PHYSIOLOGY

Asthma and Testosterone

It was previously shown[1,2] that testosterone is a powerful inhibitor of histamine and SRS* responses, and in view of the varying age incidence of status asthmaticus in the two sexes it was thought testosterone levels might have aetiological significance. Dutch workers have thought along similar lines[3]. Accordingly blood levels were measured in male and female subjects (by courtesy of Dr. J. Coghlan and Prof. Hudson) immediately after a severe attack. In two males the levels were 0·87 and 1·03 μg/100 ml. (high and one above normal: range 0·37–1·00) while in four females the levels were 0·13, 0·16, 0·19, and 0·29 μg/100 ml. (above normal: range 0·04–0·12). In another asthmatic subject, in the interval between attacks, the level was 0·24 μg/100 ml. (male), which is significantly low. I am now investigating the possibility that the level may be low in asthmatics, but that as a reaction to the stress of an attack, possibly associated with anoxia and hypercapnia, the levels rise high temporarily. Corticoid and also oestrin levels will be measured, as sometimes oestrins enhance histamine responses.

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* SRS, Slow-reacting substance.

[1] Trethewie, E. R., *Arch. Intern. Pharm. Therap.*, **149**, 3, 366 (1964).
[2] Trethewie, E. R., *Nature*, **198**, 290 (1963).
[3] Beumer, H. M., *Acta Physiol. Pharm., Neerlandica*, **10** (1962).

Active Transport of Chloride across the Cornea

The presence of an active transport of ions across the cornea has been postulated[1–3] in connexion with the loss of transparency of this membrane when it swells, after reduction of its metabolic rate or injury. The swelling and opacity, especially after exposure to cold solutions, is reversible and this has prompted the notion that an active ionic transport is performed by the cells of the epithelium or endothelium, dragging water out of the stroma to preserve the normal orientation of the fibrils.

The cornea of the American bull frog (*Rana catesbiana*) maintains a potential difference of 15–60 mV and produces short-circuit currents of 6–30 μamp/cm², when mounted as a membrane in Ussing's modified type of chamber[4]. The aqueous or endothelial side is positive and the tear or epithelial side is negative. The potential and the short-circuit current are mainly dependent on the presence of chloride ions in the aqueous side. As can be seen in Fig. 1, when all the chloride ions are replaced by sulphates in the fluid[5] bathing the corneas, the short-circuit current is markedly reduced; it recovers to control-levels, however, when chloride ions are again present in the fluid. The same effect is obtained if methyl-sulphate ions are used to replace the chlorides. The measurement of chloride fluxes with chlorine-36 in short-circuited corneas, as shown in Table 1, indicates that there is a net transport of chloride from the aqueous towards the tear side of the cornea. From 95 to 100 per cent of the short-circuit current measured could be computed as due to the chloride net transport, as shown at the bottom of Table 1. Sodium fluxes measured with sodium-22 indicate that no net transport of this cation is performed, since both unidirectional fluxes are similar. In these corneas chloride is secreted towards the outside, and then possibly sodium ions are dragged along passively, due to the potential difference. This salt movement could then induce water to follow it, keeping the hydration of the cornea at the normal level, and consequently preserving its transparency.

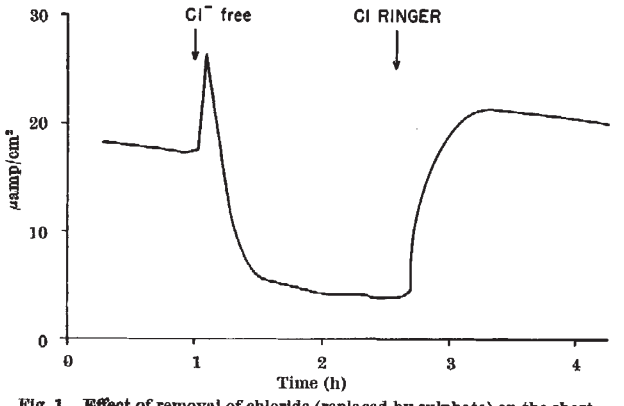

Fig. 1. Effect of removal of chloride (replaced by sulphate) on the short-circuit current produced by the isolated frog corneas

Table 1. Chloride Fluxes across Isolated Frog Cornea

Aqueous to tear side		Tear to aqueous side	
μEquiv./h/cm²	Short-circuit current (μamp/cm²)	μEquiv./h/cm²	Short-circuit current (μamp/cm²)
0·585	13·1	0·188	14·0
0·780	23·3	0·288	10·3
0·803	18·4	0·086	15·0
0·740	14·0	0·153	33·0
1·075	11·4	0·162	19·0
1·060	25·8	0·237	9·6
0·513	15·1	0·402	21·3
0·952	21·6	0·074	17·6
1·185	30·8	0·187	15·5
Mean 0·849	19·3	0·197	17·25

Chloride net flux = 0·849–0·197 = 0·652 μequiv./h/cm². Current measured = 18·2 μamp/cm². Current from chlorine transport = 17·5 μamp/cm².

When the chloride concentration is increased or decreased in steps of 10–20 mM of chloride in the inside, while regular fluid is kept in the outside or tear side, a saturation-type curve is obtained as the chloride concentration is plotted against the stable short-circuit current attained after each replacement. In double reciprocal plottings, straight lines are obtained as shown in Fig. 2, indicating saturation-type kinetics.

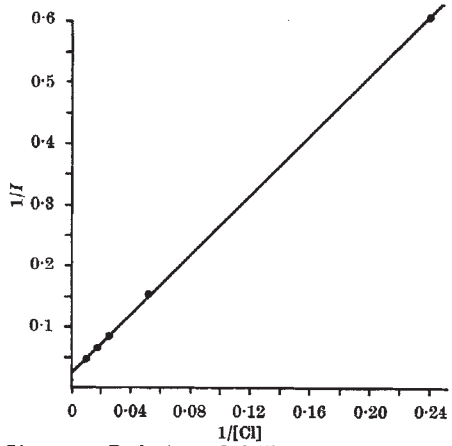

Fig. 2. Lineweaver–Burke type of plotting of short-circuit current (*I*) against chloride concentration in the fluid bathing the aqueous side of the frog cornea

The short-circuit current is sensitive to ouabain, but only at high concentrations, 10^{-4} M, and a definite drop of the current is observed only after a delay of about 1 h when the glucoside is added in the inside or aqueous side of the corneas. Though sodium ions move only passively across the corneas, the presence of these cations is necessary inside to maintain the potential.

Homogenates of the corneas exhibit ATPase activity in the presence of magnesium and in the absence of calcium. This magnesium-activated ATPase activity does not, however, show any affinity for sodium or potassium. The ATPase splitting activity is found in the microsomal as well as in the mitochondrial fraction of these corneas, and does not show any sodium, potassium or chlorine affinity. Ouabain does not affect the ATPase splitting activity of the preparations.