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Interruption of pulmonary arterial flow with inadequate ventilation leads to pulmonary infarction

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Abstract We examined the effect of interruption of pulmonary arterial flow and inadequate ventilation on the development of pulmonary infarction in rats. Pulmonary arterial flow was blocked by the injection of agar into the inferior vena cava and inadequate ventilation was produced by obstructing the left main bronchus with a polypropylene tip. Histological and angiographic examination of the lung demonstrated that: pulmonary artery embolism alone does not induce pulmonary infarction; obstruction of a bronchus does not induce significant changes, but that pulmonary infarction develops when pulmonary artery embolism and obstruction of a bronchus occur simultaneously. It has been thought that pulmonary infarction is caused by acute obstruction of a pulmonary artery, however, the alveolar walls are supplied with oxygen by both the pulmonary circulation and by ventilation. Interruption of pulmonary arterial flow alone is probably not sufficient to induce pulmonary infarction, which is probably caused by deficiency of oxygen supply to the alveolar walls by a synergy between interruption of pulmonary arterial flow and inadequate ventilation.

Key words Pulmonary infarction · Interruption of pulmonary arterial flow · Inadequate ventilation

Introduction

Pulmonary infarction is often considered to be due to obstruction of a pulmonary artery, usually due to thromboembolism [3]. Pulmonary artery thromboembolism is often seen at autopsy but pulmonary infarction is less common [4, 7, 9]. Almost all cases of pulmonary infarction are accompanied by obstruction of a pulmonary artery, but the incidence of pulmonary infarction in the cases of pulmonary artery obstruction is unexpectedly low. Moreover, interruption of pulmonary arterial flow by ligation or embolization of a pulmonary artery fails to induce pulmonary infarction in animal experiments [8]. Accordingly, interruption of pulmonary arterial flow alone may not be sufficient to induce pulmonary infarction and some additional factor, for example, inadequate ventilation may be necessary, since alveolar walls are supplied with oxygen by both the pulmonary circulation and by direct gas exchange. Some investigators have reported that pulmonary infarction tends to occur more often in association with pulmonary congestion, oedema, pneumonia and atelectasis [10, 11]; conditions which lead to extreme deficiency of oxygen supply to the alveolar walls [1, 5, 6]. The present study, undertaken in rats, sought to clarify the role of interruption of pulmonary arterial flow and of inadequate ventilation on the development of pulmonary infarction.

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Materials and methods

Fifty-two male Wistar rats weighing about 300 g were maintained in community wire-woven cages with 2–3 animals per cage under a 12–12 light-dark cycle at a temperature of 22–24° C. The animals were housed for 3 days prior to the experiments and maintained on a standard diet and water ad libitum. They were divided into four groups of 13 rats each. Group A: controls; Group B: obstruction of the left main bronchus; Group C: embolization of the pulmonary arterial branches; Group D: embolization of the pulmonary arterial branches plus obstruction of the left main bronchus.

Embolization of the pulmonary arterial branches

The abdomen was opened through an upper midline incision under ether anaesthesia and aseptic operative techniques. Agar (1 g) was dissolved in physiological saline (60 ml) by boiling and coagulated by cooling. The coagulated agar (0.07 ml), in the maximum dose avoiding death from right-sided heart failure, was injected into the inferior vena cava with 27G needles. In controls rats, physiological saline (0.07 ml) was injected. The abdominal incision was closed with sutures.

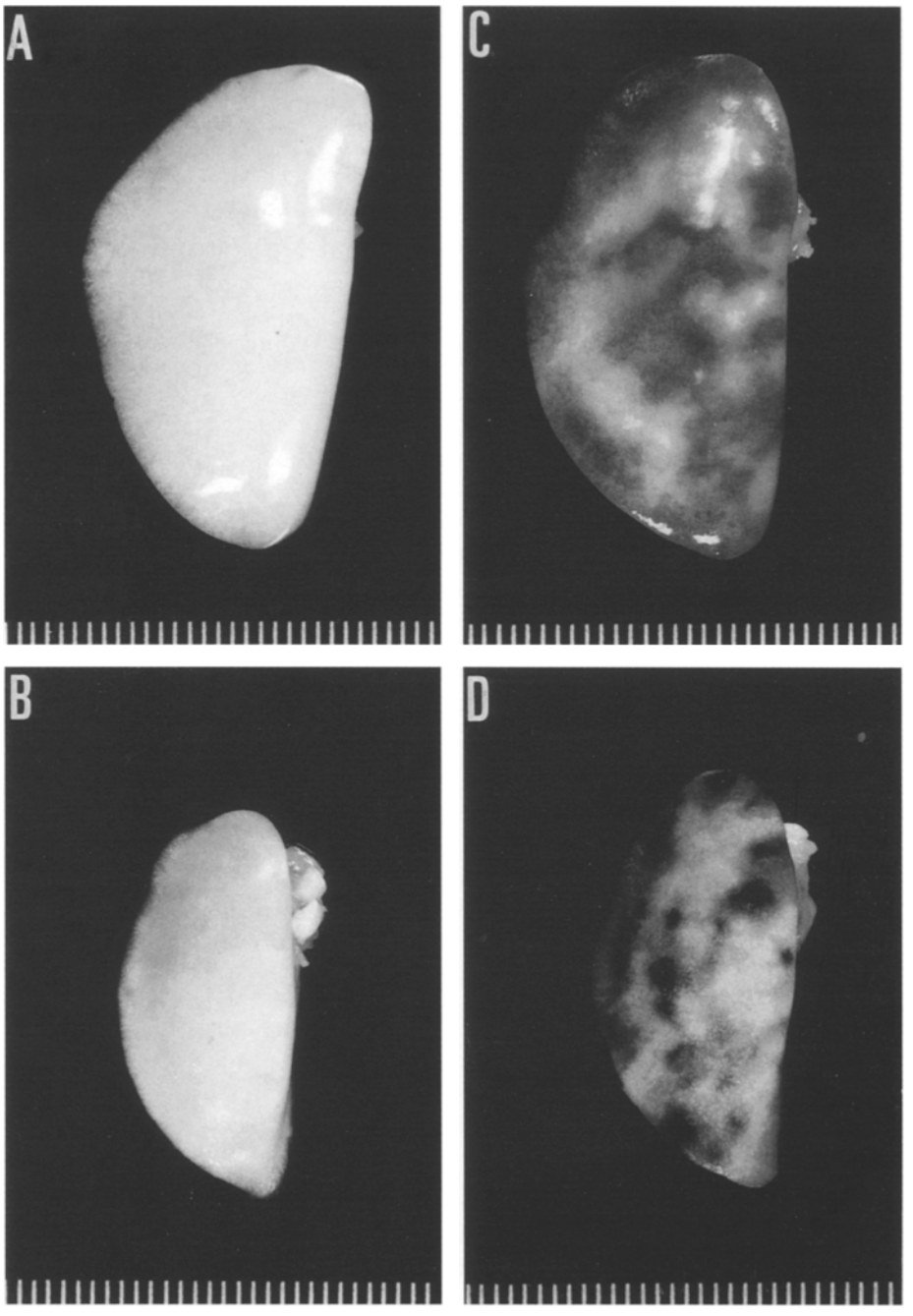

Fig. 1A–D Gross appearance of left lung (graduation=1 mm). **A** Group A (*control*). There are no conspicuous changes. The lung is perfused with physiological saline, and blood in the lung is washed out completely. **B** Group B (obstruction of the left main bronchus). The lung has collapsed. The blood in the lung is completely washed out. **C** Group C (embolization of the pulmonary arterial branches). Unperfused areas, where blood is not washed out, are seen sporadically. **D** Group D (embolization of the pulmonary arterial branches plus obstruction of the left main bronchus). Perfused, unperfused and haemorrhagic areas are seen in the collapsed lung

Obstruction of the left main bronchus

A polypropylene tube was inserted into the left main bronchus immediately after closure of the abdominal incision. The diameter of the tube was about 2 mm and the length 10 mm. Its lumen was completely obliterated by heating. In control rats, a patent tube was used.

The abdomen was reopened through an upper midline incision under ether anaesthesia 24 h after the operation. After heparinization, the animals were killed. A polyethylene cannula was inserted into the right atrium through the inferior vena cava, 100 ml of physiological saline was infused to wash out blood in the lungs and 50 ml of 20% buffered neutral formalin was infused to prevent collapse of the blood vessels (infusion pressure: 200 mm water). Then Indian ink was infused through the cannula in 8 rats for demonstration of the distribution of the pulmonary arterial blood supply, and a 50% barium sulphate emulsion was injected into the cannula in 5 rats for angiography of the lungs. Before the lungs were removed, buffered neutral formalin was infused into the lungs through the trachea (infusion pressure: 150 mm water). Angiograms were taken with a super soft X-ray apparatus. The lungs were fixed in 20% buffered neutral formalin for 7 days, embedded in paraffin and studied histologically. Sections were stained with haematoxylin and eosin and by Weigert's method for elastic fibres.

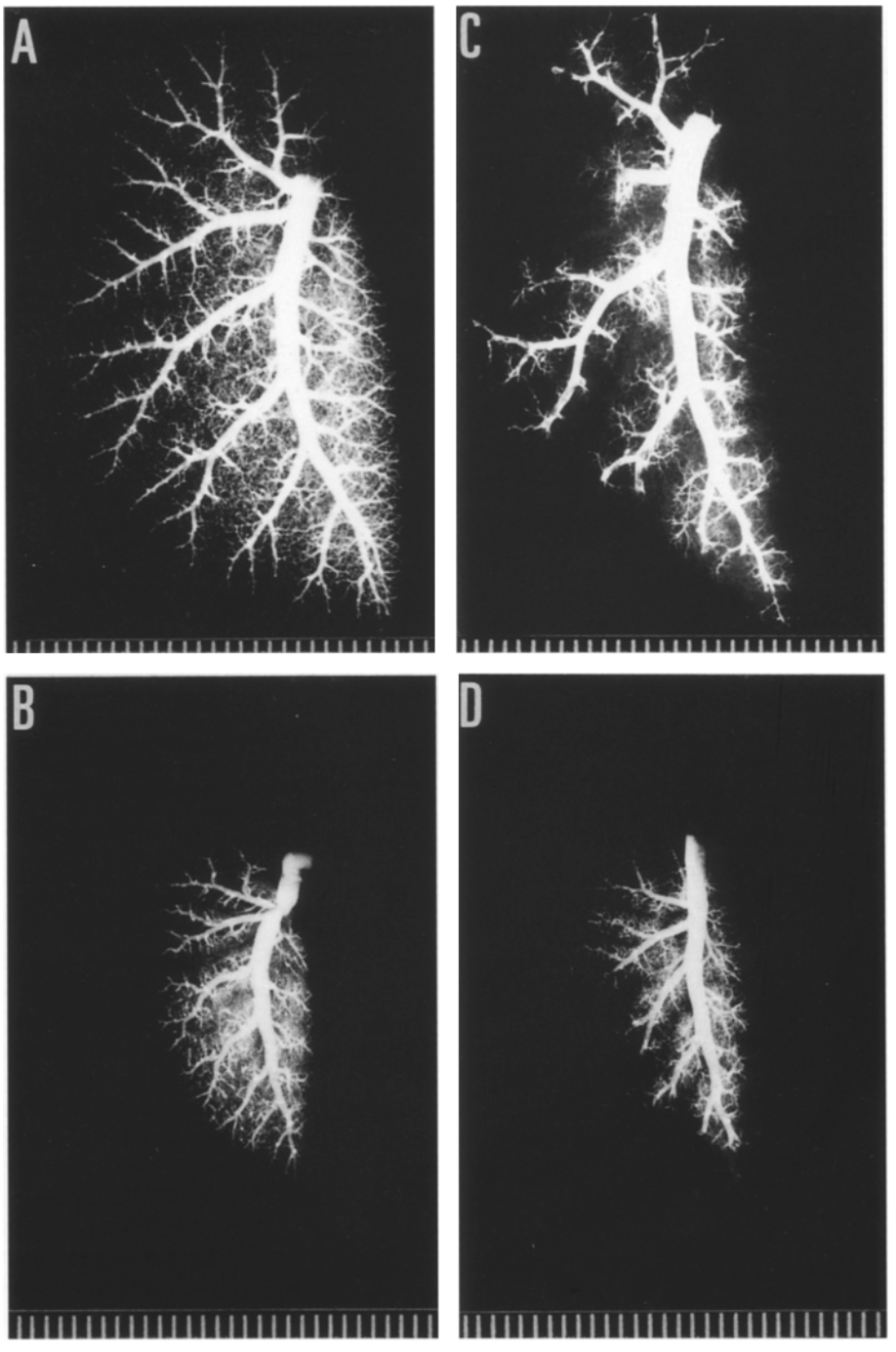

Fig. 2A–D Angiograms of the left pulmonary artery. **A** Group A (control). Contrast medium is adequately injected into every branch. **B** Group B (obstruction of the left main bronchus). A decrease in diameter and length of every branch and tortuosity of the peripheral branches are seen as results of collapse, but no obstruction is evident. **C** Group C (embolization of the pulmonary arterial branches). Medium-sized and smaller branches are completely obstructed. **D** Group D (embolization of the pulmonary arterial branches plus obstruction of the left main bronchus). Obliteration of medium-sized and smaller branches and a decrease in diameter and length of large- and medium-sized branches are seen

Results

Group A (controls)

There were no conspicuous macroscopic or histopathological changes in the lungs (Fig. 1A). Blood in the pulmonary arteries, capillaries and pulmonary veins was washed out, and particles of Indian ink were seen in them. Pulmonary arteriograms showed that contrast medium was adequately infused through every branch (Fig. 2A).

Group B (obstruction of the left main bronchus)

The left lung was collapsed (Fig. 1B). Histologically, there was no significant change except for collapse of the alveolar spaces (Fig. 3A). Neither necrosis of alveolar walls nor alveolar haemorrhage was seen. Blood in the pulmonary arteries, capillaries and pulmonary veins was washed out, and particles of Indian ink were seen (Fig. 3B). Pulmonary arteriograms showed a decrease in the diameter and length of the pulmonary arterial branches and tortuosity of the peripheral branches. However, the contrast medium adequately filled the most peripheral

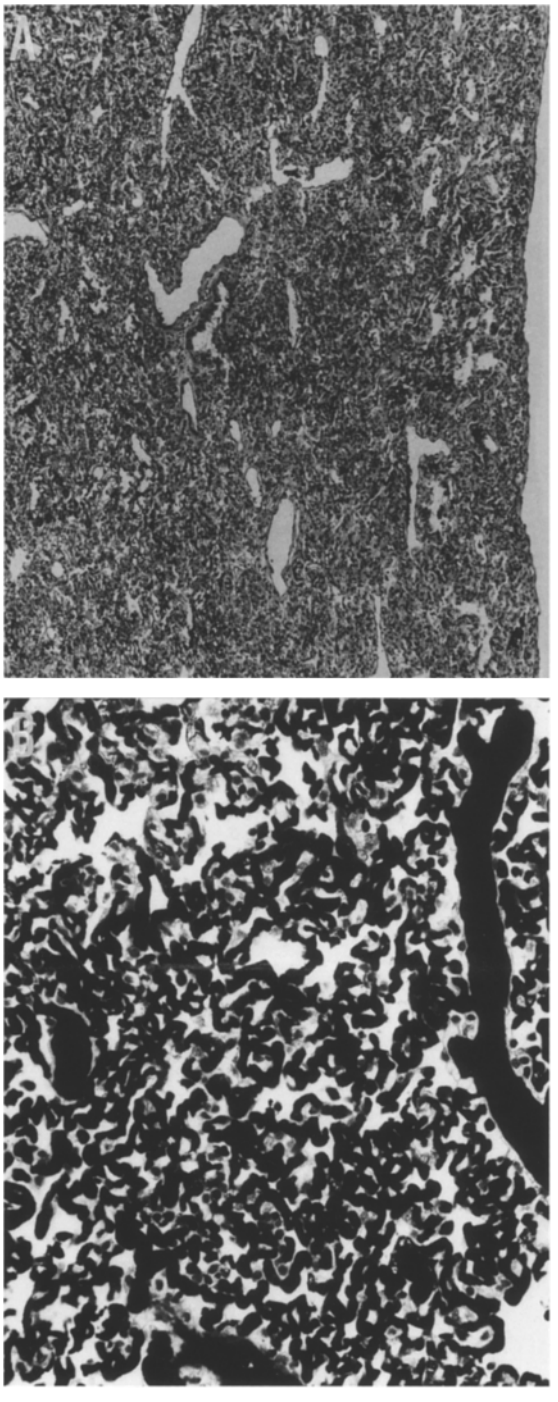

Fig. 3A, B Histology of the left lung of a rat with obstruction of the left main bronchus (Group B). **A** There is no significant change, except for collapse of the alveolar spaces. **B** Blood in the pulmonary arteries, capillaries and pulmonary veins is washed out, and particles of Indian ink are seen in them

branches of the pulmonary artery and there was no obstruction of the branches (Fig. 2B). The findings in the right lung were the same as those of Group A.

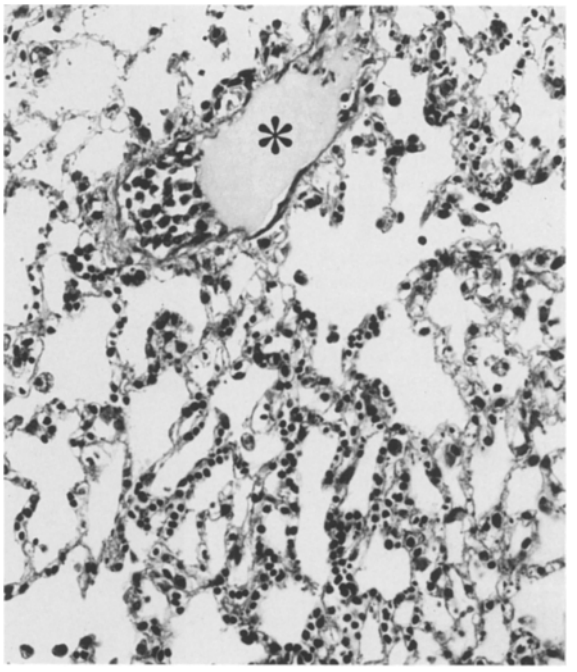

Fig. 4 Histology of the left lung of a rat with embolization of the pulmonary arterial branches (Group C). Injected agar is seen in a pulmonary arterial branch (*), and peripheral capillaries are not perfused. No necrosis of the alveolar walls or alveolar haemorrhage is seen

Group C (embolization of the pulmonary arterial branches)

Unperfused areas, where blood in the vessels was not washed out, were seen sporadically in both lungs (Fig. 1C). Histologically, the injected agar was found in many medium-sized and smaller branches of the pulmonary arteries and their peripheral alveolar capillaries were not perfused. Unperfused alveolar capillaries were packed with red blood cells, and particles of Indian ink or barium sulphate were not seen. However, no collapse, necrosis of the alveolar walls or alveolar haemorrhage was seen. Pulmonary infarction was not recognized (Fig. 4). Pulmonary angiograms showed that some medium-sized and smaller branches of the pulmonary arteries were completely obstructed (Fig. 2C). The macroscopic, histological and angiographic findings of the perfused areas were the same as in Group A.

Group D (embolization of the pulmonary arterial branches plus obstruction of the left main bronchus)

The left lung was collapsed. Perfused areas, unperfused areas and haemorrhagic areas were seen (Fig. 1D). Histologically, the injected agar was found in some medium-sized and smaller branches of the pulmonary arteries. The haemorrhagic areas were confirmed to be haemorrhagic infarction, namely coagulative necrosis of the alveolar walls and haemorrhage into the alveolar spaces.

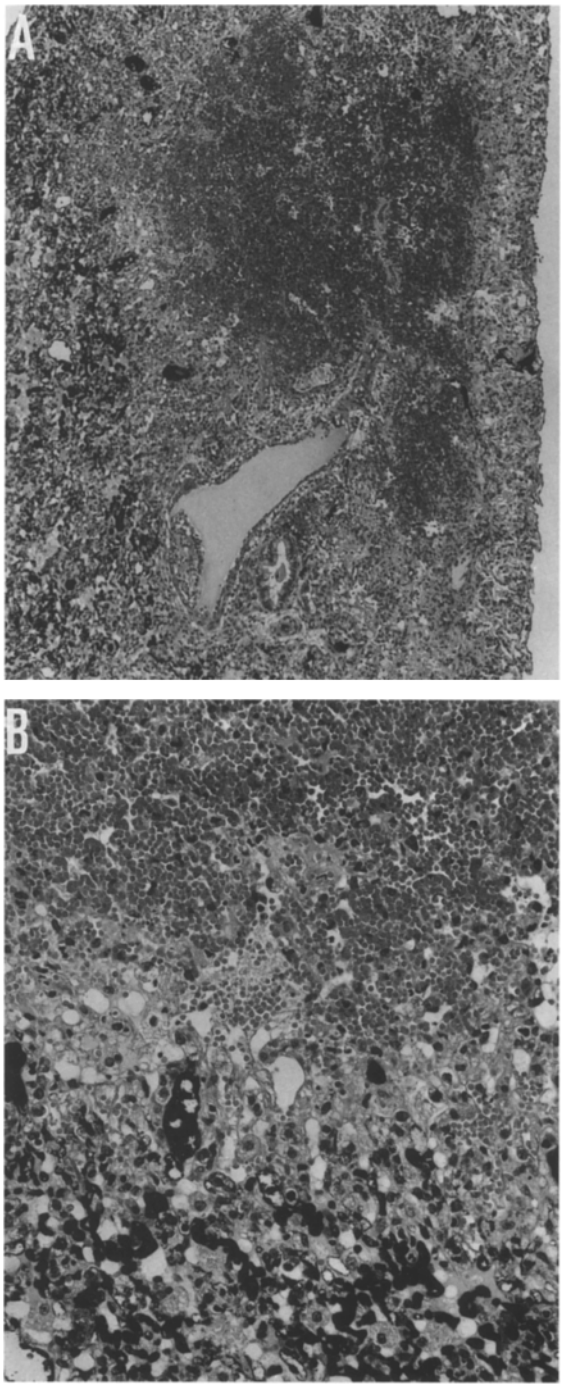

Fig. 5A, B Histology of the left lung of a rat with embolization of the pulmonary arterial branches plus obstruction of the left main bronchus (Group D). **A** The pulmonary arterial branches are obstructed with agar, and in the peripheral area coagulative necrosis of alveolar walls and alveolar haemorrhage are seen. **B** Particles of Indian ink are not seen in the infarcted area, although they are packed in the capillaries of the alveolar walls in the non-infarcted area

Particles of Indian ink were not seen in the infarcted areas. There were no significant changes in the perfused areas except for collapse (Fig. 5A, B). Pulmonary arteriograms showed evidence of collapse as seen in Group B and of obstruction of pulmonary arterial branches as seen in Group C (Fig. 2D). There was no significant change in the bronchial arterial branches. The findings in the right lung were the same as in Group C.

Discussion

An infarction is a localized area of tissue necrosis, resulting from circulatory insufficiency (ischaemia). Accordingly pulmonary infarction can be defined as necrosis of the lung parenchyma. However, the term pulmonary infarction is often used loosely and incorrectly, because clinicians and radiologists cannot distinguish complete infarction with necrosis from congestive atelectasis or incomplete infarction without necrosis. Pathologically, incomplete or incipient infarction is haemorrhage alone, which is assumed to be due to rupture of the alveolar capillaries caused by the increased bronchial arterial flow in reaction to the interruption of pulmonary arterial flow. Complete or true infarction is tissue necrosis with haemorrhage [7, 9] and pulmonary infarction in the present study describes this change.

The present study demonstrates that pulmonary artery embolism leads to interruption of blood flow in pulmonary arterial branches but does not induce pulmonary infarction. Obstruction of the bronchus does not induce significant changes, except for collapse but pulmonary infarction only develops when pulmonary artery embolism and obstruction of the bronchus occur simultaneously.

It is generally thought that infarction is caused by relative or absolute deficiency of oxygen supply due to obstruction of the arteries and that the cause of pulmonary infarction is acute obstruction of the pulmonary artery. However, it has been reported that the incidence of pulmonary infarction is as low as 10 to 30% in all cases of thomboembolism of the pulmonary artery [3, 7, 9]. The present study demonstrates that embolization of the pulmonary artery does not induce pulmonary infarction and that interruption of pulmonary arterial flow alone is not sufficient to induce pulmonary infarction. The lung is supplied with oxygen by both the pulmonary circulation, including the pulmonary arteries and the bronchial arteries and by ventilation through the respiratory tract.

Clinicopathological reviews have shown that pulmonary thromboemboli tend more often to be followed by infarction in patients with pulmonary congestion, oedema, pneumonia or atelectasis [10, 11]. These pathological conditions disturb the supply of oxygen to the alveolar walls. We may expect that the coexistence of disturbance of the pulmonary circulation and of ventilation might induce marked tissue hypoxia and lead to pulmonary infarction, as shown in the present study.

It had been thought that the bronchial arteries might play an important role on the development of pulmonary infarction, however, recent work suggests that the bronchial arterial supply contributes little to the development or prevention of pulmonary infarction [2, 4, 5, 7]. The present study also illustrates that the bronchial arterial supply is unimportant.

In conclusion, it appears that the deficiency of oxygen supply to the alveolar walls due to a synergy between interruption of pulmonary arterial flow and inadequate ventilation causes pulmonary infarction, irrespective of the bronchial arterial supply.

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