ABSTRACT

A model of chronic pulmonary venous congestion was developed by surgically damaging the mitral valve leaflets in New Zealand White rabbits and maintaining them for 12 weeks. The mitral valve damage was confirmed by (i) demonstrating presence of mitral regurgitation using echocardiography, (ii) increased left atrial pressure (5.8 ± 0.3 in these rabbits Vs 2.9 ± 0.5 mmHg in control rabbits), (iii) increased left ventricular weight / body weight ratio (1.5 ± 0.02 g/kg in these rabbits Vs 1.2 ± 0.01 g/kg in control rabbits) and (iv) *post-mortem* visual inspection of mitral valve leaflets for perforations.

Action potentials were recorded in the cervical vagus nerve from pulmonary afferent nerve fibres to study their response to manipulation of Starling forces in the pulmonary microvasculature. Starling forces in the pulmonary microvasculature were manipulated by (i) acutely elevating the left atrial pressure (LAP) (ii) obstructing the pulmonary lymphatic drainage (iii) reducing the plasma protein concentration by plasmapheresis and (iv) elevating the plasma protein concentration with an intravenous infusion of hypertonic albumin solution. 4 types of receptors were studied; (i) slowly adapting receptors (SAR), (ii) rapidly adapting receptors (RAR), (iii) pulmonary C fibre afferent receptors and (iv) Bronchial C fibre afferent receptors.

In intact control rabbits, RAR showed a graded increase in activity when the LAP was elevated 5 mmHg and 10 mmHg. Activity during initial control period, LAP + 5 mmHg, LAP + 10 mmHg and final control periods were 38.5 ± 11.9, 57.9 ± 14.2, 114.5 ± 31.9 and 39.7 ± 12.9 action potentials min^{-1}, respectively. In rabbits with chronic pulmonary venous congestion for 12 weeks, RAR did not show an increase in activity with this stimulus. The corresponding values were 30.8 ± 8.6, 25.4 ± 6.6, 32.6 ± 8 and 26.9 ± 8.2 action potentials min^{-1}, respectively. After an

intravenous infusion of hypertonic albumin solution, responsiveness of RAR to acute small elevations of LAP was restored in rabbits with chronic pulmonary venous congestion. Similarly, RAR in rabbits with chronic pulmonary venous congestion showed an increase in activity when the LAP was elevated to above 25 mmHg inducing pulmonary oedema. Bronchial and pulmonary C fibre afferent receptors in rabbits with chronic pulmonary venous congestion also did not increase their activity during small acute graded elevations of LAP, but did so when the LAP was elevated to above 25 mmHg.

RAR in control rabbits increased their activity when the pulmonary lymphatic drainage was obstructed. The RAR activity during initial control period, pulmonary lymphatic obstruction (PLO) for 1-10 min, PLO 11-20 min and the final control periods were 198.3 ± 49.0, 232.8 ± 54.6, 246.8 ± 55.1 and 204.4 ± 56.5 action potentials min^{-1}, respectively. After plasmapheresis, PLO increased the RAR activity to a greater degree. Pulmonary C fibre afferent receptors in control rabbits did not show an increase in activity with (PLO). Bronchial C fibre activity in control rabbits also did not show increase in activity with PLO.

Extravascular water content was measured in rabbits with chronic pulmonary venous congestion and in age matched intact control rabbits. This was done under baseline conditions and under different experimental conditions (e.g. LAP + 10 mmHg, LAP + 25 mmHg etc.). The extravascular water content in lower trachea, carina and bronchi was significantly higher under baseline conditions in rabbits with chronic pulmonary venous congestion compared to control rabbits (58.3 ± 1.5 % Vs 52.1 ± 1.2 %). The extravascular water content in the same region in control rabbits increased significantly when the LAP was elevated by 10 mmHg, while in rabbits with chronic pulmonary venous congestion it did not. In both groups of rabbits the extravascular

water content in the region described above as well as in the lungs increased when the LAP was elevated to above 25 mmHg.

Since it is known that pulmonary vagal afferent receptors in control rabbits are able to sense fluid fluxes across the pulmonary microvasculature, we concluded that RAR in rabbits with chronic pulmonary venous congestion increase their activity only when the LAP is acutely elevated to above 25 mmHg inducing pulmonary oedema.