Caesarian Vs Vaginal Delivery: From A Human Microbiota Perspective

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Abstract:
The route of the birth delivery influences new born’s health. Children born via Cesarean section are at increased risk of developing asthma, systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, immune deficiencies and leukemia. Part of these diseases is believed to be related to maturation of neonatal immune system. During vaginal delivery, the contact with the maternal vaginal and intestinal flora is an important source for the start of the infant's colonisation. During Caesarean delivery, this direct contact is absent, and non-maternally derived environmental bacteria plays an important role for infant's gastro-intestinal colonisation. The primary function of microbial colonisation during the foetal period, intrapartum and after the birth is crucial in maturation and development of new-born immune system. This review supports the choice of the route of birth delivery and consequently favours a decrease in unnecessary Cesarean sections. It is crucial to provide this information to pregnant women and/or couples and health workers to make informed and educated decisions.

Keywords: Human microbiota, Microbial colonization, Immune system

Introduction:
The route of birth delivery influences the newborn's health. Children born via Caesarean section are at an increased risk of developing asthma, systemic connective tissue disorders, juvenile arthritis, immune deficiencies and leukemias. Part of these diseases is believed to be related to the maturation of the neonatal immune system.

Some Studies suggest that the immune system of the newborn is widely stimulated when first exposed to microorganisms during neonatal life, while the type of delivery shapes an infant's microbial communities which consequently plays the role in his/her immune system Maturation. A significant number of Caesarian section delivery are performed for obstetrical indications; some are simply due to maternal request and may incur several risks for the child's health and wellbeing. Well known among these risks are neonatal depression due to general anaesthesia, fetal injury during hysterotomy and/or delivery, increased likelihood of respiratory distress (RD) even at term and breastfeeding complications. Concurrent with the trend of increasing Caesarean deliveries, there has been an epidemic of both autoimmune diseases such as type 1 diabetes, Crohn's disease and multiple sclerosis (MS) and allergic diseases, such as asthma, allergic rhinitis and atopic dermatitis. The interplay between the emerging microbial ecology of the gastrointestinal tract and the developing mucosal immune system serves as a backdrop for a relationship between Caesarean delivery and the emergence of some of these diseases. With the highly immune reactive intestine serving as the largest surface area of the body that is exposed to the environment, especially a vast array of the luminal microbes and antigens, it is intriguing to speculate that the intestinal environmental interaction during early development of the immune system may relate to these diseases.

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One intriguing component of this relates to the early development of the intestinal microbiota, the developing immune system and the early influence of cesarean versus vaginal delivery on these phenomena. The immune system undergoes major development during infancy and is highly related to the microbes that colonise the gastrointestinal tract. It has been suggested that the different initial exposures depend on mode of delivery. The microbes that "seed" the intestine during either Caesarean section or Vaginal delivery may lead to changes in long term colonisation and subsequent altering of the immune development. Here we will provide background about the human microbiota and its relationship to the developing immune system and the relationship of mode of delivery on the colonisation of the infant intestine, development of the immune system and subsequent childhood allergies, asthma and autoimmune diseases.

**The Human Microbiota**

The human body consisting of 100 trillion cells carrying about ten times as many microorganisms in the intestines. It is estimated that these gut floras have around 100 times as many genes in aggregate as there are in the human genome. The metabolic activities performed by these bacteria resemble those of an organ, causing some to liken gut bacteria to the “forgotten” organ. Microorganisms perform a host useful function such as:

1) fermenting unused energy substrates,
2) training the immune system,
3) preventing growth of harmful pathogenic bacteria,
4) regulating the development of the gut, and producing vitamins for the host (such as biotin and vitamin K).

Excitement about the potential of harnessing the intestinal microbiota for therapeutic purposes and health is reflected by the popularity of pro- and prebiotics and even such seemingly esoteric therapies as human fecal transplantation. Not all the species in the gut have been identified because most cannot be cultured, and identification is difficult. An effort to better describe the microflora of the gut and other body locations using newly developed non-culture-based technologies has been initiated and termed the “Human Microbiome Project”. This project has a mission of generating resources enabling comprehensive characterisation of the human microbiota and analysis of its role in human health and disease.

**Intestinal Microbiota of Newborn**

Features of a healthy microflora are its richness and evenness. Richness describes the number of bacterial species in a specific ecosystem not taking into account their relative abundance. Evenness indicates the relative abundance of each species in a specific ecosystem. These two definitions are used to describe the microbial diversity in the gastrointestinal tract. However, the initial colonization of the intestine is also important for future microflora and functions. At birth, the intestine is sterile, and bacterial colonization begins with amniotic membrane rupture. Bacteria from the mother's intestinal and vaginal sites, and from the outer environment, colonize the neonatal gut within a few hours from birth, and appear in feces shortly thereafter. Vaginally born infants have a greater abundance of Bacteroides and Bifido bacteria compared with infants born by cesarean section. Other important factors that contribute to build the microbiome composition are antibiotics, hygiene status and functional nutrients. The latter are increasingly used in infancy. Breastfed infants had 2 times the numbers of Bifido bacteria than formula fed infants, and in the latter, Atopobium and Bacteroides were found in significant counts. Moreover, in formula-fed infants, intestinal microbiota was less complex (or ‘diverse’) than in breastfed. Breastfeeding has been associated with a number of beneficial effects in infants in the short and long term and it is likely that microflora contributes many of these effects. The profile of intestinal bifidobacterial population in infants shows the simultaneous co-occurrence of a number of bifidobacterial species.

**Function of Intestinal Microbiota**

Human microbiota exerts important immune, metabolic, trophic, and protective functions that are currently interpreted with a model of symbiosis between the host and intestinal microbes.
Many of the effects by intestinal microbiota are realized with mechanisms that derive from coevolution of bacteria and in the host. The commensal microflora inhibits colonisation by pathogenic bacteria through a variety of local mechanisms.

It also interacts with the immune system at local and systemic level. The immune system in turn protects the host from potential pathogenicity of microbial communities that provide metabolic benefits. This results in a balanced homeostasis whose histological counterpart is the ‘physiological inflammation’, defined by the presence of a rich immune cell population within the intestine. A key effect of the innate immunity is to confine bacteria into the intestine preventing them from reaching the systemic immune compartment necrotising enterocolitis in preterm neonates. Similar mutually beneficial relationship exists in terms of energy and nutrition supply, between gut microbiota and the host. Bacteria provide the host with energy from indigestible dietary substrates in the form of short-chain fatty acids, whereas the host offers a nutritionally adequate environment to its commensals. A recent clinical trial showed clear associations between gut microbes and nutrient absorption indicating a possible role of microbiota in the regulation of nutrient digestion and energy harvest. Microbiota is an active player in the brain gut axis and affects levels of neurotrophins in mice. This translates in behaviour control, brain differentiation, and neuronal survival.

**Vaginal vs. Cesarean delivery:**

During vaginal delivery the contact with the maternal vaginal and intestinal flora is an important source for the start of the infant's colonisation. During Cesarean delivery, this direct contact is absent, and non-maternally derived environmental bacteria plays an important role for infant's gastro-intestinal colonisation. Some authors have suggested that the composition of the first human microbiota could have long lasting effects on the intestine in breast fed infants. For example, Gronlund, et al showed that the primary gut flora in the infants born by cesarean delivery may be disturbed for up to 6 months after the birth. Another study using culture-based techniques showed that the mode of delivery was associated with differences in the gastrointestinal microbes 7 years after delivery. The clinical relevance of these changes is unknown and even longer follow up is needed to establish how long-lasting these alterations of the primary gastrointestinal flora can be. Nevertheless, there is accumulating evidence that the gastro-intestinal bacteria play an important role in the postnatal development of the immune system. Thus, if the intestinal flora develops differently depending on the mode of delivery, the postnatal development of the immune system might also be different. Available epidemiological data show that the atopic diseases appear more often in infants after Cesarean section than after Vaginal delivery. The composition of enteric microbiota in the early days of life is an important factor for achieving and maintaining good health in the years to come. It follows that it is fundamental to identify more thoroughly the gastrointestinal ecosystem of the newborn.

**Conclusion:**

- Microbial colonisation during the foetal period, intra partum, and after birth is crucial in host-microbial mutualism; the primary function is maturation and development of newborn's immune system. The maternal vaginal microbiota provides newborns with a greater variety of colonising microorganisms, responsible for training and adapting the infant's immune system. Therefore, it is clear that vaginal delivery is ideal and only in the presence of medical indications should a Cesarean section be endeavoured.

- The implications of using this route of birth delivery involve increased foetal, neonatal, and maternal morbidity and mortality. In that sense, this study supports the choice of route of birth delivery and consequently favours a decrease in unnecessary C-sections. It is crucial to provide information to the pregnant women and/or couples and health workers to make informed and educated decisions.
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