

Effect of Chlorpromazine on Number of Mast Cells and of Certain Formed Elements of Blood. (23702)

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Recently we have suggested(1) that some of the hypothermic effects of chlorpromazine could be associated with the liberation of a variety of substances, such as histamine, serotonin and adrenaline, which individually will cause some drop in body temperature(1,2,3, 4). Some of these substances have been found in significant amounts in mast cells(5) and in some blood cells(6). The effect of chlorpromazine on mast cells and blood cells was the primary concern of the present study. Since the response to chlorpromazine is greatly reduced in acclimatized animals(1), and because of the reported changes in the number of mast cells of the same animals(7), the effect of chlorpromazine on mast cells of animals exposed to cold for varied periods of time was also investigated.

Methods. Male albino rats weighing about 300 g were used in all experiments. Chlorpromazine (10 mg/kg) was always injected intraperitoneally.* In a first experiment 1 group of 6 animals was used. Blood counts were made at 0, 4, 24 and 48 hr after injection of chlorpromazine. Blood samples were obtained by cutting the tip of the tail. The eosinophiles and total leucocytes were counted by using Henneman's method(8) and the erythrocytes and platelets, by the Rees-Ecker method(9). In a second experiment 4 groups of 6 rats were used. The first group served as control, the second received one injection of chlorpromazine, the third group, 5 injections of the same substance, and the fourth group, 5 saline injections. In the last 2 groups the injections were given at a rate of one per day. Finally in a third experiment 4 groups of rats were exposed to cold (6°C) for 0, 1, 7 and 28 days respectively. At the end of the cold exposure the animals were main-

tained at 24°C for 1 day before receiving chlorpromazine. In the last 2 experiments the mast cells in the intervacular area of the mesentery were examined 24 hr after the last injection in a manner described previously(7).

Results. Table I shows that 5 saline injections have little effect on the number of mast cells of the mesentery whereas a single injection of chlorpromazine reduces the number of these cells. This effect is greatly increased with 5 injections of chlorpromazine. The same table shows that in the preliminary stages of acclimatization (1 and 7 days) the response of mast cells to chlorpromazine is the same as the one observed in control animals. However, after 4 weeks in the cold chlorpromazine has very little effect on the number of mast cells. Table II shows that a single injection of chlorpromazine causes a very large drop in the eosinophile, leucocyte and platelet counts at 4 and 24 hr after the injection. After 48 hr a return towards normal values is observed in these counts although the initial levels have not been reached yet in the eosinophiles and platelets. A small transitory drop is observed in the number of erythrocytes. Measurements of rectal temperature have shown a marked drop in the first 2 hours after chlorpromazine injection, followed by a rapid return towards normal levels after 4 and 6 hours. Twenty-four and 48 hr after chlorpromazine injection the rectal temperature is back to normal.

Discussion. The large drop in the number of mast cells, eosinophiles, leucocytes and platelets caused by chlorpromazine is regarded as additional evidence to our previous suggestion that the hypothermic effect of chlorpromazine can be associated with the release of a variety of substances from either mast cells or blood elements(1). In the light of this hypothesis, the results obtained in acclimatized animals become somewhat easier

* Chlorpromazine was graciously supplied by Smith, Kline and French under their trade name of Thorazine.

TABLE I. Effect of Chlorpromazine on Mast Cells of the Intervascular Region of the Mesentery of Animals Exposed to Cold (6°C) for Various Periods of Time.

Treatment	0	5 saline	1 CPZ*	5 CPZ	1 CPZ	1 CPZ	1 CPZ
Length of exposure at 6°C before inj. of CPZ, days	0	0	0	0	1	7	28
Mast cells in mesentery (per 3 mm ²)	304 ± 104†	254 ± 34	160 ± 26	60 ± 14	172 ± 30	160 ± 60	252 ± 50
P value‡		>0.3	.02	<.001	.02	.02	0.3

* CPZ = Chlorpromazine (10 mg/kg).
 † Stand. dev. ‡ P is calculated by comparing untreated group with the others.

TABLE II. Effect of Chlorpromazine (10 mg/kg) on Certain Formed Elements in the Blood of Normal Rats.

Time after inj. (hr)	Eosinophiles	Leucocytes	Platelets	Erythrocytes	Rectal temp. (°C)
			(× 1000)	(× 1000)	
0	160	17,180	652	8,630	36.8
2					32.5
4	40	10,180	338	8,270	34.2
6					36.0
24	30	12,630	348	8,700	36.6
48	100	16,740	501	8,170	36.5

to interpret. Indeed, the very small destruction of mast cells caused by chlorpromazine in acclimatized animals could explain the reduced hypothermic effect of this drug under these conditions. This may not constitute the complete answer since the hypothermic effect of serotonin and histamine, which are products of secretion of mast cells, is also reduced in acclimatized animals(7).

Recently a large drop in platelet and leucocyte counts was reported in hypothermic dogs(10). Since these blood elements returned to normal levels as soon as the body temperature of the animals returned to normal, it was concluded that lowering of body temperature causes a sequestration rather than destruction of these blood cells. In our study on rats, however, the body temperature, after a drop of 4.3°C within the first 2 hours following the injection of chlorpromazine, has almost returned to normal levels in 6 hours. Consequently the fact that the blood cells studied are still at very low levels even when the body temperature has long returned to normal seems to indicate that the effect of chlorpromazine on certain blood cells is not a result of the hypothermic effect of this drug.

Summary. A single injection of chlorpromazine was shown to cause a large drop in eosinophiles, leucocytes and platelets in the

blood and in the mast cells of the mesentery. The effect of this drug on mast cells is negligible in cold acclimatized animals. This finding is associated with the smaller hypothermic effect of chlorpromazine in acclimatized animals than in control animals. It is suggested that the effect of chlorpromazine on formed elements of the blood and mast cells in the rat is not a direct result of hypothermia.

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