volume was replaced with heparinized blood from a donor); (ii) 10 rats treated as in (i) but with replacement of blood with saline; (iii) 30 rats without cannulation or transfusion from which only one sample was taken, by abdominal aorta puncture, from groups of five animals at 15, 45, 90, 180, 240 min and 24 h. Quinidine sulphate was determined by a method of Gelfman & Seligson (1961) measuring quinidine fluorescence.

Fig. 1 shows that the half life times are between 34–45 min for the three groups of animals.

Although these results are preliminary we consider the blood concentration pattern acceptable, since the rates of elimination for the three groups do not show significant differences ($P > 0{\cdot}05$).

It is also possible to overcome the limitation of the reduced blood volume (12–15 ml), even in the adult stage, by using this technique.

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September 17, 1973

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Effect of chloroquine on histamine-induced bronchial asthma in the guinea-pig

Chloroquine has direct spasmolytic effects on smooth muscles. Agarwal & Deshmanker (1963) observed that it antagonized the effects of histamine, 5-hydroxytryptamine (5-HT) and acetylcholine on the guinea-pig ileum and tracheal rings. Similar observations were made by Olatunde (1970), who quantitatively showed it to be a more potent antagonist of histamine than of 5-HT and acetylcholine. Chloroquine is concentrated in many tissues, including lung (Berliner, Earle & others, 1948; Grundmann, Virubloresky & Mikutihora, 1970), and since it has been shown to inhibit the catabolic enzyme imidazole *N*-methyl-transferase (Cohn, 1965) we have examined its actions on histamine-induced bronchoconstriction in the guinea-pig.

Bronchoconstriction was induced in guinea-pigs of either sex, 400–900 g, by exposing them to a fine histamine aerosol (1·5% histamine diphosphate solution) in a vapour chamber (Loew, Kaiser & Moore, 1945). One group was pretreated acutely with intraperitoneal injection of chloroquine (20 mg kg^{-1}) 2 h before exposure to histamine aerosol; a second group was pretreated with the same dose daily for 7 days before exposure; a third group was similarly pretreated for 7 days, after which the drug was discontinued for another 7 days before the animals were exposed to histamine. A fourth group formed the controls. A control and a chloroquine pretreated or a control and two pretreated animals were introduced into the vapour chamber together. Time of onset was when the animal showed signs of dyspnoea. Then it was exposed to the aerosol for a further 2 min after which it was removed from the vapour chamber.

Table 1. *Effect of chloroquine administration (20 mg kg^{-1}) acutely or chronically on the bronchoconstrictor effect of histamine.*

Group	No. of animals	Onset of action (s) mean ± s.e.	No. dead	Duration of action (s) in survivors
Control	19	83·9 ± 4·0*	7	95; 320; 215; 100; 95; 210; 130; 75; 95; 210; 335; 235
Acute	9	100·6 ± 16·9*	1	40; 85; 120; 5; 5; 10; 35; one did not react
Chronic	10	95·0 ± 10·5*	0	60; 55; 100; 95; 5; 5; 70; 85; 55; 85
Chronic-withdrawn	5	163·4 ± 59·95*	0	40; 35; 70; 165; 88

* There were no statistically significant differences between the groups when onset of action was compared ($P > 0·3$ for all groups compared with control).

Chloroquine administered either acutely or chronically in the dose of 20 mg kg^{-1} (i.p.) significantly protected the animals against fatal asphyxia caused by the bronchoconstrictor effect of histamine. The data are presented in Table 1. About 37% of the control animals died of asphyxia within 180 s of removal from the chamber while the remainder reacted for periods ranging from 95 to 330 s. On the other hand, 89% of the acutely pretreated animals were protected against fatal asphyxia, and they reacted to histamine for periods of 10 to 120 s. All of the animals which were pretreated chronically for 7 days, including those withdrawn from the drug treatment, were protected against fatal asphyxia but they reacted to histamine for periods ranging from 5 to 165 s. The time of onset of the reaction in the control group did not differ significantly from that of any of the chloroquine pre-treated groups, indicating that the drug did not alter the threshold of response to histamine. These results show that chloroquine confers some protection against histamine-induced bronchoconstriction. The observation that chloroquine afforded protection against the histamine reaction several days after discontinuing the drug suggests that chloroquine not only may accumulate in the lung (Berliner & others, 1948; Grundmann & others, 1970), but also may be retained in sufficient quantity to afford a long-lasting protection. It is interesting to note that although chloroquine interferes with histamine metabolism (Cohn, 1965), it does not aggravate histamine-induced bronchoconstriction but rather affords protection against fatal asphyxia.

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October 2, 1973

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