

THE EFFECT OF CORTISONE ON BRONCHIAL ASTHMA AND HAY  
FEVER OCCURRING IN SUBJECTS SENSITIVE TO  
RAGWEED POLLEN\* †

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A STUDY has been undertaken to determine whether or not cortisone will influence bronchial asthma and hay fever resulting from sensitivity to ragweed pollen. A number of general facts have suggested the possible value of such a study. Experimental data have interlinked three systems and mechanisms of the body: the adrenal cortex, lymphoid tissue, and reactions of immunity.

A pituitary-adrenal control influences the occurrence and severity of anaphylactic shock by enhancing resistance to this form of trauma.<sup>1, 2</sup> The tolerance to the deleterious effects of histamine is decreased when an animal is deprived of the function of its adrenal cortex.<sup>3-6</sup>

The transport and, likewise, the possible formation of antibodies in lymphoid tissue<sup>7-10</sup> is significant when considered with the fact that the adrenal hormones can effect a degeneration of lymphoid tissue.<sup>11, 12</sup>

Evidence suggests that the adrenal cortex can influence the titer of circulating immune bodies, and that extracts of this gland can bring about an anamnestic response.<sup>13</sup>

In this study of the allergic state we have selected for consideration the adrenal cortical fraction cortisone (17-hydroxy-11-dehydrocorticosterone). Among the several hormones of the adrenal cortex cortisone has been demonstrated to be effective in bringing about lymphocytic degeneration in tissue culture experiments,<sup>12</sup> in neoplastic lymphoid tumors,<sup>14, 15</sup> and possibly in circulating lymphoid tissue.<sup>16</sup> Cortisone, and adrenal cortical extracts containing cortisone, will effect an anamnestic response.<sup>13</sup> Cortisone is in the 11-oxysteroid fraction of adrenal cortical extract which generally has been effective in bringing about lymphocytic degeneration and in evoking an anamnestic response.<sup>13</sup>

As diseases for consideration in this study of the allergic state we have selected seasonally occurring bronchial asthma and hay fever. Among allergic disorders these diseases are unique in affording suitable methods of control in such a study. Symptoms may be severe, are of relatively constant occurrence, and afford a means of objective evaluation. The symptoms experienced in pollinosis are of sufficient duration to afford an opportunity for both control and test studies to be made on a single subject. The degree of exposure of a patient to an offending allergen may be estimated with reasonable accuracy by a day-to-day study of the pollen content of the air. Among the allergic dis-

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orders pollinosis is a most nearly "pure" extrinsic form of allergy. Complicating infections and neurogenic factors are less important than may be the case in perennial vasomotor rhinitis, perennial forms of asthma, and the allergic dermatoses.

The use of cortisone in the treatment of hay fever or less severe bronchial asthma would not be justified under present circumstances of supply and understanding. However, the advantages, as indicated, seem to justify its use in these diseases as a means of studying the mechanism of the allergic state.

As volunteer patients for this study, 3 persons having both bronchial asthma and hay fever resulting from sensitivity to ragweed pollen were selected. Such patients were given an injection either of cortisone\* or of cholesterol into the gluteal muscles. A suspension of 100 mg. was administered daily over a 4-week period starting Aug. 19, 1949. The preparations which we administered were in containers labeled only by a code number. As the cortisone and cholesterol suspensions were grossly identical in appearance, the knowledge as to which preparation was injected remained unknown to the patients and to the physicians during this study. Not until the conclusion of the study, when all observations had been made and recorded, was information concerning the dates of test and of control periods available to us. In this manner objectivity was assured. While changes from test to control suspensions were made periodically in the course of these studies, at no time was a substance given for a period of less than 6 consecutive days. By this procedure errors in interpretation as a result of delayed absorption of a suspension were minimized.

The patients in this study were observed daily by physicians from both medical and otorhinolaryngologic sections. In evaluating and classifying symptoms, several criteria were employed. The occurrence and severity of asthma in the preceding 24-hour period were evaluated, as were the symptoms of paroxysmal sneezing, nasal congestion, rhinorrhea, and conjunctival irritation. With respect to hay fever, a classification of symptoms on the basis of 1 to 4 was employed wherein grade 1 has designated minimal difficulty and grade 4 has designated maximal difficulty. Each patient selected for study was engaged in an occupation assuring a generous exposure each day to pollen-laden air.

The appearance of the intranasal and conjunctival mucous membranes was studied particularly for changes in the degree of edema, pallor, and moisture.

In addition to studies directed toward an evaluation of asthma and hay fever, the patients were observed for evidence of any untoward reaction to cortisone. Frequent determinations of blood pressure and clinical observations for disturbances of electrolyte metabolism were made. Weekly determinations of the leukocyte count and differential leukocyte count were made, particular attention being directed to the relative percentage of lymphocytes and eosinophilic leukocytes.

#### CASE REPORTS

CASE 1.—A 60-year-old man, whose occupation was that of an automobile dealer, for 35 years had had hay fever which for the past 12 years had been associated with the occurrence of bronchial asthma. His symptoms of hay fever and asthma had occurred only in the weeks between mid-August and the period immediately following a frost. An allergy

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\*The acetate derivative of cortisone was employed throughout the study.

survey including common inhalant allergens and pollens prevalent in the season of his difficulty revealed sensitivity to ragweed pollen. From 17 to 10 years prior to this study, the patient had received yearly hyposensitization with an extract of mixed ragweed pollen with an estimated 50 to 75 per cent relief from symptoms of hay fever. In recent years the patient had employed numerous remedies including large doses of ascorbic acid and numerous antihistamine drugs with partial relief of symptoms. With the exception of asthma and hay fever the patient was in excellent health.

At the time when cortisone was first administered, this patient was having severe symptoms resulting from hay fever and was having daily bronchial asthma. After the administration of cortisone the symptoms of hay fever subsided to a minimal level within 3 days and those of asthma disappeared within 1 day. During this time the concentration of pollen in the air remained high. The patient had relief from symptoms for 4 days extending into the control period. The relief of symptoms early in the control period may be ascribed to the delayed absorption of suspended cortisone from the site of its injection. On the fourth day of the control period both hay fever and asthma recurred. With the resumption of administration of cortisone, either minimal or no symptoms of hay fever were experienced and no asthma occurred. No other drugs for symptomatic relief were employed during this study (Fig. 1).

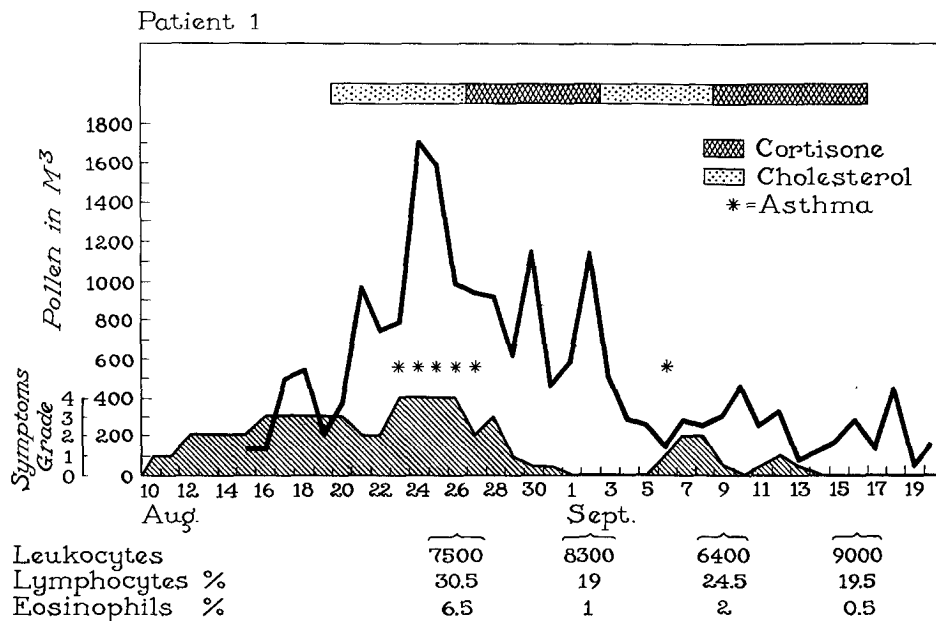


Fig. 1.—The effect of cortisone on bronchial asthma and hay fever resulting from sensitivity to ragweed pollen in Patient 1.

CASE 2.—A 57-year-old man, who was engaged in office work in an executive capacity, had had seasonal hay fever occurring between mid-August and frost since childhood. In the 10 years preceding this study an associated asthma had occurred in this season. Both hay fever and asthma were virtually entirely confined to this season. An allergy survey revealed sensitivity to ragweed pollen. In the years 1930 to 1932 he had received hyposensitization with ragweed pollen extract with an estimated 50 per cent relief of symptoms. In recent years considerable symptomatic relief had been obtained with various antihistamine drugs. The patient was otherwise in excellent health.

At the time when the second patient first received cortisone, moderate symptoms of hay fever were present as well as daily asthma for 6 consecutive days. With the administration of cortisone no further asthma and only minimal hay fever occurred until the fourth day of

the control period. On that day hay fever of moderate severity developed as well as daily bronchial asthma until the patient's symptoms abated at a time when the pollen content of the air dropped precipitously. With the resumption of administration of cortisone minimal

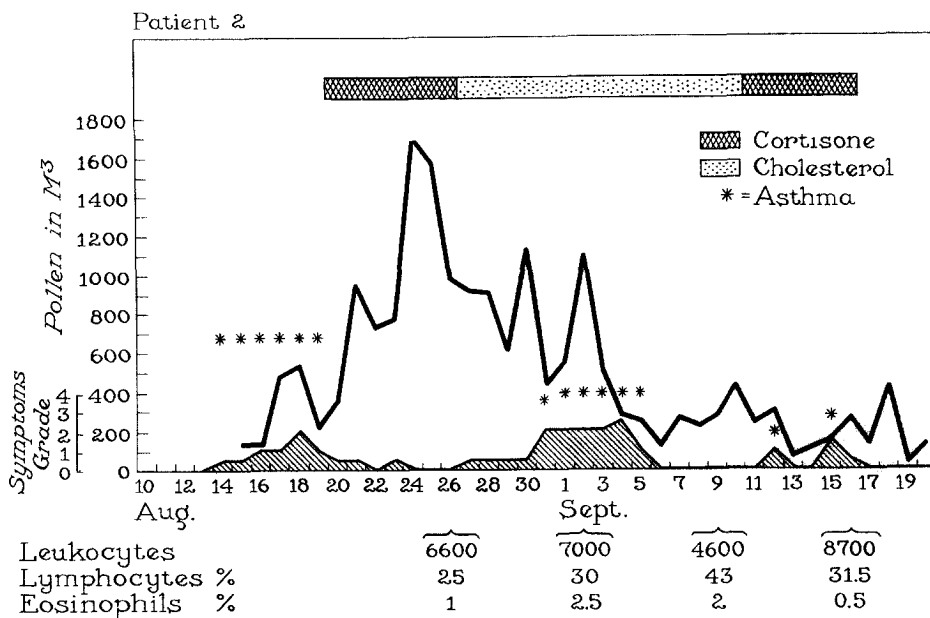


Fig. 2.—The effect of cortisone on bronchial asthma and hay fever resulting from sensitivity to ragweed pollen in Patient 2.

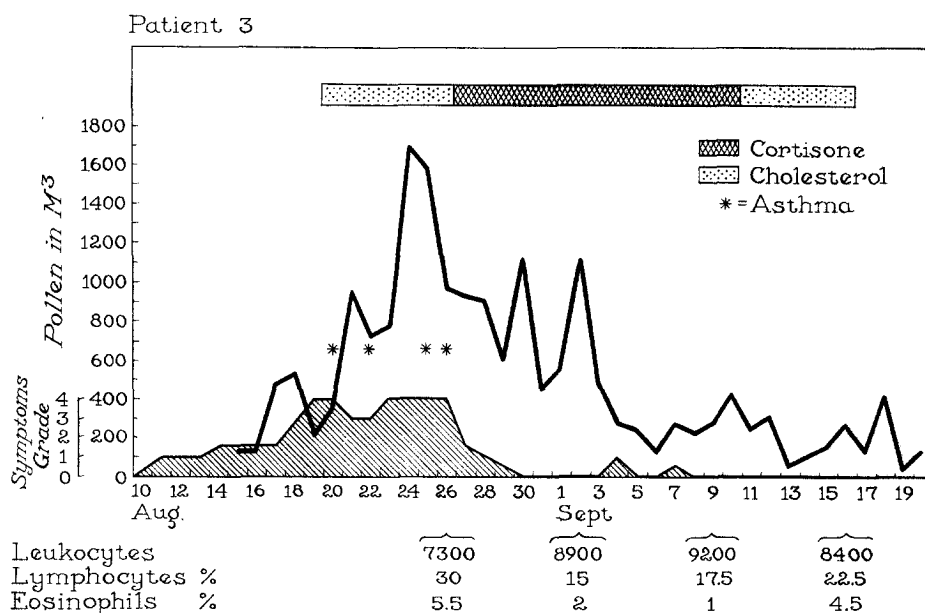


Fig. 3.—The effect of cortisone on bronchial asthma and hay fever resulting from sensitivity to ragweed pollen in Patient 3.

hay fever and minimal wheezing occurred for 1 day on two occasions. Exertion in unseasonably cold weather with a bronchitis not yet controlled may explain this occurrence. No other drugs for symptomatic relief were employed during this study (Fig. 2).

CASE 3.—A 57-year-old woman, a nurse, had had seasonal hay fever for approximately 20 years. This had been associated with bronchial asthma virtually since its onset. The hay fever and asthma began in mid-August and were improved following a frost. An allergy survey revealed sensitivity to ragweed pollen. In recent years asthma had persisted until November. Hyposensitization with mixed ragweed pollen extracts was of little benefit when used in 1935. The patient had wished no further attempts at hyposensitization. In recent years considerable symptomatic relief had been obtained from antihistamine drugs.

This patient was having extremely severe hay fever associated with bronchial asthma at the time when cortisone was first administered. After she began to receive cortisone no further asthma was experienced. The symptoms of hay fever were completely controlled and recurred in a minimal and transient form on but 2 occasions during the remainder of the period of study. Before symptoms were controlled following administration of cortisone the patient used antihistamine therapy to enable her to continue her work as a nurse (Fig. 3).

#### COMMENT

Each patient in this study experienced great relief during and immediately following the administration of cortisone from those symptoms associated with bronchial asthma and hay fever. This relief was greater than that previously achieved with hyposensitization to ragweed pollen extract or with the use of antihistamine drugs. The relief of symptoms was largely confined to the period when cortisone was being administered. The delayed absorption of injected suspended medication in all probability explains the period of relief continuing for approximately 2 or 3 days following the last administration of cortisone.

Changes in the appearance of the nasal mucosa were gradual in their occurrence. The relief of the symptoms of hay fever following the administration of cortisone was associated with a decrease in the amount of the secretion bathing the nasal mucosa, a moderate change in the amount of swelling of the middle turbinates, and a slight decrease in the pallor of the mucosa. Further reduction in the edema and pallor continued slowly over several days. The only day-to-day objective change in the nasal mucosa considered to be significant was in the moisture of this membrane. This was well correlated with symptomatic changes.

While none of these patients exhibited eosinophilia in excess of 6.5 per cent, there was in each instance a lowering of the relative eosinophil count at times when cortisone was being administered. No untoward symptoms occurred as a result of administration of cortisone. On occasions those receiving the drug appeared to have slight psychic stimulation. This was, however, indefinite in its occurrence and transitory in its duration.

In many ways ACTH and cortisone bring about parallel changes within the body. The injection of ACTH leads to the release by the adrenal cortex of cortisone-like steroid hormones. Other closely related substances, notably compound F (17-hydroxy-corticosterone), are likewise liberated. The ratio of effective doses of ACTH to cortisone is probably not constant but varies with the amount of available cortisone-like steroid hormones present in the body at a given moment. One hundred milligrams of cortisone is in a general way the equivalent of approximately 40 mg. of ACTH.

## SUMMARY

1. Three patients received injections of cortisone during the season when ragweed pollen, to which they were allergic, was in the air.
2. Each patient experienced prompt relief from the symptoms of bronchial asthma and hay fever occurring as the result of that pollen sensitivity.
3. The symptoms of bronchial asthma were relieved more quickly than were symptoms of hay fever.
4. Within 3 days following the onset of administration of cortisone, only occasional allergic symptoms, which were of a mild and transitory nature, were observed.
5. The relief of symptoms was apparently confined to the period during and immediately following the time when cortisone was being administered.

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