Histological Changes on The Liver of The Mothers Treated with Uranyl Acetate in Albino Rats.

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Abstract
This study was carried out to investigate the toxicity of the oral administration of uranyl acetate on some activity organs. For this purpose, twenty females mature Albino rats which were divided into four equal groups, control group administrated distilled water, and other three groups administrated orally by (50, 75 and 100 mg/kg/b.w. /day of uranyl acetate). The route of administration was oral intubations for 70 days (10 weeks), for 10 days before mating with untreated males, as well as during pregnancy (3 weeks) and lactation (5 weeks). liver were taken from mothers of rats.
Results of histopathological changes to the liver of rat mothers showed congestion to the central vein, congestion to the sinusoid capillaries, and swelling of the hepatocytes. Vacuolation of the cytoplasm of the hepatocytes, and necrosis to the hepatocytes, also slight hyperplasia to kupffer cells and, Lipid vacuolation in the cytoplasm.

Introduction:
Uranium(U) is found in very small amounts in nature in the form of minerals, rock, soil, and surface and under ground [1]. Water, air, plants and animals all contain varying amounts of U [2].
The etiology of this effect is unknown, although histological signs of hepatic toxicity have been observed in animals after oral exposure to U. In the available animal studies, the existing data provide evidence that U exposure can damage the liver [1]. In an acute-duration study in which Sprague- Dawley rats were given single gavages doses of 5.6 or 118 U/kg as uranyl acetate dihydrate, micro haemorrhagic foci in the liver were observed at both doses tested [3].
Hepatic toxicity was also found several other studies. In one study, Sprague – Dawl rats were exposed to U as uranyl nitrate in drinking water (males: up to 36.73 mg/kg/day; females: up to 53.56 mg/kg/day) for 91 days and then sacrificed. Hepatic lesions, which included anisokaryosis , vesiculation, increased portal density, perivenous vacuolation, and homogeneity, were observed in the liver at all doses [4] , although the dose ranging portion of this study found no effects at essentially the same doses as those discussed below [5]. However, in New Zealand rabbits exposed to U as uranyl nitrate in the drinking water (males: 0, 0.05, 0.20, 0.88, 4.82, and 28.70 mg/kg/day; females: 0, 0.49, 1.32, and 43.02 mg/kg/day) for 91 days, no treatment-related histopathological changes were found, and no changes in liver weights were noted [6].
In contrast, another study by the same investigator in male New Zealand rabbits exposed to U as uranyl nitrate in drinking water (1.36 and 40.98 mg/kg/day) for 91 days found irregular accentuation of zonation in the liver, accompanied by increased variation in hepatocellular nuclear size, nuclear pyknosis, and extensive cytoplasmic vacuolization. These changes were found to be treatment-related but not dose-related [5].
Children can not be considered as small adults in relation to their exposure to U. They differ from adults in their exposures and susceptibility to hazardous chemicals[7,8]. More resent study has examined the teratogenic and embryo toxic effect and reproductive outcome of uranyl acetate dehydrate in Swiss albino mice [9].

Materials and Methods:
Experimental Design:
Thirty (10 males and 20 females) sexually mature laboratory breed males and females Sprague- Dawley Albino rats (*Rattus norvegicus*) of an average body weight of 230±3.565 gm and 12-15 weeks old were obtained from animal house of the national center for censorship and curative researches in Baghdad.
The rats were randomly divided into four groups. Each group were kept into box cage measuring 40×25×15 cm . Female rats were mated with males (2:1) until copulation was detected. Finding of sperm indicated copulation and the day of detection were designated as Day 0 of gestation. Then the adult fertile females were treated with uranyl acetate dihydrate (UAD) by gavages 10 days w before mating with untreated males, as well as during pregnancy and lactation [10]. The first group served as a control and only receive drinking water .However three concentrations of uranyl acetate dissolved in water were administrated gavages to three other groups of females (50,75,100 mg/ kg/ B.W/ day). The dose of (UAD) is based on results of previous study [11, 12].
The animals were killed by cervical dislocation, then each group were scarified directly and liver was taken from the dams (mothers)
Histological procedure:
Animals were killed and small piece of liver tissue taken from experimental animals were fixed in 10% neutral formalin, alcohol-dehydrated, paraffin-embedded and the section to mean thickness of 4 µm. The histological examination was evaluated by assessing the morphological changes with Hematoxylin and Eosin (H&E) stains. **Results:**
The present histological examination of liver cells of mothers showed a normal hepatocytes arranged as

plates around the central vein with sinusoid between the liver plate (Fig.1).
The liver of mother G3 and G4 ,showed congestion to the central vein, and swelling of the hepatocytes as(fig.2).vaculation of the cytoplasm of the hepatocytes, necrosis to the hepatocytes, and hyperplasia to kupffer cells (Fig.3,4,5).

While Section of liver of mother G2 ,showed congestion to the central vein ,and perivascular (infiltration of inflammatory cells) as (Fig.6) increased inflammatory cells ,and necrosis to the hepatocytes (Fig.7).focal Infiltration of the kupffer cell (Fig.8).

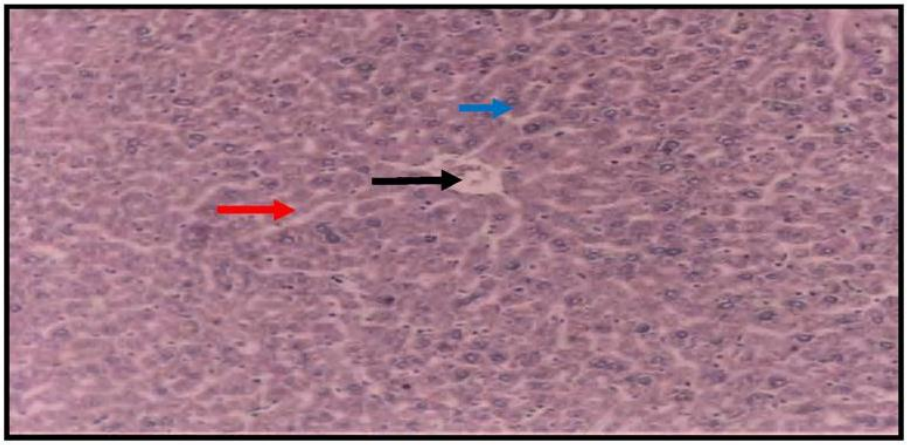

Fig.(1): Liver of control (G1) showed (→) Normal central vein, (→) normal hepatocytes, (→) Normal arrangement of liver plate , H&E (100X).

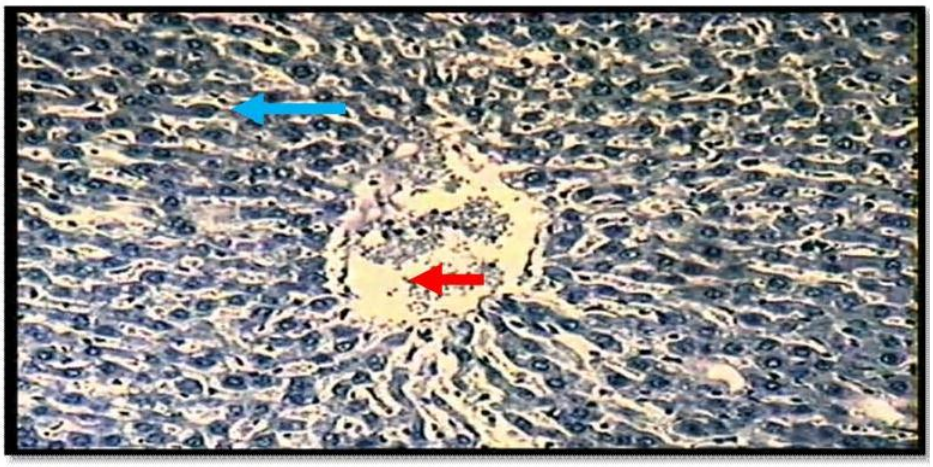

Fig. (2): Liver of mother(G4), showed (←) Congestion of the central vein, (←) Swelling of the hepatocytes,(100X).

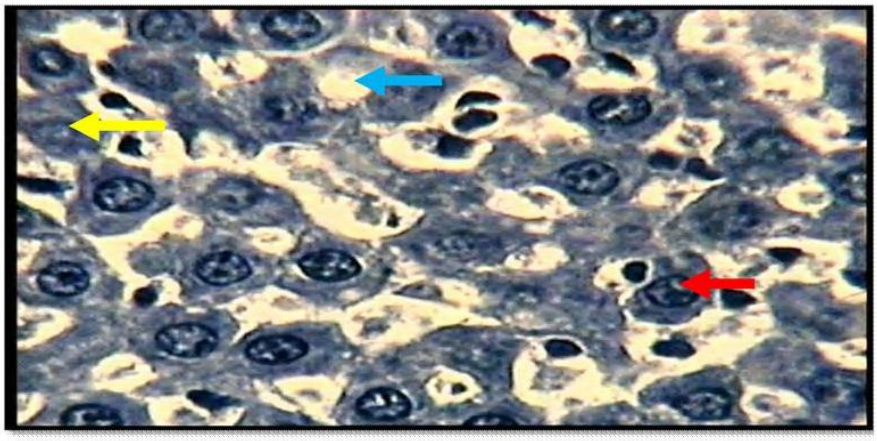

Fig.(3): Liver of mother (G4),showed ( ) Vaculation of the cytoplasm of the hepatocytes, ( ) Necrosis to the hepatocytes, ( ) hyperplasia to kupffer cells,(400X).

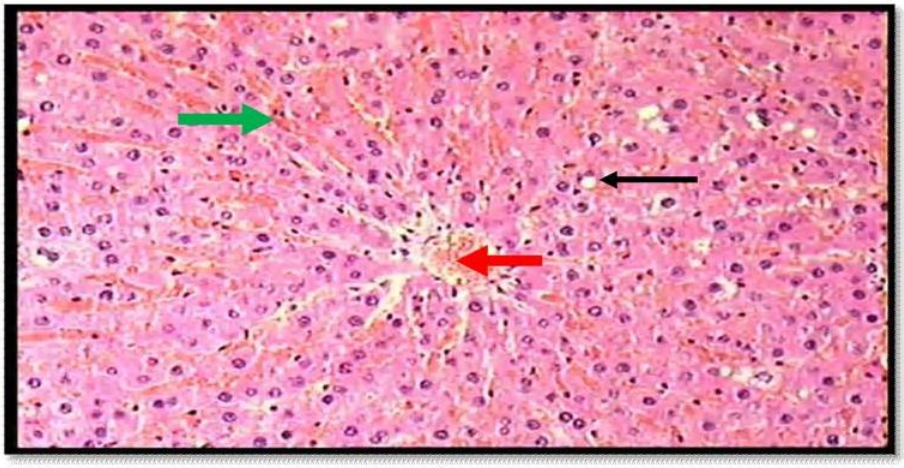

Fig. (4): Lliver of mother(G3), showed ( ) Vaculation of the cytoplasm of the hepatocytes, ( ) Congestion of the central vein, ( ) Congestion to the liver sinosoid (100X).

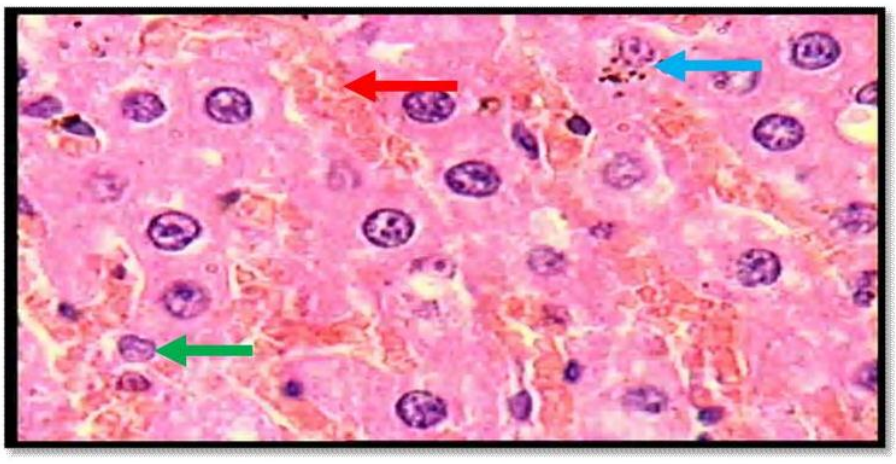

Fig.(5):Lliver of mother(G3),showed ( ) Congestion to the sinusoidal capillaries ,( ) Necrosis to the hepatocytes, ( ) Fragmentation the nucleus of hepatocyte ,(400X).

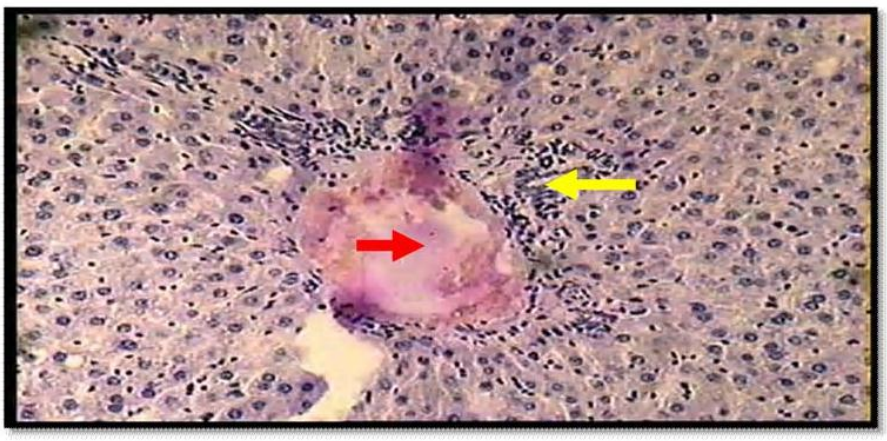

Fig.(6): Section of liver of mother (G2),showed ( ) Congestion to the central vein, ( ) Perivascular infiltration of inflammatory cells,(100X).

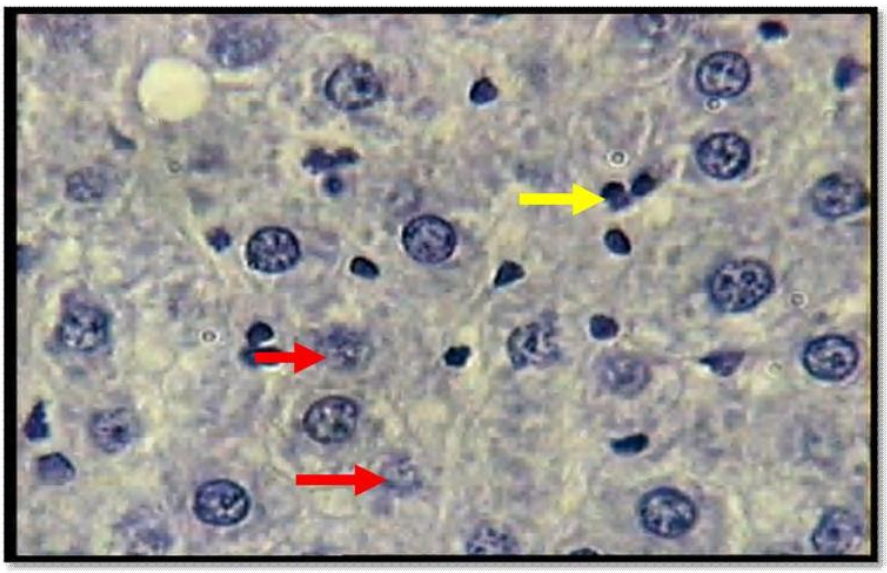

Fig.(7): Section of liver of mother (G2),showed ( ) Increased inflammatory cells , ( ) Necrosis to the hepatocytes ,(400X).

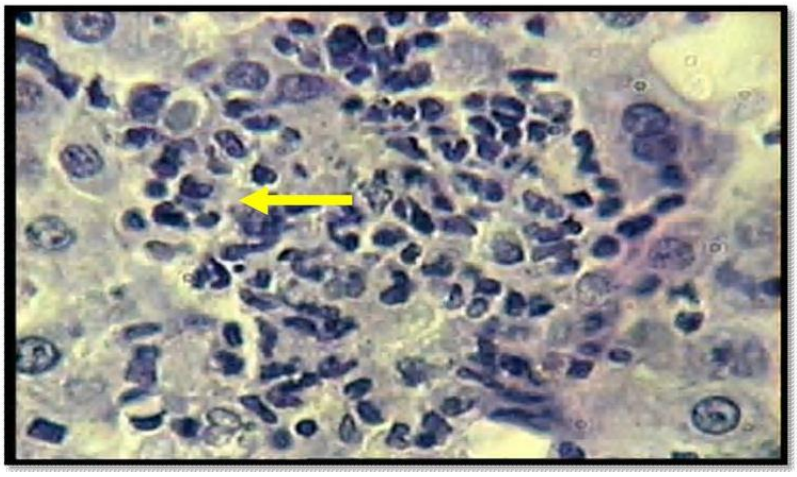

Fig.(8): Section of liver of mother(G2), showed ( ) Focal Infiltration of the kupffer cells, (400X).

Discussion:

Liver is the most sensitive organ for U toxicity in both humans [13] and animals [3,14].Section of liver of mother G4 and G3 showed congestion of the central veins and congestion to the liver sinusoidal capillaries, swelling of the hepatocytes. Vaculation of the cytoplasm of the hepatocytes, necrosis to the hepatocytes, and slid hyperplasia to kupffer cells. Necrosis to the hepatocytes, and fragmentation of nuclei of the hepatocyte and perivascular kupffer cells.

Liver of the mother G4 and G3 Showed congestion to the sinusoid capillaries, and vaculation in the cytoplasm of the hepatocytes .also, necrosis to the hepatocyte and hyperplasia to the kupffer cells.

Section of liver of mother G2 showed congestion to the central vein, and perivascular infiltration of inflammatory cells, increased inflammatory cells, and necrosis to the hepatocytes and Focal Infiltration of the kupffer cell.

UA translate to the offspring across placenta to the fetus and during the lactating [15].

Necrosis is characterized by hepatocyte vacuolation, degeneration, and necrosis in the mother and their offspring . Hemorrhage and a mild, diffuse mononuclear cell infiltrate is evident [16]

Hepatic lesions, which included anisokaryosis, vesiculation, increased portal density, perivenous vacuolation, and homogeneity, were observed in the liver at all doses these results were agree with study of Gilman *et al*., (1998a) [4]

Irregular accentuation of zonation in the liver, accompanied by increased variation in hepatocellular nuclear size, nuclear pyknosis,and extensive cytoplasmic vacuolization, these results be in agreement with Gilman *et al*., (1998c). [5]

Liver congestion, minimal hepatic lesions, mild degeneration, or fatty infiltration which appeared in this study was similar to the results of Maynard and Hodge (1949) [17] in his study on the dogs.

Heavy metals including U have a strong affinity for many biological molecules containing phosphate residues such as glucose phosphate, phospholipids, and nucleic acids, or sulphydryl groups including cysteine, glutathione, and many proteins. Because of this high affinity U does not exist as a free ion in biological systems, rather it is present in complexes with a variety of molecules(Hursh and Spoor, 1973). [18]

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التغيرات النسجية في كبد أمهات معاملة بخلات اليورانيوم في الجرذان البيض

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الملخص

أجريت هذه الدراسة للتحقق من سمية خلات اليورانيل المعطاة عن طريق الفم على الكبد في الجرذان البيض.استخدمت لهذا الغرض20 (جرذ) من الإناث الناضجة (Albino) وقسمت إلى أربع مجاميع متساوية، مجموعة السيطرة (G1) وقد جرعت بالماء المقطر، ومجموعة (G2) جرعت بتركيز (50ملغم/كغم/وزن الجسم) من خلات اليورانيل، ومجموعة (G3) جرعت بتركيز (75ملغم/كغم/وزن الجسم) من خلات اليورانيل، ومجموعة (G4) جرعت بتركيز (100ملغم/كغم/وزن الجسم) من خلات اليورانيل لمدة 70يوم (10 أسابيع)، جرعت الإناث لمدة 10 أيام قبل التزاوج من قبل ذكور غير مجرعة وكذلك أثناء فترة الحمل (3 أسابيع) وفترة الرضاعة(5 أسابيع). تم أخذ الكبد بعد تشريح الأمهات لغرض إجراء الدراسة.

أظهرت نتائج الفحص النسجي المرضي للكبد للأمهات المعاملة بخلات اليورانيل ، حدوث نزف في الوريد المركزي الكبدي والشعيرات الدموية للجيبانيات الكبدية وكذلك تكون فجوات في السايتوبلازم وتنخر في الخلايا الكبدية وتجمع خلايا كبفر البلعمية والتفجي الدهني في السايتوبلازم.