Letters to the Editor

The inhibition of analgesia in mice by thiopentone

SIR,—Clutton-Brock (1960, 1961) and Dundee (1960) have independently demonstrated that sub-anaesthetic doses of thiopentone antagonize the analgesic action of pethidine and nitrous oxide in man. We are now reporting a similar investigation in mice using morphine, heroin, pethidine and codeine.

Groups of male mice (18–24 g) were injected subcutaneously with the appropriate analgesic and the ED50 determined. The experiment was then repeated on additional groups of mice which were injected intraveously with 25 mg/kg of sodium thiopentone in addition to the analgesic and the ED50 re-determined.

Analgesia was evaluated by the tail-clip technique of Bianchi & Franceschini (1954). The method of Miller & Tainter (1944) was used to determine the ED50's. The parameters obtained from the two experiments were treated statistically.

TABLE 1. THE EFFECT OF THIOPENTONE ON ANALGESIA

	Analgesic only E.D.50 ± s.e.	Analgesic plus thiopentone E.D.50 ± s.e.	P
	mg/kg	mg/kg	
Morphine	15 ± 2·4 (60)	43 ± 11·5 (25)	<0·05
Heroin	0·95 ± 0·2 (35)	3·6 ± 0·28 (25)	<0·05
Pethidine	28 ± 3·2 (35)	54 ± 4·7 (20)	<0·05
Codeine	62 ± 11·4 (25)	110 ± 16 (20)	<0·05

Figures in brackets indicate the number of mice used.

Table 1 shows that the ED50 for all the analgesics was significantly higher for the thiopentone-treated mice than for the controls.

These experimental findings and those of Neal (1964) are in agreement with the clinical observations that thiopentone antagonizes the analgesic action of pethidine.

From the work of Brodie & others (1950), Clutton-Brock (1960, 1961) has concluded that the anti-analgesic action in man is related to the plasma level of thiopentone and Dundee (1960) relates it to the presence of sub-anaesthetic doses of thiopentone in the brain. There is no satisfactory explanation for the increased sensitivity to pain after thiopentone, though it has been suggested that the reticular system of the brain stem may be involved.

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September 14, 1964

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