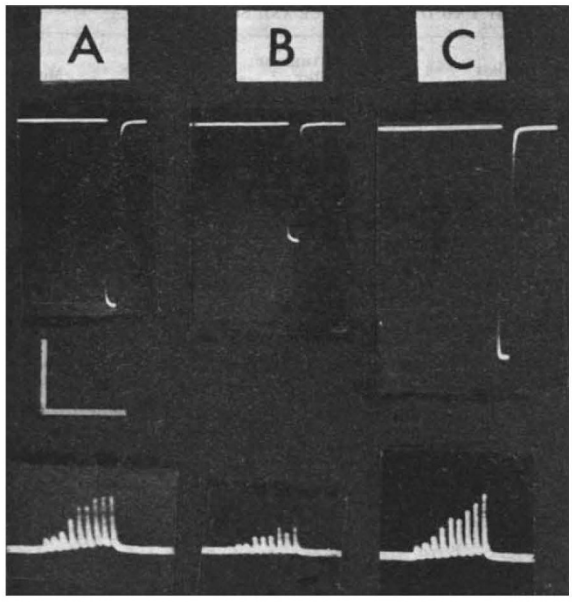

Fig. 1. ('Opener' muscle.) Effect of GABA (10^{-6} g/ml.) on the change in membrane potential resulting from a square pulse of applied current and on excitatory junctional potentials arising from stimulation of the efferent nerves. Records show excitatory junctional potentials and hyperpolarization recorded (*A*) while the muscle fibre was bathed in normal crab Ringer; (*B*) immediately after the application of 10^{-6} g/ml. GABA; (*C*) 20 min after return to normal crab Ringer. Note the large decrease in the effect of applied current and the marked decrease in the size of excitatory junctional potentials. Current was monitored periodically and was found to remain constant. Changes in resting potential are not considered significant. Scales: upper records, 4 mV, 100 msec; lower records, 2 mV, 100 msec

passing current. The efferent nerves were stimulated and excitatory junctional potentials were recorded. The effect of GABA on excitatory junctional potentials and membrane conductance was studied.

In both the 'opener' and 'closer' muscles, GABA in concentrations of 10^{-6} g/ml. or greater produced within a few sec: (1) a decrease in the size of excitatory junctional potentials of up to 80 per cent; (2) a marked decrease in the effect of applied current, indicating an increase in membrane conductance (Fig. 1).

In crab muscle the natural inhibitory transmitter reduces excitatory junctional potentials and produces a selective increase in membrane conductance, bringing the membrane potential toward a particular level—the 'reversal potential'[7,9]. Thus, in crab muscle both GABA and the natural inhibitory transmitter produce an increase in membrane conductance.

A more detailed comparison of the action of GABA and the natural inhibitory transmitter in crab muscle—such as that made by Boistel and Fatt[1] in crayfish muscle—has not as yet been made.

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ROBERT S. EISENBERG *
DAVID HAMILTON †

Nerve-Muscle Program,
Marine Biological Laboratory,
Woods Hole, Mass.

* Present address: Department of Biophysics, University College, London.
† Present address: Institute of Physiology, University of Glasgow.

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Effect of Alacreatine on the Rat

IN an earlier communication we reported that rats fed a diet containing 2 per cent of DL-α-guanidinopropionic acid (alacreatine) develop weakness during a 6-week period[1]. In subsequent work we have been unable to demonstrate either a defect in creatine metabolism in these animals or improvement of the weakness by creatine administration. Because of an odour which suggested the presence of a sulphur-containing compound in the alacreatine preparation further experiments were done with highly purified odourless alacreatine. None of the animals receiving the purified alacreatine became weak. It thus appears that the weakness was not caused by alacreatine, but by an impurity. The impurity has not been identified. However, various isothiourea and guanidine derivatives are known to be toxic in acute dose[2] and such compounds could have been present in the original preparations of alacreatine.

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COY D. FITCH
JAMES S. DINNING

Departments of Biochemistry and Medicine,
University of Arkansas School of Medicine,
Little Rock, Arkansas.

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PHARMACOLOGY

Effect of 'Methotrexate' and 'Melphalan' on the Survival of Tumour and Skin Homografts

SEMI-ISOLOGOUS (F_1 hybrid) mice surviving systemic leukæmia *L*1210 after extensive therapy with halogenated derivatives of 'Methotrexate' (MTX) were shown to be immune to re-inoculation with sensitive or resistant sublines of leukæmia *L*1210[1-3]. In other work[4-6], it was observed that MTX therapy of mice bearing homografts of MTX-resistant leukæmias abrogated the immune response. However, in a system involving differences at the strong *H*-2 histocompatibility locus, pretreatment of mice with MTX failed to promote the growth of *L*1210[7]. In the latter system, pretreatment with a number of alkylating agents (*cyclo*phosphamide, triethylene melamine, and 'Melphalan') and X-irradiation resulted in marked immune suppression. In view of the foregoing results, and the observation that MTX therapy did not interfere appreciably with the ability of an inoculum of splenic tissue to render mice immune to *L*1210[5], we decided to determine what effect a dose-level of MTX capable of abrogating the immune response to tumour homograft would have on the survival of skin homografts. Also, as part of the same experiment, the effect of pretreatment with MTX on the immune response to skin and tumour homografts was determined, since, in the present system, only minor histocompatibility differences were involved. 'Melphalan', a potent immune suppressor[7], was used as a positive control.

In the work recorded here the fates of *DBA*/2 tumour and skin homografts were compared in drug-treated *BALB*/*c* mice. The *DBA*/2 strain leukæmia used was *FR*-8 (ref. 8), an antifolic-resistant sub-line of *L*1210. Skin from stock *DBA*/2 male mice was grafted to *BALB*/*c* male mice according to the technique of Billingham and Medawar[9].

Mice of the *BALB*/*c* and *DBA*/2 strains possess the same *H*-2 histocompatibility allele ($H\text{-}2^d$), but have multiple differences at other, more minor histocompatibility loci[10]. Following subcutaneous inoculation of *L*1210 or resistant sub-lines, a local tumour develops at approximately the same rate as in isologous controls. Cessation of