

Chronic Fibrotic Changes in Experimental Pulmonary Embolization in the Rat Model

M. Mehrer, M.D.¹, J. Schroepfel, M.D.³, E. Fibuch, M.D.¹, F. Adler, M.D.³, A. Molteni, M.D., Ph.D.², B. Herndon, Ph.D.², K. Lankachandria, M.D.²

T. McIlff, Ph.D.³, A. Poisner, M.D.⁴

¹Departments of Anesthesiology, University of Missouri-Kansas City School of Medicine, Saint Luke's Hospital/Truman Medical Center ²Departments of Medicine and Basic Medical Science, University of Missouri School of Medicine, ³Departments of Orthopedic Surgery ⁴Pharmacology University of Kansas Medical Center, Kansas City, Kansas.

Introduction: Fat embolism, a subclinical event, occurs in many clinical settings, such as long bones fractures, liposuction and during cardiopulmonary bypass. Some cases, especially with trauma, result in fat embolism syndrome (FES), a serious manifestation of fat embolism. FES is reported to occur in 5-10% of major trauma cases and can produce profound respiratory problems that may culminate in adult respiratory distress syndrome (ARDS). Embolized fat is hydrolyzed by lipase into free fatty acids which have been shown by previous histological studies to be toxic to the lung. An animal model of fat embolism has been developed utilizing triolein given intravenously (i.v.) to rats (¹). We hypothesized that i.v. triolein will produce histological changes in the lung that are similar to the changes seen in human FES.

Methods: Following University animal care approval, unanesthetized Sprague Dawley rats (study n=13, control n=12) were injected with either triolein, 0.2 mL (study) or saline, 0.2 mL (control). Weights were recorded until necropsy at 3 weeks (n=13) and 6 weeks (n=12). Morphometric measurements were made on both H&E and fat-stained tissues from the lungs, heart, kidneys and spleen. All vessels were examined using high magnification fields. Arterial wall thickness (lumen patency) was calculated by vessel luminal and external diameters. The medial-adventitial ratio was calculated from the outer medial diameter divided by the outer adventitial diameter. These values were keyed into statistical software and analysis as a function of time and treatment was calculated using t-tests with significance noted at a p<0.05.

Results: Gross pathological changes were seen in lung, heart, kidneys, liver and spleen of the triolein group. Pulmonary histological examination revealed diffuse intra-alveolar hemorrhages and edema with peri-bronchial inflammation. Vasculitis was more prominent in the peri-bronchial areas as well. Pulmonary arteries revealed significant medial thickening as compared with the control groups with lumen patency p=0.004. Adventitia/media ratio, with large variability in the triolein group, was not statistically significant. **Conclusions:** Our data showed that injected triolein remains in the rat lung after 3 and 6 weeks with associated vascular and septal damage in the lung tissue compared to controls.

Discussion: This study is a continuation of our previous study showing an increase of severe pulmonary damage within 3-6 hours following triolein induced fat embolism in the rat, reaching a peak at 96 hrs post injection(¹). Despite unmedicated recovery of general condition and body weight and reopening of the pulmonary arteries and arterioles, collagen and vasculitis persisted up to 6 weeks. Further studies are needed to verify the eventual recovery or the organ evolution toward chronic fibrosis.

References:

1. McIlff TE, Poisner AM, Herndon B, Lankachandra K, Schutt S, HaileSelassie B, Patel S, Quinn T. Adler F, Molteni A. Fat Embolism: Evolution of histopathological changes in the rat lung. J. Orthopaedic Research (Accepted 19 June 2009).