Short Communication

# Histopathological Changes of Dexamethasone on Affected Lung of Rats

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## Abstract

**Background:** Dexamethasone (DEX) is a long-acting fluorinated glucocorticoid, it is used as support therapy in respiratory infections unresponsive to antimicrobials alone, or in severe-to-progressive lung infections (e.g., pneumonia) to reduce allergic response. **Objectives:** The current study aimed to search for the most important tissue changes in the lungs after long-term DEX administration. **Materials and Methods:** Twenty-four adult albino rats of both sexes weighing 220–280 g were used and grouped into two sets. The first group was treated orally with DEX 10 weeks (0.1 mg/kg b.wt.) daily and the second group was treated with distilled water only as a control group. At the end of the experiment, a post-mortem examination was done for all animal groups to preserve lung pieces in 10% formalin for tissue slice preparation then microscopic examination. **Results:** There were marked vascular changes from congestion, dilation, and thrombus-like lesion along with inflammatory response and necrotic processing occurred. Multifocal areas of necrosis with thickening of the alveolar septa by infiltration of inflammatory cells and congestion of blood vessels with degeneration of the epithelial lining of the bronchioles are seen. Others revealed per-bronchiolitis; focal aggregation of inflammatory cells extended to the mucosa with hypertrophy of smooth muscles layer and lymphocytic bronchiolitis. emphysematous alveoli and interstitial infiltration of inflammatory cells with hypertrophy of terminal blood vessels were seen. **Conclusion:** Lung tissue histopathological changes of oral administration of DEX were a toxicity indicator for the therapy of lung.

**Keywords:** Dexamethasone, lung infections, lung toxicity, oral administration, rat

## Introduction

Dexamethasone (DEX), a synthetic corticosteroid, has been successfully used in clinical practice due to its anti-inflammatory activity.[1] There are several therapeutic applications for DEX. DEX has been effective in curing extreme cases of multiple sclerosis aggravation, allergies, cerebral edema, inflammation, and shock. DEX chronic usage, even at modest dosages, is connected to substantial adverse effects.[2] As a result, a formulation with the capability for lung-targeted administration is required for the treatment of acute respiratory distress syndrome. Although there have been several publications on the transport of nanoparticles to the lungs,[3] according to Varis *et al*.,[4] DEX is effectively absorbed after being administered to dogs and rats orally and intramuscularly, reaching peak plasma levels within 30 min and 6 h, respectively. DEX is metabolized in the liver by CYP450 3A4 substrate, which produces the side-change cleaved metabolite 6-hydroxyDEX.[5] The majority of conjugated inactive metabolites are eliminated via the kidney, and gut residues are absent.[6] DEX regulates the lung's Na+-K+-ATPase. DEX increased alveolar fluid clearance by 80% when compared to the mock-run group and enhanced the expression of the Na+-K+-ATP enzyme in rat alveolar epithelial cells.[7]

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## Materials and Methods

### Preparation the dose of dexamethasone

The treated dose of DEX sodium phosphate was prepared according to Amriya Pharmaceuticals Industries, Alexandria, Egypt which was 0.25 mg/kg b.wt.[8]

### Lab animals

A total of 24 Albino adult male rats weighing 180–200 g and maturing at a rate of roughly 150 days were used in this investigation. The Veterinary Medicine College/ University of Baghdad housed the animals. All Albino rats were housed in soft-wood chips as bedding in 120 × 60 × 60 cm plastic cages with six rats per cage and temperatures between 22 and 25°C. They were given a commercially prepared base diet that included unlimited water. The animals were acclimated in the best circumstances for 2 weeks.

### Experimental design

The experimental rats were separated equally into two groups:

**Group 1**: (control group): (n = 12) rats were daily given distilled water orally by stomach tube for 1 month.

**Group 2**: (*n* = 12) rats were administered orally DEX sodium phosphate at a dose level of 0.25 mg/kg b.wt (8) orally twice weekly with 72 h interval.

## Results

### Histological changes

The treated rats were sceptered for microscopic study for their lungs which revealed multifocal areas of necrosis in the lung parenchyma and thickening of the alveolar septa by infiltration of inflammatory cells [Figure 1] and congestion of blood vessels with mild hyperplasia and degeneration of the epithelial lining of the bronchioles.

Figure 2 shows focal per bronchiolitis represented by focal aggregations of inflammatory cells from lymphocytes, macrophages, and polymorphonuclear neutrophils (PMNs) extended to the layers of bronchioles and bronchioles to cause severe necrosis.

In other lung sections, there were marked bronchiolar hypertrophy of tunica media infiltrated with inflammatory cells from mononuclear cells (MNCs) and PMNs and also there was excessive production of mucin on the mucosal surface and their lumen [Figure 3].

The pulmonary blood vessel showed marked dilation-moderate thin wall and contained thrombus-like lesion attached to internal intima [Figure 4]. The congestion of pulmonary blood vessels was the predominant change occurred due to oral administration of DEX for long time, the emphysema, and hypertrophy of small blood vessels [Figure 5].

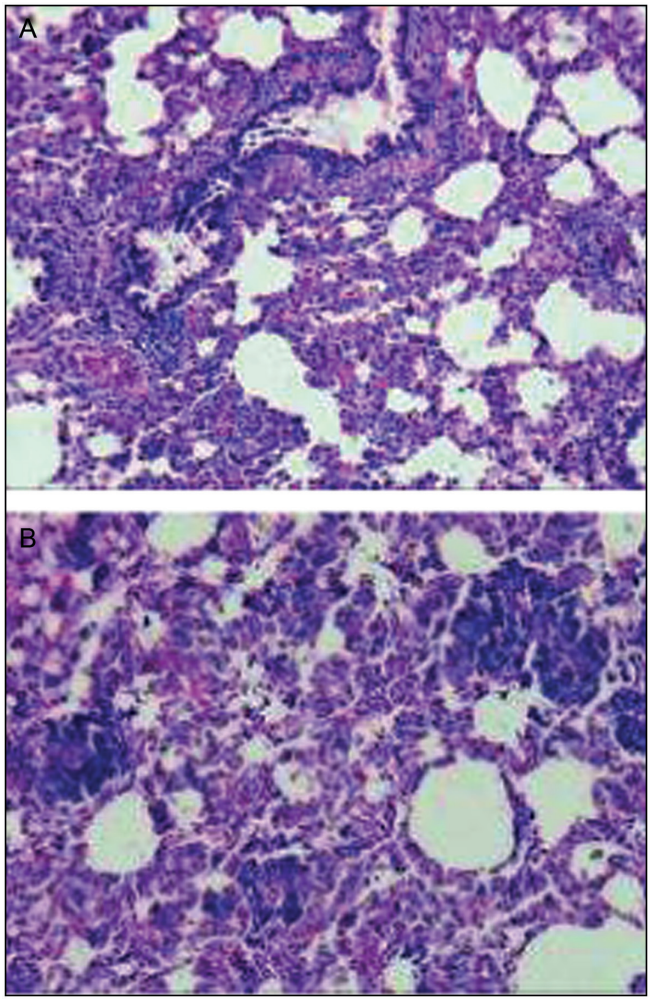


**Figure 1:** (A) Histopathological section of lung showing thinking of the alveolar septa by infiltration of inflammatory cells and congestion of blood vessels with degeneration of the epithelial lining of the bronchioles (H&E stain; 100×). (B) Histopathological section of lung multifocal area of necrosis of the lung parenchyma (H&E stain; 100×)

## Discussion

DEX may cause vascular changes and pulmonary lesions of rats after 10 weeks of treatment. Still the treatment of severe pulmonary diseases used of DEX may lead to unclear changes.[9] The use of DEX in newborns caused negative effect on cardiovascular tissue which showed present of inflammatory cells and collagen fibers deposit.[10]

Furthermore, DEX-exposed mice had early hypertension symptoms that improved with age. The severe respiratory distress syndrome and related chronic lung disease are linked to a high rate of morbidity and mortality.[11] Inflammation is considered to have a significant impact on its pathogenesis. In neonatal rats receiving DEX medication, there is lung hypoplasia and an increase in pulmonary arterial pressure.[12]

The adult rat heart suffers from cellular hypertrophy and increased collagen deposition as a result of neonatal

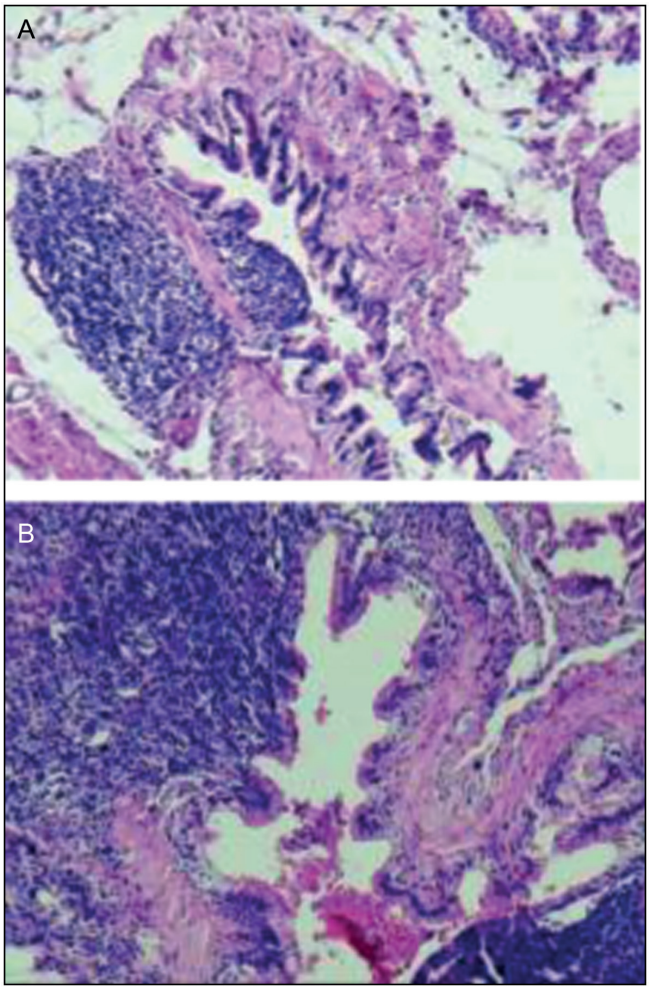


**Figure 2:** Histopathological section of lung showing (A) focal lymphocytic bronchiolitis. (B) Bronchiolar-associated lymphocytic tissue around bronchiole (BALT. (H&E stain, 100×).

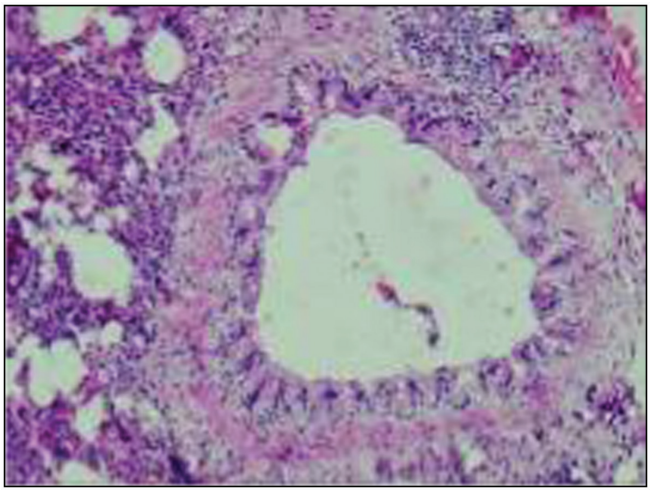

**Figure 3:** Histopathological section of lung showing marked bronchiolar hypertrophy, infiltration of inflammatory cells with mucinous secretion (H&E stain; 100X)

DEX's interference with heart development.[10] In light of past studies in rats that revealed early death suggesting

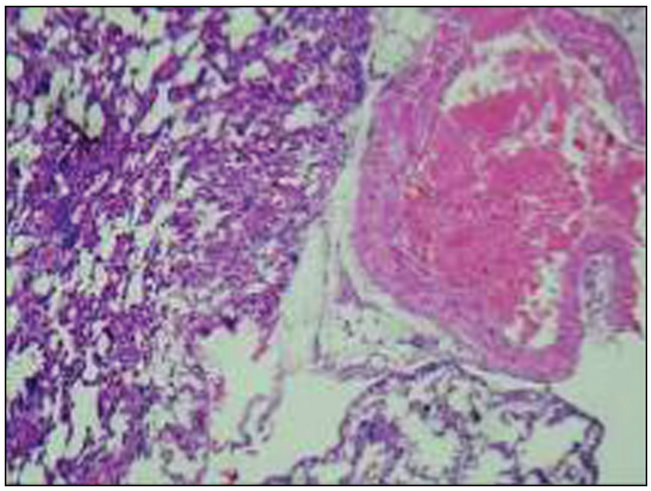

**Figure 4:** Histopathological section of lung showing marked dilation of pulmonary blood vessel with moderate thin wall and contained thrombus-like lesion attached to internal intima bronchiolar hypertrophy (H&E stain; 100X)

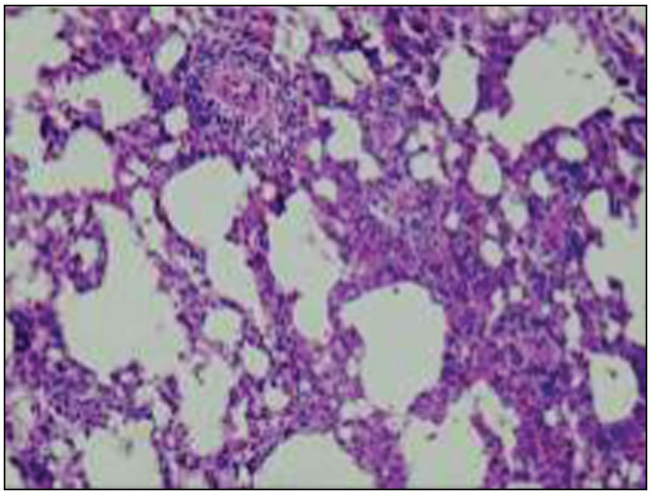

**Figure 5:** Histopathological section of lung showing marked interstitial infiltration of inflammatory cells and hypertrophy of terminal blood vessels (H&E stain; 400X)

heart failure, cardiovascular follow-up of preterm neonates treated with glucocorticoids should be taken into account. Hepatic steatosis and mild to severe aortic arteriosclerosis were likewise brought on by acute high doses of DEX (4, 8, and 16 mg/kg) given over a six-day period.[13] Blood insulin and C-peptide levels increased after receiving a single dose of DEX, which contributed to the significant blood vessel damage shown in this study.[14-16]

## Conclusion

The current investigation concluded that the lung histopathological changes treatment orally with DEX in adult rats was a toxic indicator for therapy of lung infections.

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## Conflicts of interest
There are no conflicts of interest.

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