

When Humanity is Born by Cesarean At the Dawn of a Paradigm Shift?

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Abstract: In this paper, the question of the long-term impact of cesarean birth on cultures worldwide is investigated. Extensive research is cited to support the concepts put forth.

Keywords: Birth, Cesarean, Paradigm Shift

Today the birth process is still understood in the framework of the dominant cultural conditioning, as the aftermath of thousands of years of interferences through beliefs and rituals. The basis of this deep-rooted conditioning is that a woman does not have the power to give birth by herself. It is the “*helping-supporting-coaching-managing paradigm*.” This paradigm has obviously reached its limits.

Another way to understand the birth process is suddenly emerging, inspired by modern physiology. From this perspective, the birth process is considered an involuntary process, under the control of archaic brain structures. In general, one cannot help an involuntary process. However, it can be disturbed by inhibitory situations easily identified through well-established physiological concepts, such as the concept of adrenaline-oxytocin antagonism and the concept of neocortical inhibition. Within this emerging paradigm the keyword is “*protection*” (of an involuntary process from inhibitory factors): the birth process needs to be *protected* in particular from the effects of language, light, and attention-enhancing situations such as feeling observed or feeling insecure.

As an obstetrician, Michel Odent, MD, developed the maternity unit at Pithiviers hospital in France which he ran with midwives from 1962 to 1985 with excellent results and low intervention rates. He created the Primal Health Research database which brings together research from various fields that intersects with the study of the pre- and perinatal period (www.primalhealthresearch.com). Dr. Odent is a prolific author of many articles and several books which describe the needs of the laboring woman and explore the implications of the primal period on later development and humanity as a whole, such as: *Birth Reborn* (1984), *Primal Health* (1986), *The Caesarean* (2004), *The Scientification of Love* (1999), and *Childbirth and the Future of Homo sapiens* (2013). In 1997, Michel Odent received the Thomas R. Verny Award for Outstanding Contributions to Pre- and Perinatal Psychology and Health.

A paradigm shift is undoubtedly difficult, even utopian. Simple situations that are compatible with an easy and fast birth are culturally unacceptable. Let us take an example: a woman is in labor, with nobody around, apart from one experienced and silent midwife sitting in a corner and knitting. All the components of this simple situation can easily be interpreted in the light of modern physiology, including the response to a repetitive task like knitting. However, one cannot make such a scenario acceptable without flirting with utopia.

One must also keep in mind that the cesarean section has become a fast and easy operation, with an average blood loss that is roughly the same as during a birth by the vaginal route. At the same time, one starts realizing that the negative long-term effects of pharmacological assistance – particularly the use of synthetic oxytocin – have probably been underestimated.

In such an historical context, it is plausible that in the near future the majority of humanity will be born via the surgical abdominal route. All projections of birth statistics since the middle of

the twentieth century have paved the way to this kind of prediction. At such a landmark in the history of our species, we'll pose inevitable questions: Can we learn to routinely compensate for deprivations inherent in the abdominal route of birth? Should we expect an acceleration of human evolution in relation to the modes of birth? Our questions about the future of a humanity born by cesarean are different from the usual questions about individuals currently born that way. Let us use an analogy: we are considering the future of a forest; we are not looking at particular trees.

Until now, experts in human evolution have been exploring the past: the authoritative experts were mostly paleontologists, paleoanthropologists, archaeologists, and geneticists. The dominant paradigm – often called Neo-Darwinism - was limited to the effect of the integration of genetics and Darwinian evolution, after what had been called “the modern synthesis” (Huxley, 1942). Genetic mutation was considered the ultimate source of variation within populations and natural selection was considered the main evolutionary force which could produce adaptation. Evolution of the species was understood as a very slow process, measured by mutation rates. Within this restrictive theoretical framework, there was a lack of curiosity for the possible fast and spectacular transformations of species.

The development of epigenetics - the discipline based on the processes of gene expression – and the emergence of concepts associated with the “microbiome revolution” have induced a new phase in our understanding of evolution and an unprecedented interest in the probable transformations of the genus *Homo* in the near future. Speedy transformations under the effects of environmental factors are well-documented among mammals in general. We know that it does not take a long time for the process of domestication of mammals to modify brain structures and behaviors (Kruska, 1988). For example, after only 120 years of domestication, a brain size reduction of about 20% has been observed in mink (Kruska, 1996). In the age of epigenetics, we are encouraged to pay renewed attention to studies exploring the trans-generational effects of what happens in particular during fetal life and the perinatal period. It now appears that epigenetic markers (the “epigenome”) may be, to a certain extent, transmitted to subsequent generations. Understanding one of the mechanisms through which acquired traits can be transmitted to the following generations is an important step in our understanding of the transformation of species and their adaptation to environmental factors. The epigenetic perspective appears as a landmark in the history of evolutionary biology. It can suddenly help with interpreting mysterious facts. For example, recent studies of the epigenome of Neanderthal and Denisovan make less mysterious the obvious differences between archaic humans and *Homo sapiens* despite very similar DNA sequences (Gokhman et al., 2014).

In such a scientific context, experts in human evolution are offered reasons to look towards the future. They must first realize that the period surrounding birth is the phase of modern life that has been the most dramatically turned upside down during the past decades. They must also realize that this short phase of life is deemed critical in the formation of individuals by a great variety of developing disciplines (such as ethology, epidemiology, hormonology, epigenetics, immunology, and modern bacteriology).

As a point of departure, we suggest looking towards the future within three frameworks: evolution of the encephalization quotient, evolution of the microbiome, and evolution of physiological systems such as the oxytocin system.

The Encephalization Quotient

The encephalization quotient is a measure of relative brain size defined as the ratio between actual brain mass and predicted brain mass for an animal of a given size. The main characteristic of *Homo sapiens* is an extremely high encephalization quotient, compared with all other land and sea mammals. Since our ancestors separated from the other members of the chimpanzee family (about six millions years ago) the size of the brain in the genus *Homo* has been gradually increasing. It is commonplace to claim that the evolutionary process adopted a combination of solutions to make birth possible, up to the time when the birth canal became an “evolutionary bottleneck,” so that the development of the human brain had reached its limits.

With the advent of simplified fast techniques of cesarean sections, this bottleneck has suddenly disappeared. In other words, a tendency towards an increased head circumference can

suddenly be transmitted to the following generations. It is therefore plausible that the average encephalization quotient of *Homo* will increase in the future. Have we reached a landmark in the evolution of brain size?

We must emphasize that it is the development of neocortical structures that is responsible for the gradual increased brain volume throughout the process of evolution of the genus *Homo*. This is an important fact when considering the capacity to give birth. The concept of neocortical inhibition is crucial for interpreting the specifically human difficulties during the birth process as an involuntary process under the control of archaic brain structures.

It is easy to interpret the solution to the evolutionary process found to overcome the human handicap in the perinatal period. One can observe that when a woman can give birth easily without any pharmacological assistance, her neocortical activity is significantly reduced. A laboring woman tends to forget what is happening around her. She tends to forget what she learned and what her plans were. She can behave in a way that usually would be considered unacceptable regarding a civilized woman (e.g. screaming, swearing, being impolite). She can talk nonsense. She can find herself in the most unexpected primitive postures. This obvious reduction of neocortical control makes human birth possible by increasing the similarities between humans and non-human mammals. It implies that a laboring woman needs to be protected against all stimulants of her neocortex (language, light, feeling observed, and attention stimulating situations).

If we anticipate a possible evolution of our species characterized by an increased average encephalization quotient and, therefore, a still more powerful neocortex, we have to raise questions about the future of the capacity to give birth. Will it be more and more difficult to neutralize the effects of neocortical activity during the involuntary process of parturition? In this case, one solution might be to renew the bases of pharmacological assistance by developing drugs that electively reduce neocortical activity. The other more probable solution would be to increase the rates of cesarean sections. Are we at the beginning of a self-perpetuating process, an increased need for c-sections being induced by increased rates of c-sections?

The Microbiome Revolution

The “microbiome revolution” started when bacteriologists could dramatically enlarge their horizons thanks to the power of computer processing and new DNA sequencing technologies. Today, one may present *Homo sapiens* as an ecosystem, with a constant interaction between the trillions of cells that are the products of our genes (the “host”) and the hundreds of trillions of microorganisms that colonize the body (the “microbiome”). The microbiome revolution is at the root of a real rethinking of the immune system, which needs specific stimulations to develop properly. We are in the process of learning that our health and our behavior are highly influenced by our microbiome. The immune functions of the main components of the microbiome (particularly the gut flora and the skin flora) have remained ignored until recently. Today it is acceptable to claim, for example, that our gut flora is about 80% of our immune system.

One can simplify our current knowledge by claiming that to be born is to enter the world of microbes and that the human microbiome is to a great extent established in the perinatal period. This is confirmed by an accumulation of data regarding the gut flora (Gronlund, Lehtonen, Eerola, & Kero, 1999; Palmer, Bik, DiGiulio, Relman, & Brown, 2007), the skin microbiome (Capone, Dowd, Stamatias, & Nikolovski, 2011), the oral microbiome (Lif Holgerson, Harnevik, Hernell, Tanner, & Johansson, 2011), and the milk microbiome (Cabrera-Rubio et al., 2012). The immunological perspective confirms that the perinatal period is critical as an initial phase of interaction between host and microbiome. It can be presented as critical for immune programming (Gronlund, Nuutila et al., 1999; Malloy et al., 2004). For example, a comparative study of 15 infants born vaginally and nine infants born by cesarean section followed up from the age of one week until the age of two years confirmed the reduced Th1 responses among those born by cesarean section. The low levels of Th1-associated chemokines were related to lower total microbiota diversity and particularly to a lower abundance and diversity of the Bacteroidetes phylum (Jakobsson et al., 2013).

In order to introduce these new issues in the framework of a modern lifestyle, we just need to recall that until recently human babies were born in a familiar environment via the bacteriologically rich vagino-perineal zone. The term “familiar” applies to the mother and to the

child since, compared with the placenta of other mammals, the human placenta is highly effective at transferring the maternal IgG to the fetus (Cederqvist, Ewool, & Litwin, 1978; Garty, Ludomirsky, Danon, Peter, & Douglas, 1994; Hashira, Okitsu-Negishi, & Yoshino, 2000).

Today, simplified safe techniques of cesarean sections have suddenly induced radical changes in the way human microbiomes are established. A cesarean birth is associated with a spectacular microbial deprivation in the neonatal period. At a time when the immune system is compared to a sensory organ that needs specific stimulations during critical periods of development, there are reasons to expect significant changes in the comparative prevalence of pathological conditions, even if, later on in life, dietary intake influences the structure and activity of the human microbiome (David et al., 2013).

There are reasons, in particular, to anticipate an increased prevalence of dysregulations of the immune system. The concept of dysregulation of the immune system is first evocative of allergic diseases. It is significant that all studies of atopic diseases and asthma included in the Primal Health Research Database (www.primalhealthresearch.com) provide concordant results with cesarean birth as risk factor (Bager, Wohlfahrt, & Westergaard, 2008; Pistiner, Gold, Abdulkerim, Hoffman, & Celedon, 2008; Roduit et al., 2009; Xu, Pekkanen, Hartikainen, & Jarvelin, 2001).

Interestingly, there are also published studies confirming that the perinatal period should be looked at from immunological-bacteriological perspectives in order to interpret data about risk factors for asthma and allergic diseases. For example, in a double-blind, placebo-controlled study, Finnish researchers randomized 1,223 mothers with infants at high-risk for allergy to receive a probiotic mixture or placebo during the last month of pregnancy and their infants to receive it from birth until age six months. It appeared that perinatal supplementation of probiotic bacteria to high-risk mothers and children conferred protection only to cesarean born children (Kuitunen et al., 2009). In the light of such studies, not only can we claim that a cesarean birth is a risk factor for asthma and allergic diseases, but we also have at our disposal valuable clues for interpreting correlations established by retrospective epidemiological studies and for thinking in terms of cause and effect. Since cesarean born babies are often exposed to antibiotics in the perinatal period, let us mention that pre- and perinatal exposure to antibiotics has been established as an independent risk factor for asthma and allergic diseases and also as risk factor for serious infection in infancy by antibiotic-resistant bacteria (Glasgow et al., 2005; Jedrychowski, Galas, Wyatt, & Perere, 2006; Stensballe, Simonsen, Jensenm, Bonnelykke, & Bisgaard, 2008).

Autoimmune diseases are other common dysregulations of the immune system. The pathogenesis of some of them is probably related to the way the microbiome is established in the perinatal period. There are, in particular, concordant data suggesting that cesarean section is associated with an increased risk of childhood-onset type 1 diabetes (Cardwell et al., 2008; McKinney et al., 1999).

Furthermore, we are also in a position today to offer plausible interpretations for the results of studies according to which cesarean births are risk factors for obesity in childhood and in adulthood (Blustein et al., 2013; Darmasseelane, Hyde, Santhakumaran, Gale, & Modi, 2014; Goldani et al., 2011, Huh, et al., 2012), since alterations of the gut microbiome of obese adults (and of adults with type 2 diabetes) have been clearly demonstrated (Larsen et al., 2010; Turnbaugh et al., 2006). According to a Danish study, individuals with a low microbiota diversity are characterized by more marked overall adiposity, insulin resistance, and dyslipidemia, and also a more pronounced inflammatory phenotype than other individuals (LeChatelier et al., 2013). In general, a low microbiota diversity is pathogenic. We can mention, as an example, the low microbiota diversity of colicky babies (de Weerth, Fuentes, & de Vos, 2013). Let us repeat that low gut microbiota diversity is precisely the main characteristic of cesarean born children (Gronlund, Lehtonen, Eerola, & Kero, 1999).

Not only can our current understanding of the development of the microbiome suggest interpretations to epidemiological studies, but it can also make us aware of radical differences between pre-labor and in-labor cesareans. Studies of the milk microbiome in relation to the way babies are born have detected significant differences according to the timing of the operation (Cabrera-Rutio, Collao, & Laitinen, 2012). Such differences are confirmed by a Canadian study of the gut flora of four-month-old babies (Azad et al., 2013).

The bacteriological studies demonstrating radical differences between pre-labor and in-labor cesareans pave the way to several kinds of interpretations. They underline the complexity of these issues. One way to penetrate this complexity is to reconsider the enduring premise of the sterile womb paradigm. In fact, it is probably simplistic to claim that to be born is to enter the world of microbes. According to recent studies, it appears that most infants might incorporate an initial microbiome before birth (Funkhouser & Bordenstein, 2013). This will probably be confirmed by studies of the placental microbiome (Aagaard et al., 2014).

When referring to recent advances in microbacteriology, the word “revolution” is not too strong. Today all subdisciplines of biology – including evolutionary biology - require microbiology. The microbiome has suddenly appeared important to the evolution of animals and plants. The neologism “hologenome” can help us to adapt to a new understanding of the process of evolution. It refers to a sum of information that may be transmitted from generation to generation. This total genetic information includes the cell’s DNA, the cell’s mitochondria and the microbiome (Brucker & Bordenstein, 2013; Zilber-Rosenberg & Rosenberg, 2008).

These considerations about childbirth from a bacteriological perspective suggest that some aspects of human lifestyles are now changing so quickly that we might live long enough to watch transformations of the genus *Homo* happening before our eyes: all the diseases we have mentioned are already mysteriously more common than some decades ago. The route of birth is one of the factors we should not overlook.

The Oxytocin System

Until recently, childbirth was inevitably associated with an intense activation of the oxytocin system. It will be radically different on the day when the cesarean section is the most common way to give birth. Then, the oxytocin system will offer a typical example of a function that has suddenly become underused. In the age of epigenetics, it is understood that an underused physiological function may grow weaker from generation to generation. We must add that among women who will still give birth via the vaginal route, it is probable that endogenous oxytocin will be replaced by drips of exogenous oxytocin in most cases. Taking into account what we know about the connections between birth physiology and the physiology of lactation, and what we already know about infant feeding in countries with skyrocketing rates of cesareans, we must also add that the average number of milk ejection reflexes per woman will be dramatically reduced. In other words, it is probable that among generations born by cesarean the oxytocin system will also be underused to feed babies.

There are no other examples of vital physiological systems that may become as useless under the effects of changes in lifestyle. We use the term “system” to emphasize that we are referring to the capacity to synthesize oxytocin, to secrete it, to use it as a neuromodulator, to store it in the posterior pituitary gland, to release it in a pulsatile effective way, and to develop receptors. We, therefore, have reasons to anticipate a weakening of this physiological system. This may have far reaching consequences, since oxytocin is involved in all aspects of our reproductive/sexual life, in socialization, and in all facets of the capacity to love. Furthermore, this system has strong connections with other vital physiological systems, such as the system of endorphins, the system of prolactin and the dopamine system. Should we anticipate a super-brainy *Homo* with a reduced ability to give birth, breastfeed, and empathize, and with weakened sexual functions (Odent, 2013; Odent, 2014)? Can a super-brainy *Homo sapiens* be endowed with a strong “emotional intelligence”?

Emerging Questions

At such a crossroad in our history, we are accumulating reasons to phrase emerging questions. The main questions are about the adaptability of human beings regarding new kinds of deprivations in the perinatal period and possible fast transformations of *Homo sapiens* in relation to the modes of birth.

A combination of technical advances have made cesarean births so easy and so safe that we are reaching a time when it is gradually becoming acceptable to offer most pregnant women the option of giving birth that way. In such a context the main discussion points are about the timing of the operation: pre-labor or in-labor cesarean? One must keep in mind the option of “planned in-

labor cesarean section” (Odent, 2004). It simply means that the planned operation is performed as soon as the labor has spontaneously begun. Besides the well-known increased risks of neonatal respiratory problems after pre-labor cesarean, and besides the data provided by the bacteriological perspective, new reasons for contrasting pre-labor and in-labor cesareans have suddenly been provided since the beginning of the current decade by a great variety of emerging scientific disciplines. We must mention, in particular, studies confirming the possible negative effect on the fetus of stress deprivation when the cesarean is performed before the labor starts: it appears that uterine contractions are needed for the mitochondrial uncoupled protein2 (UCP2) expression on hippocampal neurons (Simon-Areces et al., 2012). Such stress deprivation may have long term effects on behavior and personality traits. In order to underline the great variety of perspectives that offer reasons for avoiding pre-labor cesareans, we may also mention the low adiponectin levels in blood cord after pre-labor cesareans. This fact suggests that pre-labor cesarean may carry a risk of obesity independently of other risk factors (Hermansson, Hoppu, & Isolauri, 2014).

Whatever the comparative prevalence of pre-labor and in-labor cesarean sections in the future, there will be reasons to try to minimize the effects of the microbial deprivation experienced by the newborn baby in the case of a cesarean birth. If there is cohabitation between the mother and the father, we can assume that both of them are adapted to the same bacteriological environment: there are, therefore, theoretical reasons to put the newborn baby in the arms of its father as soon as possible while waiting for the mother to be ready. We must also take into consideration preliminary studies confirming the advantages of giving probiotics to the mother at the end of pregnancy and then to the newborn baby (Kuitinen et al., 2009). The “gauze-in-the-vagina technique” also makes sense: immediately after birth, the baby’s skin and mouth are gently swabbed with a gauze pad that had been previously placed in the vagina (Blaser, 2014). To facilitate the “education” of the immune system immediately after birth and to facilitate the Th1 responses among those born by cesarean section, it should be theoretically possible to test the practice of giving BCG (Bacille de Calmette et Guérin) to all babies immediately after a cesarean birth, since the mycobacteria of BCG are potent inducers of Th1-type response (Ota et al., 2002).

While we must lucidly prepare for the plausible scenario of a humanity born by cesarean, we must also prepare for other possible scenarios. We must keep in mind that the root of the problem is a deep-rooted cultural lack of understanding of the basic needs of laboring women that has been dramatically amplified since the middle of the twentieth century. Is it possible, thanks to the power of modern physiology, to reverse thousands of years of cultural conditioning?

References:

- Aagaard, K., Ma, J., Antony, K.M, Ganu, R., Petrosino, J., & Versalovic, J. (2014). The placenta harbors a unique microbiome. *Science Translational Medicine*, 6(237), 237ra65. doi: 10.1126/scitranslmed.3008599.
- Azad, M.B., Konya, T., Maughan, H., Guttman, D.S., Field, C.J., Radha, S., ..., & Kozyrskyj, A.L. (2013). Gut microbiota of healthy Canadian infants: Profiles by mode of delivery and infant diet at 4 months. *Canadian Medical Association Journal*, 185(5). doi: 10.1503/cmaj.121189
- Bager, P., Wohlfahrt, J., & Westergaard, T. (2008). Caesarean delivery and risk of atopy and allergic disease: meta-analyses. *Clinical and Experimental Allergy*, 38(4), 634-642
- Blaser, M. (2014). *Missing microbes*. London: Oneworldbook.
- Blustein, J., Attina, T., Liu, M., Cox, L.M., Blaser, M.J., Trasande, L. (2013). Association of caesarean delivery with child adiposity from age 6 weeks to 15 years. *International Journal of Obesity (London)*, 37(7), 900-906. doi: 10.1038/ijo.2013.49.
- Brucker, R.M., & Bordenstein, S.R. (2013). The capacious hologenome. *Zoology*, 116(5), 260-261. doi: 10.1016/j.zool.2013.08.003
- Cabrera-Rubio, R., Collado, M.C., & Laitinen, K., (2012). The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery. *American Journal of Clinical Nutrition*, 96(3), 544-551. doi: 10.3945/ajcn.112.037382
- Cabrera-Rubio, R., Collado, M.C., Laitinen, K., Salminen, S., Isolauri, E., & Mira, A. (2012). The human milk microbiome changes over lactation and is shaped by maternal weight and mode

- of delivery. *American Journal of Clinical Nutrition*, 96(3), 544-551. doi: 10.3945/ajcn.112.037382.
- Capone, K.A., Dowd, S.E., Stamatias, G.N., & Nikolovski, J. (2011). Diversity of the human skin microbiome early in life. *Journal of Investigative Dermatology*, 131(10) doi: 10.1038/jid.2011.168.
- Cardwell, C.R., Stene, L.C., Joner, G., Clinek, O., Svensson, J., Goldacre, M.J., ..., & Patterson, C.C. (2008). Caesarean section is associated with an increased risk of childhood-onset type 1 diabetes mellitus: A meta-analysis of observational studies. *Diabetologia*, 51(5), 726-735.
- Cederqvist, L.L., Ewold, L.C., & Litwin, S.D. (1978). The effect of fetal age, birth weight, and sex on cord blood immunoglobulin values. *American Journal of Obstetrics and Gynecology*, 131(5), 520-525.
- Darmasseelane, K., Hyde, M.J., Santhakumaran, S., Gale., & Modi, N. (2014). Mode of delivery and offspring body mass index, overweight and obesity in adult life: A systematic review and meta-analysis. *PLOS One*, 9(2), e87896. doi: 10.1371/journal.pone.0087896.
- David, L.A., Maurice, C.F., Carmody, R.N., Gootengerg, D.B., Button, J.E., & Wolfe, B., ..., & Turnbaugh, P.J. (2013). Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, 505(7484). doi: 10.1038/nature12820.
- de Weerth, C., Fuentes, S., & de Vos, W.M. (2013). Crying in infants: On the possible role of intestinal microbiota in the development of colic. *Gut Microbes*, 4(5), 416-421. doi: 10.4161/gmic.26041.
- Funkhouser, L.J., & Bordenstein, S.R. (2013). Mom knows best: The universality of maternal microbial transmission. *PLOS/Biology*, 11(8). e1001631. doi: 10.1371/journal.pbio.1001631.
- Garty, B.Z., Ludomirsky, A., Danon, Y., Peter, J.B., & Douglas, S.D. (1994). Placental transfer of immunoglobulin G subclasses. *Clinical and Diagnostic Laboratory Immunology*, 1(6), 667-669
- Glasgow, T.S., Young, P.C., Wallin, J., Kwok, C., Stoddard, G., Firth, S., ..., & Byington, C.L. (2005). Association of intrapartum antibiotic exposure and late-onset serious bacterial infections in infants. *Pediatrics*, 116(3), 696-702.
- Gokhman, D., Lavi, E., Prufer, K., Fraga, M.F., Riancho, J.A., Kelso, J., ..., & Carmel, L. (2014). *Science* 2, 344(6183), 523-527. <http://dx.doi.org/10.1126/science.1250368>.
- Goldani, H.A., Bettiol, H., Barbieri, M.A., Silva, A.A., Agranonik, M., Morais, M.B., & Goldani, M.Z. (2011). Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study. *American Journal of Clinical Nutrition*, 93(6), 1344-1347. doi: 10.3945/ajcn.110.010033.
- Gronlund, M.M., Lehtonen, O.P., Eerola, E., & Kero, P. (1999). Fecal microflora in healthy infants delivery: Permanent changes in intestinal flora after caesarean delivery. *Journal of Pediatric Gastroenterology and Nutrition* 28(1), 19-25.
- Gronlund, M.M., Nuutila, J., Pelto L, Lilius, E.M., Isolauri, E., Salminen, S., ... & Lehtonen, O.P. (1999). Mode of delivery directs the phagocyte functions of infants for the first 6 months of life. *Clinical Experimental Immunology*, 116(3), 521-526
- Hashira, S., Okitsu-Negishi, S., & Yoshino, K. (2000). Placental transfer of IgG subclasses in a Japanese population. *Pediatrics International*, 42(4), 337-42.
- Hermansson, H., Hoppu, U., & Isolauri, E. (2014). Elective caesarean section is associated with low adiponectin levels in cord blood. *Neonatology*, 105, 172-174. doi:10.1159/000357178
- Huxley, J. (1942). *Evolution: the modern synthesis*. London: Allen & Unwin.
- Huh, S.Y., Rifas-Shiman, S.L., Zera, C.A., Edwards, J.W., Oken, E., Weiss, S.T., & Gillman, M.W. (2012). Delivery by caesarean section and risk of obesity in preschool age children: a prospective cohort study. *Archives of Disease in Childhood*, 97(7), 610-616.
- Jakobsson, H.E., Abrahamsson, T.R., Jenmalm, M.C., Harris, K., Quince, C., Jernberg, C., ... & Andersson, A.F. (2013). Decreased gut microbiota diversity, delayed Bacteroidetes colonisation and reduced Th1 responses in infants delivered by Caesarean section. *GMJ Open Gastroenterology : Gut* doi: 10.1136/gutjnl-2012-303249.
- Jedrychowski, W., Gałaś, A., Whyatt, R., & Perera, F. (2006). The prenatal use of antibiotics and the development of allergic disease in one year old infants: A preliminary study. *International Journal of Occupational Medicine & Environmental Health*, 19(1), 70-76.

- Kruska, D. (1988). Mammalian domestication and its effect on the brain structure and behaviour in *Intelligence and evolutionary biology*, Jerison, H.J. & Jerison, I. (eds), p.211-250. Berlin: Springer-Verlag.
- Kruska, D. (1996). The effect of domestication on brain size and composition in the mink. *Journal of Zoology*, 239, 645-61.
- Kuitunen, M., Kukkonen, K., Juntunen-Backman, K., Korpela, R., Poussa, T., Tuure, T., ..., & Savilahti, E. (2009). Probiotics prevent IgE-associated allergy until age 5 years in cesarean-delivered children but not in the total cohort. *Journal of Allergy & Clinical Immunology*, 123(2), 335-341. doi: 10.1016/j.jaci.2008.11.019
- Larsen, N., Vogensen, F.K., Van der Berg, F.W.J., Nielsen, D.S., Andreasen, A.S., Pedersen, B.K. ..., & Jakobsen, M. (2010). Gut microbiota in Human adults with type 2 diabetes differs from non-diabetic adults. *PLoS One*, 5(2), e9085. doi: 10.1371/journal.pone.0009085.
- Le Chatelier, E., Nielsen, T., Qin, J., Prifti, E., Hildebrand, F., Falony, G., ..., & Tims, S. (2013). Richness of human gut microbiome correlates with metabolic markers. *Nature*, 500(7464), 541-546. doi: 10.1038/nature12506.
- Lif Holgerson, P., Harnevik, L., Hernell, O., Tanner, A.C., & Johansson, I. (2011). Mode of birth delivery affects oral microbiota in infants. *Journal of Dent Res*, 90(10), 1183-8. Doi: 10.1177/0022034511318973.
- McKinney, P.A., Parslow, R., Gurney, K.A., Law, G.R., Bodansky, H.J., & Williams, R. (1999). Perinatal and neonatal determinants of childhood type 1 diabetes. A case-control study in Yorkshire, U.K. *Diabetes Care*, 22(6), 928-932
- Molloy, E.J., O'Neill, A.J., Grantham, J.J., Sheridan-Pereira, M., Fitzpaterick, J.M., Webb, D.W., & Watson, R.W. (2004). Labor Promotes Neonatal Neutrophil Survival and Lipopolysaccharide Responsiveness. *Pediatric Reserves*, 56(1), 99-103.
- Palmer, C, Bik, E.M., DiGiulio, D.B., Relman, D.A., & Brown P.O. (2007). Development of the human infant intestinal microbiota. *PLOS Biology*, 5(7). doi: 10.1371/journal.pbio.0050177.
- Pistiner, M., Gold, D.R., Abdulkerim, H., Hoffman, E., & Celedon, J.C. (2008). Birth by cesarean section, allergic rhinitis, and allergic sensitization among children with a parental history of atopy. *Journal of Allergy & Clinical Immunology*, 122(2), 274-279. doi: 10.1016/j.jaci.2008.05.007.
- Odent, M. (2004). *The Caesarean*. London: Free Association Books.
- Odent, M. (2013). *Childbirth and the future of Homo sapiens*. London: Pinter & Martin.
- Odent, M. (2014). What about the future of *Homo sapiens*? *Human evolution*, 29, 229-230.
- Ota, M.O., Vekemans, J., Schlegel-Haueter, S.E., Fielding, K., Sanneh, M., Kidd, m., ..., & Marchant, A. (2002). Influence of *Mycobacterium bovis* bacillus Calmette-Guérin on antibody and cytokine responses to human neonatal vaccination. *Journal of Immunology*, 168(2), 919-925.
- Roduit, C., Scholtens S., de Jongste, J.C., Wijga, A.H., Gerritsen, J., Postma, D.S., ..., & Smit, H.A. (2009). Asthma at 8 years of age in children born by caesarean section. *Thorax*, 64(2), 107-113. doi: 10.1136/thx.2008.100875.
- Simon-Areces, J., Dietrich, M.O., Hermes, G., Garcia-Segura, L.M., Arevalo M-A, & Horvath, T.L. (2012). Ucp2 Induced by Natural Birth Regulates Neuronal Differentiation of the Hippocampus and Related Adult Behavior. *PLOS ONE*, 7(8), e42911. doi:10.1371/journal.pone.0042911
- Stensballe, L.G., Simonsen, J., Jensenm, M., Bønnelykke, K., & Bisgaard, H. (2008). Use of antibiotics during pregnancy increases the risk of asthma in early childhood. *Journal of Pediatric*, 162(4), 832-838.e3. doi: 10.1016/j.jpeds.2012.09.049.
- Turnbaugh, P.J., Ley, R.E., Mahowald, M.A., Magrini, V., Mardis, E.R., & Gordon, J.I. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*, 444, 1027-1031.
- Xu, B., Pekkanen, J., Hartikainen, A.L., & Järvelin, M.R. (2001). Caesarean section and risk of asthma and allergy in adulthood. *Journal of Allergy & Clinical Immunology*, 107(4), 732-733.
- Zilber-Rosenberg, I., & Rosenberg, E. (2008). Role of microorganisms in the evolution of animals and plants: the hologenome theory of evolution. *FEMS Microbiology Reviews*, 32(5), 723-735. doi: 10.1111/j.1574-6976.2008.00123.x.