availability of substrates to the enzyme in the carcinoid tumour, 5-hydroxytryptophan penetrating much more readily than dopa.

I wish to thank Miss Maureen Raffan for carrying out the VMA estimations.

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Liberation of noradrenaline from the dog spleen

SIR,—Recently, Haefely, Hürlimann & Thoenen (1965) published evidence on the relation of the rate of stimulation and the quantity of noradrenaline liberated from sympathetic nerve endings in the isolated spleen of the cat. This is an account of similar experiments on the isolated spleen of the dog.

Mongrel bitches were anaesthetised with pentobarbitone, 30 mg/kg, intravenously. A midline incision was made in the abdomen and the animal eviscerated from mid-duodenum to the terminal colon. The spleen was isolated and removed to a chamber containing liquid paraffin and maintained at 37°. It was perfused with McEwen's solution maintained at 37° and at a rate of 20 ml/min. The perfusion fluid contained 1 μg/ml each of cocaine hydrochloride and phenoxybenzamine. The splenic nerves were laid over bipolar electrodes and stimulated with supramaximal square wave pulses of 1 msec duration. Stimulation was for 2 min at 0·5, 1·0, 2·0 and 5·0 c/s, applied successively without interruption. The perfusate was collected in the last 30 sec of each period of stimulation in tubes containing hydrochloric acid, ascorbic and ethylenediaminetetra-acetic acids and the noradrenaline assayed spectrofluorometrically. The method of assay also served to identify the substance as noradrenaline, and fully accounted for the vasopressor activity of the samples assayed in the pithed rat.

The combined results of three experiments are shown in Fig. 1. A resting output of approximately 20 ng/ml noradrenaline was observed; whether arising from the spontaneous release of noradrenaline from the nerve terminals, or from an indirect sympathomimetic action of cocaine is not known. The output of noradrenaline increased by 20 ng/ml at 0·5 c/s which is approximately twice the resting output; the noradrenaline output per stimulus was 1·2 ng. At a frequency of 1·0 c/s the output of noradrenaline rose to 110 ng ml, i.e. about 4 ng/stimulus. When the rate of stimulation was increased to 2·0 c/s the

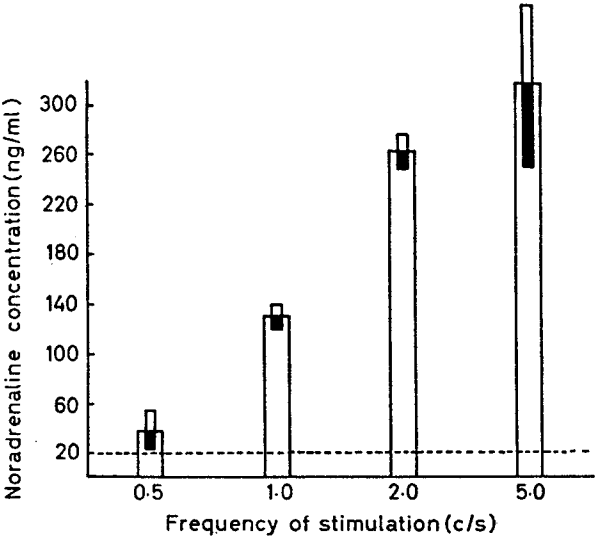

FIG. 1. Noradrenaline concentration in the perfusate of isolated dog spleen during stimulation of splenic nerves. Perfusate collected in the last 30 sec of a 2 min period of stimulation (see text). Dotted line indicates the output of noradrenaline from the spleen at rest.

concentration of noradrenaline rose to 240 ng/ml, the output per stimulus was however the same as was observed at 1 c/s. At 5 c/s the noradrenaline concentration was further increased but the increase did not parallel the increase in frequency of stimulation, thus the output per stimulus fell at 5 c/s to approximately 2 ng/stimulus. An attempt to obtain reproducible frequency/output curves for noradrenaline was unsuccessful. The results of such an experiment

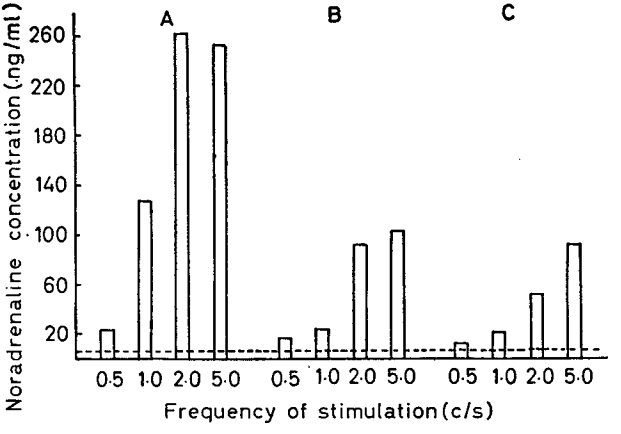

FIG. 2. Frequency/output curves for noradrenaline on isolated dog spleen. 30 min elapsed between A and B, and B and C respectively (details see text). Dotted line indicates the output of noradrenaline from spleen at rest.

are shown in Fig. 2. A period of thirty minutes was allowed between the determination of each output curve. Stimulation of the splenic nerves during the second (Fig. 2B) and third (Fig. 2 C)determinations produced much less noradrenaline in the perfusates, an effect which was most marked at the highest frequency of stimulation and may arise from exhaustion of the transmitter, as suggested by Haefely & others (1965).

Between 0·5 and 2·0 c/s the concentration of noradrenaline in the splenic perfusate during stimulation of the sympathetic nerves to the dog spleen is proportional to the frequency of stimulation employed. When the frequency of stimulation is raised from 2 to 5 c/s the concentration of noradrenaline is increased but not markedly so. In the cat this maximum lies between 4 and 8 c/s but the calculated output of noradrenaline per stimulus for the range of 0·5 to 2·0 c/s is quantitatively the same as in the dog. Thus the dog and cat spleens behave similarly in the amount of noradrenaline released by stimulation of the sympathetic nerves in the presence of phenoxybenzamine and cocaine. But, when the splenic nerves are stimulated in the absence of phenoxybenzamine and cocaine and the response of the spleen is assessed by measuring the increase in inflow pressure, maximum responses occur between 5 and 10 c/s. This response is more related to the concentration of noradrenaline in the perfusate than to the calculated output of noradrenaline per stimulus.

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Book Review

Drill's *PHARMACOLOGY IN MEDICINE.* 3rd edition. Edited by Joseph R. DiPalma. Pp. xiii + 1488 (including index). McGraw-Hill Publishing Company Ltd., Maidenhead, Berks, 1965. 180s.

Increasing specialisation within specialties is reflected in the tendency towards multi-authorship of most textbooks which purport to be comprehensive and authoritative. The obvious advantage of this arrangement is that each section can be contributed by a chosen authority on the topic; the obvious disadvantage could be discontinuity in the quality, quantity and style of the presentations. Much of the onus for the final quality of such a book falls on the editor and Professor Di Palma is to be congratulated on his successful supervision of the 3rd edition of Drill's Pharmacology in Medicine.

Drill first appeared in 1954 and was from the beginning a multi-author tome edited by Victor A. Drill. Even the first edition had 81 contributors (one of whom was Joseph R. Di Palma) and it was stated that "It is the aim of this book to present, with proper emphasis in each area, the mechanism of action, the effect on organ systems and the therapeutic uses of drugs presently used in medical practice." The success of the book and the rate of advance in the subject soon made a 2nd edition necessary and this appeared in 1958, still edited by Drill, with the number of contributors increased to 86.

For the 3rd and latest edition, published in 1965, Victor Drill has relinquished the editorship to Joseph Di Palma although he is still associated with the book