

# Mythology and rational explanation in the history of medicine The case of molar pregnancy

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## Overview

**Objective:** To analyse own set of molar pregnancies and to develop clinically relevant procedures.

**Type of study:** Historical article based on the analysis of Greek classic medicine.

**Settings:** History of Medicine Unit; Department of Medico-Surgical Sciences and Biotechnologies; Sapienza-University of Rome, Italy; Unit of Medical Humanities; Department of Cardiac, Thoracic, Vascular Sciences and Public Health; University of Padua, Italy.

**Introduction:** Molar pregnancy is a specific kind of gestational trophoblastic disease which originates from the placenta. There are two types of molar pregnancy, complete and partial. Complete molar pregnancy derives from a defect in maternal eggs, while an incomplete one derives from a defecting fertilization by paternal sperm.

**Historical analysis:** Molar pregnancy drawn the attention of ancient physicians from the classic period and they widely discussed maternal and paternal roles in causing this condition. Classic doctors drawn from mythology several suggestions and ideas, which indicates that the issue of normal and abnormal conception was a crucial problem since the most ancient past

**Conclusion:** Current scientific studies on molar pregnancy are free from ancient prejudices about male and female “nature” and their reciprocal role in embryogenesis. However, an awareness of the cultural biases that could drive scientific researches, might be useful for scientists and physicians even today.

## Keywords:

molar pregnancy – Hippocrates – Aristotle – Galen – Greek mythology

## INTRODUCTION

Hydatidiform mole, also known as molar pregnancy, is a specific kind of gestational trophoblastic disease (GTD) which originates from the placenta. GTD includes also invasive mole, choriocarcinoma, and placenta site trophoblastic tumor [13]. It is usually benign, but in some cases, it became malignant and invasive. The epidemiology of molar pregnancy and, in

general, of gestational trophoblastic diseases, is not totally understood because of different methodological problems [8, 13, 15]. Estimates from studies in Western countries have shown an incidence of molar pregnancy ranging from 0.57 to 1.1 per 1000 pregnancies, whereas studies performed in Asia suggest a higher incidence of about 2.0 per 1000 pregnancies [13]. Data from South America and Africa are limited and sparse, making impossible a correct evaluation [15].

There are two types of molar pregnancy, complete and partial, which are different for morphological, cytological and genetic features [1, 17, 18]. The complete molar pregnancy has no identifiable embryonic tissue, even if there are some exceptions [9]. Since the late 1970's, it was established that it is an "androgenic" conception, because its genome is entirely paternal in origin [10]. It is probably caused by an abnormal gametogenesis in woman [8], because it forms when a single or two sperms combine with an egg in which the DNA is either inactive or absent [13]. The partial molar pregnancy presents identifiable fetal or embryonic tissue. It is probably caused by an abnormal fertilization [8], because it forms when an apparently normal egg is fertilized by two sperm [13]. Even in this case there might be exceptions, because some partial moles are found diploid with biparental origin [3]. The molecular mechanisms underlying both these conditions are still poorly understood [3].

Although the epidemiological data are limited, it seems quite clear that molar pregnancy has a significant incidence in the population. Moreover, new infertility techniques, such as ovary hyperstimulation and intracytoplasmic sperm injection, could rarely result in that condition [14, 16]. Finally, recent advancements in epigenetics open new questions about the possible role of germline imprinting in causing the familial hydatidiform molar pregnancy [3].

## THE MOLAR PREGNANCY IN THE CLASSIC MEDICINE

By simplifying an otherwise still poorly understood question, it can be stated that, at the current state of our knowledge, complete molar pregnancy derives from a defect in maternal eggs, while an incomplete one derives from a defecting fertilization by paternal sperm. It might be of interest, therefore, to note that molar pregnancy drawn the attention of ancient physicians from the classic period and that they widely discussed maternal and paternal roles in causing this condition. Moreover, as we will see in the following discussion, classic doctors drawn from mythology several suggestions and ideas, which indicates that the issue of normal and abnormal conception was a crucial problem since the most ancient past.

Hydatidiform mole (HM) was first described in the Hippocratic treatise *De morbis mulierum* (*On Diseases of Women*), and more in particular in the third part of that book, named *De sterilibus* (*On Sterile Women*) [12] (Littré 1839-1861, vol. 8, pp. 446–449). The author used the term *μύλης* (*múles*), which etymologically derives from "grindstone" and metaphorically was used, in anatomy, for terms designating "hard" parts, such as molar tooth and rotula. Similarly, a mole was understood as a hard-fleshy production of a "false" pregnancy [2]. At the same time, there might be at work an implicit analogy between mole-grindstone and gestation. The first was used for making flour, from which bread was produced, while the second was often viewed, in classic literature and medicine, as a process analogous to bread-making. In other terms, the female womb was like a furnace where the embryo was created by cooking male and female "semen". In classic medicine, in fact, it was believed that female's ovaries were analogous to male's testes, and that also them produced a semen involved in the creation of the embryo. Galen (c. 130-210 AD), on whom we will return below, in his famous *De usu partium* (*On the Usefulness of the Parts*), stated: "Male's semen is nourished and concocted since the beginning [of gestation] by the female one" [4]. In this sense, a mole was metaphorically analogous to a hard-over-cooked piece of bread.

In the Hippocratic *De sterilibus* there is the following description: "... when abundant menstruations receive a not very abundant and weak semen, a false production is generated. The womb is full as the woman is pregnant, but nothing moves and the breasts, even if turgid,

*do not produce milk. This condition could last two and often three years. If there is just one flesh, the woman died .... If there are more fleshes, from the genital organs it comes an abundant and fleshy ejection of blood. If the ejection is moderate, the woman survives, in the opposite case the woman died because of a metrorrhagia” [12].* For curing this condition, the Hippocratic author suggested a warm vaginal purge for helping the expulsion of the mole.

As clearly indicated in that passage, the “cause” of molar pregnancy was the quality and quantity of male semen. An opposite view was advanced by Aristotle (384-322 BC), who, as well known, other than being one of the most important philosophers of the antiquity, was also the father of “biology” – even if this term has a modern origin. Then, his view was “translated” into medicine by Galen who, with Hippocrates, is traditionally considered the father of Western medicine. In his *De Generatione Animalium (On the Generation of Animals)*, Aristotle observed that a “*fleshy mass called mole*” could be produced in those women who were defective in the necessary warmth for a proper concoction of the embryo. Because of that, “*The nature is able neither to accomplish nor to terminate the generative process. [...] The missed concoction is the cause of the hardness [of the mole]*” [6]. Aristotle supported the view of a radical disparity between male and female in terms of “perfection”. In other terms, the female gender was an imperfect or even degenerated form of male. This model was accepted by Galen, who, in his *De usu partium*, stated that “*Female is less perfect than male for a simple, principal reason: she is more cold than male*” [4]. Accordingly, the cause of molar pregnancy could be nothing but a defect in women’s contribution to the process of gestation. In the same book, Galen mentioned the “mole” as an “*inactive and unformed flesh*” and attributed all kinds of defects in the embryo to a woman failure: “*... when an affection to the fetus arrives ... it is because something wrong happens in the woman, and she is no more able to give fetus enough blood, and consequently the order of nature’s works is confused and perturbed*” [4].

As mentioned, the debate around the role of male and female in the generation has an extremely old tradition in Greek mythology [19]. From an ancient phase in which gods generated without sexual intercourse (*sine congressione*), Greeks moved to embryogenesis with sexual intercourse (*cum congressione*), passing through an intermediate phase testified by the myth of Deucalion and Pyrrha. The ancient myths of the ectopic pregnancy of Zeus (who generated Dionysus in his thigh) and the delivery *sine congressione* of Gaea (who generated Uranus, the Ourea, and Pontus without intercourse), testify that Greek males considered women as even belonging to a different species than men [11]. This model surely influenced Aristotle, who, in turn, inspired Galen. Probably it represented the crucial cultural background for the conception according to which male and female each owned their own seeds, as the medical sources testify [7]. Interestingly, the myth of Deucalion and Pyrrha, survived after Zeus’s flood, tells that they re-generated mankind separately. They both thrown stones behind their shoulders: those thrown by Deucalion became males, while those thrown by Pyrrha became females [5]. It was natural, therefore, that the following debate around the mole was influenced by this entrenched cultural tradition of separation and disparity between sexes.

Interestingly, these classic ideas returned in the modern period, when several authors discussed the hydatidiform mole maintaining the polarities male-female, coldness-warmness in attributing the cause of its formation [5]. Only in the 19th century, thanks to advancements in cytology and genetics, as seen in the introductory paragraph of this paper, hydatidiform mole started to be properly understood and its different forms distinguished.

## CONCLUSIONS

Rather than being forms of knowledge separated from their specific historical and cultural contexts, science and medicine are always deeply interconnected with the so-called *zeitgeist* (“spirit of the time”). Current scientific studies on molar pregnancy are, of course, completely free from ancient prejudices about male and female “nature” and their reciprocal role in embryogenesis. However, a deep awareness, based on a sound historical knowledge, of the cultural biases that could drive scientific researches, might be extremely useful for scientists and

physicians even today.

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