LETTERS TO THE EDITOR

Histamine in Mast Cell Granules

SIR,—Recent observations on the intracellular distribution of histamine in dog liver have suggested that most of the histamine is present in the mitochondrial fraction[1,2]. However, this fraction has been shown to be highly contaminated with mast cell granules[3], in which the histamine is probably concentrated. This conclusion was supported by the finding that relatively pure fractions of mast cell granules from rat subcutaneous tissue are very rich in histamine. This tempts me to report the results of some similar experiments which I carried out on mice in 1953 in Boston, Mass.

I was attempting to locate the exact site of the histamine in mouse subcutaneous tissue. Using the method of Köksal[4], I obtained isolated mast cell granules from the pooled tissue of 5 mice, and found the granules to contain proportionately more histamine than any other fraction examined. Treatment with the histamine liberators, compound 48/80 or *d*-tubocurarine, released most of the histamine from the granules into the supernatant liquid. Acid treatment likewise freed the histamine.

Köksal showed that this granular fraction also possesses potent anticoagulant properties, and thus it appears that both histamine and heparin are normally present in the granules of mast cells of mouse subcutaneous tissue. Work on dog mast cell tumours[5] indicates that in the dog both histamine and heparin are likewise concentrated in the mast cells. These observations therefore support the suggestion of Mota *et al.*[3] that a reconsideration of the problem of the intracellular distribution of histamine seems to be necessary.

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REFERENCES

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5. Cass, Riley, West, Head and Stroud, *ibid*, 1954, **174**, 318.

The Leucocyte Response in the Rabbit to Pyrogen from *Proteus vulgaris*

SIR,—In your issue for December, 1954, Professor Todd takes me to task for some remarks I made at the Oxford Conference about three papers on pyrogens from his Department. However, in the first paper it is stated: "It was established that there was no correlation between temperature rise and white blood cell change, *i.e.* a rabbit sensitive to pyrogen by one response was not necessarily sensitive by the other." (*J. Pharm. Pharmacol.*, 1952, **4**, 977.) While referring to the second paper I may have used the term "partial correlation" somewhat carelessly, but the contents of that paper—and especially Figure 1—make it clear that correlation was established only between 2 of the 3 doses. Furthermore, in the discussion on this paper, Professor Todd himself, replying to a remark by Dr. J. I. M. Jones on this very point, admitted that "it would be wrong to pretend that the correlation had been established further" (*J. Pharm. Pharmacol.*, 1954, **6**, 323). In the third paper the results for 4 dose levels were presented and correlation was, as he says, "shown to exist." I pointed out these differences in his 3 sets of results, and expressed surprise that, in the third paper, no reference was made to them. It is difficult to understand why Professor Todd should take exception to this.

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