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The "Hidden Genetic Cause" of Mules Natural Sterility: A Fascinating Biological Dialogue between Aristotle and Ibn Sina as Outlined in "The Book of Animals"

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Abstract
This study aims to provide a comparative perspective on "The Book of Animals", contrasting Aristotle's original text with Ibn Sina's version – which serves as a commentary on Aristotle's work, while introducing pivotal insights and theories of Ibn Sina's own. It further examines the phenomenon of mule natural sterility – a subject that embarrassed thinkers in the past – and explores how early philosophers and scientists who addressed it through exposition and diligent interpretation. The term "hidden cause" originated with Ibn Sina in his great book, "The Book of Animals", when he examined the ideas and theories of Aristotle and others regarding the causes of mule sterility. Unconvinced by the explanations put forward by these scholars and philosophers, he coined this term – thereby immortalizing his name in the history of human science- as modern scientific discoveries have conclusively confirmed his insight. The person who came closest to a correct scientific understanding and explanation of this phenomenon was the Greek philosopher Democritus, who claimed that the cause of the sterility of mules is a defect in the structure of their wombs, resulting from their being born of non-homogeneous parents. This expression carries, in its profound implications, a meaning that is quintessentially genetic. The main cause of the sterility of mules and hinnies is probably related to failure of pairing of homologous chromosomes at meiosis during spermatogenesis. To understand why mules can't reproduce, we must first look at chromosomes. Horses boast 64 chromosomes while donkeys have 62. When these two species mate, their offspring—the mule—ends up with an unusual count of 63 chromosomes: 32 from the mare and 31 from the jack. This mismatch creates chaos during meiosis—the process that produces sperm and eggs. There are two types of male and female sterility; primary type affects germ cell causing arrest of germ cell development, and secondary infertility occurs as a result of systemic or syndromes' genetic defects, including developmental, endocrine, and metabolic defects. Mules these wonderful hybrids, which were born from a male donkey and a female horse, often impress them because of their strength and vitality, but despite this, they are always sterile and this sterility is rooted in their genetic structure.

Keywords: Mule Sterility, Aristotle, Ibn Sina, The Book of Animals, The Hidden Cause (Genetic Cause), Germ Cell, Spermatogenesis

1. Introduction

Mule natural sterility is one of the most significant lessons in the fields of biology and genetics; our generation learned this lesson in its modern form and grasped the genetic cause underlying this unique phenomenon. Yet, we were unaware that philosophers and scientists had addressed this very phenomenon as early as the fourth century BC-foremost among them, the "First Teacher," Aristotle. In this era-distant in time and profound in primordial knowledge – Aristotle brought together various branches of philosophy and the biological sciences, classifying them alongside logic.

It is a historical certainty that Aristotle wrote more on the natural history than on any other subject. He wrote three books on animals, "History or characteristics of Animal, "The Organs of Animals, and "On the Being of Animals [1].

Aristotle stated that: “Democritus claimed that the cause of the sterility of mules is a defect in the structure of their wombs, resulting from their being born of non-homogeneous parents. But if that were the case, then the offspring that is generated from a dog and a Wolf, as well as from a Fox and a dog, and similar pairings, would not reproduce either”. On the other hand, Empedocles claimed that the reason for sterility of the mules is the excessive softness of the both female and male semen resulting in that they do not unite in a way that allows the sold organs, as well as organs possessing depth to be formed through a strong union [2].

Aristotle revealed that, the most common cause of sterility of mules is that the mare produces very little semen and has little surplus blood. The amount of semen that is generated in her is hot; therefore, the mare's womb is not eager to attract and retain the semen, and she often expels the semen and passes it out in her urine. As for the jenny (she-ass), she possesses more seed and surplus matter than the mare, and she does not become sexually excited or aroused except when the weather gets hot, and does not give birth in cold regions. Her conception requires one of two things: either similarity of species or a balancing of the temperament of the both semen. In presenting these ideas, Ibn Sina was not entirely convinced by any of the proposed reasons for mule sterility; he articulated his critique of Aristotle’s ideas precisely, stating: “This is the entirety of what Aristotle said, and it is a conjectural view, and in such matters, there is no way except conjectural reasoning. It is likely that there is another “hidden cause” [3].

This “hidden cause”, deduced by Ibn Sina was none other than the genetic factor – a discovery made by his descendants nearly ten centuries later, thereby validating his prediction, the soundness of his reasoning, and his scientific intuition. How did this come about?

To understand why mules can’t reproduce, we must first look at chromosomes. Horses boast 64 chromosomes while donkeys have 62. When these two species mates, their offspring—the mule—ends up with an unusual count of 63 chromosomes: 32 from the mare and 31 from the jack. This mismatch creates chaos during meiosis—the process that produces sperm and eggs.

Modern scientific data in explaining the hidden cause of the sterility of mules indicated that Mules (*Equus mulus)* and hinnies (*Equus hinnus*) are the sterile hybrid offspring that result from the mating of donkeys (*Equus asinus*) to horses (*Equus caballus*) [4].

The main cause of the sterility of mules and hinnies is probably related to failure of pairing of homologous chromosomes at meiosis during spermatogenesis [5].

More advanced studied on karyotypes of fertile mules and hinnies have demonstrated indirectly that the arrangement of their chromosomes differs from that of horses and donkeys [6, 7].

Jung, etal, 2014 revealed that the deleted in azoospermia-like (DAZL) protein is localized to the cytoplasm of spermatogonia and primary spermatocytes in stallion testis [8].

Mules these wonderful hybrids, which were born from a male donkey and a female horse, often impress them because of their strength and vitality, but despite this, they are always sterile and this sterility is rooted in their genetic structure.

There are two types of male and female sterility; primary type affects germ cell causing arrest of germ cell development. This type includes premature ovarian failure (POF), polycystic ovary syndrome (PCOS) and endometriosis. Primary male sterility obstructs spermatogenesis and is associated with abnormal semen. Secondary infertility occurs as a result of systemic or syndromes’ genetic defects, including developmental, endocrine, and metabolic defects.

Genetic syndromes that manifest male or female infertility are fragile X syndrome, Kartagener's syndrome, myotonic dystrophy, Noonan syndrome, Fanconi anemia, sickle cell anemia, β-thalassemia, etc. [9-11].

2. Material of the Article

A Literal Translation of the Sixteenth Treatise of Ibn Sina’s “The Book of Animals: pages, 408-412
Title: Issues of infertility, sterility, masculinity, and femininity

Many animals mate with each other when the male and female are of the same species, or two closely related species, provided that their gestation periods are the same or similar, such as dogs and wolves, or horses and donkeys. In human infertility and sterility may be caused by the semen of either partner, also, it may be caused by the womb in women with masculine tendencies, whose womb is not suited to conception. As for men, the causes are varied, including, male organ (penis) may not be sufficiently vigorous (not abundant) in maintaining erection or the penis may be too large, becoming obstructed by the hymen so that the semen does not flow properly. Additionally, among men there are who are effeminate (**tending towards femininity**), whose semen is thin and poor in quality; if some of this semen gently thrown on the surface of the water, it would float and disperse, and would not sink as mature semen does. On the other hand, among women there are who are masculine and do not incline toward sexual intercourse.

In general, the cause of infertility and sterility is either related to the temperament **(genotype)*** of both male and female semen, or to the reproductive organs. Regarding semen, it may be of very poor quality overall or perhaps according to the (**genetic compatibility**) between male and female semen. As for the reproductive organs, the womb may have a bad/poor constitution (abnormal formation or anatomy), or its openings may be obstructed, or it may have disrupted the sperm supply for a temperamental (**genetic**) or mechanical (**organic**) reason. It may be inferred that the semen itself, or a spirit of it, or something that complements it, comes from the brain (**pituitary gland**) and passes through the region of the eyes during ejaculation: they are drawn inward, as though the brain were draining itself during ejaculation. When an organ is depleted, its effect and harm extended to what is connected with it. Something is also driven from the heart (as though the brain and heart react together during ejaculation; evidence for this is some of the symptoms accompanying ejaculation from the contraction of the psyche (arrhythmia), as though the heart moves toward the driving force which is (**the brain**).

Democritus claimed that the cause of the sterility of mules is a defect in the structure of their wombs, resulting from their being born of non-homogeneous (**heterozygotes**) parents. But if that were the case, then the offspring that is generated from a dog and a Wolf, as well as from a Fox and a dog, and similar pairings, would not reproduce either. Empedocles claimed that the reason for it (i.e., the sterility of the mules) is the excessive softness of the both female and male semen resulting in that they do not unite in a way that allows the sold organs, as well as organs possessing depth to be formed through a strong union.

Thus, what is generated from them becomes defective and diseased (**weak or malformed embryos**) because the firm proper coherence is lacking. This also applies to donkey semen and mare semen, but the reason for it (**i.e., mule sterility)** is something else, which we shall now mention- a not as a definitive/universal (**absolute**) cause, but as one that occurs in most cases.

He (**Aristotle**) said: The most common (**predominant**) cause of this is that the mare produces very little semen and has little surplus blood. The amount of semen that is generated in her is hot; therefore, the mare's womb is not eager to attract and retain the semen, and she often expels the semen and passes it out in her urine. As for the jenny (she-ass), she possesses more seed and surplus matter than the mare , and she does not become sexually excited or aroused except when the weather gets hot, and does not give birth in cold regions. Her conception requires one of two things: either similarity of species (**the same species**), or a balancing of the temperament (**genotype**) of the both semen. Thus, donkeys conceive from donkeys because of similarity of species, and she-asses conceive get from stallions because of the strength of the semen. Likewise, mares conceive from stallions because of similarity of species, and mares conceive from donkeys because the semen of each balances the other. For you find the mare's semen more abundant in heat than the donkey's semen, while the donkey's semen is more moderate than that of mare, and this moderation is suitable for generation (**fertilization**).

As for other animal species, they mate, and their temperaments (**genotypes**) are close to one another. There is no disparity between their semen as there is in the semen of the mule and the donkey. So nothing departs from the initial balance (**the zygote cell**) in a divergent way (**meaning complete genetic uniformity in the zygote cell**), because this deviation only occurs between species that are opposing and unbalanced in their composition (**genetic constitution**). As for those animals that are similar, the mean and resulting compositions (**embryos**) are closely related to both ends (**parents**). Therefore, when a mare becomes pregnant by a stallion and then a donkey mounts her, it corrupts her semen due to its coldness after conception. But if a stallion mounts her, it does not corrupt it, because it increases its heat, and heat is safer and more suitable for temperament (**genotype**) than coldness; for inclination toward cold is worse than inclination toward heat.

⁎ (The words in brackets are the author's explanations and elicitation regarding specific hidden meanings in Ibn Sina's text).

Ibn Sina's Commentary on Aristotelian text:
<u>"This is the entirety of what Aristotle said, and it is a conjectural view, and in such matters, there is no way except conjectural reasoning. It is likely that there is another "hidden cause".</u>

(This conclusion by Ibn Sina means that through his scientific intuition he was certain there was a "hidden cause" of the sterility of mule, and he was not entirely convinced by what Aristotle had said. Modern science has proven the correctness of Ibn Sina's prediction about this "hidden cause", and this perplexing "hidden cause" was nothing other than the "genetic cause", which was hidden in his distant era and is no longer so today).

After nearly a thousand years, humanity discovered the "hidden cause" with perfect clarity, and here it is: The main cause of the sterility of mules and hinnies is probably related to failure of pairing of homologous chromosomes at meiosis during spermatogenesis and oogenesis due to meiotic block.

Then Ibn Sina concluded his unique manuscript with these words: "The sixteenth article of the eighth art (The Book of Animals) of the Natural Sciences section of "al-Shifaa" has been completed, thanks to the praise of Allah and His good favor".

3. Interpretation and Discussion

3.1-A Brief Comparative Overview Between the Original Aristotelian and Ibn Sina's Versions of "The Book of Animals"

It is a historical certainty that Aristotle wrote more on the natural history than on any other subject. In addition to being considered the founder of logic, he is certainly the founder of biology, having studied more than five hundred animal species comprehensively, examining their characteristics, features, physiology, growth, reproduction, and environment. In his immense research journey, he read the works of earlier scholars such as Homer, Democritus, and Plato, and drew much knowledge from the invasions of Alexander the Great's campaign. Indeed, Aristotle even wrote to him constantly, tasking him with gathering scientific information about local animals in different countries for study and comparison [1].

Aristotle wrote three books on animals, which are: the first is "History or characteristics of Animal, consisting of ten articles "treatises" (Histoir des Animaux), the second is "The Organs of Animals, consisting of four articles (Les Parties des Animaux), and the third is, "On the Being of Animals, consisting of five articles (De is Generation des Animaux).

The Arab knew all these books by their names, based on Ptolemy, one of the three important sources for listing Aristotle's works [12].

The Arabs translated Aristotle's books under the title "The Book of Animals", noting that it comprises nineteen treatises. Once translated into Arabic, the work became a source for scholars; Al-jahiz, Al-Kindi, Al-farabi, Ibn Rushd and Ibn Sina all drew upon it and benefited from its contents. At the beginning of his exposition of the book, Ibn Sina stated: "Let's now talk about the animal, following- throughout this entire book- the example of the First Teacher" [1].

Ibn Sina placed great value on direct observation- much like Aristotle – and records his personal observations regarding the exotic birds and animals he encountered in Juzjan, Khorasan, and Transoxiana, noting the differences between the animals of the West and the East. He relies heavily on Aristotle's records corroborating them with new observations or, at times, refining and revising them [13].

It is worth noting that Ibn Sina closely links biology to the natural sciences, subjecting it to the concepts of form and matter and applying to it the laws of change and motion, as well as the theory of the hot, cold and moist, dry qualities; for him, biology is intimately connected to psychology, and both are components of natural philosophy.

The soul is the principle of life and motion in both animals and humans. Since Ibn Sina was a physician before he was a biologist, his medical expertise played a significant role in his biological studies; indeed, his "Book of Animals" contains sections that lean more toward medicine than biology. Humans receive greater converge than other animals. Moreover, the treatment of the human reproductive system and embryology is more extensive than that of other species [14].

Ibn Sina fully embraces the concept of teleology, holding that the parts of a living organism work in concert to achieve its greatest benefit. He perceives a precision and ingenuity in nature – perceptible to those with the sensibility to appreciate them – demonstrating that nothing is creating in vain; indeed, the living world abounds with wondrous sings that attest to the majesty and greatness of God – Blessed be God, the best of Creators [15].

Every living being – indeed, every one of its organs – possesses a function/benefit, even if that function is sometimes not immediately apparent to us. Ibn Sina strives to uncover and document these function, aligning in this regard with Aristotle, who asserts that "there is beauty in nature no less than in timeless works of art." [16].

3.2 Ibn Sina's Version of "The Book of Animals"

This version constitutes the eighth and final section of the natural philosophy components of "The Book of Healing" (al-Shifaa). It is the largest section – surpassing even the section of on metaphysics, which represents one of the four main divisions of the entire work. "Book of Animals" comprises nineteen treatises, each containing one or more chapters; the longest is the thirteenth treatise, which includes fifteen chapters. In terms of both form and subject matter, the two versions – Aristotle's and Ibn Sina's – share similarities, particularly regarding their lack of systematic organization and the presence of scattered repetitions. Indeed, Aristotle's biological writings themselves lacked coherence and suffered from a lack of focus, because he did not finalize it, and it was not free from the intervention of some of his students in certain parts.

In terms of form, Ibn Sina paid close attention to organization and structure; he would either write his research himself or dictates it to his devoted student, Al-Juzjani. It is notable that he addresses specific topics across multiple sections of the book rather than attempting to provide a comprehensive treatment of any given animal group in a single, continuous passage.

Substantively, Ibn Sina's work is fundamentally grounded in Aristotle's three relevant treatises – a debt he openly acknowledges. Consistent with this, his student Al-Juzjani attests that Ibn Sina modeled his book on Aristotle's book while incorporating additional material. It would be a mistake, however, to view Ibn Sina's book merely as a commentary or set of annotations on Aristotle's text; rather, it is an independent study, uniquely crafted by Ibn Sina himself.

Ibn Sina's book centers largely on five main topics: comparative zoology, anatomy, physiology, reproduction and embryology. In the twelfth, thirteenth, and fourteenth treatises, he relied primarily on Aristotle's works "The Nature of Animals" and "The Parts of Animals"; at the same time, however, he drew upon his own medical experience and made extensive use of Galen's anatomical research. He devoted as much attention to physiology as he did to anatomy, viewing it as the manifestation of God's mystery in creation and the key to understanding the reasons for existence. Ibn Sina identified three principal – or vital – organs that serve as the sources of faculties essential for the survival of the individual and the species: the heart, representing the source of the vital faculty (life force); the brain, representing the source of the faculties of sensation and movement; and the liver, representing the source of the nutritive faculty. Each of these faculties has a "servant" organ: the servants of the heart are the lungs and arteries; the servants of the brain are the organs of nutrition and the nerves; the servants of the liver are the stomach and the veins. With this insightful explanation, Ibn Sina corrected Aristotle's error of limiting the brain's function to cooling the heart through the secretion of phlegm, which prevents the temperature from rising [17,18].

Finally, Ibn Sina devotes a chapter to addressing the disagreement between philosophers and physicians regarding the origin of blood: while Plato and Aristotle held that it originates in the heart, physicians maintained that it originates in the liver. Ibn Sina aligns with the philosopher's view that the heart is the origin of blood. However, he rejects the position of held by the Peripatetics

(Aristotle's disciples) – that the heart is the seat of psychic faculties – and instead sides with the physicians, who asserted that the brain is the source of these faculties

3.3 The Genetic & Physiological Aspects of Mule's Sterility

Horses and donkeys differ phenotypically and karyotypically, although they can interbreed freely. Hybridization between different mammalian species has been reported to occasionally occur in nature (e.g., sheep × goat, tiger × lion, dog × wolf, Horse x donkey, etc.) producing a hybrid offspring which is usually sterile [19].

There are many different equine hybrid combinations, such as those crossbred between Przewalski (Equus prezwalskii, 2n = 66) and domestic horses (E. caballus, 2n = 64), wild (e.g., E. hemionus; 2n = 54) and domestic (E. asinus; 2n = 62) asses, and between various subspecies of zebras. Mules (jack ass × mare, 2n = 63) are the most common equine hybrids from E. caballus, (2n = 64) and E. asinus, (2n = 62) [20].

In **Figure 1**, hinnies (horse stallion × jenny, 2n = 63) seem to be much less common and diffused as in fact, when natural breeding between a horse stallion and a jenny occurs, significantly lower conception rates are achieved [21].

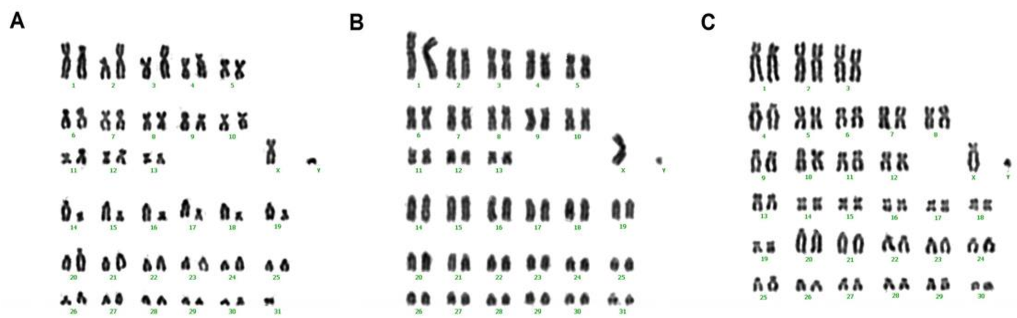


Figure 1. Hinny karyotype (A) compared with that of the stallion (B) and the Jack donkey (C). The number of chromosomes = 63 (XY), 2n = 64 (XY), and 2n = 62 (XY) in the hinny, stallion (B) and Jack donkey, respectively.

The effect of hybridization on an organism is variable. Particular traits may either be determined by one parent, be intermediate between the parental traits, be inferior to the traits of both parents, or be superior to both. Regarding morphological traits, mules inherit the best from both parents: they are stronger, carry more weight than horses of the same size, and have the sure-footedness of the donkey [22]. These characteristics made mules important as working animals for agriculture and during the First World War [23]. Today, mules are once again valued, and donkeys and mules continue to have a positive impact in developing countries; their economic value stems from work, transportation, packing, and tourism [20].

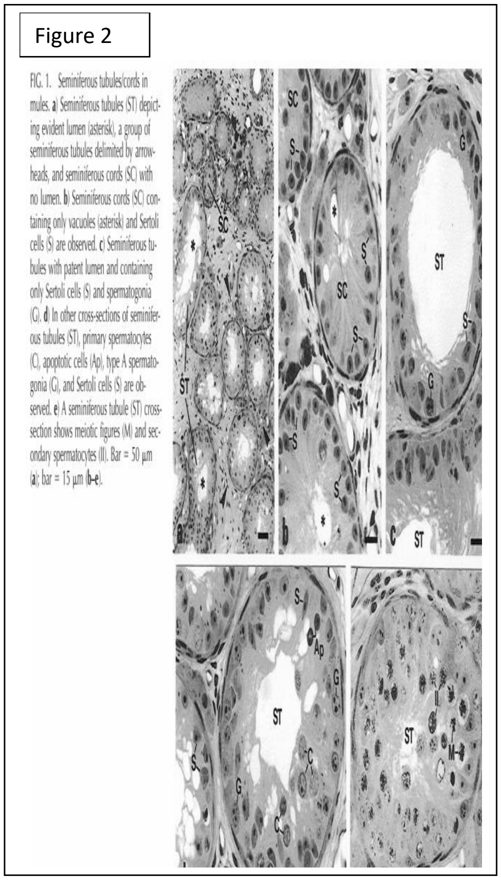
Most mules (female horse×male donkey) and hinnies (female donkey×male horse) are sterile with few reports of equine fertile hybrids.

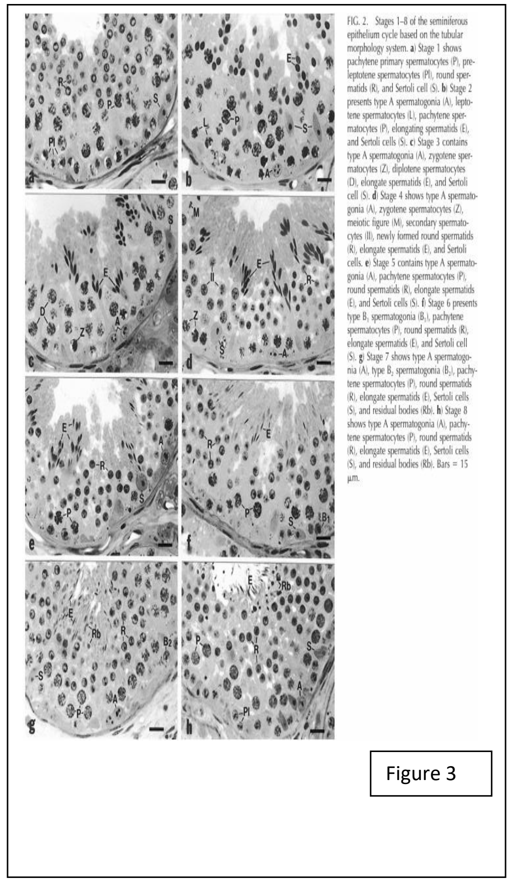
The main cause of the sterility of mules and hinnies is probably related to failure of pairing of homologous chromosomes at meiosis during spermatogenesis and oogenesis due to meiotic block. The mule (Equus mulus mulus) is a sterile hybrid domestic animal that results from the breeding of a male donkey (Equus asinus) to a female horse (Equus caballus). Usually, spermatogenesis in mules does not advance beyond spermatocytes. **Figure 2**. shows histological evaluation of the seminiferous tubules in mules. Due to the smaller testis size, lower seminiferous tubule volume density, and fewer germ cells, the total length of seminiferous tubules in mules was significantly smaller than in donkeys., the percentage of seminiferous tubules containing germ cells (spermatogonia and spermatocytes) in mules was approximately 95%

Figure 3, represents histological evaluation of the seminiferous tubules in donkeys, the total number of Sertoli cells per testis observed in donkeys and mules was very similar. However, the total number of Leydig cells in mules was approximately 70% lower than in donkeys. At least in part, this difference was probably related to the lower number of germ cells present in mule seminiferous tubules. The results found for mules suggest that the mechanisms involved in the determination of testis structure and function are probably originated from donkeys. Also, the data found for mules suggest that their seminiferous tubules are able to sustain complete spermatogenesis. In this regard, this species is a potential model for transplants of germ cells originated from donkeys and horses or other large animals [24].

Variety in hybrid sterility and the gradual progression to fertility can also be taken as a complement to the theory of how species have been formed. Hybridization is also a matter of cross wise gene flow, and if hybrid sterility is not as absolute as people usually think, and that a few individuals among hybrids can produce germ cells to cause the appearance of new types or new species, it will not be so difficult to understand how a progressive advance to fertility can be achieved [25].

In **figure 4**, the developmental features of the testes and histological analysis of spermatogenesis in male hinny is compared with normal fertile stallion and Jack donkey. Hinny testes showed a thicker tunica





albuginea, fewer blood vessels and more connective tissue in the testis parenchyma than those of the stallion and Jack donkey. The mean proportion of seminiferous tubules was lower in the hinny (p<0.01) which resulted in a smaller diameter of seminiferous tubules. The mean number of spermatogonia and spermatocytes per unit area were significantly lower in hinny testis (p<0.01) and no spermatids or mature spermatozoa cells were found during immunofluorescent analyses. These results indicated that defects in seminiferous tubule development and structure occur in the testis of hinnies. Furthermore, most spermatogonia and spermatocytes cease development in synapsis during mid-meiosis of spermatocytes, which results in a block to spermatogenesis that prevents the formation of spermatids and matured spermatozoa during meiosis in male hinnies [26].

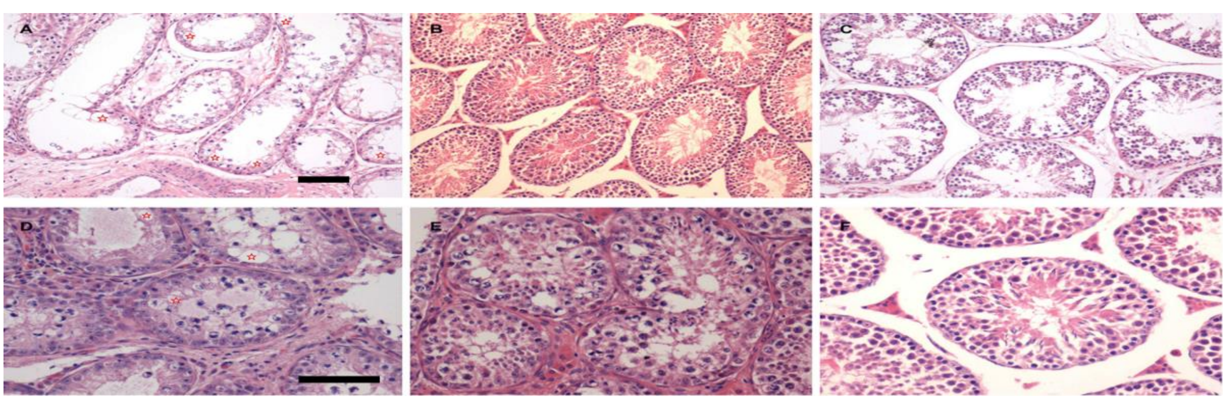


Figure 4: Developmental characteristics in the testes of the hinny, stallion and Jack donkey. The seminiferous tubules (ST) laminae were more deflated, folded and vacuolated in the hinny (A and D) than in the stallion (B and E) and Jack donkey (C and F). There were fewer germ cells and they were more irregularly distributed in the hinny than in the stallion and Jack donkey. Asterisks were highlighting the vacuole of ST in hinny. Scale bar = 100

Previous studies compared the testis weight, seminiferous tubule length, germ cell development and numbers of Sertoli and Leydig cells and seminiferous epithelium cycle length in mules and donkeys and a comparative morphometric analysis of mule, horse and donkey testes, which included assessing the hardness, weight and shape of the testes plus determining germ cell types plus the distribution of Sertoli and Leydig cells [27,28]. In both, systematic measurements were not made of the number, size and area of seminiferous tubules nor the number of germ cells at different stages of development. Furthermore, the stage at which spermatogenesis is blocked in the mules and hinnies were not determined accurately.

Female mules are hybrid, commonly considered as infertile, resulting from a cross between a donkey and a mare. Few recent studies made on the particularities of the reproductive system of the female mules. Here we present data showing consistent evidences of regular cyclicity in mules and also the first report of two births of donkey foals after embryo transfer into mule recipients with spontaneous estrous cycle. Clear evidences of cyclicity were found in 61.1% (44/72) of the ovaries, being 45.8 % (33/72) corpora lutea and 15.3 % (11/72) large antral follicles. After follicle aspiration, we obtained oocytes with regular distribution of granulosa cells and homogenous characterization of ooplasm. In contrast to the classical concept of infertile females, a higher percentage of the female mules can present ovarian activity and these animals may be considered for reproductive biotechnologies, such as embryo recipients [29].

3.4 To What Extent Can the Initial Notions of This Ancient Text Be Considered Accurate from A Modern Genetic Perspective?

It is no coincidence that the scientific assessments made by Greek philosophers and scientists were so precise; this precision stems not merely from their scientific intuition but also from accumulated scientific expertise and an early advancement in understanding and grasping the principles of biology – as evidenced by the theories of Aristotle, Galen, Democritus. In this regard, and to substantiate these hypotheses, we will focus on the following factors:

- Hippocrates and Democritus proposed that invisible "seeds" or miniaturized particles were produced by all parts of the parent's body. It is believed that these seeds moves towards the reproductive organs and combine during intercourse to form the offspring. Furthermore, Aristotle developed a theory of inheritance, according to which each sex contributes to heredity, so that the daughter resemble their mothers and sons resemble fathers. He also emphasized the importance of blood in heredity. Moreover, Aristotle was the founder of biology and the most prominent figure in formulating the ancient theories of reproduction /conception in animals, which were also applicable to humans. Democritus (460-370 BC) coined the concept of nature - nature as he stated: "more people become capable by exercise by their natural predisposition" [30].
- It can be concluded that the patterns of genetic inheritance did not appear until Mendel's work. However, history shows that humankind must have been interested in heredity long before the dawn of civilization, when the first speculations on heredity were recorded by the ancient Greek [31,32].
- In addition, early Greek philosophers and physicians made observation on the inheritance of physical traits in human, developed theoretical concepts, and proposed Eugenie methods [33].

Finally, We previously explained that Democritus came closest to a scientific diagnosis of the hidden cause of mule sterility; while he clearly grasped the correct genetic principle, he did not articulate it explicitly, but rather implied it. In translating the text into English, we took care to clarify – using between brackets- certain implicit meaning that underscore the validity of the interpretations offered by Greek philosophers, foremost among them Aristotle.

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