


Intestinal Microbiota and Metabolic Syndrome - The Influence of Food and Supplements

Cynthia L. Lieu, Pharm.D.
Associate Professor of Clinical Pharmacy
USC Mann School of Pharmacy and Pharmaceutical Sciences
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Learning Objectives

1. Discuss the relationship between the intestinal microbiota and metabolic syndrome
2. Describe how changes in nutritional intake can influence the intestinal microbiota in individuals with metabolic syndrome
3. Describe how the use of supplements can influence the intestinal microbiota in individuals with metabolic syndrome

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What did you consume in the past 24 hours?

- On a piece of paper or on your electronic device:
 - List everything that you ate and drank yesterday
 - Include all ingredients to the best of your ability
- Hold onto this information throughout this presentation

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**Metabolic syndrome (MetS):
3 or more present, or drug treatment**

- High waist circumference (WC)
 - Thresholds depend on populations & country-specific definitions
- Blood TG \geq 150 mg/dL
- Blood HDL cholesterol $<$ 40 mg/dL in men & $<$ 50 mg/dL in women
- Blood pressure (BP) \geq 130/85 mm Hg
- Blood fasting glucose \geq 100 mg/dL

Nutrients 2023; 15: 640
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**Metabolic syndrome:
Comorbidities & complications**

- Obesity
- Type 2 diabetes mellitus (T2DM)
- Dyslipidemia
- Hypertension
- Atherosclerosis
- Cardiovascular disease
- Non-alcoholic fatty liver disease (NAFLD)
- Obstructive sleep apnea (OSA)
- Osteoarthritis
- Increased incidence of cancer
- Major depressive disorder (MDD)
- Polycystic ovary syndrome (PCOS)
- Male infertility
- Cognitive impairment
- Sarcopenia
- COVID-19

Nutrients 2023; 15: 640
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Intestinal microbiota

- Dependent on:
 - Mode of birth delivery
 - Breast-feeding
 - Diet
 - Medications
 - Antibiotic use
 - Personal hygiene
 - Presence of toxins
 - Genetic factors
 - Exercise
- Production of vitamins & amino acids
- Fermentation of indigestible substrates
 - Dietary fiber
 - Endogenous intestinal mucus
- Production of short-chain fatty acids (SCFA)
- Metabolism of dietary toxins & carcinogens
- Conversion of cholesterol & bile acids
- Intestinal epithelial homeostasis
- Maturation of the immune system
- Protection against pathogens

Metab Syndr Relat Disord 2022; 20(8): 429-439
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Microbiota-derived metabolites: Short-chain fatty acids (SCFAs)

- Complex resistant carbohydrates
 - Fructo-oligosaccharides, sugar alcohols, resistant starch, inulin, polysaccharides from plant cell walls
 - Escape digestion & absorption in small intestine
 - Cecum/colon: fermentation by anaerobic bacteria
- Major SCFAs: acetate, propionate, butyrate
- Improvement of gut barrier integrity
- Regulation of blood pressure
- Regulation of energy intake & energy use
- Modulation of glucose & lipid metabolism
- Mediation of immune system
- Anti-inflammatory response

Gut Microbes 2021; 13(1): e1897212

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Microbiota-derived metabolites: Trimethylamine (TMA)

Dietary components	Dietary source
Choline	Eggs, fish, seafood, liver, beef, pork, chicken, grains, milk, dairy meat, poultry, soy products, soybeans, potatoes
Phosphatidylcholine	Eggs, dairy, meat
Betaine	Shellfish, wheat, beets, spinach, fish, shrimp, wolfberry, beans
L-carnitine	Red meat, such as beef & lamb; fish, poultry, milk

Front Endocrinol 2023; 14: 1085041

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Microbiota-derived metabolites: TMA → Trimethylamine N-oxide (TMAO)

- TMA enters portal circulation to liver
- Liver:
 - Oxidized to produce trimethylamine N-oxide (TMAO)
- Reduced kidney function
 - TMAO accumulation
- Atherosclerosis
- Heart failure
- Hypertension
- Arrhythmia
- Coronary artery disease
- CVD-related diseases
 - Diabetes
 - Chronic kidney disease

Pharmacol Res 2023; 187: 106586; Front Endocrinol 2023; 14: 1085041

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Metabolic syndrome Food & supplements

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<p>Unhealthy diet: high fat, high sugar</p> <ul style="list-style-type: none"> • Dec bacterial diversity • Dec SCFA • Dec mucus secretion • Dec gut barrier function • Inc bacterial translocation • Inc low-grade inflammation • Inc insulin resistance • Inc body weight • Inc waist circumference • Inc blood pressure • Inc dyslipidemia 	<p>Healthy diet: dietary fiber rich</p> <ul style="list-style-type: none"> • Inc bacterial diversity • Inc SCFA • Inc mucus secretion • Inc gut barrier function • Dec bacterial translocation • Dec low-grade inflammation • Dec insulin resistance • Dec body weight • Dec waist circumference • Dec blood pressure • Dec dyslipidemia
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Foods	Mediterranean Diet	Western Diet
Vegetables	Every main meal (≥ 2 servings)	Rarely
Fruits	Every main meal (1-2 servings)	Rarely
Bread/pasta/rice/couscous/other cereals	Every main meal (1-2 servings, preferably whole grains)	Rarely whole grain cereals, often refined grains
Olive oil	Every main meal (3-4 servings, especially extra virgin)	Rarely olive oil, often replaced by margarine & butter
Nuts/seeds/olives	Every day (1-2 servings)	Occasionally

Nutrients 2019; 11: 1306

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Foods	Mediterranean Diet	Western Diet
Dairy foods	Every day in moderate portions (2 servings, preferably low fat)	Often high fat dairy foods
Herbs/spices/garlic/onion	Every day (less added salt)	Less often
Legumes	Weekly (≥ 2 servings)	Less often
Potatoes	Weekly (≤ 3 servings)	Less often
Eggs	Weekly (2-4 servings)	Less often
Fish/seafood	Weekly (≥ 2 servings)	Less often
White meat	Weekly (2 servings)	Less often
Red meat	Weekly (< 2 servings)	Often
Processed meat	Weekly (≤ 1 serving)	Often
Sweets	Weekly (≤ 2 servings)	Often

Nutrients 2019; 11: 1306

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Postprandial glycemic response (PPGR)

- Glycemic index (GI)
 - How food containing carbohydrates changes blood glucose levels
 - 50 g of given food compared with reference food (white bread)
- High GI
 - Hyperglycemia, insulin resistance, development of T2DM
- Low GI (55 or less)
 - Lower & slower increase in blood glucose & insulin levels
 - Low GI diet: lower TG, LDL-C
- Glycemic load (GL)
 - Combines both quantity & quality of carbohydrates

Clin Med 2019; 8: 1306

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Reducing postprandial glycemic response

- Complement meals rich in carbohydrates with foods rich in:
 - Fiber (fruits & vegetables, whole grains, legumes, & nuts)
 - Animal protein (meat, fish, eggs, dairy products, & derivatives) or vegetable protein (legumes, nuts & seeds, & whole grains)
 - Healthy fats (extra virgin olive oil, oily fish, nuts & seeds)
- Add vinegar or incorporate pickled foods to meals rich in carbohydrates with high GI
- Prioritize the consumption of underripe climacteric fruits
- Consume foods in its original form, as little processed as possible

Front Nutr 2022; 9: 1025993

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Reducing postprandial glyceimic response

- Cook pasta, rice or other starchy foods al dente
- Prioritize microwave cooking over other cooking techniques (boiling, steaming, sauteing & frying) due to its major content of resistant starch
- Cook foods such as pasta, rice or legumes beforehand
 - Leave them to cool in refrigerator for 1 day
 - Consume them cold or reheated (< 130° C)
 - To allow for formation of resistant starch
- Reduce the proportion of liquid when cooking foods such as rice & pasta
- The order matters – preferably consume:
 - First course: vegetables with foods rich in protein
 - Second course: food rich in carbohydrates

Front Nutr 2022; 9: 1025993
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Postprandial glyceimic response (PPGR): Personalized approach

- Postprandial response to same foods varied between individuals
- Personalized predictive model
 - Unique features of individual
 - Clinical characteristics, physiological variables, microbiome
 - In addition to nutrient content
- More predictive than current dietary approaches that focus only on calorie or carbohydrate content of foods
- Better to maintain blood glucose levels within limits associated with good health

JAMA Netw Open 2019; 2(2): e188102
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Personalized diet vs Mediterranean diet: Prediabetes


- Reduced daily time with glucose levels >140 mg/dL
- Reduced HbA1c levels
- Reductions significantly greater vs Mediterranean (MED) diet
- Significant between group differences maintained at 12-month follow-up

Diabetes Care 2021; 44: 1980-1991
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**Personalized diets:
Newly diagnosed T2DM**

- Significantly lower levels of CGM-based measures vs MED diet
 - Average PPGR, mean glucose, daily time of glucose levels > 140 mg/dl
- End of 6 months
 - Significant improvements in multiple metabolic health parameters
 - HbA1c, fasting glucose, triglycerides
- 61% of participants: diabetes remission (HbA1c < 6.5%)
- Some clinical improvements significantly associated with gut microbiome changes


BMC Med 2022; 20(1): 56

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Non-caloric artificial sweeteners (NAS)

- Saccharin-fed mice
 - Intestinal dysbiosis
- In high doses, saccharin, sucralose, aspartame
 - Alter composition & function of gut microbiota
 - Led to development of glucose intolerance


Metab Syndr Relat Disord 2022; 20(8): 429-439

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**Mediterranean diet:
Prevention & management of Mets**

- Black beans
- Whole soy foods
- Fish
- Pumpkin seeds
- Flaxseed
- Walnuts
- Broccoli
- Onions
- Polyphenols
 - Olive oil
 - Grapes
 - Berries
 - Bergamot
 - Pomegranate
 - Cocoa
 - Coffee
 - Tea
 - Wine

Nutrients 2023; 15: 640;
Int J Mol Sci 2022; 23: 786;
Front Microbiol 2022; 13: 997056

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Metabolic syndrome: food & supplements

- Garlic
- Ginger
- Curcumin (turmeric)
 - With piperine
- n-3 PUFA fish oil (EPA, DHA)
- Vitamin D
- Magnesium
 - Whole grains, nuts & seeds, legumes, dark-green vegetables
 - 250-600 mg/day for 7 days to 6 months
 - Blood pressure amelioration, decrease hyperglycemia, decrease hypertriglyceridemia
- Probiotics


Nutrients 2023; 15: 640; Front Pharmacol 2022; 13: 1033026; Nutrients 2021; 13: 320

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What else can we do to modulate the intestinal microbiota?

- Herbs
 - > 50,000 PPM polyphenols: clove, cinnamon, fennel seed, thyme, oregano, onion, rosemary
 - > 30,000 PPM polyphenols: above, & ginger, tarragon, cumin, basil, allspice
 - ≥ 90,000 PPM, compounds with reported antibiotic properties: clove, cinnamon, fennel seed, thyme, oregano, rosemary, black pepper, nutmeg, cardamom
 - ≥ 30,000 PPM, compounds with reported antibiotic properties: above, & sage, bay leaf, mint, parsley, cummin, allspice
- Diversity of plant foods
 - Eating more than 30 types of unique plant foods per week
 - Different types of dietary fibers & resistant starches
 - Higher microbial diversity
 - Reduction in antibiotic resistance genes

Nutrients 2022; 14: 1981; mSystems 2018; 3(3): e00031-18

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Self-assessment questions

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The intestinal microbiota dysbiosis is associated with ____.

- A. Ischemic stroke
- B. Non-alcoholic fatty liver disease
- C. Type 2 diabetes mellitus
- D. All of the above

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Microbiota-derived metabolites include ____.

- A. Omega-3 polyunsaturated fatty acids
- B. Omega-6 polyunsaturated fatty acids
- C. Omega-9 monounsaturated fatty acids
- D. Trimethylamine N-oxide

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- A. Omega-3 polyunsaturated fatty acids
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Postprandial glycemic response is influenced by ____.

- A. Intestinal microbiota
- B. Physical activity
- C. Specific foods consumed
- D. All of the above**

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The Mediterranean diet is beneficial to reduce metabolic syndrome because it is rich in _____.

- A. Animal-derived protein
- B. Refined grain
- C. Saturated fat
- D. Vegetables

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Which of the following are beneficial in modulating the intestinal microbiota?

- A. Physical activity
- B. Polyphenols
- C. Polysaccharides
- D. All of the above

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Intestinal microbiota & metabolic syndrome


- Dysbiosis associated with metabolic syndrome, comorbidities & complications
- Modulation of the intestinal microbiota for better health
 - Limit refined grains, processed foods, foods & beverages high in sugar, saturated fats
 - Mediterranean diet
 - Reduce postprandial glycemic response
 - Increase dietary fiber intake
 - Select high quality plant foods with beneficial effects
 - Eat a diverse variety of plant foods

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What did you consume in the past 24 hours?


- On a piece of paper or on your electronic device:
 - List everything that you ate and drank yesterday
 - Include all ingredients to the best of your ability
- Give 1 point for each different plant food
- Give ¼ point for each different spice
- Calculate your total number of points for the day

- What are some changes that you can make to your diet to increase the total number of points for the day?

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Questions?

CLLLieu@usc.edu
Cynthia.Lieu@usc.edu

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