SL 6

ACUTE LUNG INJURY OR ACUTE RESPIRATORY DISTRESS SYNDROME: EXPERIMENTAL AND CLINICAL INVESTIGATIONS

Hsing I Chen
Institute of Integrative Physiology and Clinical Sciences

Since 1973, my colleagues and I have investigated the neural and hemodynamic mechanisms of neurogenic pulmonary edema. We have found that central sympathetic overactivation causes constriction of the systemic and pulmonary resistance and capacitance vessels, leading to a shift in blood volume from the systemic circulation to the lung. Pathological examinations show disruption of large and small vessels in the lung.

Later on, we invented the technique of isolated-perfused lungs *in situ*. A digital-converter is used to record the changes in body weight, which the lung weight changes. Microvascular permeability can be obtained. Using this technique, a series of studies has investigated the roles of leukocytes, platelets, nitric oxide, ischemia/reperfusion, endotoxin and other disorders in the acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

Recent work has involved clinical studies on the pathogenetic mechanisms of ALI or ARDS caused by various disorders. We have obtained several important findings. The release of nitric oxide (NO) through the inducible nitric oxide synthase (iNOS) is detrimental to the lung. The generation of NO is mainly from the lung instead of from the systemic circulation. Hsu et al. (2003) have reported acute pulmonary edema resulting from Japanese B encephalitis, lymphangitis, and fat embolism. Kao et al. (2004) have suggested that static inflation attenuates the ischemia/reperfusion ALI through the prevention of hyaline membrane formation. He and coworkers have extended the study on the mechanisms of fulminant lung injury caused by enterovirus 71 (EV 71). The clinical investigation revealed that with the onset of respiratory stress, sympathetic activity and arterial pressure increased, while parasympathetic drive and heart rate decreased. The opposite changes occurred before death. RT-PCR displays the expression of iNOS in the lung parenchyma. Viral destruction of the brain stem is mainly located in the medial, ventral, and caudal medulla. This study suggests that viral lesions in the brain stem account for the cardiopulmonary changes and iNOS is also involved. A recent experimentation in conscious rats has revealed that insulin abrogates the endotoxin-induced ALI and prevents systemic hypotension. It also inhibits the production of NO, free radicals and proinflammatory cytokines and the development of ALI. The findings indicate that insulin exerts strong anti-inflammatory actions.

Major References

1. Chen HI, Kao SJ, Wang D, Lee RP, Su CF. Acute respiratory distress syndrome. *J Biomed Sci* 10: 588-592, 2003
2. Lee RP, Wang D, Kao SJ, Chen HI. The lung is the major site that produces nitric oxide to induce acute pulmonary oedema in endotoxin shock. *Clin Exp Pharmacol Physiol* 28: 315-320, 2001
3. Hsu YH, Kao SJ, Lee RP, Chen HI. Acute pulmonary oedema: rare causes and possible mechanisms. *Clin Sci (Lond)* 104: 259-264, 2003
4. Kao SJ, Wang D, Yeh DY, Hsu K, Hsu YH, Chen HI. Static inflation attenuates ischemia/reperfusion injury in an isolated rat lung in situ. *Chest* 126: 552-558, 2004
5. Kao SJ, Yang FL, Hsu YH, Chen HI. Mechanism of fulminant pulmonary edema caused by enterovirus 71. *Clin Infect Dis* 38: 1784-1788, 2004
6. Chen HI, Yeh DY, Liou HL, SJ Kao. Insulin attenuates the endotoxin-induced acute lung injury in conscious rats. *Crit Care Med* 34: 758-764, 2006
7. Kao SJ, Wang D, Lin HI, Chen HI. N-acetylcysteine abrogates acute lung injury induced by endotoxin. *Clin Exp Pharmacol Physiol* 33: 33-40, 2006