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# **Review Article**

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# **Placentophagy: a controversial trend**

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# ABSTRACT

This work presents the latest scientific results of research in placenta, highlighting the description of the organ's associated microbiotic, whose possible deleterious effects will be of greater magnitude in a hemomonochorial placental barrier, as is the case in the human species. We want to make solid scientific evidence available to Health Professionals in the delivery and post-delivery care area, so that they may adequately inform their patients that the supposed benefits of the placentophagy are not supported by scientific studies. On the contrary, they are based on misguided popular beliefs spread on social media and untrustworthy maternity/health blogs and internet pages. None of these sources warn mothers about the fact that placentophagy involves a potential risk of exposure of the baby to vertically transmitted infections, risk of the mother developing a thromboembolism due to the estrogen content in the organ, or that the accumulation of heavy metals and/or environmental toxins in the placenta has been reported lately, because, normal prions can be transformed into the infective forms albeit by a mechanism that yet remains unclear. This adds another risk to those previously described. Therefore, it is imperative that Health Professionals warn their patients that placentophagy is not a safe practice and can constitute unnecessary risks for both mother and baby.

Keywords: Amyloidosis and placental prions, Microbiotic, Placentophagy, Placental barrier

# **INTRODUCTION**

# Legal bases for the handing-off of the placenta

The recommendations of the World Health Organization (WHO) on women's reproductive health were ratified by Chalmers et al., whom highlighted the perinatal care that should be applied to mother and child prior to and during the delivery and in the postpartum period.<sup>1</sup> Based on these recommendations, and taking into account the development and growing importance of intercultural health processes, several countries have regulated the legality of the protocol that must be followed for handing-off the placenta to those mothers who request of the Health Services.<sup>2,3</sup>

In this way, a legal modification has been introduced that allows the placenta to not be considered biological waste, and at the same time incorporates a professional procedure for the handing-off of the organ. This Technical Standard implies that the placenta's handingoff to the mother must be carried out within a framework of safe sanitary regulation, both for those who deliver the organ and for those who receive it. Such delivery is also regulated and limited by the following causes of exclusion: women who present a diagnosis of HIV, hepatitis B or C, women who after the delivery - and due to the characteristics of the placenta-a microbiological or histopathological study is indicated, as it is the case of diagnoses of microinfarcts or chorioamnionitis, among others. These legal regulations seek to respect ancestral customs and multiculturalism.<sup>4,5</sup> However, this praiseworthy concern of the authorities for legally accounting for these customs has indirectly favored placentophagy, a practice that consists in ingesting the placenta, applying various methods or preparations. Due to the above, and as members of the scientific community that investigate in placenta, we consider the increase in this practice a concern because it is not based on solid scientific studies.

The first case of placentophagy described in the literature occurred in 1979 in the USA.<sup>6</sup> Since then, it has been increasing in many countries, without being analysed or discussed at scientific level.<sup>7</sup> Consequently, the purpose of this work is to highlight the latest and important advances made in placental research, putting them within the reach of health professional teams that intervene in the delivery of the baby as well as in post-delivery care, so that in this way they can transmit to their patients the risks involved in the practice of placentophagy.

# Scientific basis of studies in placenta

It is worrisome that the supposed maternal benefits associated with human placentophagy suffer from lack of rigorous scientific evidence on which to sustain themselves, and that they are only supported on articles published on social media, blogs and/or unregulated Internet sites.<sup>7</sup> None of these sources of information warn mothers about the potential risk of exposure to infections by vertical transmission to the child. An example of this type of transmission has recently been described by Farr et al., who have reported the case of a newborn who developed recurrent infections with B-streptococcus a situation, according to the Center for Disease Control and Prevention in USA, associated to the ingestion by the mother of capsules prepared from their own placenta, which was infected with this bacterium.8 This study concludes that currently it is imperative that Health Professionals inform their patients that "the benefits of placentophagy are not supported by any scientific evidence."8 Another recent publication warns that the possible risks associated with this practice can be various infections, thromboembolism (due to the amount of estrogen present in the placenta) and/or intoxication due to accumulation of heavy metals and/or environmental toxins.9 Therefore, the author concludes that before making a decision regarding their placentas, women should be fully informed of these risks.

Currently, in a number of countries, the management and destination of the placenta is an increasing practice that is exercised by people from different social strata, belonging or not to indigenous ethnic groups.<sup>7,10</sup> This fact is related to the emergence of the office of "Doulas", which is a person who accompanies the parturient and who also cares about the management of the placenta, either to use it as an offering ritual or as a placental medicine.<sup>11</sup> The latter corresponds to the intake of small frozen pieces of the tissue added to juice-shakes, or

subjecting the organ to desiccation and then encapsulating it as powder. Among the supposed benefits of human placentophagy are the amount of hormones, opioids and minerals that are stored in the organ, which would produce in the mother a reduction in the risk of suffering postpartum depression, reduction of postpartum bleeding, increase in the milk production, etc. However, the only works that scientifically support some of these alleged benefits, are researchs carried out on animals, such as the work of Kristal et al, performed in rats,<sup>12</sup> as well as the work of González-Mariscal et al, carried out in rabbits.<sup>13</sup> To date, there is no scientific evidence from clinical trials in humans, with the exception of Gryder et al, who studied the concentration of iron in the plasma of mothers who consumed placenta capsules versus those who consumed placebo, finding no significant differences between both groups.<sup>14,9</sup>

# Types of placenta and placental barrier

An important point to be considered on this topic is the constitution of the placental barrier involved in the mother/fetus metabolic exchange, this is because the cellular mechanisms involved in the crossing of this barrier depend directly on its structural constitution. In this context, the number and type of epithelial cells that cover the chorionic villi and separate maternal and fetal blood, factors that intervene in the metabolic exchange process, must be kept in mind. Under this perspective, it is important to remember the tragic effect of the use of the Thalidomide analgesic by pregnant mothers from 1958. In 1961 Mc Bride postulated that the use of Thalidomide was possibly the cause of limb malformations observed on babies born to mothers who ingested the analgesic.<sup>15</sup> Subsequently, Somers demonstrated, in a model of pregnant rabbits, that the drug was effectively teratogenic for the embryological formation of the extremities, not affecting pregnant rats equally.<sup>16</sup> The remarkable difference in these results is explained by the different type of placental barrier present in rats and rabbits. Therefore, today the FDA uses different animal models to test the teratogenicity of new drugs, taking into account the different types of placentas they present.

In this regard, it should be noted that the type of placenta depends on the type of implantation of the blastocyst. In the case of mammalian groups such as rodents, lagomorpha, primates and humans, the placenta is hemocorial due to the intrusive type of implantation of both species. This means that the blastocyst is completely introduced into the uterine wall, destroying during the process of implantation the endometrial epithelium, the connective tissue and the endometrial glands and even the endothelium of the maternal blood vessels, thus originating a blood chamber where maternal blood circulates.<sup>17</sup> As an example, in the rat, although the implantation is also intrusive, the placenta is of the hemotrichorial type (three layers of fetal epithelial cells separate the fetal blood from the maternal blood), while

in the rabbit, is is hemodichorial (two layers of fetal epithelial cells).<sup>18</sup> Both cases (rat and rabbit) differ from the term human placental barrier, which has been classified as hemomonochorial, (a single layer of fetal epithelial cells at term).<sup>19</sup> However, herbivorous species such as the cow, have an epitheliochorial placenta, that is, the blastocyst only contacts the endometrial epithelium without entering the endometrium.<sup>17</sup> Feline species like the cat present an endotheliochorial type of placenta where, although the blastocyst is introduced into the uterine wall, it does not destroy the endothelium of the maternal blood vessels.<sup>17</sup> As the human placenta is hemochorial type monochorial subtype, its placental barrier present a thinner constitution, making the vertical infection to which the fetus is exposed, more likely to occur.<sup>20</sup> That is why, considering the different types of placentas existing in mammals in general, it is reasonable to assume that the placentophagy observed in some animals cannot be extrapolated to human placentophagy. By other hand, from a behavioral point of view, some authors have analyzed the placentophagy observed in carnivorous and herbivorous animals, concluding that this action would be related to postpartum behavior tending to keep clean the area of the birth in order to avoid the arrival of predators.<sup>21</sup>

# Placental microbiotic

Numerous investigations in placenta have shown that this organ not only acts as a barrier of metabolic exchange between mother and fetus, but also as a protective barrier for the fetus, preventing the arrival of harmful agents that could affect its normal development. In this way, those pathogens that are effectively stopped by the placental barrier are accumulated in the organ, as is the case with the hepatitis B virus. In those occasions in which the placental barrier fails to stop the pathogen, a vertical transmission of infections occurs. Therefore, it is reasonable to assume that, once the delivery has taken place, the placenta may contain a reservoir of viruses, bacteria and toxic elements, making necessary to advice that postpartum placentophagy is not necessarily beneficial for mothers.

In this line of evidence, during the last three decades, numerous studies have demolished the paradigm that considered the placenta as a niche or sterile compartment, erroneously justified by the absence of clinical infections.<sup>22</sup> Thus. Stout et al., found in the maternal face of human placentas of normal gestation, the presence of gram positive and gram negative bacteria, and in turn Prince et al, demonstrated that there is a placental microbiota that is not always accompanied by visible chorioamnionitis.<sup>23,24</sup> On the other hand, the presence of a placental microbiota that could be a cause of premature birth and was related to the microbiotic existing in the maternal oral cavity has been described.<sup>24</sup> Since the vertical infections caused by this microbiotic are very broad, some acronyms have been coined to encompass them. In this context, the authors Namhias et al, proposed

the acronym To RCH to refer to vertical or intrauterine congenital infections (Toxoplasma Gondii, Rubella virus, Cytomegalovirus, Herpes simplex virus).<sup>25</sup> In this acronym, which is still used to date, parvovirus B19 and Treponema Pallidu were not considered.<sup>26,27</sup> Another interesting and broader acronym to quote is CHEAPTORCHES, which was proposed by Ford-Jones and Kellner in, to include other pathogens.<sup>28</sup> In turn, during delivery and the passage of the fetus through the maternal vaginal canal, it is exposed to cross contamination by the presence of maternal blood (hepatitis B, HIV) or body fluids, sexually transmitted diseases (Neisseria gonorrhoeae and Chlamydia trachomatis), or normal flora of the urogenital tract (Candida albicans), situations that, if diagnosed opportunely, are treated efficiently by the Healthcare team.<sup>29</sup> Recent studies agree on the importance of taking into consideration the human vaginal microbiotic or set of microorganisms that are normally located in it.<sup>30,31</sup>

Taking into consideration the studies described in the previous paragraphs, we consider it worrisome that some mothers arrive at the time of delivery without having previously attended medical check-ups during their pregnancy (echography, ultrasound, etc.).

On the other hand, we consider relevant to mention in this work some other relevant placental studies, such as cytomegalovirus (CMV) that infects the the extravellositary trophoblast (EVT). These are placental cells that emerge from the anchor villi and migrate to reshape the maternal blood vessels (spiral arteries).<sup>32</sup> CMV replicates in the EVT and then invades both the chorionic exchange villi and the basal decidual or the maternal face of the placenta.<sup>33</sup> There are also other examples in which the placenta acts as a real barrier to viral infection, such as the Herpes simplex virus (HSV)-1 which is retained by the placental barrier at the syncytiotrophoblast level, resulting in the placenta being infected by the virus.<sup>34</sup> In turn, Bose et al, demonstrated that the human placenta is the extrahepatic site of replication of the hepatitis E virus (HEV), a virus that has an incubation period of 2-10 weeks.35

## Amyloidosis and prions

In another line of evidence, preeclampsia (PE) a pathology of pregnancy, produces hypertension and proteinuria in the mother, and would develop as a result of poor placentation.<sup>36</sup> Currently, new lines of research relate PE to placenta, for example the study of Buhimschi et al., who linked PE with the presence in both the placenta and the maternal urine of amyloid deposits, this is, misfolded proteins produced as a consequence of stress of the endoplasmic reticulum in the cells of the placental trophoblast.<sup>37</sup> In addition, Cheng et al, correlated the structural similarity of the placental amyloid deposits with the amyloid deposits observed in neurons of Alzheimer's patients.<sup>38</sup> On the other hand, Bosco et al, demonstrated that this amyloid was presented

both in placentas of women with PE and in placentas of women with intrauterine growth retardation.<sup>39</sup> It remains to be dilucidated if the accumulation in the placenta of these deposits of amyloid can cause some problem in the baby or the mother as a consequence of the placentophagy, so we estimate that it is a point that deserves a deep reflection.

It is also important to mention the work of Donadio et al. and Alfaidy et al. who demonstrated that the cellular normal prion protein (PrPc) is expressed in the plasma membrane of both the cvtotrophoblast and the human placenta syncytiotrophoblast, considering that this protein with alpha configuration is susceptible to proteolysis.<sup>40,41</sup> In turn, the authors Kubosaki et al, described the presence of PrPc in the placenta and brain of sheep which, due to mechanisms not yet well defined, although probably related to oxidative stress, can change its alpha configuration to an abnormal beta isoform (PrPSc) that is resistant to proteolysis and therefore insoluble and precipitating.<sup>42,43</sup> PrPc is a non-infecting prion protein that binds copper and would protect against oxidative stress, which Hwang et al showed increased in placentas of women with PE.44 The name prion (Proteinaceous Infectious) was applied for the first time to neurodegenerative diseases such as Creutzfeldt-Jakob disease in humans.<sup>45</sup> It should be noted that once PrPc changes to its PrPSc isoform, it acquires an infecting capacity by itself and transforms all the normal PrPc of the cell into infective PrPSc isoforms, which, being resistant to proteolysis, will accumulate forming amyloid plaques that produce vacuolization and cell death.<sup>45</sup>

Aguzzi et al, demonstrated in ovine animals that the infecting prions enter orally and cross the intestine, then travel with the blood cells first infecting the lymphatic organs, without major clinical manifestations, then leaving this system and infecting the brain.<sup>46,47</sup> The brain incubation period can vary between 2-10 years.<sup>47</sup> Since it is not clearly known how a normal prion protein is transformed into an infective prion, and taking into consideration the expression of PrPc in the human placenta, we believe that placentophagy carries a potential risk that should be avoided as it could result in an infection that can pass through the intestine of the mother, and then infects the baby through breastfeeding. The presence of amyloidosis in the placenta, as well as PrPc, led the authors Bosco and Díaz to postulate the possible existence of a parallelism between the mechanisms that lead to amyloidosis both in the placenta as in neurodegenerative diseases.<sup>37,39,48,44</sup>

## Heavy metals and environmental toxics

Finally, it is important to note that in the placenta, added to the presence of pathogens, the organ can also accumulate heavy metals such as selenium, cadmium, mercury and lead, whose accumulation has been shown to be due to the consumption of contaminated fish or exposure of the mother to environmental toxins.<sup>49,50</sup> In

these circumstances, placentophagy could favor the deleterious effect due to the presence of heavy metals, both in the mother and in the baby.

## CONCLUSION

The purpose of our work has been to scientifically document the Healthcare team about the risks of placentophagy. Animal placentophagy can not be extrapolated to humans given the structural differences of placental barriers. Infections without chorioamnionitis are not detectable by macroscopic analysis of the placenta. Scientific evidence shows that the placentophagy is not innocuous and that it can be accompanied by absorption of heavy metals accumulated in the placenta.

Also, it must be taking into account the presence of normal prions in the organ, which by a mechanism still unknown, could be transformed into infecting prions, which may affect mother and child. Finally, this work does not object those other ancestral customs related to placental rituals.

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