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RESEACH ARTICLE

Histochemical and Histological Assessment of the Lungs and Trachea in Mercury Chloride treated Wistar Rats

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Abstract

Background: Mercury is a member of the family of metallic element known as the heavy metals. Toxicity of mercury has continued to occur in Iraq, Taiwan and in Nigeria killing several thousand people thereby placing mercury among top-most toxic metals. Despite documented cases of mercury chloride poisoning showing respiratory symptoms such as dyspnea, chess pain and chemical pneuminitis, the precise anatomical mechanisms by which mercury chloride disrupt the primary respiratory areas remain inadequately understood. Most published research overlooks detailed respiratory tissue analysis focusing instead on other organs. The microscopic and chemical alterations in the respiratory tract due to mercury chloride exposure also remains underexplored, despite known exposure and systemic risk. **Methods**: This study assesses mercury chloride administration on the histology and histochemistry of the lungs and trachea. Thirty adult Wistar rats were used for the purpose of this study. The rats were grouped into three (3) groups of ten (10) rats each. They were administered 2mls of distilled water, 5mg/kg and 10mg/kg body weights of mercury chloride respectively for fourteen (14) days. The rats were weighed daily using manual weighing balance and electronic weighing balance was used to weigh the organs after sacrifice. **Results:** The results showed that mercury caused hemorrhage, collapse and coalition of the alveolar wall, necrosis of the pneumocytes as well as depletion of the epithelial lining of the trachea. Mercury also caused an increase in the production of mucins in lungs. The presence of these mucus-secreting cells suggests an adaptive response to irritation or inflammation, which is commonly observed in various respiratory conditions. **Conclusion**: mercury alters the histology and histochemistry of the lungs and trachea.

Keywords: Mercury, Histology, Histochemistry, Lungs and Trachea.

INTRODUCTION

Man is exposed to the deleterious effects of mercury. Exposure to mercury can occur orally, dermally or by inhalation (ATDSR, 2003; WHO 2016). The use of Kolhli, a cosmetic traditionally used in northern Nigeria has been identified to be one of the exposure sources of mercury in Nigeria (Onyeike *et al*., 2002). Naturally exposure can occur through anthropogenic sources like volcanoes and rock excavation (Burkholder and Johnson, 2008). Diet is another significant exposure source of mercury poisoning which caused the death of thousands of people in the mid 1950s in Nigata and Minimata Japan. In Nigeria significant amount of mercury have been found in certain species of fish in Lagos lagoon and in the Niger Delta region (Wegwu, 1999). Mercuric chloride had been used to treat syphilis; it is also a component of photographic plate and tonners (Tilles and Wallach, 1996; Goyer, 1986). Mercury and its compound have been used as diuretics, disinfectants, dewormer and laxative (US, FDA, 2007; Pimple *et al*., 2002). It is also been used to treat Constipation,

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depression and toothaches (Mayell, 2007; Pimple *et al*., 2002). One of the organs to exhibit toxicity is the brain due to the reaction between mercury and oxygen to give mercury oxide (Hallee, 1969; Goyer, 1991; Jackson, 2018). Taueg *et al*., (1992) and the UKHSA (2025) had reported respiratory distress syndrome and other range of respiratory diseases in an in-home smelting operations involving mercury. Oral exposure is the primary route for inorganic mercury salts. The rate of oral absorption of mercuric mercury compounds in laboratory rodents has been shown to be dependent on intestinal pH, age, and diet (Kostial *et al*., 1978; Endo *et al*., 1990). Mercury, once absorbed, enters oxidation-reduction cycle in the red blood cells, lungs and liver resulting in formation of divalent cation (Hg^{2+}) (ATSDR, 1989). It is believed that the rate of oxidation is dependent on concentration of catalase in the tissue; endogenous production of hydrogen peroxide; and availability of mercury vapour at the oxidation site (Magos *et al*., 1978; Ogata and Aikoh, 1983).

There is insufficient histological and histochemical analysis of respiratory tissues, particularly the lungs and trachea, in Wistar rats exposed to mercury chloride. Despite known toxicity of mercury and its significant impact on on human health, the microscopic and chemical alterations in the respiratory tract due to mercury exposure remain underexplored in existing literature. Despite extensive studies on mercury toxicity in the liver, kidney and cerebral cortex, there is a relative paucity of focused research on its impact on the lungs and trachea in Wistar rats, which serves as standard model for toxicological studies. Assessing anatomical changes through histopathology, histohemical alterations in mucin secretion in adult Wistar rats will provide comprehensive insights into the mechanisms of mercury chloride toxicity on vital respiratory centers. This research is essential for understanding mercury's systemic toxicity and improving clinical interventions for mercury poisoning.

The aim and objectives of this research is to assess the histology and to histochemically localize mucins in the lungs and trachea following acute exposure to mercury chloride in adult Wistar rats.

MATERIALS AND METHODS

Experimental Animals

Thirty (30) Adult Male Wistar rats weighing between 120 and 220g were obtained from National Veterinary research Institute Vom, Plateau State. The rats were maintained on water and standard pellet diet obtained from vital feeds Nigeria LTD. The rats were housed and allowed to be acclimatized for two weeks in the Department of Human Anatomy Faculty of Basic Medical Sciences, Northwest University, Kano, before the commencement of administration of mercuric chloride. All the experimental animals were kept in well ventilated cages.

Experimental Design

Thirty (30) adult wistar rats were divided into Three (3) groups of ten (10) rats each. Group I, served as the control, Group II, were administered 5mg/kg body weight of mercuric chloride solution and Group III were administered 10mg/kg body weight mercuric chloride solution. Administration of mercuric chloride solution was via intragastric intubation for a period of 14 days. All the groups were weighed anaesthetized using ethyl- ether and sacrificed 24 hours after the last day of administration. The lungs and trachea were excised, cleared and weighed. The rats were perfused with paraformaldehyde before immersing the tissues into the same fixative solution (Ekong, 2017)

Histological Method

The lungs and trachea were processed for histopathological studies, they were fixed in paraformaldehyde and were later processed using automated tissue processor. They were subsequently embedded using paraffin wax at 60c in tissue cassettes and were sectioned using rotary microtome at 5µm. The tissues were then stained using haematoxylin and eosin stains. Light microscope was utilized for histological observation of structural details.

Histochemical Method

The lungs and trachea were utilized for Histochemical studies. Tissues were first perfused with paraformaldehyde via the right atrium of the heart and were subsequently fixed in 10% formaldehyde, dehydrated and cleared before embedding it for sectioning. Dehydration was carried out using ascending alcohol grade *i.e*., 50, 70, 80, 90 and 100% alcohol after which clearing was done with Xylene. The tissues were then embedded in melted paraffin wax at 60c. 5-7µm sections were obtained. The sections were stained with alcian blue/periodic acid Schiff (AB/PAS) according to the manufacturers guide. Light microscope (Leica DM750) was utilized for visualization of mucins and structural details.

RESULTS

The hematoxylin and eosin stained sections shows that, lungs in the control group were observed to be normal with patent alveoli (surrounded by pneumocytes) and blood vessels. However, the mercury treated groups (GII & GIIII) shows few necrotic cells in the alveolar lining, unpatent alveoli (coalesced alveoli) and congested blood vessels. The trachea in the control group was normal with all the cell layers intact. While the mercury treated groups were observed to posses some pathological features in the form of; depletion of the mucosal lining and necrosis of the submucosal cells and the hyaline cartilage.

The AB/PAS stained sections of the lungs and trachea were reported to be stained greenish blue in areas where mucins are present in the mercury treated rats (arrows), demonstrating increased production of mucins. While the control was stained normal (blue) demonstrating few or less mucin presence.

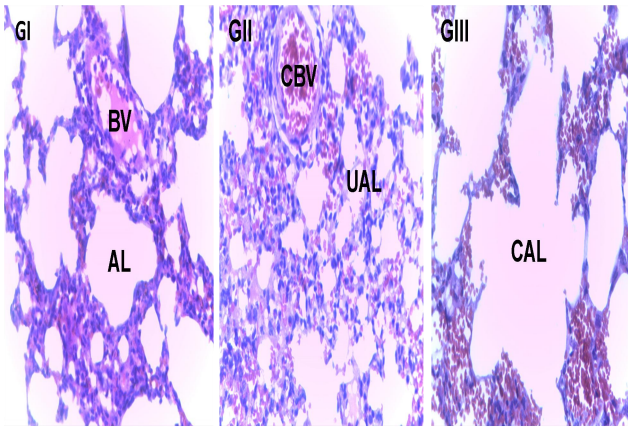

FIG 1: Comparison of histological sections of the lungs across G1 (control) rats induced with 2mls distilled water, GII induced 5mglkg of $Hgcl_2$ and GIII induced with 10mg/kg of $Hgcl_2$. AL = alveoli, BV = blood vessel, , UAL = unpatent alveoli, CBV = congested blood vessel and CAL= coalesced alveoli. H & E X400

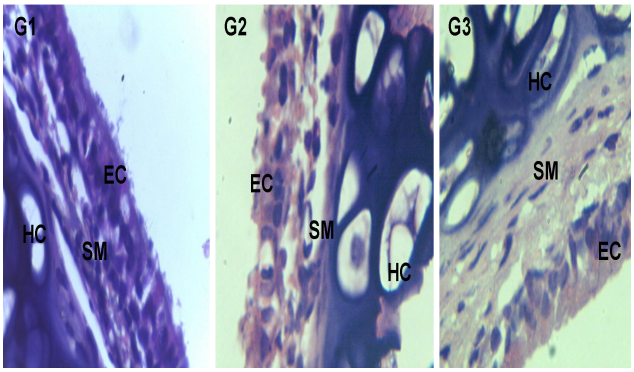

FIG 2: Comparison of histological sections of the trachea across G1 (control) rats induced with 2mls distilled water, GII induced 5mglkg of $Hgcl_2$ and GIII induced with 10mg/kg of $Hgcl_2$. EC= Epithelial cells, SM= Sub mucosa and HC = Hyaline cartilage. H &E X400

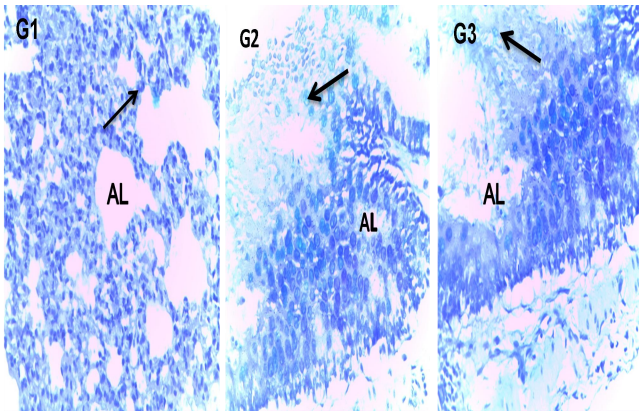

FIG. 3: Comparison of histochemical sections of the lungs across G1 (control) rats induced with 2mls distilled water, GII induced 5mglkg of $Hgcl_2$ and GIII induced with 10mg/kg of $Hgcl_2$. AL = alveoli, Arrow =mucus ABPAS X400

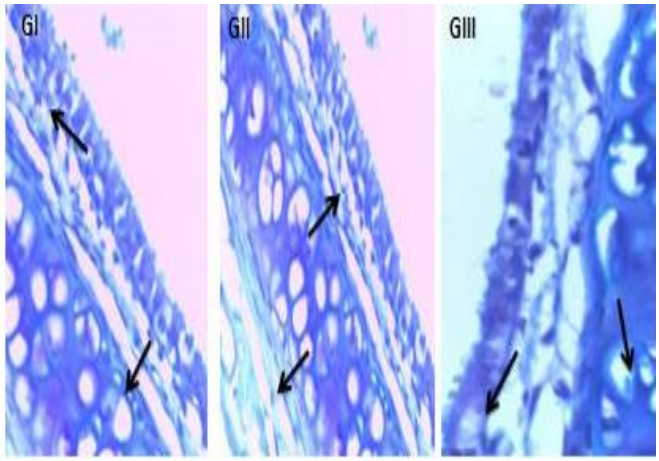

FIG. 4: Comparison of histochemical sections of the trachea across G1 (control) rats induced with 2mls distilled water, GII induced 5mglkg of $Hgcl_2$ and GIII induced with 10mg/kg of $Hgcl_2$. EC= Epithelial cells, SM= Sub mucosa and HC = Hyaline cartilage.ABPAS X400

DISCUSSION

Mercury and its metabolites have the toxic effect of denaturing biological protein, inhibiting enzyme and interrupting membrane transport, uptake and the release of neurotransmitters (Hesse, 2007; El-Shenawy and Hassan, 2008).

Inorganic mercury (e.g mercury chloride) a more reactive form of mercury, can cross the blood brain

barrier and accumulates in the brain at higher concentrations (Aschner and Aschner, 1990, Agbon *et al*., 2016). Mercury interacts with macromolecules and exhibits long latency of neurotoxicity.

In this study, the lungs and trachea have been observed to have necrotic epithelial cells in the mucosal lining as compared to the control as shown in fig 1 and 2 respectively. These might not be unconnected with the toxicity of mercury chloride. In the lungs alveoli in which the flat epithelial cells serves as a barrier for gas exchange (Bevelander and Ramaley, 1979), damage or death of the alveolar cells could greatly interfere with their function (Young, 2000). As a result of this, body's cellular respiration could be interfered with. The epithelium of the trachea is pseudo stratified ciliated, whose role is to sweep away unwanted particles in the respiratory tube. Therefore, depletion, death or any alteration of these cells could result in invasion of the respiratory space by unwanted particles; there by reducing the amount of gases moving in for exchange.

The lung section from G1 shows normal alveolar structure, with visible alveoli lined by pneumocytes and goblet cells (indicated by arrows). Blood vessels can also be observed. This normal architecture is crucial for effective gas exchange and overall lung function (Hsia *et al.*, 2010). In contrast, the lung section from GII displays some abnormalities; Unpatent alveoli are visible, indicating a reduction in alveolar patency. Pneumocytes and goblet cells are still present, but blood vessels appear congested. The presence of congested blood vessels can lead to impaired oxygenation and may reflect underlying pathological conditions (Ochs & Mühlfeld, 2013). The lung section from GIII exhibits more severe changes. Alveoli appear coalesced, suggesting a loss of alveolar integrity. Pneumocytes and goblet cells show signs of degeneration (arrows), with no visible congested blood vessels. These degenerative changes can significantly compromise lung function and indicate advanced disease processes (Weibel, 2009). These histological observations provide insights into the structural changes occurring in the lungs of different groups treated with mercury chloride. The varying degrees of alveolar patency, pneumocyte and goblet cell condition, and blood vessel congestion suggest potential differences in lung function and disease progression among the groups (Gundersen *et al*., 1988; Knudsen & Ochs, 2018).

In FIG 3 and 4, the lungs section from group 1 (control), the architecture appears normal, showcasing well-formed alveoli (AL) surrounded by type I and type II pneumocytes. Goblet cells, which are responsible for mucus production, are also present (indicated by arrows). The presence of these cells is essential for maintaining airway moisture and trapping inhaled particles, thereby contributing to the lung's defense mechanisms (Dao & Le, 2024). The blood vessels in this section appear normal, supporting adequate perfusion and gas exchange.

In contrast, the sections of mercury treated groups (groups II and III) exhibit notable alterations. Both groups showed localized mucus-secreting cells, indicated by arrows, respectively. The presence of these mucus-secreting cells suggests an adaptive response to irritation or inflammation, which is commonly observed in various respiratory conditions (Jackson, 2001; Physio-pedia, 2024). The increased number of goblet cells can lead to excessive mucus production, potentially obstructing airflow and impairing gas exchange (Li *et al.,* 2024). Mucins are high molecular weight glycoprotein that is synthesized stored and secreted by epithelial mucosal cells, especially goblet cells (Kim *et al*., 1991; Ali *et al*., 2012), it provides protective barrier against pathogens and toxins and contribute to the innate defensive system in mucosal immunology (Corfield and Shukla, 2004) and it play a role in the process of tumour progression, invasion and metastasis and also in tumour cell survival and protection against the host immune response (Komatsu *et al* 1991).

In conclusion, mercury alters the histology and histochemistry of the lungs and trachea.

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REFERENCES

ATSDR, (1989).Toxicological Profile for Mercury.*ATSDR/U.S. Public Health Service*.Pp. 169.

Agbon, A. N., Kwanashie, H. O. Hamman, W. O., Ibegbu, A. O., Akpulu, P. S., Ogirima, N. A. and Festus, F. (2016). Histological and Histochemical studies on the Neuroprotectective effect of Aqueous fruit extract of Phoenix Dactylifera L. on Mercury induced cerebeller Damage in wistar rats. *Journal of Anatomical Sciences* 7 (2) : 44- 54

Ali, U., Nagi, A.H., Naseem, N. and Ullah, E. (2012). Mucin Histochemistry in tumurs of colon, Ovaries, and Lung. Journal of cytology and Histology; 3: 163.

Aschner, M. and Aschner, J. L. (1999). Mercury neurotoxicity: mechanism of blood brain barrier transport. Neuroscience and biobehevioural reviews. 14(2):169-176.

Burkholder, M. & Johnson, L. (2008). Colonial Latin America.*Oxford University Press*. Pp. 157–159.

Dao, D.P. D., & Le, P. H. (2024). Histology, goblet cells. In StatPearls. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK553208.

Endo, T., Nakaya, S. and Kimura, R. (1990). Mechanisms of Absorption of Inorganic Mercury from Rat Small Intestine: III.Comparative Absorption Studies of Inorganic Mercuric Compounds*in vitro*.*Pharmacology and Toxicology*, 66(5):347–353.

El-Shenawy, S.M.A. & Hassan, N.S. (2008). Comparative Evaluation of the Protective Effect of Selenium and Garlic Against Liver and Kidney Damage Induced by Mercury Chloride in the Rats. *Pharmacological Reports*, 60: 199-208.

Ekong, M. B. (2017). Perfusion fixation: a vital process for neuroanatomical research. Nigerian journal of neuroscience 8(2), 2017. 38-43.

Gundersen, H. J. G., Bendtsen, T. F., Korbo, L., Marcussen, N., Møller, A., Nielsen, K., ...& West, M. J. (1988). Some new, simple and efficient stereological methods and their use in pathological research and diagnosis. *APMIS*, 96(1-6), 379-394.

Hsia, C. C., Hyde, D. M., Ochs, M., and Weibel, E. R. (2010). An official research policy statement of the American Thoracic Society/European Respiratory Society: standards for quantitative assessment of lung structure. *American journal of respiratory and critical care medicine*, 181(4), 394-418.

Hesse, R. W. (2007). Jewelry Making Through History. *Greenwood Publishing Group*. Pp120.

Jakson, A. D. (2001). Air way goblet cell mucus secretion. Trends in Pharmacological Science. 22(1):39-45 .

Jackson, A. C. (2018). Chronic neurological disease due to methylmercury poisoning. Canadian Journal of Neurological Sciences. 45(6)620-623.

Komatsu, M., Yee, L. and Caraway, K.L. (1999). Over expression of sialomucin complex, a rat homoloque of MUC4, inhibits tumor killing by lymphokine activated killer cells. *Cancer Research*. 59: 2229-2236

Kostial, K., Kello, D., Jugo, S., Rabar, I. and Maljkovic, T. (1978). Influence of Age on metal Metabolism and Toxicity. *Environmental Health Perspectives*, 25:81–86.

Knudsen, L., and Ochs, M. (2018). The micromechanics of lung alveoli: structure and function of surfactant and tissue components. *Histochemistry and cell biology*, 150(6), 661-676.

Li, K., Song, Z., Yue, Q., Wang, Q., Li, Y., Zhu, Y., & Chen, H. (2024). Disease-specific transcriptional programs govern airway goblet cell metaplasia. Heliyon, 10(13), e34105. https://doi.org/10.1016/j.heliyon.2024.e34105

Mayell, H. (2007). Did Mercury in Little Blue Pills Make Abraham Lincoln Erratic. *National Geographic News*

Ogata, M. and Aikoh H. (1983). The oxidation of Metallic mercury by catalase in relation to acatalasemia. Industrial Health; 21, 219-230.

Onyeike, E. N. (2002). Inorganic ion levels of soils and streams in some areas of Ogoni land,Nigeria as affected by crude oil

spillage.*Journal.Environmental.Monitoring. Assessments. 73:191-205*

Ochs, M., and Mühlfeld, C. (2013). Quantitative microscopy of the lung: a problem-based approach. Part 1: basic principles of lung stereology. *American journal of physiology-lung cellular and molecular physiology*, 305(1), L15-L22.

Physio-pedia. (2024). Lung Anatomy. Retrieved from Physio-pedia.

Pimple, K. D., Pedroni, J. A. and Berdon, V. (2002). Syphilis in History.Poynter Center for the Study of Ethics and American Institutions at Indiana University-Bloomington. Retrieved 17 April 2015.

WHO, (2003). World Health Organization. Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects. (Concise International Chemical Assessment Document; 50 NLM Classification: QV 293).

Wegwu, M. O. (1999). Seasonal Variations of Pollutants in Some Areas of the Niger Delta and their Toxicity on some Aquatic fauna. *Ph.D. thesis*, University of Port Harcourt,Nigeria.

Weibel, E. R. (2009). What makes a good lung? *Swiss medical weekly*, 139(27-28), 375-386.

Young, B., Woodford, P. and O'Dowd, G. (2013). Respiratory system: in *Wheaters Functional Histology*: A text and colour atlas, 6th edition. Pp. 224-238

Magos, L., Halbach, S. and Clarkson, T.W. (1978). Role of Catalase in the Oxidation of Mercury Vapor. *Biochemical Pharmacology*, 27:1373–1377.

Taueg, C., Sanfilippo, D.J, Rowens, B., Szejda, J. and Hesse, J.L. (1992). Acute and Chronic Poisoning from Residential Exposures to Elemental Mercury. *Journal of Toxicology — Clinical Toxicology*, 30(1):63–67.

Tilles, G. and Wallach, D. (1996). The treatment of syphilis with mercury: an exemplary therapeutic history. Hist Sci Med. 30(4):501-10.

UKSHA (2025). United Kingdom Health Security Agency: Elemental mercury and inorganic mercury toxicological overview.

USFDA (2007).United State Food and Drug Administration: Thimerosal HYPERLINK "http://www.fda.gov/cber/vaccine/thimerosal.htm" in Vaccines. *Center for Biologics Evaluation and Research*, Retrieved 1 October 2007.