was compared. Dogs were anæsthetized with hexobarbitone and on awakening were given chlorpromazine or the sulphoxide intravenously. Resumption of anæsthesia, indicating potentiation, was observed with both compounds, the sulphoxide being about one-eighth as active as chlorpromazine. In contrast to its activity in dogs, the sulphoxide produced only minimal sedation and potentiation of hexobarbitone in mice, rats and rabbits.

Since chlorpromazine sulphoxide induces sedation in dogs with relatively little of the orthostatic hypotension observed with chlorpromazine, it is planned to test the drug in man in the treatment of mental illness.

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Function of Heparin

BOTH heparin[1] and histamine[2] are now known to be concentrated in the tissue mast cells, and it might thus be expected that the release of histamine caused by damage to the mast cells would be accompanied by the release of heparin and a consequent increase in the clotting time of blood. So far this dual effect has been observed in only one species, the dog, in which an intravenous injection of peptone or of a chemical histamine liberator such as compound 48/80 can release sufficient heparin to render the blood incoagulable. In the rat, however, although compound 48/80 releases histamine from the numerous mast cells in the subcutaneous connective tissue, the clotting time of the rat's blood remains unchanged. We have therefore attempted to discover what happens to the heparin in the rat following a maximal release of histamine by compound 48/80.

Two groups of eight female Wistar rats, of 200–250 gm., were used. The first received intraperitoneally over a period of five days progressively increasing doses of compound 48/80 in saline, by which time 1 mgm. per 100 gm. body-weight could be given without eliciting signs of shock. The second group was given equivalent volumes of saline intraperitoneally as a control. Whole blood-clotting times were measured repeatedly by the capillary tube method, and samples of urine, collected on filter paper, were tested for metachromatism with a weak solution of toluidine blue. At the end of five days, the two groups were killed and skinned, and as much subcutaneous connective tissue as possible was scraped off. Representative tissue spreads were examined histologically for mast cells, the remaining subcutaneous tissue (about 60 gm.) in each group being then pooled and assayed for histamine and heparin as previously described[3], except that on this occasion we used the thiocyanate method[4] for the initial extraction before finally purifying the heparin by the method of Charles and Scott[5].

Compound 48/80 in the dosage used produced widespread degranulation and disruption of the mast cells in the subcutis of rats, and almost complete loss of its tissue histamine—a drop from 26 to 1·5 μgm./gm. tissue (94 per cent loss). On the other hand, the total heparin content fell only from 10·0 to 4·7 I.U./gm. (53 per cent loss), and even this loss was unaccompanied by any sign of the release of heparin into the circulating blood; the clotting time remained normal and no metachromatic material appeared in the urine. That the heparin extracted from the control series did in fact possess anticoagulant activity was confirmed by its action on normal rat blood *in vivo* and *in vitro*.

Thus the almost complete release of histamine from the subcutis of the rat by compound 48/80 is accompanied by a loss of only half the associated heparin. Some of the metachromatic material from the disrupted mast cells may be disposed of locally by macrophages[6,7], some may adhere to adjacent connective tissue fibrils[8] or cells[9], while some may be bound by the basic histamine-liberator itself[10]. Although these same basic compounds can release active heparin into the blood stream of the dog[11], they fail to do so in the rat; the rabbit and the guinea pig appear to be similar to the rat in this respect[12]. This suggests that the function of heparin may be concerned rather with events in the tissues than with the coagulability of the circulating blood.

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Inactivation of Phenyl Mercuric Acetate in Groundwood Pulp by a Mercury-resistant Strain of *Penicillium roqueforti* Thom

AN investigation was started in December 1954 into the storage qualities of groundwood pulp impregnated with 25–35 p.p.m. of phenyl mercuric acetate, compared with unimpregnated pulp made at the same time. One object of this work was to follow the course of infection of the pulps by blueing and wood-rotting fungi (Basidiomycetes), the latter frequently being responsible for the condition known