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Letter to the Editor

The solved and unsolved mysteries of human life

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DISCLOSURE: **ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.**

INTRODUCTION

A recent book by two well-known, senior Italian Obstetricians/Gynecologists entitled *Le Sorprese e gli arcani della vita prenatale* (Surprises and arcana of prenatal life) provides details about the amazing continuous talk existing between fetus and mother from the earliest stages of embryonic development, through the production by the embryo of specific hormonal and non-hormonal substances which, secreted into the maternal organism, find specific receptors capable to decode such molecular signals. Another little-known phenomenon that may produce advantages for the mother later in her life, is the transfer from the fetus of multipotent stem cells which, migrating through the placenta, allocate themselves into different organs of the mother. These amazing cells may then contribute to partially repair organs and tissues deteriorated because of aging and/or diseases.

The Authors describe in an original way the placenta as a spacecraft capable to carry the fetus – as a passenger – from the maternal womb to an unknown external world, just as the vessel flies the cosmonauts from our planet to the unknown space and planets. Another intriguing similarity they describe is that between the umbilical cord that links the mother to the placenta and therefore to the fetus, and the strings that connect the cosmonaut to its spacecraft.

The Authors stress that the intense interchange of information established through the placenta between the fetus and the mother not only at a local level but through a continuous relation investing all the mother organs, first of all after formation and development of the nervous and sensitive systems of the unborn child.

In the womb, the fetus continuously increases its relationship with the mother learning to recognize her voice and the environment' fragrances, characterized by the personal microbiota, which will be soon recognized by her milk flavor nursed after the birth.

The fetus sensorial perceptions experienced during pre-natal life will remain engraved in the memory of the child for a long period after birth and may be awaken in many different occasions. At this purpose, it is also important to remember how the microbiota differ from each one, representing a familiar patrimony jet present at placenta level.

Fetus development by the first signals

The early development of the human body following the fusion of the oocyte and spermatozoon represents an area of research still ongoing with many still unanswered questions, similar to the situation existing with studies of transmission and translation of memory at the level of the brain. We know only part of all the phenomena by which a single cell becomes an entire human organism. In a similar way, we don't know where our memories are located in the brain: we know that this organ is constituted by some 100 billion cells which continually talk to each other through about tens of thousands of contact points, the synapses.

Fortunately, scientific progress moves at an accelerating pace and has clarified a number of fundamental issues: today we know of the existence of a number of signals the embryo and the fetus send to the mother, starting well before the formation of the placenta. In a similar way it has been discovered that at level of specific parts of brain (i.e., the hippocampus), where memories are allocated for few seconds, there is a continuous production of new cells.

It has been discovered that, as a sort of “thank you” gesture to the mother for the hospitality, the fetus shares with her a number of young stem cells with the potential of ameliorating her future life. In a similar way, the brain, sending various signals to different body organs, acts as the conductor of an orchestra, induces the body, for example, to smile, eat or sleep. Interestingly, the brain and the skin are the first organs organized at the beginning of life.

The embryo starts to communicate with the maternal organism at a very early stage by sending continuous signals, inducing all the changes necessary for its development. The first of these signals is represented by a single peptide, named Pre-Implantation Factor (PIF); it communicates to the mother the presence of a new vital early embryo already at the stage of only four cells. Another early messenger is provided by the secretion of the chorionic gonadotrophin, an indispensable molecule produced by the trophoblast to create the hormonal environment necessary for the development of the fetus.

The embryo is capable to modify the maternal immune reactivity, so that the mother can accept the 50% of the embryonic genome coming from its father.

Finally, by the end of the first trimester the formation of placenta provides all the necessary exchanges between the fetus and the maternal organism (Fig. 1).

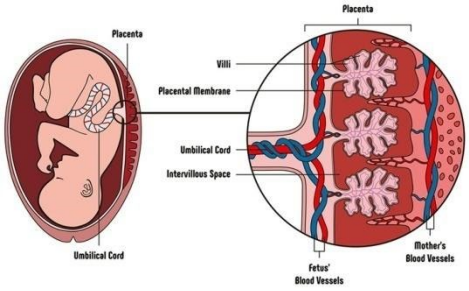

Fig. 1. *Placenta as organ of communication between embryo and the mother.*

The placenta barrier

This unique organ possesses many different functions assuring a continuous supply of oxygen, nutrients and biochemical and hormonal molecules to the embryo. The placenta acts through an exchange of fundamental signals between mother and fetus; as such, it results indispensable to fetal growth and development. Moreover, the placenta acts as a filter for compounds that may damage the fetus, such as environmental contaminants, including toxic heavy metals that, crossing this important barrier, may reach the fetus. Heavy metals, in fact, including lead, arsenic, cadmium and zinc, perfluorinated compounds and hydrocarbons, nitrogen oxides, sulphur dioxide, etc., are ubiquitous environmental air pollutants which, transported by particulate matters (PM2.5 and PM 10), are increasing worldwide because of the excessive industrialization and urbanization. All these and other pollutants, including components of many plastics, can cause Inflammation, oxidative stress and allergic responses. Additionally, these chemicals, acting also as endocrine disruptors and/or a cause of persistent vulnerabilities in immune systems functions, may further affect fetal development.

Moreover, many other complex interactions between genetic and environmental factors exist. These include fetal and parental genetic variations, maternal undernutrition or overnutrition, age, adiposity, cigarette consumption and can play important roles in fetal growth and development. It must be stressed that, although progress has been made in this field, many other different damages due to environmental contaminants have yet to be discovered. Thus, for example, it has to be better understood what happens to the fetal neuro-endocrine axis when the gonadotrophin-releasing hormone and galanin system are affected by maternal exposure to the complex mixture of air and water chemicals. Galanin, in fact, is closely involved in the modulating and inhibition of action potentials in neurons, including sleep regulation, cognition, feeding blood pressure, acting as tropic factor also.

As a consequence, the impaired fetal growth represents one of the greatest public health threats to the present generation of children, as documented by the birth of more than 30 million low-birth-weight infants annually worldwide. The birth of these infants, weighting less than 2500 g, is often associated with an increased risk of multiple diseases in adulthood, including hypertension, obesity, cardiovascular diseases and cancers. Therefore, a clean environment and the right functioning of the placenta barrier result fundamental for a healthy development and growth of the embryo.

The Microbiota functions

An important player in conditioning the fetus' early life is the microbiota that, residing within and outside our body since the beginning of our lives as hosts of the maternal uterus, can be modified by different pollutants (Fig. 2). The term microbiota refers to the estimated 30 trillion microorganisms, including bacteria, viruses and fungi that influence positively many areas of human health, from innate immunity to appetite and energy metabolism, protecting the body from pathogenic microorganisms and producing vitamins, including B, riboflavin, and K needed for blood coagulation. It is with surprise that we learn that the global genes of the microbiota have been estimated to be 100 times the number of genes of human genome!

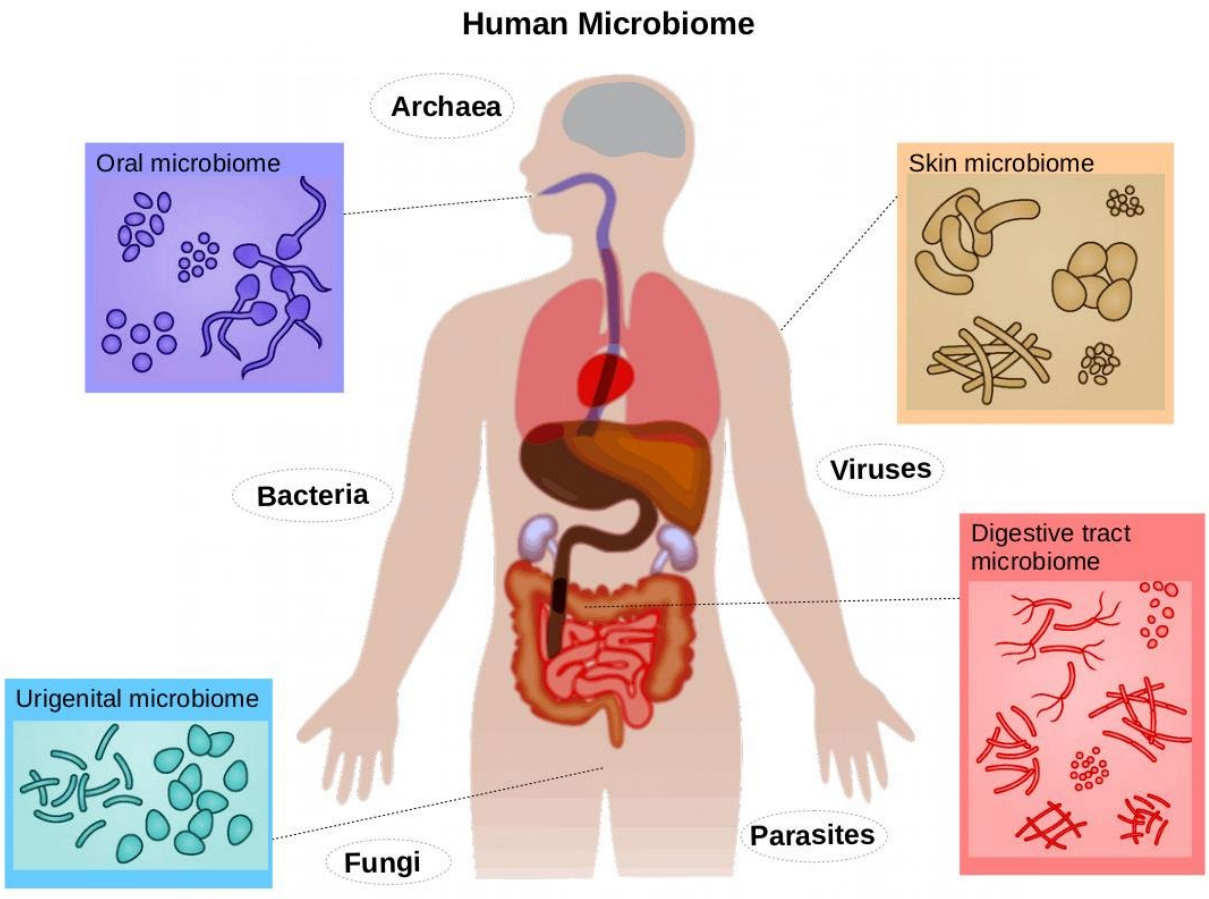

Fig. 2. *The different microorganisms living in various part of human body.*

Thus, thanks also to the microbiota, an extraordinary symbiosis begins that, while helping the fetus, fortifies the maternal organism during pregnancy and for many years after the two symbionts (mother and child) have been separated. As a consequence, the mother's cardiovascular apparatus fortifies, and her target organs, such

as the breast, are protected by the great quantity of estrogens produced and transmitted from the fetus-placenta unit to the mother. One of these molecules, namely the “Tetrol, (15α-OH-estriol)”, in fact, occupying the mother' estrogen-receptors, act as a defensive screen, while the fetal young stem cells are ready to partially regenerate her tissues and organs which in future might receive possible lesions. Thus, the authors show to the reader the benefits fetus offers to the mother as a thanking for the obtained life.

Effects of environmental degradation to human health

As we have seen, humans show the need to communicate with the internal and external environment since their earliest stages of development, when the new human genome begins to structure a new human being. They utilize transcription of molecules that, codified into the DNA, will be transmitted and decoded from the mother's organism. Thus, the environment into which the human embryo develops represents the ideal habitat for the body development pre- and post-birth. Unfortunately, during the last twenty years, air, water and many foods have been contaminated with toxic compounds coming from industrial and car emissions, and from plastic materials, including hormone-disruptors chemicals, found in the oceans by billions of microparticles (Fig. 3).

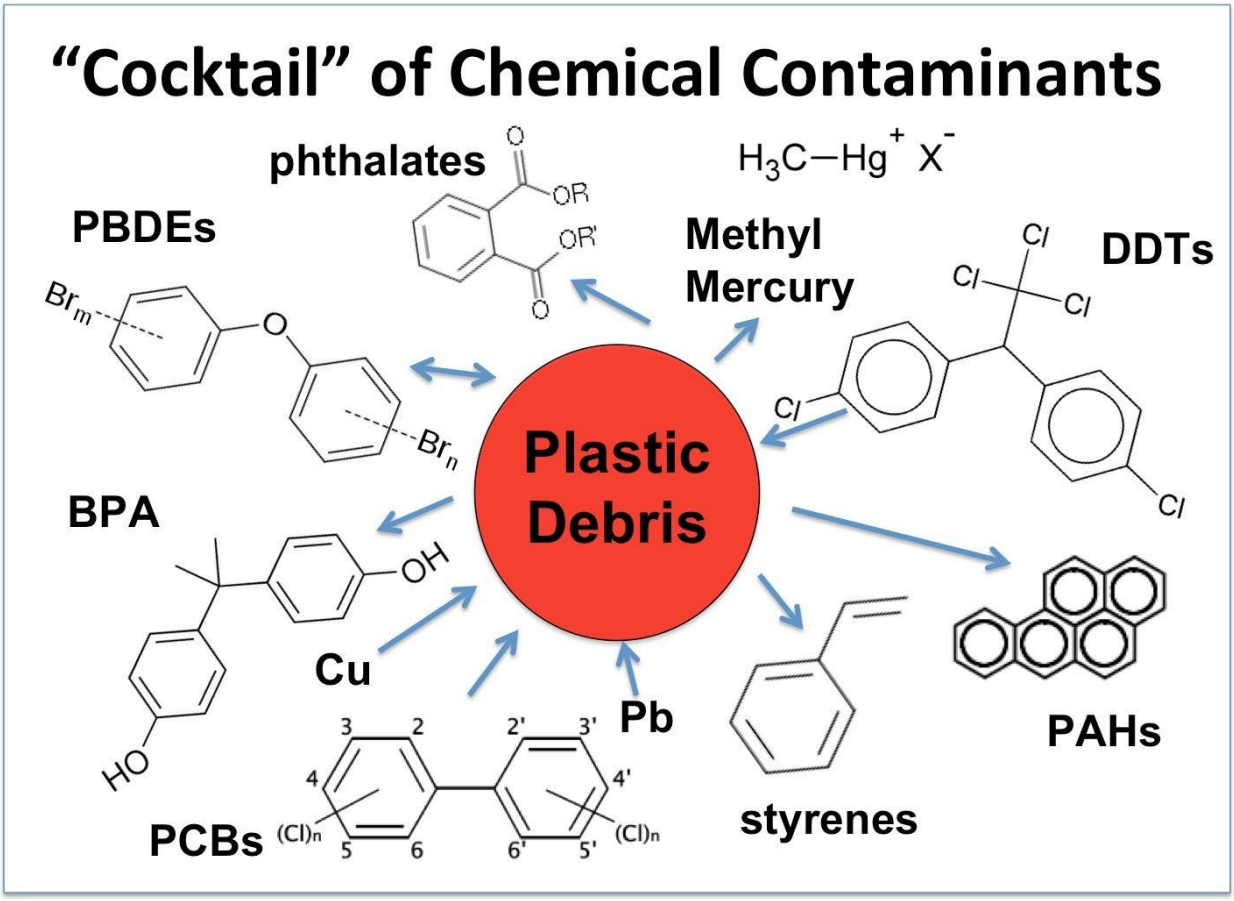

Fig. 3. *Toxic compounds released from microplastics recovered in the oceans.*

As a consequence, exposure to these pollutants have provoked and continue to provoke damages to human organs and systems, including the regulatory function of hormonal systems, the fertility of both women and men, as well as the development of various cancers.

In this connection, the World Health Organization (WHO) has estimated that every year and worldwide 4.2 million individuals die because of the effects of indoor and outdoor pollutants (Fig. 4).

Fig. 4. *The estimate worldwide deaths for the indoor and outdoor pollutants.*

Thus, as suggested from the book' authors, the need to change the way of producing, adopting sustainable technologies and a healthier lifestyle, eating preferably food at low greenhouse gas emissions and packed in biodegradable containers, generating no food waste (Fig. 5). But a sustainable consumption not only involves a reduction in consumption waste, but also a selection of better ways to consume and dispose wastes. In fact, we must remember that 30-50 % of the around 2 billion tons of all food produced on the planet is lost before reaching the human stomach. On the other hand, around one billion people are undernourished and 60% of the soil is degraded, thus augmenting the impact of natural disasters and lowering the productivity of land and marine ecosystems.

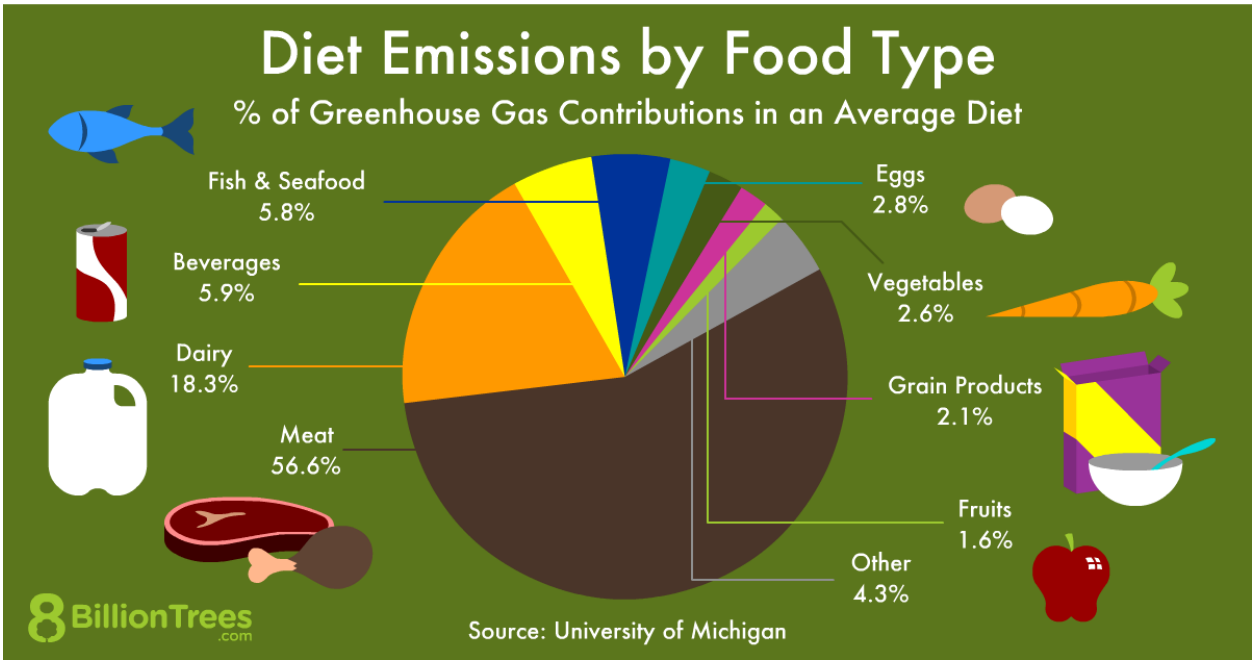

Fig. 5. *Greenhouse gas emission produced from different food.*

Therefore, the present linear economy, based on taken, making and producing waste, has to be urgently changed by the circular economy (CE), based on reducing, reusing, recycling and redesigning the products. CE, in fact, reduces the environmental degradation for its capacity to modulate the natural raw material consumption; it also reduces consumption of water and energy, producing zero waste, as focused on this precious book. At this purpose it has been underlined from the authors how the drastic reduction of natality registered in Italy over many years, has to be attributed to the daily increasing of the environmental pollution. Nevertheless, it is also caused by the shortsightedness of the policy-makers who did not and have not the capacity to develop and follow-up a policy for helping and protecting women and the family by the creation of nurseries and other benefits necessary to allow them to be part of the social and economic community. Thus, on the one hand humans have been sustained by wonderful and clear mechanisms realized and made perfect from nature during billions of years. On the other hand, the same humans continue to create waste and pollution, destroying biodiversity and the environment in which they are living.

CONCLUSIONS

In my opinion, this interesting and unusual book should be in every personal and public library as a precious source to learn the unique processes and mysteries yet to be unfolded about the future of humanity.

In conclusion, reading this book can not only increase awareness in every woman of the important role they have in society as workers and mothers and of the effort they must make to preserve during pregnancy the best pre-natal habitat. Additionally, it might be of great help also for men, enabling them to better understand the fundamental role their wives have in the creation of a new life and also to teach them to show more consideration towards women's role in respect of family and society. Moreover, politicians should pay more attention to make suitable and long-lasting laws, favoring both environment and family. These legislative reforms will give to all women the possibility to work by economic serenity and peace of mind, finally favoring the natality that should be the primary goal of the conjugal life.

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