

Steroids in treatment of pertussis

A controlled clinical trial

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Zoumboulakis, D., Anagnostakis, D., Albanis, V., and Matsaniotis, N. (1973). *Archives of Disease in Childhood*, 48, 51. **Steroids in treatment of pertussis: a controlled clinical trial.** Of 135 children with pertussis 70 were treated with steroids for 7 to 8 days and the remainder served as controls. The two groups were comparable. All children received erythromycin for 10 days. They were in the first week of the paroxysmal stage. Coughing, whooping, and vomiting episodes occurred less frequently in the steroid-treated groups, and the illness was shorter especially in babies under 1 year of age. These results indicate that steroids may have a beneficial effect on the course of pertussis if given early in the paroxysmal stage. Nevertheless, since steroids are potentially dangerous drugs we believe their use in pertussis must be limited to severe cases, particularly in infants under 6 to 9 months of age where the mortality is highest.

Pertussis and its complications remain a prominent cause of death in infancy. Unfortunately no specific treatment for this disease is available. Antibiotics and pertussis immune globulin both showed promise of affecting favourably the mortality of pertussis (McGuinness, Armstrong, and Felton, 1944; Brainerd, 1948; Schwabacher, Wilkinson, and Karran, 1949; Debré, Herzog, and Guerin, 1951; Hazen *et al.*, 1951); but both soon proved of dubious value in modifying the course of the disease (Eichlseder, 1963; Bass *et al.*, 1969; Balagtas *et al.*, 1971).

Because of the lack of effective treatment and because of current concepts regarding the pathophysiology of cough in pertussis (inflammatory lesions involving the entire respiratory tract (Krugman and Ward, 1964) associated with a possible allergic effect of *B. pertussis* on the coughing centre (Frobisher, 1965)) we thought it worth treating patients suffering from pertussis with steroids. This study represents an effort to assay the value of steroids in the treatment of pertussis.

Patients and methods

Children aged up to 3 years who were admitted to the Infectious Diseases Pavilion of the Department of Pediatrics, Athens University, between November 1968 and May 1971, with a clinical diagnosis of pertussis

were studied. Most of the patients were admitted during the first quarter of 1971 at the time of a pertussis epidemic in Athens.

Patients who had been given antibiotics and/or pertussis immune globulin before admission and those who had been coughing for more than 3 weeks were excluded.

All patients studied had a typical history of a catarrhal period followed by paroxysmal coughing; in the great majority of patients we were able to identify the source of infection. Inclusion in the study was based on clinical grounds alone and was always made by the same observer (D.Z.) throughout the period of the study.

Alternate cases of pertussis were treated with steroids regardless of the severity of the disease. We used hydrocortisone sodium succinate* intramuscularly at a dose of 30 mg/kg per day for 2 days; thereafter the dose was gradually reduced and treatment was discontinued by the 7th to 8th day.

Erythromycin was given orally to all patients for 10 days at a dose of 40 mg/kg per day in 4 divided doses.

All patients were assigned to an isolation room while in hospital. A nurse who was not aware of what therapy the patients were receiving recorded the number of coughing and whooping paroxysms and episodes of vomiting for every patient in a prepared observation sheet. At the end of the study the daily observation sheets were summarized and served as the principal basis for comparison of the two groups.

A total of 145 patients was included in the study. 8 patients were dropped from the final analysis because the hospital stay was too short for adequate study.

*Solu-Cortef (R) Upjohn.

Of the remaining 137 patients, 70 received steroids (treatment group) and 67 did not (control group).

Seventy-eight patients (57%) were female and approximately one-half of the patients (72 of 137) were under 1 year of age. The youngest patient was a 15-day-old infant.

Sex, age distribution, average estimated duration of illness until hospitalization, immunization status, leucocyte count, and number of patients with an abnormal chest x-ray on admission for both groups are illustrated in the Table. It can be seen that there were no significant differences between the studied groups in respect to the above-mentioned variables.

Patients with less than 14 coughing paroxysms and less than 4 whooping episodes daily on the day of admission were arbitrarily considered to have mild disease, whereas the remaining patients were classified as having moderately severe disease. No difference in the severity of the disease was found between the two groups (Table).

Results

No patient became worse and none died. The hospital course in each group of patients is illustrated in Fig. 1, 2, and 3.

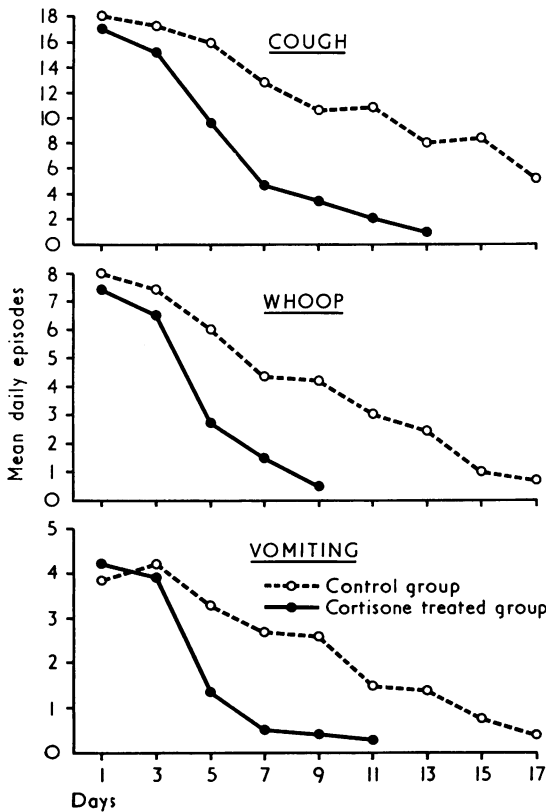


FIG. 1.—Hospital course of patients with pertussis.

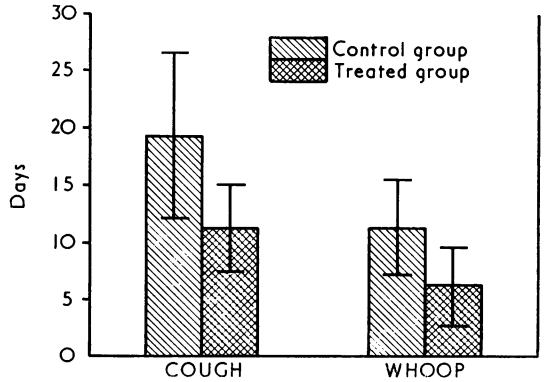


FIG. 2.—Interval in days (mean \pm SD) between initiation of treatment and the disappearance of coughing and whooping episodes in the control and steroid-treated groups.

Fig. 1 shows the mean number of coughing, whooping, and vomiting paroxysms calculated for each group from the daily episodes of each patient.

It is clear that there were no differences between the two groups during the first 3 days after initiation of treatment; thereafter, and throughout the period of study, there was a statistically significant difference ($P < 0.05$) between the two groups, the steroid treated group having less coughing and whooping paroxysms as well as vomiting episodes than the control group.

Fig. 2 shows the interval between the initiation of the treatment and the day when patients were free from coughing and whooping paroxysms. Here again we arbitrarily considered that the patients were free from coughing episodes when they had no more than one daily. Patients in the

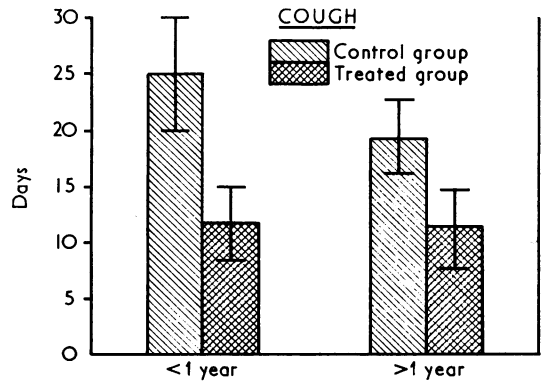


FIG. 3.—Interval in days (mean \pm SD) between initiation of treatment and the disappearance of coughing episodes in patients under and above 1 year of age.

TABLE
Comparability of patients with pertussis in treatment and control groups

Criteria	Cortisone-treated group	Control group
Total number of patients	70	67
Sex		
Female	41 (58.5%)	37 (55.3%)
Age		
< 12 months	38 (54.3%)	34 (50.7%)
> 12 months	32 (45.6%)	33 (49.2%)
Days of illness before admission (mean \pm SD)	10.9 \pm 6.95	12.05 \pm 6.42
Immunization status (number of patients)		
None	64 (91.4%)	63 (94.5%)
Incomplete	6 (8.6%)	4 (5.5%)
Number of patients with total WBC on admission		
5,000–15,000	19 (27.1%)	13 (19.4%)
15,000–25,000	23 (32.9%)	29 (43.2%)
> 25,000	28 (40%)	25 (37.3%)
Number of patients with abnormal chest x-ray on admission	17 (24.3%)	11 (16.4%)
Number of patients with subsequent pulmonary infiltrates	8 (11.4%)	6 (8.9%)
Severity of illness on admission		
Mild	41 (58.5%)	32 (47.7%)

steroid-treated group improved more rapidly; they were coughing for only 10.7 ± 3.8 days, as compared to the 19.3 ± 6.5 days in the group of patients not taking steroids ($P < 0.001$). The same is true for the whooping episodes: the mean duration of whooping was 11 (± 4.5) days in the control and only 6.5 (± 3.0) days in the steroid-treated group.

Fig. 3 shows the effects of steroids on coughing episodes in relation to the age of the patients. Here only the moderately severe and severe forms of the disease were considered. It is evident that the beneficial effect of steroids was more pronounced in patients under 1 year of age. The incidence of pulmonary complications was similar in the two groups. 6 of 56 patients in the control group and 8 of 53 in the steroid-treated group who had a normal chest x-ray on admission subsequently developed pulmonary infiltrates (Table).

Discussion

The great difficulties encountered in evaluating a therapeutic agent in pertussis have been repeatedly emphasized (Chassagne, 1964; Balagtas *et al.*, 1971). It is well known that the clinical expression and the course of the disease vary from one epidemic to another and that both may be influenced by the age of the patient, his status of immunization, and

his idiosyncrasy (Chassagne, 1964; Brooksaler and Nelson, 1967).

Furthermore, spontaneous improvement occurs and the stage of the disease during which a therapeutic agent is administered is of considerable importance (McGuinness *et al.*, 1944). In view of these and other variables, controlled studies are necessary in order to evaluate any form of therapy.

The results of the present study, in which comparable groups of patients were investigated, seem to indicate that steroids have a beneficial effect on the course of pertussis. This beneficial effect was more pronounced in babies under 1 year of age. We were unable to find an explanation for this observation. A significant point is that the incidence of complications in the steroid-treated patients was not higher than in patients who had received only erythromycin.

In no patient in either group did the disease relapse at least for the 6-month period during which we had contact with the patients' parents. Cortisone did not have any side effect in any patient, probably because it was given in relatively small doses for a short period.

Nevertheless, since steroids are potentially dangerous drugs the authors believe that their use is not justified for mild cases which generally do not require therapy of any type but must be limited to moderately severe or severe cases, particularly

in infants under 6 to 9 months of age where most of the mortality occurs.

The mode of action of steroids in pertussis is not clear. It may be related to their anti-inflammatory effect on the inflammatory lesion of the respiratory tract, especially of the bronchi and bronchioles, caused by *B. pertussis*. Another possible explanation is that steroids may interfere with the allergic mechanisms of cough in pertussis.

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Proposed European Society for the Study of Paediatric Dermatology

The need for a society to discuss and advise on paediatric dermatology in Europe emerged from informal meetings which were held during the recent International Dermatological Congress at Venice, and it is hoped to hold the inaugural meeting of the Society in the Summer of 1973. The membership of the Society will be open to all who are interested in diseases of the skin in infancy and childhood, who are resident in Europe or the countries of the Mediterranean Littoral. Membership will not be restricted to dermatological paediatricians. Geneticists, pathologists, and those engaged in fundamental developmental research in biology will be welcomed. Those who are interested should contact Dr. E. J. Moynahan, The Hospital for Sick Children, Great Ormond Street, London, W.C.1.