FERMENTATION, CIVILIZATION AND THE MICROBIOME

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FERMENTATION—what comes to mind?

I think I'm beginning to ferment
Fermentation

- Fermentation is a metabolic process in which an organism converts a carbohydrate, such as starch or a sugar, into acid, gas or alcohol.
Two Fermentation Processes

**Ethanol Fermentation**
Beer, Wine, Bread

- Yeast and certain bacteria perform ethanol fermentation where pyruvate (from glucose metabolism) is broken into ethanol and carbon dioxide

**Lactic Acid Fermentation**
Yogurt

- The pyruvate molecule from glucose metabolism is fermented into lactic acid
- Lactic acid fermentation is used to convert lactose into lactic acid in yogurt production
- It also occurs in animal muscles when the tissue requires energy at a faster rate than oxygen can be supplied
Fermentation’s Effects

• It’s believed that the establishment of fermentation facilitated the shift from a hunter/gatherer society to an agricultural society because it allowed people to settle in one area and preserve food vs. following the food sources
Fermentation of Food

• For over 6000 years, humans have been preserving foods with the process of fermentation

1. Preserved food= improved food safety
2. Degrading of toxic components and anti-nutritive factors (phytic acid)
3. Enriching of diet with amino acids, vitamins, probiotics
4. Enhancing the bio-availability of nutrients
5. Enriching the sensory quality of foods
6. Multiple health benefits
Health Benefits-Fermentation/probiotics

- Manufacture of vitamins
- Support and increase the rate of metabolism
- Detoxification of chemicals
- Promote cell growth including RBC
- Enhance immune and nervous system function
- Increase production of enzymes improving food assimilation and absorption of nutrients
- Crowd out pathogenic organisms
All Things Fermented….

- **Bean-based**: Cheonggukjang, doenjang, miso, natto, soy sauce, stinky tofu, tempeh, oncom, soybean paste, Beijing mung bean milk, kinama, iru
- **Dough-based**: Proofing-sourdough
- **Grain-based**: Batter made from rice and lentil prepared and fermented for baking idlis and dosas, Amazake, beer, bread, choujiu, gamju, injera, kvass, makgeolli, murri, ogi, rejuvelac, sake, sikhye, sourdough, sowans, rice wine, malt whisky, grain whisky, idli, dosa, vodka, boza
- **Vegetable-based**: Kimchi, mixed pickle, sauerkraut, Indian pickle, gundruk, tursu
All Things Fermented....

- **Fruit-based**: Wine, vinegar, cider, perry, brandy, atchara, nata de coco, burong mangga, asinan, pickling, višinatǎ, chocolate, rakı
- **Honey-based**: Mead, metheglin
- **Dairy-based**: Some cheese also, kefir, kumis (mare milk), shubat (camel milk), cultured milk products such as quark, filmjölk, crème fraîche, smetana, skyr, and yogurt
- **Fish-based**: Bagoong, faseekh, fish sauce, Garum, Hákarl, jeotgal, rakfisk, shrimp paste, surströmming, shidal
- **Meat-based**: Chorizo, salami, sucuk, pepperoni, nem chua, som moo, saucisson
- **Tea-based**: Pu-erh tea, Kombucha
Let’s Explore…….

• How does fermentation and its effects make us healthier?
Microbiome

- Describes all the organisms that live in and on our bodies (bacteria, viruses, fungi, protozoa, helminths) along with their genes
- Considered a counterpart to the human genome
Microbiome

• During birth baby is colonized by bacteria- thus begins the evolution of our individual microbiome
• Our unique microbial footprint develops over our lifetime and is altered by just about everything: C-section, vs vaginal delivery, breast milk vs bottle, food, hygiene, exposure to chemicals, pets, farm animals, toxins, medications and even emotions
Was this you growing up?
Or this??

Please

USE HAND SANITIZER

Thank You

Antibiotics

CLEAN!
Microbiome

- The end result of our individual microbial salad is so unique and distinctive that it’s more specific than our own DNA
- We have about 23,000 human genes and 8,000,000 microbial ones
- Some studies suggest that gut bacteria play a critical role in carbohydrate metabolism, enzymatic detoxification and even determining whether or not a disease you are genetically predisposed to actually develops
- This may explain why identical twins with inherited diseases don’t always manifest the disease; the genes may be the same but the microbes are different
Microbiome

- Disruption of the microbial ecosystem can cause disease
- As adults there are ways we can keep our microbiome healthy
- As physicians, it is our duty to keep our patients’ healthy microbiome in mind
The Human Microbiome Project

- Established in 2008
- Funded by NIH
- Goal: characterize the human microbiome and analyze its role in human health and disease
BATTLE for the BIOME

Researchers explore skin microbiome to exploit bacteria for treatments

46. What are the seven steps to MIPS success?

54. How can you hire and nurture good medical assistants?

68. What has the AAD done for you lately?
- Certain diseases carry with them certain types of bacteria
- Healthy skin shows a balance of bacteria
- Dysbiosis causes an imbalance and results in a pro-inflammatory state
- This leads to dysregulation of the immune system
- NIH is currently evaluating trial of skin autologous microbiome transplant to decrease S. aureus colonization
- ‘The option of rebalancing and rediversifying the skin microbiome, instead of eliminating pathogens randomly will add to the arsenal of treating skin diseases’
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Microbiome-studies

- Study *Nature*, 2006 “An obesity-associated gut microbiome with increased capacity for energy harvest” found that germ free mice colonized with the gut flora of obese mice became obese.
- They correlated this to fewer Bacteriodetes than Firmicutes in gut flora.
- It’s postulated that the flora in obese mice is more efficient at extracting energy from food.
Microbiome

• In a similar study (published in Science in 2013) researchers at Washington University in St. Louis took gut bacteria from identical twins, one was lean and one was obese, and transplanted them into germ-free mice
• Within a few weeks, the mouse that received the microbes from the obese twin became obese and the one who received them from the lean twin remained lean
• What happens when you put the lean mice with the fat mice? Or vice versa?
Microbiome

• As stated in the book, The Microbiome Solution, by Dr. Robynne Chutkan, ‘the microbiome has one of the biggest impacts on our genes, turning them on and off and determining which ones are ultimately expressed as disease’

• She goes on to discuss how the study of ‘epigenetics’ evaluates how the environment affects heritable traits without actually changing the DNA material in our genes, and suggests that the gut bacteria you inherit might be far more important than the genes you inherit.
Microbiome

• Studies have shown that children prescribed large amounts of antibiotics are at higher risk of obesity later in life
• Antibiotic exposure before birth can affect children the same way
The word antibiotic literally means “against life” from its Greek roots. And, that’s exactly what this form of medicine is designed to do: antibiotics stop or slow down the growth of microscopic organisms (bacteria, fungi, and some parasites), in turn treating potentially dangerous infections.
• Compared with previous recommendations, there are currently relatively few patient subpopulations for whom antibiotic prophylaxis may be indicated prior to certain dental procedures.
• In patients with prosthetic joint implants, a January 2015 ADA clinical practice guideline, based on a 2014 systematic review states, “In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection.”
Antibiotics and the microbiome

- Antibiotics influence the function of the immune system, our ability to resist infection, and our capacity for processing food, and storing energy
- Now more important than ever to revisit how we use antibiotics
- We have a better understanding of the long term effects on diseases such as malnutrition, obesity and diabetes
Antibiotic Overkill

• Between 2000-2010 world wide use of antibiotics has increased by 35%
• US ranks #1 in per capita consumption
• Average American child receives 17 rounds of antibiotics by their 18th birthday
• Incidence of antibiotic resistant infections rising sharply-2015-over 50,000 deaths in US and Europe- expected to rise to 10 million worldwide by 2050
• The resultant antibiotic resistance and the superbugs created are killing more Americans each year than murders and car accidents combined
• One round of antibiotics can kill off over 30% of the bacteria in the gut and create an imbalance that can take months to years to recover from
How does the microbiome effect the immune system?

• The relationship between the mammalian host and its microbiota is symbiotic, and this shapes the host’s immune system.
• There exists a type of ‘cross-talk’ between the two via the exchange of chemical signals.
• This allows the immune system to recognize bacteria that are ‘harmful’ and find ways to remove them while allowing the good bacterial to remain intact.
• It is thought that the microbiome directly influences immune reactivity and targeting.
How does the microbiome effect the immune system?

- It is suggested that connections between the microbiome and a growing number of diseases exist, including:
  - 1. Crohn’s disease
  - 2. UC
  - 3. Irritable bowel syndrome
  - 4. Type 1&2 diabetes
  - 5. Rheumatoid Arthritis
  - 6. Periodontal disease
Am J Gastroenterol, 2010- authors DJ Margolis, et al suggested that while the risk of IBD from Isotretinoin appears to be minimal, it appears that there is a potential association between the oral tetracycline class of drugs used to treat acne and inflammatory bowel disease.

They also found a hazard ratio of 2.25 for the development of Crohn’s disease with the use of doxycycline, with the risk evident only after 2 months of use.
How does this affect dermatology?


• Cross-sectional analysis on 239 patients with HS seen at Johns Hopkins from 2010-2015.

• Concluded that antibiotic therapy for HS treatment may be inducing antibiotic resistance.

• Raised the question regarding the balance of antibiotic use versus potential harms associated with antibiotic resistance.

• A controversial proposal: no more antibiotics for acne!
• Muhammad M, Rosen T

• Use of antibiotics, often for prolonged periods, has become the de facto standard of care for acne (and rosacea). However, the world is now facing a health crisis relating to widespread antibiotic resistance.

• The authors provide current evidence to suggest that dermatologists should consider a radical departure from standard operating procedure by severely curtailing, if not outright discontinuing, the routine and regular use of antibiotics for acne.
• Trends in the treatment of acne vulgaris: are measures being taken to avoid antimicrobial resistance?
• Kinney MA, Yentzer BA, Fleischer AB Jr, Feldman SR.

• CONCLUSION: The development of antibiotic resistance is of concern. Greater awareness of retinoid use for maintenance therapy, using topical benzoyl peroxide to prevent resistance, and limiting use of oral antibiotics to as short a time period as possible are measures to contribute to better eco-responsible acne treatment.
Systematic review of Propionibacterium acnes resistance to systemic antibiotics.

Cooper AJ

Research since 1978 has suggested an association between poor therapeutic response and antibiotic-resistant propionibacteria. The overall incidence of P. acnes antibiotic resistance has increased from 20% in 1978 to 62% in 1996. Resistance to specific antibiotics varied and was most commonly reported with erythromycin and clindamycin, tetracycline and doxycycline, and trimethoprim. Resistance to minocycline is rare.

CONCLUSIONS:

In many patients with acne, continued treatment with antibiotics can be inappropriate or ineffective. It is important to recognize therapeutic failure and alter treatment accordingly. The use of long-term rotational antibiotics is outdated and will only exacerbate antibiotic resistance
What do we do???

• Figuring out how to undo the damage done by antibiotics and an unhealthy lifestyle might be the answer to undo the damage
How do we build a better biome and improve our general health?
It’s never too late to get dirty....
7 ways to embrace more microbes

• Stay away from hand sanitizers
• Exposure yourself to the great outdoors
• Stop destroying your personal army of microbes
• Make your microbes flourish with greens
• Get rid of artificial sweeteners and other chemicals
• Discover prebiotics- non digestible short chain fatty acids that help your bacteria flourish-artichokes, garlic, beans, oats, onions and asparagus
• Protect your microbiome with probiotics
Probiotics

• Evidence-based reviews indicate that certain strains of probiotics help to balance the microbial colonies in the gut.
• The inhibition of pathogenic bacteria may be due in part to pH as well as antimicrobial activity of the probiotic colonies (good guys vs bad guys).
• Touted for an array of diseases: eczema, acne, IBS, autism, food allergies, etc.
• In the US the products are unregulated and not subject to FDA oversight.
• Very difficult to find products with consistent strains, dosages and populations of bacteria.
• Nearly 40 billion dollar industry.
Benefits of Probiotics-Eczema

- 2012 Journal of Allergy and Clinical Immunology: Infants whose mothers took probiotics during pregnancy and breastfeeding were less likely to develop eczema.
- 23 randomized, placebo-controlled studies examining the effects of probiotics on the development of eczema and food allergies-60% of these studies show a favorable outcome during first year of life.
Benefits of Probiotics- Antibiotic Associated Diarrhea (AAD)

- May 2013, review in the Cochrane Database of Systematic Reviews, looked at 23 studies testing a total of 3938 children 2 weeks to 17 years of age who received a probiotic along with an antibiotic

- Probiotic usage was associated with a significant 64% reduction in the risk of AAD
Probiotics Affect Brain Activity?

• June 2013, *Gastroenterology*, utilized a functional MRI that demonstrated women who consume probiotic-containing yogurt on a regular basis have altered activity in the regions of the brain that control central processing of emotion and sensation.
• Not yet determined if these effects are beneficial according to the lead author, Kirsten Tillisch, MD.
• Study funded by Danone Research.
Probiotics and The Skin

• Gut-brain-skin axis originally proposed over 70 years ago by dermatologists John H. Stokes and Donald M. Pillsbury
• Many studies show acne and rosacea patients are at higher risk for GI and emotional issues
• Theory: anxiety <-> GI issues → alter gut microbial flora → promotes local and systemic inflammation
• As early as 1961 there were published case reports showing the benefits of probiotics for the treatment of acne
• One study showed 80% clinical improvement when patients consumed a probiotic
• Other studies from Italy and Russia have also shown improvement
Probiotics and the Skin

• 2008 study published in Clinical Gastroenterology and Hepatology noted that SIBO (small intestinal bacterial overgrowth) was 10 times more prevalent in rosacea patients, and correction of SIBO led to marked improvement in rosacea.

• Other recent studies are looking at the topical application of probiotics for acne and rosacea.
Looking to the future…

• Our control over microbial disease is diminishing
• Pathogens are outsmarting every new antibiotic we develop
  1. Anti-quorum sensing
  2. Anti-toxin production
  3. Enhancing microbiota
  4. Fecal transplants
  5. Phage therapy
  6. Probiotics