

## Facilitation of histamine release in the *Haemophilus influenzae* vaccinated experimental animal

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Literature data suggest the involvement of *Bordetella pertussis* in immunopharmacological processes including histamine sensitization and blocking effects on  $\beta$ -adrenergic mechanisms (Munoz & Bergman, 1968; Szentivanyi, 1968). Therefore the *B. pertussis* vaccinated animal is considered to be a model of atopy. However the model lacks direct clinical significance: atopic patients usually are not infected by *B. pertussis*.

Considering the frequency of *Haemophilus influenzae* in chronic asthmatic bronchitics and the effect of *H. influenzae* in experimental animals (Terpstra, 1975), the possibility exists that this bacteria could maintain the chronic asthmatic bronchitis or that *H. influenzae* could act as a causative agent in the exacerbations of chronic asthmatic bronchitis.

Therefore the effects of *H. influenzae* were investigated in rats on peritoneal mast cell, lung and plasma histamine levels and on ovalbumin induced anaphylactic histamine release from isolated guinea-pig lung.

Wistar rats (male, 125 g) were vaccinated with  $500 \times 10^6$  killed *H. influenzae* cells i.p.. Four days later peritoneal mast cell, plasma and lung histamine levels were determined fluorometrically. For ovalbumin induced anaphylactic shock guinea pigs (male, 350 g) were sensitized to ovalbumin (Piper & Vane, 1969) and four days before the experiment vaccinated with  $500 \times 10^6$  killed *H. influenzae* cells per 100 g body weight i.p. Sensitized lungs were perfused with Krebs solution at 10 ml/min and shocked with ovalbumin (2  $\mu$ g) injected into the pulmonary artery. Histamine release was measured in the supernatant of perfusate by means of an enzymatic double isotopic assay.

Four days after vaccination plasma histamine levels were enhanced significantly ( $128.8 \pm 8.9$  vs.  $90.7 \pm 3.6$

ng/ml,  $n = 10$ ,  $P < 0.01$ ). Lung histamine levels were also elevated significantly ( $2.85 \pm 0.31$  vs.  $1.29 \pm 0.32$   $\mu$ g/g,  $n = 10$ ,  $P < 0.01$ ). Furthermore it was demonstrated that the mast cell histamine content was increased ( $121.4 \pm 14.8$  vs.  $62.7 \pm 9.7$  ng/g  $1.5 \times 10^4$  cells,  $P < 0.001$ ). Lungs from *H. influenzae* vaccinated guinea pigs released more histamine as a result of the ovalbumin shock ( $P < 0.05$ ).

From the results it may be concluded that the histamine levels are elevated in the investigated tissues of the *H. influenzae* vaccinated experimental animal. Further sensitivity to exogenous stimuli is increased in the vaccinated animal. In analogy chronic asthmatic bronchitics are also more sensitive to environmental stimuli than normal individuals (Jenne, Chick, Strickland & Wall, 1977; Townley, Ryo, Kolotkin & Rang, 1975). Therefore this animal model might be a tool for investigating the influence of *H. influenzae* in chronic asthmatic bronchitis.

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