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Pulmonary Effects of Prolonged Sympathetic Stimulation[1] (38102)

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Previous clinical studies (1–3) have shown that the sympathetics play a major role in the development of acute pulmonary injury associated with mechanical CNS damage, surgical trauma, and severe nonspecific stress. Similar findings in animals exposed to experimental head injury (4–7), hyperbaric oxygen (8), and sympathetic nerve stimulation suggest that, in addition to possible hemodynamic changes, the sympathetics may alter the alveolar surfactants prior to the subsequent development of pulmonary congestion and edema (9, 10). Previous work has shown that short-term stimulation of the sympathetics results immediately in a decreased lung compliance and altered surfactants in the absence of any initial gross lung injury (10), as evidenced by normal or even decreased lung wt/body wt ratios. In the present study, experiments were carried out in order to determine what effect prolonged continuous sympathetic nerve stimulation in cats might have on lung compliance and lung wt/body wt ratios.

Methods. Fifteen adult cats were anesthetized with ketamine (30 mg/kg, im), the femoral artery catheterized, and the right stellate ganglion isolated via a lateral incision while avoiding rupture of the thoracic pleura. Wire electrodes were attached to the ganglion and stimulation applied by a Grass S-7 stimulator (10 V, 0.5 msec, 10/sec, square wave). A vinyl esophageal balloon 2 in. long was inserted into the stomach and then retracted 2 in. so that it was located in the esophagus. The cat was then placed in a whole-body pressure plethysmograph which, after equilibration was established, was calibrated for the measurement of tidal volume. Periodic measurements of esophageal pressure and tidal volume were made prior to stimulation of the pulmonary sympathetics and for a 3 hr period during continuous stimulation. After such stimulation, the lungs were carefully excised, grossly examined, photographed, weighed, dried, the dry weight determined, and the lung wt/body wt and lung wt/dry wt ratios calculated.

Results. The results from the present study show that continuous sympathetic nerve stimulation results in an initial 38% compliance decrease which persists for at least 3 hr. Such a compliance decrease occurs in the absence of gross pulmonary congestion and edema. In 15 cats exposed to sympathetic stimulation the control lung compliance based on tidal volume and esophageal pressure at points of zero airflow was 0.037 ± 0.005 (SE) liter/cm H_2O compared to 0.023 ± 0.004 immediately after stimulation, $P < 0.05$. Lung wt/body wt ratios increased only 4% in 11 stimulated cats, 0.0072 ± 0.001 compared to four normal controls, 0.0069 ± 0.003, showing no significant change. Furthermore, there was no significant change in lung wet wt/dry wt ratios. Three control values were 4.46 ± 0.12 compared to 4.44 ± 0.06 for 11 stimulated cats. There was little or no evidence of gross hemorrhage or edema in any of the cat lungs.

Discussion. Previous work showed that stimulation of the pulmonary sympathetics immediately decreased dynamic lung compliance and airway resistance in the absence of any gross lung pathology (9, 10). The present experiments indicate that prolonged continuous sympathetic nerve stimulation results in a decrease in lung compliance in the absence of any significant pulmonary congestion and edema, as shown by normal lung wt/body wt ratios, normal wet wt/dry wt ratios and the

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absence of any gross pathology. Previous work suggested that the initial compliance decrease during sympathetic nerve stimulation is due to an alteration in the alveolar surfactants (9). These subsequent changes may also be a result of surfactant changes. Recent experimental evidence has shown that the intra-alveolar protein content increases after this sympathetic nerve stimulation (11). The initial compliance decrease is apparently not due to systemic hemodynamic factors, as suggested by only a minimal rise in pulmonary artery and left atrial pressures (1–3 mm Hg) during stimulation of the pulmonary sympathetics in cats (10). Previous findings (9) showed that lung compliance decreases and altered surfactants occurred immediately after mechanical head injury in the absence of gross lung pathology. These compliance decreases were blocked by various sympathetic agents (9), as was also the decrease found after stress from exposure to hyperbaric oxygen (12). In view of such findings, it is not surprising that stimulation of the pulmonary sympathetics via the stellate ganglion in cats resulted in a decreased lung compliance in the absence of pulmonary congestion and edema even after prolonged continuous stimulation.

Summary. Previous work in monkeys and cats showed that sympathetic stimulation via mechanical head injury and exposure to hyperbaric oxygen resulted in an immediate decrease in lung compliance and altered alveolar surfactants in the absence of any evidence of gross pulmonary edema or congestion as evidenced by normal lung wt/body wt ratios. Such effects were ameliorated by pretreatment with sympathetic blocking agents but not with atropine. Similar results were found during short-term sympathetic stimulation via the stellate ganglia. In the present study, using cats, a 3-hr continuous electrical stimulation of the stellate ganglion decreased lung compliance by 38% in the absence of any increase in lung wt/body wt ratio or lung wet wt/dry wt ratio. Such evidence suggests that this sympathetic-induced compliance decrease was due to factors other than cardiovascular.

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1. Ducker, T.B. J. Neurosurg. **28**, 112 (1968).
2. Hess, L. Wein Med. Worchenschr. **84**, 285 (1934).
3. Weisman, S. Surgery **6**, 722 (1939).
4. Ducker, T.B., and Simmons, R.L. J. Neurosurg. **28**, 118 (1968).
5. Eichbaum, F.W., Gazetta, B., Bissetti, P.C., and Pereira, C.B. Z. Gesamte Exp. Med. **139**, 721 (1965).
6. Ivanhoe, F., and Meyers, F.H. Dis. Chest **46**, 211 (1964).
7. Visscher, B., Haddy, F.J., and Stephens, G. Pharmacol. Rev. **8**, 389 (1956).
8. Bean, J.W. Physiol. Rev. **25**, 1 (1945).
9. Beckman, D.L., Bean, J.W., and Baslock, D.R. J. Appl. Physiol. **30**, 394 (1971).
10. Beckman, D.L., and Mason, K.F. Life Sci. **12**, 43 (1973).
11. Beckman, D.L., Sexton, J.D., and Bergren, D.R. Fed. Proc. **33**, 346 (1974).
12. Beckman, D.L., Houlihan, R.T. Aero. Med. **44**, 422 (1973).

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