of decamethonium can be largely prevented by previous treatment with *d*-tubocurarine[5]. This effect of the antagonist has been confirmed by preparing transverse sections, and also by a different method the results of which are shown in Fig. 3. These autoradiograms were obtained by placing intact hemi-diaphragms in contact with slides which had been coated with emulsion. At the end of the exposure the muscles were removed and the autoradiograms were developed and photographed. The left side of Fig. 3 shows a dark band of silver grains which correspond to the position of the endplates in the stained diaphragm[6]. The right side of Fig. 3 was obtained from a rat which had received *d*-tubocurarine chloride (0·8 mg/kg) 10 min before injection of decamethonium. The density of silver grains in the band at the endplate region was much reduced, and with a larger dose of antagonist the band could be abolished.

Diaphragm muscles which have taken up labelled decamethonium lose their radioactivity at a slow rate. Fig. 4 shows autoradiograms from muscles which were removed 2 h and also 7 days after injection. After 7 days the band of silver grains is considerably wider, and this appearance is consistent with slow diffusion of decamethonium along the fibres.

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Diffusion of Decamethonium in the Rat

Creese and Maclagan have reported evidence that labelled decamethonium enters the fibres of striated muscles when the drug is injected into rats (preceding communication). It was found that this radioactivity is lost slowly from the muscles and can still be detected after days or weeks.

The upper histogram in Fig. 1 shows the distribution of radioactivity in a diaphragm which was removed 2 h after injection of decamethonium-(^{3}H-methyl) dichloride into the tail vein of a rat. The dose (1·64 mg/kg) produced a transient weakness in some animals and no obvious effect in others. The left diaphragm was removed, frozen, sectioned into strips 1 mm wide and the radioactivity was expressed as counts min^{-1} mg^{-1}. The counts showed a peak in the region of the endplate, as found[1] previously, and a Gauss curve could be fitted to the results.

The lower histogram in Fig. 1 was obtained from a rat which was injected with the same dose of decamethonium and kept for 10 days before the diaphragm was removed. Considerable radioactivity remained in these muscles and it appeared that less than half had been lost. The Gauss curve is more dispersed, and this would be expected if there had also been some degree of diffusion along the fibres[2]. This interpretation is supported by the spread of radioactivity among the muscle which was shown in autoradiograms (preceding communication).

Curves can be fitted to the histograms of the form

$$y = d + A \exp\{-(x-\mu)^2/2\sigma^2\} \quad (1)$$

where y represents counts min^{-1} mg^{-1} and x is the distance in millimetres from the tendon. The Gauss curves were found by a method to be described separately in which the parameters d, A, μ and σ were computed to give a fit with least squares. In twelve muscles removed after 2 h the mean standard deviation σ_1 was 0·802 mm (range 0·614–1·17), while for twelve muscles removed after 10 days σ_2 was 1·64 mm (range 1·33–2·03). Intermediate values were obtained which were consistent with these results. The lower curve of Fig. 1 is still diminishing at the ends, and with longer times the effects of reflexion may become significant[3].

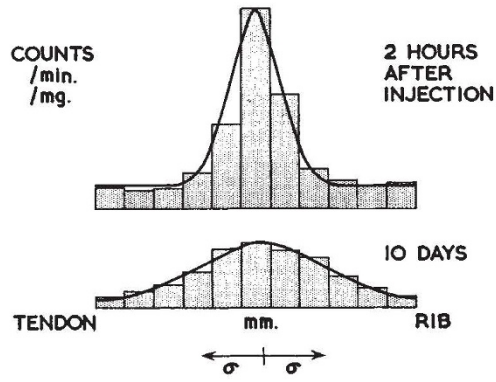

Fig. 1. Upper histogram shows radioactivity of rat diaphragm which was removed 2 h after injection of labelled decamethonium. The muscle was cut into strips 1 mm wide, and a Gauss curve has been fitted to the counts. The lower histogram was obtained from a rat which was injected and kept for 10 days before removal of the diaphragm. The standard deviation σ of the lower curve is indicated.

For longitudinal diffusion

$$\sigma_2^2 - \sigma_1^2 = 2D't \quad (2)$$

where D' is the apparent diffusion coefficient and t is the time. Thus D' is $1{\cdot}2 \times 10^{-8}$ cm^2 sec^{-1}. This rate is very slow, and differs from the unidirectional transport which has been demonstrated in nerve axons[4]. The diffusion coefficient of labelled decamethonium in the interspaces of isolated rat diaphragm was found to be $2{\cdot}4 \times 10^{-6}$ cm^2 sec^{-1}—the method being similar to that used previously[5]. The figure for internal diffusion is 200 times smaller than that for the interspaces, which in turn is less than in free solution[6].

Decamethonium enters the fibres of rat muscle in the region of the endplate, and then migrates towards the ends of the fibres and is slowly lost. These results apply to the labelled compound which remains after injection, and the early distribution of the drug has not been explored.

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