
DISCUSSION

Dr. Turner-Warwick: Did you differentiate your asthmatics in terms of severity of their disease, and did you find any differences between groups in their response to isoprotroenol beyond an hour's time?
Dr. Brooks: That is a good question. We did differentiate asthmatics in terms of disease severity. All our patients were stable for a period of months. We assessed severity of disease using clinical and physiologic criteria. We did study one actually ill asthmatic patient. She had decreased alprenolol binding which increased with her clinical improvement during hospitalization. Serial studies on more patients need to be performed in order to determine the duration, magnitude and significance of these changes in alprenolol binding.
Dr. Chick: Were any of your patients recently on beta-adrenergic drugs?
Dr. Brooks: This is important since the use of beta-adrenergic agonist drugs has been shown to depress in vitro beta-receptor binding. We selected patients who had either never taken beta-adrenergic agonist agents or who had not received them for weeks to months prior to study.
Dr. Oren: Is there a dose-response relationship in the effect of glucocorticoid on binding, and is it different for different patients, depending on the severity of illness?
Dr. Brooks: In vitro studies suggest that this may be true, but this is as yet unstudied.

In vitro Studies on the Mechanism of Respiratory Virus-induced Asthma*

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The mechanism of virus-provoked episodes of asthma is not established. One of several plausible hypotheses is an impairment by virus or some product of virus-infected cells of homeostatic mechanisms that maintain normal bronchial caliber. Release of granulocyte (PMN) lysosomal enzyme, beta-glucuronidase, follows incubation with complement activated zymosan. In asthma, isoproterenol (ISO) and histamine (HIS) inhibition of enzyme release is impaired while prostaglandin E1 (PGE,) response is normal (Am Rev Resp Dis 115:783, 1977; J Clin Invest 59:1080, 1977). During respiratory infection-provoked asthma, the response to ISO is further impaired. A similar, but less severe reduction in ISO and HIS response occurred in normal subjects during an experimental rhinovirus 16 infection (J Allergy Clin Immunol, in press).

Impairment in PMN response to the agonists, ISO, HIS, and PGE, (10^-8 to 10^-4 M) develops during in vitro incubation with several respiratory viruses: rhinovirus 16, influenza A (England/42/72[H3N2]), and two live attenuated influenza vaccines (bivalent: A [H3N2] and B; WRL-105 type A). Bivalent vaccine affects PMNs from normal (n=15) and asthmatic (n=29) donors similarly. Asthmatics with a history of virus-provoked episodes of wheezing with colds did not differ from other asthmatics. Vaccine did not impair agonist response on PMNs collected from patients receiving systemic corticosteroids and in vitro cortisol (50 × 10^-4 M) restored the vaccine-induced impairment in response to agonists.

Preliminary observations show the change in agonist response is proportional to the concentrations of the virus preparation, is retained following virus inactivation (heat, ultraviolet light), and is restored by washing after virus incubation.

DISCUSSION

Dr. Stechschulte: Do you have any evidence that phosphodiesterase activity or that cyclic nucleotide levels are altered by the 30 minute incubation?
Dr. Busse: The baseline levels of cAMP are not changed. We do not have measurements of phosphodiesterase activity.
Dr. Oren: Are these effects you see with viral incubation due to infection or to some other mechanism, perhaps immunologic?
Dr. Busse: In studies in which the viruses have been killed we see the same results as with the live virus. Whether it is some viral product or an effect of the virus particle itself, we do not know.
Dr. Chester: Have you had an opportunity to do in vitro studies on leukocytes from non-asthmatic normal subjects during and after viral infections?
Dr. Busse: Yes, and they were similarly affected.

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