Seeding Lifelong Health:

The Impact of Pregnancy, Birth, and Infant Care on the Baby's Developing Microbiome

1

by

Lori Nicholson, MPA, HBCE, CH, NLPP

Joyful Birth HypnoBirthing®

lori@joyfulbirthhypnobirthing.com

www.joyfulbirthhypnobirthing.com

Disclaimer

Nothing in this presentation should be construed as medical advice. This document is educational in nature, prepared by a childbirth educator who is not a medical provider. It is strictly intended to provide a general overview of the research literature; the topics may not apply to you as an individual. It is not intended to be, nor should it be used as, a substitute for prenatal care and advice from a medical provider (e.g., midwife, nurse, nurse practitioner, doctor, etc.). Prenatal care is important; please see your medical provider for consultations, care, and advice. The author assumes no responsibility for your actions or decisions based upon your reading of this presentation.

Photo Credit: American Microbiome Institute:
http://www.microbiomeinstitute.org/

The Microbiome: What is It?

- Our microbiome consists of all of the organisms that live within and on us (e.g., bacteria, fungi, viruses, protozoa)
  - 1,000 species in the intestines
  - 700 species in the mouth
  - 300-400 species in the vagina
  - 700 species on the skin
- We need diversity in our microbes in order to fight pathogens and stave off disease—they are integral to our immune and metabolic health—but we have collectively lost about 1/3 of our microbes due in large part to:
  - Antibiotics and antimicrobial products (which kill off the good bacteria as well as the pathogens)
  - Lifestyle/diet (Blaser, as quoted in Harman T, Wakeford A 2014)
- The National Institutes of Health (NIH) launched the Human Microbiome Project in 2007 to study how our microbiomes may lead to various non-communicable diseases (NCDs)

(All information from Harman T, Wakeford A 2014)

5

The Microbiome: Why Does it Matter?

Unbalanced microbiome results in "a low-grade, long-lasting inflammatory response"

"Leakiness" of the child's intestinal lining results in abnormal processing of food (protein and carbohydrates find their way into the bloodstream)

Potentially chronic conditions later in life

(Reference: Sloan 2012)

The Microbiome: Why Does it Matter?

The health of the microbiome has been associated with several non-communicable diseases:

- Allergies
- Asthma
- Celiac disease
- Diabetes
- Eczema
- Irritable bowel syndrome (IBS)
- Mental health issues, such as Autism Spectrum Disorder
- Necrotic enterocolitis (NEC) in newborns
- Obesity (Harman T, Wakeford A 2014)

Summary of the factors affecting gut microbiota colonization in infants

Factors affecting colonization of gut microbiota before birth	Factors affecting colonization of gut microbiota during/at birth	Factors affecting colonization of gut microbiota after birth
Intra-uterine environment	Mode of delivery (Cesarean vs. vaginal delivery)	Breastfeeding vs. formula feeding
Maternal exposures or practices: Stress	Environment at the time of delivery	Weaning or food supplementation
Maternal exposures or practices: Antibiotic use	Contact with the mother	Antibiotic exposure
Maternal exposures or practices: Smoking	Contact with the health care staff	Home or family setting (rural vs. urban)
Length of gestation (term vs. pre-term)		Home structure (contact with siblings, other family members)

Reference: Munyaka PM, Khafipour E, Ghia J-E 2014

Factors affecting colonization of gut microbiota in neonates and infants or children

Factor	Observed effect on microbiota	Specific health condition/disorder/disease
Intrauterine environment	Presence of bacteria in the uterus, amniotic fluid, or meconium	Remote history of antenatal infections such as urinary tract infection during the first trimester; could contribute to preterm birth
Stress during pregnancy	Low counts of beneficial bacteria	Allergic reactions
Probiotic use during pregnancy	Increased colonization by beneficial bacteria, increased bacterial diversity	Reduced incidence of allergic reactions
Antibiotic use during pregnancy	Delayed colonization or reduced abundance of beneficial bacteria	Increased allergic reactions (asthma, allergic sensitization, allergic rhinitis), Irritable bowel syndrome (IBS), Inflammatory bowel disease (IBD)
Smoking during pregnancy	Microbial dysbiosis	Increased risk of IBD

Reference: Munyaka PM, Khafipour E, Ghia J-E 2014

Factors affecting colonization of gut microbiota in neonates and infants or children (continued)

Factor	Observed effect on microbiota	Specific health condition/disorder/disease
Length of gestation period – preterm	Slow rate of bacterial colonization, reduced bacterial diversity, high interindividual difference in colonization, increased level of potential pathogenic bacteria	Necrotic enterocolitis (NEC)
Length of gestation period - term	Increased abundance of beneficial bacteria, high bacterial diversity	Lower incidence of NEC
Cesarean delivery	Reduced bacterial richness and diversity, reduced colonization by beneficial bacteria, increased colonization by potential pathogens	Increased risk of asthma, allergic reactions, Type 1 diabetes, atopic eczema, obesity and NEC
Vaginal delivery	Increased microbial diversity	Decreased risk of asthma, allergic reactions

Reference: Munyaka PM, Khafipour E, Ghia J-E 2014

The Microbiome: Why Does it Matter?

Photo Credit: http://www.babyknowledge.co.uk/wp-content/uploads/2013/08/bk-laughing-baby_postcard.jpg

In other words:

We lay the groundwork for the life-long health of our children through the way in which we prepare our bodies for conception, care for our bodies during pregnancy, birth our babies, and feed our babies

The Development of the Microbiome

- Human microbial colonization begins in utero and develops in a non-random way (i.e., the starting point determines the development); essentially the baby inherits its microbiome from its mother
- The gastrointestinal tract is the largest source of microbial exposure, which is why mothers-to-be should address their gut health ***before*** conception (Mueller et al. 2015)

Photo Credit: www.healthcastle.com

Prenatal Nutrition and The Microbiome

- Our gut microbes impact our brain tissues and nervous system tissues through the "Brain-gut-enteric microbiota axis" (Horvath Marques et al. 2013)
- One study showed a reduction in gestational diabetes when women took probiotics early in pregnancy (Barrett et al. 2014); other research on the use of prebiotics and probiotics during pregnancy and labor show mixed results (Mueller et al. 2015)
- The fetal microbiome, and therefore the development of the baby's immune system, depends on adequate maternal nutrition; certain micronutrients (and a fatty acid) are especially important:
  - Folate and other B-vitamins
  - Iodine
  - Vitamin D
  - Docosahexanoic acid (DHA), an omega-3 fatty acid

Prenatal Nutrition and The Microbiome: Folate

- Folate (or folic acid, the synthetic form of folate) is necessary for normal fetal spine, brain, and skull development, thus protecting against neural tube defects (Morse 2012)
- Is needed for DNA methylation, which helps cells to control gene expression (Martino D, Prescott S 2011)
- Helps modulate epigenetic mechanisms that help the immune system develop, protecting against allergic risk and asthma development (Martino D, Prescott S 2011)
- New research suggests that prenatal folic acid supplements may lower the risk of severe language delay (Roth et al. 2011), autistic disorder (Surén et al. 2012), and autism spectrum disorders (Schmidt et al. 2012)
- Dark green vegetables like broccoli and spinach, and dried legumes such as chickpeas, beans and lentils, are good sources of folate

Prenatal Nutrition and The Microbiome: Iodine

- Essential for thyroid hormone production, which is necessary for: normal brain and nervous system development (Morse 2012); and modulating immune response (De Vito et al. 2011)
- Helps prevent mental retardation (Trumpff et al. 2013)
- Sea vegetables, cranberries, organic yogurt and cheese, and strawberries are good sources of iodine

Photo Credit: chefjjs.com

Prenatal Nutrition and The Microbiome: Vitamin D

- Helps maintain the pregnancy and lower the risk of preeclampsia (Morse 2012)
- Is crucial in skeletal and brain development and the development of the immune system (Morse 2012)
- Regulates antimicrobial innate immune responses, can inhibit lymphocyte proliferation, and can decrease the risk of respiratory syncytial virus (RSV) infection during an infant's first year of life (Wang et al. 2004; Horvath Marques et al. 2013)
- Current animal research implies that it may decrease the risk of neurodevelopmental disorders as well (Horvath Marques et al. 2013)
- Fish, fish oils, mushrooms, beef liver, cheese, milk and egg yolks are high in Vitamin D ("the sunshine vitamin")

Photo Credit: www.pinterest.com

Prenatal Nutrition and The Microbiome: DHA

- Necessary for cell membrane formation in the brain and central nervous system, which ensures proper fetal growth (Morse 2012)
- Prolongs gestation in high-risk pregnancies (Morse 2012)
- Increases baby's birth weight, head circumference, and birth length (Morse 2012)
- Enhances baby's visual acuity, hand/eye coordination, attention processing, problem solving ability, information processing and neurological outcomes (Morse 2012)
- Good dietary sources of DHA include: algae, fatty fish (salmon, halibut, anchovies, tuna), liver (organ meat), fish oil, and egg yolks

The Development of Baby's Healthy Microbiome

- The intrauterine environment, the environment in which the baby is born, and the people with whom the baby comes in contact all help form the baby's microbiome
- Early exposures impact the intestinal microbiota of the baby—they "train the baby's immune system" (Mueller et al. 2015)
- The baby's brain tissues and nervous system tissues are dependent upon the "seeding" and diversity of microbes in the gut
- Exposure to pathogens, and/or lack of exposure to beneficial microbes, are associated with childhood diseases that may persist into adulthood
- The greatest challenges to the healthy development of the baby's microbiome are:
  - Cesarean delivery
  - Antiobiotic exposure before, during, or after birth
  - Formula feeding (Mueller et al. 2015)

The Development of Baby's Microbiome

According to the experts interviewed for the documentary <u>MICROBIRTH,</u> there are three crucial steps in the formation of an infant's healthy microbiome:

- Step 1: Vaginal birth
- Step 2: Immediate skin-to-skin contact with the mother following birth
- Step 3: Breastfeeding (Harman T, Wakeford A 2014)

The Healthy Microbiome Model

Vaginal Birth → Skin-to-Skin Contact → Breastfeeding → **Healthy Microbiome**

The Microbiome: Step 1
Vaginal Birth

Vaginal Birth → Skin-to-Skin Contact → Breastfeeding → **Healthy Microbiome**

The Microbiome: Step 1 Vaginal Birth

- Birth is a "programming event" where genes can be switched on and off (epigenetics) (Schulfer A, Blaser MJ 2015)
- Key bacterial species gather in the vagina and the breasts in the days leading up to the birth
- The baby acquires the mother's bacteria while coming down the birth path (swallowing amniotic fluid)
- This is the "major seeding event" for the infant's gut microbes, which are crucial to the development of the child's immune system
- Disrupting this "major seeding event" due to a C-section delivery may increase the risk of asthma, allergies, Type 1 diabetes, eczema, and obesity in the baby
- Using antibiotics during birth may have a much greater impact genetically than using antibiotics at other times during your life (Schulfer A, Blaser MJ 2015)

The Microbiome and Cesareans

From the perspective of the microbiome, babies born via C-section are not getting the "seeding" of their immune system that they require:

- Have less diverse and less rich gut microbiota than vaginally delivered babies (Arrieta et al. 2014; Azad et al. 2013)
- Difficult for their immature immune systems to determine which bacteria are good (and should be tolerated) and which are harmful (and should be attacked)
- Induction, antibiotics, Pitocin, C-section, forceps—all of these interventions ***may*** change the baby's epigenome
- The baby's metabolism may not stabilize
- The baby's immune system may not mature (or may be "incomplete")
- If you have one non-communicable disease (NCD) early in life, you are at greater risk for other NCDs later in life (association—not causation) (Harman T, Wakeford A 2014)

The Microbiome and "The Completed Self"

Dietert and Dietert have created an immunological model called "The Completed Self":

- The Completed Self forms in the neonate, so prenatal and perinatal protection of the development of The Completed Self is crucial
- Three major components affect the formation and integrity of The Completed Self: "1) useful epigenetic programming, 2) effective immune development, and 3) complete microbiota acquisition"
  - Will the child's microbiome become "complete," leading to a life of health?

  OR

  - Will the child's microbiome remain "incomplete," leading to a life of disease?

(Dietert R, Dietert J 2012)

The Microbiome and Cesareans

- It is possible to “seed” the baby born via C-section
- These “seeded” babies look more like vaginally born babies than like C-section babies, from the perspective of the microbiome
- If babies are born via C-section, they should have the benefits of:
  - Immediate skin-to-skin
  - “Seeding” through vaginal swabbing, to help establish their microbiome
  - Extended breastfeeding (6 months or more)

Photo Credit: www.oneworldbirth.net

The Role of the Birthing Environment

Photo Credit: www.drperlmutter.com

- When the baby is born, s/he is "seeded" with mom's microbes ***and*** the microbes in her/his environment
- As discussed, the foundation for baby's long-term health is laid at this time
- We have no research to inform what impact different birthing environments may have on the baby's microbiome; however:
  - Being in one's home environment may support this "seeding" process—exposing baby only to his/her own family's microbes
  - Babies born in a hospital or birthing center may benefit from being exposed only to those items that have been brought from home (e.g., blankets, clothing) immediately following birth

Antibiotic Exposure and the Baby's Microbiome

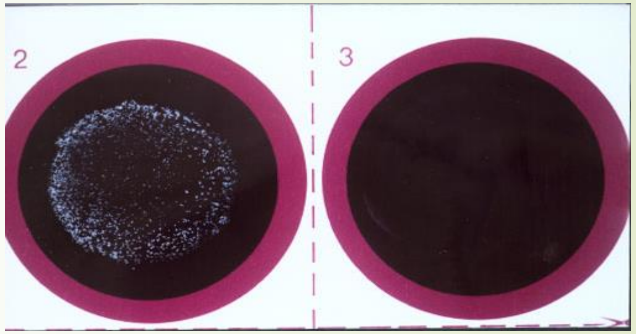
- One small study examined the gut microbiota of nine newborns who were given IV ampicillin and gentamicin within 48 hours of birth (the research did not look at the infant's gut microbiota as a result of the mother receiving IV antibiotics during labor) (Fouhy et al. 2012)
- Stool samples were taken at 4 weeks and 8 weeks after the infants completed their antibiotics, and these were compared to the stool samples of nine untreated infants
- At 4 weeks after completing the course of antibiotics, the treated infants had:
  - Significantly lower levels of beneficial *Actinobacteria*, including *Bifidobacterium* and *Lactobacillus*
  - Significantly higher levels of *Proteobacteria*
  - Less diversity of their gut microbe (Fouhy et al. 2012)

Antibiotic Exposure and the Baby's Microbiome

- By week 8, the treated infants had:
  - Significantly higher *Proteobacteria* levels (still)
  - Recovered levels of *Actinobacteria*, *Bifidobacterium*, and *Lactobacillus* similar to those in the control samples
  - Fewer different *Bifidobacterium* species present (i.e., less diversity still) (Fouhy et al. 2012)
- The authors concluded that "the combined use of ampicillin and gentamicin in early life can have significant effects on the evolution of the infant gut microbiota, the long-term health implications of which remain unknown" (Fouhy et al. 2012)

Perinatal Maternal Antibiotic Usage and the Baby's Microbiome

- When women are given antibiotics during labor, it is often because they have tested positive for Group B Strep, a common bacterium carried in the intestines or lower genital tract (Mayo Clinic 2015)
- 12-27% of pregnant women worldwide are "colonized" with GBS (they carry it in their bodies, but are not harmed by it) (Johri et al. 2006)
- Although typically harmless to adults, GBS can cause life-threatening complications in infants, including:
  - "Inflammation of the lungs (pneumonia)
  - Inflammation of the membranes and fluid surrounding the brain and spinal cord (meningitis)
  - Infection in the bloodstream (bacteremia)" (Mayo Clinic 2015)



Positive agglutination GBS is present

Negative agglutination GBS is not present

Photo Courtesy of Dr. Richard Facklam, CDC, Laboratory Slide Set, http://www.cdc.gov/groupbstrep/guidelines/slidesets.html

Perinatal Maternal Antibiotic Usage and the Baby's Microbiome

- The standard of care for GBS-positive women during labor is multiple doses of IV antibiotics, administered four hours apart (CDC 2010)
- IV antibiotics are effective at protecting babies from GBS infection; in clinical trials, the risk of early GBS infection dropped by 83% when antibiotics were administered (Ohlsson A, Shah VS 2014, as referenced in Dekker 2014)
- However, we do not understand the long-term impact of this antibiotic exposure on the baby's developing microbiome, so researchers are seeking alternatives; one option is maternal probiotic usage

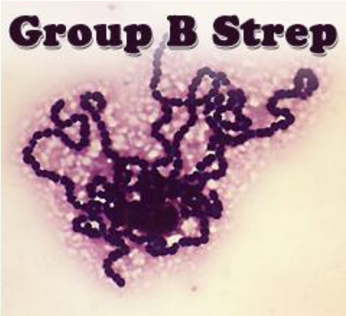


Photo Credit: www.families.com

Probiotic Usage and the Baby's Microbiome

- Three studies have found that probiotics (various strains of *Lactobacilli* and *Florajen* 3) strongly inhibit the growth of GBS in vitro (i.e., in a petri dish), thus supporting probiotics as a potential preventative for neonatal GBS infections (Açkigöv et al. 2005—article in Turkish; Zárate G, Nader-Macias ME 2006; Ephraim et al. 2012)
- Other research has found that prenatal probiotic therapy has the potential to reduce GBS colonization, but that the intervention is correlated with daily adherence to taking the probiotic regimen (i.e., those who took their probiotics regularly had lower levels of GBS colonization than those who skipped days of taking their probiotics) (Hanson et al. 2014)

Probiotic Usage and the Baby's Microbiome

- Non-pregnant women in a small clinical trial were able to increase the level of *Lactobacilli* in the vagina from wearing panty liners saturated with probiotics; the women with higher levels of *Lactobacilli* in the vagina also had lower levels of GBS (Rönnqvist PD, Forsgren-Brusk UB, Grahn-Håkansson EE 2006)
- A large clinical trial is currently underway at Stanford University "to determine if oral probiotic supplementation during the second half of pregnancy decreases maternal GBS recto-vaginal colonization at 35-37 weeks' gestational age, thereby decreasing need for maternal antibiotic administration at time of labor": https://clinicaltrials.gov/ct2/show/NCT01479478?term=probiotics+AND+group+b+strep&rank=1

The Microbiome: Step 2
Immediate Skin-to-Skin Contact (SSC) (aka Kangaroo Care)

Vaginal Birth → **Skin-to-Skin Contact** → Breastfeeding → **Healthy Microbiome**

The Microbiome: Step 2 Immediate Skin-to-Skin Contact (SSC) (aka Kangaroo Care)

- "Separation of human mothers and newborns is unique to the 20th century and is a complete break from natural human history" (Dekker 2013)
- Kangaroo Care, or Kangaroo Mother Care (KMC) includes three major components:
  1) Skin-to-Skin Care/Contact (SSC)
  2) Frequent and exclusive (or nearly exclusive) breastfeeding
  3) Treating the mother and baby as a dyad—what is sometimes referred to as "couplet care"

  (Conde-Agudelo A, Diaz-Rossello JL 2014; Wildner 2012; Dekker 2013)

Photo Credit: www.ecobabysteps.com

The Microbiome: Step 2
Immediate Skin-to-Skin Contact (SSC)
(aka Kangaroo Care)

- When researchers study **human** mother-newborn contact, keeping mothers and babies together is always considered the "experimental" intervention
- When researchers study **non-human mammals**, the "experimental" intervention is separating newborns from their mothers (Moore et al. 2012, as reported in Dekker 2013)

Photo Credits: www.fanpop.com and www.dailymail.co.uk

The Microbiome: Step 2
Immediate Skin-to-Skin Contact (SSC)
(aka Kangaroo Care)

- Neuroscientists believe that the newborn period is a “sensitive time” that meets the mom’s and baby’s biological needs—helping program physiology and behavior for the future (Hung KJ, Berg O 2011)
- Skin-to-skin promotes:
  - Neurobehavioral development (Ludington-Hoe SM, Swinth JY 1996)
  - Infant temperature stabilization (Moore et al. 2007; Bergman NJ, Linley LL, Fawcus SR 2004)
  - Less infant crying (Moore et al. 2007)
  - Higher infant blood glucose (Moore et al. 2007)
  - Increased maternal satisfaction and confidence (Moore et al. 2007)
  - Improved breastfeeding relationship (Ferber SG, Makhoul IR 2004; Radzyminski 2005; Moore et al. 2007)

The Microbiome: Step 2
Immediate Skin-to-Skin Contact (SSC)
(aka Kangaroo Care)

- Immediate skin-to-skin for the mom-baby dyad following birth leads to the skin-to-skin transfer of skin bacteria to the baby
- Baby has to get his or her microbes from somewhere; we want the baby's immune system primed with the right type of bacterium (as discussed, this impacts the choice of birthing environment/facility as well)
- This is when the baby's immune system learns what is friend versus foe
- Scientists believe the microbes have one chance to do this—during birth and immediately thereafter: you can correct the "balance" of microbes with probiotics later in life, but you cannot retrain the immune system

Skin-to-Skin after Cesarean

- C-sections are getting safer, so the threshold of risk at which OBs and women resort to C-sections is getting lower and lower (Philip Steer, Emeritus Professor of Obstetrics, Imperial College, London, as quoted in Harman T, Wakeford A 2014)
- Yet, in 2009 only 32% of US hospitals implemented SSC for most mother-baby dyads within two hours of an uncomplicated C-section (CDC 2009, as reported in Dekker 2012)

Photo Credit: www.pinterest.com, Kristin Jent Photography

Skin-to-Skin after Cesarean and the Development of the Microbiome

- Babies born vaginally have a microbial profile resembling their mother's vagina
- Babies born via Cesarean acquire their first microbes from the skin of people who contact them (preferably a parent)
- C-section babies tend to have microbiota more associated with the skin than with the gut or the vagina, which may lead to less diverse and less rich gut microbiota, and thus, a less robust immune system (Schulfer A, Blaser MJ 2015; Arrieta et al. 2014)

Photo Credit: www.keloland.com

The Microbiome: Step 3 Breastfeeding

Vaginal Birth → Skin-to-Skin Contact → **Breastfeeding**

Healthy Microbiome

The Microbiome: Step 3 Breastfeeding

- Breastfeeding is the postnatal method for mother-baby microbial exchange; it "seeds" and selects for particular populations of bacteria (Mueller et al. 2015)
- Breastmilk has anti-inflammatory hormones, antibodies, and sugars (oligosaccharides), which are indigestible by the baby
- Those sugars (oligosaccharides) are eaten by the good bacteria that are newly seeded in the baby's gut; in other words, breastmilk helps the good bacteria thrive
- By the end of baby's first year, the microbiome has become more complex and stable
- The child's microbiome will be similar to an adult microbiome by three years of age; in other words, the child's microbiome at three years old is likely to be that individual's "lifelong signature" of microbiota (Mueller et al. 2015; Groer et al. 2014)

Breastfeeding and The Microbiome

- One study found that the microbiota in breast milk differed between women who delivered vaginally versus those who had an elective Cesarean (Cabrera-Rubio et al. 2012)
- One study observed more than two times more "good bacteria" cells in breastfed infants compared to formula-fed infants (Berzirtzoglou E, Tsiotslas A, Weilling GW 2011)
- Rich in prebiotics, breast milk "selects for the persistence of beneficial bacteria and limits colonization of harmful ones" (Song SJ, Dominguez-Bello MG, Knight R 2013)
- Formula, even in small amounts while breastfeeding, "can alter the structure (Mackie et al. 1999) and relative abundances (Guaraldi F, Salvatori G 2012) of the bacterial communities in the breastfed infant's gut"
- Exclusive breastfeeding may help restore bacterial abundance to previously formula-fed infants (Mueller et al. 2015)

Photo Credit: www.birthbootcamp.com

Breastfeeding and The Microbiome

- Breast milk may provide the gut microbiome with greater plasticity to ease the transition into solid foods (Thompson et al. 2015)
- Introduction of solid foods, the types of solid foods consumed, and certain nutrients such as iron and fatty acids influence the diversity and composition of gut bacteria (Dewey 2013)
- There is little information on how dietary composition or nutrient intake affects the microbiome of children and the health consequences of differences in the gut microbiome (Dewey 2013)
- A new project entitled the Breast Milk, Gut Microbiome, and Immunity (BMMI) Project aims to discover new ways to promote healthy growth in infants and children through studying the development of the microbiome (Dewey 2013)

The Microbiome

Further information can be found at:

- American Microbiome Institute: http://www.microbiomeinstitute.org/?gclid=CJDxpefzksgCFdYUHwodF3wDRQ
- Gut Microbiota Worldwatch (the European Society of Neurogastroenterology and Motility): http://www.gutmicrobiotawatch.org/en/home/
- *Microbiome*, the journal: http://www.microbiomejournal.com/
- NIH Human Microbiome Project: http://hmpdacc.org/

Summary: Development of the Microbiome

- We need diversity in our microbes in order to fight pathogens and stave off disease; they are integral to our immune and metabolic health (Harman T, Wakeford A 2014)
- Human microbial colonization begins in utero and develops in a non-random way—the baby inherits its microbiome from its mother (Mueller et al. 2015)
- The "seeding" of microbiota that the baby receives from his/her mother "trains the baby's immune system" (Mueller et al. 2015)

Summary: Development of the Microbiome

- The fetal microbiome, and therefore the development of the baby's immune system, depends on adequate maternal nutrition; the mother's intake of the micronutrients folate, iodine, and Vitamin D, and the fatty acid DHA, is especially important
- An unbalanced microbiome has been associated with several health challenges including: asthma, eczema, diabetes, and obesity (Munyaka PM, Khafipour E, Ghia J-E 2014)
- The greatest challenges to the healthy development of the baby's microbiome are: Cesarean delivery; antibiotic exposure before, during, or after birth; and formula feeding (Mueller et al. 2015)
- The most important steps that can be taken to ensure the proper "seeding" of the baby are:
  - Step 1: Vaginal birth
  - Step 2: Immediate skin-to-skin contact with the mother following birth
  - Step 3: Exclusive breastfeeding (preferably for at least six months) (Harman T, Wakeford A 2014)

Summary: Vaginal Birth and the Microbiome

- The baby acquires the mother's bacteria while coming down the birth path (swallowing amniotic fluid)
- Vaginal birth is the "major seeding event" for the infant's gut microbes, which are crucial to the development of the child's immune system
- Disrupting this "major seeding event" due to a C-section delivery may increase the risk of asthma, allergies, Type 1 diabetes, eczema, and obesity in the baby (Schulfer A, Blaser MJ 2015)
- From the perspective of the microbiome, babies born via C-section are not getting the "seeding" of their immune system naturally that they require
- It is possible to "seed" the baby born via C-section immediately following birth
- These "seeded" babies look more like vaginally born babies than like C-section babies, from the perspective of the microbiome (Harman T, Wakeford A 2014)

Summary: Skin-to-Skin Care and the Microbiome

- Immediate or very early SSC has both physiologic and psychologic benefits to the mother-baby dyad, at a very sensitive developmental time for both bonding and the microbiome
- Early SSC has a positive effect on: breastfeeding, respiration, blood glucose, and lessened crying for the babies; and less breast engorgement and anxiety for the mothers—all with "no apparent short- or long-term negative effects" (Moore et al. 2012)
- SSC may be even more important for low birthweight babies than for normal babies, as it leads to: lower rates of mortality, sepsis, hypothermia, severe illness, respiratory problems, and long hospital stays, while assisting those low birthweight babies with better growth, breastfeeding, temperature regulation, and bonding with their mothers (Conde-Agudelo A, Diaz-Rossello JL 2014; McCall et al. 2010)
- Skin-to-skin care is the second stage in the all-important development of the baby's microbiome, and thus the baby's immune system for life—there is no "do-over" for this critical contact

Summary: Breastfeeding and the Microbiome

- Breastfeeding is extremely beneficial—in both the short-run and the long-run—to both babies and their mothers (WHO 2015; Stuebe 2009; WebMD 2015; WHO 2013; LLL 2015; Horta et al. 2007)
- Breastfeeding is the third crucial step in helping the baby develop a healthy microbiome (Harman T, Wakeford A 2014; Mueller et al. 2015; Berzirtzoglou E, Tsiotslas A, Weilling GW 2011; Cabrera-Rubio et al. 2012; Song SJ, Dominguez-Bello MG, Knight R 2013; Praveen et al. 2015; Guaraldi F, Salvatori G 2012; Thompson et al. 2015; Dewey 2013)
- Rich in prebiotics, breast milk "selects for the persistence of beneficial bacteria and limits colonization of harmful ones" (Song SJ, Dominguez-Bello MG, Knight R 2013)
- Breast milk may provide the gut microbiome with greater plasticity to ease the transition into solid foods (Thompson et al. 2015)

What Would Baby Want?

As the baby who wants to be conceived, I want:

- My mom to be of healthy weight, with a good, healthy microbiome herself (i.e., vaginal microbiome rich in lactobacilli, which is typically found in normal, healthy pregnancies) (Mueller et al. 2015)
  - Following good nutritional guidelines
    - Fermented foods and those with live cultures are especially good for gut health
    - Following the micronutrient/fatty acid recommendations, per a discussion with her care provider
  - Exercising regularly
  - Non-smoker
  - Low stress levels

Photo Credit: Lori Nicholson. Picture of Grace Kuhlmann, my youngest daughter.

What Would Baby Want?

As the baby who has been conceived, I want:

- To experience a vaginal birth, where I will be "seeded" with my mom's healthy microbes
- To experience birth without the use of any antibiotics or other interventions
- To birth at home (in my own bacterial environment) and to have only blankets and clothes from that environment touch me

As the baby who has been born, I want:

- To experience immediate skin-to-skin with my mom and no separation from mom (to experience rooming-in, if in a hospital)
- Care providers to do any newborn checks while I am experiencing SSC with my mom—"hands-off" from the care providers, as much as possible
- My mom to exclusively breastfeed me for six months, at which time I will be introduced to solid foods
- My mom to continue breastfeeding me from six months up to two years (or longer!) as I also eat solid foods

References

Aagaard K et al. The placenta harbors a unique microbiome. *Sci Transl Med*. 2014;6.

Abrahamsson TR et al. Low diversity of the gut microbiota in infants with atopic eczema. *J Allergy Clin Immunol*. 2012;129:434.

Abrahamsson TR et al. Low gut microbiota diversity in early infancy precedes asthma at school age. *Clin Exp Allergy*. 2014;44:842.

Açikgöz ZC et al. [Inhibitor effect of vaginal lactobacilli on group B streptococci.] [Article in Turkish.] *Mikrobiyol Bul*. 2005;39(1):17-23. http://www.ncbi.nlm.nih.gov/pubmed/15900833

Arrieta M-C et al. The intestinal microbiome in early life: health and disease. *Front Immunol*. 2014;5:427. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4155789

Azad MB et al. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. *CMAJ*. 2013;185:385. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3602254/

Azad MB et al. Impact of cesarean section delivery and breastfeeding on infant gut microbiota at one year of age. *Allergy Asthma Clin Immunol*. 2014;10(Suppl 1):A24. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126027

Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med*. 2002;347:911.

Bailey MT, Lubach GR, Coe CL. Prenatal stress alters bacterial colonization of the gut in infant monkeys. *J Pediatr Gastroenterol Nutr*. 2004;38:414.

Barrett HL et al. Probiotics to prevent gestational diabetes mellitus. Cochrane Collaboration review:CD009951. 2014. http://www.cochrane.org/CD009951/PREG_probiotics-to-prevent-gestational-diabetes-mellitus

Bergman NJ, Linley LL, Fawcus SR. Randomized controlled trial of skin-to-skin contact from birth versus conventional incubator for physiological stabilization in 1200- to 2199-gram newborns. *Acta Paediatrica*. 2004;93:779-785.

Berzirtzoglou E, Tsiotslas A, Weilling GW. Microbiota profile in feces of breast- and formula-fed newborns by using fluorescence in situ hybridization (FISH). *Anaerobe*. 2011;17(6):478.

References

Bianconi E et al. An estimation of the number of cells in the human body. *Annals Human Biol*. 2013;40:463–471.

Biedermann L et al. Smoking cessation induces profound changes in the composition of the intestinal microbiota in humans. *PLoS One*. 2013;8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597605/

Bisgaard H et al. Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic disease at school age. *J Allergy Clin Immunol*. 2011;128:646.

Black RE, Victora CG, Walker SP, and the Maternal and Child Nutrition Study Group. Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet*. 2013;published online. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2813%2960937-X/fulltext. Accessed online 10/04/15.

Butel MJ et al. Conditions of *Bifidobacterial* colonization in preterm infants: a prospective analysis. *J Pediatr Gastroenterol Nutr*. 2007;44:577.

Cabrera-Rubio R et al. The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery. *Am J Clin Nutr*. 2012;96:544-551.

Cardwell CR et al. Caesarean section is associated with an increased risk of childhood-onset type 1 diabetes mellitus: a meta-analysis of observational studies. *Diabetologia*. 2008;51:726.

Carlisle EM, Morowitz MJ. The intestinal microbiome and necrotizing enterocolitis. *Curr Opin Pediatr*. 2013;25:382.

Centers for Disease Control and Prevention (CDC). Maternity practices in infant nutrition and care (mPINC) survey. 2009. http://www.cdc.gov/breastfeeding/data/mpinc/index.htm

Centers for Disease Control and Prevention (CDC). Early-onset Group B Streptococcal disease prevention: for clinicians. Overview of CDC prevention guidelines, 2010. November 19, 2010. http://www.cdc.gov/groupbstrep/clinicians/obstetric-providers.html#slidesets. Accessed online 12/04/15.

References

Conde-Agudelo A and Diaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Collaboration review:CD002771. 2014. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002771.pub3/abstract

De Vito P et al. Thyroid hormones as modulators of immune activities at the cellular level. *Thyroid*. 2011;21:879-890.

Dekker R. The evidence for skin-to-skin care after a cesarean. Evidence Based Birth review. 2012. http://evidencebasedbirth.com/the-evidence-for-skin-to-skin-care-after-a-cesarean/

Dekker R. Can hospitals keep mothers and babies together after a cesarean? Evidence Based Birth review. 2013. http://evidencebasedbirth.com/can-hospitals-keep-moms-and-babies-together-after-a-cesarean/

Dekker R. Group B strep in pregnancy: evidence for antibiotics and alternatives. Evidence Based Birth review. 2014. http://evidencebasedbirth.com/groupbstrep/

Dewey KG. Diet, child nutrition and the microbiome. Presentation to human microbiome science: vision for the future, Bethesda, MD, July 24 to 26, 2013. https://www.genome.gov/Multimedia/Slides/HumanMicrobiomeScience2013/28_Dewey.pdf. Accessed online 10/04/15.

Dietert R, Dietert J. The Completed Self: an immunological view of the human-microbiome superorganism and risk of chronic diseases. *Entropy*. 2012;14:2036-2065. http://www.mdpi.com/1099-4300/14/11/2036

DiGiulio DB et al. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: a molecular and culture-based investigation. *PLoS One*. 2008;3. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2516597/

Dominguez-Bello MG et al. Development of the human gastrointestinal microbiota and insights from high-throughput sequencing. *Gastroenterology*. 2011;140:1713.

References

Dominguez-Bello MG et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proc Natl Acad Sci U S A*. 2010;107:11971. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900693/

Dominguez-Bello MG et al. Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer. *Nature Medicine*. Published online February 1, 2016. http://dx.doi.org/10.1038/nm.4039. http://www.nature.com/nm/journal/vaop/ncurrent/abs/nm.4039.html#supplementary-information

Droste JH et al. Does the use of antibiotics in early childhood increase the risk of asthma and allergic disease? *Clin Exp Allergy*. 2000;30:1548.

Ephraim E et al. In-vitro evaluation of the antagonistic effects of the probiotics *Lactobacillus Rhamnosus HN001* and *Florajen 3* against Group B *Streptococci*. *Int J of Probiotics and Prebiotics*. 2012;7(3/4):113-120.

Faa G et al. Factors influencing the development of a personal tailored microbiota in the neonate, with particular emphasis on antibiotic therapy. *J Matern Fetal Neonatal Med*. 2013;26(S2):35.

Ferber SG, Makhoul IR. The effect of skin-to-skin contact (kangaroo care) shortly after birth on the neurobehavioral responses of the term newborn: a randomized, controlled trial. *Pediatrics*. 2004;113:858-865.

Fouhy F et al. High-throughput sequencing reveals the incomplete, short-term recovery of infant gut microbiota following parenteral antibiotic treatment with ampicillin and gentamicin. *Antimicrob Agents Chemother*. 2012;56:5811. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3486619/

Galley J et al. Maternal obesity is associated with alterations in the gut microbiome in toddlers. *PLoS One*. 2014;9(11):e113026. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4237395

Gewolb IH et al. Stool microflora in extremely low birthweight infants. *Arch Dis Child Fetal Neonatal Ed*. 1999;80. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720923/

Groer MW et al. Development of the preterm infant gut microbiome: a research priority. *Microbiome*. 2014;2:38.

References

Guaraldi F, Salvatori G. Effect of breast and formula feeding on gut microbiota shaping in newborns. *Front Cell Infect Microbiol*. 2012;2:94.

Hällström M et al. Effects of mode of delivery and necrotising enterocolitis on the intestinal microflora in preterm infants. *Eur J Clin Microbiol Infect Dis*. 2004;23:463.

Hanson L et al. Feasibility of oral prenatal probiotics against maternal Group B *Streptococcus* vaginal and rectal colonization. J of Obstetric, Gynecologic & Neonatal Nursing. 2014;43(3):294-304. http://onlinelibrary.wiley.com/doi/10.1111/1552-6909.12308/

Harman T, Wakeford A. MICROBIRTH: Revealing the microscopic events during childbirth that could hold the key to the future of humanity. DVD. Alto Films: 2014.

Horta BL, Bahl R, Martinés JC, Victora CG. Evidence on the long-term effects of breastfeeding: systematic reviews and meta-analysis. Geneva: World Health Organization. 2007. http://www.who.int/maternal_child_adolescent/documents/9241595230/en/. Accessed online 10/03/15.

Horvath Marques A et al. The influence of maternal prenatal and early childhood nutrition and maternal prenatal stress on offspring immune system development and neurodevelopmental disorders. *Front Neurosci*. 2013;7:120. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3728489

Hung KJ, Berg O. Early skin-to-skin after cesarean to improve breastfeeding. *MCN, Am J Matern Child Nurs*. 2011;36(5):318-324. http://www.ncbi.nlm.nih.gov/pubmed/21743355

Hviid A, Svanstrom H, Frisch M. Antibiotic use and inflammatory bowel diseases in childhood. *Gut*. 2011;60:49.

Hwang JS, Im CR, Im SH. Immune disorders and its correlation with gut microbiome. *Immune Netw*. 2012;12:129. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3467411/

Hyde MF, Modi N. The long-term effects of birth by caesarean section: the case for a randomized controlled trial. *Early Hum Dev*. 2012;88:942-949.

References

Jakobsson HE et al. Decreased gut microbiota diversity, delayed Bacteroidetes colonization and reduced Th1 responses in infants delivered by caesarean section. *Gut*. 2014;63:559.

Jimenez E et al. Is meconium from healthy newborns actually sterile? *Res Microbiol*. 2008;159:187.

Jimenez E et al. Isolation of commensal bacteria from umbilical cord blood of healthy neonates born by cesarean section. *Curr Microbiol*. 2005;51:270.

Johri AK et al. Group B *Streptococcus*: global incidence and vaccine development. *Nat Rev Microbiol*. 2006;4(12):932-942. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2742968/

Keski-Nisula L et al. Maternal intrapartum antibiotics and decreased vertical transmission of Lactobacillus to neonates during birth. *Acta Paediatr*. 2013;102:480–485.

Khafipour E, Ghia JE. Mode of delivery and inflammatory disorders. *J Immunol Clin Res*. 2013;1:1004.

Kondrashova A, Hyoty H. Role of viruses and other microbes in the pathogenesis of type 1 diabetes. *Int Rev Immunol*. 2014;33(4):284.

Kozyrskyj AL, Bahreinian S, Azad MB. Early life exposures: impact on asthma and allergic disease. *Curr Opin Allergy Clin Immunol*. 2011;11:400.

La Leche League International (LLL). Benefits of breastfeeding. http://www.llli.org/nb/nbbenefits.html. Accessed online 10/04/15.

Lahtinen SJ et al. Prenatal probiotic administration can influence *Bifidobacterium* microbiota development in infants at high risk of allergy. *J Allergy Clin Immunol.* 2009;123:499.

Li M, Wang M, Donovan SM. Early development of the gut microbiome and immune-mediated child disorders. *Semin Reprod Med*. 2014;32:74.

References

Lozupone CA et al. Diversity, stability and resilience of the human gut microbiota. *Nature*. 2012;489:220. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3577372/

Ludington-Hoe SM, Swinth JY. Development aspects of kangaroo care. *Journal of Obstetric, Gynecologic & Neonatal Nursing*. 1996;25:691-703.

Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. *Am J Clin Nutr.* 1999;69:S1035–1045.

Madan JC et al. Gut microbial colonisation in premature neonates predicts neonatal sepsis. *Arch Dis Child Fetal Neonatal Ed*. 2012;97. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3724360/

Martino D, Prescott S. Epigenetics and prenatal influences on asthma and allergic airways disease. *Chest*. 2011;129:640-647.

Mayo Clinic. Group B strep disease. Mayo Clinic website. http://www.mayoclinic.org/diseases-conditions/group-b-strep/basics/definition/con-20033853. Accessed online 12/04/15.

McCall EM et al. Interventions to prevent hypothermia at birth in preterm and/or low birthweight infants. Cochrane Collaboration review:CD004210. 2010. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004210.pub4/abstract

Metsala J et al. Mother's and offspring's use of antibiotics and infant allergy to cow's milk. *Epidemiology*. 2013;24:303.

Moore ER et al. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Collaboration review:CD003519. 2012. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003519.pub3/abstract

Morse NL. Benefits of docosahexaenoic acid, folic acid, vitamin D and iodine on foetal and infant brain development and function following maternal supplementation during pregnancy and lactation. *Nutrients*. 2012;4(7):799-840. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3407995

References

Mueller NT et al. The infant microbiome development: mom matters. *Trends Mol Med*. 2015;21(2):109-117. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4464665

Munyaka PM, Khafipour E, Ghia J-E. External influence of early childhood establishment of gut microbiota and subsequent health implications. *Front Pediatr*. 2014;2:109. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4190989

Nolan A, Lawrence C. A pilot study of a nursing intervention protocol to minimize maternal-infant separation after cesarean birth. *J Obstet Gynecol Neonatal Nurs*. 2009;38(4):430-442.

O'Connor TG et al. Prenatal maternal anxiety predicts reduced adaptive immunity in infants. *Brain Behav Immun*. 2013;32:21-28. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3686987/

Ohlsson A, Shah VS. Intrapartum antibiotics for known maternal Group B streptococcal colonization. Cochrane Collaboration review:CD007467. 2014. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007467.pub4/abstract

Penders J et al. Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics.* 2006;118:511–2110.

Penders J et al. Establishment of the intestinal microbiota and its role for atopic dermatitis in early childhood. *J Allergy Clin Immunol*. 2013;132:601.

Pertea M, Salzberg SL. Between a chicken and a grape: estimating the number of human genes. *Genome Biol*. 2010;11:206. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2898077/

Praveen P et al. The role of breast-feeding in infant immune system: a systems perspective on the intestinal microbiome. *Microbiome*. 2015;3:41. http://www.microbiomejournal.com/content/3/1/41

Radzyminski S. Neurobehavioral functioning and breastfeeding behavior in the newborn. *Journal of Obstetric, Gynecologic & Neonatal Nursing*. 2005;34:335-341.

References

Ravel J et al. Human microbiome science: vision for the future, Bethesda, MD, July 24 to 26, 2013. *Microbiome*. 2014;2:16. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4102747/

Roberts SE et al. Perinatal and early life risk factors for inflammatory bowel disease. *World J Gastroenterol*. 2011;17:743. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3042652/

Rönnqvist PD, Forsgren-Brusk UB, Grahn-Håkansson EE. Lactobacilli in the female genital tract in relation to other genital microbes and vaginal pH. *Acta Obstet Gynecol Scand*. 2006;85(6):726-735. http://www.ncbi.nlm.nih.gov/pubmed/16752267

Romero R et al. The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women. *Microbiome*. 2014; 2:4. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916806

Roth C et al. Folic acid supplements in pregnancy and severe language delay in children. *JAMA*. 2011;306:1566-1573. http://www.ncbi.nlm.nih.gov/pubmed/21990300

Russell SL et al. Early life antibiotic-driven changes in microbiota enhance susceptibility to allergic asthma. *EMBO Rep*. 2012;13(5):440–447. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3343350/

Sakata H, Yoshioka H, Fujita K. Development of the intestinal flora in very low birth weight infants compared to normal full-term newborns. *Eur J Pediatr*. 1985;144.

Satokari R et al. *Bifidobacterium* and *Lactobacillus* DNA in the human placenta. *Lett Appl Microbiol*. 2009;48:8.

Savage DC. Microbial ecology of the gastrointestinal tract. *Annu Rev Microbiol*. 1977;31:107–133.

Schmidt R et al. Maternal periconceptional folic acid intake and risk of autism spectrum disorders and developmental delay in the CHARGE (Childhood Autism Risks from Genetics and Environment) case-control study. *Am J Clin Nutr*. 2012;96:80-89. http://www.ncbi.nlm.nih.gov/pubmed/?term=Maternal+periconceptional+folic+acid+intake+and+risk+of+autism+spectrum+disorders+and+developmental+delay+in+the+CHARGE+%28Childhood+Autism+Risks+from+Genetics+and+Environment%29+case-control+study

References

Schulfer A, Blaser MJ. Risks of antibiotic exposures early in life on the developing microbiome. *PLoS Pathog*. 2015;11(7):e1004903. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4489621

Shaw SY, Blanchard JF, Bernstein CN. Association between the use of antibiotics in the first year of life and pediatric inflammatory bowel disease. *Am J Gastroenterol*. 2010;105:2687.

Sloan M. Unintended consequences: cesarean section, the gut microbiota, and child health. *Science & Sensibility*. 2012 (July 12). http://www.scienceandsensibility.org/unintended-consequences-cesarean-section-the-gut-microbiota-and-child-health/. Accessed online 09/25/15.

Song SJ, Dominquez-Bello MG, Knight R. How delivery mode and feeding can shape the bacterial community in the infant gut. *CMAJ*. 2013;185(5):373-374. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3602250

Stensballe LG et al. Use of antibiotics during pregnancy increases the risk of asthma in early childhood. *J Pediatr*. 2013;162:832.

Stuebe A. The risks of not breastfeeding for mothers and infants. *Rev Obstet Gynecol*. 2009;2:222-231.

Surén P et al. Autism spectrum disorder, ADHD, epilepsy, and cerebral palsy in Norwegian children. *Pediatrics*. 2012;130:e152-e158. http://www.ncbi.nlm.nih.gov/pubmed/22711729

Thavagnaman S et al. A meta-analysis of the association between caesarean section and childhood asthma. *Clin Exp Allergy*. 2008;38:629.

Thompson AL et al. Milk- and solid-feeding practices and daycare attendance are associated with differences in bacterial diversity, predominant communities, and metabolic and immune function of the infant gut microbiome. *Front Cell Infect Microbiol*. 2015;5(3). http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4318912

Torraza RM, Neu J. The altered gut microbiome and necrotizing enterocolitis. *Clin Perinatol*. 2013;40:93.

Trumpff C et al. Mild iodine deficiency in pregnancy in Europe and its consequences for cognitive and psychomotor development of children: a review. *J Trace Elem Med Biol*. 2013;27:174-183.

References

Turnbaugh PJ et al. The human microbiome project. *Nature*. 2007;449:804–810. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3709439/

Villarreal AA et al. Use of broad-spectrum antibiotics and the development of irritable bowel syndrome. *WMJ*. 2012;111:17–20.

Wang TT et al. Cutting edge: 1,25-dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. *J Immunol*. 2004;173:2909-2912.

WebMD. Breastfeeding overview. http://www.webmd.com/parenting/baby/nursing-basics. Accessed online 10/04/15.

Westerbeek EA et al. The intestinal bacterial colonization in preterm infants: a review of the literature. *Clin Nutr*. 2006; 25:361.

Wildner K. Kangaroo Care. *Midwifery Today*. 2012;101. http://www.midwiferytoday.com/articles/kangaroocare2012.asp

Wlodarska M et al. Early life antibiotic-driven changes in microbiota enhance susceptibility to allergic asthma. *EMBO Rep*. 2012;13:440.

World Health Organization (WHO). 10 Facts on breastfeeding. http://www.who.int/features/factfiles/breastfeeding/facts/en/. Accessed online 10/04/15.

World Health Organization (WHO). Short-term effects of breastfeeding: a systematic review on the benefits of breastfeeding on diarrhoea and pneumonia mortality. Geneva: World Health Organization. 2013. http://www.who.int/maternal_child_adolescent/documents/breastfeeding_short_term_effects/en/. Accessed online 10/03/15.

Zárate G, Nader-Macias ME. Influence of probiotic vaginal lactobacilli on in vitro adhesion of urogenital pathogens to vaginal epithelial cells. *Lett Appl Microbiol*. 2006;43(2):174-178. http://www.ncbi.nlm.nih.gov/pubmed/16869901