
An overview of complementary and alternative medicine in IBD: Hope or Hype?

Jami Kinnucan, MD
Assistant Professor of Medicine
University of Michigan

Director of IBD
Metro Health, University of Michigan



Disclosures

- Advisory board member
 - Abbvie
 - Janssen
 - Pfizer
- Crohn's and Colitis Foundation
 - National Scientific Advisory Committee Chair, Patient Education Committee

Outline

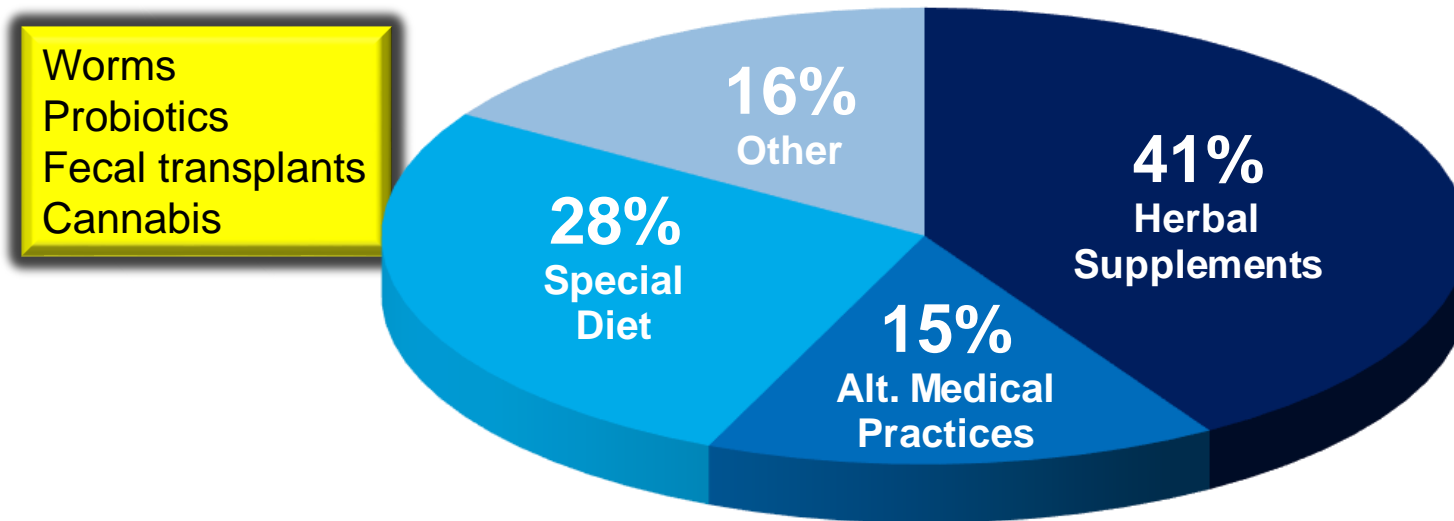
- Overview of complementary and alternative medicine (CAM) in IBD
- Provide overview of evidence (*if any*) for various CAM-based approaches
 1. Dietary modifications
 2. Supplements
 3. Probiotics
 4. Cannabis
 5. Hypnotherapy
 6. Low dose naltrexone (not covered)
 7. Exercise and yoga (not covered)

Outline: Disclaimer

While this is meant to be an overview of more common patient driven discussions about CAM in IBD, it is not meant to be a complete comprehensive overview.

What do we mean by “complementary and alternative medicine” (CAM)?

- A group of diverse medical and health care systems, practices and products not presently part of conventional medicine
- 30-50% of IBD patients report CAM use



Hilsden RJ, et al. *Am J Gastroenterol.* 2003;98(7):1563-1568.

Top reasons why IBD patients use CAM

Direct disease benefits

Search for optimum therapy

Want better control of symptoms and disease

Avoidance of steroid-based therapies

Unable to deal with the side effects of conventional therapies

Ineffective conventional medical therapies

Indirect disease benefits

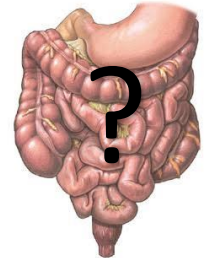
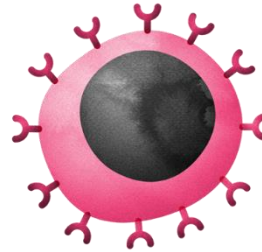
Take control over treatment

Better quality of life due to control of treatment options

Considered “safer” than conventional therapy

Dietary Modifications

Dietary Modifications? Is there a role?



Dietary modifications

Alteration of the
gut bacteria

Immune system
alteration

Effects in Crohn's disease
& ulcerative colitis

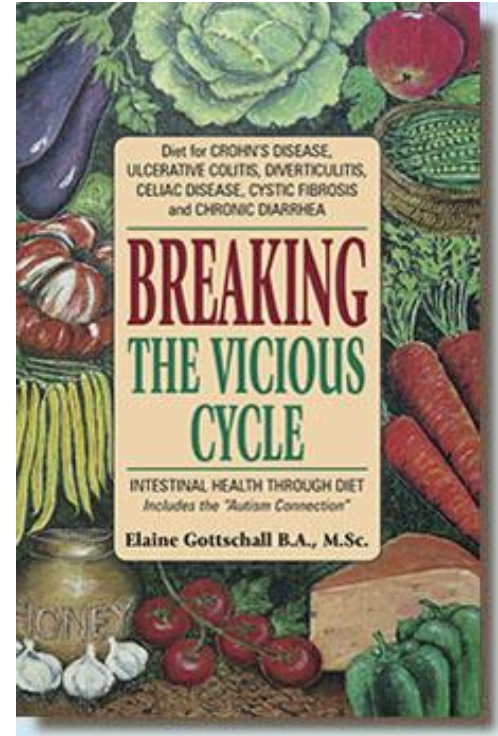
If only it were that simple...

Dietary modifications are difficult to study in a
human population

Hope or Hype: Specific Carbohydrate Diet (SCD)

- Proposed by Dr. Sydney Haas in 1924 for management of celiac disease
- Avoidance of di- and poly-saccharide carbs
- Small case series of self-reported SCD among IBD patients (n=50)
 - Patients noted improvement in **clinical** symptoms with SCD diet, most still taking their IBD therapies
 - Caution: case series so there was no report on patients NOT on SCD diet for comparison

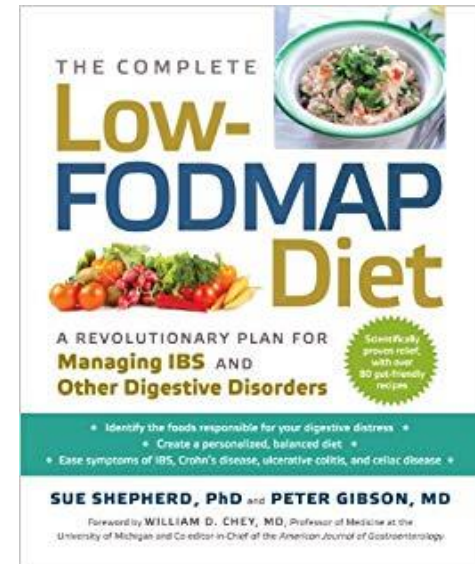
Lack of data= **Hype**



Kakodkar S et al. *Journal of the Academy of Nutrition and Genetics*.

Hope or Hype: Low FODMAP Diet

- FODMAPs are highly fermentable but poorly absorbed carbohydrates
- Elimination of high FODMAP foods for 6-8 weeks
- Significant improvement in patients with visceral hypersensitivity (IBS)
- Studies in IBD patients have shown symptomatic improvement
 - No assessment of disease activity



Hope as adjuvant therapy

Hope or Hype: Omega-3 Fatty Acids

- Fish oils containing Omega-3 Fatty Acids:
 - Naturally found in fish, fish oil, canola oil, soybean oil and dietary supplements
- Results from small trials are inconsistent
- Large trial in over 700 Crohn's disease patients
 - **No benefit** over placebo



Hope as adjuvant therapy

Feagan BG, et al. *JAMA*. 2008;299:1690-1697.

Summary: Diet in IBD

- Most of the evidence shows that patients can FEEL better when they perform dietary modifications
- No significant data to show that dietary modifications CHANGE disease activity
- More studies need to be completed to show overall effects in Crohn's and colitis
 - Crohn's and Colitis Foundation's DINE study



Supplements/Probiotics

Hope or Hype: Curcumin (turmeric)



- Curcumin (1100-2000 mg/day)
 - Large pilot study as **adjuvant therapy** UC (89 patients) showed decrease in clinical relapse @ 6 months¹
 - Pilot study of **adjuvant therapy** in UC and CD (n=10): Decrease 5ASA dosage in UC, improved symptoms in CD²
 - What is needed?
 - Large prospective, randomized controlled trials to show benefit
 - Current studies with no **objective** evaluation/follow-up
 - Initial **small** studies show some promise
 - Standardization of dosing

Hope as adjuvant therapy

1. Hanai H, et al. *Clin Gastroenterol Hepatol*. 2006;4:1502-1506.
2. Holt PR, et al. *Dig Dis Sci*. 2005;50:2191-2193.



Hope or Hype: Vitamin D

- Vitamin D is a hormone with immune system effects
- Normal levels >30 ng/ml
 - 60-70% of IBD patients are deficient in Vitamin D
- Low Vitamin D levels have been linked to more severe disease
 - Increased risk for surgery, hospitalization
 - Colon cancer, *C. diff* infection
- Small studies (n=18-20) show that supplementation leads to improved disease activity and quality of life
- It is easy and safe to supplement

Hope as adjuvant therapy



Hope or Hype: Probiotics

- Based on the idea that inflammation is driven by a gut bacteria **dysbiosis** and that restoration of a **healthy** microbiome can improve inflammation
- Probiotics
 - Traditional, commensal species, genetically engineered
 - Symptom benefit reported with use
 - Many do not colonize the gut, not able to recover in stool samples after 1-4 weeks
 - **Remember:** Not all probiotics are created equal or regulated!

Ciorba M. Clin Gastroenterol Hepatol. 2012;10:960-968.



Hope or Hype: Probiotics

- **Crohn's disease**

- Sing study showing *E. coli Nissile 1917* improved clinical symptoms in Crohn's disease (not available)
- No improvement with VSL#3[®] or others in post-surgery prevention of recurrence

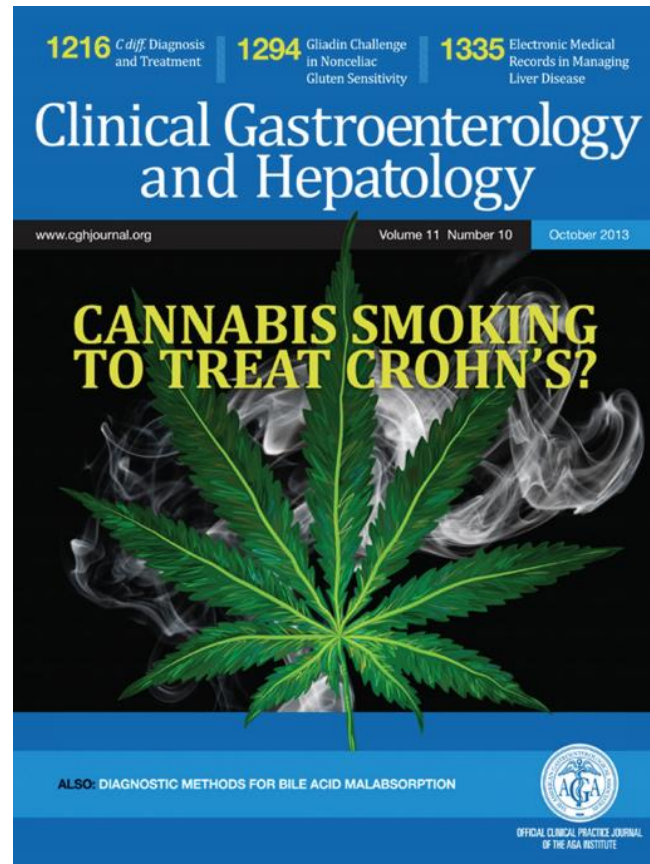
- **Ulcerative colitis**

- Multiple studies showing *E. coli Nissile 1917* showed equal benefit to mesaslamine (5-ASA) in mild disease (not available)
- VSL#3[®] - with benefit as **adjuvant** therapy in ulcerative colitis and for patients with recurrent pouchitis

Hope as adjuvant therapy in UC

Cannabis

Hope or Hype: Cannabis to treat IBD



Hope or Hype: *Cannabis sativa*

- Cannabis also known as marijuana
- Composed of hundreds of active compounds or phytocannabinoids
 - Delta-9-tetrahydrocannabinol (THC)
 - Cannabidiol (CBD)
- Cannabinoids act at cannabinoid receptors in to endocannabinoid system
- Synthetic THC cannabinoids exist but have not been tested in IBD

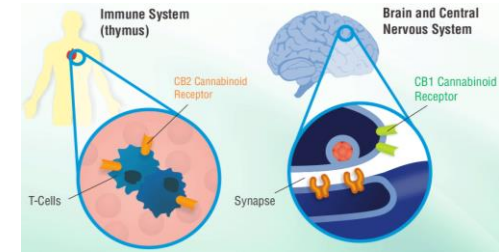
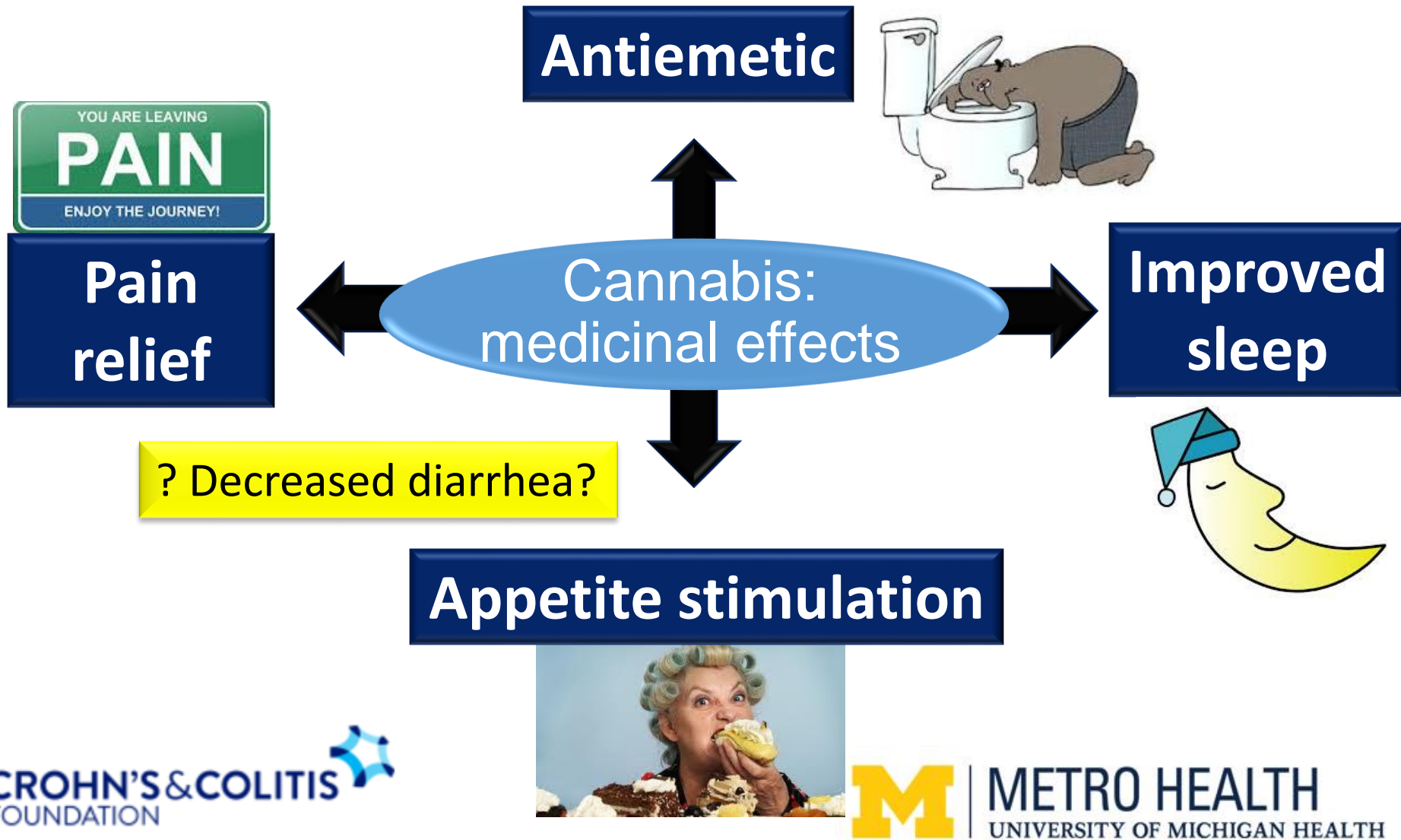
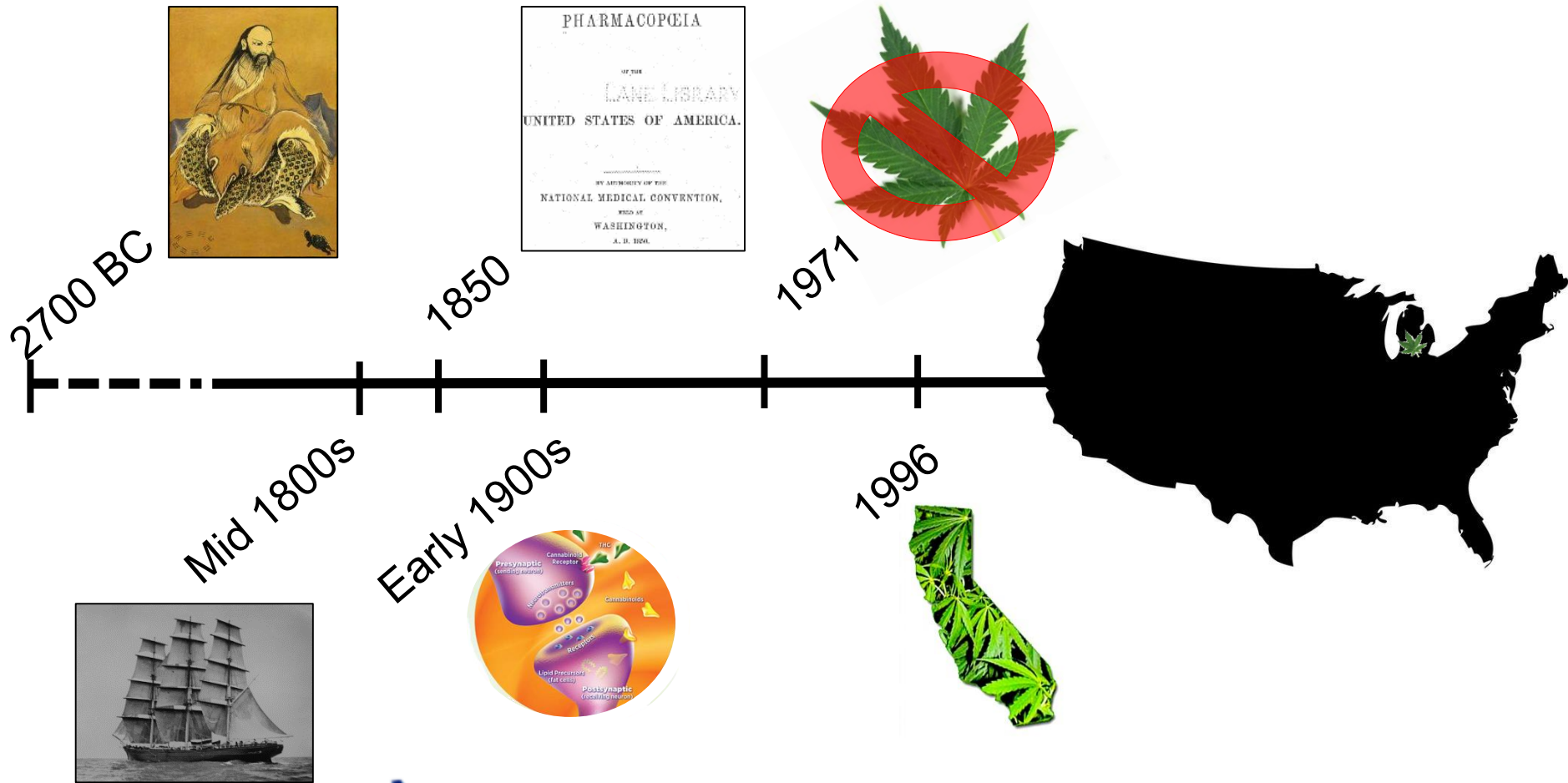


Image adapted from Peak Pharma

What are the clinical effects of cannabinoids (cannabis)?

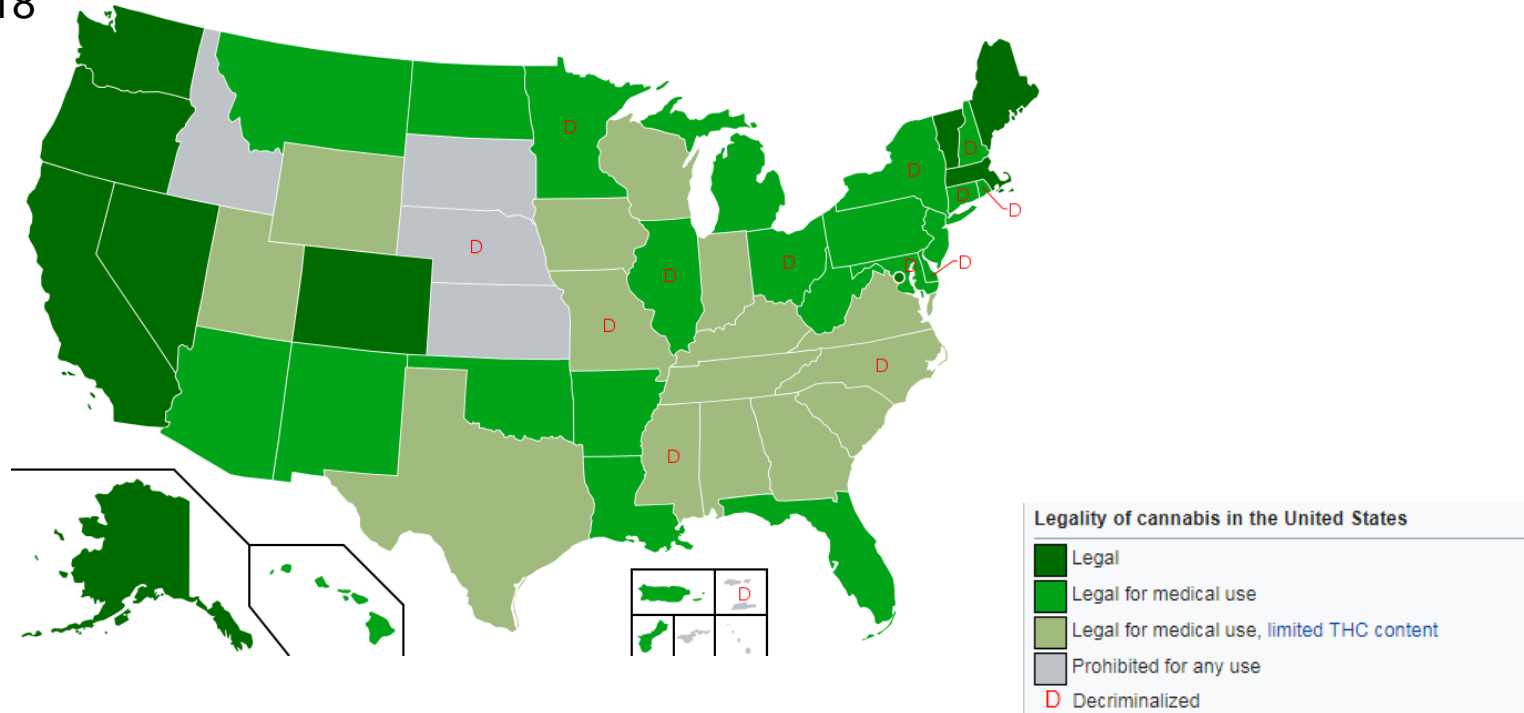


Cannabis timeline



Where is cannabis legal NOW?

As of March 2018



DISCLAIMER: It is still considered Schedule I drug under the Federal Controlled Substance Act

Image adapted from Wikipedia, Sept 1, 2018

IBD patients are using cannabis

- 15-20% IBD patients report active cannabis use
 - Up to 40% report prior use of cannabis
 - They indicate use to relieve IBD-related symptoms
 - To improve pain, appetite and diarrhea, nausea
- More than 50% express interest if it were to become legalized
- Majority mention that they do not discuss use with their health care provider

What are the benefits of cannabis in Crohn's disease patients?

- First small study showed decreased steroid requirement associated with cannabis use
- Follow-up first randomized control trial in 21 patients showing overall clinical improvement
 - *Smoked* 2 cannabis cigarettes/day x 8 weeks
 - Significant improvement in clinical symptoms and quality of life
 - 45% patients achieved clinical remission, however no statistical difference from placebo
 - **No** change in hemoglobin or C-reactive protein (inflammation marker)
- Small study looking at *oral* cannabidiol (no THC) showed no difference in clinical symptoms or lab assessment

What are the benefits of cannabis in **ulcerative colitis** patients?

- Limited data in ulcerative colitis
- First randomized controlled trial in 60 patients with ulcerative colitis on mesalamine therapy
 - Only 59% of patients completed assigned therapy vs. placebo
 - No difference in remission rates
 - Trend towards improved quality of life
- Preliminary data presented in 28 patients with ulcerative colitis showed improvement in clinical symptoms and endoscopic (colonoscopy) change

So what are the risks?

- Long-term effects have not been well studied
- Large study published looking at risks in all cannabis users
 - Risk for addiction to other substances, diminished life achievement, increased motor vehicle accidents, chronic bronchitis, psychiatric disturbances
 - Cannabis hyperemesis syndrome
- Most studies in IBD show no significant adverse effects
 - However the studies have been small in size
- Risks that have been shown in studies
 - Increased risk for discontinuation of conventional therapy and relapse of disease
 - Increased risk for surgery in Crohn's disease

Summary: Cannabis in IBD

- Large percentage of IBD patients have used or are using cannabis to manage IBD-related symptoms
- Studies have shown some benefits of cannabis use in IBD, however no studies have shown significant impact on disease activity and some showing possible risk
- Important to discuss use with health care provider, important to not stop conventional medical therapy
- More studies are needed

Hope as adjuvant therapy

Gut-Directed Hypnotherapy

Hope or Hype: Gut-Directed Hypnotherapy



- Small study show that gut-directed hypnotherapy showed possible disease modifying benefit
 - 17 patients who had a single session of gut-directed hypnotherapy had reduced mucosa levels of inflammatory proteins
- Randomized-control trial (only) in 54 ulcerative colitis patients showed prolonged clinical remission
 - Attended 7 sessions of gut-directed hypnotherapy
 - Remission 2.5 months greater than placebo
- University of Michigan has GI-specific psychologist who performs gut-directed hypnotherapy (Dr. Megan Riehl)

Slide content c/o Dr. Megan Riehl

Hope or Hype: Complementary and alternative medicine

In general there are several CAM therapies that have **HOPE** as adjuvant therapy in the management of ongoing symptoms

Important for patients to work with health care providers about how they incorporate CAM therapies into existing treatment plans
(not replace!)

Thank you

Questions will be taken at the end of the discussions today

Some other therapies (not discussed today)

- Low dose naltrexone
- Exercise/yoga

Hope or Hype?: Low-dose naltrexone (LDN)

- LDN is inexpensive, daily oral therapy with low risk profile that has been minimally studied
- Mechanism: opioid antagonist that can act in the gut, central nervous system and immune cells
- Two small studies
 - Small open-label (no placebo) study in 17 patients showed clinical improvement in majority of patients, improvement in quality of life
 - Small (n=34) placebo-controlled study showed clinical response but no clinical or endoscopic remission at 12 weeks
- Side effects present: diarrhea, abdominal pain, insomnia, nausea and vomiting

Likely **Hype**: No clear evidence

Hope or Hype?: Exercise/Yoga

- Exercise

- Low to moderate physical activity may improve symptoms of IBD
- Walking with improvement in mood, fatigue, weight maintenance and osteoporosis



- Yoga

- 100 patients (60 UC, 40 CD) in **remission**
- Decreased joint pain, abdominal pain, anxiety

Hope as adjuvant therapy

