Short communications

Adrenaline-induced acute massive pulmonary oedema in the dog

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Pericardiotomy followed by intravenous injection of adrenaline (1 mg/kg body weight) provides a reliable method for the production of acute massive lung oedema in the dog. The lung wet weight: heart wet weight ratio is found to be the best assessment of the degree of lung oedema. A ratio greater than two represents massive lung oedema.

Lung oedema occurred in man after accidental injection of a large dose of adrenaline (Ersoz & Finestone, 1971), and a large dose of adrenaline consistently induced acute massive oedema in the rat, rabbit and other small laboratory animals (Cheng, 1958; Worthen, Placik, Argano, MacCanon & Luisada, 1969). The haemodynamic changes of adrenaline-induced lung oedema have been little studied because of the exceptional difficulty in producing the condition in large experimental animals such as the dog (Jordan & DeLaney, 1951; Saitoh, Kinoshita, Tokumasa, Nakamura, Usami & Doba, 1967). For instance, Paine, Smith, Butcher & Howard (1952) produced lung oedema by means of adrenaline in only two out of nine intact dogs, and Chan & Cheng (1971) could not produce it in open-chest dogs by injecting up to 20 mg/kg of adrenaline. As a result, recent studies of adrenaline-induced lung oedema in dogs involved supplementing the adrenaline injection with a liberal infusion of fluid (Saitoh *et al.*; Worthen *et al.*), but this procedure undoubtedly complicates the issue, especially since a massive transfusion *per se* can lead to lung oedema (Wakisaka, Inoguchi & Yano, 1967).

This paper describes the successful production of acute massive lung oedema by means of adrenaline in the open-chest dog after removal of the pericardial sac.

Methods.—Experiments were carried out on 30 mongrel dogs weighing from 5 to 25 kg and anaesthetized with sodium pentobarbitone (30 mg/kg body weight) intravenously. Artificial ventilation of the lung was given through an endotracheal tube (Portex, England) by the use of a Starling Ideal pump (Palmer, London), with the tidal volume varying between 150 ml and 450 ml according to the size of the dog, and the respiratory rate at 10 to 12 per minute. The chest was opened from the right side in the fourth intercostal space, to expose the pericardium. For pericardiotomy, the parietal layer of the pericardium was incised longitudinally from over the root of the ascending aorta to over the apex of the heart. Then the pericardial sheath at the root of the great vessels was divided, followed by a transverse cut in the pericardium over the coronary sulcus. The heart was delivered through the opening in the pericardial sac. (−)-Adrenaline (Koch-Light Lab., England), 0·1 mg/ml distilled water, was injected intravenously in a dose of 1 mg/kg body weight at the rate of about 2 ml per minute.

The animals were killed 3 min after the administration of adrenaline. Acute massive lung oedema was indicated by pinkish froth in the tracheo-bronchial tree or on the cut surface when the lung was slightly compressed. The degree of lung oedema was graded by gross examination as described by Singer, Hessen, Pick & Katz (1958). The controls consisted of dogs with the chest opened but with intact pericardium when adrenaline was administered, and dogs with the pericardium removed which were given 0·9% w/v NaCl solution (saline) in place of adrenaline.

For quantitative assessment of lung oedema the dog was killed and the lungs and heart immediately removed and weighed separately to obtain the ratio between total lung weight and the heart weight. The lungs were then dried in an oven at 85°–90° C for five days, and the wet weight: dry weight ratio of the lungs was also determined. Twenty-four results were compared statistically.

Results.—Of 30 experimental dogs, 21 showed gross evidence of acute massive lung oedema, 5 died of ventricular fibrillation or cardiac arrest during or immediately (<3 min) after adrenaline injection, and 4 failed to produce pulmonary oedema. In the oedema group, 18 lungs were graded 3+ or 4+ according to the

TABLE 1. *Lung weight: heart weight ratio and lung wet weight: dry weight ratio in oedema-positive and oedema-negative dogs which had undergone pericardiotomy and in control dogs.*

Treatment of dogs	Results of treatment	Number of dogs	Lung weight: heart weight ratio Mean±s.e.	Lung wet weight: dry weight ratio Mean±s.e.
Pericardiotomy plus adrenaline	Oedema-positive	21	2·40±0·15	7·92±0·52
	Oedema-negative	4	1·31±0·10‡	4·82±0·27†
	Immediate death	5	1·20±0·08‡	5·30±0·49
Pericardiotomy plus saline	Oedema-negative	4	1·13±0·19†	4·89±0·14†
Adrenaline alone	Oedema-negative	7	1·32±0·06§	4·71±0·28‡

Control dogs were those with an intact pericardium which were treated with adrenaline or dogs which had undergone pericardiotomy but received saline instead of adrenaline. † Mean significantly different from oedema positive value at $P < 0·05$. † Mean significantly different from oedema positive value at $P<0·02$. ‡ Mean significantly different from oedema positive value at $P<0·01$. § Mean significantly different from oedema positive value at $P<0·001$.

criteria of Singer *et al.* (1958) and only 3 were graded 2+. The control groups did not show gross evidence of acute lung oedema. Table 1 shows that lung wet weight: heart wet weight ratio in the oedema-positive group is significantly higher than in the other groups. The wet weight: dry weight ratio also rose significantly when acute massive lung oedema was present.

Discussion.—In the present study, adrenaline-induced lung oedema was successfully produced in 70% of open-chest dogs in which the pericardium had been opened. If dogs which died from ventricular fibrillation caused by the large dose of adrenaline are discarded, the percentage rises to 87%, and if we are more selective about the health of the dogs used the percentage should be further improved. The relation of pericardiotomy to adrenaline-induced massive lung oedema in the dog is obscure and under investigation.

Electrical conductance (Lambert & Gremels, 1926) and lymphatic outflow (Uhley, Leeds, Friedman & Sampson, 1958) were initially measured to assess the degree of lung oedema but were unsatisfactory. The best, and the simplest, method for such assessment was the gross observation of the lung with measurement of the ratio of the lung wet weights to the heart wet weights. For the latter, the grading by Singer *et al.* (1958) was preferred to that by Jordan & DeLaney (1951). Thus, in the present study, the lung wet weight: heart wet weight ratio showed a clear correlation to the degree of oedema, with a ratio greater than 2 representing massive lung oedema. The lung wet weight: dry weight ratio also increased in massive lung oedema but had a wider range, possibly due to marked individual variation of pulmonary parenchymatous and fibrous tissues. Moreover, five days of drying were required to obtain the ratio while the total lung wet weight: heart wet weight ratio could be determined immediately.

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