# LEAD INTOXICATION: NATURE OF STRUCTURAL DAMAGE IN THE KIDNEY, LIVER, LUNG, TESTIS, EPIDIDYMIS AND SPLEEN

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## ABSTRACT

The damaging effects of lead poisoning to various organs of the body have been severally reported; as well as the health complications they produce. There are however relatively few reports on the nature of such effects on body tissues- histology, most publications have rather addressed the resulting complications. The proper understanding of the nature of the effects of lead poisoning on body tissues could help in understating the cause of the complications and may provide insights into better ways of managing lead poisoning effects. This research investigated the effects of lead poisoning on a number of vital body tissues histology. Twelve Wistar rats were distributed into two groups: Group A being the control and Group B was administered 50mg/kg body weight of lead-in-water for a period of 28 days that the experiment lasted. The tissues were excised, fixed in formal saline and processed using the routine Haematoxylin and Eosin staining technique. Photomicrographs were obtained and analysed critically using qualitative histological principles. Lead produced observable deleterious effects on all tissues tested, the extent however vary greatly: from its extensively disruptive effects on the kidney tissues. Kidney glomeruli tubules were morphologically distorted while tubular cells show signs of assault and morphological distortions. Testis histo-architecture and epididymis epithelium were also disrupted. The spleen pulps, especially white, show sign of damage while bone marrow cells are fewer in the lead intoxicated group. Liver cells and

alveolar epithelium showed signs of damage; Lead poisoning effects was observed in all the tissues.

**Keywords**: Lead Poisoning Tissues Histology Wistar Rat

## INTRODUCTION

Lead could get into the body via various means including drinking water (Maas *et al.*,, 2005), intoxicated food (Goyer and Clarkson 2001; ATSDR, 2005), contaminated air, occupational and industrial exposures (Hurst and Martin, 2004; Mudipalli, 2007) and ingestion of lead-containing materials among other ways. One of the major problems associated with lead poisoning is the possibility of its prolonged half-life in the body in tissues, especially the bones (Pounds *et al.*,1991), from where it can be re-introduced into the body during bone resorption and remodelling and transported in the blood circulation to every part of the body where it could produce continuous ill effects .The overlapping effects of the continuously circulating metallic poisoning in the body is what is responsible for the seriously compromising effects; hence the real effects of lead poisoning on the body can best be appreciated by investigating such effects on the whole body rather than individual tissue at a time. This is no doubt one of the strengths of the current investigation- a critical histological observation of the lead exposure on body's vital tissues under the same biological and environmental conditions.

The interactive mechanisms through which lead affects cells have been reported in a number of publications. These include induction of oxidative stress (Adonaylo and Oteiza, 1999; Sharma *et al.*, 2010; Upasani *et al.*, 2001).), mimicking or acting as antagonist of biological ions and chemicals (Aleksandrov et al.,1996) among others. Also, lead could inhibit enzymes activities, alter the structure

of cell membranes and receptors and could bind with proteins required for cellular functions (Hurst and Martin, 2004). There are existing reports on lead poisoning but several are case studies and epidemiological reports. It is however important to model the specific nature of lead poisoning in order to appreciate the specific nature and effects. This understanding will contribute to developing measures of management and possibly, rejuvenation of body tissues. The main objective of this investigation is to observe the effects of lead poisoning on a number of body tissues including kidney, lung, spleen and liver and reproductive tissues including testis and epididymis. The study included the observation of the histoarchitectural organisation of the tissues in terms of the cytological elements, considering morphologies and spatial distribution- as well as the extracellular materials. Very importantly, attention is paid to the characteristic histological architecture of the tissues.

## MATERIALS AND METHODS

Experimental animals were twelve [n=12] adult male Wistar rats. They were randomly divided into two Groups- A and B of six rats each and were allowed to acclimatise. Group A animals served as the controls and the animals were fed *ad libitum* throughout experiment. Group B were administered 50mg/kg body weight of lead, using water as a vehicle. Administration was done orally using suitable gavages. The treatment of animals lasted twenty eight days and animals were sacrificed by cervical dislocation twenty four hours after the last administration. Animals were sacrificed by cervical dislocation. The tissues were carefully excised through surgical dissections. Processing of fixed tissues was carried out using the haematoxylin and eosin staining technique [Baker, 1962]. Histological slides of the tissues were studied, analysed; [representative] photomicrographs were also taken using the Accuscope Phomicrographic Set. Tissues were thereafter analysed using qualitative histological

principles with emphasis on cytological features integrity, spatial organisation of cells, and general histoarchitectural organisation.

## RESULTS

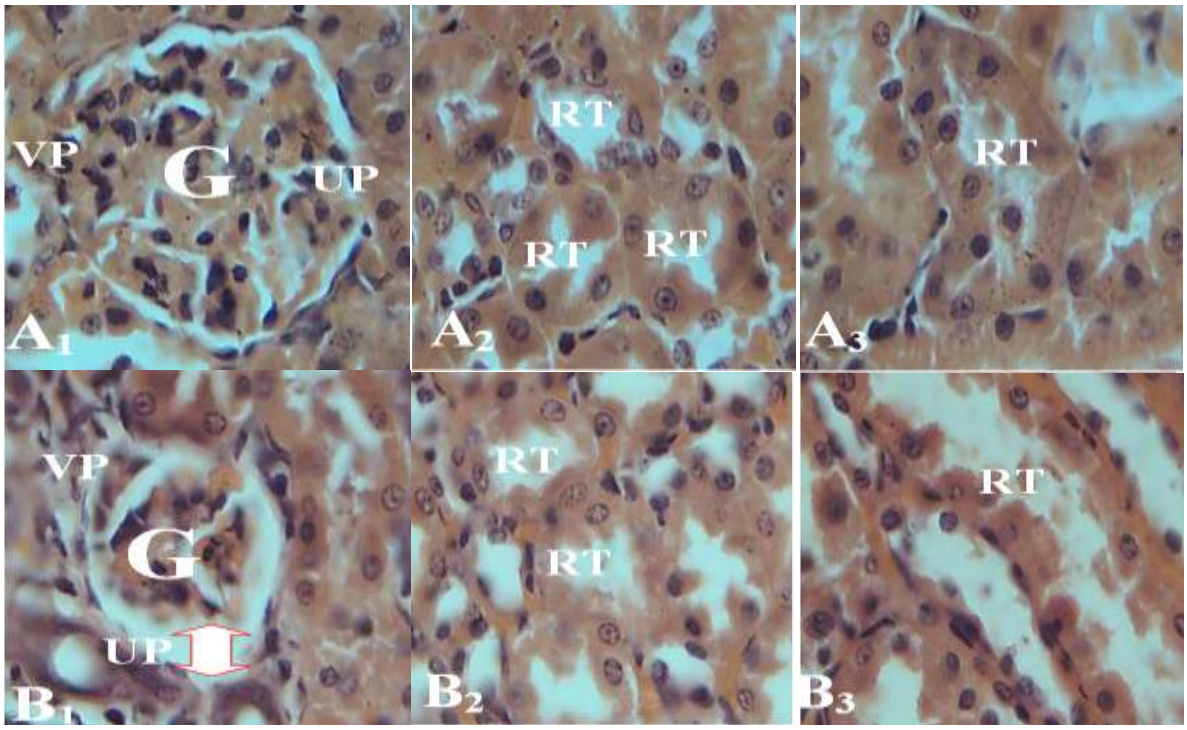


**Figure 1:** Photomicrographs of the kidney of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A kidney at X640 [glomerulus] X640 [small renal tubules] and X640 [large renal tubules]. All photomicrographs portray features of normal kidney; tubules and glomeruli are identifiable and well defined. $B_1$, $B_2$ and $B_3$ are photomicrographs of the Group B exposed to lead poisoning at X640 [glomerulus] X640 [small renal tubules] and X640 [large renal tubules]; glomerulus appears distorted and relatively shrunken and tubular epithelial cells present heterogeneous morphology in some parts. [G= Glomerulus; VP= Vascular Pole; UP= Urinary Pole; RT = Renal Tubules]

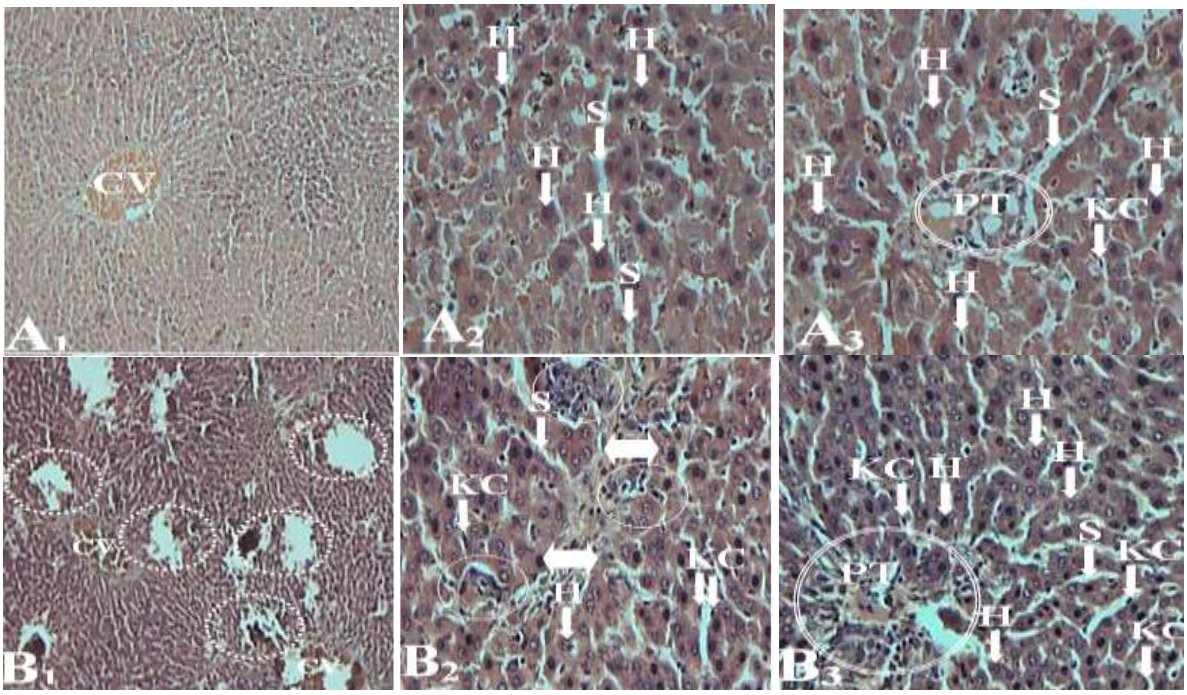


**Figure 2:** Photomicrographs of the liver of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A liver X160[general histo-architecture] X640 [cellular organisation] and X640 [characteristic features]. Photomicrographs portray features of normal liver; histo-architecture is well defined. $B_1$, $B_2$, $B_3$ are photomicrographs of the Group B exposed to lead poisoning at X160[general histo-architecture] X640 [cellular organisation] and X640 [characteristic features]; there are features of extensive tissue damage and altered cell morphology resulting from lead toxic assault. [H= Hepatocyte; CV= Central Vein; S= Sinusoids; KC= Kupfer Cell; PT= Portal Triad]

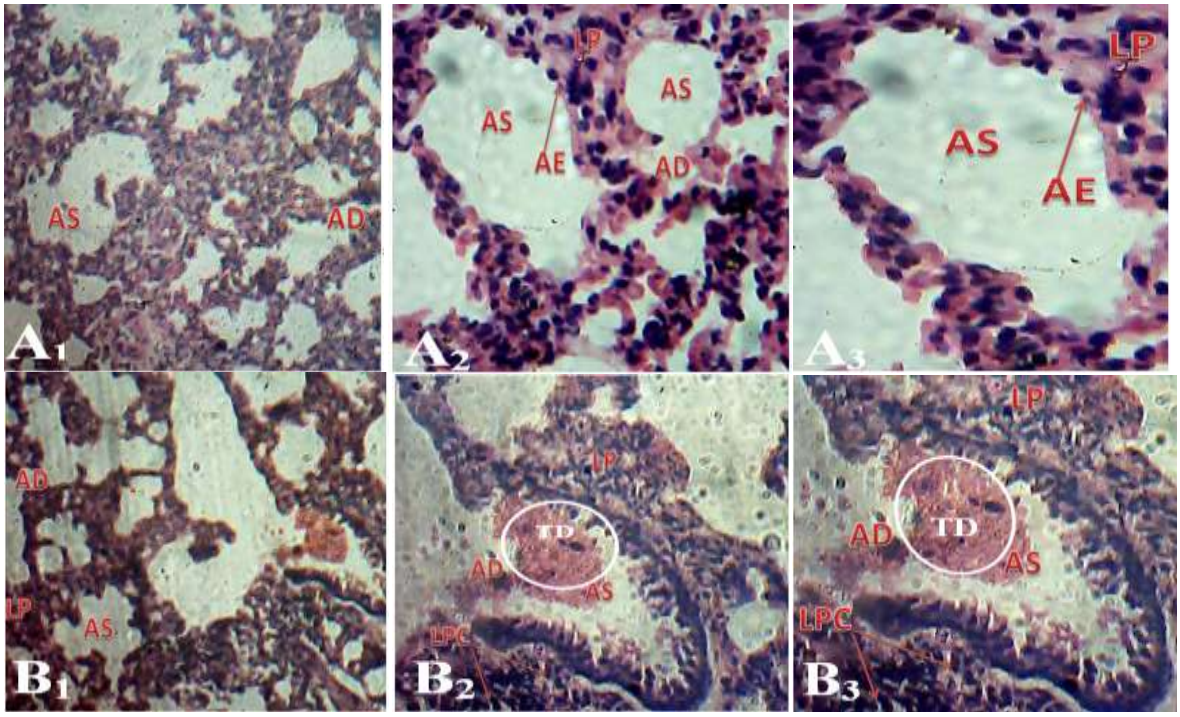


**Figure 3:** Photomicrographs of the lungs of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A lung X160[general histo-architecture] X640 [alveolar ducts and sacs] and X640 [alveolar sac and epithelium]. Photomicrographs portray features of normal lung; histo-architecture is well defined. B1, B2, B3 are photomicrographs of the Group B exposed to lead poisoning at X160[general histo-architecture] X640 [alveolar ducts and sacs] and X640 [alveolar sac and epithelium]; there are features of tissue damage including altered alveolar morphology and presence of tissue debris within alveolar sacs. [AS= Alveolar Sac; AD= Alveolar Duct; AE= Alveolar Epithelium; LP= Lung Parenchyma; TD= Tissue Debris]

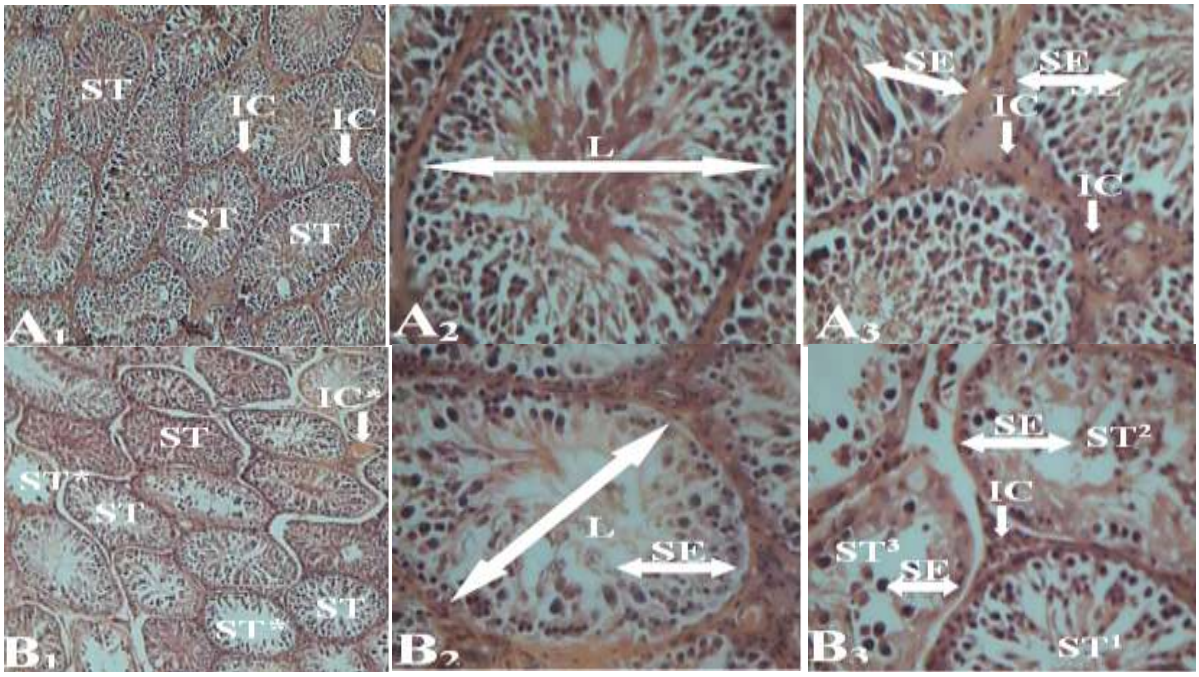


**Figure 4:** Photomicrographs of the testis of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A testis at X160[general histo-architecture] X640 [seminiferous tubule cross section] and X640 [tubules-interbubular organisation]. Photomicrographs portray features of normal testis; histo-architecture is well defined. B1, B2, B3 are photomicrographs of the Group B exposed to lead poisoning at X160[general histo-architecture] X640 [seminiferous tubule cross section] and X640 [tubules-interbubular organisation]; there are disruptions to the seminiferous tubules and their epithelium as well as damage to interstitial tissues. [ST= Seminiferous Tubules; L= Lumen; SE= Seminiferous Epithelium; IC= Interstitial Cells].

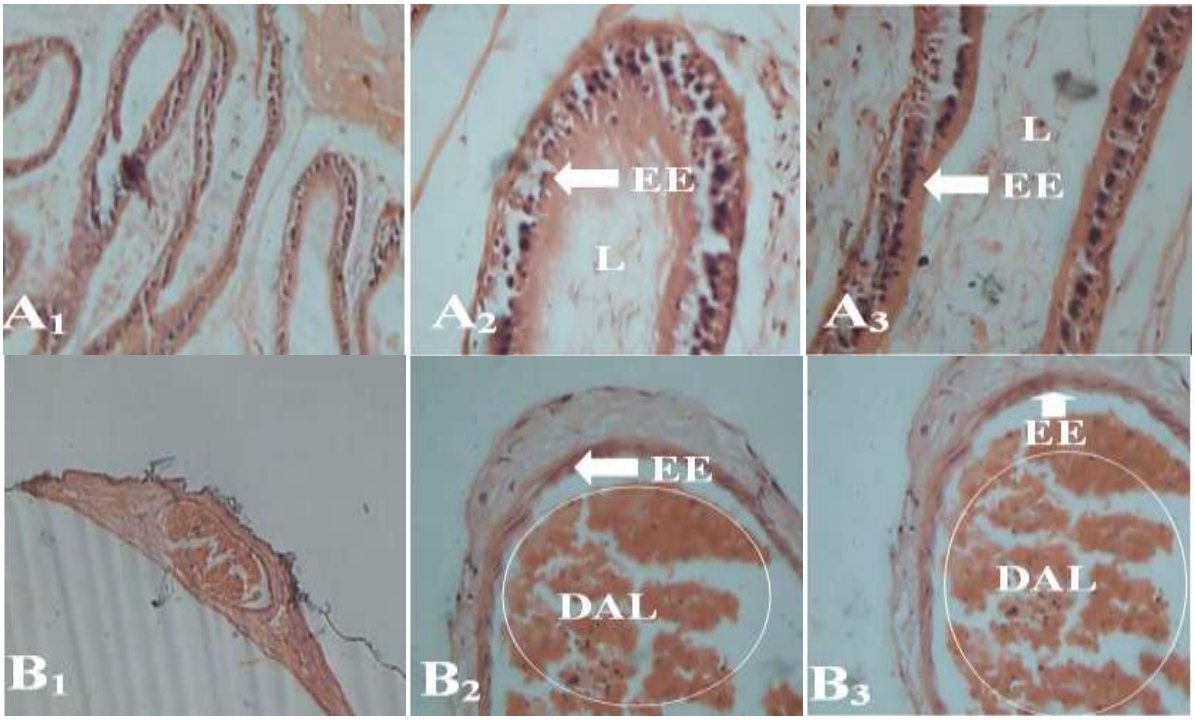


**Figure 5:** Photomicrographs of the epididymis of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A epididymis at X160 [cross sections], X640 [epithelium and lumen] and X640 [epithelium]. All photomicrographs portray features of normal epididymis; epithelium of the hippocampus is well defined. $B_1$, $B_2$, $B_3$ are photomicrographs of the Group B exposed to lead poisoning at X160 [cross sections], X640 [epithelium and lumen] and X640 [lumen and debris]; there is extensive epithelial disruption of the epididymis, and unusual lumen-filled debris accumulation. [EE= Epididymis Epithelium; L= Lumen; DAL= Debris Accumulation in the Lumen].

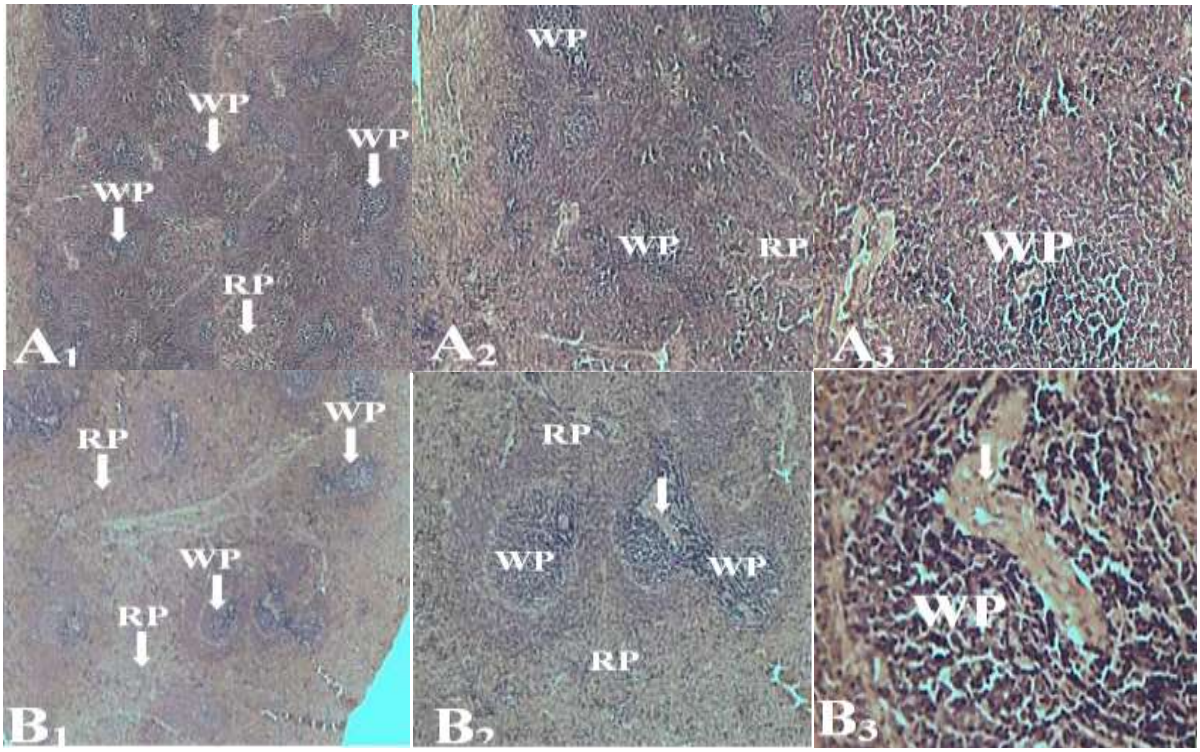


**Figure 6:** Photomicrographs of the spleen of experimental animals; $A_1$, $A_2$ and $A_3$ are illustrations of the Control Group A spleen at X64 [general histo-architecture] X160 [pulps and supportive tissues] and X640 [white and red pulps]. Photomicrographs portray features of normal spleen; histo-architecture is well defined. $B_1$, $B_2$, $B_3$ are photomicrographs of the Group B exposed to lead poisoning at X64 [general histo-architecture] X160 [pulps and supportive tissues] and X640 [white and red pulps]; overall histo-architecture is poorly defined and there are disruptions to the white pulp. [WP= White Pulp; RP = Red Pulp]

## DISCUSSION

### Kidney

The kidney of the Control Group A animals illustrated as Figure A1 [glomerulus], Figure A2 [renal tubules] and Figure A3 [renal tubules]. All basic features are well defined and normal in histo-morphological appearance. Figures $B_1$, $B_2$ and $B_3$ are photomicrographs of the kidney of the Group B animals exposed to lead poisoning-glomerulus and renal tubules

respectively. The glomerulus is a vital component of the kidney cortex; Group B glomerulus [labelled G in figure B1] is relatively smaller and poorly defined. There are fewer cells [podocytes] within the glomerulus and the few observable cells are not well defined morphologically. The peri-glomerular space appears unusually wide especially in the region of the urinary pole [UP]; even around the vascular pole [VP] the histological integrity appears compromised as the glomerulus appears partially detached from the adjacent tissues. There are features that suggest tissue or cellular damage within the glomerulus such as presence of damages tissue and blood vessels. The small renal tubules in $B_2$ also show signs of tissue distortion are they are relatively disproportionate especially in terms of their average width and epithelial organisation. Figure $B_3$ illustrates the large renal tubules; several cells appear to constitute a squamous epithelium contrary to the supposedly predominant simple cuboidal type- only the ascending thin limb is basically squamous of the tubules. There are other features, such as the heterogeneous appearance of the tubular cells with respect to their morphology, likely indicating an assaulting effect of lead on the tubules. The kidney of the animal group esposed to lead poisoning therefore show histo-morphologcally observable signs of the deletrious effects of lead on its basic features especially the glomerulus of the cortex and all tubules- whether within the cortex or the meddula. This would most likely produce compromising effects on renal fucntions. A number of investigations have re[ported deleterious effects of lead poisoning on kidney tissues, especially, tubular necrosis (Greenberg, 1990; Vvskocil et al., 1995; Loumbourdis, 2003; Durgut *et al.*, 2008).) and glomerular tuft degeneration (Sageb et al., 2001) and these are in line with the current findings.

**Liver**

The first three photomicrographs- $A_1$, $A_2$ and $A_3$ are illustrations of the liver tissue of the Control Group A animals. The general histo-architecture can be appreciated, the plates of hepatocytes [H] are separated regularly by sinusoids [S] and the central vein [CV] [Figure 1A] can be observed. The Kupfer cells are also present. Other features include the portal triad of structures- hepatic artery, vein and the bile duct. The liver tissue of the Group B animals exposed to lead poisoning is being illustrated at various magnifications in $B_1$, $B_2$ and $B_3$. $B_1$ [lowest magnification] shows areas of extensive tissue damage [encircled]. Figure 8- $B_2$ also shows areas of deformed tissues- aggregates of cells that have lost their normal individual forms or morphology as well as the normal organisation to form tissues. The encircled areas show clustered cells that are typically smaller in sizes than the normally organised neighbouring cells and they appear not separated by sinusoids. Kupfer cells are hardly defined or observable in such clusters. In Figure 2- $B_3$, the illustrated area of portal triad appear to have mildly lost its integrity. All the aforementioned unusual observations on $B_1$, $B_2$ and $B_3$ are obviously abnormal and could constitute tissue malfunctions. Deformed hepatocytes could malfunction as well as distorted tissues in terms of organisation. Obviously, several vital functions of the liver as an organ could be compromised. Though there are large portions of normally appearing cells and tissues, the deformed areas would reduce efficiency of liver functions or even general compromise. A number of previous investigations had reported cell necrosis and tissue vacuolization (Nehru and Kaushal, 1993; Abd El-aal *et al.,* 1989). Liver, as well as the kidney are most affected soft tissues by lead poisoning and hepatotixicy due to lead poisoning has been reported (Jankeer and El-Nouri, 2009;

Lyn, 2006; Goswani *et al.*, 2005; Sipos *et al.,* 2003). Other histological observations reported include tissue degeneration, necrosis of the parenchyma of hepatic lobule and disruption of the normal morphology of hepatocytes (Jankeer and El-Nouri, 2009; Piasek et al., 1989 ; Kojima et al., 2005; Durgut et al., 2008)

**Lung**

The photomicrographs $A_1$, $A_2$ and $A_3$ illustrate the histological architecture of the lung tissue of the control Group A at various magnifications and with emphasis on the various vital features of the tissue. The alveolar sacs are lined by the simple squamous that though quite thin by virtue of its cell sizes and thickness- a vital functional factor- could still be observed. The supportive tissues are also present; the alveolar ducts lead into the sac as air conduits. The Group B lung tissue shows signs of extensive disruption- there are deformed alveolar sacs, some others appear to have merged with neighbouring sacs and this is most likely due to destroyed thin alveolar walls due to the destruction of the lining cells. Other alveolar sacs are partially opening into others due to partially damaged walls. At the higher magnifications, alveolar epithelium- the simple squamous epithelium- is greatly compromised, it is either non-existent of closely apposed to the underlying supportive tissues. Whichever of the cases it might be, the regular physiological diffusion of air across the membrane would no doubt be compromised. The abnormally enlarged or rather *pathologically compound* alveolar sacs are separated by unusually thick layers of tissues; this would no doubt reduce the overall surface are of the lung that would be available for air gases exchange. A feature that would be of serious functional complication for the lung tissue is the presence of tissue debris

in some of the disrupted alveolar sacs. The lung utilises the alveolar sac space as its functional interactive medium that should only accommodate air in the normal condition. The presence of abnormal tissue debris could render such sacs functionally incompetent, thus limiting the efficiency of the lung as a tissue. All these observations show that lead poisoning would disrupt lung histo-architecture is manners that would produce serious functional compromises and limitations in efficiency. Previous reports on lead poisoning mentioned thickening in the interalveolar septa as well as accumulation of inflammatory cells (Onarlioglu *et al.*, 1999).

**Testis**

The testis tissue of the control Group A [seminiferous tubules] is being illustrated in Figure 4- $A_1$, $A_2$ and $A_3$. The seminiferous tubules are well defined in their transverse cross-sections- the epithelium of developing male gamete cells is well defined and well as the central lumen [L] that it surrounds. The tubules have between them the interstitial tissues. In contrast, the general histo-architecture in the Group B, exposed to lead poisoning is disrupted. At the lowest magnification employed [Figure 11- $B_1$], There are certain seminiferous tubules [ST*] that appear disrupted and abnormal even when compared with their neighbouring tubules. More so, the interstitial spaces appear shrunken and poorly defined; the few observable ones show signs of damage [IC*] suggesting loss or deformation of the cells within these areas. The larger magnifications in $B_2$ and $B_3$show that the epithelia of the various tubules are truly disrupted, the severity however varies considerably. For instance in $B_3$, the tubule below on the right [$ST_1$], appears less severely disrupted [especially in terms of its epithelium] than the one directly above it [$ST^2$]. The most severely affected one, histo-morphologically, is however the one on the lower

left corner [$ST^3$] in which most cells of the seminiferous tubule germinal epithelium are already lost. The particular tubule also appears detached from the adjacent tissues and the tissue of the interstitial space above it in the photomicrograph presentation] is also largely disorganised. All these effects would point to a simple reality-compromise in spermatogenesis. While the staining procedure employed is primarily targeted at giving the best general histo-architectural representation and not at targeting individual cells [as in the case of special staining procedures]; it is logical to note from the observations that the process of production and maturation of spermatozoa is largely compromised; and cells at various stages of development at the time of exposure would be affected. Subsequently, the end product-matured spermatozoa are either not obtained or they rather become morphologically deformed. It is also important to note that this may not mean that the animals would be immediately sterile by being unable to produce spermatozoa, since some seminiferous tubules appear not seriously as affected as the rest and could still manage to produce gamete cells. Yet, the assaults of lead effects could lead to the production of abnormal cells that may give rise to infertility due to morphologically determined spermatozoa inability to fertilise eggs or on the other hand, introduction of congenital anomalies possibly due to altered chromosomal or genetic structures [these are simply possible complications]. Lead has been severally reported to be toxicant for testicular tissue (Hsu *et al.,* 1998a; Hsu *et al.,* 1998a; Barratt *et al.,* 1989; Saxena *et al.,* 1986); the current investigation confirms the reports. Lead poisoning could reportedly halt spermatogenesis (Batra *et al.,* 2001). Furthermore, lead poisoning has been associated with reductions in sperm count and sperm concentration (Naha et *al.,* 2000; Telisman *et al.,* 2000; Apostoli *et al.*, 1998;

Alexander *et al.,* 1998) and reduced volume of ejaculate (Naha et *al.,* 2000; Alexander *et al.,* 1998). Anomalies such as asthenospermia, hypospermia, and teratospermia and others were also reported (Lancranjan *et al.,* 1975; Viskum *et al* 1999).

**Epididymis**

The Control Group A epididymis is represented in Photomicrographs $A_1$, $A_2$ and $A_3$. The epithelium is observable, being normal in morphology and clearly defined in cross section. The lumen can also be observed. Photomicrographs $B_1$, $B_2$ and $B_3$ are representations of the histo-architecture of the epididymis of the Group B exposed to lead poisoning. The epithelium is greatly disrupted- the component cells are lost and the epithelium organisation is non-existent or rather abnormal; the sub-epithelial supporting tissue is however unusually thickened in cross section, though this is most likely predominantly connective tissues or fibres as cells are not closely arranged as they should have been in a muscle. The lumen has unusual accumulation of tissue [DAL] that appears like tissue debris. This is supposed to be the debris of damaged epithelial tissues and possibly in addition, abnormally accumulated spermatozoa. All the mentioned unusual features of the Group B epididymis, especially relative to the normal control Group A are pointers to the deleterious effects of lead poisoning in Group B. These effects would not doubt compromise the fertility of these animals as the epididymis where the spermatozoa are stored [temporality] and nurtured is being compromised; the accumulation of abnormal tissue debris within the lumen that should basically contain spermatozoa also suggests that the health of the spermatozoa would be compromised. Possible implications of these observations would include the presence of abnormal spermatozoa in ejaculates which may not achieve fertilisation or that could rather introduce congenital anomalies into the formed

embryo if such would eventually survive. On the other hand, the anomalies of the conditions during storage and nurture of the spermatozoa within the epididymis may lead to their destruction and subsequently lack or inadequate quantity of spermatozoa in the ejaculate leading to sterility or infertility. The ultimate consequence of the observed effects of lead action on the epididymis would thereof be primarily infertility; other possibilities would include teratogenesis or congenital anomalies. Lead has been reported to reduce the population of spermatozoa within the epididymis (Wadi and Ahmad, 1999); it has also been found to affect the epididymis itself as well as the associated reproductive structures negatively (Ronis *et al,* 1996; Sokol, 1990).

**Spleen**

The spleen red pulps [RP] and the white pulps [WP] are well defined in the control Group A as illustrated in the photomicrographs at the various magnifications employed [figure 6- $A_1$, $A_2$ and $A_3$]. The pulps are also observable in the Group B exposed to lead poisoning; there are however, evidences of tissue damage especially in the white pulp. The white pulps are relatively smaller or less clearly defined. The surrounding areas of red pulp also have evidences of deleterious effects of lead poisoning as the larger-than-usual areas of red pulps show signs of fibrous tissues. More prominent is the damage to the tissue of the red pulp [indicated with an arrow in $B_3$]; giving the appearance of a tissue *scar* within the white pulp. These signs altogether point to the fact that lead produced deleterious effects on the spleen that are of histological relevance and importance. The implication of these effects would include a compromise of the spleen functions especially as an immune organ; thus negatively affecting the body's state of immunity and compromising certain regulatory functions of

the spleen such as the destruction of the worn-out red blood cells. Previously reported similar effects of lead include splenic necrotic lesions which were attributed to oxidative stress (Muselin *et al.*, 2010); and decrease in splenic cellularity and white blood cells in mice exposed to lead during pregnancy and lactation (Synder *et al.*, 2000).

## CONCLUSION

Lead poisoning produced abnormal structural effects in all the tissues. Kidney glomeruli tubules were morphologically distorted while tubular cells show signs of assault and morphological distortions. Testis histo-architecture and epididymis epithelium were also disrupted. The spleen pulps, especially white, show sign of damage in the lead intoxicated group. Liver cells and alveolar epithelium showed signs of damage. This investigation confirmed the compromising effects of lead poisoning on the body health and show why conscientious efforts should be made to prevent the occurrence of lead poisoning. In observed cases, timely and effective critical medical and remedial solutions with the best outcomes would be vital.

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**Reference** to this paper should be made as follows *Joshua O Owolabi & Philip O Ogunnaike* (2017), Lead Intoxication: Nature of Structural Damage in the Kidney, Liver, Lung, Testis, Epididymis and Spleen. *J. of Medical and Applied Biosciences,* Vol. 9, No. 2, Pp. 19- 40