Module 5 and Module 6 Review
Brain-Gut Connection

A bidirectional communication network
Involves central, autonomic and enteric nervous systems, the neuroendocrine, enteroendocrine and neuroimmune systems
Mediates genetic and environmental factors on brain development and function
Where does it start?

The relationship starts in the gut

It plays a regulatory role for brain and nervous system function

In return the brain and nervous system signals the gut

Many parts needed by the brain and nervous system such as GABA, glutamine, serotonin etc are made in the gut.
Enteric Nervous System

Embedded in the gastrointestinal lining
Governs the function of the GI tract
Acts independent of the sympathetic and parasympathetic nervous systems
But can be influenced by them
The 2nd Brain
Vagus Nerve

More than one nerve

Main communication between the brain and the gut

Gut activating the Vagus nerve can affect the brain, behavior,

Plays a role in metabolic disease, diabetes, obesity, inflammation, asthma, migraines, seizures, depression
Five Ways To Communicate

1. The Autonomic Nervous System
2. The Microbiome Immune Loop
3. Microbial Metabolites
4. Environmental Influences
5. Endocannabinoid system
Stress and Emotions

Limbic system - emotion, behavior, motivation, long-term memory, and olfaction

Stress affects the limbic system – home of the fight or flight response

The limbic system then plays a role reducing good bacteria and increasing the virulence of bad

Cortisol is the key hormone the gut uses to communicate to the brain
Disrupters of Brain - Gut

Antibiotics

Studies have shown anywhere from 6 months – 2 years of disruption of the brain gut from one course of antibiotics

Depends on what type of antibiotic

Fluoroquinolones – used for respiratory, ear, sinus infections the worst
Disrupters

2. Elevated LPS (Lippopolysaccharide)

Considered an endotoxin

It’s normal in the lumen - Should be contained in the gut and excreted

80% of all bacteria (including good) produce it

It is used for communication in the gut and with immune system –

Been linked to numerous health conditions in the body
Disrupters

3. Glyphosate
Disrupts the shikimate pathway of good bacteria
Has been found in core blood of babies
Inhibits Cytochrome P450 enzymes
Linked to autism, Alzheimer’s, Parkinson’s, allergies, heart disease, ALS, MS, cancer, obesity, depression
Studies show it interferes with gut bacteria
Probiotics vs Prebiotics

High fat or high sugar diets do not help

Probiotics have limitation because they do not colonize in the gut

Prebiotics such as FOS and GOS have been shown to reduce anxiety in mice with high LPS and lower inflammatory markers

In humans - supplementation with GOS for three weeks lowered cortisol levels and increased positive attitude
Supplementation with Omega 3 (DHA/EPA) helped correct gut dysbiosis in baby rats who suffered early life stress. Also increases Akkermansia muciniphila. So does FOS and polyphenols, navy beans. Whole grains and high fibre foods also show benefits.
Candidiasis

• Yeast overgrowth – generally candida albicans

• Yeast is natural

• Not all yeast strain are problematic but no yeast strain is helpful if there is too much

• Yeast can only be in excess if there is too little good bacteria

• Can be fatal is it gets into the blood and reaches vital organs
Candida Auris

• A rising issue – CDC calls it “a new emerging global threat”
• It is difficult to identify with standard lab test
• Caused outbreaks in hospital settings – can spread patient to patient
• Most strains are treatable with antifungal drugs but resistant strains are developing
Study

In mice, dietary refined carbohydrate supplementation leads to higher rates of *Candida* growth in the gastrointestinal tract and favors mucosal invasion.

28 healthy volunteers fed high sugar diet with measurement of C. Albicans counts before, during and after

High sugar (refined diet) did not increase counts in healthy individuals

However, in those with higher Candida levels, high sugar did increase the amount of Candida
SIBO

- Small Intestinal Bowel Overgrowth
- A chronic bacterial infection of the small intestine
- Caused by bad bacteria such as E Coli and Clostridium migrating to the small intestine
- There is not enough good bacteria to deal with it in the small intestines (remember the numbers are low)
Causes

• Problem with intestinal anatomy or intestinal muscles
• Can include anatomy changes caused by gastric bypass or intestinal bypass
• Diverticulitis, tumours or any type of bowel obstruction, Ileocecval valves issues
• Drugs that affect gut motility (too much good bacteria?)
• Opportunistic infections caused by antibiotic and non-antibiotic causes
Diet Controversy

• Many say diet for both SIBO and Candidiasis die are the same – low sugar, removed processed food, increase whole foods

• Some SIBO diets say no grains or fibre

• Whereas some Candida diets says eat grains

• Sticks with the “diets are the same” scenario

• The key is the antimicrobials and probiotics
Histamine

Found in the skin, lungs, stomach, brain and heart

It is made and stored in white blood cells (mast cells) so it can act as a “first defender” and inflammatory mediator

It is an important chemical that helps many body systems

A neurotransmitter that helps regulate communication between cells

Regulates gastric function

Helps with the permeability of blood vessels

Helps with brain function

Aids muscle contractions
Breaking Down Histamine

Two enzymes in particular:

N-methyl transferase (HNMT) – primarily from the liver and kidneys

Diamine oxidase (DAO) – made in the intestines

In an animal (pigs) study – when DAO was blocked, histamine level rose to 160 ng/ml when administered 60 mg histamine whereas the control’s levels did not rise
What Is The Mucus Lining?

Cells on the surface of the intestinal lining produce mucus.

It lines the digestive tract and acts as a protective barrier.

Cells secrete mucin – which are glycoproteins rich in amino acids such as threonine and serine.

Mucin and water make up mucus.
The small intestines has a single layer of mucus that is not attached to the intestinal wall.

The stomach and the colon has two mucus layers, - one attached and one not.

The outer layer in the colon is home to the good bacteria.

Inner mucus is replace every hour by secretions from goblet cells (which essentially just secretes mucus).
Enzymes secreted by parasites and some bad bacteria can dissolve the mucus (outer layer)

There are also mechanisms that can allow the inner layer to be penetrated by bacteria but they are more related to the issues with the immune system function.

Once bad bacteria reaches the intestinal epithelia surface, inflammation is triggered.

This is a mechanism that could be play a role in ulcerative colitis.
Role of Mucus Lining

Protects the lining

Helps move pathogenic bacteria away from the epithelial lining layer and helps with their removal

It’s slippery making it difficult for them to latch on and allows for smooth movement

Mucus can also provide food for good bacteria

An antibacterial protein secreted by the absorption cells of the intestinal wall lining in small intestines prevent bad bacteria from getting near the lining

They are stored in the mucus layer
What Helps

Colostrum, Aloe Vera
Hyaluronic Acid
Omega 3 – Fish oil
B vitamins, A, D and magnesium
Turmeric
Plant Sterols
Collagen (Bone Broth)
Glutamine
Digestive Plaque (Biofilm)

A combination of bacteria and fungi that has worked together

They link together to form a film they can hide under

Similar in principal to the plaque on our teeth

Allows fungi to become more pathogenic and bacteria to become more resistant to antibiotics

Harder for immune system to get at them
Bad Biofilm:
1. Prevents nutrient absorption
2. Protects disease-causing microorganisms
3. Promotes inflammation
4. Inter-relationship with heavy metals

Heavy metals could promote it and they may also make up part of the plaque
Issues

May be connected to:

- Candida overgrowth and parasites
- Acid Reflux, heartburn
- CFS and fibromyalgia
- Intestinal conditions IBS, colitis, and Crohn's disease
- Can be connected to bloating, gas, brain fog, joint pains, stomach cramps, acne, and skin issues
Other Recommendations

Proteolytic enzymes like protease, papain, and pepsidase FP on an empty stomach between meals

Apple cider vinegar, may help strip minerals from the biofilm matrix

Cloves

Other Enzymes

Psyllium husk with bentonite clay

Activated charcoal
Leaky Gut

Is not holes in the gut lining
It’s natural openings being open too often
It’s normal for the gap junctions to open and close
Part of normal immune function
Allows water to flood the intestinal system – immune response

“I’m still thirsty. Maybe I’ve got leaky gut syndrome.”
Think of the gap junctions more like a pathway
Closed by a gate which are the coupling proteins
Receptors are locks
Molecules that lock onto receptors are like keys in lock to open the gate
Pathogens lock onto receptors - triggers zonulin to open the “gate”

This is not to let the pathogen in

Its to let water out and try to flush pathogens away from the opening

Some get it to the blood stream along with food particles, yeast etc.

Innate (inflammatory markers) and adaptive (antibody formation) jump into action
It’s not about how many pathogens, parasite, yeast or food particles get into the blood. It’s about what happens to them. Balance of T-reg cells to antibodies determines reaction. IgG antibodies mean substance contained – should be no symptoms.
IgG Testing:
Screening test – not a diagnostic test – client gets the report - no direct cause and correlation – potential guide
Allergies Refresher

IgG reactions – chemicals, food particles enter through leaky gut and IgG antibodies are formed to the substance

IgG antibodies can last up to three weeks

This is all part of the adaptive immune system that has to be learned and remembered
Secretory IgA

Intestinal cells secrete IgA (SIgA) which promote the removal of antigens and pathogens

SIgA prevents them from locking onto intestinal wall receptor sites

SIgA’s relationship with the good bacteria allows the immune system to leave the good bacteria alone and target the pathogens

Further research has found that good gut microbes play a role to stimulate the production of SIgA

So they are not just sitting there – they are active players
Gut Microbes

There are many ways in which the gut microbes affect the immune response.

Germ–free mouse studies show that these mice have a lower number of immune cells than normal mice.

Introduction of bacteria in young mice allows for them to quickly gain immune cells.

Does not happen in adult mice.

The total exact nature of the relationship is not known.
T-Regulatory Cells

Refers to the lack of reaction by the immune system to a substance or body tissue.

They modulate the immune system and maintain tolerance despite the presence of self-antigen T cells.

Promote anti-inflammatory cytokines which suppresses self-antigen T cell activity.

T-reg cells are produced in higher numbers to enable control and protect immune tolerance by suppressing self-reactive T cells.
T-Regulatory Cells

Studies show that people with lower levels of T-reg cells are more prone to allergy. T-reg cells promote the production of IL-10 which suppresses allergic inflammation. TGF-Beta is also involved in promoting T-Reg cells and lowering immune response to allergies.
Gut Connection

T-reg cells are also produced in the intestines from naïve T-cells promoted by metabolites (butyrate) made by the good bacteria

Having sufficient good bacteria is the key to maintaining a normal response (to promote T-reg cells)

The maintenance of immune homeostasis by the gut is the key to preventing or resolving allergies
Other Advantages of Immune Tolerance

Studies have shown that good immune tolerance also means:

- Better ability to fight pathogens
- More robust microbiome
- Increased nutrient absorption
- Better gut-brain connection
- Less ability for pathogens to colonize
Endocannabinoid System

ECS is biological system that plays many roles in the human body

It was not really known until about 30 years ago

Discovered when trying to understand how cannabis works

Endo: Endogenous meaning in the body

Cannabinoid: Name for chemicals
ECS is a series of receptors – 2 types: CB1 and CB2

They are triggered into action by neurotransmitters we make called cannabinoids

It’s complex

They interact with other hormones, neurotransmitters and systems in the body

Two majors ones we make: Anandamide and 2-arachidonoylglycerol
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The Gut

May be the communication system between gut and brain – at least part of it

Both receptors line the gut and CB1 helps with sIgA levels

Regulates inflammation in the gut

Body recruits more CB2 receptors when there’s a lot of inflammation in the gut

Colitis patients show high levels of anandamide (body’s way of protecting from damage)
L. Acidophilus (NCFM) stimulates CB2 which may be why it’s been linked to probiotics ability to combat inflammation and permeability

CB1 receptors inhibit acetylcholine and therefore, slow motility and creates smooth muscle contractions

There’s link between CB1 receptors and obesity and fat metabolism
The Gut

CB1 and CB2 receptors are present throughout the GI tract and the lining

ECS regulate gut motility and inflammation in the gut

Research has shown that Cannabis can help with IBS and this may be why

Dis-regulation of the ECS and it’s relationship with the gut has been link to obesity

Gut protocol and gut foods should be part of the ECS support protocol and visa versa
Metabolic Syndrome

Short chain fatty acids butyrate and acetate have been shown to protect against diet-induced obesity and insulin resistance.

Dysbiosis is associated with poor glucose metabolism and insulin intolerance – research focusing on specific types of bad bacteria.

Akkermansia muciniphila helps regulate glucose metabolism.
Study

Three probiotic strains, *Lactobacillus paracasei*, *Lactobacillus rhamnosus*, and *Bifidobacterium animalis* were administered to mice subjected to a high fat diet for 12 weeks. Each of the 3 strains prevented weight gain and markedly improved glucose-insulin homeostasis.

All three probiotic strains shifted the gut microflora of mice in the high fat group to resemble that of lean fed mice and thus could potentially be used to attenuate the effects of high fat diet-induced obesity.
Bacteria fermenting fiber produces succinate

Linked to improving glucose metabolism

Rodent study found too much production of SCFA acetate by gut bacteria increase insulin and ghrelin and is linked to weight gain

Fed a high fat diet to get them to produce more acetate
Fecal transplants have shown benefits for reversing obesity and metabolic syndrome.

Obese mice extract more calories from food than lean mice (due to gut bacteria).

Gut bacteria may be responsible for yo-yo dieting effect.
Diabetes Gut Connection

Gut bacteria helps regulate blood sugar and insulin

Gut supports liver function – many Type II do not convert glucose to glycogen well (increasing glucose to fat conversion)

Gut relationship to adrenals and stress also plays a role

High cortisol causes blood sugar to swing up and down
Cholesterol has benefits to the microflora itself as it has mild antibacterial properties, inhibiting bad bacteria when excrete in the colon.

Plant sterols increases the ability of cholesterol in food being excrete as opposed to being absorbed into the body, keeping the system for the benefits of the microflora.
B. longum SPM1207 reduced serum total cholesterol and LDL levels significantly, and slightly increased serum HDL. B. longum SPM1207 also increased fecal LAB levels and fecal water content, and reduced body weight and harmful intestinal enzyme activities.

Studies have found Lactobacillus helveticus and Saccharomyces cerevisiae lowered LDL and raised HDL.

Other strains also have similar benefits.
Blood Pressure

◦ A lot of interest in probiotics for regulating blood pressure
◦ C-reactive protein – an inflammatory marker is considered a precursor to the development of hypertension
◦ CRP, as a pro-inflammatory agent, it is associated with the release of interleukin-6 and is a factor in IBD
◦ The good bacteria lowers IL-6 and increases IL-10 (an anti-inflammatory marker)
◦ IL-6 has been indicated as a factor in hypertension
Osteoporosis

Good bacteria aids the absorption of calcium

L reuteri, L casei and L gasseri help with calcium absorption and increasing bone density

Chronic inflammation affects bone re-absorption (osteoclasts) and decreases bone formation (osteoblasts)

Good bacteria lowers chronic inflammation
*Lactobacillus reuteri* increases vitamin D levels by about 25%.

In a study of 25 women 50-79 years of age, analysis of their microorganisms status found higher levels of bad bacteria than the healthy women in the control group indicating dysbiosis was present.

Other studies (animal and one human) show probiotics can help build bone density.
Osteoarthritis

Predisposition to GIT disturbances is common in people with musculoskeletal conditions.
The gut microflora regulates inflammation in the body.
Free radicals and inflammation linked to cartilage destruction.
Pro-inflammatory cytokines increase nitric oxide – too much can damage tissues and inhibit collagen formation in cartilage.
Good Bacteria regulates cytokines
Liver function also involved in inflammatory response
NSAIDs, aspirin and ibuprofen further damage the gut lining and increases dysbiosis exacerbating the condition
Sulfur essential to maintaining cartilage
Glycosaminoglycans (GAGs) - building blocks of joint cartilage, and GAG molecules linked together in chains by disulfide bonds – contains two sulfur molecules
Sulfur maintains cross-linking of connective tissue and strengthens them
Bad bacteria, especially Streptococcus, enterococcus and prevotella, turn sulfur into hydrogen sulfide gas.
CFS

90% of CFS people have IBS

A recent study looked at colon strains of 50 people with CFS and 50 healthy people

Found an elevated levels of these species of bacteria in all CFS people:

Faecalibacterium, Roseburia, Dorea, Coprococcus, Clostridium, Ruminococcus, Coprobacillus
Fibromyalgia

In one study of 84 patients with fibromyalgia and 111 with IBS tested positive in a LBT (Lactulose Breath Test) which measures abnormal bacterial levels. Low endocrine and immune function are also factors – both of which can be affected by bacteria in the intestines. Whether this is a cause or another factor is still unknown.