SHOULD STEROIDS BE USED IN TREATING BRONCHIOLITIS?

Since their introduction into clinical use, corticosteroids have been employed as therapeutic agents in virtually every known disease state, ranging from minor dermatologic disorders to major and serious diseases. These agents have undoubtedly altered the clinical picture and prognosis of certain diseases. However, the use of corticosteroids is always potentially associated with a variety of untoward effects, some of which may be life threatening, i.e., decreased resistance to infection, growth retardation, neurological reactions, hypertension, peptic ulcerations, and many others. The time honored principle—first do no harm—should always be the guideline of therapy, especially when a definite indication for a particular therapeutic agent has not been established.

In recent years corticosteroids have been employed in the treatment of bronchiolitis on the hypothesis that their anti-inflammatory action would decrease swelling, inflammation, and the consequent respiratory obstruction. The opinions of different investigators on the efficacy of corticosteroids in this disorder have varied greatly; some have regarded their use as ineffective and others as lifesaving. It is the purpose of this report to review the findings from various studies and to outline the current status of the use of corticosteroids in this common disorder of infants and children.

Bronchiolitis is a common, acute respiratory syndrome characterized by infection of the bronchioles and respiratory distress of varying degrees due to obstructive emphysema. It is common in the first year of life and is rare in the child over 2 years of age. It frequently occurs in outbreaks. The great majority of cases are due to viruses, especially the respiratory syncitial, influenza B, and parainfluenza viruses, but it may be due to bacteria and other respiratory pathogens. The walls of the bronchioles and small bronchi are infiltrated with inflammatory cells and the lumina may be markedly reduced by the presence of inflammatory debris and edema; this occlusion leading to widespread areas of obstructive emphysema and patchy atelectasis expressed clinically by expiratory wheezing. The clinical severity is dependent on the degree of respiratory obstruction and varies from mild to severe. The chief aim of treatment is the relief of respiratory obstruction and the management of secondary complications. The mortality rate has been reported in different series to range from 1 to 5.5%. Heycock and Noble reported a mortality rate of 5.5% in 1,230 cases, with the highest fatality rate in infants less than 6 months of age. If patients with milder cases of bronchiolitis are included, the overall death rate probably does not exceed 1%.

A number of reports have appeared in the literature relating to the therapeutic use of corticosteroids in bronchiolitis. Many of the studies reporting favorable results with these agents were uncontrolled ones. In general, controlled studies have failed to identify significant favorable effects.

One of the earliest and better controlled studies was that by Dennis, which showed significant benefits from corticosteroids in a double-blind study of 98 patients with bronchiolitis. Sussman and co-workers found no difference in the mean time required for improvement or recovery among 26 infants given dexamethasone in a dose of 0.2 mg/lb for 9 days as compared to 23 patients receiving a placebo. Likewise, Dabous, et al., using a "bronchiolitis score" to quantitate severity (similar to the Silverman retraction score of the respiratory distress syndrome) and determining blood gases and pH, did not find any therapeutic difference attributable to corticosteroids in a controlled study of 22 matched pairs of children with bronchiolitis. Damus, in a placebo-controlled study, noted no beneficial effect in 30 infants receiving prednisone 1 mg daily for 4 days. Oski and co-workers, in 1961, reported a therapeutic effect from corticosteroids in a group of patients as compared to controls. Subse-
quentely, these workers extended their studies to a larger group and found no therapeutic effect from corticosteroids. Most of the studies have been characterized by the small number of patients studied, failure to differentiate between the mildly and critically ill infant, and paucity of controls.7

Recently the results from a large, controlled, collaborative study of corticosteroids in bronchiolitis have been reported.13 This study evaluated in a double-blind fashion the effect of beta-methasone sodium phosphate in the treatment of 297 infants and children with acute bronchiolitis studied at five hospitals from December 1963 to June 1965.

For this study the investigators designed a common protocol and standard case report forms for use at the five collaborating centers. All patients in the study were less than 30 months of age and were hospitalized. To qualify for admission to the study, only patients who had, on admission, acute respiratory distress characterized by expiratory grunt, hyperinflation of the lungs on x-ray, cyanosis, and scattered expiratory or inspiratory rales were included. Initially and every 6 hours each patient was evaluated for the presence and degree of the following manifestations: restlessness, retraction, flaring of alae nasi, wheezing, grunting, respiration, rales, impaired air exchange, and congestive heart failure. Roentgenograms of the chest were obtained on admission, during therapy, and as required at end of the treatment period. All patients received the same general supportive care and, in a double-blind fashion, either betamethasone sodium phosphate 1.0 mg/5 lb body weight or the aqueous vehicle alone were given intramuscularly or intravenously as an initial dose; subsequently, doses of 0.5 mg/5 lb body weight were given intramuscularly every 12 hours over a 72-hour period, for a total of six doses. The total dose administered was usually 3.5 mg/5 lb for a 72-hour period. Supportive measures included mist, oxygen, and parenteral fluids. Antibiotics were not administered to the patients during the first 48 hours (preferably 72 hours) of treatment (except for control of specific bacteria isolated from the initial cultures or in the presence of signs of bacterial infection). Antibiotics were administered subsequently if required. A total of 116 patients (53 in the corticosteroid group and 63 in the placebo group) received antibiotics. The double-blind design used in this study resulted in an almost equal partition of patients into each of the two treatment groups at all five study centers. All pretreatment aspects proved, moreover, to be similar in both groups of patients. Cluster analysis of admission signs did not reveal any meaningful single clusters either in the individual hospital data or in the pooled data.

The authors state, "There were no significant differences between the results obtained in patients treated with betamethasone sodium phosphate injections and those receiving the placebo. Neither were there any medically important differences among the results obtained at each of the five hospitals where the study was carried out." Although there was an earlier disappearance of fever and cyanosis in the corticosteroid treated group, these differences were not significant statistically. There was no statistical difference among the two groups in the duration of the signs of bronchiolitis: respiratory rate was unaffected, duration of restlessness was the same in both groups; the obstructive respiratory signs (retraction, flaring of the alae nasi, wheezing, grunting) were all comparable. No untoward effects attributable to the use of steroids were observed. Analysis of the two groups for cluster differentiation and for family history of asthma did not reveal any difference. Approximately 45% (135) of the patients in the study had a family history of allergy, usually asthma. Previous attacks of the bronchiolitis were reported for 52 patients (18%). Seventeen patients (6%) had a past history of asthma, asthmatic bronchitis, or both. Results were similar in patients with, or without, a family history of allergy.

Certain minor criticisms may be directed
toward the study by Leer, et al. These include the failure to utilize an index of severity, the failure to match patients in the treatment and placebo groups according to degree of severity, and the absence of pulmonary function studies. However, in the main this is a well executed, controlled study involving a large number of patients in several different pediatric centers which clearly shows no significant benefit from corticosteroids in the treatment of bronchiolitis, lending further support to the findings of earlier controlled studies but which involved fewer patients. Despite this clear cut evidence of no therapeutic effect from corticosteroids, the authors unfortunately do not advise firmly against their use in bronchiolitis and, in fact, by omission hint that, because no detrimental effects attributable to corticosteroids were noted, they may be employed in this disorder. It has been stated that one physician out of three prescribes adrenal cortical hormones for the treatment of bronchiolitis. The physician who might succumb to the temptation to use corticosteroids in "clinically severe" bronchiolitis because these substances are unlikely to produce harm when used for a brief period should recall the findings of Dennis, which showed that beneficial effects attributable to corticosteroids could not be identified in a controlled study of patients critically ill with bronchiolitis.

It is hoped that the results of this recent study, which parenthetically points up the unique contributions which a collaborative, investigative effort can make, as well as other controlled studies, will convince the practicing physician that there is no scientific basis for the routine administration of corticosteroids in bronchiolitis.

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REFERENCES
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