BRAIN GUT 7: INTRO TO YOUR GUT MICROBIOME

READERS SUMMARY:

1. WHAT CONTROLS OUR LOOK OR BODY COMP?

2. IS LEPTIN TIED TO THE GUT FLORA?

3. WHAT IS THE PURPOSE OF THE GUT MICROFLORA IN HUMANS?

4. IS OUR GUT LIKE A MONOPOLY BOARD?

5. HOW ARE PREGNANCY AND OBESITY ALIKE, YET QUITE DIFFERENT?

In the human gut and mouth, two other domains of microbial life are involved in human physiology. Archaea and Eukaryotic fungi and possibly protozoa, likely play an as-yet-undetermined role in optimal health maintenance. The human mouth and gut are a teeming microbial cauldron of life, which covers such intimate vital tissues, like our teeth and gut that remain exposed to our current environment. No longer can a human being be viewed as simply an individual produced from a diploid genome from its parents germ cells (Mom and Dad). Throughout the last 15 years, paradigm-shifting studies have shown the how gut microbial metabolism can truly alter human health and disease states. Today we will discuss how pregnancy and obesity are very closely related but yet different because of the hormone surges that each present with in humans. That hormone difference is all that separates a normal physiologic state (pregnancy) from a neolithic disease state (obesity). Because of this new knowledge, I now recognize that modern man is a cyborg like “superorganism” colonized with a huge variety of microbial life that can positively and negatively alter the course of health and well-being. Understanding the anatomy or the physiology in textbooks often just falls short of the entire story of human

metabolism. It is complex and is tied to modern epigenetics, and this ultimately determines ***"our look and body composition."***

THE LEPTIN LINK OF "GUT FLORA" TO OBESITY:

Many of you know I believe obesity if an inflammatory disease of the brain. Where this disease begins may surprise some of you. It begins in our eyes and gut flora. How does this happen? Read this link! Sub optimal bacteria which contain bacterial toxins called lipopolysaccharides (LPS) which are found in bacterial cell membranes. As gut LPS rises, it has been shown to cause a rise in serum leptin levels. Once leptin levels are raised high enough it stimulates SOCS 3 signaling in the hypothalamus to cause LR. The overweight seem to physiologically 'guard' their elevated weight once it has transpired. In many mammal models of diet-induced obesity, leptin resistance is seen initially at and within the signaling though the vagal afferents into the area postrema. This blunts the actions of satiety incretin hormones centrally, and causes low brain dopamine levels. These things, along with the gastrointestinal bacterial-triggered SOCS3 signaling, are all implicated in the etiology of human obesity. In humans, dietary fat and fructose elevate systemic lipopolysaccharide, while dietary glucose also strongly activates SOCS3 signaling. Protein seems immune to this signaling of SOCS3 and it is why protein and AM light exposure of the eye are keys to reversal in my Leptin Rx.

This information implies that the gut flora can directly induce leptin resistance and be a cause of obesity. Gut bacterial LPS also raises blood levels of triglycerides as do simply refined dietary sugars and industrial seed oils found in most western diets. Both of these things are the modern principal causes of leptin resistance at the blood-brain barrier near the hypothalamus. It is also clearly established that eating a diet high in refined carbohydrates with or without a combo of industrial seed oils "simplifies the gut

flora" in both species and in shear numbers, and these changes selects out for bacteria that cause inflammation at the blood brain barrier by increasing SOCS3 signaling.

NON GEEKS: Low numbers and amounts of bacteria happen to people who eat lots of processed foods and industrial seed oils. This leads to constipation and hard stools like we see in grade 1 and 2 of the Bristol Stool Chart.

So far in the Brain Gut series we have focused mostly on the brain side of this equation. Today we begin to work a bit on the other side of the equation were the gut is located. We are going to talk about the gut microflora. The key frontier questions now for scientists and clinicians are to figure out what is the purpose of the gut microflora? In Brain Gut one and two, I make the case, that the ***gut microflora is our casino dealer*** who shuffles the deck of genes that we collect from viruses. It also appears that the gut microflora helps in presenting these viral components to the immune system and they are neutralized and made less virulent so that we can carry their spare parts in our genome to use at a later date when we see fit based upon our genomic and epigenomic needs.

These viral genes are '**humans junk yard**' for new gene creation. We learned from Barbara McClintock's work that these collected genes are then purposefully and systematically inserted into parts of genome where we have the most genomic or epigenomic needs based upon the stresses the organism faces in its current environment. The human body is roughly made up of one trillion cells. The latest number science gives us about the numbers of bacteria in our gut now is close to ***100 trillion***! Just a few years ago we thought this number was ten trillion cells. This means we have 100 times as many bacteria in our own guts that we do in our body. What might this imply? When you are on a process of discovery you always want to ask really good questions and try to avoid old answers with dead ends. So todays blog asks this question, "What is the purpose of the gut microflora in humans?" It is a loaded

question for sure, but let us explore it.

When we consider the non-digestive microbiota benefits, they can be broadly segregated into two large areas:

1. gut homeostasis

2. immune system education.

What is becoming clear to clinicians and scientist alike now, is that human beings are truly a cyborg like creatures. Our genome and things that make us humans unique are made up from large amounts of retrotransposons from viruses and the bacteria in our gut truly take this concept to a new level as we explored in Brain Gut 2. We technically are "super-organisms." As a result of this co-evolution, our guts shortened in length from our immediate ancestors, and our gut bacteria ecology became quite complex, to offset the change in length to facilitate the dietary changes we saw in the East Rift zone to make a human brain. These evolutionary moves also dramatically also improved our immune system's ability to present antigens to our cellular immunity arm to better protect us from the ecology that the transitional apes found themselves in. We explored this in Brain Gut 5 in some detail. The immune system had to undergo great expansion because of how we evolved using viruses and bacteria as our path to our humanness. By once again harnessing the power of diversity of bacteria from our vertebrate ancestors with in our own guts, it allowed us to digest ***more new food sources*** that we used to fuel the blueprint to build a human brain. This diet is called the Epi paleo Rx.

While 99{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of the adult gut microbiota is dominated by two bacterial phyla Bacteroides and Firmicutes, a full-term infant who is breast-fed, has a radically different gut microbiota from adults which is dominated by Bifidobacterium species

along with Lactobacillus species for the first few months of post natal life. This persists until solid food ingestion begins and a transition to a normal adult microbiota occurs. Moreover, the human microbiota also evolves as we age as well.

Recent studies have shown that delivery type (Cesarean versus vaginal), birth weight, breast feeding, and diet all influence which gut microbes colonize the sterile newborn gut. This implies that the early colonization window of an infant is **environment-dependent** (epigenetic) rather than host-dependent action in humans.

Moreover, this gut microbial plasticity is quite temporary because shortly after birth, at approximately 100-300 days, most of the infant's gut microbiota transforms to a more adult-like composition mentioned above.

GUT REAL ESTATE:

All along the gastrointestinal tract, there is a distinct gradient of immune tissue type, chemical acidity, and a specific rate of transit that controls the microbiota composition. I consider the GI tract as a "monopoly board" where some places are very different like the Boardwalk and Oriental Avenue properties found in the board game. I have recently began to mention this in many of my educational consults I have done recently. For example, in the stomach, Proteobacteria dominate, but in the distal gut (colon), Firmicutes and Bacteroides, which are barely detectable in the upper GI tract, become the dominant super organisms in a normal gut. This transition is very likely epigenetically and host-mediated (by antimicrobial peptide production). The precise physiologic and immunologic mechanisms which control these compositional changes have not yet been delineated by modern science, but we now know this happens in health and in disease states.

The microbiota composition, in the distal gut at least, is probably evolutionarily ancient, given the dominance of Bacteroides and Firmicutes **amongst all mammals** studied so far to date by science. This implies it is a highly conserved finding in the mammalian clade for an evolutionary reason. The parasympathetic nervous system controls the connections between the gut and the brain in humans. On each end of this conduit are two specialized membranes to control the optimal health milieu of both the gut and the brain at all times. The policeman of this system is the vagus nerve. In humans, the distal gut is also not innervated by the vagus nerve which is the tenth cranial nerve. The remainder of the gut is innervated by this nerve. This means the distal gut has no direct conduit to the brain. This is why most neolithic disease happens in this area. This is a direct connection of the gut to the brain in 90{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of its length. The fact that most neolithic diseases occur in this uncovered gut real estate by this cranial nerve seems to imply that the brain directly is involved with monitoring the gut microbiotic mix in health.

I mentioned earlier in this series that I believe their has been a massive co-evolution of the gut microbiota with the host immune system. I believe this arrangement has allowed the host physiology to become optimized for survival of some bacterial lineages over others, but no direct scientific evidence for this effect has yet been presented as far as I know of today. The findings we have found today in the lab in humans are now strongly pointing in this direction.

Microbiota and Progesterone:

The bacterial survival issue also appears to be carried directly over to reproductive fitness too in humans. Women's gut microbe populations change as pregnancy advances, becoming more like those of people who might develop diabetes. It now appears there is a special microbiota for pregnant women that

develops during the first 5 months of pregnancy to allow them to put on massive amounts of weight without developing diabetes in a normal pregnancy. The reason they do not appear to develop diabetes is because during pregnancy their progesterone levels are massively raised (by their placenta if it is functioning well) while their cortisol levels stay flat to decreased. This is true of most normal pregnancies, but today in the modern world due to the older age of women at conception, now infertility issues and obesity are skyrocketing and as a result those switches no longer work well. Many obese, infertile, and older women have low progesterone and high cortisol's before they get pregnant and this radically alters the gut flora to favor an obeseogenic status as their pregnancy progresses. This is why we often see gestational diabetes develop in these women with low progesterone levels as their fetus gets larger.

Morevover, if you go back and re read point 12 in Brain Gut 5 you will see another hormone, called E3 or estriol, has a massive affect on the gut microbiota. This diminishes the risk or cancer development both to the fetus and to the mother's breast. This is precisely how epigenetics has direct actions on a fetus and mom.

WHAT MAKES METABOLIC SYNDROME AND PREGNANCY DIFFERENT?

In pregnant women overall, the diversity of their gut bacteria declines between the first and third trimesters. Simultaneously there is a massive change in species. Certain types, such as the Proteobacteria and Actinobacteria, are increased dramatically from pre-pregnancy to pregnancy states.

The Proteobacteria are a major group (phylum) of bacteria. They include a wide variety of pathogens, such as Escherichia, Salmonella, Vibrio, Helicobacter, and many other notable genera. Actinobacteria are a group of Gram-positive bacteria with high guanine and cytosine content. They can be terrestrial or aquatic.

These species, ironically, are also more common in people who are obese or have metabolic syndrome associated with T2D. Proteobacteria in particular are often the bad guys in research studies checking stool samples of pregnant women. They are associated with inflammation, elevated cytokines and lowering of DHEA and progesterone further. They also are implicated in causing leptin resistance. This also allows for even higher cortisol levels to develop quickly. Remember what I told you in the Hormone 101 blog post about high cortisol levels? A high cortisol level can not be sustained forever and eventually adrenal fatigue is the end result. Go re-read the blog to understand what is happening both in a suboptimal pregnancy and in obesity.

Dr. Kjersti Aagaard, an OB/GYN from Baylor University, published some data comparing vaginal microbiomes in pregnant and non-pregnant women; those in the pregnant women were dominated by Lactobacillus species, which are thought to prevent the growth of harmful bacteria and help aid human digestion. Many probiotics are loaded with these bacteria but in too few a dose to make a ton of immediate help in a diseased state without the help of higher progesterone and lower cortisol levels. The ideal way to have both of these situations is to have an optimal hormone panel that pays strict attention to circadian light and dietary signals.

Furthermore the research also shows that the process is reversible after birth. It appears the shifts in microbial diversity did not affect mothers' health during pregnancy. What it did show is that their stools (PCR analysis) collected during the third trimester contained more inflammatory markers than those collected during the first trimester.
These trends held firm thoughout whether or not the women were of normal weight or overweight before falling pregnant, had actually developed diabetes, or had taken antibiotics or probiotics (supplements taken to provide or boost populations

of ‘healthy’ bacteria) during pregnancy. Meanwhile, after birth, the children’s microbiota’s resembled those of the mothers’ first trimester samples. This implies the status of mom’s gut health and pre pregnancy and her hormone panels are of **primary importance** to the developing fetal brain. In my opinion, this link best explains why we are seeing record increases in autism and spectrum disorders today. I don’t believe that vaccines are the major issue in spectrum disorders as some do. I believe hormone changes in the mother prenatally are to blame. This is due to sub optimal circadian biology (artificial light, EMF’s, and diet) which cause subsequent changes to the gut microflora pre-pregnancy are of primary importance in these epigenetic diseases. This also implies it is reversible and can be made optimal before a child is conceived if the mother decides to become proactive and understands how much power her decisions truly yield in forming an optimal brain for her child.

When researchers transplanted gut bacteria from stool samples into mice that had been raised under sterile conditions, they found that mice receiving microbiota from third-trimester samples became fatter and insulin resistant than mice that were given first-trimester samples. This was not a surprising result to me because there is quite a bit of information in the literature today that obesity has its own inherent gut microbiota that is highly inflammatory and blocks normal gut signals and eventually leptin at the blood brain barrier.

The reality appears today that that the microbiome is a contributing factor to this change. Some of us believe that it maybe the driving force behind it completely. It may be that obesity is due to a change in signaling between the gut microbiome and the leptin receptor in the brain. The link is both ingenious and fascinating and of course how it ties the hormone panels together is something that modern medicine remains quite blind too. You no longer should be blind to this link. It maybe the critical first link in reducing your

risk for obesity. CT helps destroy inflammation while increasing energy expenditure and it too changes your gut flora.

It appears in pregnancy direct hormone surges dramatically alter the gut microbiota, and these changes give you the changes in metabolism to foster massive growth of the body and brain of a fetus. This implies that food and hormones are cut from the same cloth with regards to physiology. This eerily sounds like the quote I made in Brain Gut 5. It said, **“Think of food as hormone information, not as a metabolic fuel. Think of the Epi-paleo template as human jet fuel for the human nervous system.”**

Here is another piece of the QUILT in how the gut and brain are married and dance a beautiful dance together when circadian biology is optimally matched.

You should mind your gut health and it might help you repair your hormones and all this can help heal an adult ‘bad brain’ or one that is forming your own uterus right now!

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