteoporosis, severe hypoglycemia, nutrient deficiency.
- Increased risk of substance use, new-onset depression/anxiety

Weight is a Heavy Issue



Weight & Respect

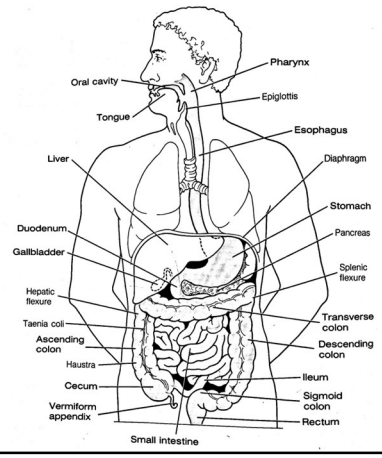
If weighing is questioned or refused:

- Be mindful of possible prior stigmatizing experiences
- Consider the value of weight monitoring - is it needed to inform treatment decisions?

Situate scales in a private area or room

Measure and report weight non-judgmentally

Take care to regard weight and BMI as sensitive health information



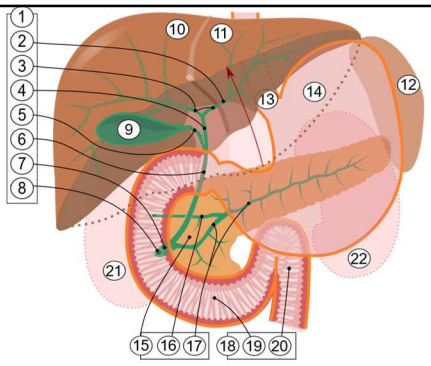
Small Intestine

Small intestine is the mover of the intestinal system

300 feet of mucous lined membrane that propels the food forward, absorbing nutrients along the way.

Small Intestine – Whole lot of Shaking

- Duodenum & Digestive Enzymes
  - duodenum curves around the head of the pancreas
  - receives digestive enzymes from the pancreas and bile from the gallbladder
  - through the common bile duct or ampulla of Vater -which is controlled by the sphincter of oddi
  - Duct can get blocked by gallstones causing gallbladder disease and increasing risk of pancreatitis.
- Pancreas contributes digestive enzymes to help emulsify fat and break down nutrients (some people with type 1 & 2 may benefit from enzyme replacement therapy).
- Pancreas also provides exactly the right amount of insulin to keep blood sugars on target (unless with diabetes)
- Gallbladder contributes bile to help with emulsification of fats.
- We can live without a gall bladder, but it's really hard to live without a pancreas.



Bile duct and pancreas 1. Bile ducts: 2. Intrahepatic bile ducts 3. Left and right hepatic ducts 4. Common hepatic duct 5. Cystic duct 6. Common bile duct 7. en:Sphincter of Oddi 8. Major duodenal papilla 9. Gallbladder 10-11. Right and left lobes of liver 12. Spleen 13. Esophagus 14. Stomach 15. Pancreas: 16. Accessory pancreatic duct 17. Pancreatic duct 18. Small intestine 19. Duodenum 20. Jejunum 21-22: Right and left kidneys

By Jmarchn - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=14612350

Diabetes Education SERVICES

Table 19.2 Digestive Enzymes—Their Locations and Functions

Location	Enzyme	Function
Mouth	Ptyalin	*Carbohydrate digestion*: converts starch into dextrins and maltose
Stomach	Pepsin	*Protein digestion*: converts proteins into polypeptides
Small Intestine *Pancreatic juice*	Pancreatic amylase	*Carbohydrate digestion*: breaks starch into the disaccharides maltose and isomaltose
	Trypsin Chymotrypsin	*Protein digestion*: break proteins into peptones, proteoses, and dipeptides
	Carboxypeptidase	*Protein digestion*: reduces proteins or protein derivatives to free amino acids
	Pancreatic lipase	*Lipid digestion*: reduces fats into monoglycerides and free fatty acids
Intestinal juice	Maltase Isomaltase Sucrase Lactase	*Carbohydrate digestion*: complete digestion into glucose, galactose, lactose, and/or fructose
	Aminopeptidase Dipeptidase	*Protein digestion*: reduce small polypeptides and dipeptides into amino acids
	Intestinal lipase	*Lipid digestion*: intracellular digestion of monoglycerides into fatty acids and glycerol

Pancreatic Enzyme Replacement Therapy

People with diabetes may have diminished pancreas exocrine function*.

Pancrelipase (Creon) – Medication harvested from porcine pancreatic glands.

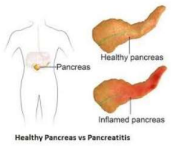
Contains combo of lipase, amylase and protease. Work in duodenum to break down fats, protein and starch.

No absorption, excreted in feces

*https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7113197/

Pancreatitis

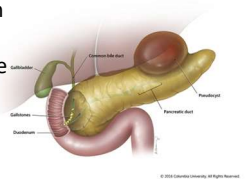
- People with diabetes 2xs risk of acute pancreatitis
- After episode of pancreatitis, one third of people will get prediabetes or diabetes
- Pancreatitis is an exocrine dysfunction:
  - Disrupts global architecture or physiology of pancreas
  - Results in both exocrine and endocrine dysfunction



Healthy Pancreas vs Pancreatitis

Pancreatitis

- Pancreatitis caused by digestion of the organ from pancreatic enzymes normally carried to the SI through pancreatic duct.
- Detected through elevated Amylase levels & pain
- Causes:
  - HIV meds and other meds
  - Alcohol ingestion
  - Gallstones blocking pancreatic enzyme flow to SI
  - Elevated triglycerides
  - Cancer, injury and other



Exocrine Pancreatic Insufficiency

- Fatty stools
- Abdominal pain especially after high fat meals
- Can happen with both type 1 & 2 diabetes
- May need to take fat soluble vitamins
- Avoid smoking, excess alcohol to protect pancreas.
- Cystic fibrosis https://www.webmd.com/digestive-disorders/video/video-epi-symptoms-vitamins

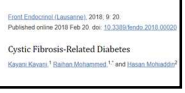
Cystic Fibrosis Related Diabetes (CFRD)

- Cystic fibrosis
  - Affects >40,000 in U.S.
    - 1000 children dx each year
  - Abnormally thick mucus clogs lungs along with pancreas exocrine dysfunction.
  - Partial fibrotic destruction of islet cell mass leads to hyperglycemia in 20-30% of those with cystic fibrosis
  - Due to improved treatment and emerging medications, CF survival rates improving

https://www.cff.org/managing-cf/cystic-fibrosis-related-diabetes

Cystic Fibrosis Related Diabetes (CFRD)

- CFRD distinct clinical entity
  - Insulin deficient but not prone to ketosis
  - Slow moving – 2-4 yrs before diagnosis
  - Abnormal glucose tolerance associated with progressive clinical deterioration
  - Associated w/ poor nutritional status, lung disease, resp failure
  - Lowers survival rate at 30 yrs
    - Only 25% live to 30 w/ CFRD
    - 60% live to 30 years or longer when no CFRD



Cystic Fibrosis Related Diabetes (CFRD)

- CFRD Magnitude with CF
  - 20% of adolescents
  - 40-50% of adult pts, develop CFRD
- CFRD Consensus Panel recommends:
  - OGTT yearly after 10 yrs age or symptoms
  - A1c may not be accurate (false low)
  - CGM also being utilized
  - Monitor BG closely during steroid therapy

Clinical Practice Recommendations for CFRD 2010

Cystic Fibrosis-Related Diabetes (CFRD)

Annual screening starting at age 10

Use oral glucose tolerance test

A1C is not recommended as a screening test for CFRD.

Treat with insulin to attain individualized glycemic goals.

Beginning 5 years after the diagnosis of CFRD, annual monitoring for complications of diabetes is recommended

2. Classification and Diagnosis of Diabetes: *Standards of Care in Diabetes—2023*

Cystic Fibrosis Related Diabetes (CFRD)

- Treatment Philosophy
  - "Eat, we will cover"
- Goal of therapy: maintain glucose/ weight
  - Daily cals – 120 to 150% RDA (2,400 – 3000)
    - 40% fat, 15-20% protein,
  - May be on steroid pulses
- Med regimen needs flexibility
  - Bolus insulin w/meals, carb counting + basal
- Monitor BG levels annually or if s/s of DM

23 yr old newly diagnosed CFRD

- A1c 8.3%
- Lost 6 lbs BMI 21
- Creat 0.9
- On and off steroids

- Insulin – Basal + bolus scale
- Food- Eat, we cover
- Activity – keep moving
- Monitoring - 2 to 3 times a day
- Plan for steroid adjustments

Quick Question

- JL has cystic fibrosis and newly diagnosed diabetes. Which of the following is the best management strategy?

A. Limit overall carb intake

B. Encourage maintaining current caloric intake

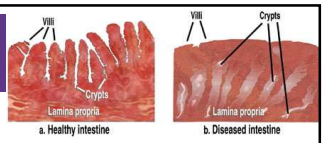
C. Avoid all concentrated sweets

D. Increase activity to reach glucose goals.

Small intestine

- The villi of the small intestine help move stomach contents forward and absorb nutrients, giving the small intestine a velvety appearance.
- Food is broken down through intestinal glands and pancreatic enzymes that act on protein, fat, carb.
- Bile helps breakdown lipids.
- Most absorption and digestion of food happens in the small intestine.
- There are not many bacteria in this section. The main goal to move things forward and maintain cleanliness of the mucous lining.
  - SIBO or Small Intestine Bacterial Overgrowth is associated with severe inflammation and GI Distress
- Celiac disease causes villi inflammation, decreasing absorption of nutrients.

Celiac Disease



- Type 1 – Affects 1-16%
- Immune reaction to gluten - affects function of villi in intestine, decreasing nutrient absorption
- S/S: bloating, malabsorption, wt loss, fatty stools, diarrhea, muscle tenderness, failure to thrive
- Diagnosis: measure either anti-endomysial antibodies (EMA) titers or tissue transglutaminase.
- If positive, refer to GI specialist for endoscopy and biopsy of small intestine to confirm diagnosis.

Celiac Disease

- Treatment for celiac disease is a lifetime gluten-free diet
  - Eliminate all wheat (including durum, semolina, spelt, and farro) and the related grains of rye, barley, and triticale.
  - Caution with oats – may be contaminated with wheat
  - Remember "BROW" – Barley, Rye, (some) Oats, Wheat
- Refer to a dietitian for help with food selection/label reading

Nutrition Interventions: Celiac Disease

Gluten Free Whole Grains & Starches include:

- Quinoa
- Potatoes
- Beans & Peas
- Cassava
- Corn
- Oats*
- Flax
- Amaranth
- Millet
- Rice
- Wild rice
- Buckwheat
- Job's Tears (Hato Mugi)
- Montina (Indian rice grass)
- Sorghum
- Teff

**Oats are inherently gluten-free may be contaminated with wheat during growing or processing.*

What links Diabetes and Cancers?

- Hyperinsulinemia
- Hyperglycemia
- Inflammation

> CA Cancer J Clin. 2010 Jul-Aug;60(4):207-21. doi: 10.3322/caac.20078. Epub 2010 Jun 16.

Diabetes and cancer: a consensus report

Edward Giovannucci [1], David M Harlan, Michael C Archer, Richard M Bergenstal, Susan M Gapstur, Laurel A Habel, Michael Pollak, Judith G Regensteiner, Douglas Yee

Affiliations + expand

PMID: 20554718 DOI: 10.3322/caac.20078

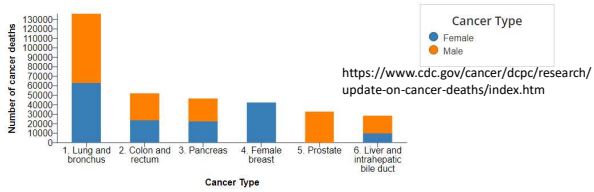
What were the leading causes of cancer death in 2020?

Lung cancer was the leading cause of cancer death, accounting for 23% of all cancer deaths. Other common causes of cancer death were cancers of the colon and rectum (9%), pancreas (8%), female breast (7%), prostate (5%), and liver and intrahepatic bile duct (5%). Other cancers individually accounted for less than 5% of cancer deaths.

In 2020—

- 136,084 people died of lung cancer (63,135 females and 72,949 males).
- 51,869 people died of colorectal cancer (23,826 females and 28,043 males).
- 46,774 people died of pancreatic cancer (22,495 females and 24,279 males).
- 42,275 females died of breast cancer.
- 32,707 males died of prostate cancer.
- 28,227 people died of liver and intrahepatic bile duct cancer (9,591 females and 18,636 males).

Figure 2. Number of deaths by leading cancer types and sex, United States, 2020



https://www.cdc.gov/cancer/dcpc/research/update-on-cancer-deaths/index.htm

The American Cancer Society's estimates for pancreatic cancer in U.S. for 2023 are:

- About 64,050 people will be diagnosed with pancreatic cancer.
- About 50,550 people will die of pancreatic cancer.
- Pancreatic cancer accounts for about 3% of all cancers in the US and about 7% of all cancer deaths.

https://pancan.org/

Type 1 and Cancer

- Rates of stomach, liver, pancreatic and kidney cancer increased in both men and women
- Rate of cancer doubled during first year of diagnosis
  - Then returns back to population levels after that
- Both type 1 and type 2 have increased risk of cancer, but type 1s a little less

Diabetologia
May 2016, Volume 59, Issue 5, pp 980–988

Cancer incidence in persons with type 1 diabetes: a five-country study of 9,000 cancers in type 1 diabetic individuals

Type 1 and Cancer – Risk compared to general population

Increased Risk

- Stomach
- Liver
- Kidney
- Pancreatic
- Endometrial

Decreased Risk

- Breast
- Prostate

Due to hormone levels
More frequent doctor visits?

Diabetologia, published online Feb. 29, 2016

Type 2 Diabetes and Cancer

- People with prediabetes and type 2 Two fold higher risk for cancers of
  - Liver
  - Pancreas
  - Endometrium
- 1.2 to 1.5 fold risk of cancers of
  - Colon
  - Breast
  - Bladder.
- Lower risk of prostate cancer

Diabetes and Cancer: A Consensus Report Cancer J Clinic 2010
Joint statement American Cancer Society and American Diabetes Assoc

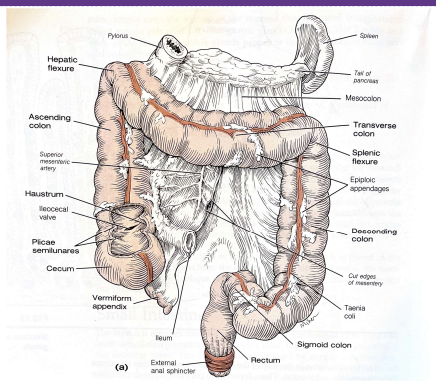
Risk Factors Common to Both Conditions

- Aging
- Extra weight
- Diet
- Physical inactivity
- Ethnicity
- Alcohol (more than 2 drinks a day)
- Smoking
- Changes in the DNA?

Biologic links incompletely understood

Cancer Screenings and a Commitment to Health Saves Lives

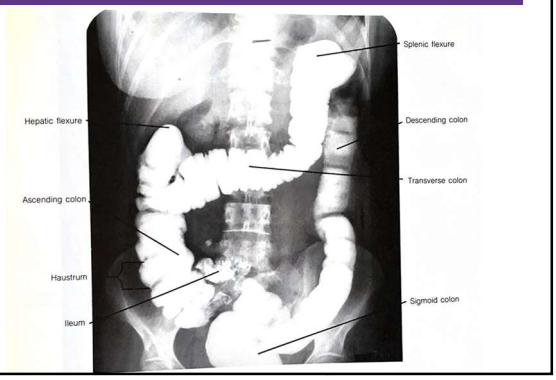
Almost There – Ileum to Anus



Ileum to Anus

- Ileum is the last 2 meters of the intestine. To move from the ileum to the cecum (first part of large intestine), food passes through the ileocecal valve.
- The appendix hangs out near this juncture. It traps harmful bacteria and contains cells lymphoid cells similar to your tonsils. If appendix gets blocked with bacteria and white blood cells, can lead to appendicitis
- Large intestine – The bacterial party center of your GI Tract
  - Ascending
  - Transverse
  - Descending
  - Sigmoid colon makes and Sideway S as it enters the iliac fossa
  - Then the rectum
  - Anus – 2 sphincters internal and external
  - External sphincter anal skeletal muscle under voluntary control and internal anal muscle not

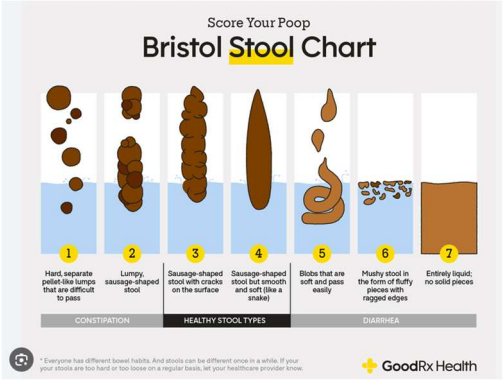
Large Intestine Barium Enema Post Meal



Colorectal Cancer Screening Recommendations – Am Cancer Soc

- All people at age 45 need screening for colon cancer
- Blacks and higher risk individuals need earlier screening
- Prostate cancer screening discussion at age 45 for Blacks
- Chadwick Bozeman died at age 43 after a 4 year battle with colon cancer

Look at your Poop – Stool Chart

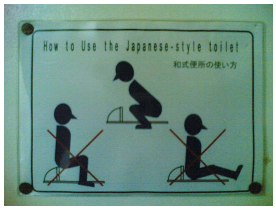


Bowel Issues

Constipation

- Defined as less than 3 bowel movements a week.
- More common in diabetes
- GLP-1 RA can contribute
- Treatment
  - Get glucose to target
  - Increase fiber, activity, H2O
  - Bulking agents (psyllium)
  - Laxatives or other agents
  - Bathroom habits review

Japanese Style Toilets – Past to Present



Pooping Position

Bowel Issues - Diarrhea

Defined and Treatment

- 3 or more bowel movements a day
- **Treat & Determine Cause**
  - Improve glucose levels
  - Eat whole foods — including whole grains and fiber.
  - Drink plenty of water.
  - Get regular exercise.
  - Quit smoking and using tobacco products.
  - Limit alcohol.
  - Take medications as necessary.

- **Possible Causes**
  - Elevated glucose
  - Autonomic neuropathy
  - Metformin
  - GLP-1 RA's
  - Celiac disease
  - Bacterial /yeast infection
  - Exocrine pancreatic insufficiency
  - Irritable bowel syndrome
  - Sugar free foods
  - Other

Let's Check in with EV

4. Comprehensive Medical Evaluation and Assessment of Comorbidities

- Person centered communication, strength-based language, active listening, literacy, quality of life
- It is necessary to take into account all aspects of a person's life circumstance
- It is important to integrate medical eval, engagement and lifestyle changes.
- Interdisciplinary teams provide best care

4. ADA – Complete Medical Evaluation

- At initial visit :
  - Whole person care and psychosocial evaluation
  - Explore diabetes self-management and health status
  - Evaluate if changes in diabetes treatment would improve well being.
- Engagement in formulation of a care management plan
- Develop a plan for continuing care

ABC's of Diabetes

- A1c less than 7% (individualize)
  - Pre-meal BG 80-130
  - Post meal BG <180
  - AGP - Time in Range (70-180) 70% of time
- Blood Pressure < 130/80
- Cholesterol
  - Statin therapy based on age & risk status
  - If 40+ with ASCVD Risk, decrease 50%, LDL <70
  - If 40+ with ASCVD, decrease 50%, LDL <55

Lab Eval

- A1C (each 3-6 mo's)
- Time in Range
- Each year
  - Lipids
  - **Liver function tests**
  - Spot urinary albumin-to-creat ratio (UACR)
  - Serum creat and GFR
  - TSH (type 1) and Type 2 as needed
  - B12 check (with anemia, nerve pain or on metformin therapy)
- Serum K
  - If on ACE, ARBs or diuretics

Physical Exam

- Height, weight, BMI, signs of insulin resistance
- Blood pressure
- Fundoscopic exam
- Skin exam – insulin insertion sites, fungus, sores
- Oral health
- Digestive issues

EV Arrives and Requests Help

- 58 yr old complains of 4 lb wt gain for past month. BMI 31, wt 90 kg. B/P 142/96. A1C 8.3%
- Meds include:
  - Sitagliptin, Metformin
  - Actos 15mg ac breakfast
  - Basaglar 58 units
  - Semaglutide 0.5mg weekly
  - Levothyroxine (ran out)
  - Lisinopril 10mg
  - Tums prn

What story do these meds tell?
Any med(s) missing?
Any med needs to be stopped?

EV Arrives and Requests Help

- 58 yr old complains of 4 lb wt gain for past month. BMI 31, wt 90 kg. B/P 142/96. Checks BG in morning; 150ish. A1C 8.3%
- Meds include:
  - Sitagliptin (DPP-IV), Metformin
  - Actos 15mg
  - Basaglar 58 units (Basal)
  - Semaglutide 0.5mg wk (GLP-1)
  - Levothyroxine (ran out)
  - Lisinopril 10mg (ACE)
  - Lovastatin 20mg (Statin)
  - Tums as needed

What does this tell us about EV?

- Struggling with weight
- B/P & A1C above target
- Overbasalized (max dose 0.5 units/kg a day)
- Why not taking thyroid med?
- Lower extremity pain?
- Elevated CV risk?
- GI issues?

EV Has GI Issues and is Tired

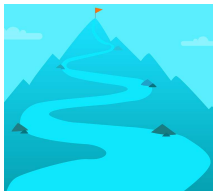
- 58 yr old complains of 4 lb wt gain for past month. BMI 31, wt 90 kg. B/P 142/96. Checks BG in morning; 150ish. A1C 8.3%
- Meds include:
  - Sitagliptin, Metformin
  - Actos 15mg ac breakfast
  - Basaglar 58 units
  - Semaglutide 0.5mg weekly
  - Levothyroxine – ran out
  - Lisinopril 10mg
  - Takes Tums for GI upset

Labs
A1C – 8.3%
UACR 26 GFR >60
TSH 10.6
LDL 98 mg/dl, Trig 158
ALT 85 IU/L, AST 90 IU/L
Platelets 217
ADA ALT 29-33 men
ALT 19-25

Life situation
Smokes ½ pack a day
Gums inflamed
No eye doctor for year
Struggles with heartburn, diarrhea

Advocating for Best Health for people with Diabetes

- Modifiable
  - Sleep
  - Activity
  - Smoking
  - Dietary Habits
  - Glucose
  - Blood Pressure
  - Lipids
  - Oral Care
  - Immunizations
  - Psychosocial care



- Make small, achievable goals. We are in this for the long run.

Diabetes is a long path

Get at least 7 hours of sleep a night – Check for sleep apnea

Keeping Oral Healthy

- Oral disease linked with heart disease
- Dental exams (every 6 mo's)
- Brush Twice Daily, Floss at least once daily.
- Quit smoking
- Treat infections with ATB'x
  - Lowers A1C by 1-2%.
  - Lowering BG shortens infection.
- Cost a barrier to getting care

Where are we on this continuum?

Only about 50% of us are meeting activity goals

Benefits of Exercise and Diabetes

- Increase muscle glucose uptake 5-fold
- Glucose uptake remains elevated for 24 - 48 hours (depending on exercise duration)
- Increases insulin sensitivity in muscle, fat, liver.
- Reduce CV Risk factors (BP, cholesterol, A1c)
- Maintain wt loss
- Contribute to well being
- Muscle strength
- Better physical mobility

Exercise decreases:

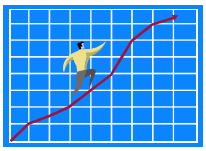
- Sleep apnea
- Diabetic kidney disease, retinopathy
- Depression
- Sexual dysfunction
- Urinary incontinence
- Knee pain
- Need for medications
- Health care costs
- Fatty liver disease

Smoking and Diabetes

Smoking increases risk of diabetes 30%

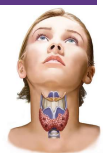
- **Ask at every visit**
- **Assess**
- **Advise**
- **Assist with stop smoking**
- **Arrange for referrals**
- **Organize your clinic**

EV asks why the weight gain?



- Fluid retention - diabetes doubles risk for Congestive Heart Failure (CHF). Check lower extremities.
- Inaccurate nutrition knowledge
- Actos (TZD) associated with edema
- Blood sugars improving
- Thyroid disease under treated
- Depression / Increased intake

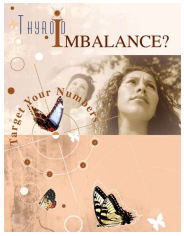
Thyroid Disease and Diabetes



- 15 to 30% of people w/ diabetes & their siblings or parents are likely to develop thyroid disease
- Up to 60 percent of those with thyroid disease are unaware of their condition.
- Women are 5-8x's more likely than men to have thyroid problems.
- Check TSH on Type 1 & 2 annually or if indicated.
- Hashimoto's thyroiditis – autoimmune thyroid
  - most common cause of hypothyroidism w/ dm
  - Associated with:
    - Elevated cholesterol levels
    - Increased risk of CV disease
    - Weight gain

AACE Website

Thyroid & TSH* Levels



AACE Guidelines

- *Thyroid Stimulating Hormone - secreted by pituitary gland
  - controls thyroid hormone thyroxine production
  - first and best test
  - TSH Norm = up to 4.5 mIU/mL
  - Treatment based on TSH plus symptoms.
    - 4.5 – 10 based on risk, s/s
    - 10 or more = treat
  - Lower = hyperthyroidism
  - Higher = hypothyroidism

A TSH above 10 mIU/L, in combination with a subnormal free T4 characterizes overt hypothyroidism.

If TSH in range, but person is symptomatic, Check for thyroid peroxidase atb or TPO antibodies

A low TSH indicates hyperthyroidism (0.1 ish)

Collaborative Action Plan

- Increase semaglutide to 1.0mg
- Decrease basaglar by 10 units
- Switch to Metformin XR
- Stop sitagliptin, pioglitazone (Actos)
- Walk after lunch during work week
- Restart levothyroxine, Re-Check TSH - Re-evaluate in 4 weeks.
- Eat one serving of veggie a day and decrease meat intake to 4 nights week.
- Meet with RD/RDN
- Get liver eval

What about alcohol intake?

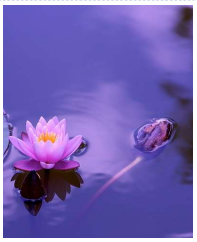
Smoking?

GI issues?

Are these goals realistic?

Social History and Med Taking

- Eating Patterns & weight history
- Sleep behaviors – goal 7 hrs
- Tobacco, alcohol, substance use
- Social supports and coping skills
- Medication taking behaviors
  - How many times a day/week are you taking this medication?
  - Complimentary meds
  - Evaluate for hyper and hypo glycemia



Supplements – "Nutraceuticals"

Non-Alcoholic Fatty Liver Disease

NAFLD is when fat reaches 5% to 10% of the liver's weight

Without consumption of significant amounts of alcohol defined as:

- Ingestion of less than 21 standard drinks per week in men and
- Less than 14 standard drinks per week in women

over a 2-year period preceding evaluation) or the presence of other secondary causes of fatty liver disease.

Non-Alcoholic Fatty Liver Disease (NAFLD)

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023*

Fatty Liver Disease & Steatohepatitis

Adults with type 2 diabetes.

- NAFLD is prevalent in >70%
  - Of those 50% have NASH*
- 12-20% have fibrosis
- Need evaluation for nonalcoholic steatohepatitis and liver fibrosis for those:
  - At high risk: type 2 or prediabetes with cardiometabolic risk factors plus
  - Elevated liver enzymes (ALT) or
  - Fatty liver on imaging or ultrasound

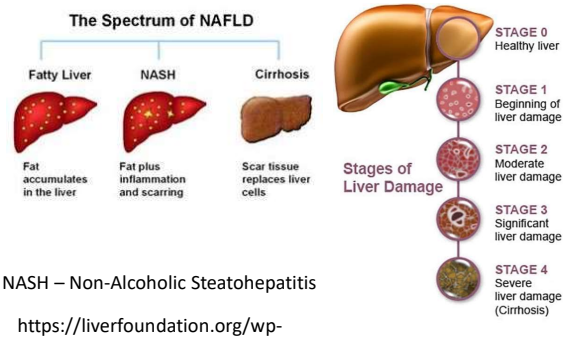
Associated with :

- Increased BMI (30+)
- Cardiometabolic risk factors
- Over 50 yrs
- ALT & AST 30 units/L +

*Non-Alcoholic Steatohepatitis (NASH)

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023*

Natural History of NAFLD to NASH



NASH – Non-Alcoholic Steatohepatitis

https://liverfoundation.org/wp-content/uploads/2020/11/StagesFibrosis.jpg

Stages of Liver Failure

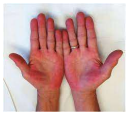
- NAFLD – nonalcoholic fatty liver disease
  - NAFL – simple fatty liver, doesn't usually progress to cause liver damage
  - NASH or MASH nonalcoholic / metabolic steatohepatitis
    - Liver inflammation and cell damage.
    - Can cause fibrosis, scarring
    - Leading cause of hepatocellular carcinoma and liver transplants (ADA)
- Cirrhosis – degeneration of cells, inflammation, fibrous thickening
- End-stage liver disease & Liver Cancer

https://liverfoundation.org/for-patients/about-the-liver/the-progression-of-liver-disease/#fibrosis-scarring

Symptoms of Fatty Liver

If symptoms do appear, they may include:

- A feeling of fullness in the middle or upper right side of the abdomen
- Abdominal pain, nausea
- Loss of appetite or weight loss
- Weakness
- Jaundice



- Swelling of the abdomen and legs
- Mental confusion
- Extreme fatigue or tiredness
- Signs of advanced disease include:
  - Portal hypertension, spider angiomas, reddening of palms, declining platelet counts

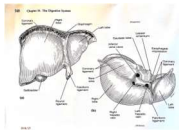
Mayo Clinic

https://dermcollective.com/palmar-erythema/

Quick Question: Detecting Fatty Liver Disease

EV is 58 years old with type 2 diabetes and a BMI of 33. In addition, EV has hypertension and hyperlipidemia, with elevated liver enzymes (ALT and AST). To determine if EV is at risk for liver fibrosis and cirrhosis, which of the following would provide a risk calculation?

A. UACR
B. FIB-4
C. GAD or ICA
D. Weight in (kg) divided by the square of height in meters (m2)



Screening for NASH – FIB-4

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required va
It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)}\ 58 \times \text{AST Level (U/L)}\ 90}{\text{Platelet Count } (10^9/L)\ 217 \times \sqrt{\text{ALT (U/L)}\ 85}} = 2.61$$

- The American College of Gastroenterology considers Upper limit of normal ALT levels:
- 29–33 units/L for males
- 19–25 units/L for female individuals

(mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis).

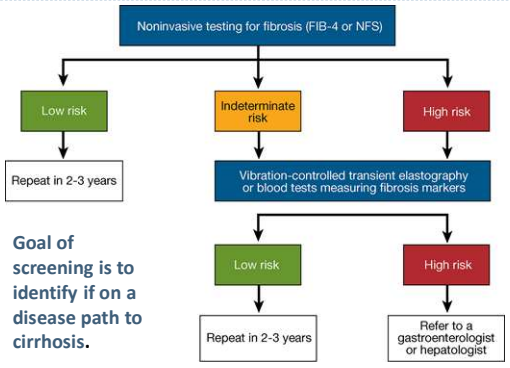
FIB-4 estimates risk of hepatic cirrhosis (age 35+):

- Calculated by imputing:
  - Age
  - plasma aminotransferases (AST and ALT)
  - and platelet count
- FIB-4 Risk Levels
  - Lower risk is <1.3
  - Intermediate 1.3 to 2.67
  - High risk >2.67
    - considered as having a high probability of advanced fibrosis (F3–F4).

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023*

www.DiabetesEd.net

Screening for Fibrosis Risk



Goal of screening is to identify if on a disease path to cirrhosis.

Finding Liver Disease

- Imaging procedures used to diagnose NAFLD include:
- **Abdominal ultrasound,** which is often the initial test when liver disease is suspected.
- **Transient elastography,** an enhanced form of ultrasound that measures the stiffness of liver. Liver stiffness indicates fibrosis or scarring.
- **Magnetic resonance elastography,** works by combining MRI imaging with sound waves to create a visual map (elastogram) showing the stiffness of body tissues
- **Biopsy** by liver specialist confirms definitive diagnosis

Referral to Hepatologist or GI specialist may be needed

Mayo Clinic

Ultrasound Liver results

COMPARISON: None

TECHNIQUE: Real-time grayscale and color doppler ultrasound images of the abdomen were obtained

FINDINGS:

LIVER: Increased echogenicity of the liver, suggestive of hepatic steatosis. Fatty sparing noted along the gallbladder fossa. Enlarged liver measuring 20.7 cm length. No mass detected.
GALLBLADDER: No gallstones. No wall thickening or pericholecystic fluid. Negative sonographic Murphy's sign.
BILE DUCTS: Normal diameter of the common duct, measuring 3 mm. No intrahepatic biliary dilation.
PANCREAS: Limited visualization due to overlying bowel gas.
SPLEEN: Normal size, measuring 9.7 cm in length.
KIDNEYS: Right kidney measures 11.3 cm in length and the left measures 13.0 cm. Likely duplicated left renal collecting system. No hydronephrosis. No renal calculus detected.
ABDOMINAL AORTA. No aneurysm detected.
Intrahepatic IVC: Unremarkable where visualized.
ASCITES: None detected.

IMPRESSION:
1. Hepatic steatosis and hepatomegaly.

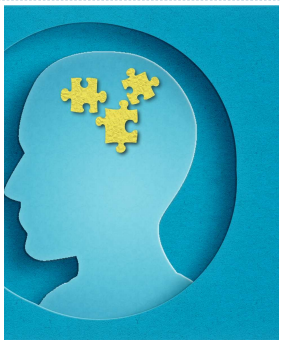
2. Likely duplicated left renal collecting system.

Ultrasound showed more light-colored tissue in your liver than normal. The presence of this light-colored tissue can be a sign of a fatty liver.

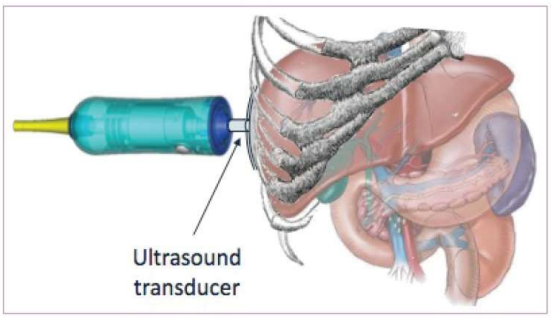
Question: What does a Liver Elastography reveal?

The provider is sending JR for a Liver Elastography or FibroScan test since JR has elevated ALT and AST levels along with an elevated Fib-4 score. Which of the following are measured during this liver ultrasound procedure?

A. Liver diameter and density.
B. Liver scarring and ductal health.
C. Hepatocyte density and distribution.
D. Liver stiffness and fat density.



Liver Elastography or FibroScan



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3594956/

FibroScan or Elastography

Fibroscan Results
- CAP & kPa
- CAP Fat Score S0 - S3
- kPa Fibrous Score F0 – F4

CAP Score	Steatosis grade	Portion of your liver affected by fatty change
238 to 260 dB/m	S1	Less than ⅓ (11% to 33%)
260 to 290 dB/m	S2	Between ⅓ and ⅔ (34% to 66%)
290 to 400 dB/m	S3	More than ⅔ (67%)

Non-alcoholic Fatty Liver Disease (NAFLD or NASH)	2 to 7 kPa	F0 to F1	Is normal.
	7.5 to 10 kPa	F2	Has moderate scarring.
	10 to 14 kPa	F3	Has severe scarring.
	14 kPa or higher	F4	Has cirrhosis.

EV has NAFLD

CAP Fat Score is 243 – S2
Fibrosis kPa Score is 8 - F2
Along with elevated ALT and AST

Fatty Liver Interventions

- Nutrition
  - Weight loss goal of 5-10% or more
  - Mediterranean Diet
  - Avoid alcohol
  - Decrease processed foods, meats and sugary foods.
  - Increase vegetables and other high fiber foods.
- Move more – including aerobic activity and strength training.
- Close follow-up and ongoing monitoring
- Can be associated with worsening renal function

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023* FREE

Other Treatments for NAFLD and NASH

- Meds that lower glucose, cholesterol and weight
- Bariatric surgery
- Pioglitazone (Actos)
  - Improves lipid and glucose metabolism
  - Reverses steatohepatitis in prediabetes/diabetes
  - Causes 1-2% wt gain at 15 mg
  - 3-5% wt gain at 45 mg
- GLP-1 Receptor Agonists

Support lifestyle changes

Actions To Decrease Fatty Liver

- Increase activity
  - Strength training
  - Yoga or Thai Chi
  - Walking & aerobics
- Thoughtful eating
  - More fiber
  - Less processed foods & less added sugar
  - Avoid alcohol
- Treatment
  - Actos
  - GLP-1
  - Statin
- Prevention
  - Cancer Screenings
  - Decrease inflammation

Initial Eval – Looking for Comorbidities

- Other conditions that may appear
  - Cancer
  - Fatty liver disease
  - Bowel issue
  - Pancreatitis
  - Periodontal disease
  - Cardiovascular disease
  - Cognitive impairment
  - Hyper/Hypoglycemia
  - Psychosocial/Emotional Issues
  - Low Testosterone in Men
  - Hearing Impairment
  - Fractures

EV is feeling Empowered

- A1C is improved by med tune up, needs less insulin.
- GI feels a lot better through healthier eating, metformin XR and increased activity.
- Back on thyroid medication and has more energy.
- Decreased smoking.
- Saw Dentist. Brushing teeth on regular basis.
- Has appt with eye doctor.

"NAFLD is the hepatic manifestation of metabolic syndrome."

AASLD

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

No More NAFLD

The NAFLD nomenclature is changing.

The NAFLD nomenclature is changing

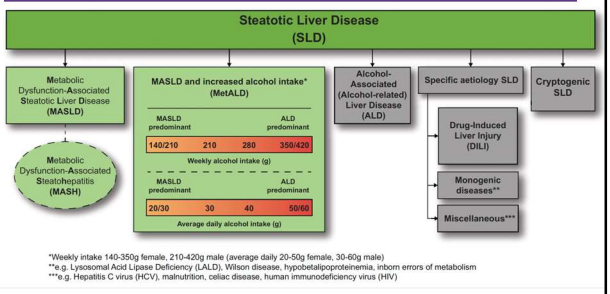
***Cardiometabolic criteria**

Adult Criteria	Pediatric Criteria
At least 1 out of 5:	**At least 1 out of 5:**
☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent	☐ BMI ≥ 85th percentile for age/sex [BMI z score ≥ +1] **OR** WC > 95th percentile **OR** ethnicity adjusted equivalent
☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes	☐ Fasting serum glucose ≥ 5.6 mmol/L [≥ 100 mg/dL] **OR** serum glucose ≥ 11.1 mmol/L [≥ 200 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol [140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** already diagnosed/treated type 2 diabetes **OR** treatment for type 2 diabetes
☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment	☐ Blood pressure age < 13y, BP ≥ 95th percentile **OR** ≥ 130/80 mmHg (whichever is lower); age ≥ 13y, 130/85 mmHg **OR** specific antihypertensive drug treatment
☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment	☐ Plasma triglycerides < 10y, ≥ 1.15 mmol/L [≥ 100 mg/dL]; age ≥ 10y, ≥ 1.70 mmol/L [≥ 150 mg/dL] **OR** lipid lowering treatment
☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment	☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [≤ 40 mg/dL] **OR** lipid lowering treatment

AASLD

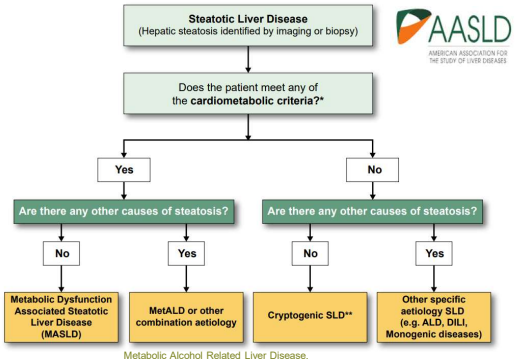
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Consensus Nomenclature



Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) or Steatohepatitis (MASH)

Decision Support Tool



Metabolic Alcohol Related Liver Disease.

ADA Assess and Treatment Plan

- **Assess risk of diabetes complications**
  - ASCVD risk factors and heart failure history
  - Stage chronic kidney disease
  - Hypoglycemia risk
  - Assess for neuropathy, retinopathy
  - GI and Liver Health
- **Goal setting**
  - Set A1C/blood glucose targets & Time in Range
  - Address hypertension and lipids
  - Diabetes self-management goals

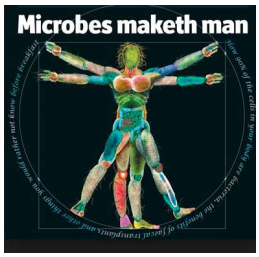
- **Therapeutic treatment plans**
  - Lifestyle management – referral to RD, DSME and specialists
  - Pharmacologic therapy: glucose lowering
  - Pharmacologic therapy: cardiorenal risk factors
  - Use of glucose monitoring and insulin delivery devices

Bacterial Cells Outnumber Human Cells 10 to 1

Bacterial Taxis?

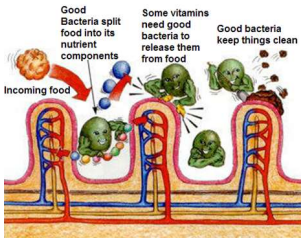
Gut Microbiome

- Part of endocrine axis
- Stabilized by 3 years of age
- Influenced by:
  - Birth method
  - Breast fed
  - Early Antibiotic use
  - Environment
  - Travel
- Help us
  - utilize energy
  - fight off invaders



How do our bacteria help us?

- Maintain physiological homeostasis and metabolism.
- Other benefits
  - pathogen displacement
  - immune system development
  - barrier fortification
  - vitamin production
  - nutrient absorption
- Forgotten organ



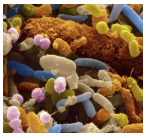
Quick Question

- How much does your gut bacteria weigh?

A. 24 ounces
B. 3 pounds
C. Less than 1 pound
D. 1.5 pounds

3 lbs of Microbes in our Gut

- This community of bacteria can be thought of as an extra 'organ' "microbiome".
- We have evolved together with our microbiome over millions of years.
- Ratios of these communities has changed over the past 30 years
- Mirrors global spikes in obesity, diabetes, allergic and inflammatory diseases
- What are we doing to change these bacteria?



Standard American Diet is SAD

- 70% of food consumed is processed
- Low fiber, high sugar
- Intake of fruit and veggies decreasing
- We are starving our good bacteria

United States: The Revis family of North Carolina. Food expenditure for one week: $341.98. Favorite foods: spaghetti, potatoes, sesame chicken.
Peter Menzel, from the book, "Hungry Planet: What the World Eats."

Guatemala: The Mendozas of Todos Santos - Food expenditure for one week: 573 Quetzales or $75.70. Family Recipe: Turkey.... VIEW MORE
Peter Menzel, from the book, "Hungry Planet: What the World

19 of 27

Reduce refined Carbs, Added Sugars - ADA

- Reduce risk of CVD and fatty liver disease
- ADA strongly discourages consumption of:
  - Sugar sweetened beverages
  - Processed "low-fat" or "non-fat" foods with high amounts of refined grains & added sugar

Sugary and processed foods can displace healthier, more nutrient dense food choices

ADA MNT Standards 2023

Until there is more evidence:

- Emphasize non starchy vegetables
- Minimize added sugars and refined grains
- Choose whole foods over highly processed foods to the extent possible
- Healthful approaches include:
  - Mediterranean-style, low-carb and plant based or vegetarian, DASH
- Plate method good getting started approach
- Refer to RD/RDN

Quick Question

- In general, how does immigrating to the U.S. impact individual's gut microbiota?

A. Increased diversity due to new food exposure.
B. A generational decline in bacterial diversity
C. They experience a sudden increase in Akkermansia muciniphila
D. Decrease in helicobacter pylori.

HEALTH

Just Months of American Life Change the Microbiome

Immigrants' gut bacteria "westernize" soon after they move to the U.S., which might influence obesity in immigrants and Americans alike.

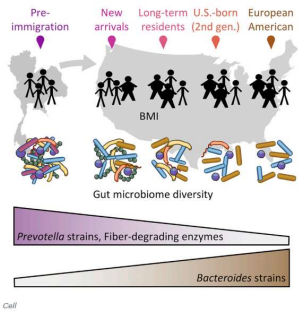
OLGA KHAZAN NOV 1, 2018 Atlantic.com Nov 2018

A Hmong woman carries grass in Vietnam. (NGUYEN HUY KHAM / REUTERS)

From Vietnam to America – Hmong immigrants microbiome shifts associated with worse health

- In Minneapolis—scientists followed a group of Hmong immigrants for 9 months.
- Increased intake of protein, sugar, and fat and processed food.
- Researchers found that the immigrants' gut microbiomes "westernized" and became less diverse
- Within a generation, Hmong women experiencing a BMI of >30 increased from 5% to 30%.

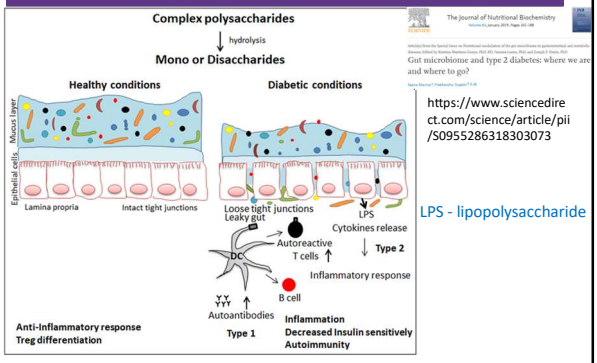
Moving to America isn't good for your health



Researchers don't know if eating a less-healthy diet increases the rate of obesity *and* changes the microbiome, or if a less healthy diet changes the microbiome *so* it makes people experience higher BMI.

Atlantic.com Nov 2018

Gut Microbiome and Diabetes



The Journal of Nutritional Biochemistry

Gut microbiome and type 2 diabetes: where we are and where to go?

https://www.sciencedirect.com/science/article/pii/S0955286318303073

LPS - lipopolysaccharide

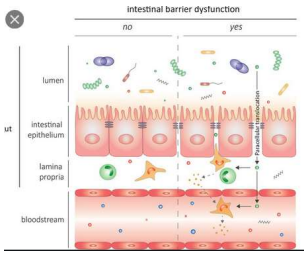
Fig. 1. Interplay between diet and the gut microbiome. Regulatory role of diet and microbiota in healthy (left) and diabetic conditions (right) has different mechanisms. In T1D, the bacterial population in gut modulates gut permeability and signaling mechanisms, thereby initiating an autoimmune response. In T2D, dysbiosis due to carbohydrate hydrolysis causes low-grade inflammation and decrease in insulin sensitivity.

Metformin helps gut microbiota in diabetes

- Induces GLP-1 secretion
- Changes in *Bacteroidetes/Firmicutes* ratio
- Capacity to induce mucin expression similar to *Akkermansia* muciniphila
- Improves the metabolic profile by lowering tissue inflammation in the presence of extra weight

Especially increases Akkermansia and Bifidobacterium.

Akkermansia Muciniphila



A. muciniphila in our mucus lining is inversely correlated with obesity and diabetes in both mice and humans.

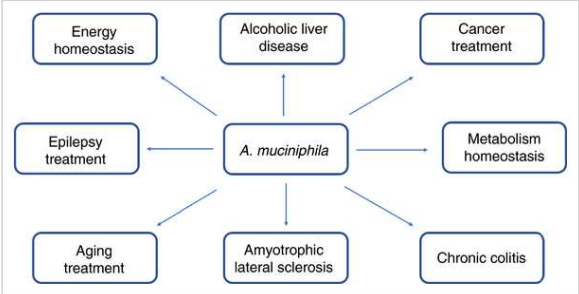
Mucus lining protector and increases presence of short chain fatty acids.

High levels of A. muciniphila is associated with improved health.

"AKK" is associated with enhanced intestinal barrier function and incretin secretion from intestinal endocrine cells. Together, these actions suppress obesity, insulin resistance, and intestinal inflammation.

Depommier C, Everard A, Druart C, et al. Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study. *Nat Med*. 2019. doi: 10.1038/s41591-019-0495-2.

The benefits of *Akkermansia muciniphila* for the host physiology



https://sfamjournals.onlinelibrary.wiley.com/doi/10.1111/jam.14911

Plant & Fiber Diet = Less inflammation

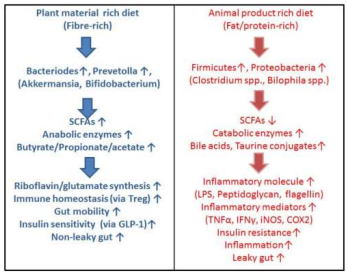


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Fig. 2. Flowcharts representing the effect of diet pattern on bacterial population in the human gut. The flowchart on the left panel (blue) indicates fiber-rich diet and the right panel (red) indicates fat/protein-rich diet.

SCFA – short chain fatty acids

https://www.sciencedirect.com/science/article/pii/S0955286318303073

Fiber – the New "F" Word

- Goal:
  - 14 gms / 1000 calories ~ 30 gms a day
- How?
  - Whole, intact grains, beans, fruits, veggies, nuts, avocados
- Why?
  - Associated with lower mortality for people with type 2.
  - Fiber intake inversely associated with type 2 diabetes
- Avoid highly processed foods
  - If label says 0-2gms of fiber per serving, low fiber food.

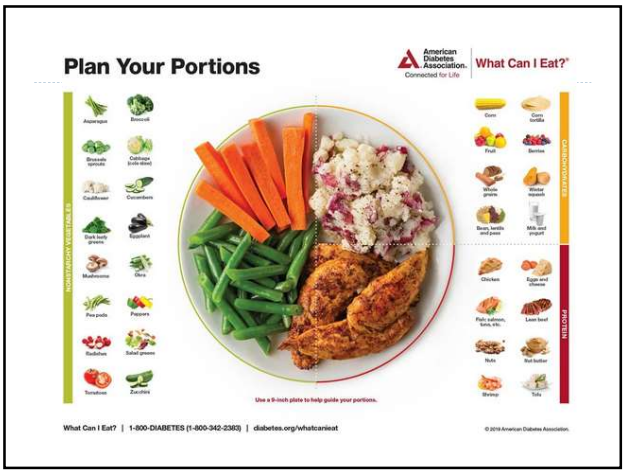
Nutrition Facts

99% Fat Free Vegetarian Chili with Beans

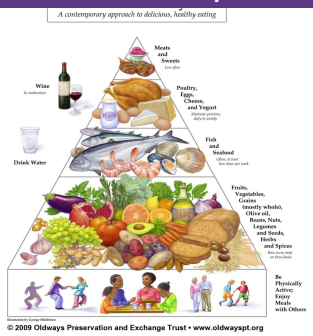
Serving Size 1.00 cup(247g)
Serving Per Container about 2

Amount Per Serving	
Calories	190
Calories from Fat	10
	%DV
Total Fat 1g	2%
Saturated Fat 0g	0%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 780mg	33%
Total Carbohydrate 35g	12%
Dietary Fiber 10g	40%
Sugars 6g	
Protein 11g	
Vitamin A 25%	Vitamin C 0%
Calcium 6%	Iron 15%

*Percentage Daily values are based on a 2,000 calorie diet. Your Daily values may be higher or lower depending on your calorie needs



Mediterranean Diet Pyramid



Getting to Better Gut Bacterial Health

Eat more PREbiotics

- Foods with indigestible fibers that nourish the good bacteria:
  - High fiber foods like, whole grains, fruits, veggies, nuts
  - High in prebiotic fibers include: Jerusalem artichokes, onions, kale, Brussels sprouts, bananas, dandelion greens & more

PRObiotics

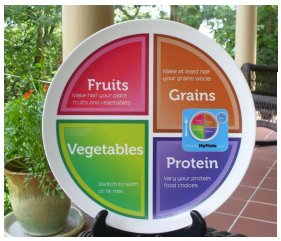
- These foods contain healthy bacteria like *Bifidobacterium* and *lactobacillus.*
  - Yogurt, Kefir – look for "live or active cultures"
  - Fermented foods like: Sauerkraut, Kimchi, Miso soup, kombucha

Kefir – Fermented Milk

From the Turkish word *keyif*, which means "feeling good" after eating

GET Lots of Diverse Fiber Foods
Goal is 25 – 30 gms day

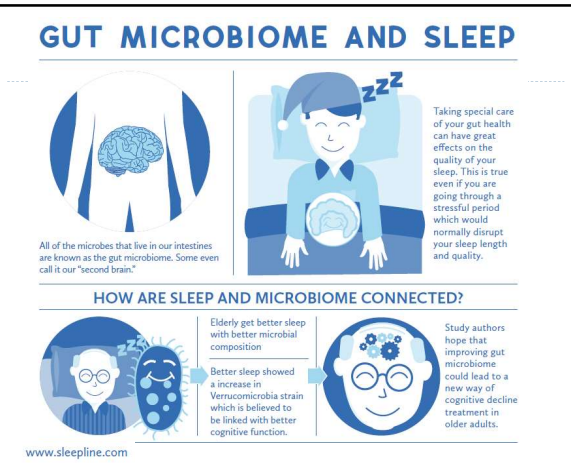
American Food Project **Full Plate Diet**



- Helps increase fiber in usual meals

Fiber is suddenly hip. Grandma, it turns out, was just ahead of her time.

—*Health & Nutrition Letter*
Tufts University
February 2009



https://www.gutmicrobiotaforhealth.com/how-to-eat-for-a-diverse-microbiota/

Take Home Message

- Get Dirty
- Limit Unnecessary C-Sections
- Breastfeed if possible
- Limit early antibiotics
- Eat a wide variety of fiber foods

100 Trillion Friends to Call Your Own

From way back when, to current time
man and bacteria have been intertwined.

Start with your head, it's a happening place,
there's staphylococcus all over your face.

Next up is gums, teeth and mouth,
You'll find streptococcus inside and out!

Now to your stomach, to keep the pH,
H. pylori is on the case!

Inside the intestines, 30 feet of tube,
3 pounds of bacteria digesting your food.

From Bacteroidetes to keep you lean,
to Firmicutes, a junk food digesting machine!

Prevotella another bug on the scene,
breaks down fiber, veggies and beans!

Lactobacillus is a newborn's friend,
lining birth canal from tip to end.

Down to your feet, in-between the toes,
that's where lots of pseudomonas grows!

Short chain fatty acids, you wanna keep them around
Protects gut mucous lining from breakin' down

So here's my message, always nourish your gut
With fresh fruit, grains, veggies, beans and nuts

More kefir, miso, sauerkraut, kimchi
Less sugar and fast foods to keep away disease

Breast feed, get dirty, limit antibiotic use
Let newborns come out through the natural shoot

Be reassured that you're never alone
You've got 100 trillion friends to call your own!

100 Trillion Friends to Call Your Own by Beverly Thomassian, RN, MPH, CDE, BC-ADM to the tune "Yeah" in the style of Usher.

Mahalo

- Questions?
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