Intranasal Injection of Corticosteroids

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• **Intranasal injections into the inferior turbinates of a slightly soluble form of prednisolone TBA (Hydeltra® TBA) into persons with complaint of nasal obstruction gave considerable relief in 78 per cent of cases. Nasal hyperfunction due to seasonal allergic rhinitis, vasomotor rhinitis and secondary nasal edema from sinusitis was the indication for use. No local or general reactions other than a small amount of bleeding at the time of injection was noted. This method allows full utilization of the anti-inflammatory activity of corticosteroids at the local tissue level without producing a systemic effect.**

A DECADE has passed since recognition was first given to changes in the mucosa of the upper air passages under stimulation of the pituitary adrenocorticotropin hormones and the adrenal corticosteroids.[5,18] Following reports of Bordley and his co-workers,[2,3,4] many authors indicated relief of symptoms of allergic diseases with administration of these hormones parenterally and orally.[9,10,17] The severest forms of nasal allergic reaction and bronchial asthma often subsided completely. Swelling of affected nasal mucous membranes subsided, a more normal pink color returned and the thick gelatinous mucus characteristic of allergic reaction disappeared. The nasal turbinates became smaller and the air space became larger. Nasal polyps lost their translucence, began to shrink and in many instances disappeared.

Later topical use of corticosteroids by nasal sprays was reported to avert many systemic side effects. An early report in 1951 by Dill and Bolstead[6] indicated that cortisone nasal spray produced a more or less temporary effect. Objectively, the use of the solution lessened nasal secretions and decreased edema of the nasal mucosa. They noted too, that many patients had relief of mild asthmatic symptoms such as wheezing, cough and tightness of the chest. Also headache of allergic origin was relieved and polyps shrank. They noted no untoward effects and no atrophy of nasal mucosa. Subsequently, in 1952 Dill and Bolstead[7] stated that only half their patients had some relief of allergic symptoms from cortisone sprays and only while using the spray.

Williams[20] in 1952 observed that results of giving cortisone by mouth for reduction of nasal polyposis were disappointing. Other medical and surgical measures gave more lasting results, he believed.

Semenov[13] described injections of cortisone directly into nasal polyps. One patient a minute or two after the injection had weakness, dyspnea, substernal pressure, flush of the entire face, wheezing, rapid, weak pulse and collapse. All these symptoms disappeared within an hour. In a later discussion[8] Semenov said that hydrocortisone is twice as potent and more effective topically than cortisone. He stated he had injected 5 mg. of Cortone® acetate into the nasal mucosa hundreds of times without mishap, whereas a dose of 25 mg. evoked severe reactions in three patients.

In 1952 a very favorable report was issued by Wall and Shure[19] after intranasal injection of cortisone in 52 patients with unmistakable allergic rhinitis; 42 had pronounced improvement. In all cases of acute allergic rhinitis, results were excellent, they said. They also reported two severe, immediate, unexplainable constitutional reactions which left no after-effects. At the conclusion of their report they advocated the intranasal injection of cortisone into the inferior turbinates for prolonged symptomatic relief of allergic rhinitis, especially of the acute seasonal variety.

Multiple studies using cortisone as packs and drops in allergic rhinitis followed. Evans[8] in 1954 recommended continuous and more widespread use of these methods by the medical profession.

Grace, in discussing Evans' paper, stated he had used cortisone topically "without any startling results." However, he said that injections of cortisone into the nasal mucosa gave "splendid" results. The dosage he used was 2.5 mg. in a series of four injections and no bad reactions occurred.

In 1954 Smith[16] used hydrocortisone in a nasal jelly in allergic rhinitis, together with specific hyposensitization. He reported topical therapy more effective than submucosal injection into the nasal turbinates in relieving symptoms.

In 1955, Sidi and Tardif[14] reported on intranasal injections of hydrocortisone acetate (compound F) into the anterior third of the inferior turbinates of the nose for treatment of allergic rhinitis. They noted favorable results in 30 of 50 cases. Two of the 50 patients complained of a sensation of thoracic constriction after the injection followed by pain in the lumbar region. This reaction did not last more

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than four minutes. The dosage these investigators used was never more than 6 mg. of hydrocortisone acetate at one time.

All patients with allergic rhinitis treated by Anderson and Ogden[1] were helped by nasal sprays of prednisolone. These investigators said that pharmaceutically prednisolone is considered several times more potent than hydrocortisone.

In 1958 Myers[11] reported on the treatment of allergic nasal polyps by intrapolyp injection of prednisolone TBA.* He noted no untoward reactions and said that results were excellent.

Doses of about 30 to 40 mg. were employed at each treatment.

MECHANISM OF ACTION

Several properties of the corticosteroids may explain why they are effective in nasal disease. The human organism attempts to maintain homeostasis through the pituitary-adrenal axis hormonal secretions. Allergic reaction may well be due to inability of the organism to either produce sufficient, effective cortical hormones or inability of specific shock organs to utilize them. Why many patients respond poorly to stress—whether due to allergy, infection or emotions—may be explained on the basis of inadequate function of the pituitary-adrenal axis.

Nasal inflammation and hyperfunction is produced in susceptible persons by any stress whether due to allergy, infection or emotions. Edema is primary in this inflammation and believed located in the gel of connective tissue. The enzyme hyaluronidase present in connective tissue is liberated. In inflammation the enzyme liquefies the gel with resultant edema. Hyaluronidase also disrupts the integrity of the capillary endothelial cell, increasing capillary permeability and enhancing edema. The corticoids are believed to neutralize hyaluronidase, hence controlling the inflammatory edema. A good deal of evidence that large doses of the corticoids lower resistance to infection but small doses increase resistance,[12,15] has accumulated. Acute infectious rhinitis appears to improve with small doses of corticoids.

In other words, these hormones help keep a good peripheral vascular bed, improve smooth muscle tone, maintain a healthy capillary endothelium and preserve the ground substance of connective tissue. Since corticosteroids are effective in all inflammatory disorders, steroid injections need not be confined to allergic nasal disease. In many cases, it is impossible to make specific delineation between nasal allergic disease and infectious rhinitis or nasal changes from emotions or weather changes. Finding eosinophils in the nasal smear is not pathognomonic of nasal allergic disease. Wolfe[21] showed that eosinophilia locally and in the peripheral blood occurs with nasal hyperfunction associated with emotional stress. He also observed that polymorphonuclear leukocytes occurred with the eosinophils in emotional stress with no apparent allergic reaction or infection. Wolfe demonstrated that the nose reacts similarly in any disease that affects that organ—namely, with hyperemia, nasal obstruction, turbinal and mucosa swelling and increased secretions. Sneezing may occur. This reaction represents a defense to shut off from the organism what is harmful or unpleasant whether it is a viral, bacterial, pollen or a disagreeable emotional reaction. Color changes of the nasal mucosa from pale violet to scarlet may give a clue as to whether allergic disease or infection predominates. But, here again specificity is absent.

The effectiveness of the pituitary-adrenal axis theoretically determines the extent of the reaction and the speed to which normal conditions return. Seemingly, local injection of the corticosteroids, especially in a transitory episode, should hasten return to normal function of the nose. In addition, increased concentration of the hormone in the tissues may act as protection against assault by pollen, bacteria or emotional stress.

INDICATIONS

The indication for the use of intranasal prednisolone is primarily the relief of nasal obstruction caused by edema of the inferior turbinates. Vasomotor rhinitis is a generic term reserved for this condition. Edema may occur in seasonal allergic rhinitis, in infection as in bacterial rhinitis secondary to infectious sinusitis, and in emotional reactions as described by Wolfe.[21] Acute nasal edema as in coryza lasts but a few days and is self-limited. Intranasal injections of prednisolone are recommended for longstanding and recurrent nasal edema recalcitrant to other therapy. No contraindications exist.

PRESENT STUDY

The basis of this report is the use of a series of three nasal turbinate injections of corticosteroids in the treatment of 419 patients with vasomotor rhinitis of various causes. There were no side reactions of importance. Some psychological anxiety existed with the mention of a needle. When the patient realized that the procedure is painless no further apprehension was apparent. A slight amount of cocaine solution may be sprayed on the anterior ends of the inferior turbinates before injection. A small amount of bleeding occurs at the time of each injection, especially if considerable congestion exists. The bleeding ceases within a few minutes. Although clinically

*In the form of suspension Hydeltra® TBA—Produced by Sharp & Dohme, Division of Merck & Co.

successful results were obtained with cortisone and hydrocortisone, my impression was that Hydeltra® TBA* (prednisolone) was so much more effective that the use of the other corticosteroids was soon discontinued. Hydeltra® TBA, a very slightly soluble ester of prednisolone, is capable of producing a longer and more pronounced local anti-inflammatory effect when injected than does hydrocortisone or cortisone. The manufacturers state that, since Hydeltra® TBA is so very slightly soluble, 18 to 24 hours may elapse following injection before there is a change in its chemical structure with subsequent absorption in local tissues and effective relief of symptoms. My experience agrees with that claim.

Initially, 0.2 cc. (8.0 mg.) was injected into each anterior end of the inferior turbinate as superficially as possible. This was repeated usually in three to four days, and again about a week after the second injection. The patients usually had relief for varying periods up to a year or more. If the patient returned with a recurrence of symptoms, larger doses appeared necessary at the second series to give the same relief—0.3 cc. (12 mg.) Hydeltra® TBA for each turbinate at each treatment.

During the year 1958 questionnaires were mailed to 419 individuals who had received a series of three injections for various nasal complaints, the last injection more than one year previous. Of this number, 195 returned the questionnaire. Reporting only their own subjective observation, 152 (78 per cent) stated that they had had considerable relief of their nasal complaints for at least six months, 67 (44 per cent) saying they had had no return of their symptoms for at least one year. Many had had complete relief since the time of therapy for as long as three years.

Of the 419 persons who received the series of three injections, 298 (71 per cent) had typical histories of seasonal allergic rhinitis. Vasomotor rhinitis was the diagnosis in 109 patients (26 per cent) who complained of perennial nasal obstruction. The cause was uncertain but the majority admitted being tense and anxious. Allergic sensitivity is difficult to prove in this group. Sinusitis resulting in secondary nasal edema was confirmed in 12 patients (3 per cent).

A diagnosis of allergic seasonal rhinitis had been made in 110 (72 per cent) of 152 patients who stated in the questionnaires that they had had relief of symptoms. The remaining 42 (28 per cent) had long-standing vasomotor rhinitis of uncertain cause.

Several days following an injection, the nasal mucosa, whether pale blue or violet from allergic reaction or bright red or pink from infection, returns to a normal pink color. A noticeable subsidence of edema becomes evident, with pronounced decrease of secretions. At the end of the third injection, oftentimes, the turbinal bodies appeared fibrous. Cardinal relief noted by the patients was ease in breathing and lack of a feeling of obstruction. Many also commented on the disappearance of postnasal drip and regaining a sense of smell. Sometimes one injection of prednisolone relieved the symptoms when the obstruction had been present for a number of days to several weeks. The symptoms did not recur.

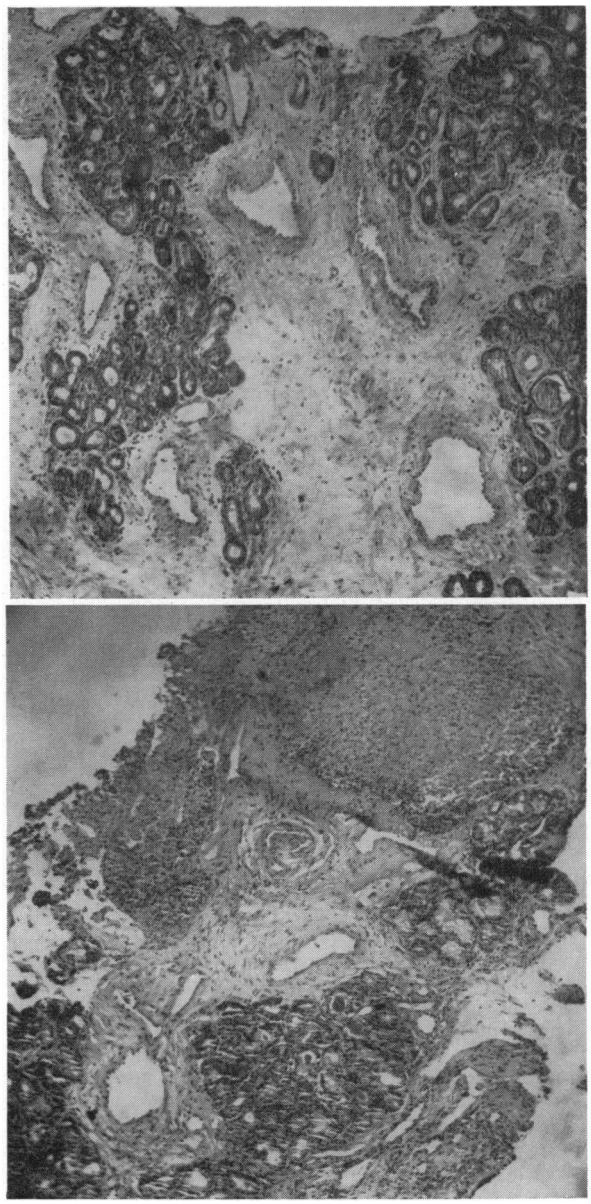

Figure 1.—*Above:* Section of inferior turbinate of individual complaining of nasal obstruction. Note marked edema, engorged blood spaces and increased thickness of the connective tissue layer. *Below:* Section of same inferior turbinate one month later following three injections of prednisolone. Edema has subsided, the blood spaces are smaller and the connective tissue layer is reduced considerably. (×100)

*Supplied by Sharp & Dohme, Division of Merck & Co.

In biopsy of tissue taken from the inferior nasal turbinates in some cases, no pronounced microscopic changes were noted aside from decrease in edema of the tissue. The amount of connective tissue present was neither greater nor less than normal, nor was there any evidence of the injected material within the tissues. (See Figure 1.)

Direct injection of Hydeltra® TBA into polyps was disappointing. Some shrinkage was noted but never complete disappearance. Surgical removal of large polyps was always necessary. I believe that prednisolone injections offer an expediency in relieving transitory nasal hyperfunction regardless of the etiologic factor, whether allergic sensitivity, infection or emotional disturbance. They are also a help sometimes in chronic nasal disease if irreversible changes have not already taken place.

Time-tested methods of pollen desensitization and surgical operation on the nasal septum and on polyps are still in order when indicated. Sinus disease may be a result of nasal dysfunction or complicated by it. The principles of drainage and ventilation may require very conservative sinus operations, but seldom are such procedures indicated. Hydeltra® TBA intranasal injections will promote drainage and ventilation of the sinuses by decreasing nasal edema.

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