CONDITIONING AS A CAUSE OF ASTHMATIC ATTACKS; A LABORATORY STUDY

by Egbert Dekker, M.D., Henk E. Pelser, M.D., and Juda Groen, M.D.

Introduction

A number of authors have written on the role which conditioning may play as a cause of attacks of asthma. Their evidence, however, was mostly indirect, mainly based on clinical histories as obtained from the patients. Some of our former observations on asthmatic attacks provoked by emotional stimuli under controlled laboratory conditions also seemed in line with a conditioning mechanism although they did not represent classical examples of such a mechanism.

Strictly speaking, a conditioned attack of asthma should contain the following elements:

1. One or more attacks of asthmatic dyspnoea.
2. A conditioning stimulus or situation, which originally does not in itself produce an attack but coincides with these attacks.
3. The occurrence of attacks after exposure to the conditioned stimulus or the conditioned situation alone.

In this paper, observations on two patients are presented which seem to fulfil these requirements. In both patients the conditioning took place under experimental conditions in the laboratory and the effect could be measured by the standard technique used in the former investigation.

Methods

The experiments were carried out in the course of investigations during which patients were exposed to allergic and emotional stimuli. To register the effect, we used a modification of the method developed by Herxheimer (16, 17) and ten Cate and Orie (4, 5) for the detection of inhalation allergy by provocation tests. In this method the vital capacity is
used as the parameter. The patient is seated in front of a spirograph. Every 4 min. the vital capacity is determined; between these determinations, the patient is not connected to any apparatus. After the vital capacity has been registered a number of times and a baseline value has been obtained, the patients are exposed to various stimuli. During the experiment the determination of the vital capacity is continued every 4 min. for at least 20 min., as far as the condition of the patient allows.

For the present investigation into the possibility of the production of asthmatic attacks by conditioning under laboratory conditions, an unconditioned stimulus was provided by the inhalation of nebulized allergens to which the patients were hypersensitive.

An aerosol† of grass-pollen extract (5000 Noon units per ml.) was administered to the first patient; the second patient inhaled an aerosol of a 5% solution of house-dust extract as prepared in the University of Groningen (5).

The allergens were nebulized in glass atomizers‡ by means of a stream of oxygen with a flow-rate of 4 l./min. The atomizers were placed, hidden from the patient's view, in a wooden box. The box contained a number of holes through which rubber tubing carried the aerosol to the patient. The tubes from any atomizer could be made to leave the box through any hole; this prevented the patient from knowing what substance he or she was given to inhale. The inhalation took place by means of an exchangeable glass-tube mouthpiece, held loosely between the half-opened lips through which the patient was quietly breathing outside air.

A regularly progressive decrease of the vital capacity of more than 10% of the mean of the baseline values was accepted as a positive reaction, according to the standards laid down by ten Cate and Orie (4, 5).

The figures give the mean value for all the determinations of the vital capacity during a 20-min. observation after the end of the provocation or, in other instances, up to the moment when an attack had to be stopped by drugs. The effect of drugs has been indicated as the maximal increase in the vital capacity which was observed.

After one or more positive reactions to the inhalation, we gradually changed the inhalation situation and studied the influence of these changes on the effect. These “fragments” of the inhalation situation acted as conditioned stimuli. Registration and evaluation of these reactions took place in the same manner as those of the allergic reactions. This determined the sequence of the experiments described below.

**Observations**

**Case 1. A.**

A 37-year-old unmarried housekeeper suffered from serious bronchial asthma. Skin reactions to grass pollen and tree pollen were strongly positive.

26 April: First control inhalation test with the neutral solvent of the allergen extracts,* caused a slight subjective dyspnoea and a decrease of the

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* Trademark: LIFA, Groningen. † Trademark: Wiesbadener Doppelinhalator.
* Coca solution: A watery solution of sodium chloride, sodium bicarbonate with a trace of phenol.