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Research Article

Polyamine Metabolism Related to Reproductive Processes in the Woman

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1. Abstract

This paper provides information on polyamine metabolism under different physiological conditions in female reproduction. Although information obtained from experimental models is included, special relevance is given to reproductive processes in the women, Polyamine metabolism has been studied in the ovary, uterus, endometrium, and myometrium, in maternal blood, urine, placenta, and embryo development as pregnancy progresses, as well as in women with spontaneous abortion and preeclampsia. Inhibition of polyamine synthesis in immature female mice inhibits ovarian development and delays puberty. In the uterus polyamine synthesis is regulated by hormones, injection of 17-β estradiol into young female rats increases uterine ornithine decarboxylase activity 14- to 25-fold 4 hours after hormone administration. The concentration of polyamines increases in the plasma and urine of pregnant women as the pregnancy progresses. They exert significant effects on embryonic development, implantation, placentation, and fetal development. In rats, specific and irreversible inhibition of polyamine synthesis with DL-α-difluoromethylornithine causes inhibition of embryonic development and embryo resorption. Polyamines are oxidized by polyamine oxidase. It has hypothesized that this enzyme has a protective role in the physiology of pregnancy and that polyamine oxidase at high levels protects the mother and fetus from high concentrations of biogenic amines. On the other hand, acrolein, a highly reactive aldehyde, is formed by oxidation of polyamines. Since acrolein is highly reactive to molecules containing amine groups such as nucleic acids, proteins and aminophopholipds forming advanced glycation end products, it can be speculating the participation of this metabolite in toxemia development, but this remain to be demonstrated.

2. Keywords: Polyamines; Putrescine; Spermidine; Spermine; Polyamine Metabolism; Human Female Reproduction; Woman; Preeclampsia

3. Introduction

Polyamines putrescine, spermidine and spermine are small molecules whose main characteristic is to possess two or more amino groups in their structure (Figure 1). There are many molecules in nature with these characteristics, however, these three amines have been the most studied since there is a close relationship in their biosynthesis and interconversion in different organisms including mammals. Since its discovery in 1677 by Antonie van Leeuwenhoek,[1] its function has been intensively studied in both prokaryotes and eukaryotes.

As polycations, polyamines are involved in numerous functions within cells. They influence cellular growth, cellular differentiation, and the function of cell membranes, and play a role in protein synthesis by regulating nucleic acids synthesis.

POLYAMINE	CHEMICAL STRUCTURE
PUTRESCINE	H_2N-CH_2-CH_2-CH_2-CH_2-NH_2
SPERMIDINE	H_2N-CH_2-CH_2-CH_2-$NHCH_2$-CH_2-CH_2-CH_2-NH_2
SPERMINE	H_2N-CH_2-CH_2-CH_2-NH-CH_2-CH_2-CH_2-CH_2-NH-CH_2-CH_2-CH_2-NH_2

Figure 1: Chemical structures of polyamines.

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4. Presence in Human Tissues and Fluids

Polyamines putrescine, spermidine and spermine are present in human tissues, and body fluids including blood, milk, urine, and amniotic fluid. They were discovered in the human semen through the formation of crystals.[1-3] A wide variety of studies have been conducted using samples obtained from humans and from experimental models to understand two aspects: first, their metabolism and second, their role in reproductive physiology in health and disease.

5. Polyamines in Female Reproduction

In female reproduction, polyamine metabolism has been studied in tissues and fluids of the reproductive system including ovary, metabolic changes during the menstrual cycle, in maternal blood, urine, placenta, and in amniotic fluid as pregnancy progresses, as well as in women with spontaneous abortion and preeclampsia [4-6].

Some publications have been made by our group on the role of polyamines in human reproduction [7]. Here, although information obtained from studies in experimental models is included, special relevance is given on the role of polyamines in reproductive processes in women.

It is important to mention that polyamines can be acquired from the diet [8], but they are also produced by gut microbiota [9]. Their relevance to longevity has been enhanced [10]. Their synthesis in mammals including humans is well known [2, 5].

6. How Polyamines are Synthesized in the Human Body

Putrescine is formed from ornithine in a reaction catalyzed by ornithine decarboxylase followed by another decarboxylase, S-adenosyl methionine decarboxylase, and two synthases: spermidine synthase and spermine synthase. Polyamines are catabolized by polyamine oxidases [5, 11-15]. The ornithine available for these reactions is formed by the action of arginase on arginine. Arginase is an enzyme that is part of the urea cycle but is also found in extrahepatic tissues [16, 17]. This enzyme provides the ornithine required for polyamine biosynthesis and regulates the initial phase of polyamine biosynthesis in addition to its well-known role in the urea cycle.

7. Polyamine Metabolism in Reproductive Tissues and Fluids

7.1. The Ovary

Several studies on ovarian polyamine metabolism have been performed in hamsters, mice, rats, and rabbits. Ornithine decarboxylase activity is high during the prepubertal period in rabbit and mouse ovaries [18, 19]. The activity of this decarboxylase is hormonally regulated as has been demonstrated with the use of follicle-stimulating and luteinizing hormones and by equine and human placental gonadotropins [20-22]. Some observations on the role of polyamines in ovarian development and function have been made through the specific inhibition of this enzyme. Inhibition of polyamine synthesis in immature female mice inhibits ovarian development and delays puberty [19].

7.2. The Uterus

Estrogen stimulation of spermidine synthesis has been demonstrated in the uterus of ovariectomized rats and in chicken oviducts [23, 24], as well as on ornithine decarboxylase activity [24, 25]. Injection of 0.5 μg of 17-β estradiol into young female rats increases uterine ornithine decarboxylase activity 14- to 25-fold 4 hours after hormone administration [26], demonstrating hormonal regulation of the gene that codes for the synthesis of this enzyme.

7.3. The Menstrual Cycle

7.3.1. Endometrium and myometrium: Ornithine decarboxylase activity and polyamine levels have been determined in the endometrium and myometrium.[27] Ornithine decarboxylase activity is high in normal endometrium (723 ± 286.4 picomoles of putrescine/mg of protein, n = 27), and undetectable in myometrium (n = 12). Ornithine decarboxylase activity in endometriosis has been associated with the high biological activity of this tissue due to its continuous morphological and functional modifications. In contrast, the myometrium, which has a different activity, does not show detectable ornithine decarboxylase activity, and presents low values in polyamine concentrations. From a comparative point of view, polyamine concentrations are higher in the endometrium than in the myometrium. In both tissues, spermine concentrations are higher than spermidine and spermidine higher than putrescine (Normal endometrium, n = 27, spermine = 125.0 ± 36.1, spermidine = 94.5 ± 31.2 and putrescine 40.2 ± 17.1 (S. D.) picomoles /mg of DNA, respectively); Normal myometrium, n = 12, (spermine = 113.2 ± 30.9, spermidine = 62.5 ± 19.1, putrescine = 10.8 ± 3.5 (S.D.) picomoles /mg of DNA, respectively)

7.3.2. The Urine: Urinary polyamine concentrations have been studied during the menstrual cycle of healthy women and total excretion of all three polyamines has been found to be highest during menstruation [28]. In some cases, urinary polyamines were elevated during the early follicular phase. In addition to the increased excretion of polyamines observed during menstruation, all women who participated in the study exhibited one or more mid-cycle spikes in polyamine excretion during the time that ovulation was expected. During the luteal and follicular phases, polyamines accumulated in the urine of some women. However, the elevated levels of urinary polyamines in these phases did not occur consistently in all women and do not seem to reflect events related to the menstrual cycle; rather, these peaks may occur as a function of diet. Other observations have suggested that food composition may modify urinary polyamine excretion [28]. It has been speculated that the increase in the concentration of polyamines in urine during menstruation may be related to endometrial cell necrosis. Polyamines may accumulate in the extracellular fluid as result of cell death [29].

7.4. Polyamines in Placenta

The concentration of polyamines increases in the plasma and urine of pregnant women as the pregnancy progresses [30, 31]. The con-

tent of polyamines in the human placenta at different stages of fetal development has been studied [32]. The placenta plays a central role in the growth and development of the embryo, which is why this tissue constitutes a primary source for the increased biosynthesis of polyamines observed during pregnancy. High concentrations of putrescine in the placenta occur as soon as it forms. During placental development, putrescine levels decline and are almost negligible before term. spermidine concentrations decline during gestation and remain at nearly constant low levels from the 25th week of pregnancy. Spermine levels rise continuously almost to term.

The increased synthesis of polyamines and their accumulation in the human placenta may be related to the active protein synthesis required for growth and the production of protein hormones. These may be associated with early events in the development of the placenta and for its function in late pregnancy [31].

Studies conducted using physiological concentrations of polyamines indicate that these amines stimulate the phosphorylation of specific proteins in placenta extracts [33]. The order of potency of the polyamines from highest to lowest is; spermine, spermidine and putrescine that coincides with their levels in placental tissues during gestation [32]. The phosphoproteins induced by spermine in the human placenta are distinct from those induced by cyclic adenosine monophosphate and Ca-dependent phosphorylation. Spermine inhibits both cyclic adenosine monophosphate-dependent phosphorylation and calcium-dependent phosphorylation in the placenta. Polyamines can act directly through phosphorylation by a polyamine-dependent reaction, or indirectly through inhibition of phosphorylation induced by other known inducers. These observations arise from the possibility that polyamines or their metabolites are primary effectors for the specific cascade of events associated with pregnancy [33].

8. Polyamines and Embryo Development

Polyamines play essential role in cell proliferation, growth, and differentiation. These molecules exert significant effects on embryonic development, implantation, placentation, and fetal development [34]. Evidence has been obtained for several years that ornithine decarboxylase (and/or the polyamines generated through its action) play an essential role in reproductive processes.

8.1. Inhibition of Polyamine Synthesis

The role of polyamines in normal growth in culture and in animal tissues has been understood with the development of inhibitors of polyamine synthesis [35, 36]. In mice, rats, and rabbits, oral administration of DL-α-difluoromethylornithine, a specific and irreversible inhibitor of ornithine decarboxylase (Figure 2), results in inhibition of the activity of this enzyme, affecting embryonic development [37]. In rats, the intrauterine or intraperitoneal administration of DL-α-difluoromethylornithine causes the blockage of embryonic development with its consequent reabsorption [38, 39].

DL-α-difluoromethylornithine [40], inhibits the synthesis of polyamines (LD50 for mice and rats: PO 5 g/ Kg, IP 3 g/Kg). This substance decreases the concentrations of cellular polyamines in vivo [41- 43]. It has been widely used to explore the role of polyamines in a wide variety of physiological and pathological processes. It has therefore been logical to explore the physiological importance of polyamines, using DL-α-difluoromethylornithine in systems exhibiting rapid cell differentiation and growth.

Early embryogenesis in mammals presents one of the most active division and differentiation systems, numerous studies have described marked increases in ornithine decarboxylase activity associated with this process [37]. In the mouse uterus, ornithine decarboxylase activity begins to increase close to nesting and reaches a peak on day 8 of gestation. During this time, putrescine and spermidine concentrations also increase, but spermine levels are severely affected. The peak of biochemical changes corresponds to a sudden increase in embryonic growth. This is associated with early somite formation which in the mouse occurs on days 7 to 8. The effects of DL-α-difluoromethylornithine treatment during days 5 to 8 of gestation are unequivocal; the increase in ornithine decarboxylase activity and putrescine and spermidine concentrations is abolished and embryonic development does not progress beyond day 7. Arrested embryos are reabsorbed [37, 44]. The effects of DL-α-difluoromethylornithine can be completely reversed by the simultaneous administration of putrescine whose half-life is relatively long [45], implicating the inhibition of putrescine biosynthesis as the mechanism of contragestational effect. DL-α-difluoromethylornithine also inhibits early embryonic development in rats and rabbits when administered in the pre- and post-implantation period [37-39]. Thus, an increase in ornithine decarboxylase activity leading to a rapid rise in putrescine concentration appears to be essential during a critical period after implantation for continued embryonic growth in mammals.

DL-α-difluoromethylornithine has been proposed as an effective postcoital antifertility agent in females [38], which provides a new area of research in contraception.

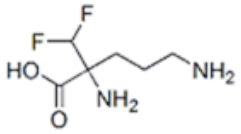

Figure 2: Chemical structure of DL-α-difluoromethylornithine, an irreversible inhibitor of ornithine decarboxylase (chemicalbook.com).

9. Polyamine Catabolism

9.1. Amine Oxidases and Pregnancy

The enzymes involved in the oxidation of polyamines have long been associated with pregnancy. Diamine and polyamine oxidase activities show a progressive increase with gestational age at or after 21 weeks, declining to very low levels on days 3 to 4 postpartum [46-48]. The placenta is generally considered a source of amine oxidases, although some authors suggest that these enzymes may be of decid-

ual origin [49]. Several attempts have been made to purify and characterize placental amine oxidases and to determine the specificity of their substrates [50, 51]. Both mono- and diamine oxidases from placenta homogenates have been shown to oxidize various amines, although the affinity of the enzymes for their substrates varies considerably. Therefore, it is believed that there is a large group of catalytic proteins capable of oxidizing amines, and another that uses polyamines or their acetylated derivatives as substrates.

It has been proposed that the apparent lack of specificity of amine oxidases may be a consequence of the lack of information on the conditions in which these enzymes function in vivo, leading to confusion in the definition and classification of amine oxidases in the literature [52].

Amine oxidases have been classified according to their prosthetic groups into 2 classes: monoamine oxidases or flavin adenine dinucleotide amine oxidases and cupper-amine or diamine oxidases [53]. The term polyamine oxidase was initially used to describe amine oxidases capable of catalyzing oxidative deamination of spermidine and spermine regardless of enzymes acting on mono- or diamines as substrates [15, 49].

In human pregnancy, diamine oxidase oxidizes both; histamine and putrescine circulate in maternal serum. Its levels rise as the pregnancy progresses. This enzyme was originally called histaminase since it uses histamine as a substrate [54], later it was called diamine oxidase due to its activity on putrescine [55].

In other investigations, it was shown that the enzyme obtained and partially purified from serum of pregnant women had affinity for putrescine and spermidine and acted on a wide range of substrates of which N1-acetyl spermidine was the best substrate [56]. This suggested that N1-acetylespermidine constitutes an important metabolite in human pregnancy since this molecule can be recycled to maintain the polyamine pool. In addition, amine oxidase could participate in the conversion of products that can be toxic to the organism, as has been proposed for rat liver polyamine oxidase, which also uses N1-acetylspermidine as a substrate. The presence of spermidine oxidase in the serum of pregnant women has also been reported. For this, labeled spermidine was used as a substrate, separating the reaction products by ion exchange chromatography, and thus determining some kinetic constants that were similar, to those of diamine oxidase [47].

Spermidine oxidase activity can be detected 8 weeks after the last menstrual cycle and increases with gestational age parallel to the increase in amino oxidase activity, stabilizing at 20 weeks of gestation. On the other hand, spermine oxidase activity has been detected in maternal serum in the tenth week of gestation. This suggests that this enzyme may be the same, polyamine oxidase [48].

Polyamine oxidase activity has also been measured in amniotic fluid and in fetal membranes between 15 and 40 weeks of gestation [57]. Enzyme activity increases as pregnancy progresses, like to that found in maternal serum, although levels are lower. The fetal membranes, chorion, and amnion, also show the presence of enzyme activity, with levels lower compared to those of the decidua, but significantly higher than those found in the placenta. This suggests that the enzyme found in amniotic fluid may be a consequence of diffusion from the decidua through the membranes [57].

10. Polyamines and Human Milk

Polyamine content has been measured in human milk, the concentration is highest during the first weeks of lactation and varies across mothers. They are essential for optimal maturation of the neonatal gut [58].

Polyamine ingestion from milk is believed to have an essential role in this accelerated development of the small and large intestines [59]. The polyamine concentration is significantly higher in human milk for preterm than for term infants, and this and the different spermidine/spermine ratios could influence the gut development of premature babies [60].

Polyamines also have been associated to promote a healthy gut microflora, seeding of the bacteria populations occurs during neonatal life. The resulting composition of gastrointestinal microflora is very important for establishing nutrient and energy balance, a healthy immune system and development of other physiological systems.[61]

11. Polyamine Oxidase and Abortion

Polyamine oxidase activity is highest in the intervillous circulation where the first and closest contact between fetal and maternal surfaces occurs [33, 62]. This has led to the hypothesis that polyamine oxidase has a protective role in the physiology of pregnancy and that this enzyme at high levels protects the mother and fetus from high concentrations of biogenic amines. Another hypothesis arose from the suggestion that the placenta releases an immunosuppressive factor that “turns off” potentially harmful maternal lymphocytes [37]. Some in vitro studies have shown that the action of polyamine oxidase on polyamines produces non-cytotoxic compounds which are inhibitors of cell proliferation.

Human pregnancy serum inhibits lymphocyte proliferation in vitro in the presence of exogenous spermine [63], the effects being proportional to polyamine oxidase content [64]. Other observations, such as the suppressive effects of the polyamines spermidine and spermine on components of the immune system in vitro and the observation that the placenta is rich in spermine and polyamine oxidase activity in retroplacental blood, suggest that the interaction products of polyamines and polyamine oxidase contribute to the protection of the fetus against maternal immune rejection due to the possible involvement of immunological factors in recurrent and spontaneous abortion [65, 66].

In a group of patients who miscarried between weeks 11 and 22 of pregnancy, serum polyamine oxidase activity was found to be significantly lower in patients with miscarriage than in the control group [67]. Although the authors noted that the low levels of this enzyme

found in women who had miscarried were not necessarily related to each other, suggesting that certain levels of polyamine-polyamine oxidase interaction may play an important role in maintaining normal pregnancy by protecting the fetus from maternal rejection, thus participating in embryonic growth. Other evidence [68] also supports the notion that a localized immune barrier malfunction may be related to reduced amine oxidase activity and may lead to spontaneous abortion [37].

12. Polyamine Oxidase in Preeclampsia-Eclampsia

Preeclampsia, also called gestosis or toxemia, generally appears in women after the 24th week of pregnancy. In some case it appears in the first postpartum hours [69]. Although the etiology of this condition is unknown, its pathophysiology and impact on target organs are well defined [70]. Toxic patients show concomitant hypertension with severe alterations in the vascular structure, proteinuria, and edema, in complicated cases seizures and coma may occur. Various pathological manifestations have been associated with this syndrome, such as a low platelet count, alterations in coagulation mechanisms, increased plasma viscosity, elevated levels of immunoglobulin G, and rheumatoid factor [71]. In addition, changes in the levels of nucleic acids and proteins have been observed in the placenta [72].

In the uterine veins of toxemic women, trophoblast levels are 20 times higher compared to those in women with normal pregnancy. This can induce a challenge of the mother's immune response against the fetus. It was also shown that macrophage migration can be inhibited by microsomal fractions of placental origin [73].

Polyamines modify the structure and function of nucleic acids. Thus, alterations in polyamine metabolism can result in abnormal synthesis of proteins and other molecules. In women with preeclampsia, the permeability of cell membranes is altered causing a protein to leak out to the urine. This process can be regulated by polyamines [74, 75].

During normal pregnancy, polyamine oxidase increases along with spermine, while putrescine and spermidine concentrations decrease. It is possible that spermidine binds to the enzyme to produce the polyamine oxidase-polyamine complex that exerts an inhibitory effect, regulating placental growth and limiting its extension to prevent invasion of the myometrium. In toxemic women, the myometrial vessels show swelling in the intima layer and hyperplasia in the muscular layer [69], for this reason an abnormality in trophoblast invasion is suspected [37]. These changes in the spiral vessels ensure intervillous irrigation, causing vasoconstriction that raises pressure and increases vascular permeability, causing a normal interaction between platelets and vascular endothelium.

To better understand the correlation between polyamine metabolism and preeclampsia, serum polyamine oxidase activity has been measured in women with preeclampsia. These patients, who were selected for their blood pressure of 160/110 mm Hg or higher, maintained for a period of 6 hours associated with edema extended to the abdomen or generalized, and proteinuria above 3 grams per liter [76]. Symptoms were diagnosed after 35 weeks of reliable amenorrhea, and cases of postpartum toxemia were excluded. The control group was made up of women with a normal pregnancy. The polyamine oxidase activity values of preeclamptic patients did not show significant differences compared to the values of the control group (toxemic women, n= 20, 8.48 ± 3.23 vs. normal women, n= 20, 6.91 ± 2.53 picomoles of Δ1-pyrraline/mg of protein/hour, respectively) [76]. However, it is recommended that the enzyme activity should be measured from the first trimester of pregnancy to determine if the enzyme arises from early significant changes.

A high incidence of toxemia has been found between weeks 39 and 41 (65%) and week 43 (5%), while in women with normal pregnancy it was evenly distributed throughout the third trimester. This observation suggests that week 39 to 41 are the critical weeks in which toxemia appears.

13. Discussion

The evidence of the participation of polyamines in the reproductive processes of women is widely documented, since these molecules are involved in all phases of female physiology and embryonic development. Here, its participation in normal reproductive processes has been briefly described, and in experimental models it has been demonstrated how these processes are affected with the use of specific inhibitors of polyamine synthesis. In addition to this, it has been demonstrated that in rats with chemically induced diabetes on day 4 of gestation, delayed embryonic growth and resorption is presented as signs of embryotoxicity [77]. These effects of hyperglycemia can be prevented by the administration of putrescine, spermidine, and spermine [78].

On the other hand, it has been reported that acrolein (Figure 3) also called acrylaldehyde or 2-propenal, a monoaldehyde, highly reactive to proteins is a major toxic compound produced from spermine and spermidine oxidation by polyamine oxidase and that acrolein is accumulated in plasma of patients with chronic renal failure [79].

Furthermore, the main amine oxidase producing acrolein from spermine and spermidine is polyamine oxidase [79]. So, if preeclamptic women have increased polyamine oxidase levels and renal abnormalities, they may accumulate acrolein and possible develop uremia. From chemical point of view, it can hypothesize that acrolein could reacts not only with amino groups of proteins but also with amino group of nucleic acids and aminophospholipids, which can then rearrange to form advanced glycation end products [80] or advanced lipid end products. This hypothesis is supported in a study that shows that advanced glycation end products accumulated markedly in the plasma and collagenous tissues in normoglycaemic uremic patients [81, 82].

Experimentally, it has been shown that acrolein reacts with a lysine residue to form an adduct which partly explains the oxidative mod-

ification of low-density lipoproteins. The structure of this adduct was identified as N-α-acetyl-N-ε-(3-formyl-3,4-dehydropiperidino) lysine [83].

Previously, was suggested by our group that urea can be used as a glycation protector.[84] Due to the renal abnormalities in preeclampsia, the urea levels in blood may be increased [85], then urea can react with acrolein forming end products like to glycation end products [84]. Based on the information that uremic sera contain unknown precursors for the Maillard reaction [86], it can suspect on the formation of compounds between acrolein formed by oxidation of polyamines and its reaction with amino groups of proteins, nucleic acids and aminophospholipids in preeclampsia, however, it remains to be demonstrated.

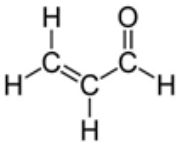

Figure 3: Acrolein (acrylaldehyde or 2-propenal), formed from oxidation of polyamines, is an aldehyde highly reactive to proteins. (https://study.com/learn/lesson/acrolein-structure-safety-uses.html).

14. Conclusions

In conclusion, polyamines are involved in all stages of the reproductive process in women. Valuable results obtained in experimental models complement this information. From the maturation of the ovary, the menstrual cycle, the implantation process, embryonic development, growth, and lactation are regulated by polyamines, in turn, the activity of enzymes that biosynthesize polyamines is regulated by hormones, as is the case of ornithine decarboxylase. If the synthesis of polyamines stops, embryonic development is blocked, which clearly demonstrates its participation in this process.

Finally, there are several hypotheses about the activity of the polyamine oxidase enzyme. One of them is related to the formation of acrolein, a highly reactive aldehyde. Whether or not the formation of this aldehyde is related to the development of preeclampsia remains to be demonstrated.

References

1. van Leeuwenhoeck A, Observationes D. Anthoni Leeuwenhoeck, de Natis e Semine genitali Animalculis. Phil. Trans. Roy. Soc. London. 1677; 12: 1040.
2. In the path of Leuwenhoeck, Vauquelin, Charcot, et al. Chapter 1. In: Introduction to the Polyamines. Prentice-Hall Inc. Englewood Cliffs, New Jersey. U.S.A. 1971; 1.
3. Méndez JD. The other legacy of Antonie van Leeuwenhoek: The polyamines. J. Clin. Mol. Endocrinol. 2017; 2: e107.
4. Pavine L, Lefevre C, Palin MF, Murphy BD. Polyamines on the reproductive landscape. Endocrine Reviews. 2011; 32: 694.
5. Pegg AE. Functions of polyamines in mammals. J. Biol. Chem. 2016; 291(29):14904.
6. Lenis Y, Elmetwally M, Maldonado-Estrada J, Bazer F. Physiological importance of polyamines. Zygote. 2017; 25(3): 244.
7. Méndez JD. Polyamines and human reproduction. In: Bachrach, U., Heimer, Y. editors, Volume 1: The Physiology of Polyamines. C.R.C. Press, Inc. Florida, U.S.A., 1989; 23.
8. Muñoz-Esparza NC, Latorre-Moratalla ML, Comas-Basté O, Toro-Funes N, Veciana-Nogués MT, Vidal-Carou MC. Polyamines in food. Front. Nutr. 2019; 6:108.
9. Tofalo R, Cocchi S, Suzzi G. Polyamines and gut microbiota. Front. Nutr. 2019; 6:16.
10. Soda K. Overview of polyamines as nutrients for human healthy long life and effect of increased polyamine intake on DNA methylation. Cells. 2022; 11(1): 164.
11. Bachrach U. Function of Naturally Ocurring Polyamines. Academic Press, New York, 1973.
12. Pegg AE, Williams-Ashman HG. Biosynthesis of putrescine- In: Polyamines in Biology and Medicine. Morris DR, Marton LJ, Eds., Marcel Dekker, New York. 1981; 3.
13. Pegg AE, McCann PP. Polyamine metabolism and function. Am. J. Physiol. 1982; 243: C 212.
14. Tabor CW, Tabor H. Polyamines: Annu. Rev. Biochem. 1984; 53: 749.
15. Höltta E. Oxidation of spermine and spermidine in rat liver: purification and properties of polyamine oxidase. Biochemistry. 1977; 16: 91.
16. Oka T, Perry JW. Arginase affects lactogenesis through its influence on the biosynthesis of spermidine. Nature. 1974; 250: 660.
17. Méndez JD, Yañez R, Wong C, Hicks JJ. Uterine arginase inhibition affects the rat embryonic development. Contraception. 1986; 33(6): 597.
18. Young Lai EV, Byskov AG. Relationship of meiotic prophase and ornithine decarboxylase in the neonatal rabbit ovary. Cell Tissue Res. 1983; 231:565.
19. Bastida CM, Cremades A, Castells MT, López-Contreras AJ, López-García C, Tejada F, Peñafiel R. Influence of ovarian ornithine decarboxylase in folliculogenesis and luteinization. Endocrinology. 2005; 146: 666.
20. Johnson DC, SashidaT. Temporal changes in ovarian ornithine decarboxylase and cyclic AMP in immature rats stimulated by exogenous or endogenous gonadotrophins. J. Endocrinol. 1977; 73:463.
21. Nureddin A. Ovarian ornithine decarboxylase regulation in the immature, the pubescent, and the pseudopregnant rat. Proc. Natl. Acad. Sci. USA. 1978; 75:2530.
22. White SS, Ojeda SR. Changes in ovarian luteinizing hormone and follicle-stimulating hormone receptor content and in gonadotropin-induced ornithine decarboxylase activity during prepubertal and pubertal development of the female rat. Endocrinology. 1981; 109:152.
23. Moulton BC, Leonard SL. Hormonal effects on spermidine levels in male and female reproductive organs of the rat. Endocrinology. 1969; 84:1461.

24. Russell DH, Taylor RH. Polyamine synthesis and accumulation in ovariectomized rats after estradiol 17-β-administration. Endocrinology. 1970; 88: 1397.
25. Cohen S, O´Malley BW, Stastny M. Estrogenic induction of ornithine decarboxylase in vivo and in vitro. Science. 1970; 170: 336.
26. Kaye Am, Iceckson I, Linder HR. Stimulation by estrogens of ornithine and S-adenosylmethionine decarnboxilases in inmature rat uterus. Biochim. Biophys Acta. 1971; 252: 150.
27. Romano M, Cecco L, Santacrose MA, Cerra M, Rasquinelli R, Pagnano AM, Paladini A. Polyamine levels and ODC activity in the normal human endometrium and myometrium in the myoma and the endometrial carcinoma, in Advances in Polyamines in Biomedical sciences, Caldarera, CM and Bachrach U., Eds., CLUEB, Bologna, Italy. 1984; 145.
28. Osteberg S, Rose S, Heby O. Urinary polyamine excretion during the menstrual cycle. Clin. Chem. 1978; 24(5): 769.
29. Heby O, Anderson G. Tumor cell death: The probable cause of increased polyamine levels in physiological fluids. Acta Pathol. Microbiol. Scand. Sect. A. 1978; 86: 17.
30. Russell DH, Giles HR, Christia CD, Campbell JL. Polyamines in amniotic fluid, plasma and urine during normal pregnancy. Am. J. Obstet. Gynecol. 1978; 132: 649.
31. Hiramatsu Y, Eguchi K, Yonesaw M, Hasaye R, Sekeba K. Alteration of blood red cells polyamines during pregnancy and neonatal period. Biol. Neonate. 1981; 40:136.
32. Porta R, Servillo L, Abruzzese A, Della Pietra G. Automated chromatographic análisis of human placenta polyamines Biochem. Med. 1978; 19: 143.
33. Moore JJ, Cardaman RC, Lundgren DW. Spermine-enhanced protein phosphorylation in human placenta. Proc. Soc. Exp. Biol. Med. 1984; 176: 313.
34. Hussain T, Tan B, Ren W, Rahu N, Hussain Kalhoro D, Yin Y. Exploring polyamines: Functions in embryo/fetal development. Animal Nutrition. 2017; 3: 7e10
35. Heby O. Role of polyamines in the control of cell proliferation and differentiation. Differentiation. 1981; 14:11.
36. Jane J, Posso H, Raina A. Polyamines in rapid growth and cancer. Biochim. Biophys. Acta. 1978; 473: 241.
37. Fozard JR, Part ML, Prakash NJ, Grove J, Schechter PJ, Sjoerdsma A. Koch-Weser J. L-Ornithine decarboxylase: an essential role in early mammalian embryogenesis. Science. 1980; 208: 505.
38. Reddy PRK, Rukmini V. α-Difluoromethylornithine as a postcoitally effective antifertility agent in female rats. Contraception. 1981; 24 (2): 215.
39. Méndez JD, Diaz-Flores M, Durán G, Hicks JJ. Inhibition of rat embryonic development by the intrauterine administration of -difluoromethylornithine. Contraception. 1983; 28(1): 93.
40. Metcalf BN, Bey P, Danzin C, Jung MJ, Casara P, Vevert JP. Catalytic irreversible inhibition of mammalian ornithine decarboxylase (E.C. 4.1.1.17) by substrate and product analogs. J. Am. Chem. Soc. 1978; 100: 2551.
41. Mamont PS, Bey P, Koch-Weser J. Biochemical consequences of drug-induced polyamine deficiency in mammalian cells. In: Polyamines in Biomedical Research. Gaugas JM, Ed., John Wiley & Sons, Chichester England, England. 1980. 147.
42. Fozard JR, Part ML, Prakash NJ, Grove J. Inhibition of murine embryonic development by α-difluoromethylornithine, an irreversible inhibitor of ornithine decarboxylase. Eur. J. Pharmacol. 1980; 60: 379.
43. Slotkin TA, Seidler FJ, Trepanier PA, Withmore WL, Larea L, Barnes GA, Weigel SJ, Bartolome J. Ornithine decarboxylase and polyamines in tissues of neonatal rat: effects of α-difluoromethylornithine, a specific irreversible inhibitor of ornithine decarboxylase. J. Pharmacol. Ther. 1982; 222(2): 741.
44. Fozard JR, Koch-Weser J. Pharmacological consequences of inhibition of polyamine biosynthesis with D, L-α-difluoromethyl ornithine. Trends Pharmacol. Sci. 1982; 3(3): 107.
45. Barkai U, Kraicer PF. Definition of period of induction deciduoma in the rat using ornithine decarboxylase as a marker of growth onset. Int. J. Fertil. 1978; 23(2): 106.
46. Southren AL, Kobayashi Y, Carmody MC, Weingold AB. Serial measurements of plasma diamine oxidase during normal human pregnancy by an improved method. Am J. Obstet. Gynecol. 1966; 95: 615.
47. Gahl WA, Vale AM, Pitot HC. Spermidine oxidase in human pregnancy serum: probable identity with diamine oxidase. Biochem J. 1982; 201:161.
48. Illei G, Morgan DML. Polyamine oxidase activity in human pregnancy serum. Br. J. Obstet. Gynaecol. 1979; 86: 878.
49. Illei G, Morgan DML. The distribution of polyamine oxidase activity in the fetomaternal compartments. Br. J. Obstet. Gynaecol. 1979; 86: 873.
50. Bardsley WG, Crabbe MJ, Scott IV. The amine oxidase of human placenta and pregnancy plasma. Biochem J. 1974; 139: 169.
51. Amicosante G, Oratore A, Crito C, Finazzi Agro A. Rapid characterization and partial purification of various animal amine oxidases. Experientia. 1984; 40:1140.
52. Morgan DML. Commentary: amine oxidases and pregnancy. Br. J. Obstet. Gynaecol. 1982; 89: 177.
53. Mondovi B, Guerrieri P, Costa MT. Sabatini S. Amine oxidase inhibitors and boiogenic amines metabolism. In: Advances in Polyamine Research. Vol. 3. Caldarera CM, Zappia V, Bachrach U. Eds. Raven Press, New York, 1981. 75.
54. Morgan DML. Polyamine oxidase and cellular interactions. In: Advances in Polyamine Research. Vol. 3. Caldarera CM, Zappia V, Bachrach U. Eds. Raven Press, New York. 1981; 65.
55. Andersson AC, Henninsson S, Rosengren E. Diamine oxidase. In: Polyamines in Biomedical Research. Gaugas JM. Ed. John Wiley and Sons. Chichester. 1980. 273.
56. Gahl WA, Pitot C. Acetylated polyamines as substrates for human pregnancy diamine oxidase. Life Sci. 1981; 29(21): 22177.
57. Illei G, Morgan DML. Polyamine oxidase activity in amniotic fluid and fetal membranes. Br. J. Obstet. Gynaecol. 1980; 87: 413.
58. Milligan Newmark L. Gut Check: Polyamines in human milk are es-

sential for intestinal maturation. IMGC International Milk Genomics Consortion. 2017; 62.

59. Löser C. Polyamines in human and animal milk. Br. J. Nutr. 2000; 84(S1): 55.
60. Plaza-Zamora J, Sabater-Molina M, Rodriguez-Palmero M, Rivero M, Bosch V, Nadal JM, et al. Polyamines in human breast milk for preterm and term infants. Br. J. Nutr. 2013; 110(03): 524.
61. Williamson P. Polyamines promote a healthy gut microflora. IMGC International Milk Genomics Consortion. 2014; 28.
62. Klopper A, Hughes G. placental secretion of oestrogens and protein hormones. Arch. Gynäkol. 1978; 225:171.
63. Gaugas JM, Cursen P. Polyamine interaction with pregnancy serum in suppression of lymphocytes transformation. Lancet. 1978; i: 18.
64. Morgan DML, Illei G. Polyamine-polyamine oxidase interaction: part of maternal protective mechanism against fetal rejection. Br. Med. J. 1980; 280: 1295.
65. Bresniham B, Grogor RR, Lewkonia RM, Hughes GRV, Lovins RE, Faulk WP. Immunological mechanism for spontaneous abortion in systemic lupus erythematosus. Lancet. 1977; ii: 1205.
66. Taylor C, Faul WP. Prevention of recurrent abortion with leucocyte transfusion. Lancet. 1981; ii: 68.
67. Illei G, Morgan DML. Serum polyamine oxidase activity in spontaneous abortion. Br. J. Obstet. Gynaecol. 1982; 89: 199.
68. Labib RS, Tomasi TB. Enzymatic oxidation of polyamines relationship to immunosuppressive properties. Eur. J. Immunol. 1981; 11:266.
69. López-Llera M, Fisiología patológica de la toxemia del embarazo. In: La toxemia del embarazo. Temas de Terapéutica. 1977. Publicación particular limitada. México. 1978; 1.
70. De Voe SJ, O´Shaugghnessy R. Clinical manifestation and diagnosis of pregnancy-induced hypertension. Clin. Obstet. Gynecol. 1984; 27(4): 836.
71. Mathews JD, Mason TW. Plasma viscosity and pre-eclampsia. Lancet. 1974; 8:409.
72. Samour MB, Ibrahim FK, Fattah MMA, Ramadan MA. Nucleic acids and protein changes in normal and pre-eclamptic placentae. Acta Obstet. Gynecol. Scand. 1979; 58: 535.
73. Toder V, Eichenbrenner I, Amit S, Serr D. Nobel L. Cellular hyperreactivity to placenta in toxemia of pregnancy. Eur. J. Obstet. Gynecol. Reprod. Biol. 1979; 9(6): 535.
74. Koening H, Goldstone A, Lu Ch Y. Polyamines regulate calciun fluxes in a rapid plasma membrane response. Nature. 1983; 305(5934): 530.
75. Elgavish A, Wallace RW, Pillion DJ, Meezan E. Polyamines stimulate D-glucose transport in isolated brush-border membrane vesicles. Biochim. Biophys Acta. 1984; 777:1.
76. Méndez JD, Aguilar-Hernández M, Méndez-Valenzuela V. Polyamine oxidase activity in women with preeclampsia-eclampsia. World Appl. Sci. J. 2007; 2(3): 184.
77. Palomar-Morales M, Baiza LA, Verdín L, Román-Ramos R, Altamirano M, Méndez JD. Fetal development in alloxan treated rats. Reprod. Toxicol. 1998; 12(6): 659.
78. Méndez, J.D. and Palomar-Morales, M. Prevention by L-arginine and polyamines of delayed development and embryotoxicity caused by chemically induced diabetes in rats. Reprod. Toxicol. 1999; 13(6): 501.
79. Sakata K, Kashiguagi S, Sharmin S, Ueda S, Igarashi K. Acrolein produced from polyamines as one of the uraemic toxins. Biochem. Soc, Trans. 2003; 31: 371.
80. Vlasara H, Bucala R, Striker L. Biology of Disease. Pathogenic effects of advanced glycosylation: Biochemical, biological, and clinical implications for diabetes and ageing. Lab. Invest. 1994; 70: 138.
81. Makita Z, Radoff S, Rayfield EJ, Yang Z, Skolnic E, Delaney V, Friedman EA. Advanced glycosylation end products in patients with diabetic nephropathy. N. Engl. J. Med. 1991; 325: 836.
82. Miyata T, Ueda Y, Zhinzato T, Lida Y, Tanaka S, Kurokawa K, van Ypersele de Strihou C, Maeda K. Accumulation of albumin-linked and free.formed pentosidine in the circulation of uremia patients with end.stage renal failure: renal implications in the pathophysiology of pentosidine. J. Am. Soc. Nephrol. 1996; 7: 1198.
83. Uchida K, Kanematsu M, Morimitsu Y, Osawa T, Noguchi N, Niki E. Acrolein is a product of lipid peroxidation reaction. Formation of free acrolein and its conjugate with lysine residues in oxidized low density lipoproteins. J. Biol. Chem. 1998; 26; 273(26): 16058.
84. Méndez JD, Aguilar-Hernàndez M, Méndez-Valenzuela V. Polyamine oxidase activity in women with preeclampsia-eclampsia. World Appl. Sci. J. 2007; 2(3): 184.
85. Yang B, Bankir L. Urea and urine concentrations ability: new insights from studies in mice. Am. J. Physiol. 2005; 288: 881.
86. Wada T, Miyata T, Kurokawa K. Implication of carbonyl stress in long -term uraemic complications. Nephrol. Dial. Transplant. 1999; 14(Suppl.1): 79.