

Pathological Outcomes of Cadmium Chloride and Lead Acetate Exposure in Offspring of Exposed Male White Rats: Implications for Toxicology

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ABSTRACT

A laboratory study was conducted to evaluate the negative effects of cadmium chloride and lead acetate on the offspring of male albino rats, at the Department of Life Sciences/Faculty of Pure Sciences Education/University of Tikrit during 2023. The experiment included dividing the males into six groups: the first was a control group, the second was injected with 5 mg/kg of cadmium chloride, the third was injected with 10 mg/kg of cadmium chloride, the fourth was injected with 75 mg/kg of lead acetate, the fifth was injected with 150 mg/kg of lead acetate, and the sixth was injected with 5 mg/kg of cadmium chloride and 75 mg/kg of lead acetate per body weight. The injection was applied for 30 days. Groups of females (5 animals per group) were mated with 2 of the males that were injected with pollutants. After mating healthy female albino rats with male albino rats injected with different concentrations of cadmium chloride and lead acetate, the results were as follows: The presence of an effect of cadmium chloride at a concentration of 60 mg/kg on the embryos, as half of the number of embryos were deformed. The deformity was shortening of the forelimbs, protrusion of the mouth, difference in the curvature of the back, small size of the embryo, and difference in the shape and size of the placenta. At a concentration of 120 mg/kg of cadmium chloride on the embryos, the number of embryos was eight embryos and all were abnormal. At a concentration of 600 mg/kg of lead acetate after five days, one of the females died. A concentration of 1200 mg/kg of lead acetate recorded deformities that included small size of the embryo, straight back, body crack, swollen placenta, and black color. The effect of a concentration of 60 mg/kg of cadmium chloride and 60 mg/kg of lead acetate was that the first female gave birth after 20 days and the second female gave birth after 22 days and an abortion occurred in the third female after 14 days. Upon dissection, it was found that the embryos were not equal in the horns of the uterus, the size of the fetus was small, and the placenta was large.

Keywords: Cadmium Chloride, Lead Acetate, Offspring.

INTRODUCTION

Humans and animals are constantly exposed to environmental pollutants, which are one of the external sources of reactive oxygen species and free radicals, especially industrial pollutants, especially heavy metals such as cadmium and lead [1]. Heavy metals are one of the serious problems that are widespread these days, and pollution with them causes many serious diseases, due to the tendency of these compounds to accumulate and accumulate within living ecosystems [2].

Heavy metal toxicity causes an imbalance in oxidative stress. These minerals cause an increase in the formation of free radicals and a decrease in the number of antioxidants, which work to reduce the serious damage caused by free radicals. These metals have the ability to interact with DNA and nuclear proteins, leading to oxidative degradation of biological macromolecules [3]. Cadmium is considered one of the most important heavy metals and is not necessary for the body. It is characterized by its high toxicity and health risks to both humans and animals. It is also a dangerous environmental pollutant resulting from agricultural and industrial activities [4]. Cadmium is absorbed through the respiratory system at a rate of 10 to 40% of the ingested amount and at a rate of 5% through the digestive system with food or water [5]. It is concentrated and stored in the liver and kidneys, and distributed to various organs of the body, with a long half-life of up to years, which increases the risk that it accumulates in the body's tissues and causes multiple toxic effects in the body. organism. organs of the body [6]. The toxic effects of

cadmium are characterized by liver and kidney damage, testicular necrosis, hypertension, diabetes, damage to the intestinal mucosa, emphysema, osteoporosis, osteocalcin, neurotoxicity, especially in the brain, as well as teratogenic effects. In embryos, cancerous tumors, genetic mutations in humans and animals and oxidative stress [7]. Lead is a heavy metal that is widely distributed throughout the world. It is a toxic element that poses a great danger to the life of living organisms, since it causes a variety of physiological, behavioral and biochemical risks for both humans and animals [8]. This includes the central nervous system, kidneys, liver, hematopoietic system, reproductive system, and cardiovascular system [9].

Lead causes many very serious health effects, such as congenital malformations in fetuses, hereditary diseases such as weakness in the reproductive organs, chromosomal abnormalities, and an increase in deaths due to an increase in cancer cases [10]. Regarding genetic effects, exposure to lead for a long period leads to the development of chromosomal aberrations in human cells [11]. The current study aims to investigate the morphological effects in rat fetuses caused by exposure to cadmium chloride and lead acetate.

MATERIALS AND METHODS

Experimental Animals

35 male and 30 female albino rats were used in the study. They were obtained from the Animal House at the College of Veterinary

Medicine, University of Tikrit. They were between 14 and 16 weeks old and weighed between 230 and 190 grams. They were raised in the Animal House at the College of Veterinary Medicine, University of Tikrit.

Experimental Design

The experiment was carried out according to a completely randomized design (CRD) with three replicates, each replicate including a pair of mice. First- Male Groups (3 animals per group): 1. Control group: Oral gavage with normal water (tap water) for 30 days. 2. Cadmium chloride (CdCl_2) 5 mg/kg body weight group: Oral gavage with CdCl_2 for 30 days. 3. Cadmium chloride (CdCl_2) 10 mg/kg body weight group: Oral gavage with CdCl_2 for 30 days. 4. Lead acetate ($\text{Pb}(\text{CH}_3\text{COO})_2$) 75 mg/kg body weight group: Oral gavage with $\text{Pb}(\text{CH}_3\text{COO})_2$ for 30 days. 5. Lead acetate ($\text{Pb}(\text{CH}_3\text{COO})_2$) 150 mg/kg body weight group: Oral gavage with $\text{Pb}(\text{CH}_3\text{COO})_2$ for 30 days. 6. Mixed exposure group: Oral gavage with CdCl_2 5 mg/kg and $\text{Pb}(\text{CH}_3\text{COO})_2$ 75 mg/kg for 30 days. Second- After the end of the 30-day dosing period, they were mated with females not exposed to pollutants to determine whether the negative effect was transmitted to their fetuses through this mating. Third- Each group of males that had been dosed with pollutants was mated with a group of healthy females, and the groups were distributed as follows: 1. Mated with the control group that was orally gavaged with distilled water for 30 days. 2. Mated with the group that was gavaged with cadmium chloride 5 mg/kg body weight for 30 days. 3. Mated with the group that was gavaged with cadmium chloride 10 mg/kg body weight for 30 days. 4. Mated with the group that was gavaged with lead acetate 75 mg/kg body weight

for 30 days. 5. Mated with the group that was gavaged with lead acetate 150 mg/kg body weight for 30 days. 6. Mated with the group that was gavaged with cadmium chloride 5 mg/kg and lead acetate 75 mg/kg body weight for 30 days

Mating Procedure

After selecting healthy female rats between 10 and 12 weeks of age and weighing 250-300 grams, they were placed with males of the same strain in a plastic cage overnight. In the morning, the females were examined. The presence of a vaginal plug or sperm in the vaginal fluid indicates that fertilization has occurred. The females are considered to be on day 0 of pregnancy [12].

Results and Discussion

After mating healthy female albino rats with male albino rats gavaged with different concentrations of cadmium chloride and lead acetate, we observed the effect of chemical pollutants on the offspring after birth when compared to the control group.

Control Group Fetuses

We did not observe any malformations in the control group fetuses in Figure (1). Three healthy female albino rats were mated with one male albino rat that was not gavaged with any substance. The results were the birth of healthy fetuses without malformations. The birth occurred 21 days after the formation of the vaginal plug, meaning that the birth occurred on schedule. The number of fetuses was equal in the two horns of the uterus, and 10-12 fetuses were born per female.

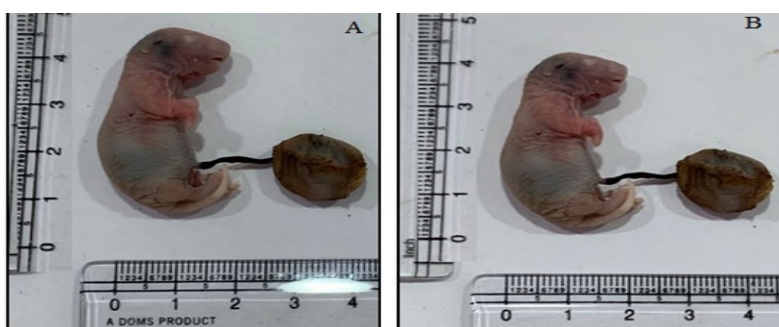
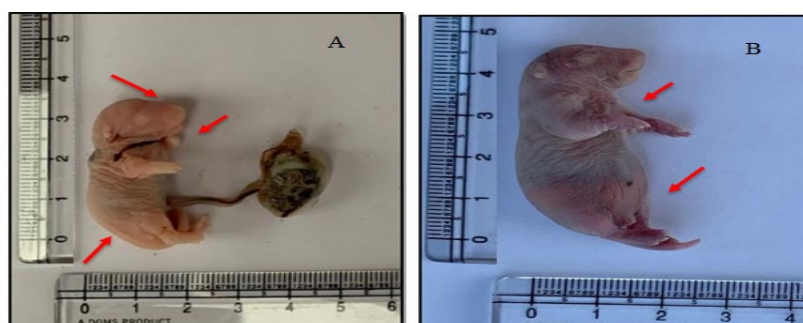


Figure 1: Control Group Embryos

Fetuses of the Second Group Treated with 60 mg/kg of Cadmium Chloride: We observed the effect of cadmium chloride at a concentration of 60 mg/kg on the fetuses. The number of fetuses in the first female was eight, and four of these fetuses were malformed compared to the control group. The malformation was shortening of the forelimbs, protrusion of the front of the mouth, as well as a difference in the curvature of the back, small size of the fetus, and a difference in the shape and size of the placenta, as shown in Figure (2-

A). The fetuses in the second female were only two, and the malformation was also shortening of the forelimbs and they had a swollen belly, as shown in Figure (2-B). The fetuses in the third female rat were small in size, the forelimbs were fused and short with the disappearance of the eye socket, as shown in Figure (2-C). One of the fetuses had a small head and the disappearance of the front of the mouth and the change of the eye socket location, as shown in Figure (2-D).



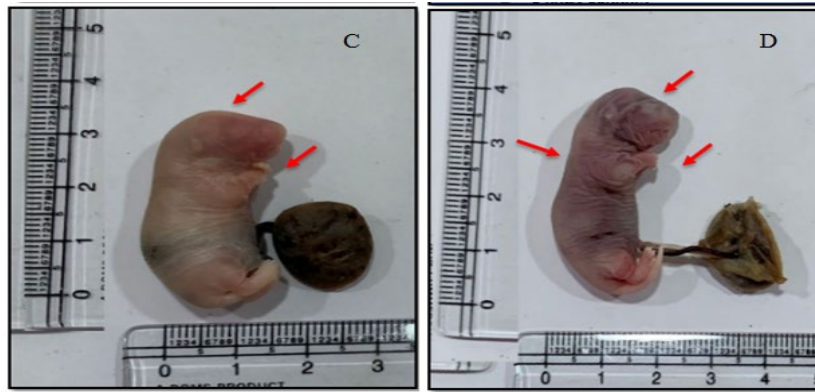


FIGURE 2: Fetuses of Females that were Mated with a male that was Gavigated with 60 mg/kg of Cadmium Chloride. A- One of the Fetuses of the First Female, B- One of the Fetuses of the second Female, C- One of the Fetuses of the Third Female, D- One of the Fetuses of the Third Female.

Fetuses of the Third Group Treated with 120 mg/kg of Cadmium Chloride: We observed the effect of cadmium chloride at a concentration of 120 mg/kg on the fetuses. Three female albino rats were mated with a male gavaged with cadmium chloride. The first female gave birth after 20 days of pregnancy. Eight fetuses were born, and all of them were abnormal. The malformations included a small

mouth, short forelimbs, a difference in the curvature of the back, a shorter length of the fetus than normal, and a difference in the shape and size of the placenta, as shown in Figure (3-A). Twenty-one days after pregnancy, the second female gave birth to only four fetuses. All of them were abnormal, as they were very small in size, unclear in outline, and had an unnatural color, as shown in Figure (3-B).

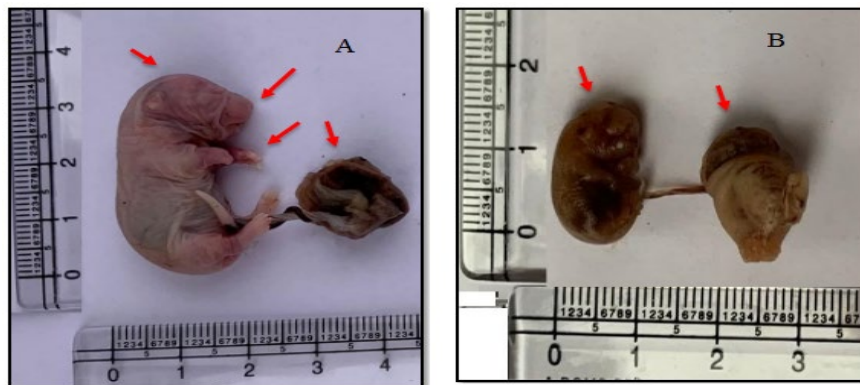


FIGURE 3: Fetuses of Females that were Mated with a Male that was Gavaged with 120 mg/kg of Cadmium Chloride. A- One of the Fetuses of the First Female, B- One of the Fetuses of the Second Female.

Fetuses of the Fourth Group Treated with 600 mg/kg of Lead Acetate: The current study investigated the effects of 600 mg/kg of lead acetate after gavaging males and mating them with non-treated females to assess the effects on their fetuses.

Three females were mated with a male, and one of the females died after five days. The pregnancies continued for the remaining two females, and the first gave birth after 16 days and the second gave birth

after 17 days. The effects of lead acetate on the fetus of the first female included malformations, such as a small fetus, a change in the shape of the palate, a split body, and an abnormal placenta with a black color, as shown in Figure (4-A). The fetus of the second female also showed malformations, such as a small fetus, a shrunken and curved body, and a black and slightly swollen placenta, as shown in Figure (4-B).

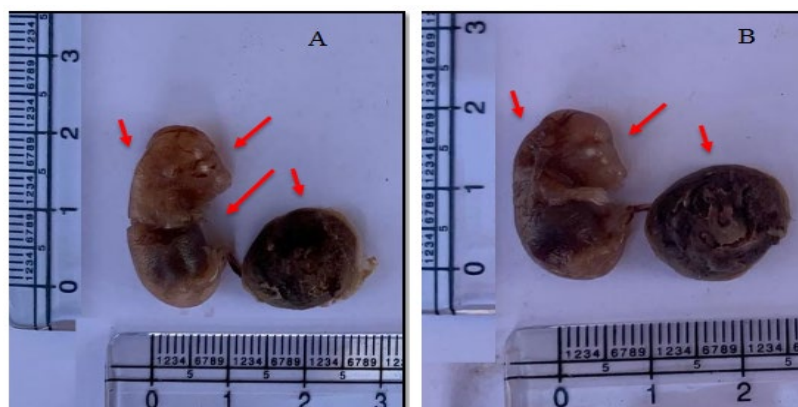


FIGURE 4: Fetuses of Females that were Mated with a male that was Gavaged with 600 mg/kg of Lead Acetate. A- One of the Fetuses of the First Female, B- One of the Fetuses of the Second Female.

Fetuses of the Fifth Group Treated with 1200 mg/kg of Lead Acetate: The current study investigated the effects of 1200 mg/kg of lead acetate after gavaging males and mating them with non-treated females to assess the effects on their fetuses. Three females were mated with a male, and the first female gave birth after 19 days, the second female gave birth after 18 days, and the third female gave birth after 20 days. The effects of lead acetate on the fetus of the first female, as shown in Figure (5-A), included malformations, such as a slight decrease in the size of the fetus, a straight back, a split body, and a

swollen placenta with a black color. The fetus of the second female, as shown in Figure (5-B), was completely deformed. It was observed that the eardrum was missing, the upper lip was cleft, the upper and lower limbs were fused to the body, the body was twisted, and the tail was absent. The fetus in the third female, as shown in Figure (5-C), was very small and was attached to a very large placenta compared to the size of the fetus. The placenta was swollen and had an irregular shape. The second fetus in the second female, as shown in Figure (5-D), was also small in size and had a large placenta with an irregular shape.

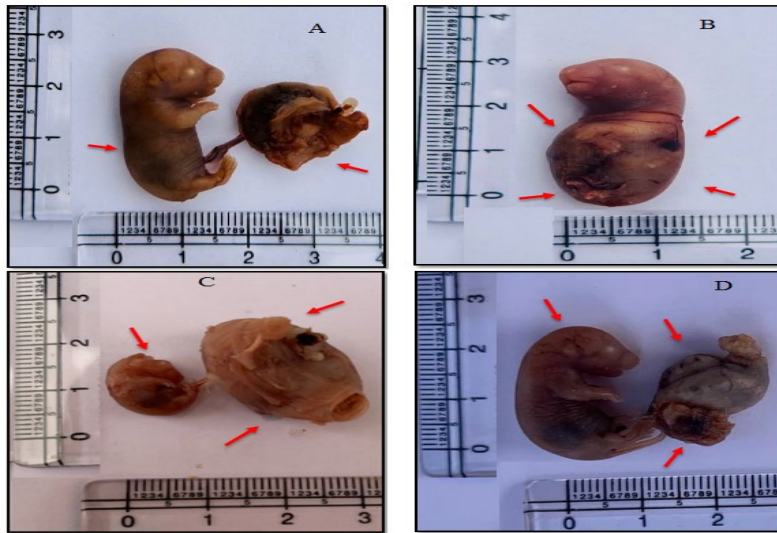


FIGURE 5: Fetuses of Females that were Mated with a Male that was Gavaged with 1200 mg/kg of Lead Acetate. A- One of the Fetuses of the First Female, B- One of the Fetuses of the Second Female, C- One of the Fetuses of the Third Female, D- One of the Fetuses of the Third Female.

Fetuses of the Sixth Group Treated with 60 mg/kg of Cadmium Chloride and 60 mg/kg of Lead Acetate: We note from the current study the effect of 60 mg/kg of cadmium chloride and 60 mg/kg of lead acetate after dosing them to males and mating them to undosed females, and explaining their effect on their fetuses, as three females were mated with a male.

The first female was born after twenty days and the second female was born after Twenty-one days later, the third female had a miscarriage after fourteen days. We notice the effect on the fetus of the

first female, as in picture (6-A): deformities in the fetus's body, a slightly extended neck, which is believed to be a deformity in the nervous and skeletal system, a straight back, and shortened forelimbs. As for the fetus. The second female is as in the picture (6-B).

We notice the shortness of the front limbs, as well as the shortness of one of the legs, with a twist in the tail. The third female was dissected as in the picture (6-C). We notice that the fetuses are not equal in the horns of the uterus, as well as the fetus in the third female, as in the pictures (6-D). It is small in size and the placenta is large.

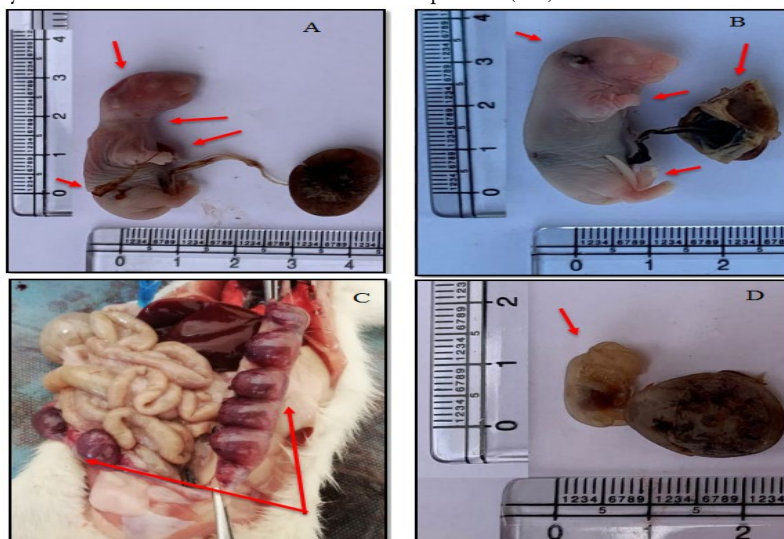


FIGURE 6: Female Embryos that were Mated with a Male that was Dosed with 60 mg/kg of Cadmium Chloride and 60 mg/kg of lead acetate. A- One of the Embryos of the First Female, B- One of the Embryos of the Second Female, C- The Uterine Horns of the Third Female, D- One of the Embryos of the Third Female.

Although rare, cadmium, a non-essential metal, poses a significant threat to unborn babies and pregnant women. It readily accumulates in the mother's body and crosses the placenta, reaching the developing fetus. This exposure disrupts essential gene expression in the fetus, leading to abnormal development and congenital malformations. The harmful effects of cadmium extend beyond its effect on the placenta. It directly affects the fetus, altering genetic expression and making healthy growth difficult. This intervention can cause structural and functional abnormalities in some tissues and organs, which can lead to lifelong health problems for offspring [13]. Additionally, exposure to cadmium during pregnancy can increase the risk of premature death and various diseases in the fetus. Its ability to generate free radicals and stimulate cell death damages the kidneys and also affects bone health. Decreased bone mineralization and increased risk of fractures and osteoporosis are possible consequences of cadmium exposure. This damage is likely due to decreased calcium absorption, leading to a condition called osteomalacia [14]. When young mice are exposed to cadmium during critical periods of bone growth, they suffer severe skeletal deformities. These conditions include fused legs, shortened arms, complete loss of limbs, abnormal bone formation in the chest and ribs, deformed bones in the face and hind legs, and swelling. Studies in several animals confirm cadmium's ability to harm developing fetuses and cause birth defects. It accumulates in the human placenta and high maternal exposure results in elevated levels in the baby's umbilical cord blood. This toxic metal can constrict small blood vessels in the placenta, preventing nutrients from reaching the fetus. Additionally, excess connective tissue around the baby's blood vessels disrupts protein and fluid balance, while decreased growth factors contribute to the possibility of cadmium causing birth defects [15]. Cadmium, a hidden villain in the body, does not need to penetrate cells to cause problems. By changing the receptors on the surface of the cell, you disrupt communication and alter its internal processes. But that is not all! This tricky mineral love to play with essential minerals like zinc, iron, and calcium. It binds them together, prevents them from doing their job and causes an imbalance throughout the body. This interference leads to significant changes in the structure and function of different organs and ultimately leads to disease [16]. Lead, a common but highly toxic metal, easily reaches our bodies and causes harm to babies. It acts as a master of disguise, mimicking essential minerals and bypassing the defenses of the placenta and even the baby's brain. Once inside, it begins its dirty work, causing widespread changes in the baby's genes and the small messengers that control its development. This leads to a variety of birth defects and lifelong health problems [17]. Think of driving as a bully attacking a child's red blood cells, their source of oxygen. It alters their production, weakening and deforming them, which causes anemia and difficulty breathing. But the evil power of bullets extends far beyond blood. It alters the nervous system, making learning and thinking difficult. It affects the kidneys, heart, and even the child's ability to have children in the future [18]. Lead, the insidious villain lurking in our environment, not only harms the

bones of adults but also poses a serious threat to babies developing in the womb. Studies have shown that it is one of the main causes of osteoporosis, because it weakens bones through several mechanisms: (a) Leads to bone breakdown: Lead causes the body to produce too many bone cells (bone cells), which leads to faster bone growth. Loss. (b) Oxidative stress: It creates an imbalance of harmful molecules, which further damages bone cells. (c) Alteration of vitamin D: Lead alters vitamin D levels, which is critical for bone health. (d) Mineral disorganization: It interferes with the way minerals such as calcium are incorporated into bones, causing them to weaken [19]. but this is not all! Lead also penetrates the placenta, which is the umbilical cord that connects the mother and the baby. Here's how it harms fetuses: (a) It reaches the fetus: Lead travels through the umbilical cord, directly affecting the baby's development. (b) Calcium mimicry: During spermatogenesis, lead can replace calcium and enter the developing fetus. (c) Placental damage: Accumulation of lead in the placenta impairs its function, affects fetal growth, and potentially causes mutations and birth defects [20].

Our research confirmed this, showing thick placental walls due to lead and cadmium accumulation. This thickening cuts off the flow of nutrients and oxygen to the baby, stunting his growth. Lead may seem harmless, but this hidden metal hides a dark secret. It can wreak havoc on your body, attacking various systems such as your heart, digestion, nerves, and most importantly, your ability to have children.

For men: Lead can play with sperm, making them fewer, weaker, and even oddly shaped. This can make it more difficult to have a baby. For women: Lead can cross the protective barrier between you and your baby, which can cause miscarriage, premature birth, or even birth defects. This is because it can interfere with your reproductive system and even harm the developing brain and bones of your baby. The Damage Doesn't Stop There: Lead can also affect your heart, making it work harder and increasing your risk of heart disease. It can mess with your digestion, causing stomach aches and constipation. And it can even damage your nervous system, making it harder to think clearly and move your body easily. Remember: Lead exposure is preventable. Taking steps to avoid lead in your environment, like using lead-free paint and avoiding contaminated water sources, can protect your health and the health of your future family [21].

Conclusion

We conclude from the above that cadmium chloride and lead acetate have an effect on the embryos at all the studied concentrations, leading to the occurrence of malformations in at least half of the resulting embryos.

These malformations include shortening of the forelimbs, protrusion of the mouth, difference in the curvature of the back, small size of the embryo, difference in the shape and size of the placenta, and non-equal distribution of embryos in the horns of the uterus. In some cases, the effects have reached the death of mothers, as well as the occurrence of cases of abortion of embryos before the due date of birth.

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