BI 358 Lecture 5

...Lab today! Yes, personal, lifetime data!
+ Outline update.

I. **Announcements**
   Today DietController Nutritional Analyses in lab. Save 6 .pdfs/screenshots, flashdrive/send to your e-mail!

II. **GI Physiology Connections**
    G&H ch 72, 64, 65, 66, LS +…
    A. **Control**
       local, nervous, hormonal fig 63-2, 61-3, tab 63-1…
    B. **Secretions**
       mucus, H₂O +…, enzymes, hormones
    C. **Hydrolysis**
       Central theme of digestion ch 66 p 833-42
       1. **Carbohydrate** fig 66-1
       2. **Fat** fig 66-3+4
       3. **Protein** fig 66-2
    D. **Overview**
       Stomach, small intestine, accessory organs, large intestine fig 64-2, 66-6, 66-7, 65-10, 65-11, 64-5, 64-6…

III. **Plant-based Diet: Mounting Evidence**
    Multiple sources
    A. **American Institute for Cancer Research** Recommendations
    B. Blue Zones? What do the longest lived people do?
    C. **Okinawan Longevity Diet?** Why plant-based?
    D. Why eat carbohydrates & whole grains?
    E. Pondering Paleo? How much protein? USDA bias? WHO?
    F. **TMAO, Neu5GC & disease risk?**
    G. Environmental impact? Plant phytochemicals?
    H. How to prevent disease?
    ? I. Longevity, weight loss & intermittent fasting?
Figure 65-7 Phases of gastric secretion & their regulation.
G&H 2016 fig 65-7 p 824; G&H 2011 fig 64-7 p 780.
Cholecystokinin → Gallbladder contraction + Pancreatic enzymes

Gastrin → HCl, Pepsinogen by stomach

Motilin → ↑ Motility

Secretin → HCO$_3^-$, H$_2$O by pancreas

Cholecystokinin → Gallbladder contraction + Pancreatic enzymes

What about feedback for hunger-satiety?

Ghrelin (stomach fundus, pancreas, ...) Leptin (adipocytes)

Motility ↔ GIP

Motility ↔ GLP-1

Cl$^-$ ↔ Guanylin

↑ NaCl + H$_2$O in feces

↓ Motility ↔ Insulin

↑ Insulin

↑ Insulin

↑ Cl$^-$
Sleep More, Eat Less

Wondering why you’re so hungry? Maybe it’s because you’re not getting enough sleep.

Researchers allowed 12 healthy young lean men to sleep for either four or eight hours in a laboratory. After one night of four hours of sleep, the men ate 22 percent more calories the next day than they did after eight hours. They also reported being more hungry before breakfast and dinner.

In a separate study, scientists found that a single night with only four hours of sleep led to insulin resistance in nine healthy lean men and women in their 40s. After the night of restricted sleep, the participants were less able to move blood sugar into their cells, which suggests that their bodies were at least temporarily resistant to insulin. Insulin resistance can lead to heart disease, diabetes, and possibly breast cancer.

What to do: Get enough sleep. Most adults need 7 to 8 hours a night. (School-aged children need at least 9 hours.) Other studies that limit adults’ sleep find higher levels of ghrelin (which makes people hungry) and lower levels of leptin (which makes people feel full) in their blood. Changes in ghrelin, leptin, and insulin resistance may explain why studies find a higher risk of obesity, heart disease, diabetes, and high blood pressure in people who get too little sleep.


Promotes Leptin release!

Ghrelin

Leptin

Times of Need!

Times of Plenty!

http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/gi/ghrelin.html
## Gut Secretions

<table>
<thead>
<tr>
<th>Secretion</th>
<th>Release Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mucus</td>
<td>into GI Lumen</td>
</tr>
<tr>
<td>2. Enzymes</td>
<td>into GI Lumen</td>
</tr>
<tr>
<td>3. $\text{H}_2\text{O}$, acids, bases+</td>
<td>into GI Lumen</td>
</tr>
<tr>
<td>4. Hormones</td>
<td>into Blood</td>
</tr>
</tbody>
</table>
Hi gang!!
You need me for digestion!!

$\text{H}_2\text{O}$  +  Enzyme
Polymer to Monomer
(Many to One)

Carbohydrate

Protein + Fat

Fat

Protein

Glucose

Amino Acids

Fatty Acids + Glycerol

...Central-linking theme, again!!
Disaccharide

Monosaccharides

Peptide (portion of protein molecule)

Amino acid

Fat

Fatty acids

Glycerol

cf: G&H 2011 pp 789-93, G&H 2016 p 833-7
Carbohydrate Digestion = 1° Energy Nutrient

Starches
- Ptyalin (saliva) - 20–40%
- Pancreatic amylase - 50–80%

Maltose and 3 to 9 glucose polymers
- Maltase and α-dextrinase (intestine)

Glucose

Lactose
- Lactase (intestine)

Galactose

Sucrose
- Sucrase (intestine)

Fructose
Why Do Some People Have Trouble Digesting Milk?

- Ability to digest milk carbohydrates varies
  - Lactase
    - Made by small intestine
- Symptoms of intolerance
  - Gas, diarrhea, pain, nausea?
- Milk allergy?
- Nutritional consequences
- Milk tolerance and strategies
HIGH FAT FOODS

An LDL to HDL ratio greater than 5 to 1 in men or 4.5 to 1 in women.

Increased risk of heart disease.
Fat Digestion = $2^0$ Energy Nutrient

1. Fat + (Bile + Agitation) → Emulsified fat
2. Emulsified fat → Fatty acids and 2-monoglycerides by Pancreatic lipase.

G&H 2011 fig 65-4 p 792
G&H 2016 fig 66-4 p 836
HIGH PROTEIN (FAT?) FOODS?
Where does enzymatic digestion of protein begin?
Zymogen = inactive precursor

Gastric lumen

Autocatalysis

Pepsinogen → Pepsin

Digestion

HCl

Protein

Peptide fragments

Various amino acids

= Enzymatic splitting of a chemical bond

LS2 2006
G&H 2011
fig 64-4
G&H 2016
fig 65-4
Protein Digestion = 3° Energy Nutrient

Proteins → Pepsin → Proteoses, Peptones, Polypeptides

Trypsin, chymotrypsin, carboxypolypeptidase, proelastase

Polypeptides + Amino acids → Peptidases → Amino acids
What is the major function of the small intestine?

Absorption!!
Why is the pancreas so unique?
Enzymes specific for all 3 energy nutrients!

The glandular portions of the pancreas are grossly exaggerated.
Poor motility causes greater absorption, and hard feces in transverse colon cause constipation.

Excess motility causes less absorption and diarrhea or loose feces.
Questions + Discussion
Plant-based diet benefits: Mounting evidence
Recommendations for CANCER PREVENTION

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 minutes every day.
3. Avoid sugary drinks. Limit the consumption of energy-dense foods particularly processed foods high in added sugar, or low in fiber, or high in fat.
4. Eat more of a variety of vegetables, fruits, whole grains & legumes such as beans.
5. Limit consumption of red meats (such as beef, pork & lamb) & avoid processed meats.
6. If consumed at all, limit alcoholic drinks to 2 for men & 1 for women a day.
7. Limit consumption of salty foods & foods processed with salt (sodium).
8. Don't use supplements to protect against cancer.
The World’s Longest-Lived People! ● Blue Zones! ●

- Lomo Linda, CALIFORNIA
- Sardinia, ITALY
- Okinawa, JAPAN
- Nicoya, COSTA RICA
- Ikaria, GREECE

M Poulain & Coworkers. Experimental Gerontology, Sep 2004
1. Eat a little bit better!
2. Move a little bit more!
3. Socialize more!
4. Strong sense of purpose!

https://en.wikipedia.org/wiki/Blue_Zone
https://bluezones.com/
70% Sweet Potatoes
12% Rice
7% Grains & Wheat
6% Soy & legumes
4% Additional vegetables
3% Fruit
2% Oils
1% Nuts (Protein)
1% Other potatoes
1% Seaweed
1% Sugars
1% Fish
1% Dairy
1% Eggs
1% Pork-Meat
1% Flavorings & Alcohol

85% Carbohydrates
9% Protein
6% Fat
85-10-5
1785 Calories

96% Vegan Diet
98% Vegetarian
99% PescaVeg
<4% Animal Prod
<1% Fish
<1% Meat-Pork

Note: These are the Actual Food Measurements of the Centenarians, not the diet of All island Okinawans or the ones who died, but the ones who lived.
I prefer glucose!
Me too!
Me three!
Me too!
Why Eat Whole Grains?

Based on existing evidence, eating whole grains is definitely good for our health.

Shengmin Sang, Professor of Food Science & Human Health North Carolina A&T

Fiber  
- ↑ fullness, motility, beneficial bacteria, wt control
- ↓ cholesterol, insulin response, inflammation, diabetes and CVD risk...

B-vitamins  thiamin, niacin, riboflavin  ↑ energy metabolism

Folate  
- ↑ red blood cells, ↓ neural tube defects

Iron  
- ↑ O₂ carrying, ↓ iron-deficiency anemia in women

Magnesium  
- ↑ bone building & muscle energy release

Selenium  
- an anti-oxidant, protects body cells & ensures a healthy immune system...

https://www.choosemyplate.gov/grains-nutrients-health
Pondering Paleo?

Evolutionary Biologist
Behavioral Ecologist
U Minnesota
How much protein do you need?

Not much! 0.8 g/kg or 0.36 g/lb of body wt/d

50 kg or 110 lb female? ~ 40 g/d
80 kg or 176 lb male? ~ 64 g/d

Boneless, skinless, cooked chicken breast 6-8 oz, 53 -70 g of protein!

Average US woman gets 35% > RDA!
Average US man 65% > RDA!
MyPlate launched June 2, 2011

1. **Vary your veggies.** Fill ½ your plate with fruits & vegetables!

2. **Focus on fruits.** Whole fruit preferable to juice, but any fruit counts! Fill ½ your plate with fruits & vegetables!

3. **Make at least ½ of your grains whole grains!**

4. **Go lean with protein.** Keep protein to < ¼ plate! Nuts, beans, peas, seeds, poultry, lean meat, seafood,…

5. **Get your calcium-rich foods.** Buy skim or 1% milk. Go easy on cheese!
Dietary Protein, Shakes, Supplements &…?

Dietary Protein and EARLY Cancer

http://www.aicr.org/about/advocacy/the-china-study.html
http://www.nutritionfacts.org/
WHO says to cut down on meat?

When I saw the headlines in October that meat was linked to cancer, I braced myself for the inevitable brouhaha. The news was that the International Agency for Research on Cancer (IARC), part of the World Health Organization (WHO), concluded that processed meats like hot dogs, bacon, and ham almost certainly increase the risk of colorectal cancer—by 18% per daily serving—and that red meat probably does as well.

But we've heard about this link many times before. Over the past 20 years, many observational studies have found that people who regularly eat red or processed meats have higher rates of several cancers, notably of the colon and rectum. And lab studies have shown that compounds formed when meat is processed (that is, smoked, salted, or cured) or cooked at high temperatures can cause cancer in animals or cells. All that research served as the basis of the IARC conclusions. But even in 2007 the World Cancer Research Fund, another key group of experts, concluded that there was “convincing” evidence that these meats increase the risk of colorectal cancer. And since 2002, WHO has advised people to moderate their consumption of processed meat, as do the still-pending 2015 Dietary Guidelines for Americans.

What elicited the most heated reaction in the press and blogosphere and especially from the meat industry was the fact that the IARC put processed meats in its Group 1—“carcinogenic to humans”—which includes tobacco smoking and asbestos. (It put red meats in Group 2A—“probably carcinogenic.”) The IARC clearly explained that this classification merely indicates the strength of the evidence that something causes cancer, not the degree of risk. In fact, it said that the increased risk from red or processed meat is “small” for individuals, though potentially important for public health since so many people eat meat.

What about that 18% increase in risk? The IARC estimated that for every serving of processed meat (just under 2 ounces) or red meat (3½ ounces) eaten daily for years, the lifetime risk of colorectal cancer goes up by about 18%. But this is what’s known as relative risk, which can be misleading. For instance, the lifetime risk of developing colorectal cancer in the U.S. is about 5%. An 18% increase does not mean 5% + 18% = 23%, but rather 5% + (18% of 5%) = 6%. That means one extra case of colorectal cancer per 100 meat eaters. In contrast, smoking increases the lifetime risk of lung cancer by roughly 2,000%—from about 1 per 100 people to about 20 per 100. So while IARC may classify both processed meat and smoking as Group 1 carcinogens, there's no comparison in their risks.

In fact, IARC cited estimates that 34,000 cancer deaths per year worldwide can be attributed to diets high in processed meat. In contrast, tobacco causes nearly 2 million cancer deaths per year.

I should add that I don’t think it has been clearly established that meat causes cancer. Proving that foods cause or help prevent cancer is difficult for many reasons. Notably, the observational studies upon which the IARC classifications were largely based can only find associations—they cannot prove cause and effect.

That said, there are plenty of other reasons to moderate your intake of red meats and limit processed ones. There's strong evidence linking them to cardiovascular disease and a variety of other disorders, though it's not clear which compounds in them are the possible culprits. What's more, eating more plant-based foods and less meat is better for the planet, resulting in less greenhouse gas production.

And there's a far surer way to reduce the risk of colorectal cancer than tinkering with your diet: Get screened.
Gut Bacteria Involved in **Inflammation & Atherosclerosis**?

Meat & Eggs → L-Carnitine & Choline → Trimethyl Amine (TMA) → TMAO → **Inflammation & Atherosclerosis**

The pathway linking diet, gut microbes and TMAO to a growing collection of disease states.

- Dietary Choline & L-Carnitine
- Gut Flora
- TMA = Trimethyl Amine
- Hepatic FMOs
- TMAO
- Choline
- Heart Failure
- Atherosclerosis
- Kidney Disease
Red Meat-Derived Glycan Promotes Inflammation & Disease

- N-Glycolylneuramic acid (Neu5GC)
- Ab to Neu5GC
- Neu5GC Ab

Immune System

Atherosclerosis
- Chronic Inflammation
- Amyloid-A
- Acute Phase Proteins
- IL-6

Cancer

Xeno Auto-Antigen!
- Anti-Neu5GC Ab

Source: After AN Samraj, PNAS, 2015, 112(2), 542-7. http://m.pnas.org/content/112/2/542.long
Environmental Impact

Grain required for:

- ~61 kg 1 kg of Beef
- ~38 kg 1 kg of Pork
- ~13 kg 1 kg of Fish

~33% of H₂O farm animal footprint due to beef production

Phytochemicals ≡ Plant chemicals

1️⃣ **Anti-oxidants**
   - protect DNA from oxidative damage

2️⃣ **Protein synthesis**
   - regulation/control

3️⃣ **Hormone-like action**
   - endocrine mimicry

4️⃣ **Blood effects**
   - modify blood chemistry

Potential regulators of health!

10s of thousands!

*Phytochemicals* ≡ *Plant chemicals*

aroma, color, taste
Broccoli sprouts may contain ~ 10,000 unique phytochemicals!
≥ 5 tomato-containing meals per week may protect from cancers of the esophagus, stomach & prostate!
...but, the phytochemical candidate, lycopene with anti-oxidant activity is also in guava, papaya, pink grapefruit & watermelon!
With the right food choices, physical activity, and not smoking, we could prevent about 90% of diabetes, 80% of heart disease, about & 70% of stroke!
10 CANCER PREVENTION RECOMMENDATIONS

1. Maintain a healthy weight
2. Move more
3. Eat well
4. Enjoy a plant-based diet
5. Reduce red meat, avoid processed meat
6. Cut down on alcohol
7. Eat less salt
8. After treatment, cancer survivors should follow the cancer prevention recommendations
9. If you can, breastfeed your baby
10. For cancer prevention, don’t use supplements

And always remember – do not smoke or chew tobacco.
An Anti-Aging Diet?
CALERIE STUDY
Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy

- 2-yr kcal restriction, assess biomarkers longer, healthier life
- 218 people, 21 – 51 yr, ½ ~ overwt, ½ normal wt
- Usual diet or cut kcal by 25% (achieved ~ 12% so < ½ goal)
- If cut calories, lost 10% body wt ~ 17 lb & kept off for 2 yr
- Cardiometabolic Δs: ↓ Cholesterol, ↓ Inflammatory markers, ↑ control blood sugar control w/o adverse sexual or immune function Δs

Some bone loss, but attributed to weight loss.

5:2 Intermittent “Fasting”

2 Days a Week

500-CALORIE DAY

**Breakfast**
Plain low-fat yogurt with berries
200 calories

**Dinner**
Mixed greens with grilled chicken
300 calories

NAHL 2017 May
5:2 Intermittent “Fasting”

600-CALORIE DAY

**Breakfast**

- Oatmeal with peaches, berries, and milk
- 250 calories

**Dinner**

- Baked salmon with asparagus and tomatoes
- 350 calories
Human Intermittent Fasting Studies

- ~100 overweight or obese women
- ½ cut 25% kcal every day
- ½ ate normally 5 d, but only 650 kcal/d for 2 d/wk
- After 3–6 mo, each group lost ~ same amount of wt but women on 5:2 diet had better insulin function!
- Likely easier for most humans to restrict for only 2 d/wk!


Intermittent Fasting Metabolic Adaptations

Liver (hepatocyte) → FGF21 → β-HB → Muscle (myocyte) → ATP production

Liver (hepatocyte) → FGF21 → β-HB → Heart (myocyte) → Improved performance

Liver (hepatocyte) → Acetoacetate → β-HB → ATP production

Liver (hepatocyte) → Acyl CoA → FFA → Muscle (myocyte) → ↑ Mitochondrial biogenesis

Liver (hepatocyte) → Acyl CoA → FFA → Heart (myocyte) → ↑ Mitochondrial biogenesis

Liver (hepatocyte) → Acyl CoA → FFA → Brain (neuron) → ↓ mTOR pathway

Intestine → Fat (adipocyte) → FFA → Vasculature → Improved performance

Intestine → Fat (adipocyte) → TG → Vasculature → Stress resistance

Intestine → Microbiota → FFA → Vasculature → BDNF signaling

Intestine → Microbiota → FFA → Vasculature → Synaptic plasticity

Intestine → Microbiota → FFA → Vasculature → Neurogenesis