Sequential Stool Testing to Monitor Progress in People with Rheumatoid Arthritis

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Founder and Director, Blum Center for Health

Author, The Immune System Recover Plan

November 16, 2016

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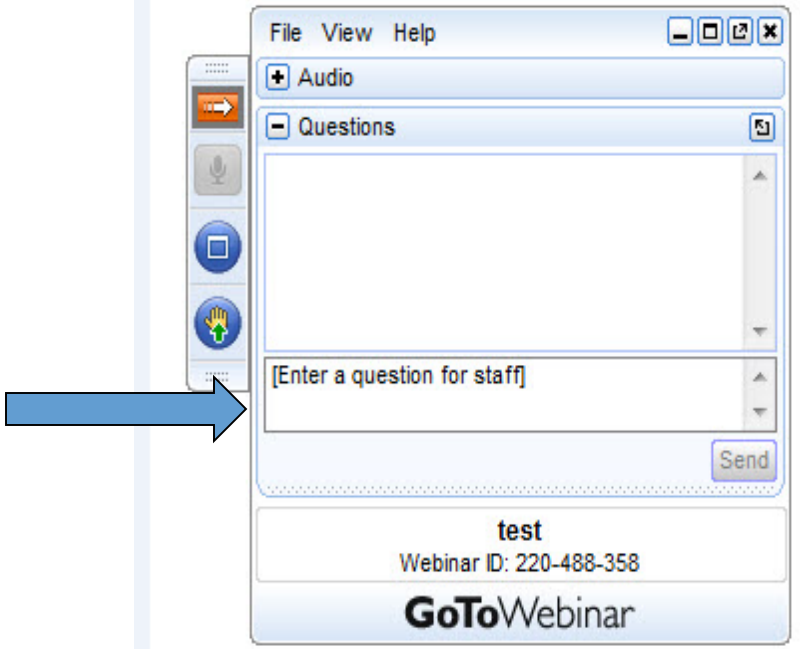
Technical Issues & Clinical Questions

Please type any technical issue or clinical question into either the “Chat” or “Questions” boxes, making sure to send them to “Organizer” at any time during the webinar.

We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.



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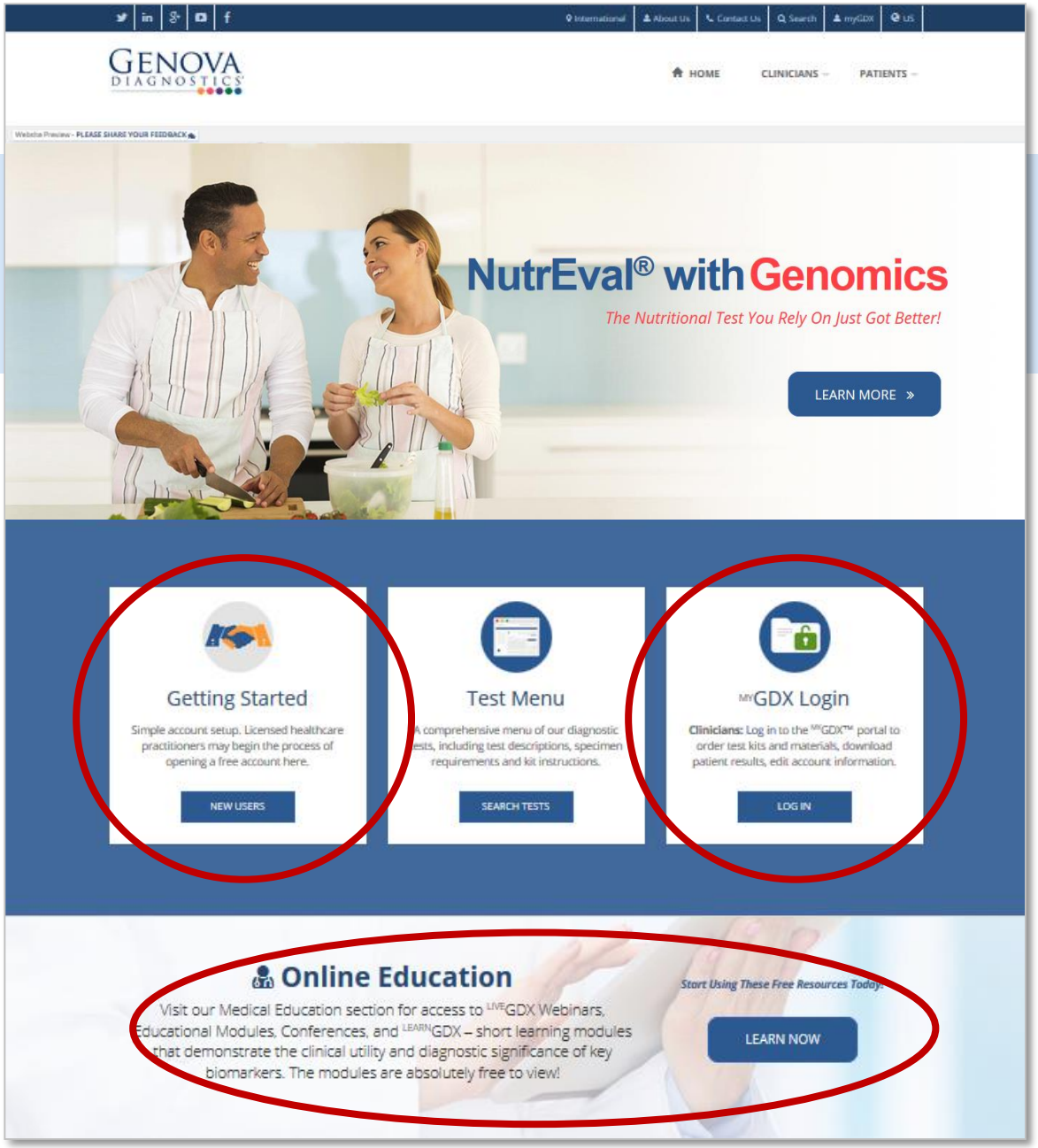

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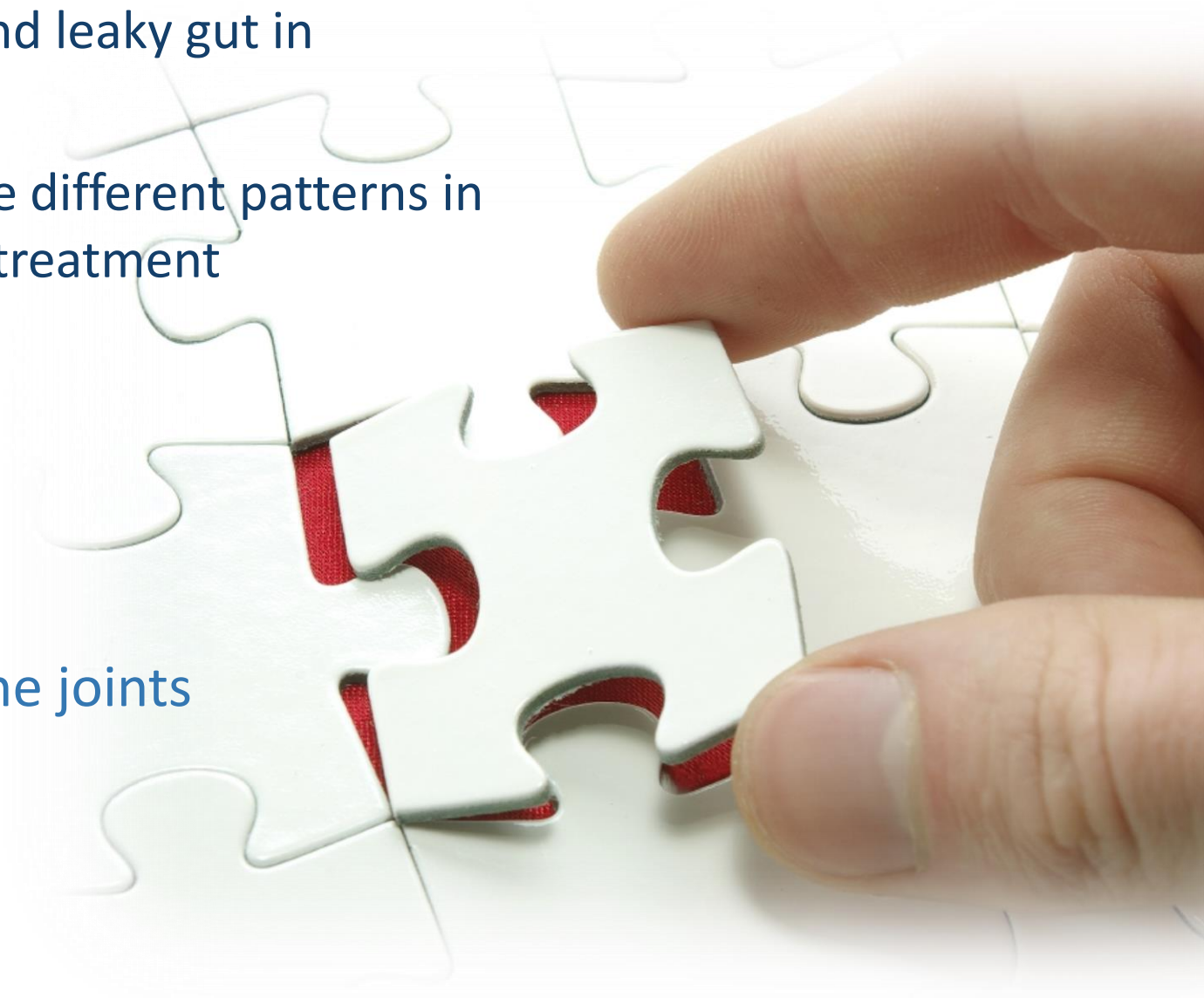
What We Will Talk About…

- The role of gut microbial dysbiosis and leaky gut in triggering inflammatory arthritis
- The role of stool testing to determine different patterns in the gut microbiome and direct your treatment
- Case studies:
  - Sequential stool tests
  - Treatment protocols
  - How to treat the gut to treat the joints



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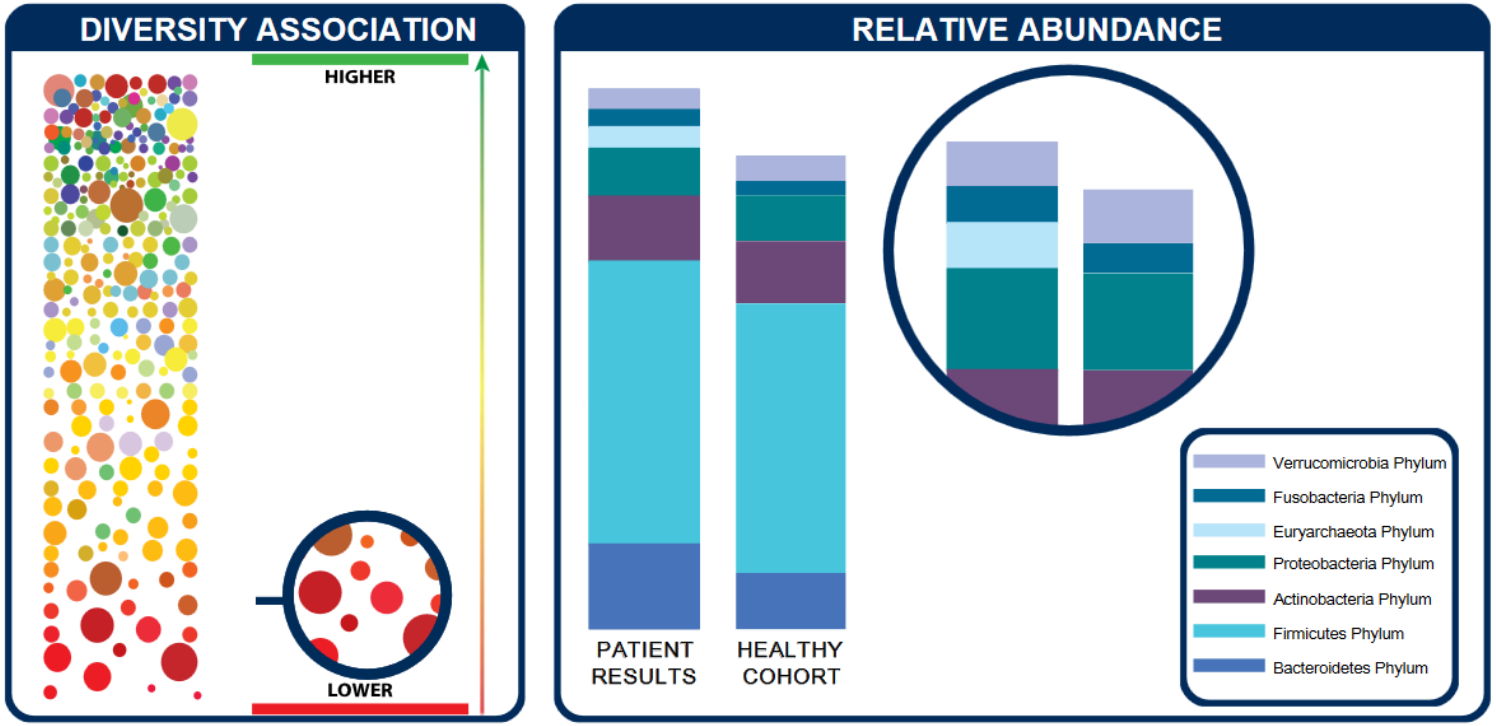
Dysbiosis and Inflammation

Dysbiosis is a common feature of those with inflammatory arthritis and appears to trigger a whole cascade of inflammation that ends up in the joints



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Dysbiosis and Arthritis

- Healthy gut microbiome:
  - Ferments food (fiber) and makes SCFA : butyrate, propionate, acetate
  - Helps protect and maintains barrier
  - Immune system development: T regulator cells
  - Anti-inflammatory cytokines
- Dysbiosis: altered state of gut bacteria.
  - Promotes increased intestinal permeability
- Leaky gut:
  - Cell walls of gut bacteria have been found in the joints
  - Increased **systemic inflammation** and **oxidative stress**

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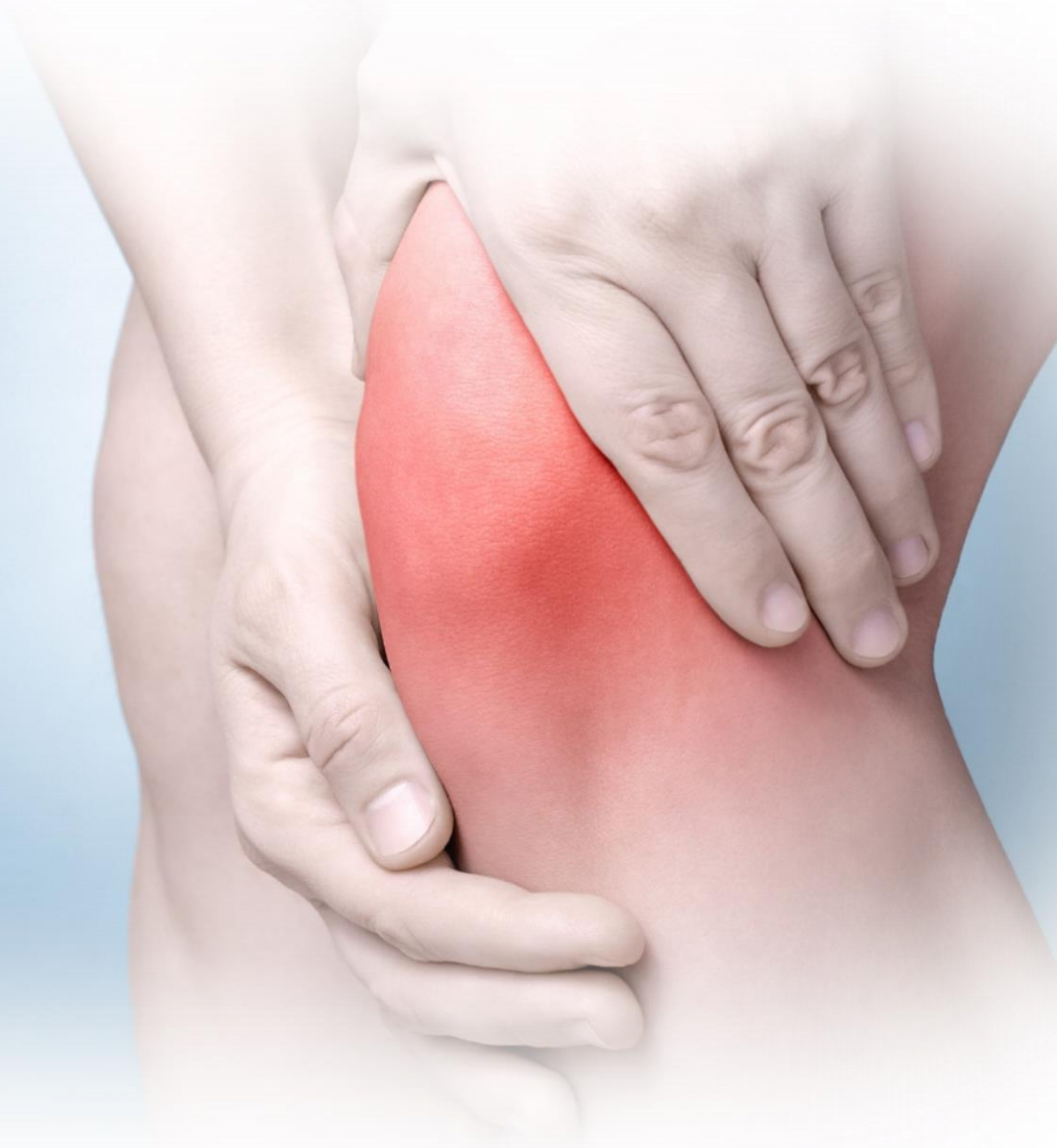
Sandhya P, Danda D, Sharma D, et. al. Does the buck stop with the bugs?: an overview of microbial dysbiosis in rheumatoid arthritis. International Journal of Rheumatic Diseases 2015.

Oxidative Stress

- High levels of oxidative stress in the joints
- Causes synovial hyperplasia, then tissue and joint damage
- Dysbiosis and leaky gut: system wide immune activation, generates free radicals
- Immune complexes in the joints generate reactive oxygen species
- Poor absorption of nutrients causes deficiency of much needed antioxidants



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Bacterial Triggers for RA

Studies showing possible bacterial triggers

- *Proteus mirabilis* in the gut or urine
  - Treating the gut with herbs can lower anti-proteus antibody levels
    - Cock, I. E., Winnett, V., Sirdaarta, J., & Matthews, B. (2015). The potential of selected Australian medicinal plants with anti-Proteus activity for the treatment and prevention of rheumatoid arthritis. Pharmacognosy Magazine, 11(Suppl 1), S190–S208
- Many studies linking dysbiosis to RA
  - *Prevotella copri* specifically
  - Studies consistently find different bacterial patterns in people with inflammatory arthritis vs controls. Some high in *bacteroides*, some high in *prevotella*
  - Pro-inflammatory bacteria: *Enterobacter aerogenes, Klebsiella pneumonia, Strep viridans, Bacteroides fragilis, Bacteriodes uniformis, Clostridium ramosum*

Treating Dysbiosis

- Researchers have not conclusively connected different patterns of dysbiosis with different diseases
- For now, best not to focus on the exact strains of bacteria that are out of balance
- Broad spectrum herbs to reduce bacterial populations
- Many herbs, like berberine, spare lactobacillus and bifidus while selectively killing inflammatory bacteria strains
- Rotate different blends
- Targeted treatment for candida

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Chae, Suck-Hee . Growth-Inhibiting Effects of *Coptis japonica* Root-Derived Isoquinoline Alkaloids on Human Intestinal Bacteria. *J. Agric. Food Chem.*, **1999**, *47* (3), pp 934–938

Information to Guide Gut Treatment

- Test for presence of these inflammatory microbes
  - Yeast (candida)
  - Parasites: Inflammatory bacteria
    - Aerobic: *Klebsiella, Pseudomonas, Citrobacter, Bacillus*
    - Anaerobes: very high amounts of bacteroidetes including *Prevotella*
  - SIBO
- Test for absence of beneficial flora

Information to Guide Gut Treatment

- **Metabolic markers of dysbiosis and inflammation**
  - Fecal fat: when high may indicate SIBO. Follow this with treatment
  - SCFA: very low need more fiber, or reflects low amounts of beneficial flora. Directs treatment towards diet and probiotics
  - Beta glucuronidase: enzyme produced by bad bugs. When high, let's you know that you need to continue treatment
- **Immune:**
  - Calprotectin: inflammatory marker, directs treatment to include anti-inflammatory support like curcumin and fish oil. Requires you to follow until it is normal
  - EPX: allergy marker, look harder for parasite and yeast. Food allergy testing

Conventional Assessment

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Conventional Assessment

- Stool for calprotectin and fecal fat
- SIBO breath testing
- Stool for ova and parasites
- Endoscopy
- Colonoscopy
- ENT for reflux evaluation

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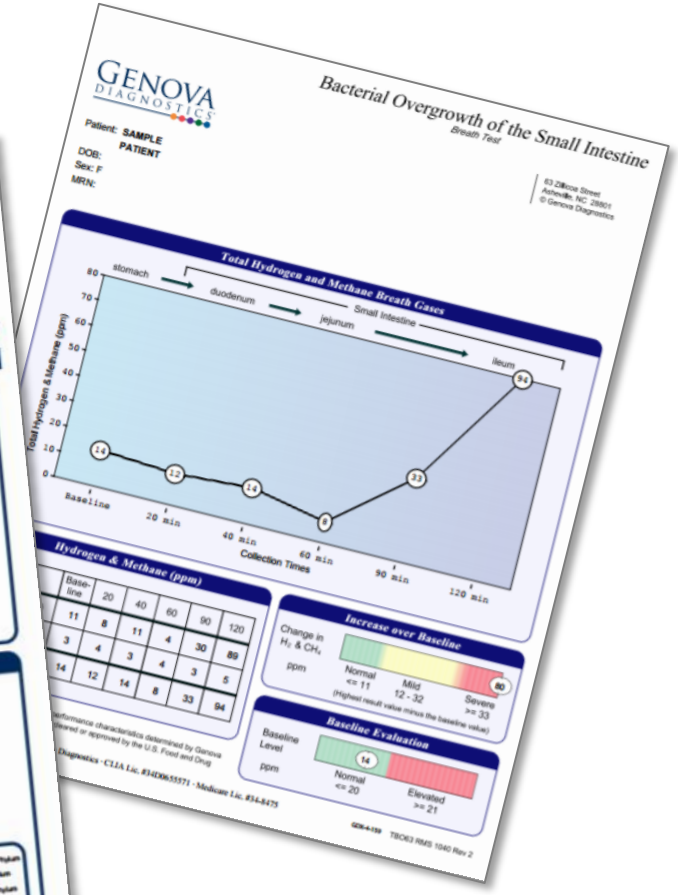
Integrative Assessment

Stool Tests



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Stool Test: GIFX or CDSA 2.0

- Use for initial assessment to determine what to treat and for how long
  - SIBO
  - Bacterial dysbiosis without SIBO
  - Candida
  - Parasites
  - Low good bacterial
  - Problems with digestion: need enzymes?
- Sequential testing to direct treatment as-you-go
- Finish what you started!
- People with inflammatory arthritis need multiple courses of gut treatment over months to years

Outcomes: Case Study

- Sequential stool tests
- Treatment protocols
- How to treat the gut to treat the joints

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Case Study: “June”

- 63 y.o. woman with RA x 2 years
- Very aggressive quickly
- Pain and deformity in both hands: couldn’t open water bottles, put rollers in her hair, hold a toothbrush, clasp her bra
  - Despite being on Plaquenil, methotrexate, and prednisone
- Long history of living abroad, including Asia and Africa, and treated for parasites multiple times, including worms, giardia and amebic dysentery
- History of ulcerative colitis while living in Japan
- Most recently moved back to Connecticut and RA started when she went back to work as a teacher

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RA Case “June”: Initial labs

- CCP antibodies 47 (<20 is normal). Best specificity for RA
- RF was normal
- CRP 1.0 (c-reactive protein, marker for inflammation)
- ESR 18 (sed rate, marker for inflammation)
- ANA negative
- Vit D 50
- DHEA-S 21 (very low, sign of chronic stress)

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RA Case “June”: Initial labs

- Elimination diet
- Ultrainflammx plus 360 shakes with ProEFA liquid fish oil and vitamin D
- Within 1 month: dropped her prednisone in half (to 2.5), relieved digestive issues, and pain was much improved in hands though not in knees
- At second visit we reviewed her stool test. It was done in May, end of school year
  - Candida 1+ and high beta glucuronidase, NG LACTO with low butyrate
  - The stool test was not as bad as her symptoms suggested

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Test Results

Digestion/Absorption

Analyte	Result	Reference Range
1. Pancreatic Elastase 1 •	401	>= 201 mcg/g
2. Putrefactive SCFAs (Total*)	4.7	1.3-8.6 micromol/g

*Total values equal the sum of all measurable parts.

Gut Immunology

Analyte	Result	Reference Range
3. Eosinophil Protein X	1.2	<= 7.0 mcg/g
4. Calprotectin •	<17	<=50 mcg/g

Metabolic

Analyte	Result	Reference Range
5. Beneficial SCFAs (Total*)	31.9	>= 13.6 micromol/g
6. n-Butyrate	4.6	>= 2.5 micromol/g
7. pH	6.5	6.1-7.9
8. Beta-glucuronidase	4,933	337-4,433 U/g
Secondary Bile Acids		
9. Lithocholic acid (LCA)	1.55	0.65-5.21 mg/g
10. Deoxycholic acid (DCA)	2.20	0.67-6.76 mg/g
11. LCA / DCA Ratio	0.70	0.39-2.07

*Total values equal the sum of all measurable parts.

Additional Tests

	In Range	Out of Range
15. HpSA- H.pylori	Negative	

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Test Results

Parasitology

Microscopic Exam Results:

No Ova or Parasites seen

Macroscopic Exam for Larvae

No larvae seen macroscopically.

PARASITOLOGY EIA TESTS:

	In Range	Out of Range
Cryptosporidium	Negative	
Giardia lamblia	Negative	
Entamoeba histolytica/dispar	Negative	

Microbiology

Bacteriology

12. Beneficial Bacteria

Lactobacillus species	*NG
Escherichia coli	4+
Bifidobacterium	1+

13. Additional Bacteria

alpha haemolytic Streptococcus	NP	1+
gamma haemolytic Streptococcus	NP	1+
Citrobacter youngae	NP	1+

14. Mycology

Candida albicans/dubliniensis	NP	1+

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.

*NG	NP	PP	P
*NG			
No Growth	Non-Pathogen	Potential Pathogen	Pathogen

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RA Case “June”: Treatment

- Herbal gut cleanse:
  - 1 month of oregano 2 BID
  - 1 month of Tricycline by ADP: 2 BID
  - Followed by 1 month of Nystatin: 500k TID
- Gut support
  - Ultrainflammx 360 plus
  - L-glutamine BID
  - Therbiotic complete (Klaire) 50 billion at bedtime
- Gluten, dairy, eggs and night shade free diet
  (she had reintroduced and found these were the problems)
- EPA/DHA/GLA oils

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RA Case “June”: Visit 2 Summer

- Follow-up 4 months later
- Symptoms much improved, happy
- Still following food plan
- Most of the time, with minimal pain she can now:
  - open water bottles
  - fix her hair and brush it
  - get clothes and bra
- Knee has finally improved. Was 6/10, now 8/10
- Energy is better, now 8/10. was 5/10
- Taking Alleve less often. Was daily, now 3-4 days/week
- Stool test was improved but not completely resolved

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2nd Stool Test

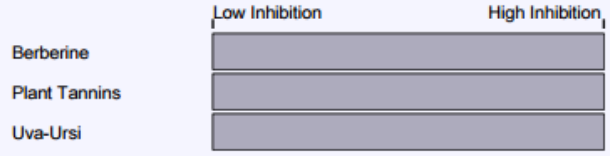
Prescriptive Agents

BACILLUS SPECIES

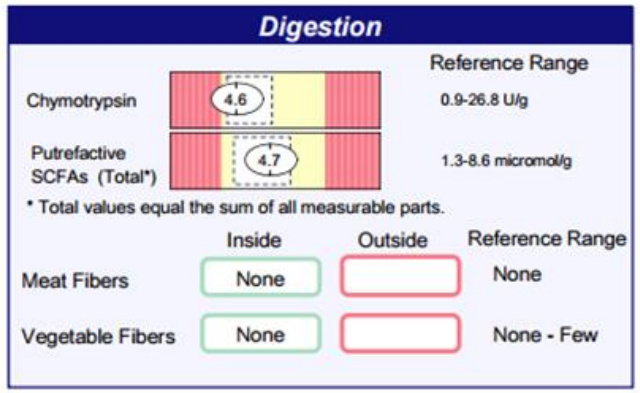
In general, *Bacillus species,* not *B. cereus,* demonstrate variable susceptibility to the penicillins and the cephalosporin antibiotics. Clindamycin and Vancomycin have shown effective activity when used to treat serious infections.

Natural Agents

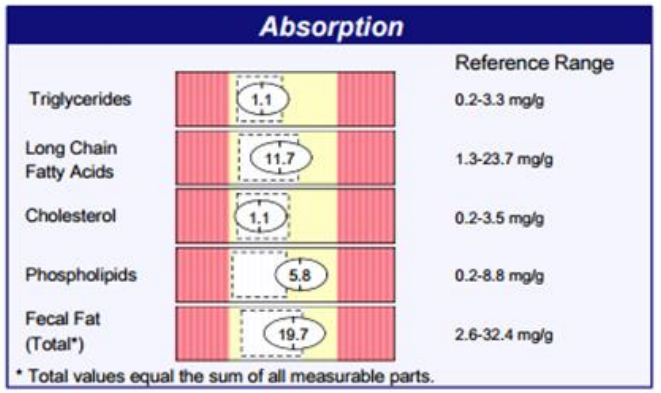
BACILLUS SPECIES



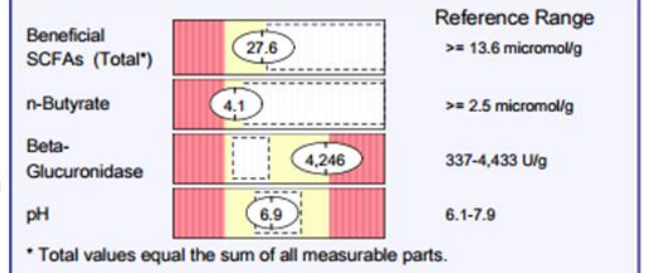
Digestion



Absorption

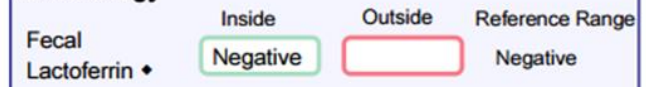


Metabolic Markers



SCFA distribution

Immunology

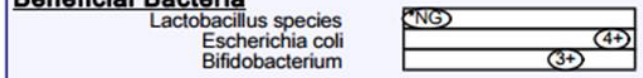


Macroscopic

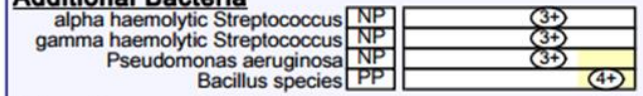
Microbiology

Bacteriology

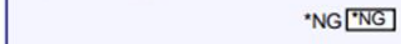
Beneficial Bacteria



Additional Bacteria



Mycology



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RA Case “June”: Interpretation and Treatment

- Beta glucuronidase dropped slightly, but still high suggesting presence of harmful anaerobes
- 3+ pseudomonas and 4+ bacillus need treatment
- Lactobacillus still not growing and butyrate still low
- Fecal fat is ok, lessening likelihood of SIBO
- Blood in stool: She reported seeing blood on tissue and having some hard stool
  - Referred to GI
- Treatment:
  - Candibactin BR: 2 BID for 1 month
  - Continue the rest of the GI support program

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RA Case “June”: Visit 3

- She came back 4 months later, in December
- STRESS from work. Very physically demanding, too
- Gave up on diet completely
- FLARE of symptoms
- Blood work:
  - CCP was higher 82
  - CCRP: 13.1 (marker for inflammation)
- No stool test this visit
- Decided to treat gut again with
  - GI MicrobX by DFH: 2 BID for 1 month
  - Oregano by DFH: 2 BID x 1 month

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RA Case “June”: Visit 4

- End of school year in May
- Had the flu and strep during the winter, took antibiotics
- Following the food plan only some of the time but overall eating less processed food and sugar
- Was still on the lowered dose of prednisone 2.5, but afraid to change it during the school year
- Symptoms were stable from initial improvement, but not changed from last visit
- We reviewed the CDSA:
  - Beta glucuronidase finally resolved, normal
  - No more blood in stool
  - 1+ proteus, still low butyrate

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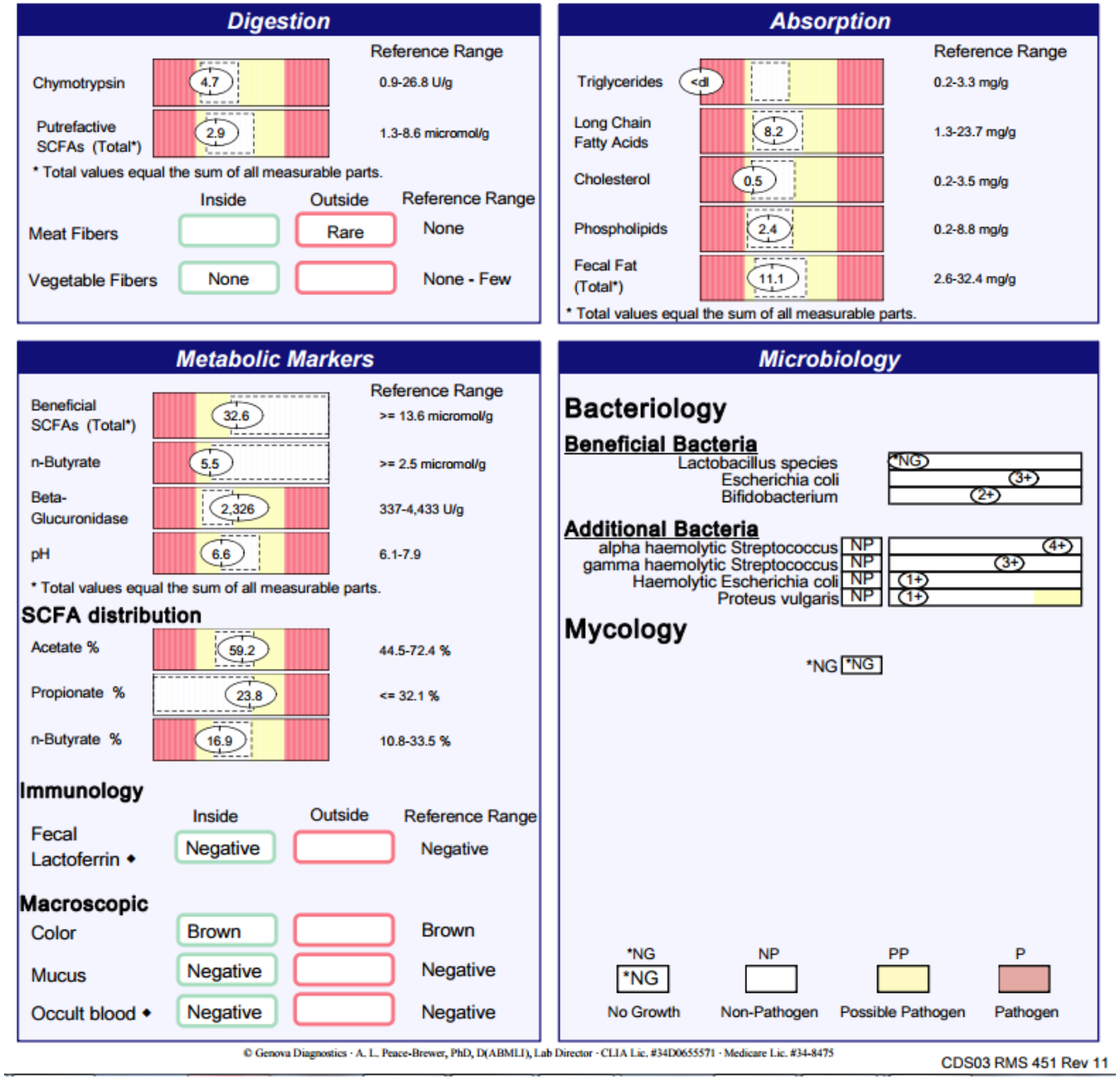
RA Case “June”: CDSA



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RA Case “June”: Assessment and Treatment

- Given her high amounts of stress, winter flare, and the flu, stool test and symptoms pretty stable
- Plan: Over the summer focus on food, mind-body practice, and another short round of gut cleanse herbs
- Tricycline (ARG) 2 BID for 2 weeks
- Return end of summer with repeat blood testing, SIBO and NutrEval to check dysbiosis markers

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RA Case “June”: Visit 5

- Joint pain, energy and gut all improved again over the summer
- Blood work: CCP 7.6!!!
- RA testing now normal
- SIBO was normal
- NutrEval: showed high dybiosis markers including yeast
- Based on NutrEval
  - Treat the yeast with Diflucan: 100 mg daily for 2 weeks.
  - Add digestive enzymes: low amino acids
  - She also needed lots of support for OXIDATIVE STRESS: NAC. Lipoic acid

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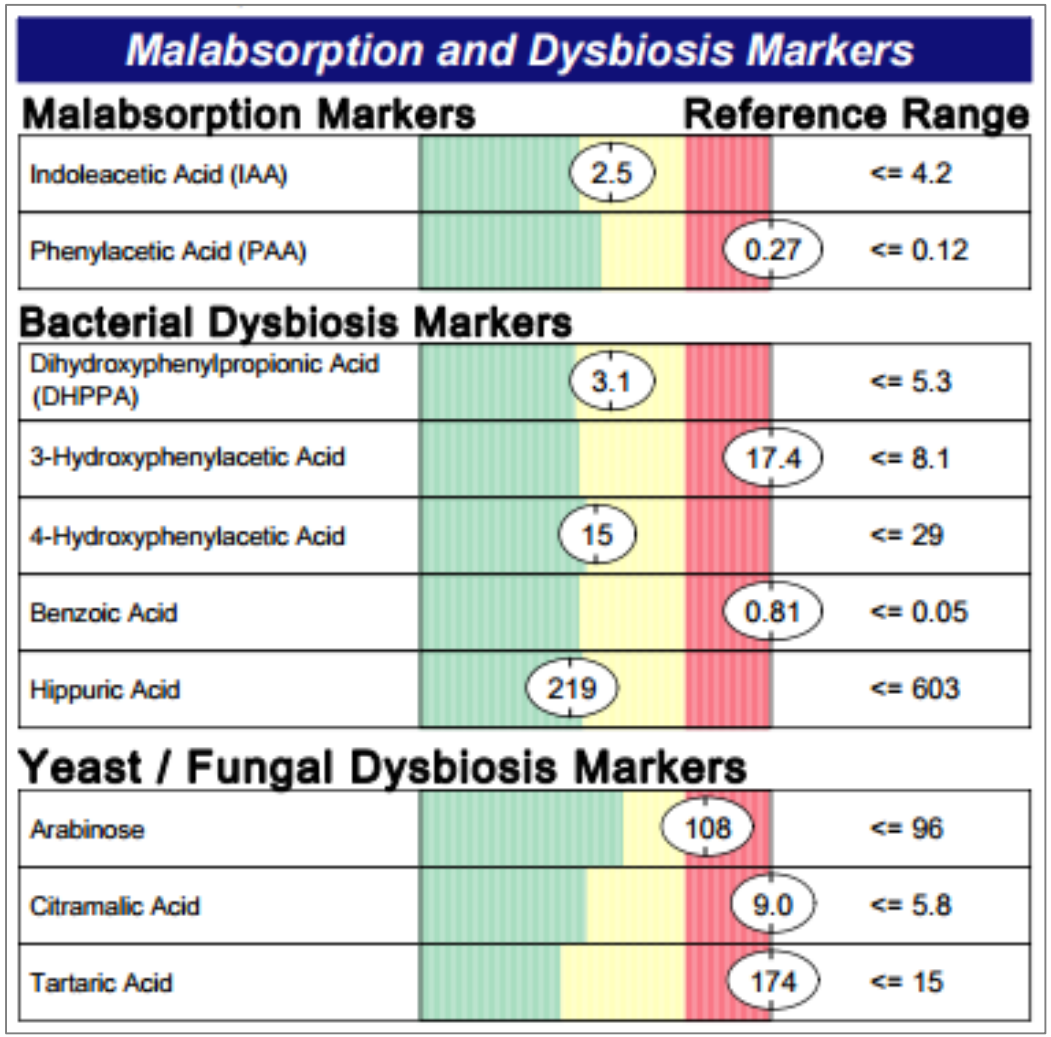
RA Case “June”: NutrEval Dysbiosis Markers



Malabsorption and Dysbiosis Markers

Malabsorption Markers		Reference Range
Indoleacetic Acid (IAA)	2.5	<= 4.2
Phenylacetic Acid (PAA)	0.27	<= 0.12
Bacterial Dysbiosis Markers		
Dihydroxyphenylpropionic Acid (DHPPA)	3.1	<= 5.3
3-Hydroxyphenylacetic Acid	17.4	<= 8.1
4-Hydroxyphenylacetic Acid	15	<= 29
Benzoic Acid	0.81	<= 0.05
Hippuric Acid	219	<= 603
Yeast / Fungal Dysbiosis Markers		
Arabinose	108	<= 96
Citramalic Acid	9.0	<= 5.8
Tartaric Acid	174	<= 15

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RA Case “June”: Visit 6

- She returned mid-school year
- She still felt great! This is the first year she can remember that she didn’t have a flare in the winter
- Only has pain when she overworks her hands
- Blood tests: CCP and RF still normal
- Retiring in 6 months
- CDSA 2.0:
  - SCFA are lower; need to focus here now
  - Enzymes a little low: stay on enzymes
  - Only 3+ bacillus

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Assessment and Treatment

- We decided to focus on gut healing for the next 6 months, no more herbs
- Increase probiotics to 100 billion/day
- Focus on prebiotics, digestion and leaky gut with glutamine
- She returned at the end of the school year, very excited for her retirement
- NO FLARE FOR ONE YEAR
- Can open jars, carry books, fix her hair, all without pain and consistently
- Moved boxes herself during the move out of her office
- Maintaining 95% night shade free, gluten and dairy free diet
- Has brandy a few nights each week with her husband
- We made a plan to start tapering prednisone

Case Study: “Robert”

- 60 year old man with high cholesterol and high PSA
  Working together for 2 years
- No digestive symptoms, but hx of celiac as a child he “out grew” and hx of ulcer and gastritis @ 16 y.o.
  - We had never done a stool test
- Sudden onset of pain and swelling in two fingers
  Couldn’t bend them
  - No obvious trigger other than STRESS
- Orthopedist: not OA, joints looked normal
  - Alleve didn’t help
- Sent him home with
  - Inflammatone (DFH, 4 x 3), Ultrainflamx
    increased his dose of EPA/DHA/ GLA
  - Arthritis diet: elim diet: gluten, dairy, soy, corn, eggs, night shades
  - Resources to begin a meditation practice

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Inflammatory Arthritis Case “Robert”: Visit 2

Returned 6 weeks later:

- 25% reduction in pain and swelling
- My testing: RF, ACPA, CRP, ANA, Sjogrens, Lyme, all neg
- Undifferentiated inflammatory arthritis
- GIFX: Candida, Prevotella
- NutrEval: high dysbiosis markers

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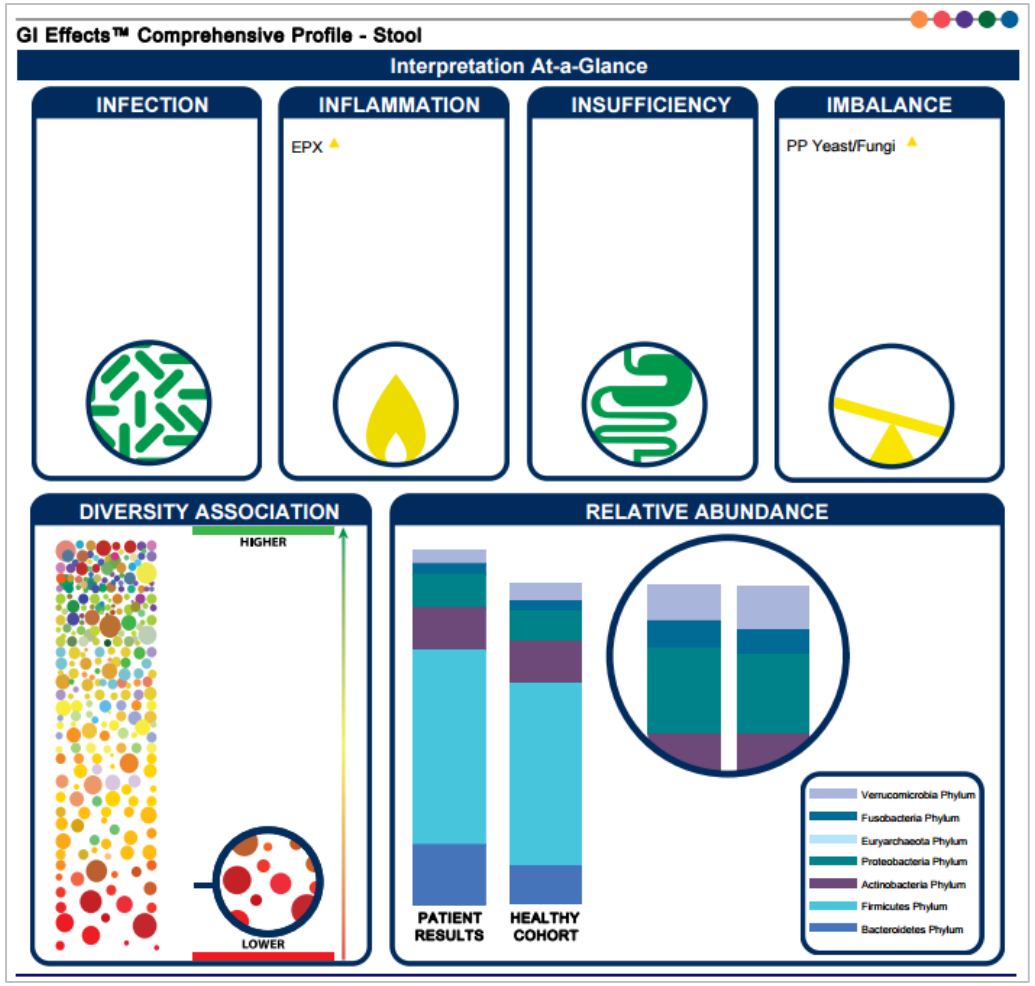
Test Results



GI Effects™ Comprehensive Profile - Stool

Methodology: GC/MS, Automated Chemistry, EIA

	Results	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 † •	359	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	4.9		1.8-9.9 micromol/g
Fecal Fat (Total*)	6.8		3.2-38.6 mg/g
Triglycerides	0.8		0.3-2.8 mg/g
Long-Chain Fatty Acids	3.5		1.2-29.1 mg/g
Cholesterol	1.4		0.4-4.8 mg/g
Phospholipids	1.1		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin † •	<17	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	1.5	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	64		<=885 mcg/g
Gastrointestinal Microbiome			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	61.9		>=23.3 micromol/g
n-Butyrate Concentration	13.2		>=3.6 micromol/g
n-Butyrate %	21.3		11.8-33.3 %
Acetate %	58.9		48.1-69.2 %
Propionate %	19.8		<=29.3 %
Beta-glucuronidase	3,188		368-6,266 U/g

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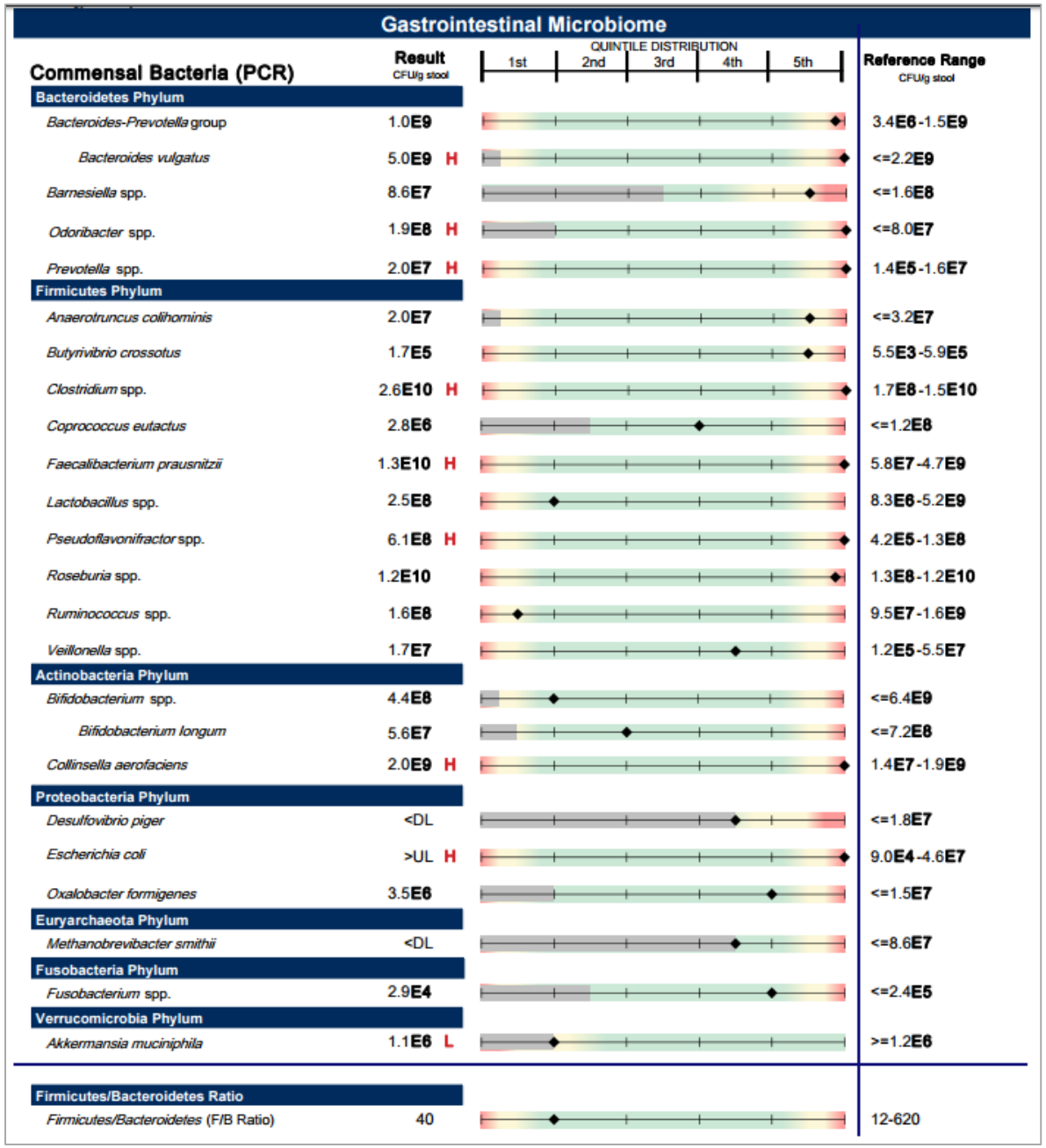
Test Results



Gastrointestinal Microbiome

Commensal Bacteria (PCR)	Result CFU/g stool		QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum				
Bacteroides-Prevotella group	1.0**E9**			3.4**E6**-1.5**E9**
Bacteroides vulgatus	5.0**E9**	H		<=2.2**E9**
Barnesiella spp.	8.6**E7**			<=1.6**E8**
Odoribacter spp.	1.9**E8**	H		<=8.0**E7**
Prevotella spp.	2.0**E7**	H		1.4**E5**-1.6**E7**
Firmicutes Phylum				
Anaerotruncus colihominis	2.0**E7**			<=3.2**E7**
Butyrivibrio crossotus	1.7**E5**			5.5**E3**-5.9**E5**
Clostridium spp.	2.6**E10**	H		1.7**E8**-1.5**E10**
Coprococcus eutactus	2.8**E6**			<=1.2**E8**
Faecalibacterium prausnitzii	1.3**E10**	H		5.8**E7**-4.7**E9**
Lactobacillus spp.	2.5**E8**			8.3**E6**-5.2**E9**
Pseudoflavonifractor spp.	6.1**E8**	H		4.2**E5**-1.3**E8**
Roseburia spp.	1.2**E10**			1.3**E8**-1.2**E10**
Ruminococcus spp.	1.6**E8**			9.5**E7**-1.6**E9**
Veillonella spp.	1.7**E7**			1.2**E5**-5.5**E7**
Actinobacteria Phylum				
Bifidobacterium spp.	4.4**E8**			<=6.4**E9**
Bifidobacterium longum	5.6**E7**			<=7.2**E8**
Collinsella aerofaciens	2.0**E9**	H		1.4**E7**-1.9**E9**
Proteobacteria Phylum				
Desulfovibrio piger	<DL			<=1.8**E7**
Escherichia coli	>UL	H		9.0**E4**-4.6**E7**
Oxalobacter formigenes	3.5**E6**			<=1.5**E7**
Euryarchaeota Phylum				
Methanobrevibacter smithii	<DL			<=8.6**E7**
Fusobacteria Phylum				
Fusobacterium spp.	2.9**E4**			<=2.4**E5**
Verrucomicrobia Phylum				
Akkermansia muciniphila	1.1**E6**	L		>=1.2**E6**
Firmicutes/Bacteroidetes Ratio				
Firmicutes/Bacteroidetes (F/B Ratio)	40			12-620

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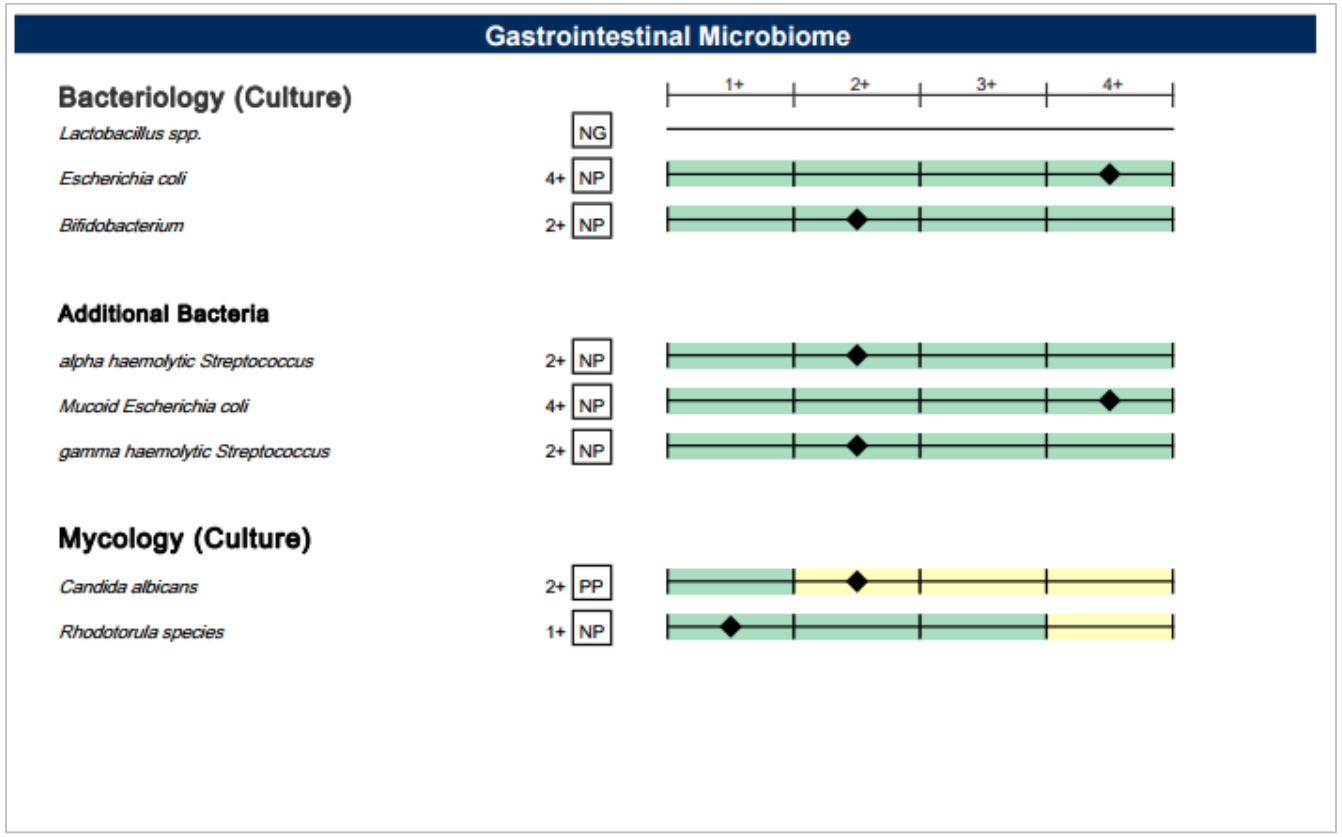
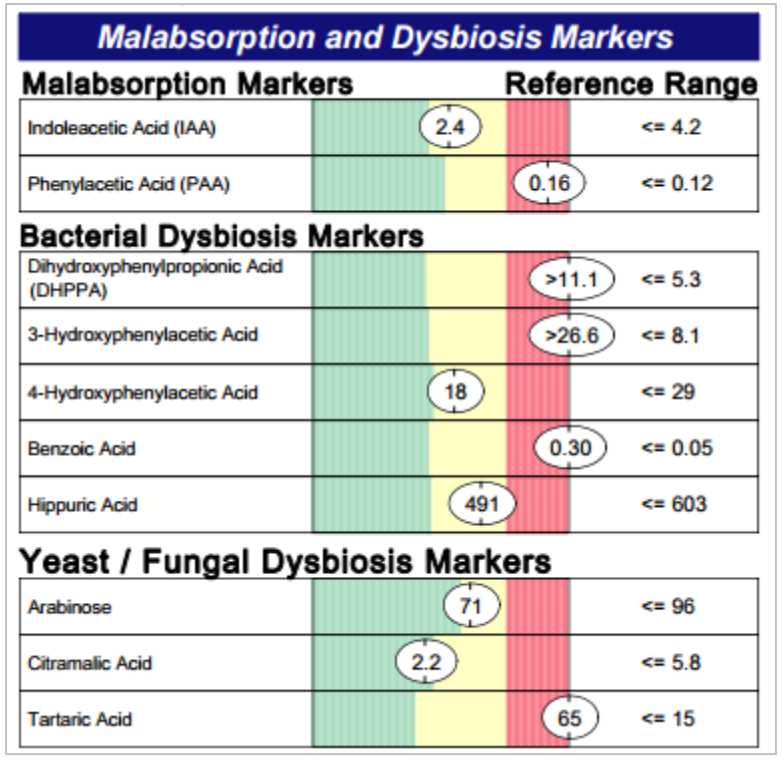
Test Results





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Inflammatory Arthritis Case ”Robert”: Treatment

- Treated him for bacterial and yeast dysbiosis
- GI MICROBx DFH: 2 BID x 1 month
- Oregano 2 BID x 1 month
- Followed by Diflucan 100 mg daily x 1 month
- He hasn’t returned yet with his follow up stool test, but he reported by phone that his arthritis was completely resolved

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Take Home

- Marathon not a sprint: Finish what you started
- Multiple rounds of herbal treatment guided by stool test
- Need to know when to stop: When to add extra treatment for yeast
- Use dysbiosis markers in urine if the clinical picture doesn’t fit with the stool test

Moderator:
Michael Chapman, ND

Presenter:
Susan Blum, MD

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Questions?

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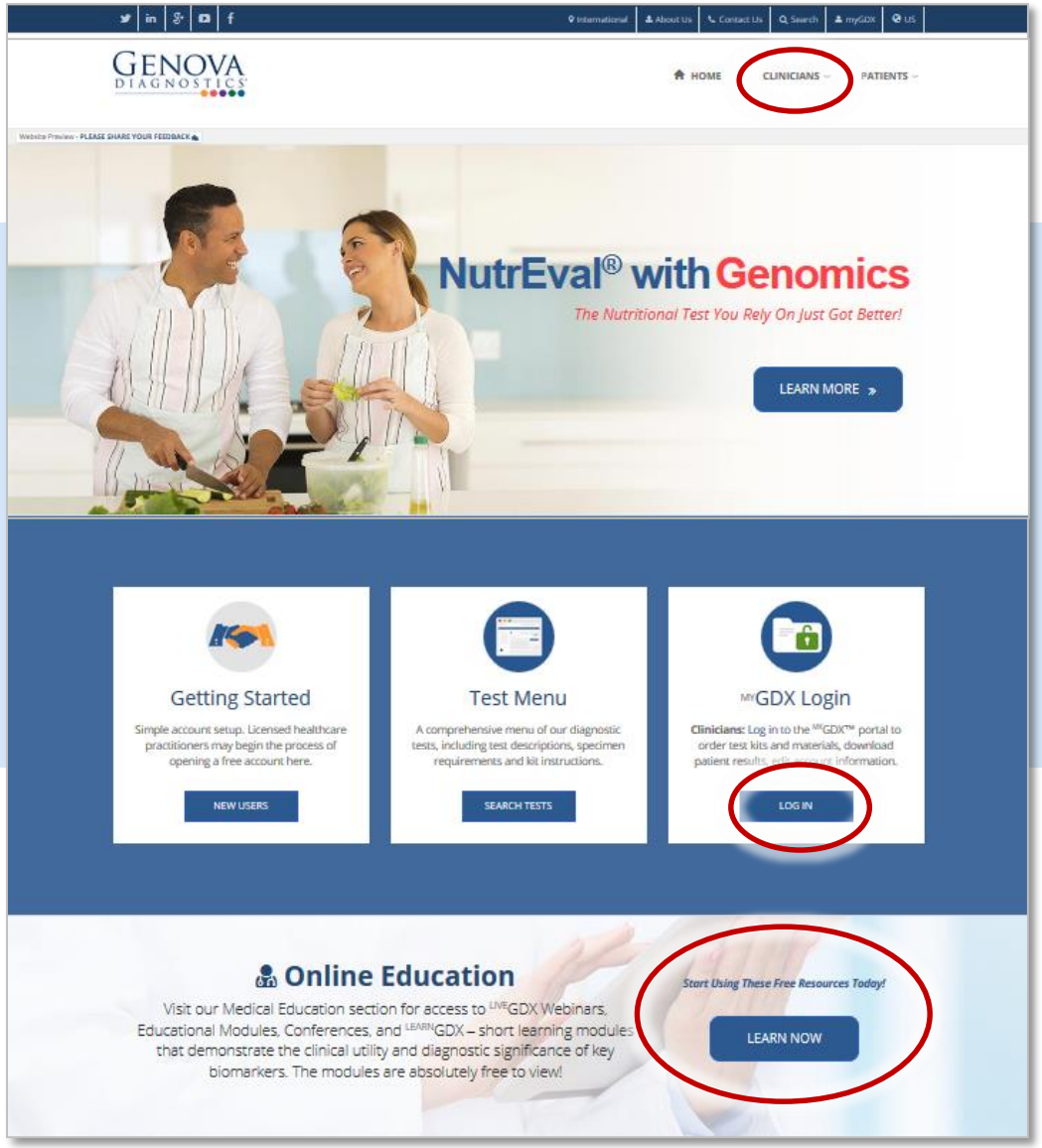
Additional Education Materials:

WWW.GDX.NET

Sample Reports,
Support Guides,
Kit Instructions, FAQs,
Payment Options, and
much more!



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Additional Questions?

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Please schedule a complimentary appointment with one of our Medical Education Specialists for questions related to:

- Diagnostic profiles featured in this webinar
- How Genova's profiles might support patients in your clinical practice
- Review a profile that has already been completed on one of your patients

We look forward to hearing from you!

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– Michael Chapman, ND

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Sequential Stool Testing to Monitor Progress in People with Rheumatoid Arthritis

Susan Blum, MD, MPH