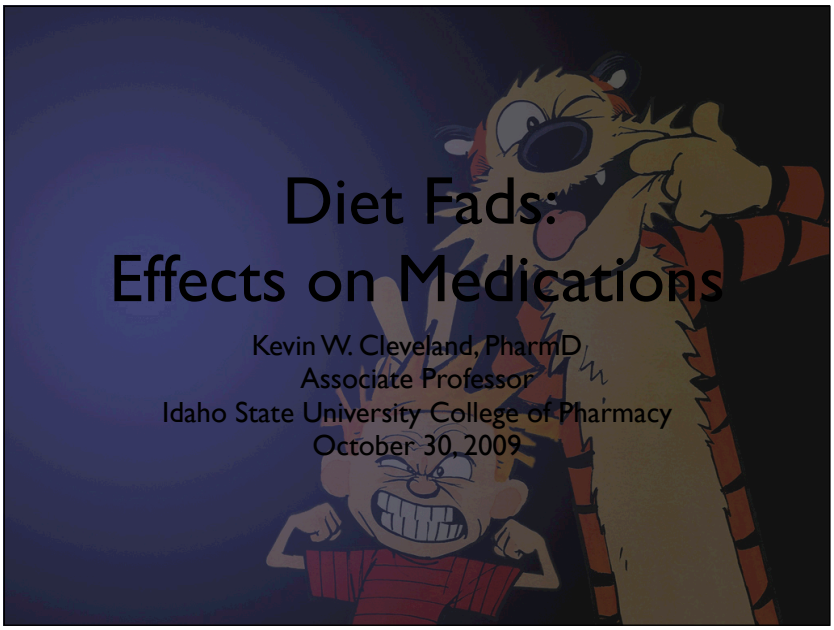

Diet Fads: Effects on Medications

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Objectives

- Understand the mechanisms of drug-food interactions and their impact on healthcare
- Understand the difference between pharmacokinetic and pharmacodynamic food interactions
- Be able to differentiate between different diet alternatives - focus on macronutrients
- Be able to identify potential drug-food interactions base on the composition of a diet
- Know where to find clinically relevant information on drug-food interactions

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Introduction

- More than 1 billion adults are considered overweight
  - ✦ Current trends predict by 2030 – 86.3% will be overweight or obese**
- Second leading cause of preventable mortality in the US
- Obesity and being overweight are risk factors for many disease states
  - ✦ Associated with increase in healthcare costs

Ref: WHO;Wolf;Allison DB; Kassirer JP, Zhu S, Calle; Mokdad; **Wang Y, Beydoun MA, Liang L, Caballer B, Sumanyika SK. Will all Americans become overweight or obese? Estimating the progression and cost of US obesity epidemic. *Obesity* 2008;16(10):2323-2330.

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The Heavy Burden of Weight

- 9.1% of U.S. medical expenditures
  - ✦ Estimated $92.6 billion/year
  - ✦ Direct costs <$50 billion
  - ✦ Indirect costs <$40 billion
- Costs of obesity is projected to reach $860 billion by 2030
- HTN, hyperlipidemia, DM-type 2, CAD, and stroke - 85% of these costs
- Healthcare costs - non-obese < obese patients

National Health and Nutritiohn Examination Survey 1999-2000
Finkelstein EA, etal. Health Affairs 2003;W3:219-226

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Introduction

- Each year it is estimated 15-35% of Americans try to lose weight
- Weight loss schemes are big business
  - ✦ Estimated $30-50 billion spent each year - with little to no improvement in body weight
  - ✦ Most of the expense is on various diet programs
- The clinical rub - most individuals do not know that changes in their diet regime can have dramatic effects on their pharmacotherapy

Ref: Willamson DF, Lissner L, Eonomist; Schmidt LE)

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Diet Overview

- Caloric intake is critical factor in weight loss
  - ✦ Diet of 1400-1500 calories/day → weight loss
  - ✦ Debate of quantity vs. quality
- Some studies indicate that extremes alterations in macronutrient content of the diet (protein, fat, or carbohydrates) will result in significant weight loss

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Macronutrient Overview

- Protein
- Fat
  - ✦ Saturated (no double bonds, solid)
  - ✦ Unsaturated (one or more double bonds, liquid)
    - ✳ MUFA & PUFA
- Carbohydrates
  - ✦ Simple carbohydrates – refined sugars
  - ✦ Complex carbohydrates
    - ✦ Starch
    - ✦ Whole grains
    - ✦ Fiber

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Drug-Food Interaction Overview

- Drug-food interactions - clinical importance
  - ✦Decrease the response of the drug
  - ✦Acute or chronic drug toxicity
  - ✦Drug alters the nutritional status
- Drug-food interactions contribute to morbidity

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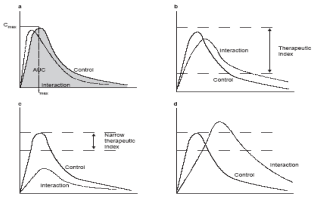
Mechanism of Drug-food Interactions

- Pharmacokinetic interactions
  - ✦Food effects the absorption, distribution, metabolism or elimination
- ✦ Pharmacodynamic interactions
  - ✦Food effects on the pharmacologic action of medications



Clin Pharmadokinet 1999; 36(3):235

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Mechanism of Drug-food Interactions

- Characteristics of the drug
  - ✦Physical and chemical properties
  - ✦Drugs in the same class will exhibit similar reactions

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Mechanism of Drug-food Interactions

- Characteristics of the meal
  - ✦Fat content
  - ✦Fiber content
  - ✦Protein content
  - ✦Carbohydrate content
  - ✦Acidic foods
  - ✦Basic foods

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Mechanism of Drug-food Interactions

- ✦Availability and the effect are closely related
  - ✦Dependent on absorption and first-pass metabolism
- ✦Most important drug-food interaction is one that affects the absorption
  - ✦Direct binding or change in environment
  - ✦Either increased or decreased absorption

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Mechanism of Drug-food Interactions

- Interactions affecting metabolism, distribution, or elimination are not as common
  - ✦Increase risk of therapy failure
  - ✦Increase risk of toxicity
  - ✦Grapefruit juice and CYP 3A4

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Mechanism of Drug-food Interactions

- Nutritional Effects
  - ✦Antinutrient effect
  - ✦Malabsorption via competitive binding
  - ✦Altered food intake
    - Stimulants, antidepressants decrease
    - Alcohol, antidepressants increase
  - ✦Alter electrolyte balance
    - Most diuretics will cause potassium loss
    - ACE-Inhibitors will cause potassium retention

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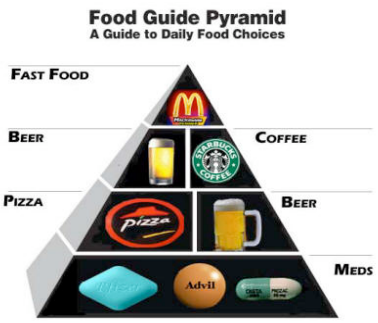
America's Food Pyramid



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Macronutrient Breakdown of Diet Fads

Type of Diet	Fat (% calories)	CHO (% calories)	Protein (% calories)
High-fat/low-CHO/ high-protein	55-60	<20 (<100g)	25-30
Moderate-fat, balance nutrient reduction (isocaloric)	20-30	30-40	30-40
Low to moderate fat/ high-CHO/low to moderate protein	20-30	55-60	15-20
Low-Fat to Very-low-fat/high-CHO/ moderate protein	<20 (VLF<10)	>65	10-20

Characterization of diets as percentage of calories

(Adapted from Freedman MR, etal. pg. 3S)

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High-protein/Low-CHO/High-fat Diets

- Popularized by: Atkin's Diet Revolution, South Beach Diet, Sugar-Busters, Protein Power Diet
- High protein leads to high satiety, decreased BG and insulin levels - leading to utilization of fat stores and subsequent weight loss
- High levels of dietary fat tends to slow gastric emptying

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Drug Interactions with High-protein/Low-CHO/High-fat Diets

- Levothyroxine - competitive binding at absorption sites
- Levodopa - inhibition of BBB penetration of medication via competitive binding to LNNA carriers
- Theophylline
  - Some theophylline SR formulations dose dumps with high fat meals
  - Theophylline increased clearance with high protein intake
- Phenytoin - decreased absorption with diet high in protein

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Drug Interactions with High-protein/Low-CHO/High-fat Diets

- Propranolol - increased clearance with high protein
- MAOIs - diet composition of certain Low-CHO diets
- Fat-soluble drugs – carbamazepine, spironolactone, diazepam
  - Enhanced absorption with higher dietary fat intake
- Atovaquone - increased absorption with higher dietary fat intake
- Warfarin - increase protein binding leading to decrease in INR
- Griseofulvin availability is increased when taken with high-fat meals

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High-protein/Moderate-fat - Isocaloric Nutrient Diets

- Popularized by: The Zone Diet and Body-for-LIFE diet
- Higher protein content will lead to increased satiety, metabolism, and lean mass retention
- Lower CHO intake leads to lower blood glucose and insulin levels - increased body fat utilization

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Drug Interactions with High-protein/ Moderate-fat - Isocaloric Nutrient Diets

- Same concerns with high protein diets
- Moderate fat intake not a big concern since it is similar to what is recommended for daily intake
- Since these diets promote high fiber intake - can lead to potential medication interactions

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Drug Interactions with High-protein/ Moderate-fat - Isocaloric Nutrient Diets

- Decreased absorption with fiber
  - Digoxin
  - Lovastatin
  - Metformin
  - Penicillins
  - Furosemide
  - Acetaminophen
- Levodopa - high fiber diets increase availability

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High-CHO/Low- to Moderate-protein/Low- to Moderate-fat Diets

- Popularized by: Weight Watchers, DASH Diet, Dietary Guidelines for Americans (USDA Food Pyramid)
- Claim - healthiest way to lose weight due to increased intake of fruits/vegetables, whole grains
- Weight loss most likely due to high fiber intake - increased bulk and satiety

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Grapefruit Juice Interaction

- Mechanism: inhibition of CYP 3A4 enzyme in the GI tract
- Generally leads to increase availability and concentration of medication

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Grapefruit Juice Interaction

- Amiodarone
  - GFJ significantly increases availability
  - Leading to clinically unpredictable results and increasing risk of toxicities
- Sildenafil
  - GFJ delays absorption but increases availability leading to unpredictable clinical effects
  - Possible increase risk of CV toxicities

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Grapefruit Juice Interaction

- Methadone
  - GFJ increases absorption significantly
  - Increased risk of toxicity but clinically not been shown to be significant
- Diazepam
  - GFJ increases diazepam blood concentration via metabolism inhibition
  - Increased effects of diazepam
- Management: Avoid concomitant administration of GFJ and problem medications

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Grapefruit Juice Interaction

- Statins - lovastatin, atorvastatin, simvastatin
  - Availability increased by 1400%, 200%, 1500% respectively
- Calcium channel blockers
  - Felodipine availability increased by 284%
- Antihistamines
  - Fexofenadine absorption decreased by 24-68%
  - Loratadine absorption enhanced with grapefruit
- Cyclosporin increased availability by 47-60%

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Pomegranate Juice

- Has positive effects on BP and lipids
- ACE-Inhibitors
- Antihypertensives
- Cytochrome P450 Inhibitor
  - 2D6 – Amitriptyline, codeine, fluoxetine, tramadol, tamoxifen
  - 3A4 – CCBs, indinavir, midazolam propranolol, statins

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Low-fat to Very-low-fat Diets

- Popularized by Ornish Diet Program and Pritikin Diet
- High-CHO content from fiber and extreme reduction in fat intake leads to weight loss and other health benefits

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Low-fat to Very-low-fat Diet Interactions

- Same concerns as mentioned with high fiber intake
- Phenytoin levels may increase with high-CHO intake
  - Due to delay in gastric emptying resulting in improved absorption
- Decreased absorption of fat soluble medications
  - Vitamins A,D,E, and K

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Recommendations

- Best resources
  - Drug Interaction Facts (Herbal Supplements and Food)
  - Micromedex
  - Lexi-comp
  - Drug information compendiums
  - Primary literature (Pubmed, IPA)
  - Idaho Drug Information Service
    - (208) 282-4689

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Recommendations

- Administration of drugs in regards to meals
  - Medications need to be taken on empty stomach
    - Wait 1 hour after taking medication
    - Wait 2 hours after the meal to take medication
- **Most importantly: patients need to take medication consistently independent of the mechanism of**

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Questions

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