the transmitter release process, then under these conditions four sodium ions compete with one calcium ion.

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[1] Birks, R. I., and Cohen, M. W., *Symposium on Muscle* (Academic Press, 1965). Kelly, J. S., *Nature*, **205**, 296 (1965).
[2] Liley, A. W., *J. Physiol.*, **132**, 650 (1956).
[3] Liley, A. W., *J. Physiol.*, **134**, 427 (1956). Hubbard, J. I., *J. Physiol.*, **159**, 507 (1961).
[4] Del Castillo, J., and Katz, B., *J. Physiol.*, **128**, 396 (1955).
[5] Takeuchi, A., and Takeuchi, N., *J. Gen. Physiol.*, **45**, 1181 (1962).
[6] Lüttgau, H. C., and Niedergerke, R., *J. Physiol.*, **143**, 486 (1958).

An Anti-anti-inflammation Concept

The induction of the inflammatory process has been ascribed to the local release of cellular agents such as histamine, serotonin, or other excitants. Such excitants have been considered as inflammatory agents or, more recently, as mediators of inflammation. A diametrically different perspective of this situation, or the concept of anti-anti-inflammation, is presented here. This concept is based on the hypothesis that the body is in a balanced state between inflammation and anti-inflammation as opposed to the state of absence of inflammation. An increase in local concentration of the excitant could therefore induce an anti-anti-inflammatory condition. Furthermore, a decrease in an anti-inflammatory agent could have as great importance in inducing inflammation as the increase in an anti-anti-inflammatory agent.

The model used to demonstrate this concept utilizes the steady state observable experimentally when epinephrine is used as the agent to maintain the anti-inflammatory condition and serotonin as the anti-anti-inflammatory agent. (This concept is in contrast to the previously held concept of regarding serotonin as an inflammatory agent.)

In this experiment, rat paw oedema was used as the index of inflammation. Oedema was induced in the hind paw of 100–150 g intact rats (Sprague–Dawley-*CD* from Charles River Laboratories)[1]. Each dose group was comprised of 7 animals. Volume (ml.) of the paw was determined prior to and 1, 2, 4 and 6 h after the injection into the paw of 0·1 ml. of an aqueous solution or suspension of varying concentrations of either serotonin creatinine sulphate (Nutritional Biochemicals Corp.), or *l*-epinephrine bitartrate ('Suprarenin', Winthrop Stearns), or combinations of these concentrations. Mustard, in 2 per cent concentration, was present (as an irritant) in all solutions for a first experiment but omitted in an accessory experiment.

Fig. 1 (left) shows the results 1 h after injection. Increasing quantities of epinephrine, in the absence of serotonin, depending on dose, decreased the amount of oedema induced by mustard; admixed increasing quantities of serotonin depending on dose decreased the inhibiting potential of the respective concentrations of epinephrine. Comparable results were observed at 2, 4 and 6 h. Fig. 1 (right) shows that a similar inter-relationship existed in the absence of mustard.

The results of these experiments with epinephrine and serotonin support the proposed anti-anti-inflammation concept. The concept is also supported by the belief expressed by Dougherty[2], that cortisone acted by moderating the degree of inflammation in that it did not act against the inflaming agent, but rather against the substance or substances released by the inflaming agent and which in turn induced the phenomenon of inflammation.

The actual physiological importance of the proposed 'anti-anti' concept in the evaluation of the inflammatory process can only be determined by future laboratory experimentation with the possible extension of this model to other systems involving excitants like histamine and anti-inflammatory agents like cortisol.

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[1] Levy, A. C., Beaver, T. H., Strain, R. D., and Holtkamp, D. E., *Proc. Soc. Exp. Biol. and Med.*, **111**, 576 (1962).
[2] Dougherty, T. F., *Rec. Prog. in Hormone Res.*, edit. by Pincus, G., **7**, 307 (Academic Press, New York, 1952).

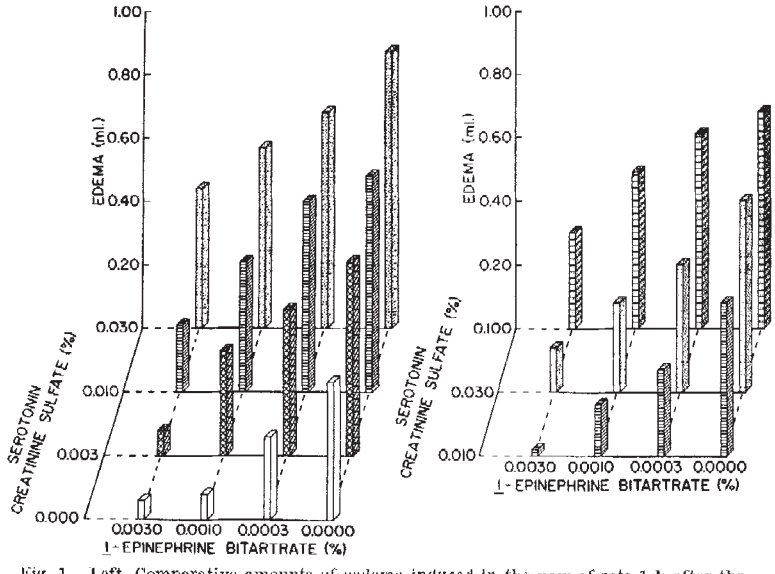

Fig. 1. Left, Comparative amounts of oedema induced in the paw of rats 1 h after the injection of 0·1 ml. of 2 per cent aqueous mustard containing varying concentrations of either serotonin creatinine sulphate, *l*-epinephrine bitartrate, or both; right, comparative amounts of oedema induced in the paw of rats 1 h after the injection of 0·1 ml. of an aqueous solution containing varying concentrations of either serotonin creatinine sulphate alone or in combination with *l*-epinephrine bitartrate

Effect of Attention on Evoked Responses in the Classical Auditory Pathway

Hernández-Peón, Scherrer and Jouvet[1] have reported marked decrements in the amplitude of click-evoked responses in the cochlear nucleus in cats attending to stimuli of other sensory modalities. It was argued that this reduction was brought about by efferent inhibition from the brain-stem reticular formation. In a later investigation, Jane, Smirnov and Jasper[2] were unable to demonstrate any reduction in evoked potential amplitudes in the medial geniculate body and the auditory cortex during 'attention'. In view of these conflicting results, it was decided to examine the effect of the act of 'attention' on evoked potentials recorded simultaneously from three levels in the primary auditory pathway of unanaesthetized cats.

Five cats were chronically implanted, stereotaxically, with bi-polar stainless steel electrodes in the cochlear nucleus (CN), inferior colliculus (IC), and medial geniculate body (MG). Testing commenced four weeks after the operation. The evoked potentials were recorded electroencephalographically. The animals were tested in a wire cage which permitted reasonably free movement. This wire cage was located in a shielded box (Fig. 1). 0·2 msec clicks of 85 dB sound pressure-level, measured with a General Radio impact noise analyser