Effect of high pressure oxygen on the duration of anaesthesia in mice

SIR,—Anaesthesia modifies the toxicity of hyperbaric oxygen (Bean, 1945). Conversely, hyperbaric oxygen may be expected to modify the action of anaesthetics, but no such experiments appear to have been reported. The only reference to such an action is that by Bean (1931) who stated that high pressure oxygen lightens anaesthesia, and that higher doses of an agent are required to provide anaesthesia in experimental animals exposed to high pressure oxygen for prolonged periods. We had also observed that animals under high pressure oxygen seemed less deeply anaesthetised than animals similarly anaesthetised in air. The present work provided quantitative data to support these impressions. Further impetus was given to this study by the finding that the biochemical action of amylobarbitone in blocking electron transport reactions *in vivo* can be reversed, at least in part, by hyperbaric oxygenation (Chance, Jamieson & Williamson, 1966).

Sleeping times in mice anaesthetised with pentobarbitone sodium were measured as a test for anaesthetic duration. The six-compartment pressure chamber has been described previously (Jamieson & van den Brenk, 1963). Twelve male albino mice, 22–27 g, were injected intraperitoneally with pentobarbitone sodium for each experiment. Each mouse was weighed and dose prescribed per unit weight. The total time taken to inject each group of mice was approximately 3·5 min. Each of the six containers inserted in the pressure vessels was centrally partitioned to house each mouse separately. Alternate cages were pressurised, the remainder being maintained under ambient air conditions as controls. Chambers were pressurised at a rate of 1·3 atmospheres per min, a maximum time of 8 min elapsing between injection and attaining the required pressure. Oxygen flowed continually through the pressurised

TABLE 1. THE EFFECT OF HYPERBARIC OXYGEN [ATMOSPHERES ABSOLUTE (ATA)] ON THE DURATION OF PENTOBARBITONE SODIUM ANAESTHESIA IN MICE

Dose pentobarbitone Na (no. of animals)	Treatment	Awakening time min ± s.e.	P value
35 mg/kg (16)	air	46·5 ± 3·8	<·001
,, (17)	6 ATA O_2	27·2 ± 1·3	
,, (18)	air	40·6 ± 3·3	<·001
,, (17)	5 ATA O_2	24·7 ± 1·4	
,, (18)	air	37·9 ± 2·6	<·001
,, (18)	4 ATA O_2	25·7 ± 1·2	
,, (18)	air	35·5 ± 2·2	N.S.
,, (18)	3 ATA O_2	31·3 ± 2·1	
50 mg/kg (18)	air	64·1 ± 2·0	<·02
,, (18)	3 ATA O_2	56·7 ± 1·5	

TABLE 2. CONVULSIVE TIMES IN MICE EXPOSED TO HYPERBARIC OXYGEN [ATMOSPHERES ABSOLUTE (ATA)]

Treatment (no. of animals)	Time to convulsion min ± s.e.
6 ATA O_2 (12)	10 ± 1
5 ATA O_2 (12)	30 ± 2
4 ATA O_2 (12)	45 ± 2
3 ATA O_2 (12)	(no convulsions)

chambers at a rate of 1 litre/min to maintain gas tensions and temperatures constant. The chamber temperatures were monitored individually and ranged from 19° to 24° in different experiments, a variation of $\pm 0{\cdot}5°$ in any one experiment. Three trials were made at each pressure and the results pooled (Table 1). The "awakening time" was the duration between time of injection and the time when the animal could stand, grip the grate in the cage, and attempt to walk. The induction of hypnosis failed in a very small number of animals in both control and pressurised groups and these mice have been excluded from the results. All other animals lost their righting reflex within 5–7 min after injection.

In preliminary experiments a dose of pentobarbitone sodium of 35 mg/kg gave satisfactory sleeping times for animals compressed to 4–6 atmospheres absolute, in that the mice awoke before severe signs of oxygen toxicity (largely based on pulmonary damage) had occurred. Pressures above 6 atmospheres were not used since pulmonary toxicity occurs too rapidly at this pressure.

The difference in duration of anaesthesia between animals breathing ambient air and oxygen at 4, 5 and 6 atmospheres respectively was highly significant (Table 1). There was a slight gradation in effect for this pressure range. At 3 atmospheres, a dose of 35 mg/kg pentobarbitone sodium produced a slight but not statistically significant difference in length of sleeping time. If the dose was increased to 50 mg/kg to prolong sleeping times and correspondingly increase the duration of exposure to 3 atmospheres oxygen, a slight but significant reversal of anaesthetic effect occurred (Table 1).

There was no clear correlation of convulsive times in unanaesthetised mice (Table 2) and duration of anaesthesia under hyperbaric oxygen, the dose-effect relationship being much steeper for oxygen convulsions than for reversal of anaesthesia in relation to oxygen pressure.

It is known that barbiturate anaesthesia can protect against convulsions and pulmonary damage produced in oxygen toxicity (Bean, 1945; Jamieson & van den Brenk, 1962), and can also potentiate a spastic motor paralysis resulting from hyperbaric oxygen (van den Brenk & Jamieson, 1964). It has now been shown that hyperbaric oxygen decreased the anaesthetic effect of barbiturate drugs.

Although the results do not exclude the possibility of chemical or metabolic inactivation of the barbiturate *in vivo* due to high pressure oxygen, it seems most likely that hyperbaric oxygen is able to directly reduce the action of barbiturates on the central nervous system by in itself altering the sensitivity of cells to the anaesthetic agent.

Radiobiological Research Unit,
Cancer Institute,
278 William Street,
Melbourne, Australia.
March 8 1966

D. JAMIESON

References

Bean, J. W. (1931). *J. Physiol., Lond.*, **72**, 27–48.
Bean, J. W. (1945). *Physiol. Rev.*, **25**, 1–147.
Chance, B., Jamieson, D. & Williamson, J. R. (1966). *3rd International Conference on Hyperbaric Medicine*, Duke University. In the press.
Jamieson, D. & van den Brenk, H. A. S. (1963). *J. appl. Physiol.*, **18**, 869–876.
Jamieson, D. & van den Brenk, H. A. S. (1962). *Aust. J. exp. Biol. Med.*, **40**, 51.
van den Brenk, H. A. S. & Jamieson, D. (1964). *Biochem. Pharmac.*, **13**, 159.