Inhalation Cortisone Therapy in Bronchial Asthma*

ALEXANDER A. DOERNER, M.D., CHARLES F. NAEGELE, M.D.,
FREDERIC D. REGAN, M.D. and
WILLIAM WEINGARTEN, M.D., F.C.C.P.
Staten Island, New York

In its original concept, the term "allergy" was used to denote the changed state of the organism that followed the parenteral introduction of an antigen. Although the role of the adrenal corticoids in relation to this altered tissue state is not clear, it appears that in some way they interfere with tissue production of substances which are detrimental to cellular integrity, and thus permit a return to normal cellular homeostasis. This concept offers a rational therapeutic basis for the beneficial effects observed to date in the treatment of acute bronchial asthma with cortisone and/or ACTH.

The predominant pathological findings in bronchial asthma are dilatation of capillaries, edema of the bronchial wall, spasm of bronchial musculature, hyperplasia of goblet cells, and eosinophilic infiltration of the bronchial wall, and peri-bronchial tissue. In addition, thick inspissated mucus plugs are frequently present. Because of the favorable response of allergic inflammatory reactions associated with certain diseases of the eye and skin, it was felt that the disturbed tissue alterations of bronchial asthma might be similarly benefited by direct contact with cortisone. The undesirable side-effects and complications noted in some instances with other methods of administration of this corticosteroid appeared to make it even more important to investigate this therapeutic approach. It was therefore decided to administer cortisone by inhalation to patients with bronchial asthma, and to compare this method of therapy with parenteral cortisone administration in these patients.

**Method and Material**

Three patients were selected for study who had been known to have typical attacks of bronchial asthma for eight to 23 years. They were of the male sex, and ranged in age from 29 to 54 years.

*From the Department of Medicine, U. S. Marine Hospital, Staten Island, New York; Chief of Medicine (Dr. Doerner); Deputy Chief of Medicine (Dr. Naegele); Deputy Chief of Medicine (Dr. Regan); Senior Medical Resident (Dr. Weingarten).

Cortisone was made available through a special grant from the Division of Hospitals, U. S. Public Health Service.
Only one of these patients had a familial history of asthma. All had required frequent treatment with standard methods of therapy, showing transient beneficial response. During a carefully controlled week of hospital observation prior to cortisone administration, these patients continued to show objective and subjective manifestations of bronchial asthma, with intermittent exacerbations of symptoms requiring parenteral use of adrenalin and aminophylline. For two days immediately prior to cortisone administration a placebo solution, consisting of normal saline, was given to two patients by inhalation, four times daily. The use of this inert substance did not alter their symptomatology or clinical course in any way. A saline suspension of cortisone was then administered by aerosol to the patients, one receiving a concentration of 6.25 mg. per cc., and the other two, 12.5 mg. per cc. Each patient inhaled one cc. of cortisone solution four times daily for a two week period. Following this, two patients received 100 mg. of cortisone by intramuscular injection daily for five days. All inhalation administrations were given under standardized conditions,* with oxygen flow regulated at seven liters per minute.

**Results**

In each of the three patients studied, the administration of cortisone by inhalation was without effect in alleviating the subjective and objective manifestations of bronchial asthma. In two patients, exacerbation of symptoms required occasional parenteral use of adrenalin and aminophylline. This was necessary in one individual despite the administration of cortisone aerosol coincidentally with an acute asthmatic attack.

The patients who received cortisone by intramuscular injection began to experience relief of symptoms within 48 hours, and at the end of four days of therapy demonstrated complete subsidence of all signs and symptoms previously noted. In no instance were any untoward effects of cortisone observed.

**Comment**

Several recent reports7,8 have recorded the favorable response of bronchial asthma to cortisone and/or ACTH administration. It is apparent that the use of these corticosteroids in this potentially chronic illness will become more widespread. Although the asthmatic attack may be temporarily controlled, the disease state is not abolished. Because of the observations of the authors9 and other workers10,11 of the possible unfavorable effects resulting from the prolonged use of these adrenal corticoids, a method was

---

*OEM Blue-Dot Bronchial Nebulizer Unit No. 301, with latex rebreathing bag No. 717, Oxygen Equipment Manufacturing Co., Norwalk, Conn.*
investigated which might allow their safer use in bronchial asthma. Small amounts of cortisone were administered by aerosol directly to the shock tissue involved. In the cases treated, no beneficial effect was observed in response to nebulized cortisone. The two patients who subsequently received parenteral cortisone demonstrated marked subjective and objective improvement.

Several reasons may be postulated to explain the failure of inhalation cortisone therapy in the cases studied. It is possible that local changes in the bronchial wall due to the long duration of the disease process in these patients prevented proper absorption of the corticoid. True irreversibility of the underlying tissue pathology did not seem to have occurred because of the ability of parenterally administered cortisone to produce profound improvement in these patients. Another possibility is that the bronchospasm associated with the asthmatic state was not relieved by the tissue level of cortisone attained, although the inflammatory changes may have been favorably influenced. It is also possible that in bronchial asthma the action of cortisone is not affected by direct contact at the local tissue level at all, but that a systemic level of the corticoid must be attained to alter the asthmatic state. This hypothesis would seem to be substantiated by the success of nebulized cortisone recorded in a case of bacterial pneumonia, where a satisfactory systemic level was probably achieved by the administration of a total of 313 mg. over a 33 hour period. If it is necessary to attain such levels by aerolization, the possible undesirable effects of parenteral cortisone would not be excluded by this method.

Further investigation is thus warranted before definitive conclusions can be reached, and the final place of inhalation cortisone therapy in bronchial asthma evaluated.

SUMMARY

1) Three patients with long-standing bronchial asthma were treated with cortisone by inhalation, without demonstrable effect.
2) This method of therapy was compared with parenteral cortisone administration in two of these patients.
3) Several reasons are postulated to explain the lack of response to nebulized cortisone in contrast to the favorable response obtained with parenteral cortisone.
4) The observations recorded are the initial results of a continuing study. Further investigation seems warranted.

RESUMEN

1) Tres enfermos con asma de larga duración fueron tratados con cortisona por inhalación sin resultados demostrables.
2) Este método de tratamiento fue comparado con la administración de cortisona por vía parenteral en dos de estos enfermos.
3) Varias razones son presentadas para explicar la falta de resultados a la cortisona nebulizada en contraste con los obtenidos por la vía parenteral.
4) Las observaciones referidas son los resultados iniciales de un estudio en marcha. Las investigaciones ulteriores están justificadas.

RESUME
1) Trois malades atteints d'asthme ancien ont été traités par inhalation de cortisone, sans effet notable.
2) Pour deux de ces malades, cette méthode a été comparée avec celle de l'administration par voie parentérale.
3) Plusieurs raisons sont invoquées pour expliquer le manque d'action de la cortisone par aérosol en contraste avec l'action favorable de la cortisone par voie parentérale.
4) Les observations mentionnées sont les résultats initiaux d'études qui sont en cours. De nouvelles investigations emblent justifiées.

REFERENCES
10. Thorn, G. W., et al.6