**Adrenergic mediation in the antagonism between desipramine and reserpine**

SIR,—It is well known that tricyclic antidepressant drugs, including desipramine, counteract the hypothermia induced by reserpine (Garattini, Giachetti, Jori, Pieri & Valzelli, 1962; Askew, 1963) through an effect which is probably of central origin (Bernardi, Jori, Morselli, Valzelli & Garattini, 1966). It was also reported that desipramine potentiates the hyperthermia (Jori & Garattini, 1965) and other pharmacological responses elicited by noradrenaline (Sigg, 1959; Thoenen, Huerlimann & Haefely, 1964; Bonaccorsi, 1966; Hrdina & Garattini, 1966), probably as a result of the inhibition of the catecholamine uptake at the nerve endings (Hertting, Axelrod, Whitby & Patrick, 1961; Iversen, 1965).

This allowed the suggestion that desipramine increases the relative concentration of noradrenaline at the receptor sites and that this effect is a mechanism by which desipramine antagonises the reserpine syndrome (Matussek, Rüther & Titus, 1964; Sulser, Bickel & Brodie, 1964; Jori, Paglialunga & Garattini, 1966).

We report some preliminary experiments designed to test if the effect of desipramine on reserpine-hypothermia could be interpreted as an interaction of desipramine with the adrenergic system.

Sprague-Dawley rats were injected intravenously with reserpine (2·5 mg/kg) and kept in Makrolon cages at an environmental temperature of 20°. 16 hr later desipramine was given intravenously at a dose of 1·5 mg/kg. Adrenergic blocking agents were injected intraperitoneally 30 min before desipramine.

When desipramine was given, rats were placed in individual cages to record the body temperature continuously during 2 hr automatically (Jori & Paglialunga, 1966).

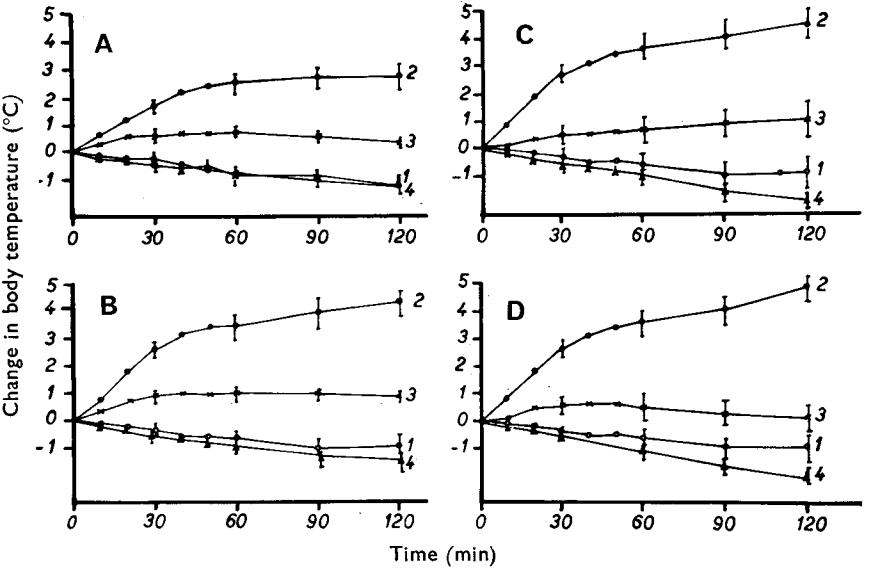


FIG. 1. Changes of body temperature in rats treated with reserpine (2·5 mg/kg i v.) 16 hr before test. At zero time, the animals (average temperature 30 ± 1°) received saline (curves 1/A; 1/B; 1/C; 1/D) or desipramine 1·5 mg/kg i.v. (curves 2/A; 2/B; 2/C; 2/D) or phentolamine plus desipramine 2·5 mg/kg i.p. (3/A), phenoxybenzamine plus desipramine 10 mg/kg i.p. (3/B); pronethalol 15 mg/kg i.p. (3/C), desipramine plus propranolol 10 mg/kg i.p. (3/D) or phentholamine (4/A), phenoxybenzamine (4/B), pronethalol (4/C), propranolol (4/D).

The results in Fig. 1 show that the adrenergic blocking agents tested—phenoxybenzamine, phentolamine, pronethalol and propranolol—inhibit the hyperthermic effect induced by desipramine in fully reserpinised rats.

Other experiments we have made show that an infusion of noradrenaline induces a significant increase of body temperature in rats made hypothermic by reserpine.

Since the synthesis of noradrenaline is not impaired by reserpine (Hillarp & Malmors, 1964) our results are compatible with the hypothesis that desipramine increases body temperature in reserpinised animals by increasing the concentration of free noradrenaline at the receptor sites because of the inhibition of noradrenaline uptake.

This mechanism may be also relevant to the explanation of the clinical antidepressant activity of imipramine-like drugs.

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# Book Review

*CHEMICAL ASPECTS OF THE AUTONOMIC NERVOUS SYSTEM.* By D. J. Triggle. Pp. ix + 329 (including index). Academic Press, London and New York, 1965. 75s.

In Chapters I, II and III (51 pages in all) Dr. Triggle sets out what he considers chemists should know about the workings of the autonomic nervous system and the peripheral connections of striated muscle. In Chapter IV (23 pages) he discusses, in general terms, the interaction of drugs with receptors. The next part of the book (97 pages) is devoted to cholinergic synapses; Chapter V deals with compounds believed to have a presynaptic action at the neuromuscular junction, Chapter VI with compounds which are agonists at acetylcholine receptors, Chapter VII classifies antagonists of acetylcholine, which