A more detailed account of the results of this investigation will be published in due course in Swedish journals of botany.

ELIAS MELIN
TORSTEN WIKÉN
KARIN ÖBLOM

Institute of Physiological Botany,
University of Uppsala.
March 26.

¹ Wikén, T., *Ark. Bot.*, **33** A, No. 3 (1946).

² Lindeberg, G., *Sym. Bot. Upsal.*, **8**, No. 2 (1944).

³ Melin, E., *Svensk. Bot. Tidskr.*, **37**, 115 (1943).

⁴ Norkrans, Birgitta, *Svensk. Bot. Tidskr.*, **38**, 121 (1944).

⁵ Melin, E., *Sym. Bot. Upsal.*, **8**, No. 3 (1946).

⁶ Abraham, E. P., Chain, E., Fletcher, C. M., Florey, H. W., Gardner, A. D., Heatley, N. G., and Jennings, M. A., *Lancet*, **241**, 177 (1941).

Use of Potassium in the Assay of Curare

Now that tubocurarine, one of the curare alkaloids, is gaining importance in medicine, it is important that this compound and other curare-like substances should be biologically standardized. A suitable method has been described by Chou¹, utilizing the rat's phrenic nerve-diaphragm preparation of Bulbring²; but we have been unable to obtain consistent results with this technique. By using temperatures lower than usual for mammalian tissue work (namely, room temperature, about 20° C.), we have obtained satisfactory results. The preparation lasts for a much longer period of time, shows little sign of fatigue after eight hours, and contractions are more regular. Larger doses of tubocurarine are needed than those used at 37° C., and a reduction in contraction of approximately 50 per cent is obtained with 0.15 mgm.

The difficulty with this technique is that the preparation requires a long time for complete recovery (more than 30 min.); but this has been overcome by the addition of small amounts of potassium ions to the bath during recovery phase, after the curare action has been shown for 3–5 min., according to the preparation. The anti-curare action of potassium is well known. When recovery is complete, the potassium is washed out and the next dose of curare-like substance is added (a total of 6–10 min. after the last dose). Potassium chloride itself exerts a stimulating action in this preparation in small doses (20–30 mgm.), whereas in larger doses (80–100 mgm.) the depressant effect predominates. These quantities refer to an isolated organ bath of 75 ml. capacity.

P. GA. DE JALON
G. B. WEST

College of the Pharmaceutical Society,
London, W.C.1.
April 12.

¹ Chou, *Brit. J. Pharmacol.*, **2**, 1 (1947).

² Bulbring, *Brit. J. Pharmacol.*, **1**, 38 (1946).

Leukotaxine and Histamine

INFLAMMATORY exudates contain a polypeptide, leukotaxine, which has, among other properties, that of inducing increased capillary permeability on intracutaneous injection^{1,2,3}. Other observations suggest that histamine may play a fundamental part in wheal formation of allergic and non-allergic origin⁴⁻⁶. It has therefore been suggested that the active factor in inflammatory exudates is really histamine and not leukotaxine, or that leukotaxine, if it exists, induces an increased permeability of the capillaries only through the mediation of histamine⁸.

That leukotaxine is not histamine is suggested by the observations^{1,2} that: (1) leukotaxine does not cause contraction of the isolated guinea pig ileum; (2) histamine is not chemotactic for leucocytes, but leukotaxine is; (3) intravenous injection of leukotaxine does not lower the blood pressure of the cat.

Moreover, crude preparations of leukotaxine, prepared by the method of Cullumbine and Rydon³, when extracted for histamine (Barsoum and Gaddum's method¹⁰) and assayed on the isolated guinea pig ileum, yield insignificant quantities of histamine; for example, 6 mgm. (550 'units') of crude leukotaxine contained less than 2 µgm. of histamine.

We have used the anti-histamine substance 'Neoantergan', or 2786 R.P., which prevents or diminishes the action of histamine in increasing capillary permeability^{11,12} in further studies on the mode of action of leukotaxine and the production of oedema following cutaneous burning.

We have observed that rabbits burned under nembutal anaesthesia, by exposing their depilated abdomens for 90 sec. to a glass vessel containing water at 70° C., develop extensive subcutaneous oedema of the abdominal wall within two to four hours of burning. The subcutaneous injection of 'Neoantergan' in a 10 mgm./kgm. dose (half the subcutaneous dose of this drug required to produce toxic symptoms in the rabbit) 30 min. before, or immediately after, or one hour or two hours after burning did not apparently affect the rate of development of the oedema or the degree of oedema produced by the burning.

Each burned area of skin yielded 30,000–60,000 'units' of leukotaxine. The intracutaneous injection of 60,000 'units' of leukotaxine into the abdominal wall of normal rabbits or rabbits medicated with 'Neoantergan' (10 mgm./kgm.) produced an oedema comparable to that induced by the burning.

If 1.25 c.c./kgm. of a 5 per cent solution of Pontamine Blue in 0.6 per cent saline is injected intravenously into a rabbit, and then a solution (0.2 c.c.) of leukotaxine or of histamine is injected intracutaneously into the depilated abdominal wall of the rabbit, blue areas rapidly develop at the sites of the cutaneous injections. 'Neoantergan' administered: (1) subcutaneously in a 10 mgm./kgm. dose and 30 min. before the test agents (0.2 c.c. of solutions containing 0.1 mgm. crude leukotaxine/c.c. or 0.1 mgm. histamine/c.c. respectively); or (2) intracutaneously (0.2 c.c. of a solution containing 40 mgm./c.c.) at the sites of injection of the test agents and immediately after the test agents; or (3) intracutaneously in a solution containing 40 mgm. 'Neoantergan'/c.c. and 0.1 mgm. crude leukotaxine/c.c. or 0.1 mgm. histamine/c.c., did not prevent the development or diminish the intensity of the blue staining at the sites of injection of the leukotaxine solution, but did completely prevent the blue staining at the sites of the histamine injection.

These observations suggest that the local liberation of histamine is not necessary for the production of subcutaneous oedema after cutaneous burning in the rabbit, and that leukotaxine does not induce an increased capillary permeability through the mediation of histamine. But the evidence is not conclusive, since the doses of 'Neoantergan' used, although large, may have been inadequate to deal with the amount of histamine that may have been liberated locally by the leukotaxine preparations. Higher concentrations of 'Neoantergan' cannot be used locally, since this drug itself, on intracutaneous injection in high con-