

# Influence of long-term intermittent exposures to hypoxia on decompression-induced pulmonary haemorrhage<sup>1</sup>

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**Fang, H. S. and Chen, C. F. (1976).** *Thorax*, 31, 91-93. **Influence of long-term intermittent exposures to hypoxia on decompression-induced pulmonary haemorrhage.** Healthy male rats were acclimatized by being placed in a decompression chamber at a simulated altitude of 18 000 feet (5486 m) for three hours daily for 84 days. The altitude acclimatized rats paired with unacclimatized rats were rapidly decompressed together. The range of decompression was performed from one atmospheric pressure to an ambient pressure of 30 mmHg in 0.2 seconds. It was found that in control rats, 14 of 20 lungs (70%) exhibited pulmonary haemorrhage following rapid decompression. In altitude acclimatized rats, however, only 6 of 20 (30%) revealed decompression-induced haemorrhage. The difference was statistically significant. The present findings indicate that long-term intermittent exposures to hypoxia might increase the resistance of pulmonary tissue to rapid decompression, resulting in a decrease in frequency and severity of pulmonary haemorrhage. The possible mechanism of such a phenomenon is discussed.

It has been shown that hypoxia may induce striking hypertrophy of smooth muscle of small pulmonary arteries in men, dogs, calves, and rats (Naeye, 1965; Naeye and Bickerman, 1959). It is also known that pulmonary haemorrhages are the most common lesions seen in experimental animals subjected to rapid decompression (Whitehorn, Lein, and Hitchcock, 1947; Hall, 1955; Hitchcock, 1953). The purpose of this study is to ascertain whether prolonged intermittent exposures to hypoxia would influence the incidence of pulmonary haemorrhages following rapid decompression.

## METHODS

Healthy male rats (Long Evans strain) were acclimatized by being placed in a low-pressure chamber at a pressure of 379 mmHg (simulated altitude: 18 000 feet (5486 m); rate of ascent: 1500 feet (457 m) per minute) for 3 hours each day (except Sunday) for a period of 84 days. To produce such a low pressure within the chamber, air was withdrawn faster than it entered so that there

was no possibility of carbon dioxide accumulation during chamber flight. Twenty-four hours after the last altitude acclimatization each experimental rat was rapidly decompressed together with a control male rat. Rapid decompression was accomplished by the rupture of a sheet of x-ray film separating an animal chamber at one atmospheric pressure from a large vacuum chamber using the method described previously (Fang, 1966). The small animal chamber was kept open to room air until immediately before the rapid decompression. The rate of decompression was measured by means of a Statham model PM6±15-350 transducer through a Grass polygraph. The range of decompression was from an initial pressure of 760 mmHg down to a final pressure of 30 mmHg in 0.20 seconds. In order to avoid hypoxia acting as a complicating factor, all rats were recompressed immediately following decompression. The lungs were then carefully examined for gross evidence of haemorrhage thereafter. The severity of decompression-induced haemorrhage was graded according to the following scale: 0 no haemorrhage; + slight haemorrhage (a few petechial haemorrhages); ++ moderate haemorrhage (haemorrhagic area covering less than 25%

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of the lungs); and +++ severe haemorrhage (haemorrhagic area covering 25–50% of the lungs).

### RESULTS

The Table shows the results obtained. It will be noted that in control animals, 14 of 20 lungs showed mild to severe pulmonary haemorrhages, while in experimental animals subjected to prolonged intermittent exposures to 18 000 feet (5486 m) altitude for 3 hours each day for 84 days, the frequency of occurrence of pulmonary haemorrhage was markedly decreased. This was indicated by the fact that haemorrhages were found in only 6 out of 20 lungs on necropsy, among which 5 were mild and 1 was severe. The difference in occurrence of pulmonary haemorrhage between the control and experimental groups was statistically significant ( $P < 0.025$ ,  $\chi^2$  test).

### DISCUSSION

During the 14-week period of altitude acclimatization, an increased weight from 165 g to an average weight of 335 g, a gain of 107%, was noted in the experimental rats. The respective figures in the control animals were from 145 g to 328 g, a 128% gain. The differences, though statistically insignificant, indicated that the growth of male rats was not retarded by long-term intermittent exposures to 18 000 feet (5486 m) altitude. This

finding is quite in accord with those of Thorn *et al.* (1942) and Fang and Chen (1973).

The effect of hypoxia on pulmonary vascular changes was extensively studied by Naeye (1965). He reported that when dogs' lungs were poorly ventilated for longer than three weeks, the small pulmonary arterial muscle increased in mass. Prolonged hypoxia also led to an increase of pulmonary muscle mass in yearling steers and calves. In the calves exposed to chronic hypoxia both medial smooth muscle hyperplasia and hypertrophy were shown in the small pulmonary veins. In some infants with unilateral diaphragmatic defects, pulmonary arterial muscle mass was found to be much greater in the poorly ventilated lungs than in the better ventilated lungs. Naeye and Bickerman (1959) also demonstrated that in human subjects with alveolar hypoventilation due to obesity, and in native residents at high altitude, the smooth muscles of the pulmonary arteries showed marked hypertrophy. On investigating the effect of chronic hypoxia upon pulmonary arteries in adult rats, they again observed similar pulmonary vascular changes to those found in hypoxic humans. It is generally accepted that two mechanisms may be involved in the development of pulmonary lesions during rapid decompression (Whitehorn *et al.*, 1947; Hitchcock, 1953; Fang, 1966; Fang, Liu, and Chen, 1971). One is the sudden expansion of the lungs which results in stretching to eventual rupture of the alveolar wall. The other is a sudden rise of intrapulmonary pressure which produces a bruising effect by pushing the inflated lungs against the rigid

TABLE

FREQUENCY AND SEVERITY OF PULMONARY HAEMORRHAGE IN CONTROL AND EXPERIMENTAL RATS (18 000 ft altitude for 3 hr each day for 84 days) FOLLOWING A SINGLE RAPID DECOMPRESSION FROM ONE ATMOSPHERIC PRESSURE TO AN AMBIENT PRESSURE OF 30 mmHg IN 0.2 s

| Control                            |             |           |                  | Experimental                       |         |                |             |           |                  |                                    |         |
|------------------------------------|-------------|-----------|------------------|------------------------------------|---------|----------------|-------------|-----------|------------------|------------------------------------|---------|
| Rat No.                            | Body Weight |           |                  | Pulmonary Haemorrhage <sup>1</sup> |         | Rat No.        | Body Weight |           |                  | Pulmonary Haemorrhage <sup>1</sup> |         |
|                                    | Initial (g) | Final (g) | Diff. %          | Rt Lung                            | Lt Lung |                | Initial (g) | Final (g) | Diff. %          | Rt Lung                            | Lt Lung |
| 1                                  | 127         | 332       | 142              | ++                                 | +       | 2              | 160         | 345       | 116              | ++                                 | ++      |
| 3                                  | 145         | 322       | 122              | +                                  | 0       | 4              | 149         | 324       | 117              | 0                                  | 0       |
| 5                                  | 154         | 330       | 114              | +++                                | +++     | 6              | 213         | 407       | 91               | 0                                  | 0       |
| 7                                  | 137         | 340       | 148              | +                                  | +       | 8              | 165         | 315       | 91               | +                                  | 0       |
| 9                                  | 116         | 275       | 137              | 0                                  | 0       | 10             | 174         | 321       | 85               | 0                                  | 0       |
| 11                                 | 137         | 335       | 145              | 0                                  | +       | 12             | 133         | 280       | 111              | 0                                  | 0       |
| 13                                 | 130         | 320       | 146              | +                                  | +       | 14             | 160         | 359       | 124              | +                                  | +++     |
| 15                                 | 155         | 354       | 128              | 0                                  | 0       | 16             | 222         | 363       | 64               | 0                                  | 0       |
| 17                                 | 195         | 313       | 61               | +++                                | ++      | 18             | 146         | 330       | 126              | 0                                  | 0       |
| 19                                 | 147         | 355       | 141              | +                                  | +       | 20             | 125         | 305       | 144              | 0                                  | +       |
| Av.                                | 145         | 328       | 128 <sup>a</sup> |                                    |         |                | 165         | 335       | 107 <sup>a</sup> |                                    |         |
| No. of lungs revealed haemorrhage: |             |           |                  | 14 <sup>b</sup>                    |         | 6 <sup>b</sup> |             |           |                  |                                    |         |

<sup>1</sup>0 No haemorrhage  
+ Slight haemorrhage  
++ Moderate haemorrhage  
+++ Severe haemorrhage

P (a:a) 0.08  
P (b:b) < 0.025

thoracic cage. It is possible that the hypertrophy of the pulmonary vessels following prolonged intermittent exposures to hypoxia might increase the resistance of pulmonary tissues to rapid decompression. The frequency and severity of decompression-induced pulmonary haemorrhage may thus be lessened. On the other hand, Fang and Lin (1972) observed that toads, after fasting for 257 to 271 days, showed marked atrophy of smooth muscle fibres in the pulmonary vessels as well as in the alveolar septa. Working with rats, Lin and Fang (1973) also found that prolonged semistarvation for 45 to 90 days led to a certain degree of lung atrophy. Such atrophy, occurring in the pulmonary vessels and possibly some other pulmonary tissues, lowered the resistance of the lung to rapid decompression. The results obtained from both the previous experiments on toads and from the present study on rats are not inconsistent.

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