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Inhibition of effects of isoprenaline and adrenaline by *Haemophilus influenzae* vaccination

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Szentivanyi (1968) postulated that the pathogenesis of atopy is due to malfunctioning of the β-adrenoceptors resulting in an imbalance of α and β-adrenoceptors. This postulate was based on experiments with *Bordetella pertussis*. However, for *B. pertussis* no causative relation with chronic asthmatic bronchitis has been shown. On the other hand *Haemophilus influenzae* can be isolated from the upper respiratory airways in normal individuals and also from the deeper airways in asthmatic patients (see Hirschmann & Everett, 1979). Therefore we studied the influence of *H. influenzae* on functioning of the β-adrenoceptors in vaccinated animals (500×10^6 killed cells 100 g body weight i.p. administered 4 days prior to the experiments).

Lungs from guinea-pigs sensitized to ovalbumin were isolated and perfused with Krebs solution at 10 ml/min and shocked by ovalbumin injection into the pulmonary artery. Cascade superfusion apparatus was prepared and release of thromboxane A_2 and prostaglandins were measured (Piper & Vane, 1969). Minimal ovalbumin doses needed to detect release of prostaglandins and thromboxanes were determined in *H. influenzae* vaccinated and control lungs.

The vaccinated animals responded to lower doses of ovalbumin (threshold doses 0.4 ± 0.1 vs 1.9 ± 0.5 µg ovalbumin, $P < 0.01$, $n = 8$–11). Correcting for differences in sensitivity, in lungs and tissues, by means of internal and external standards (arachidonic acid and PGE_2), did not alter the significance. A significant inhibition of prostaglandin release was demonstrated in control animals during 6×10^{-9} M isoprenaline into the pulmonary artery. However in *H. influenzae* vaccinated animals no significant inhibition could be achieved with isoprenaline (2×10^{-9} and 6×10^{-9} M).

To obtain equal contractions of the bioassay tissues before and during isoprenaline infusion, the dose of ovalbumin had to be increased with the following factors: 2×10^{-9} M isoprenaline 2.7 ± 0.6 (*H. influenzae*) vs. 5.8 ± 2.7 (controls, n.s.; 6×10^{-9} M isoprenaline 2.7 ± 0.3 vs. 8.7 ± 2.8, $P < 0.05$. Prostaglandin and thromboxane A_2 release induced by these doses of ovalbumin were reproducible. Release of prostaglandins by histamine and bradykinin and conversion of arachidonic acid in prostaglandins did not differ in vaccinated and control animals.

In a second series of experiments we investigated the effect of adrenaline on the eosinophilic blood count which is believed to be mediated through β-adrenoceptors. Adrenaline was administered to rats (2 mg/kg body weight s.c.) and mice (0.3 mg/kg body weight i.p.) and the eosinophilic response was investigated 30 min later. This effect was inhibited in vaccinated animals (50% increase in *H. influenzae* and 130% increase in controls, $P < 0.02$). Furthermore the response to several drugs in different groups of mice was tested. LD_{50} values to isoprenaline in *H. influenzae* vaccinated mice were increased (26.4 mg and 172 mg resp., $P < 0.05$). In contrast LD_{50} values to noradrenaline were decreased (10.7 mg and 3.2 mg resp., $P < 0.05$).

In different experimental set ups and in different species the effects on isoprenaline and adrenaline were attenuated. This suggests a decreased functioning of β-adrenoceptors in *H. influenzae* vaccinated animals.

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