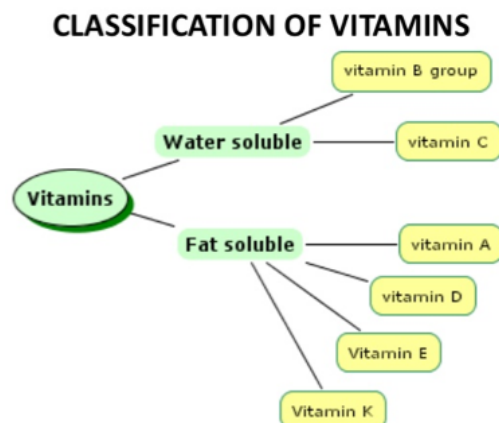


## **Vitamins (Ch. 81)**

### **Vitamins**

- Organic compounds required in small amounts for energy transformation & metabolic processes
- Fat soluble vitamins can be stored for later.
- Water soluble vitamins get used up by the body, and whatever is leftover is immediately excreted
- Mixed evidence → ‘don’t stop - don’t start’
  - Mixed evidence regarding taking multivitamins. There’s no evidence saying that you should stop taking the vitamins if you already are - there’s no evidence indicating that it’s bad for you. At the same time, there’s no evidence to support that you should start taking them either.
- Healthy diet = best behavior
- Watch out for excessive vitamin A & E, could be detrimental in very large amounts
- Evidence for 3 individual vitamins:
  - Vitamin B12 → everyone 50+ years old
  - Folic acid (B9) → childbearing age women
  - Vitamin D + calcium → postmenopausal women



### **Dietary Reference Values**

- Adequate intake
  - Estimation of RDA when not enough evidence available
- Estimated average requirement
  - Level required for 50% of individuals (regardless of conditions)
  - Used to establish the RDA following extensive research
- Tolerable upper level intake
  - Maximum dose without significant ADR risk → safety index
- Recommended daily allowance
  - Average daily intake necessary for healthy individuals
  - Varies according to sex, age, pathologies

### **Vitamin A (Retinol)**

<b>Functions</b>	Dim light adaptation Embryogenesis & spermatogenesis Skin & mucous membrane integrity Immunity & growth
<b>Deficiency</b>	Night blindness Corneal or conjunctiva lesions Skin/mucous membrane lesions
<b>Toxicity</b>	Liver injury

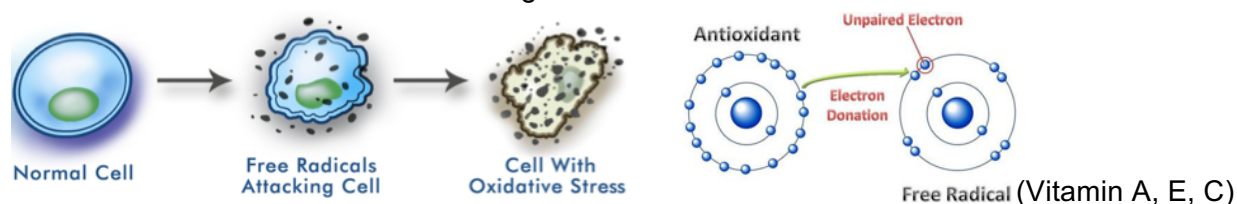
	Bone-related disorders Birth defects
<b>Therapeutic use</b>	Deficiency prevention Retinol derivatives → acne & skin disorders

### Vitamin E

<b>Functions</b>	Antioxidant with unknown metabolic role
<b>Deficiency</b>	Neurologic deficits
<b>Toxicity</b>	Increased heart failure risk & cancer progression & all-cause mortality Inhibit exercise benefits on insulin sensitivity Inhibit platelet aggregation → increased hemorrhagic stroke risk
<b>Potential benefits</b>	Hemolysis & age-related macular degeneration prevention Many other false claims

### The Case Against Antioxidants

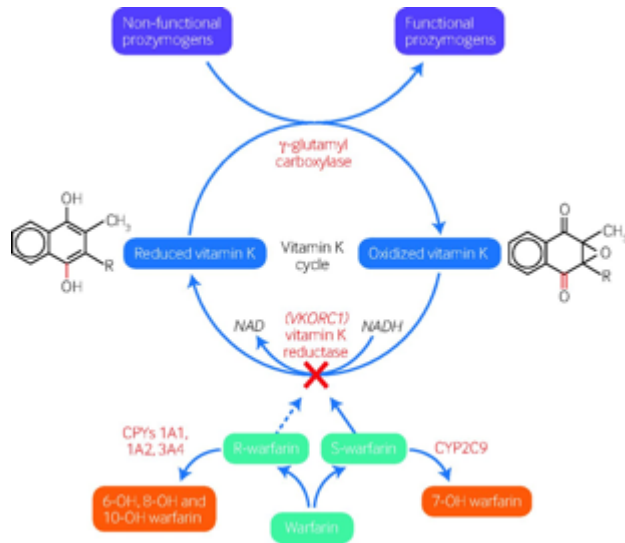
- Theory & observational studies → promising results!!
- Actual robust scientific inquiries
  - Excessive beta-carotene (vitamin A) → increase lung cancer risk in smokers
  - Excessive vitamin E → increase prostate cancer risk & strokes
  - Other antioxidants → drug interactions



- Meta-Analysis conclusion:
  - “There is no evidence to support the use of vitamin and antioxidant supplements for prevention of cardiovascular diseases.”
  - “The meta-analysis of randomized controlled trials indicated that there is no clinical evidence to support an overall primary and secondary preventive effect of antioxidant supplements on cancer. The effects of antioxidant supplements on human health, particularly in relation to cancer, should be overemphasized because the use of those might be harmful for some cancer.”

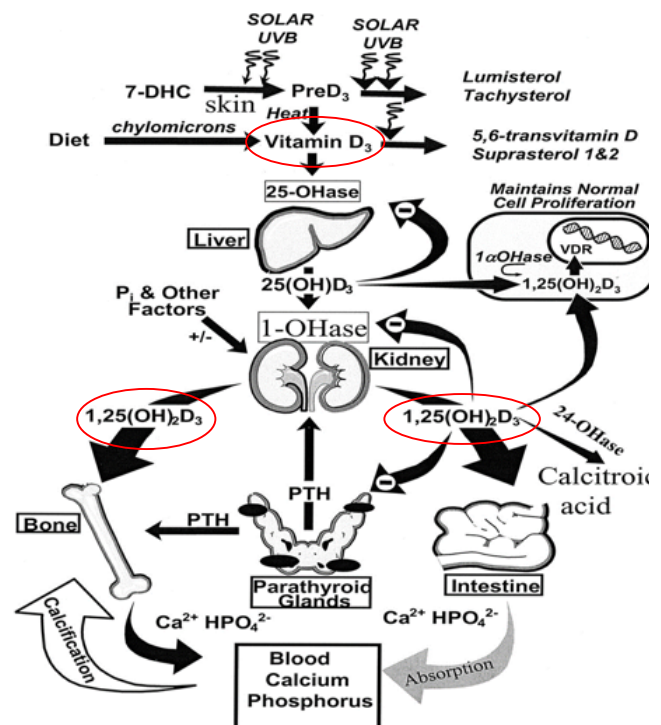
### Vitamin K

<b>Functions</b>	Prothrombin synthesis Activation of clotting factors VII, IX & X
<b>Deficiency causes</b>	Malabsorption syndrome or decrease (bile salts) Antibiotics → decrease GI flora vit K synthesis Warfarin toxicity
<b>Deficiency symptoms</b>	Prophylaxis injection in newborns Warfarin antidote
<b>Adverse effects</b>	IV administration → hypersensitivity/anaphylaxis risk Hyperbilirubinemia → kernicterus of newborn

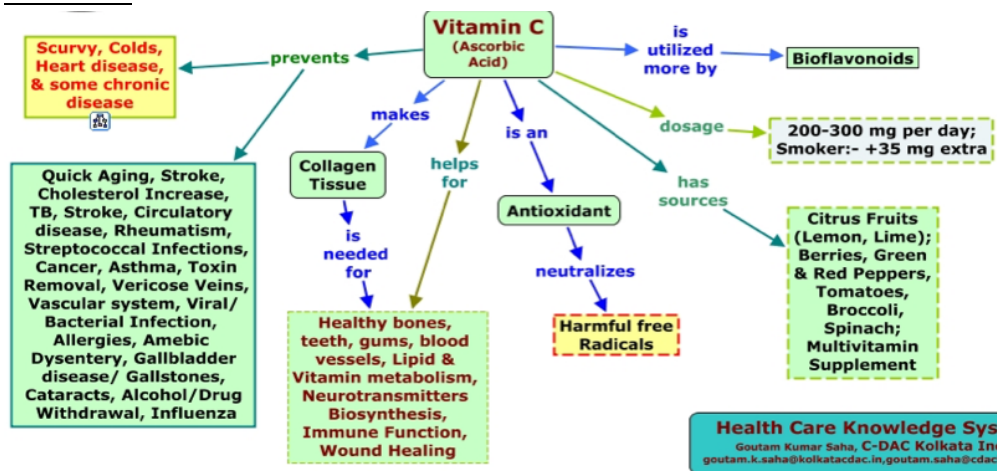


### Vitamin D

- Proven benefit = bone homeostasis
- Debated evidence → prevention of:
  - Arthritis & autoimmune disorders
  - Breast, prostate & colon cancer
  - Heart disease & T1DM
- Most important in children because, as adults, our growth period is over and we already have lots of calcium.



## Vitamin C



<b>Deficiency</b>	Scurvy → lethal collagen tissue/matrix dysfunction
<b>Therapeutic use</b>	Scurvy prevention/treatment All other claims disproved (ex. Wound healing, common cold, etc)
<b>Adverse effects</b>	GI Sx: nausea, diarrhea, cramps

## Vitamin B Group

### Niacin (B3)

<b>Functions</b>	Precursor of NAD & NADP → major coenzymes
<b>Deficiency</b>	Pellagra: <ul style="list-style-type: none"> <li>• Dermatitis, skin scaling</li> <li>• GI distress (cramps, diarrhea)</li> <li>• CNS: irritability + insomnia + memory loss</li> </ul>
<b>Therapeutic use</b>	Pellagra prevention & treatment
<b>Adverse effects</b>	Low doses = none Very high dose = dizziness + nausea

Nicotinamide = preferred for Pellagra Tx

- Less toxicity
- No vasodilation

### Pyridoxine (B6)

<b>Functions</b>	Amino acid synthesis coenzyme
<b>Deficiency causes</b>	<b>Isoniazid (tuberculosis) therapy</b> Poor diet Inborn metabolism error
<b>Deficiency symptoms</b>	Peripheral neuritis, Convulsions, Depression, anemia, seborrheic dermatitis
<b>Therapeutic use</b>	Deficiency prevention & treatment
<b>Adverse effects</b>	Low doses = none Very high dose = neurologic injuries <b>Drug interaction: decrease L-DOPA efficacy</b>

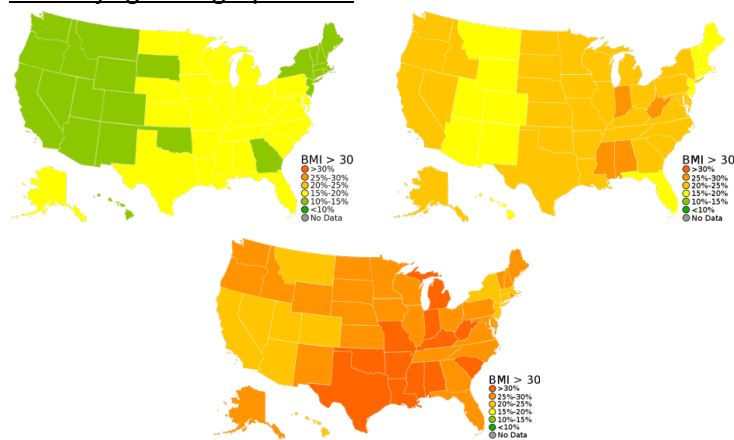
### Folic Acid (B9) & Cyanocobalamin (B12)

- Discussed in the hemodynamic lecture
- Involved in RBC development
- Review those slides for information on actions & deficiencies

### Drugs For Weight Loss (Ch. 82)

#### **PATHO REVIEW**

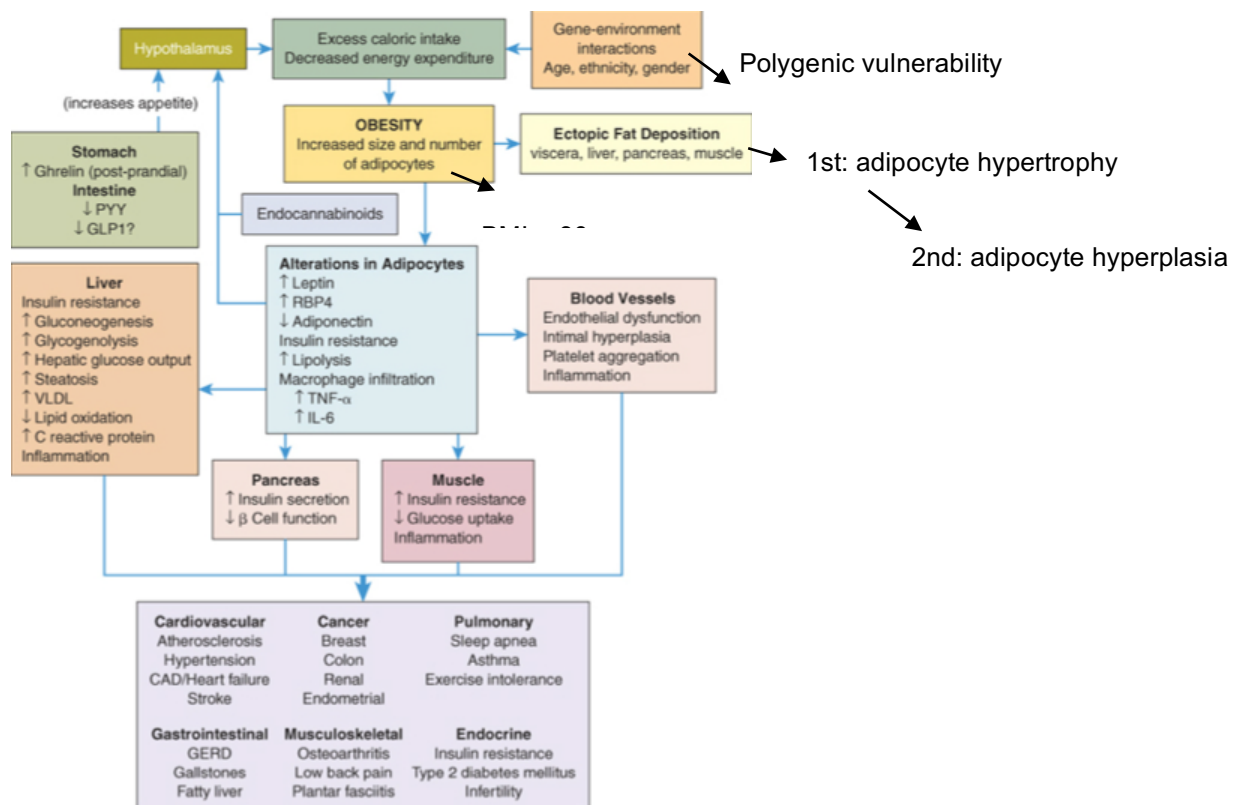
#### Obesity: growing epidemic



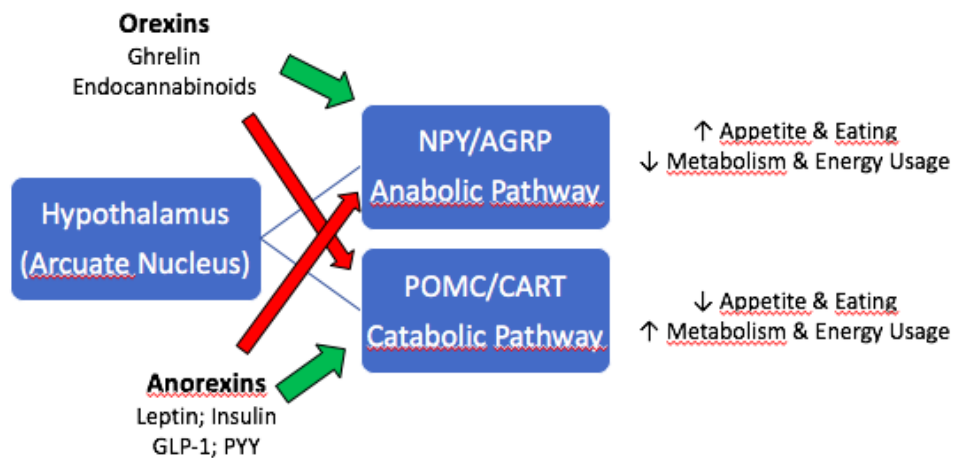
#### Obesity

- Caloric (appetite) input-output imbalance
- Increase body fat & metabolic disorder
- Association with:
  - Mental retardation (down syndrome)
  - Endocrine alterations (cushing's hypothyroidism)
  - Mutations: (increased appetite, obesity genes, leptin)

- Many adverse physical & psychosocial outcomes



### Appetite Regulation



### Adipocytes

- Fat (energy) storage cells + endocrine cells → release adipokines
  - Ex. Leptin & adiponectin
- Regulate multiple processes:
  - Appetite & satiety
  - Lipid storage & metabolism

- Insulin sensitivity
- Female reproduction
- Inflammation & immune responses
- General energy metabolism
- Obesity → low grade inflammation & adipokine pattern alterations → T2DM & cardiovascular diseases

### Leptin vs. Adiponectin

#### Leptin

- Anorexin molecule acting on Hypothalamus
- Decreases appetite & increases energy expenditure
- Healthy:
  - Eat → adipocytes full of fat → increases leptin
  - Fast → adipocytes empty → decrease leptin
- Obesity
  - Increase adipocyte → increase ++ leptin resistance
  - Leptin resistance → overeating → weight gain
  - Hyperleptinemia → increase sympathetic activity → hypertension

#### Adiponectin

- Anti-inflammatory & anti-atherogenic
- Increases insulin sensitivity
- Obesity:
  - Decreases adiponectin release → increase in insulin resistance → T2DM + increased inflammation & atherosclerosis

### Apple vs. Pear

#### Visceral (apple) obesity

- Men > women
- Metabolic lipid activity > peripheral obesity
- Increased risk:
  - Cardiovascular complications
  - T2DM
  - Cancer

#### Peripheral (pear) obesity:

- Women > men
- Metabolic lipid activity < visceral obesity
- Increased risk < visceral obesity

## BACK TO PHARM

### BMI

$$\text{BMI} = \frac{\text{Weight in pounds} \times 703}{(\text{Height in inches})^2}$$

OR

$$\text{BMI} = \frac{\text{Weight in kilograms}}{(\text{Height in meters})^2}$$

### Weight-Related Health Risk

- Waist circumference
- Measure of abdominal fat
- Pear vs. apple shape
- Independent risk factor

	Men	Women
Normal	78–94cm	64–80cm
Overweight (Elevated Risk)	94–102cm	80–88cm
Obese (High Risk)	>102cm	>88cm

### Overall Health Risks

- MOST individuals with BMI > 30
- MOST individuals with BMI > 25 + obese waist circumference
- Cardiovascular heart risks further increase health risk for all

## Obesity Management

### Obesity Therapy: Overview

- In theory: calories burned > calories intake
- In practice: complex struggle between internal homeostasis & behavioral habits

For whom?	BMI > 30 or > 25 + 2 more risk factors	
Benefits	Decreased risk for cardiovascular events, T2DM & mortality	
Goals	<ul style="list-style-type: none"> <li>- Lower BMI as much as possible</li> <li>- Reach new BMI with significant risk improvement vs. starting BMI</li> <li>- 10% weight loss in 6 months → maintain loss for next 6 months</li> </ul>	
Modalities	Caloric restrictions	1st line option, fat reduction = easiest
	Exercise	1st line option, minimum 150mins/week
	Behaviour modification	Reinforce eating & exercise habit changes
	Bariatric surgery	Very effective → 110-220 pounds lost in 6 months Very risky → 4.6% 1 year mortality
	Drug therapy	Introduce only after 6 months of diet + exercise



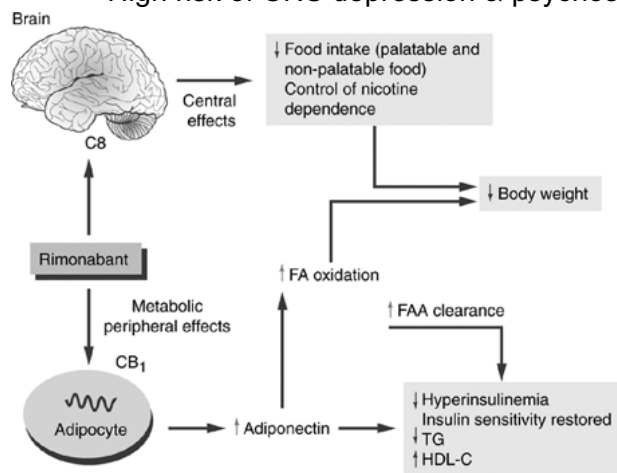
### Weight-Loss Drugs

- Only modest benefits → huge \$\$ market → once on market, widespread use & abuse → many receive approval and then get withdrawn due to serious toxicity discovery
- Remember: losing weight is extremely hard. Everyone wants the simple/easy solution
- Smoking & stimulants (cocaine, amphetamines) are often abused for weight loss purposes.

<u>Drug class</u>	<u>Prototype</u>
<b>Lipase inhibitor</b>	Orlistat (least benefits)
<b>5-HT<sub>2C</sub> receptor agonist</b>	Lorcaserin
<b>Sympathomimetic</b>	Diethylpropion & Phentermine
<b>GLP-1 Agonist</b>	Liraglutide
<b>Combination products</b>	Phentermine + topiramate (most benefits) Naltrexone + Bupropion

### Cannabinoid Inhibitors: Rimonabant

- They figured that if stimulating the cannabinoid receptors stimulated appetite, then inhibiting it would suppress hunger.
- Marketed in 2005 → withdrawn in 2008
- Therapeutic window too narrow
- High risk of CNS depression & psychosis



### Combination Products

#### Phentermine + Topiramate (Qsymia)

- Phentermine:
  - Sympathomimetic amine
  - Decreases appetite @ the hypothalamus

- Topiramate
  - Anticonvulsive drug
  - Increases satiety feeling
- Adverse effects:
  - Dry mouth, dizziness, insomnia
  - Serious ADRs: HTN tachycardia & birth defects
- Interactions
  - Antidiabetic agents → increases hyperglycemia
  - Oral contraceptives → increases estrogen levels
  - MAO inhibitors → contraindicated

#### Naltrexone + Bupropion (Contrave)

- Naltrexone
  - Opioid antagonist
  - Decreases appetite @ hypothalamus
- Bupropion
  - DA/NE reuptake inhibitor
  - Decreases reward feeling of food
- Adverse effects:
  - Nausea, vomiting, constipation, dizziness
  - Serious ADRs: depression, mania & suicidal ideation
- Interactions:
  - Other drugs with bupropion
  - Strong CYP2D6 inhibitor
  - Opioids & MAO inhibitors → contraindicated

#### **Is obesity a problem intrinsically or is it a symptom associated to other issues?**

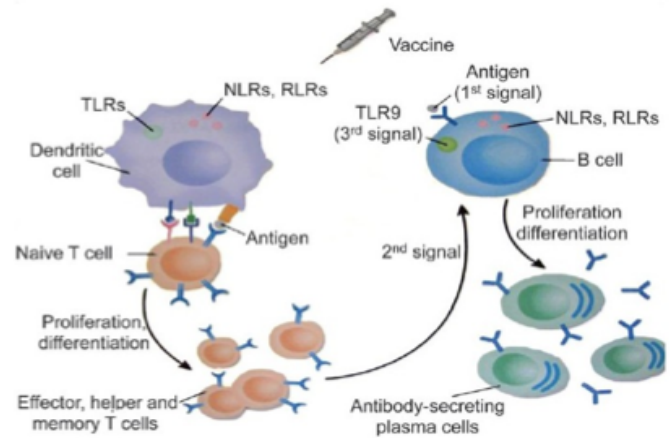
##### Quick word on fat-shaming & weight-related myths

- Many studies show that weight gain is unrelated to:
  - Motivation / personality / bad health / nutrition quality
- Some individuals are predisposed to accumulate fat if the environment favors it → evolutionary advantage
- Obese individuals are not lazy and could be in better health than many individuals within the 'healthy BMI range'
  - Cardiovascular fitness test is a better predictor of health outcomes than BMI
- Fat-shaming takes on many forms and only makes their health worse/scare them away from HCP
  - Intimidation / social isolation / many HCP spend less time with obese patients
  - Phrases such as: "Congrats for doing something about your weight" or "it's cool that he loves you so much despite your weight"

## **Childhood Immunization (Ch. 68)**

### **Vaccine Types**

- Immunization = process of increasing strength of immune system
  - Active immunity → endogenous antibody production (ex. vaccination)
  - Passive immunity → performed antibodies injection (ex. Specific immune globins)
- Live vs. killed vaccine
- Toxoid = harmless bacterial toxin
  - Ex. diphtheria or tetanus toxoid vaccines



### **History Capsule: Because Why Not Some Perspective?**

- Variation in 15th century China
  - Used powdered scabs of infected smallpox patients
- Western Europeans notice that milkmaids are resistant to smallpox
- 1796: Edward Jenner vaccinates first patient
  - Vaccination refers to cowpox (vacca) vaccine against smallpox
- 1886: Louis Pasteur uses 1st laboratory designed vaccine (rabies)
- 1998: Dr. Wakefield publishes study linking vaccines with autism
- 2010: scientific journal The Lancet retracts his article
  - Dr. Wakefield loses license after discovery of falsified data

### **Vaccines: (Actual) Adverse Effects**

**Adverse Effects of Some Vaccines and Toxoids**

Preparation	Mild Effects	Serious Effects
Measles, mumps, and rubella virus vaccine	Local reactions; rash; fever; swollen glands in cheeks and neck and under the jaw; pain, stiffness, and swelling in joints	Anaphylaxis, thrombocytopenia <sup>a</sup>
Diphtheria and tetanus toxoids and acellular pertussis vaccine	Local reactions, fever, fretfulness, drowsiness, anorexia, persistent crying	Acute encephalopathy, convulsions, shock-like state
<i>Haemophilus influenzae</i> type b conjugate vaccine	Local reactions, fever, crying, diarrhea, vomiting	None
Varicella virus vaccine	Local reactions, fever, mild varicella-like rash (local or generalized)	None
Hepatitis A vaccine	Local soreness, headache, anorexia, fatigue	Anaphylaxis
Hepatitis B vaccine	Local discomfort, fever	Anaphylaxis
Pneumococcal conjugate vaccine	Local reactions, fever, irritability	None
Influenza vaccine (inactivated)	Local reactions, fever	None
Influenza vaccine (live attenuated)	Runny nose, headache, cough, fever	None
Meningococcal conjugate vaccine	Local reactions, headache, fatigue	None
Rotavirus vaccine	Diarrhea, vomiting, ear infection, runny nose, sore throat	Intussusception (rare)
Human papillomavirus vaccine	Local reactions, fainting	None

<sup>a</sup>A study showing a connection with autism was disproved.

(need to know)

## Vaccines: Contraindications

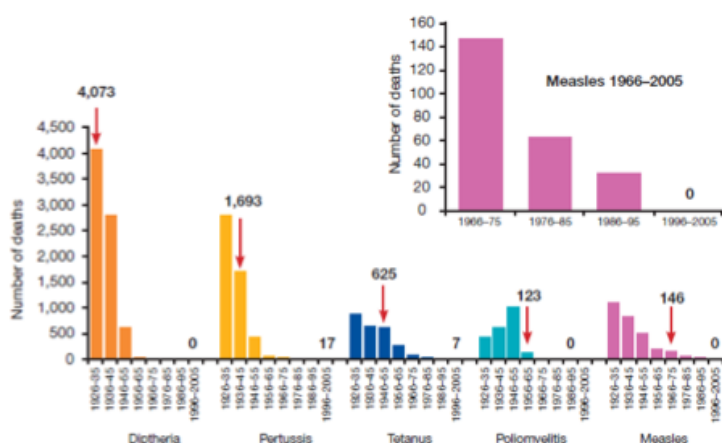
### Contraindications That Apply to All Vaccines and Conditions Often Incorrectly Regarded as Contraindications

True Contraindications (Vaccine Should Not Be Administered)	Not Contraindications (Vaccine May Be Administered)
<p>Anaphylactic reaction to a specific vaccine: Contraindicates further doses of that vaccine</p> <p>Anaphylactic reaction to a vaccine component: Contraindicates use of all vaccines that contain that substance</p> <p>Moderate or severe illnesses with or without a fever</p>	<p>Mild to moderate local reaction (soreness, erythema, swelling) following a dose of an injectable vaccine</p> <p>Mild acute illness with or without low-grade fever</p> <p>Diarrhea</p> <p>Current antimicrobial therapy</p> <p>Convalescent phase of illnesses</p> <p>Prematurity (same dosage and indications as for normal, full-term infants)</p> <p>Recent exposure to an infectious disease</p> <p>Personal or family history of either penicillin allergy or nonspecific allergies</p>

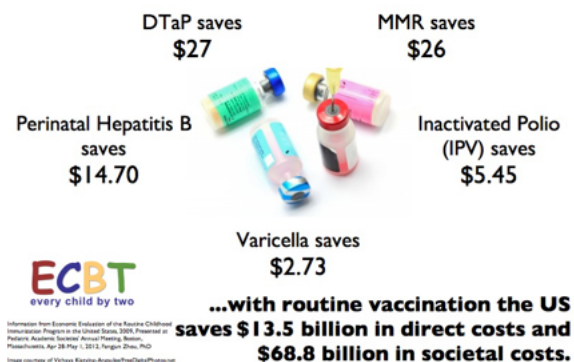
- Vaccines have one of the best benefit:risk ratio of all Rx
- Minimize pain during administration → EMLA patch, quick IM injections
- Avoid prophylactic NSAIDs/Acetaminophen → decreases vaccine efficacy + hide early adverse effects
- Avoid live vaccines in immunocompromised children

## Vaccines: Public Health Impacts

- Polio eradicated from all but 2 countries
- Smallpox eradicated from the planet!

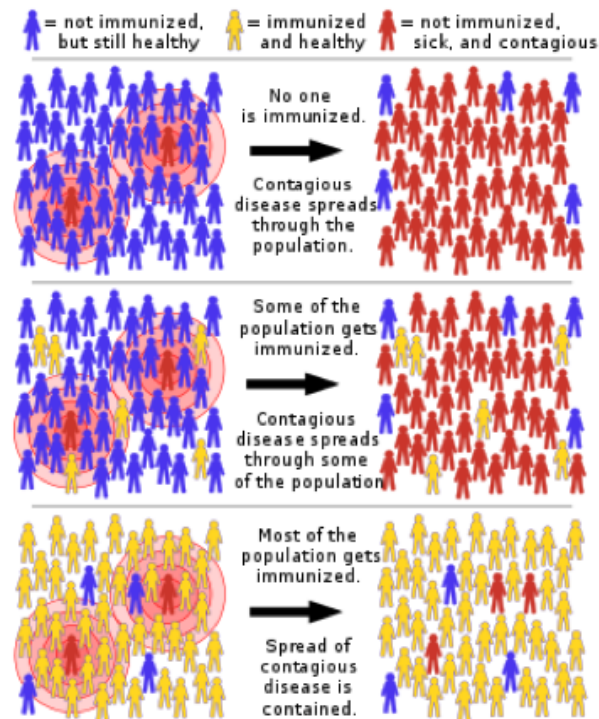


### For every \$1 spent on a vaccine in the US...



## Vaccines: Herd Immunity

- Arguably the most important action of immunization
- If everyone who can receive vaccines is immunized, this protects those who cannot receive vaccines
- Very newsworthy today with anti-vaxx campaigns



### Childhood Vaccination Schedule

Vaccine protecting against:	At 2 months	At 4 months	At 12 months	At 18 months	Between 4 and 6	Elementary 4	Secondary 3
Diphtheria-tetanus-whooping cough-hepatitis B-polio-Hib	✓	✓	✓ (without hepatitis B)				
Pneumococcus	✓	✓	✓				
Rotavirus	✓	✓					
Meningococcus C				✓			✓
Measles-mumps-rubella-varicella			✓	✓			
Diphtheria-tetanus-whooping cough-polio					✓		
Diphtheria-tetanus							✓
Hepatitis A-hepatitis B				✓			
Human papillomavirus						✓	

#### IMPORTANT

For optimal protection for your child, do not forget any vaccines and have the child vaccinated at the recommended ages.

**It's up to you to make an appointment** with the CLSC or with your doctor to have your child vaccinated (except for vaccines given at school).

### Some Target Diseases

Disease	Type	General Comments
Measles	Virus	Highly contagious, risk of death by encephalitis
Mumps	Virus	Attacks parotid glands
Rubella	Virus	Mild in adults, but extremely teratogenic
Diphtheria	Bacteria	Potentially fatal, In US: 5 cases only between 2006-16
Tetanus	Bacteria	Painful muscle spasms caused by endotoxin
Pertussis	Bacteria	Whooping cough, affects mostly very young children
Poliomyelitis	Virus	Attacks CNS neurons leading to paralysis; 37 cases worldwide in 2016
Varicella	Virus	Highly contagious, most serious in adults
Hepatitis A & B	Viruses	Serious Liver infections
Type B Influenza	Virus	May cause permanent neurological deficits in children
Pneumococcal Infection	Bacteria	Affects airways & hearing, mortality = 10%
Meningococcal Infection	Bacteria	Leading cause of meningitis, mortality = 10-14% despite antibiotics
Rotavirus	Virus	Gastrointestinal infection which can lead to fatal dehydration
Human Papillomavirus	Virus	Cause of almost all anogenital warts & cervical cancers

(don't need to memorize)

### MMR Vaccine

#### Measles, Mumps & Rubella Live Virus

- Efficacy:
  - 97% success within 2-6 weeks
- Adverse effects
  - Mild: fever, local rash, pain, stiffness
  - Severe: anaphylaxis & thrombocytopenia (very rare), gelatin allergy → extreme caution
- Precautions & contraindications
  - Pregnancy
  - Severe immunocompromisation
  - Severe febrile illness
- Schedule
  - 1st dose = 12 months
  - 2nd dose = 18 months
  - Boosters for HCPs

### DTaP Vaccine

#### Diphtheria + Tetanus toxoids + acellular Pertussis

- Efficacy
  - Protection success = 80-90% after 3rd dose
  - Lasts 6 years (pertussis) or 10 years (tetanus + diphtheria)
- Adverse effects
  - Mild: local rash, fever, anorexia, drowsiness
  - Severe: convulsions, shock-like state, acute encephalopathy
- Precautions & contraindications
  - Contraindicated if severe febrile illness
  - History of anaphylaxis reaction to previous DTaP shot

- Schedule
  - Routine immunization: 2, 4, 12 months & 4-6 years
  - Booster DTaP → 10-12 years old
  - Booster every 10 years henceforth

#### Polio Vaccine: IPV

##### **Inactivated polio vaccine (IPV) against polio types 1, 2 & 3**

- Efficacy
  - Success is 97-100% after 2+ shots lasting several years
- Adverse effects
  - Mild local pain/reactions
  - Potential allergic reactions to antibiotics in vaccine
- Routine immunization = 2, 4, 12 months & 4-6 years old

#### Varicella Virus Vaccine

##### **Live attenuated varicella vaccine**

- Efficacy
  - 99% success with 2-dose series
- Adverse effects
  - Only mild ones: local varicella-like rash, fever, & soreness
- Precautions & contraindications
  - Contraindications: pregnancy, leukemias, neomycin or gelatin allergy
  - Avoid aspirin for 6 weeks after → reye's syndrome
- Schedule
  - 1st dose: 12 months; 2nd dose: 18 months; 3rd dose: 4-6 years
  - Administered with MMR

Rates of varicella vaccination are declining due to misconceptions:

- Anti-vaccine groups' scare tactics
- Low incidence of diseases providing false sense of eradication
- Majority of cases being mild in children

#### Hepatitis A & B Vaccine

##### **Hep A vaccine = inactivated virus**

##### **Hep B vaccine = Hepatitis B surface antigen**

- Efficacy
  - Hep A success = 100% 1 month after 2nd dose
  - Hep B success = 90% after 3rd dose
- Adverse effects
  - Among safest vaccines: mild soreness and headache
- Precautions & contraindications
  - Hep A booster for risk populations (ex. Homosexual men, travelling to outbreak countries, illicit drug use, chronic liver disease, etc)
  - Hep B contraindicated if previous anaphylactic reactions

- Schedule
  - Hep B given with DTap at 2 & 4 months
  - Combined Hep A & B: 18 months & 4th grade school year

#### HPV Vaccines: Gardasil-9

#### **Virus sized empty capsid proteins - routine pap smear tests still recommended**

- Efficacy
  - Protection against cervical, vaginal and anal cancer
- Adverse effects
  - Very safe, mild symptoms only
  - No causality with serious effects
- Who should get vaccinated?
  - Routine vaccination of males & females recommended
  - 11-12 years since it only protects, cannot treat
- Precautions & contraindications
  - Contraindicated in pregnant & breast-feeding women
- Schedule
  - 3 doses over 6 months whenever the patient decides
  - Now part of routine schedule during 4th grade school year

#### Seasonal Flu Vaccines

#### **Developed twice per year due to rapid mutations of influenza**

#### **Inactivated or live-attenuated**

- Efficacy
  - Varies from year to year
  - Reduces risk of contracting infections & boosts recovery
- Adverse effects
  - Very safe
  - Transient fever
  - Muscle soreness in about 10% of cases
- Who should get vaccinated?
  - Healthcare professionals
  - Vulnerable populations: elderly (75+), respiratory diseases, children, pregnant women
- Precautions & contraindications
  - Individuals allergic to previous flu vaccines
- Schedule
  - Yearly around october

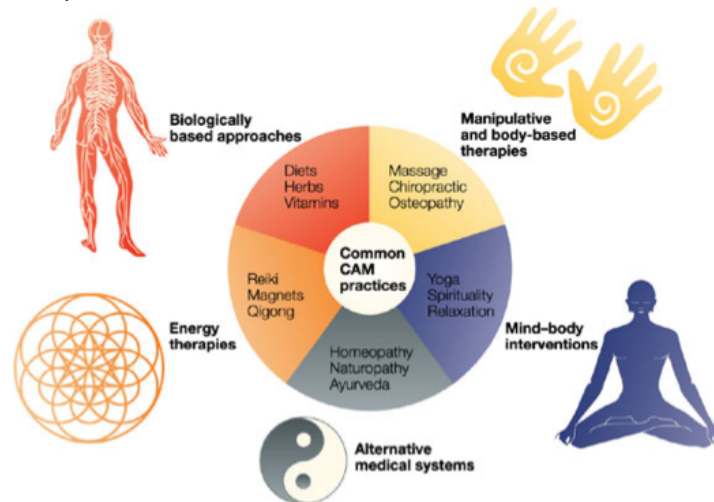
#### **Complementary & Alternative Medicine (CAM) (Ch. 108)**

#### **CAM: Overview**

- Benefit claims more or less evidence-based
- Complementary:
  - Non-mainstream approaches IN ADDITION to conventional medicine



- Alternative:
  - Non-mainstream approaches INSTEAD of conventional medicine
- 3 important aspects of CAM:
  - Marketing & money \$\$
  - Individual empowerment
  - Skepticism of medicine



### Dietary supplements

= vitamins, minerals & herbal supplements

### Why People Use Dietary Supplements

- Perception that supplements are safer and healthier than conventional drugs
- Sense of control over one's care
- Emotional comfort from taking action
- Cultural influence
- Limited access to professional care
- Lack of health insurance
- Convenience
- Media hype and aggressive marketing
- Recommendation from family and friends

### Regulation of Dietary Supplements

- Dietary supplements health & education act (1994)
  - Reversed burden of proof → safe until proven hazardous
  - Investigate safety concerns or false efficacy claims ONLY after marketed
  - Manipulative labelling semantics (see next section)
  - No control on quality and actual content or products
- Dietary supplement & nonprescription drug consumer protection act (2006)
  - Serious adverse effects must be reported within 15 days
- Current good manufacturing practice (GMP) ruling (2007)
  - Addresses issues with quality control

- Content of product must match labelling → most obtain “seal of approval” from a private laboratory
- Standardization
  - Differences in plant active ingredient depending on sunshine, rainfall, soil, etc.
  - Adjust concentration of extract to ensure consistency between batches produced
  - Allows for accurate dosing & safety/efficacy data interpretation

#### Dietary Supplements Labeling

- Shady labeling - super vague because you can't disprove it.
- Because it can't be proved wrong, it does not fall under false labelling.
- Not obliged to state adverse effects on the labels, because it is technically not a drug.

#### Adverse Interactions With 'Conventional Drugs'

- Many unknown interactions due to lack of safety/efficacy studies
- CYP3A4 induction
  - St John's Wort → decrease therapeutic efficacy of many drugs (ex. statins)
- Platelet aggregation inhibition
  - Interaction with warfarin, heparin, etc. → increase risk of bleeding
  - Ex. Ginko Biloba, feverfew, garlic
- Cardiovascular effects
  - Ma Huang = ephedrine → increased BP, HR & CNS
  - Interactions with beta-blockers, antidepressants, etc.
- 2 major issues:
  - Prescriber knowledge - some prescribers don't know all the effects of those agents, thus they can't properly educate patients about their effects.
  - Patient disclosure - they don't disclose they are taking those products because they don't think it matters.

#### Editorial Comment - NEJM

*It is time for the scientific community to stop giving alternative medicine a free ride. There cannot be two kinds of medicine—conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously, it no longer matters whether it was considered alternative at the outset. If it is found to be reasonably safe and effective, it will be accepted. But assertions, speculation, and testimonials do not substitute for evidence. Alternative treatments should be subjected to scientific testing no less rigorous than that required for conventional treatments.*

Unfortunately, two decades later, little has changed.

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- New England Journal of Medicine Editorial

### Editorial Comments - W.A.

- The capitalization of health → age of skepticisms
- Internet: democratization of information → individual empowerment
  - Ex. anti-vaccine movement; big pharma & lobbying groups
- Looking for simple solutions to complex problems vs. using judgement & nuance (see youtube clip)
  - [https://www.youtube.com/watch?v=j5U\\_6Vdm07w](https://www.youtube.com/watch?v=j5U_6Vdm07w) → Dallas Buyers Club – Judge Ruling(1 min)
- Rationalization: when you must adapt to your behaviour - when you start doing something, such as using natural products, well your attitude/beliefs towards it tends to change → “if i am using natural products, that must mean that I do not trust the use of medication, ergo i believe in it more.”

### Logical Fallacies

- Pharmachien Tome 3 - Logical Fallacies Bible
  - Debunks a lot of myths
- “It’s not that people are stupid. It’s that life is hard.” - prof. Richard Thaler (Nobel Prize of Economics)

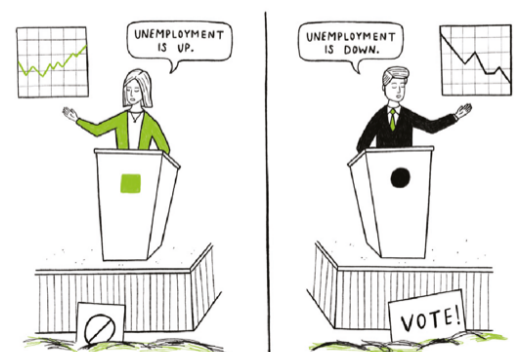
### Anecdotes - Scientist’s Kryptonite

- Be careful when you are reading papers/articles when people are using arguments “i heard something..., i read something... “



### Cherry Picking

- <https://www.youtube.com/watch?v=yJD1lwy5IUy> - If Google was a Guy (Part III) – Watch at 45 seconds
- Using an anecdote that fits your story rather than looking at the whole picture

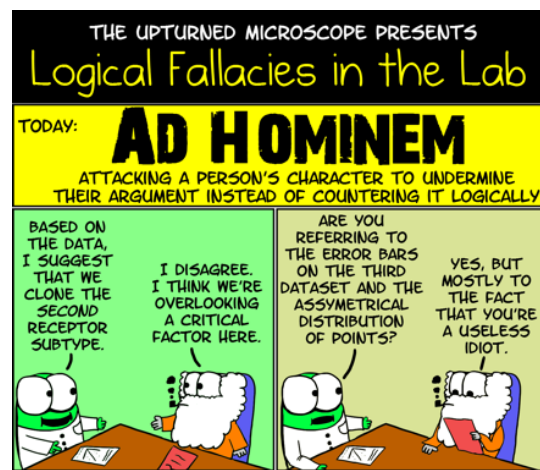
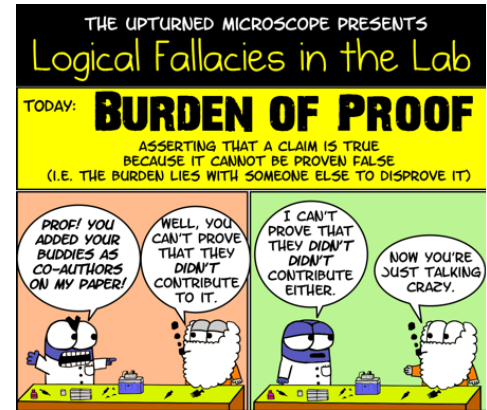


### Burden of Proof

- Who needs to prove what and when - the person making the allegation should be the one to prove it and not the other person to disprove it.
- A hypothesis is said to be false, unless proven otherwise
- Extraordinary claims require extraordinary (robust) evidence
- Complex problems (most often than not) require complex solutions

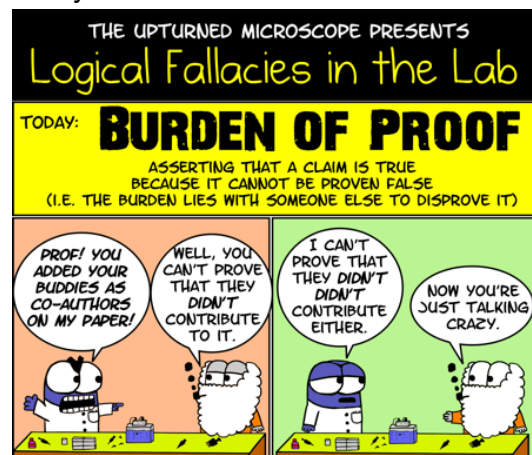
### Ad Hominem

- Instead of attacking the claim, you attack the person making the claim



### Strawman Fallacy

- Misrepresent an argument so that it is easier to destroy
- Anti-vaccine argument seen online: 'if you are for vaccines, then you should not mind me when i stab your children'



### Appeal to Traditions

- 'Marriage should be between a man and a woman. It has been that way for hundreds of years.'
- It's much easier to stay with traditions than to have to change that. It gives us a sense of control.

### Appeal to Authority

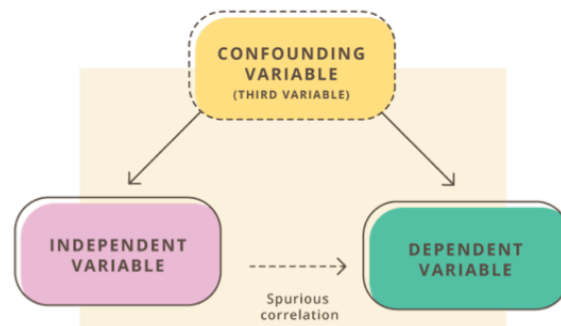
- Target authority figures to try and prove something. Such as cigarettes are healthy because even doctors smoke them.
- Becomes a cult of personality. I like this actress/blogger, so i like this too.

### Appeal to Nature

- Your body doesn't care if it's natural or made in a lab, it can't tell the difference. It only cares about what it does to your body.

### Correlation vs. Causation

- 2 big traps:
  - Reverse causation: when there is a correlation between two items, we don't know which one caused the other to change. We just know that when one changes, the other also changes.
  - 3rd confounding variable: 2 things have changed, it's not because one affected the other. There is another factor affecting them.



### Many More Logical Fallacies

Please check out this website when you have an argument or just a moment to practice critical thinking.

<https://yourlogicalfallacyis.com/>

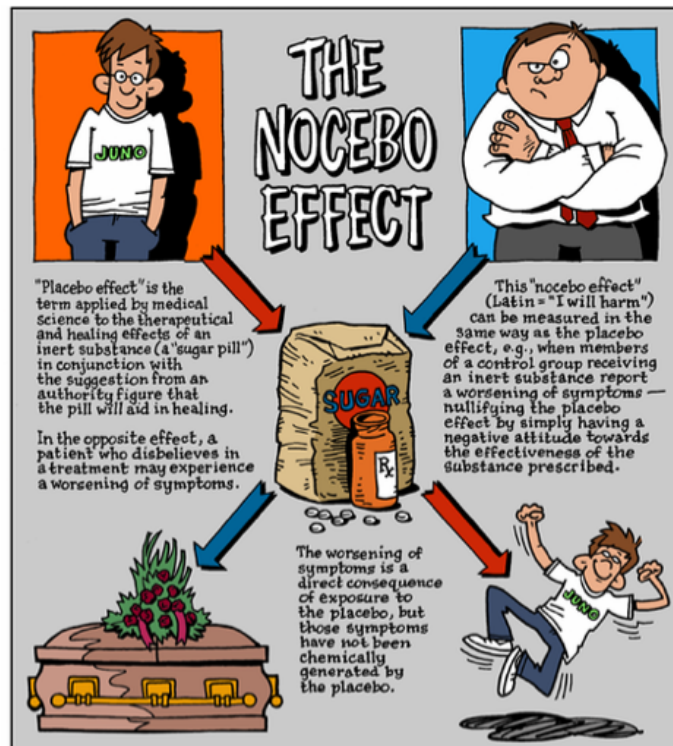


## 24 Cognitive Biases



## Placebo Effect

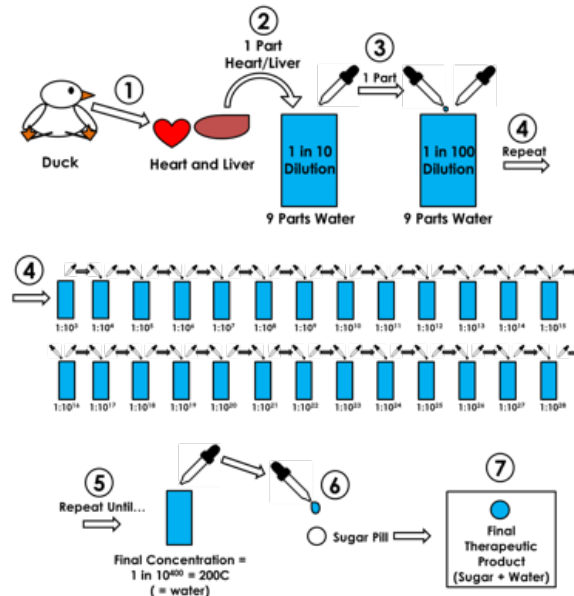
- Psychological fraction of drug response based on patients' attitude and expectations of the Rx.



### Case Study: Homeopathy

#### Founding principles:

- Likes cures likes - if someone has a heart disease, you're going to give them a heart extract of something else.
- Water potentization power - belief that water has a memory. That the more diluted it is, the better it is. They believe that the dilution is stronger because the water remembers. If the water was exposed to the molecule of that product, it will remember it and keep this property. They think that if you take that water, and place some in a different jar of water, it will give that property to the other jar.



#### Homeopathy: When it is Good

- For mild conditions like common cold, minor fatigue, headache or winter blues, the placebo effect of homeopathy can be sometimes more beneficial rather than taking medication for it.
- Placebo effect + sense of self-efficacy + social support of authority figure = very strong placebo
- 'Homeopathy users who saw a practitioner were significantly more likely to feel that homeopathy was 'very important in maintaining health and well-being' and that it helped their health condition "a great deal" than were homeopathy users who did not see a practitioner. Homeopathy users who did not see a practitioner were significantly more likely than were supplement users to find the modality they used helpful.'

#### Homeopathy: When it Goes Too Far

- Homeopathy only becomes a problem when it goes too far, such as trying to cure hepatitis C with homeopathy.
- It also becomes a problem when patients refuse proper treatment because they truly believe that homeopathy is helping them.

### **Some Commonly Used Dietary Supplements**

#### Garlic

<b>Active Ingredients</b>	Allicin & Ajoenes
<b>Claims</b>	Decrease cholesterol synthesis Antiplatelet effect Increase nitric oxide vasodilation
<b>Effectiveness</b>	Recent robust NCCIH review included: <ul style="list-style-type: none"> <li>- No effect on LDL cholesterol</li> <li>- Modest decrease in BP &amp; atherosclerosis development</li> </ul>
<b>Adverse effects</b>	Bad breath & odor Potential GI irritation
<b>Interactions</b>	Warfarin, aspirin, heparin, etc → antiplatelet effects Increase metabolism of cyclosporine & Saquinavir

#### Ginkgo Bilboa

<b>Active ingredients</b>	Flavonoids (24%) & Terpenoids (6%)
<b>Claims</b>	Increase memory / decrease dementia & erectile dysfunction
<b>Effectiveness</b>	Early findings = promising More robust & recent research = conflicting results No evidence for dementia prevention in alzheimer's study
<b>Adverse effects</b>	Well tolerated - mild vertigo or dizziness Eating raw or roasted seeds = extremely toxic
<b>Interactions</b>	Warfarin, aspirin, heparin, etc → anticoagulation effects Increase seizure risk drugs & patients (ex. antipsychotics)



### Probiotics

<b>Active ingredients</b>	Normal GI gut flora bacteria: lactobacilli & bifidobacteria
<b>Claims</b>	Tx of irritable bowel syndrome, ulcerative colitis & diarrhea
<b>Effectiveness</b>	Some evidence of decrease in diarrhea duration & increased UC recovery Larger more robust studies required
<b>Adverse effects</b>	Flatulence & bloating = most common Infections only in severely immunocompromised patients
<b>Interactions</b>	Abx & antifungal drugs → administer probiotic 2h post-Tx

### Ginger Roots

<b>Claims</b>	Suppress vertigo & nausea/vomiting
<b>Effectiveness</b>	Monitoring sickness prevention: good evidence! Other types of nausea/vomiting: conflicting results Rheumatoid arthritis Sx alleviation: potential but weak evidence
<b>Adverse effects</b>	Very well tolerated Very excessive doses: CNS depression, GI disturbances, dysrhythmias Theoretical risk of effects on fetus but no evidence
<b>Interactions</b>	Warfarin, aspirin, heparin, etc. → anticoagulation effects insulin/antidiabetic agents → decrease blood sugar

### Resveratrol

<b>Sources</b>	Skin of grapes, red wine, blueberries, cranberries, peanuts
<b>Claims</b>	Antioxidant with anti-aging properties
<b>Effectiveness</b>	Clear benefits in animal studies: decreased mortality of obese mice Increased bone density, CVS or motor functions in healthy mice Decreased tumor growth in mice & blood glucose in diabetic rats Early human studies show promising results
<b>Adverse effects</b>	Antiplatelets action + estrogen analog + increased insulin sensitivity
<b>Interactions</b>	

### St-John's Wort

<b>Active Ingredients</b>	Hyperforin & hypericin extracts
<b>Claims</b>	Antidepressant Mild anti-inflammatory & analgesics
<b>Effectiveness</b>	Mild to moderate depression: better than placebo Severe depression: inferior to antidepressants
<b>Adverse effects</b>	Skin allergic reactions, CNS effects & GI disturbances High dose therapy: risk of phototoxicity
<b>Interactions</b>	CYP3A4 induction → decreases therapeutic effects Increases P-glycoprotein synthesis → decrease therapeutic effects Increase serotonin transmission → risk of serotonin syndrome

### Harmful Supplements

#### Comfrey

- Carcinogenic
- Veno-occlusive hepatic disease → 2001 FDA advisory of removal
- Still available online

#### Kava

- Promoted as alternative of benzodiazepines
- Risk of severe hepatotoxicity → 2002 FDA public warning
- Sales restricted in Canada

#### Ma Huang (Ephedra)

- High-dose Ephedra associated with stroke, myocardial infarction & death
- 17 000+ ADR reported → 2004 FDA ban

#### Nursing Capsule: Patient Education

- When asked for advice, use evidence-based approaches
- SBN time: respect patient's beliefs → don't ruin their placebo effect
- Explain to them the importance of disclosing all the dietary supplements they use
  - Adverse effects undocumented
  - Potential interactions with other drugs

### **About the final exam**

- FINAL exam is on Dec 12th at 9h00 in the gym most likely...
- Don't forget the bonus question :) refer to the link on the first slide:
  - <http://revisionisthistory.com/episodes/09-generous-orthodoxy>
- Final exam breakdown
  - About 9 MCQs on the pre-midterm courses (none on the 1st short lecture)
  - 10 or 11 MCQs / post-midterm lectures
    - 1 passage with 4-5 questions associated / post-midterm lecture
  - 1 bonus question based on the podcast
- Pre midterm material to review:
  - 4 main class of drug receptors
  - Kinetic vs. dynamic interactions
  - Ideal general anesthetic
  - Dose-dependent selectivity or neurological agents
- Material to review:
  - Endocrine pharmacology:
    - Mechanisms of action of antidiabetic drugs
    - Insulin administration
  - OTC pharmacology
    - Best migraine management practices
    - Differences between types of laxatives
  - Cardiovascular pharmacology
    - Monitoring of anemia deficiencies
    - Advantages vs. drawbacks of drugs with similar action/within the same class
    - Combination of cardiovascular drugs to manage toxicity
    - Digoxin
    - Angina & STEMI complications
  - Respiratory/ADHD pharmacology
    - Asthma vs. COPD management similarities/differences
    - Cocaine vs. amphetamine
  - Complementary & alternative medicines
    - Main application of each vitamins
    - Examples of cognitive biases → play at spotting them in newspaper ads and pseudoscientific websites!