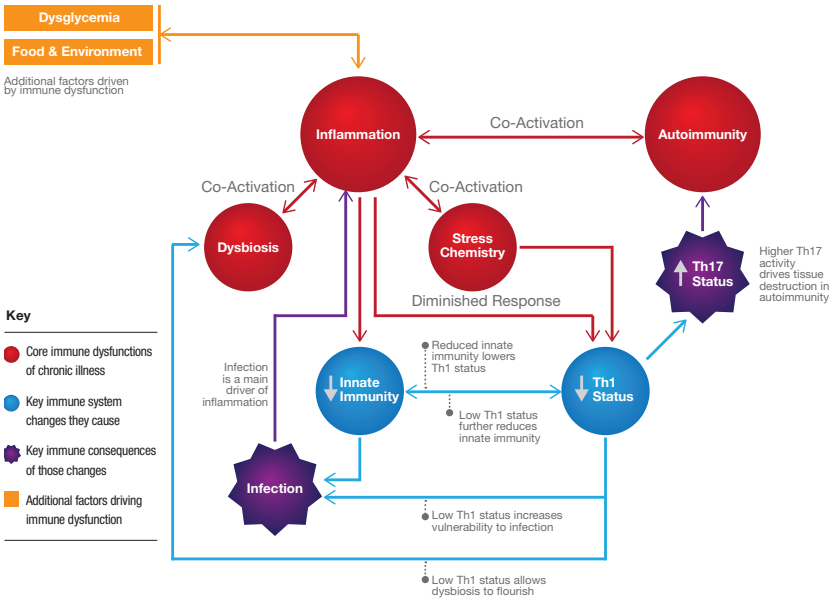
Dory – A case of spreading autoimmune process

Cogence
Shaping the Future of Functional Immunology

Complaints: Hashimoto's disease, fatigue, clumsiness, occasional left arm numbness

Dory's case involves most of the factors in the infographic. She reports recent changes in digestion. She's not aware of infections or allergies. She knows her stress level is high, but doesn't connect it to her illness process.



Dory – 52-year-old attorney. She's had thyroid problems since the birth of her second child in her 30's. She was diagnosed with Hashimoto's disease at 41. She's recently been feeling that her movements are clumsy. She also observes occasional left arm numbness.

In any patient with an existing autoimmune disease, the risk of developing another autoimmune process is greater. Neurological symptoms are present, so a panel of brain-related antibodies was run.

Functional Medicine Symptom Inventory:

Inventory of functional medicine symptoms suggests mild dysbiosis, very high stress, significant fatigue, and the expected set of thyroid-related symptoms.

Labs:

Myelin basic protein antibody elevation. MRI shows diffuse white matter changes. WBC's 5.5. Neutrophils 79%. Lymphocytes 14% Monocytes 6%. EOS 1%. Increased viral burden for EBV, with EBV VCA IgG >600 (about 28x the range), EBNA IgG >600 (28x the range), EBV EA IgG 88 (any elevation indicates virus pushing cells into the cell cycle, so the virus can hijack the cell replication machinery). Elevated IgG responses to gluten and several other foods.

Interpretation:

The primary concern here is that the new onset of occasional clumsiness and arm numbness raise concerns about the development of a demyelinating disorder, in a patient who already carries an autoimmune disease diagnosis. The elevated myelin basic protein antibody level corroborates this concern. Negative MRI suggests the autoimmune process hasn't created enough destruction to yield an abnormal MRI result. Expansion of the neutrophil compartment, relative to the rest of the wbc types, suggests an increase in the activity of neutrophils, driven by Th17 cell activation, a key component of autoimmune tissue destruction. Research suggests chronic EBV infection is a driver of MS development in susceptible individuals. This patient doesn't meet diagnostic criteria for MS, and should not be told she has MS. She has an autoimmune process related to myelin as a target of autoimmunity. She doesn't have the disease associated with those antibodies. The clinical task is to inhibit the further progression to the disease state.

Cogence Brief Immunological Assessment

Please CIRCLE the number that reflects whether the statement applies to you:

0 = Does not apply | 1 = Rarely applies | 2 = Sometimes applies | 3 = Applies | 4 = Strongly applies

Th1 Polarization Support Factors						Th2 Modulation Factors					
Chronic inflammation	0	1	(2)	3	4	Childhood asthma	No=0				Yes=3
High stress level	0	1	2	3	(4)	Childhood intestinal problems	No=0				Yes=3
Autoimmune disease flares	0	1	2	(3)	4	Childhood ear infections	No=0				Yes=3
Tendency to intestinal problems	0	(1)	2	3	4	Tendency to asthma or other lung issues	(0)	1	2	3	4
Current intestinal problem	(0)	1	(2)	3	4	Active or medicated asthma	(0)	1	2	3	4
Catch colds that are going around	(0)	1	2	3	4	Active or medicated other lung problem	(0)	1	2	3	4
Stay sick longer once you get sick	(0)	1	2	3	4	Tendency to sinusitis	(0)	1	2	3	4
Get cold sores	(0)	1	2	3	4	Headache in forehead, cheek, face	(0)	1	2	3	4
Tendency to bladder infections	(0)	1	2	3	4	Current sinus problem	(0)	1	2	3	4
Current bladder infection	(0)	1	2	3	4	Produce copious nasal mucous	(0)	1	2	3	4
Tendency to sinus infections	(0)	1	2	3	4	Mucous in stool	(0)	1	2	3	4
Current sinus infection	(0)	1	2	3	4	Allergy to environment (pollen, mold, etc.)	(0)	1	2	3	4
Tendency to respiratory infections	0	1	2	3	4	Food sensitivities/reactions	0	1	2	(3)	4
Current respiratory infection	(0)	1	2	3	4	Tendency to IBS, SIBO, Dysbiosis, etc.	0	(1)	2	3	4
Chronically elevated viral burden	0	1	2	3	4	IBS, SIBO, Dysbiosis, other GI currently	0	1	(2)	3	4
Age: add 2 points for every 5 years over 50					0	Chronic Stress	0	1	2	3	(4)
Total of the numbers you circled plus any for age					16	Work with toxic chemicals	(0)	1	2	3	4
						Age: add 2 points for every 5 years over 50					0
						Total of the numbers you circled plus any for age					10

Number of days with symptoms of autoimmune flare in the past month 14 **in the past week** 3

Number of days with symptoms of inflammation in the past month 18 **in the past week** 5

Can be body inflammation (aches & pains, body fatigue, GI symptoms, etc.) or brain inflammation (mental fatigue, brain fog, etc.)

Dory's Questionnaire Scores:

Clinician Interpretation Section

Th1 polarization support may be useful based on scores:

≥ 8 = 1 cap bid | ≥ 14 = 2 caps bid | ≥ 18 = 3 caps bid

Labs suggesting the need for support of Th1 response:

CBC hallmark: monocytes ≤ 6%. TGFβ >3000. Low normal Natural killer cells absolute or %. Viral IgG's higher than 5x the range for EBV, CMV, HSV-1, HSV-2, HHV-6, Parvovirus. EBV EA any elevation. High salivary cortisol. Chronic susceptibility to infection of any kind suggests the need for Th1 support.

Innate immune system support may be useful based on Th1 polarization scores:

≥ 8 = 1 cap qd | ≥ 14 = 1 bid | ≥ 18 = 2 bid

Labs suggesting the need for support of innate immune response:

WBC's <5 & TGFβ >3000 suggests the utility of at least 1 bid

Other indices:

NK % in lower 1/3 of range. Neutrophils ≤ 48%.

Monocytes ≤ 6%. Increased viral or bacterial burden.

Th2 down-regulation may be useful based on scores:

≥ 8 = 1 cap bid | ≥ 14 = 2 bid | ≥ 20 = 3 bid

Labs suggesting the need to down-regulate Th2 response:

CBC hallmarks: Eosinophils ≥ 5%, or Basophils ≥ 2%.

Low CD8 count and/or high CD4/CD8 ratio. Stool parasite.

The presence of asthma, environmental allergies, or any eosinophilic GI disorder strongly suggests Th2 dominance and the utility of dampening excessive Th2 response.

Inflammation / Autoimmune Support

Consider the following doses:

Number of flare days or inflamed days per month:

≥ 10 days = 3 caps tid (some patients will need 4 caps tid)

≥ 6 days = 3 caps bid ≥ 2 days = 2 caps bid

Dory's Recommendations

Recommendation pertaining to inflammation and inflammasome activation:

- Dory has substantial ongoing inflammation, and a substantial number of days per month involving autoimmune flare activation. It's appropriate to consider substances that downregulate NFkB, STAT3, and inflammasomes, starting at 3 caps 3x per day. If this dose does not yield a report within a couple of weeks of substantially fewer days of inflammation and autoimmune flare, consider increasing the dose.

Recommendations for inflammation, autoimmunity, and T cell polarization imbalances:

Starting doses as follows:

- Downregulation of NFkB, STAT3, inflammasomes: 3 caps 3x per day.
- Th1 polarization support: 2 caps twice per day.
- Innate immune system support: 1 cap twice per day.
- Th2 modulation support: 1 cap twice per day.

As always, doses need to be tailored to each patient's needs, based on clinical judgement.

In Dory's case, infection, dysbiosis, and chronic stress all drive the inflammation/autoimmunity axis.

Addressing these factors is essential to the success of her case.

Additional comments:

- Supporting Th1 response and the innate immune system are appropriate in cases involving increased viral burden. Improving the patient's Th1 response capacity will also help dampen Th17-mediated autoimmune tissue destruction.
- Tracking the neutrophil percentage will be important in this case, with a goal of bringing it down closer to the normal 60%. Th17 cells make IL-17a and IL-17f that drives neutrophils into tissue. Inhibiting the NFkB-STAT3 axis enough that Th17 polarization is substantially decreased is a key in this case.
- Addressing dysbiosis will be important in this case.
- Adaptogens will be important to diminish stress chemistry.

General Guidelines

Addressing inflammation:

A baseline dose of substances intended to dampen NFkB and inhibit inflammasome formation, at appropriate concentrations, is 2 capsules 2x per day, for anyone whose goal is to influence inflammatory activation. Some people may need higher doses, to offset factors that are driving more inflammation. Generally, clinicians should consider using doses that yield few or no days per month of aches and pains, fatigue, brain fog, fluctuating weight that suggests inflammatory fluid retention, or other symptoms suggestive of chronic inflammation.

Addressing autoimmune flares:

The goal should be to inhibit the NFkB-STAT3 axis, with the goal of zero flare days for a given week or month. If the patient is having fewer flare days with each subsequent time they fill out the questionnaire, you're on the right track with dosing. If the number of flare days has increased since the patient's previous visit, increasing doses may be needed.

For patients not yet using NFkB-STAT3 inhibitors, (new patients, example), it is useful to consider the following doses:

Number of flare days or inflamed days per month:

≥ 10 days = 3 caps tid (some patients will need 4 caps tid)

≥ 6 days = 3 caps bid ≥ 2 days = 2 caps bid

For patients in ongoing care, each patient will likely have two different dose levels:

1) The dose that quiets down flares

2) The dose that keeps them quiet between flares

The first dose is usually higher than the second dose. It's useful to instruct patients that this is their "flare dose," which they can go to when they feel a flare coming on. This is often the dose you start with to help them quiet down initially.

Once the case is ongoing and flares are occurring much less frequently, they can use the lower dose. You can determine the lower dose by having the patient gradually decrease the dose and observe if they do well at each reduced level (no flares). If the patient has a flare, you've gone too low.

Marnie – Multiple systems dysfunction without autoimmunity

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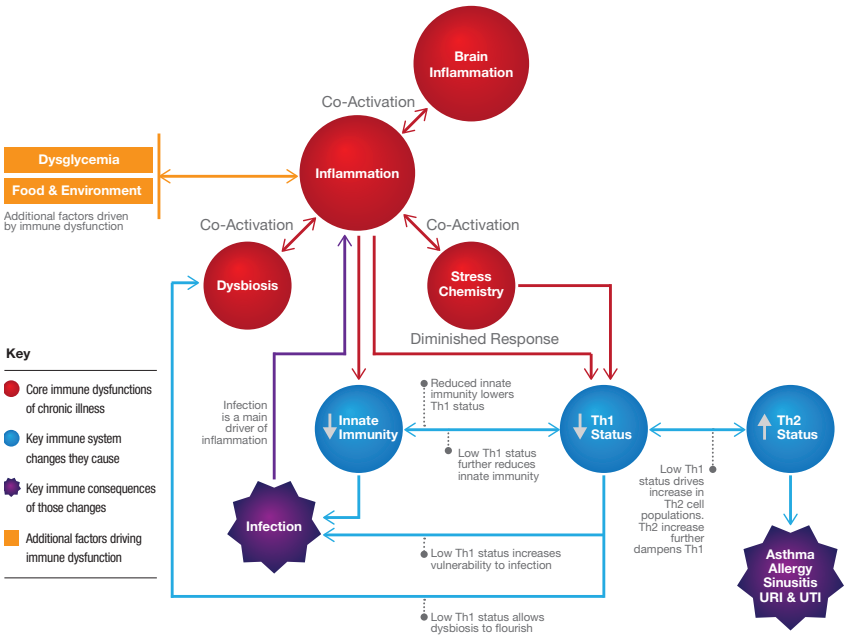
Chief Complaints: Fatigue, IBS

Marnie's case involves inflammation, dysbiosis, and stress chemistry (red circles), immune dysfunction (blue circles), effects driven by immune dysfunction (purple stars), and dysglycemia.

Notably, no autoimmune process has yet been detected



Marnie – 38-year-old female college assistant professor. She got tenure three years ago, got divorced two years ago, and is raising two children, ages 9 and 7.

Chief complaint is fatigue, onset 2.5 years ago, accompanied by mild depression, which she attributes to her fatigue, and the fact that she grapples with long standing IBS/SIBO, which puts her in a persistent state of discomfort and narrows her repertoire of foods. Childhood history of asthma. Occasional bladder infections. No significant surgical or injury history.

Functional Medicine Symptom Inventory:

Inventory of functional medicine symptoms corroborates her IBS/SIBO, and reveals a cluster of symptoms suggesting chronic hypoglycemia.

Labs:

WBC's 4.2 (functionally low). TGFb 6854 lab high. Monocytes 6%. Increased viral burdens for HHV6 (12x the range), and EBV, including EBV VCA IgG of 455 (20x the range), EBNA IgG >600 (>28x the range), EBV EA IgG 58 (any elevation indicates virus in lytic phase, pushing cells into the cell cycle, so the virus can hijack the cell replication machinery). Elevated IgG responses to various foods.

Interpretation:

The patient's inflammation is driven by stress, digestive dysregulation, and hypoglycemia. Inflammation interferes with mitochondrial integrity, driving her fatigue. Body inflammation drives brain inflammation, inviting / worsening the depression (brain inflammation contributes powerfully to diminished neuronal function). The increased viral loads, SIBO, and vulnerability to bladder infections are indications her immune system is less than efficient at addressing pathogen burdens, a hallmark of low Th1 status and low innate immune response status. The increased pathogen burden further drives her chronic inflammation. Any inadvertent exposures to foods to which she has IgG-mediated food sensitivity also drive her inflammation. The presence of IBS/SIBO, the bladder involvement, and the childhood history of asthma are three signs of suboptimal mucosal function, hallmarks of a tendency toward Th2 dominance. Thus, her history and lab results suggest the need for innate immune support, Th1 support, and Th2 modulation.

Cogence Brief Immunological Assessment

Please CIRCLE the number that reflects whether the statement applies to you:

0 = Does not apply | 1 = Rarely applies | 2 = Sometimes applies | 3 = Applies | 4 = Strongly applies

Th1 Polarization Support Factors					
Chronic inflammation	0	1	**2**	3	4
High stress level	0	1	2	**3**	4
Autoimmune disease flares	**0**	1	2	3	4
Tendency to intestinal problems	0	1	2	3	**4**
Current intestinal problem	0	1	**2**	3	4
Catch colds that are going around	0	**1**	2	3	4
Stay sick longer once you get sick	**0**	1	2	3	4
Get cold sores	**0**	1	2	3	4
Tendency to bladder infections	0	1	**2**	3	4
Current bladder infection	**0**	1	2	3	4
Tendency to sinus infections	**0**	1	2	3	4
Current sinus infection	**0**	1	2	3	4
Tendency to respiratory infections	**0**	1	2	3	4
Current respiratory infection	**0**	1	2	3	4
Chronically elevated viral burden	**0**	1	2	3	4
Age: add 2 points for every 5 years over 50				**0**	
Total of the numbers you circled plus any for age				**17**	

Th2 Modulation Factors					
Childhood asthma	No=0				**Yes=3**
Childhood intestinal problems	**No=0**				Yes=3
Childhood ear infections	**No=0**				Yes=3
Tendency to asthma or other lung issues	0	**1**	2	3	4
Active or medicated asthma	**0**	1	2	3	4
Active or medicated other lung problem	**0**	1	2	3	4
Tendency to sinusitis	**0**	1	2	3	4
Headache in forehead, cheek, face	**0**	1	2	3	4
Current sinus problem	**0**	1	2	3	4
Produce copious nasal mucous	**0**	1	2	3	4
Mucous in stool	**0**	1	2	3	4
Allergy to environment (pollen, mold, etc.)	**0**	1	2	3	4
Food sensitivities/reactions	0	1	2	**3**	4
Tendency to IBS, SIBO, Dysbiosis, etc.	0	1	2	3	**4**
IBS, SIBO, Dysbiosis, other GI currently	0	1	2	**3**	4
Chronic Stress	0	1	2	3	**4**
Work with toxic chemicals	**0**	1	2	3	4
Age: add 2 points for every 5 years over 50					**0**
Total of the numbers you circled plus any for age					**18**

Number of days with symptoms of autoimmune flare in the past month 0 **in the past week** 0

Number of days with symptoms of inflammation in the past month 23 **in the past week** 6

Can be body inflammation (aches & pains, body fatigue, GI symptoms, etc.) or brain inflammation (mental fatigue, brain fog, etc.)

Marnie's Questionnaire Scores:

Clinician Interpretation Section

Th1 polarization support may be useful based on scores:

≥ 8 = 1 cap bid | ≥ 14 = 2 caps bid | ≥ 18 = 3 caps bid

Labs suggesting the need for support of Th1 response:

CBC hallmark: monocytes ≤ 6%. TGFβ >3000. Low normal Natural killer cells absolute or %. Viral IgG's higher than 5x the range for EBV, CMV, HSV-1, HSV-2, HHV-6, Parvovirus. EBV EA any elevation. High salivary cortisol. Chronic susceptibility to infection of any kind suggests the need for Th1 support.

Innate immune system support may be useful based on Th1 polarization scores:

≥ 8 = 1 cap qd | ≥ 14 = 1 bid | ≥ 18 = 2 bid

Labs suggesting the need for support of innate immune response:

WBC's <5 & TGFβ >3000 suggests the utility of at least 1 bid

Other indices:

NK % in lower 1/3 of range. Neutrophils ≤ 48%.

Monocytes ≤ 6%. Increased viral or bacterial burden.

Th2 down-regulation may be useful based on scores:

≥ 8 = 1 cap bid | ≥ 14 = 2 bid | ≥ 20 = 3 bid

Labs suggesting the need to down-regulate Th2 response:

CBC hallmarks: Eosinophils ≥ 5%, or Basophils ≥ 2%.

Low CD8 count and/or high CD4/CD8 ratio. Stool parasite.

The presence of asthma, environmental allergies, or any eosinophilic GI disorder strongly suggests Th2 dominance and the utility of dampening excessive Th2 response.

Inflammation / Autoimmune Support

Consider the following doses:

Number of flare days or inflamed days per month:

≥ 10 days = 3 caps tid (some patients will need 4 caps tid)

≥ 6 days = 3 caps bid ≥ 2 days = 2 caps bid

Recommendations For Marnie

Recommendation pertaining to inflammation and inflammasome activation:

- Marnie has substantial ongoing inflammation, but no discernable autoimmune disease expression at this point. It's appropriate to consider substances that downregulate NFkB and inflammasome activation, starting at 3 caps 3x per day. If this dose does not yield a report within a couple of weeks of substantially fewer days of inflammation and autoimmune flare, consider increasing the dose.

Recommendation pertaining to immune imbalances:

Starting doses as follows:

- Downregulation of NFkB and inflammasomes: 3 caps 3x per day.
- Th1 polarization support: 2 caps twice per day.
- Innate immune system support: 1 cap twice per day.
- Th2 modulation support: 2 caps twice per day.

As always, doses need to be tailored to each patient's needs, based on clinical judgement.

Additional comments:

- Marnie's case involves SIBO, which is known to drive systemic inflammation and thus brain inflammation, which may be a central driver of her fatigue. Supporting a robust Th1 response and downregulating (modulating) the Th2 response is likely to be crucial to the restoration of her GI balance. Directly addressing the restoration of a healthy microbiome is also likely to be central.

- Adaptogens are likely to be important to diminish stress chemistry.
- Antibodies to thyroid, parietal cells, intrinsic factor, pancreas, ASCA/ANCA, ANA, etc. are all currently negative. However, given the tendency of increased viral loads to drive autoimmune development, any case involving substantially increased viral burdens may need to include surveillance of antibodies related to the case at least annually, or more often if the patient is not responding to care.
- If TGF beta levels remain high, it may be necessary to supplement with N-acetyl-cysteine or glutathione.

General Guidelines

Addressing inflammation:

A baseline dose of substances intended to dampen NFkB and inhibit inflammasome formation, at appropriate concentrations, is 2 capsules 2x per day, for anyone whose goal is to influence inflammatory activation. Some people may need higher doses, to offset factors that are driving more inflammation. Generally, clinicians should consider using doses that yield few or no days per month of aches and pains, fatigue, brain fog, fluctuating weight that suggests inflammatory fluid retention, or other symptoms suggestive of chronic inflammation.

Addressing autoimmune flares:

The goal should be to inhibit the NFkB-STAT3 axis, with the goal of zero flare days for a given week or month. If the patient is having fewer flare days with each subsequent time they fill out the questionnaire, you're on the right track with dosing. If the number of flare days has increased since the patient's previous visit, increasing doses may be needed.

For patients not yet using NFkB-STAT3 inhibitors, (new patients, example), it is useful to consider the following doses:

Number of flare days or inflamed days per month:

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For patients in ongoing care, each patient will likely have two different dose levels:

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Once the case is ongoing and flares are occurring much less frequently, they can use the lower dose. You can determine the lower dose by having the patient gradually decrease the dose and observe if they do well at each reduced level (no flares). If the patient has a flare, you've gone too low.

Mark – Long standing type 1 diabetes and new Crohn's disease

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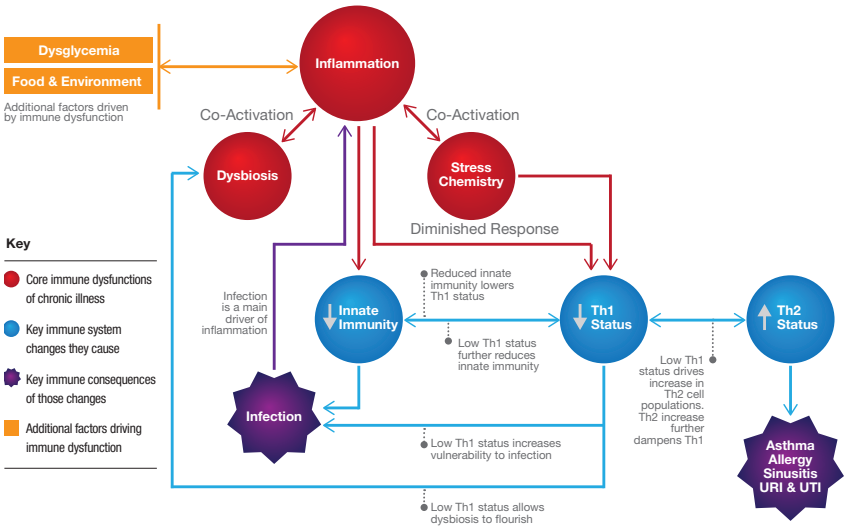
Chief Complaint: New abdominal pain in the context of 20-year history of Type 1 Diabetes.

Mark's case is focused on the axis of co-activation between inflammation and autoimmunity. Factors driving the inflammation / autoimmune axis are SIBO, blood sugar dysregulation, and food reactions.



Mark – 55-year-old chef with chief complaint of new abdominal pain.

In any patient with an existing autoimmune disease diagnosis, there is a clinical concern that the immune system can develop an interest in other tissue targets, yielding the development of other autoimmune processes. In Mark's case, the long-standing type 1 diabetes raises concerns that his new onset of burning abdominal pain and changes in stool consistency may indicate an expansion of the targets of his autoimmune process to include his digestive tract.

Functional Medicine Symptom Inventory:

An inventory of functional medicine symptoms suggests significant GI dysregulation, antibody mediated reactions to foods, and the expected set of blood sugar imbalance symptoms related to his T1D.

Labs:

Antibodies to insulin, GAD65, IA2, ZnT8 all markedly elevated, as expected for T1D. ASCA antibodies are also markedly elevated, consistent with a new expression of Crohn's disease. Colonoscopy confirms the diagnosis. WBC's 8.4. Neutrophils 69%. Lactulose breath test is abnormal, suggesting SIBO. Viral burdens are normal. IgG food testing shows an abundance of sensitivities.

Interpretation:

Mark has a new expression of Crohn's disease. Because inflammation is a primary driver of autoimmune tissue destruction, it will be very important clinically to inventory all factors that could contribute to Mark's inflammation. GI dysfunction, food reactions, and blood sugar dysregulation are three drivers of inflammation that push his autoimmune activation, which now has targeted his GI tract, in addition to his pancreas. Mark's blood sugar balance has always been adequate, so he thought he was taking proper care of his condition. He never paid attention to the content of his food, except as regards blood sugar balance. So, he's consistently eaten foods known to instigate autoimmune activation, likely driving further autoimmune expression, particularly given his many IgG mediated food sensitivities. In addition to reorganizing his immune response, he will need long term avoidance of the involved foods.

Recent evolution of the immunology research has clarified that Th17 cells, not Th1 cells, drive autoimmune tissue destruction, and that Th1 cells inhibit Th17 expression. Mark's T cell polarization questionnaire indicates the need for Th1 support as an important factor in quieting his autoimmunity.

Cogence Brief Immunological Assessment

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Th1 Polarization Support Factors					
Chronic inflammation	0	1	2	3	(4)
High stress level	0	1	(2)	3	4
Autoimmune disease flares	0	1	2	3	(4)
Tendency to intestinal problems	0	1	2	3	(4)
Current intestinal problem	0	1	2	3	(4)
Catch colds that are going around	(0)	1	2	3	4
Stay sick longer once you get sick	(0)	1	2	3	4
Get cold sores	(0)	1	2	3	4
Tendency to bladder infections	(0)	1	2	3	4
Current bladder infection	(0)	1	2	3	4
Tendency to sinus infections	(0)	1	2	3	4
Current sinus infection	(0)	1	2	3	4
Tendency to respiratory infections	(0)	1	2	3	4
Current respiratory infection	(0)	1	2	3	4
Chronically elevated viral burden	0	(1)	2	3	4
Age: add 2 points for every 5 years over 50				2	
Total of the numbers you circled plus any for age				21	

Th2 Modulation Factors					
Childhood asthma	No=(0)				Yes=3
Childhood intestinal problems	No=(0)				Yes=3
Childhood ear infections	No=(0)				Yes=3
Tendency to asthma or other lung issues	(0)	1	2	3	4
Active or medicated asthma	(0)	1	2	3	4
Active or medicated other lung problem	(0)	1	2	3	4
Tendency to sinusitis	(0)	1	2	3	4
Headache in forehead, cheek, face	(0)	1	2	3	4
Current sinus problem	(0)	1	2	3	4
Produce copious nasal mucous	(0)	1	2	3	4
Mucous in stool	0	1	2	(3)	4
Allergy to environment (pollen, mold, etc.)	(0)	1	2	3	4
Food sensitivities/reactions	0	1	2	(3)	4
Tendency to IBS, SIBO, Dysbiosis, etc.	0	1	2	3	(4)
IBS, SIBO, Dysbiosis, other GI currently	0	1	2	3	(4)
Chronic Stress	0	1	(2)	3	4
Work with toxic chemicals	(0)	1	2	3	4
Age: add 2 points for every 5 years over 50					0
Total of the numbers you circled plus any for age					16

Number of days with symptoms of autoimmune flare in the past month 0 **in the past week** 0

Number of days with symptoms of inflammation in the past month 23 **in the past week** 6

Can be body inflammation (aches & pains, body fatigue, GI symptoms, etc.) or brain inflammation (mental fatigue, brain fog, etc.)

Mark's Questionnaire Scores:

Clinician Interpretation Section

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Inflammation / Autoimmune Support

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Recommendations For Mark

Recommendation pertaining to inflammation and inflammasome activation:

- Mark has substantial ongoing inflammation, and a substantial number of days per month involving autoimmune flare activation. It's appropriate to consider substances that downregulate NFkB, STAT3, and inflammasomes, starting at 3 caps 3x per day. If this dose does not yield a report within a couple of weeks of substantially fewer days of inflammation and autoimmune flare, consider increasing the dose.

Recommendation pertaining to immune imbalances:

Starting doses as follows:

- Downregulation of NFkB, STAT3, inflammasomes: 3 caps 3x per day.
- Th1 polarization support: 3 caps twice per day.
- Innate immune system support: 2 caps twice per day.
- Th2 modulation support: 2 caps twice per day.

As always, doses need to be tailored to each patient's needs, based on clinical judgement.

Additional comments:

- Mark's case revolves around the development of new autoimmune process in a person with existing autoimmune disease. Inhibition of the NFkB-STAT3 axis is crucial to the dampening of this mechanism ongoing. Thus, in Mark's case, it's likely to be essential to address the underlying immunological mechanisms driving the inflammation/autoimmunity, and also to address the autoinflammation / autoimmunity directly. The following factors are thus worthy of attention…

- Mark's case involves SIBO, which is known to drive systemic inflammation, which will drive NFkB-STAT3 axis activation, and thus autoimmune flares. Supporting a robust Th1 response and downregulating (modulating) the Th2 response is likely to be crucial to the restoration of his GI balance. Directly addressing the restoration of a healthy microbiome is also likely to be central.
- Addressing dysglycemia. For Mark, who has developed significant expertise in blood sugar management, but hasn't yet accounted for the way foods can drive autoimmunity, it will be crucial to coordinate any recommendations with his existing expertise in keeping himself safe from a type 1 diabetes point of view.
- Consistent elimination of problematic foods.

General Guidelines

Addressing inflammation:

A baseline dose of substances intended to dampen NFkB and inhibit inflammasome formation, at appropriate concentrations, is 2 capsules 2x per day, for anyone whose goal is to influence inflammatory activation. Some people may need higher doses, to offset factors that are driving more inflammation. Generally, clinicians should consider using doses that yield few or no days per month of aches and pains, fatigue, brain fog, fluctuating weight that suggests inflammatory fluid retention, or other symptoms suggestive of chronic inflammation.

Addressing autoimmune flares:

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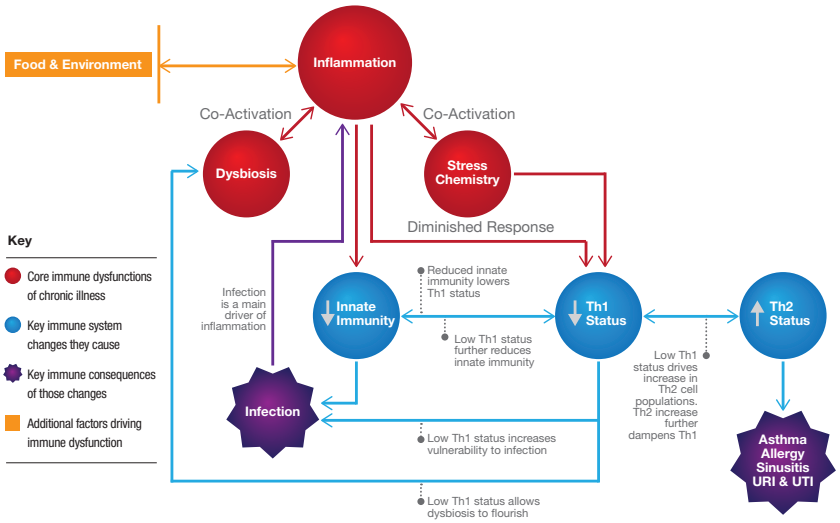
Jill – Classic Th2 dominance

Cogence
Shaping the Future of Functional Immunology

Complaints: Asthma, Environmental Allergies, Food Sensitivities

Jill's case is primarily focused on the issue of Th2 dominance.



Jill – 44-year-old administrator. She has a lifelong history of asthma and environmental allergies. She's recently become aware that the consumption of certain foods worsens her condition.

Her chief complaint is asthma, lifelong, worse at times when her environmental allergies are also active. She exercises daily, though exercise triggers her asthma, especially in cold weather. She is married, has two children, rates her stress level as mild, and sleeps well. She has no significant surgical or injury history. She has a childhood history of ear infections and a family history of environmental allergies (mother and father), and sinus problems (father).

Functional Medicine Symptom Inventory:

Inventory of functional medicine symptoms corroborates her asthma, environmental allergies and food sensitivities, and suggests a mild level of digestive dysregulation, with symptoms primarily in the colon. While she endorses these symptoms in discussion, she doesn't think of them as abnormal, since they are so longstanding.

Labs:

WBC's 3.9 (functionally low). Neutrophils 41%. Lymphocytes 43%. Eosinophils 9% (lab high). TGFb 8247 (lab high). Elevated IgG responses to various foods.

Interpretation:

Jill's immune system matures too many naïve CD4 T cells into T helper cells type 2 (Th2 cells). Her asthma and her GI tract problems (food intolerances) reflect this tendency. The purpose of the Th2 response is to protect the body against debris (pollen, etc.) by making mucous to carry away debris or to fight pathogens in hollow spaces (lungs, sinuses, GI tract, bladder). This mechanism is mainly for killing parasites, which are large enough that a single white blood cell can't eat it. Th2 cells signal groups of eosinophils to bombard parasites with eosinophilic granules. Thus, Jill's tendency to make too many Th2 cells drives her eosinophil elevation. However, no parasite is needed to instigate the Th2 response in a susceptible individual like Jill. The response can be driven by substances like pollen in the sinuses or lungs, or problematic foods in the GI tract. The eosinophils then drive inflammation. The tendency to mature too many naïve T cells toward a Th2 polarization is at the root of Jill's pattern of dysfunction.

Cogence Brief Immunological Assessment

Please CIRCLE the number that reflects whether the statement applies to you:

0 = Does not apply | 1 = Rarely applies | 2 = Sometimes applies | 3 = Applies | 4 = Strongly applies

Th1 Polarization Support Factors					
Chronic inflammation	0	1	**2**	3	4
High stress level	0	1	2	**3**	4
Autoimmune disease flares	**0**	1	2	3	4
Tendency to intestinal problems	0	**1**	2	3	4
Current intestinal problem	0	**1**	2	3	4
Catch colds that are going around	**0**	1	2	3	4
Stay sick longer once you get sick	**0**	1	2	3	4
Get cold sores	**0**	1	2	3	4
Tendency to bladder infections	**0**	1	2	3	4
Current bladder infection	**0**	1	2	3	4
Tendency to sinus infections	**0**	1	2	3	4
Current sinus infection	**0**	1	2	3	4
Tendency to respiratory infections	0	1	**2**	3	4
Current respiratory infection	**0**	1	2	3	4
Chronically elevated viral burden	**0**	1	2	3	4
Age: add 2 points for every 5 years over 50				**0**	
Total of the numbers you circled plus any for age				**9**	

Th2 Modulation Factors					
Childhood asthma	No=0				**Yes=3**
Childhood intestinal problems	**No=0**				Yes=3
Childhood ear infections	No=0				**Yes=3**
Tendency to asthma or other lung issues	0	1	2	3	**4**
Active or medicated asthma	0	1	2	**3**	4
Active or medicated other lung problem	**0**	1	2	3	4
Tendency to sinusitis	**0**	1	2	3	4
Headache in forehead, cheek, face	**0**	1	2	3	4
Current sinus problem	**0**	1	2	3	4
Produce copious nasal mucous	**0**	1	2	3	4
Mucous in stool	**0**	1	2	3	4
Allergy to environment (pollen, mold, etc.)	0	1	2	**3**	4
Food sensitivities/reactions	0	1	2	**3**	4
Tendency to IBS, SIBO, Dysbiosis, etc.	**0**	1	2	3	4
IBS, SIBO, Dysbiosis, other GI currently	**0**	1	2	3	4
Chronic Stress	0	1	2	**3**	4
Work with toxic chemicals	**0**	1	2	3	4
Age: add 2 points for every 5 years over 50					**0**
Total of the numbers you circled plus any for age					**22**

Number of days with symptoms of autoimmune flare in the past month 0 **in the past week** 0

Number of days with symptoms of inflammation in the past month 17 **in the past week** 7

Can be body inflammation (aches & pains, body fatigue, GI symptoms, etc.) or brain inflammation (mental fatigue, brain fog, etc.)

Jill's Questionnaire Scores:

Clinician Interpretation Section

Th1 polarization support may be useful based on scores:

≥ 8 = 1 cap bid ≥ 14 = 2 caps bid ≥ 18 = 3 caps bid

Labs suggesting the need for support of Th1 response:

CBC hallmark: monocytes ≤ 6%. TGFβ >3000. Low normal Natural killer cells absolute or %. Viral IgG's higher than 5x the range for EBV, CMV, HSV-1, HSV-2, HHV-6, Parvovirus. EBV EA any elevation. High salivary cortisol. Chronic susceptibility to infection of any kind suggests the need for Th1 support.

Innate immune system support may be useful based on Th1 polarization scores:

≥ 8 = 1 cap qd ≥ 14 = 1 bid ≥ 18 = 2 bid

Labs suggesting the need for support of innate immune response:

WBC's <5 & TGFβ >3000 suggests the utility of at least 1 bid

Other indices:

NK % in lower 1/3 of range. Neutrophils ≤ 48%.

Monocytes ≤ 6%. Increased viral or bacterial burden.

Th2 down-regulation may be useful based on scores:

≥ 8 = 1 cap bid ≥ 14 = 2 bid ≥ 20 = 3 bid

Labs suggesting the need to down-regulate Th2 response:

CBC hallmarks: Eosinophils ≥ 5% or Basophils ≥ 2%.

Low CD8 count and/or high CD4/CD8 ratio. Stool parasite.

The presence of asthma, environmental allergies, or any eosinophilic GI disorder strongly suggests Th2 dominance and the utility of dampening excessive Th2 response.

Inflammation / Autoimmune Support

Consider the following doses:

Number of flare days or inflamed days per month:

≥ 10 days = 3 caps tid (some patients will need 4 caps tid)

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Recommendations For Jill

Recommendation pertaining to inflammation and inflammasome activation:

- Jill has symptoms of inflammation about half the days of the month, and has had symptoms of inflammation every day for the past week, so her symptoms are very active. It's appropriate to consider substances that downregulate NFkB and inflammasome activation, starting at 3 caps 2x per day. If this dose does not yield a report within a couple of weeks of substantially fewer days with symptoms of inflammation, consider increasing the dose.

Recommendation pertaining to immune imbalances:

Starting doses as follows:

- Downregulation of NFkB and inflammasomes: 3 caps 3x per day.
- Th1 polarization support: 1 cap twice per day.
- Innate immune system support: 1 cap per day.
- Th2 modulation support: 3 caps twice per day.

As always, doses need to be tailored to each patient's needs, based on clinical judgement.

In Jill's case, asthma, allergies, food sensitivities, and GI symptoms all reflect dysfunction of organs that are hollow and lined with epithelial tissue. These spaces tend to rise and fall together in their function, with Th2

dominance as the theme. Addressing Th2 dominance as the core clinical strategy is essential to making real changes in the underlying immunology of these cases.

Additional comments:

- For Jill, the absence of any history of chronic infection suggests that her Th2 dominance may be more constitutional, rather than a secondary effect of loss of Th1 status from inflammation and stress. In these cases, the inflammatory process may itself be a secondary consequence of her constitutional Th2 dominance. It becomes useful in these cases to focus on the Th2 dominance and its modulation, and to focus on the inflammatory process, both in terms of nutritional modulation, and in terms of avoidance of triggers like problematic foods or other factors in the environment.
- Patients with Th2 dominance often need to diminish their histamine burden, both by taking adequate amounts of quercetin, and by pursuing a low histamine diet.
- It will be useful to track Jill's eosinophil percentage going forward. If it doesn't go down, higher doses of substances intended to modulate Th2 response may be useful. Since cytokines made by Th1 cells inhibit Th2 polarization, and vice versa, it may be necessary to support adequate Th1 response as a secondary way to downregulate (modulate) excessive Th2 polarization.
- If TGF beta levels remain high, it may be necessary to supplement with N-acetyl-cysteine or glutathione.
- In some patients, downregulating inflammation and the primary Th2 dominance will not be enough to turn the tide. If the patient doesn't respond adequately with through the measures described, it may be necessary to directly address dysbiosis and to use adaptogens to diminish stress chemistry. Or, if symptoms suggest that these features play an important role in the activation of inflammation and the loss of Th1 response and innate immunity, these measures can be adopted at the start. In Jill's case, her score for Th1 deficiency is modest, suggesting a focus on downregulating a primary Th2 dominance and inflammatory process are a good starting point.

General Guidelines

Addressing inflammation:

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