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### Short Communication

# Placenta-'The Least Understood Human Organ'-From Animistic Origins to Human Placental Project

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### Abstract

Background: Despite its importance, the structure and function of the placenta remains poorly understood.

Objective: To describe the progress of theories regarding structure and function of the placenta from ancient to modern times

Design/Methods: Review of literature regarding history of the placenta.

**Results:** In ancient times, virtually all recorded concepts of the placenta described it as animistic or possessing mind or spirit. For example, the ancient Egyptians believed that the placenta contains part of the child's soul, which will only emerge if treated well. The Royal Placenta used to be carried in ceremonial procession as a standard before the Pharaoh. Each Pharaoh had an official "Opener of the King's Placenta".

The transition from animistic to functionality began with the Greeks. Diogenes of Apollonia (480 BC) is credited with the idea that the placenta is an organ of fetal nutrition. Hippocrates (460-370 B.C.) believed that fetus 'sucks nutrition from 'uterine paps'. Aristotle (384-322 BC) was the first to postulate delivery of nutrition through the umbilical cord.

The Renaissance marked the beginning of rapid progress in understanding the structure and function of the placenta. J.C. Arantius (1530-1589) was the first to describe separate maternal-fetal circulation in dissected specimens. In the following century, John Mayow (1643-1679) proposed that the placenta was the respiratory organ of the fetus and shifted the concept of the placenta from HeparUterinumto PulmoUterinus.

The 19<sup>th</sup> century witnessed a fast growth in understanding the structure of the placenta. William Hunter was the first to give a sophisticated description of the structure of the placenta. Biscoff (1842) made many contributions to the understanding of placental barrier. Charles Sedwig Minot (1891) published a detailed description of the placentas of different species.

In the 20<sup>th</sup> century, the placenta was recognized for the first time as an endocrine organ and the new focus became the transfer of solutes across the placenta. Despite this journey of evolving understanding of the complexities of the placenta, significant knowledge gaps remain in understanding placental functions. The Human Placental Project sponsored by National Institute of Health (NIH) described eloquently the need for continuing research in this field. "The Placenta is the least understood human organ and arguably one of the most important...The Human Placental Project, would make substantial inroads".

**Conclusions:** Our understanding of the human placenta has progressed from an animistic tissue to a multi-functional fetal organ. The NIH's Human Placental Project should continue to improve our knowledge of this mysterious "least understood organ".

### **INTRODUCTION**

In spite of its importance, the placenta has been subject to almost pure conjecture in the course of human history until the Renaissance. Since then, good progress has been made in understanding the structure and function of placenta, but it is still considered as the least understood human organ and arguably one of the more important, not only for the health of a woman and her fetus during pregnancy, but also for the lifelong health of both. This perspective article will review six currents of thoughts about the understanding of placenta in the following chronology.

## Animistic concepts of primitive man and the ancient Egyptians

The placenta had a good deal of animistic significance in

the mind of primitive man [1]. Ploss and Bartels found that the most striking thing about placenta was the almost universal concept of this organ as a sort of alter ego, being the symbol of preservation of good fortune or talisman in case of danger. The Old Testament has an animistic Egyptian conception of placenta as the container of king's soul (first book of Samuel XXV:29) [1-3]. The ancient Egyptians believed that the placenta contains part of child's soul and will come out only if treated well [1-4]. This belief gained significance when the royal placenta was carried as a symbol before the Pharaon, a practice that continued to the time of the Ptolemies (ca. 325-45 B.C) [1,3].A sculpture on an Egyptian ceremonial slate from Hierakonpolis depicts a Pharaoh, in what appears to be a ceremonial procession, preceded by five attendants, one of whom is bearing a standard interpreted

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as representing the Royal placenta with umbilical cord – the Pharaoh's "soul" or "secret helper" (Seligman and Murray, 1911) [5] (Figure 1).

### The Hippocratic theories of fetal nutrition

Man's first recorded utterances tending toward a rational interpretation were those of Diogenes of Apollonia (480 B.C.), a little known physician from Ionia. He was the first man to hold the theory that the placenta is the organ of fetal nutrition. Many of the philosphers of that era, and the Hippocratic School also agreed to the concept that the placenta is an organ for fetal nutrition. During that time, they believed that the fetus feeds and respires by 'sucking' nourishment and 'Pneuma' through what they called "uterine paps" or the cotyledons of the decidua formed by subepithelial cells of the uterine lining during pregnancy [1].

### The Aristotelian theories

Aristotle (384-322 B.C) argued against the prevalent Hippocratic theories of uterine paps by citing the fact that the fetus is enclosed in membranes which would prevent this method of intra-uterine nursing. He postulated that the embryo takes form from the menstrual blood and concluded that maternal and fetal circulations are in direct connection.

Nonetheless, he did much to establish the science of the study of fetal membranes. In his great embryological treatise De generatione animalium [On the generation of animals] (circa 340 B.C.E.), Aristotle stated that "The [umbilical] vessels join on the uterus like the roots of plants and through them the embryo receives its nourishment.

### The Arantian theory of heparuterinum

Renaissance represented the age of historical and cultural transition between classical and modern scientific paradigms. Scholars in every field approached their subjects in a new way, without being conditioned from any authorities and Medieval dogmas. This resulted in the development of modern theories both regarding the Universe and Mankind.J.C Arantius (Aranzi) (1530-1589) introduced an extremely important idea. This was his 'a priori conception of the placenta as the hepar uterinum, i.e., the placenta functioned for the fetus in hemopoiesis and blood 'purification' [1,3]. Although future researchers proved this idea to be exaggerated, it was the first positive theory of



**Figure 1** The Royal Placenta: Four standard bearers carrying two falcon standards, a dog, wolf or jackal standard and 'The Royal Placenta'.

the dynamics of placental function. He was the first to make an emphatic statement, based on actual dissection, that the fetal and maternal circulations are separate1.Girolamo Fabrizio [Fabricius ab Aquapendente] (1533-1619), of Padua, who wrote at length on embryology, attacked Arantius (Aranzi) for questioning the Galenic doctrine regarding the confluent fetal and maternal vascular channels. Because Fabricius mistook the cotyledon crypts of the sheep placenta as the opening of blood vessels, which match equivalent openings in the uterine caruncles, he concluded that there must be vascular continuity, so that the fetal vessels were "plugged into" those of the mother. Pointing out this mistake, however, should not lead the reader to discount his many contributions to comparative embryology and placentology [3].

William Harvey (1578-1657) made a shrewd speculation that 'the fetus at term can live in the uterus without air, yet die at delivery on compression of umbilical cord, if it does not breathe'. This reasoning about fetal respiration by William Harvey helped later workers to fruitful researches in this filed [1]. In regards to the placental circulation, Harvey stated, "the Extremities of the Umbilical vessels, are no way conjoined to the Uterine vessels by an Anastomosis; nor do extract blood from them ..." [3]. By logic based on his knowledge of the circulation, he held the maternal and fetal circulations to be separate, each following in an opposite direction to the placenta by way of the arteries and returning by the veins. Harvey postulated that substances absorbed by the umbilical cord stimulated organ development, while the fetus received its main nourishment from the amniotic fluid. Following Arantius (Aranzi), he also referred to the placenta as the hepar uterinum [uterine liver] and mamma uterina [uterine breasts]. It was not until a decade later that Marcello Malpighi (1628-1694) first described the capillary bed connecting arteries and veins, and made possible an understanding of the anatomical basis of regional circulation [6]. Lacking this knowledge, Harvey could not understand completely certain details of the circulatory system in either the adult or the fetus. Jean Claude DeLa Courveé (1615-1664), a contemporary of Harvey's and one of the first adherents to Harvey's De generatione... (1651), gave considerable insight into the role of the placenta in fetal nutrition.

### The Mayowian theory of pulmo uterinus

A young physician in 'The Invisible College' at Oxford, John Mayow (1643-1679) argued that the uterus is 'naturally adapted for separating aerial particles from the arterial blood' [1]. He therefore decided in favor of the opinion that the placenta is the respiratory organ of the fetus and proposed the replacement of Arantius' concept of the placenta as the hepar uterinum by that of the pulmo uterinus. Armed with these conclusions, he refuted the belief of intra-uterine lung respiration in the fetus [5].

### The modern theories

The period of Enlightenment was dominated by two brothers, John (1728-1792) and William Hunter (1718-1783) in England. William Hunter was the first to give a sophisticated description of the structure of human placenta. His brother, John Hunter, showed that decidua was a product of uterine mucosa [6]. Biscoff (1842) made many contributions to the understanding of the placental barrier. Charles Sedwig Minot (1852-1914) published a document entitled "A theory of the Structure of Placenta". It appeared in 1891. He showed the difference between the structures of placenta between difference species. The transfer of solutes across the placenta and its recognition as an endocrine organ is being studied since 1900s. Throughout fetal development, the placenta functions both as a unique agent of human symbiosis and as the fetal renal, respiratory, hepatic, gastrointestinal, endocrine, and immune systems [7]. Yet, our understanding of the human placenta is woefully limited. Past studies of the human placenta have focused largely on the organ after delivery. To fully understand the placenta and how it works, we need to be able to study it during pregnancy, while it's still doing its job. Given modern approaches and technologies and the ability to develop new methods, The Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institute of Health has recently proposed a coordinated 'Human Placenta Project', with the ultimate goal of understanding human placental structure, development, and function in real time [7]. A common theme of this project is the quest for real-time evaluation of the human placenta, and for cutting edge technologies that can be developed, deployed, assessed, and optimized in order to address the biological and pathological challenges in placental implantation, morphogenesis, differentiation, metabolism, maternal-fetal signaling, transport, pharmacology, immunology and the placenta's role in parturition [8].

### **CONCLUSIONS**

The Renaissance represents the age of historical and cultural transition between classical and modern scientific paradigms. This new culture led to deep progress in medical knowledge, including understanding of the structure and function of the placenta. But the placenta still remains the least understood human organ. By increasing understanding of the placenta and the ability to prevent and treat placental abnormalities, we could improve not only pregnancy outcome but the lifelong health of the child and the mother. The Human Placenta Project should have an historic impact on research and on the health of all who ever have been or will be attached to a human placenta.

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