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The effect of alternate-day prednisone on the white blood count in children with chronic asthma

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Children requiring alternate-day steroid therapy for chronic asthma were examined to establish changes that might occur in the total and differential leukocyte counts on the day-on and the day-off prednisone. It was found that the majority showed no total count changes on either day, and the totals were not dose-dependent. Marked changes in the differential, independent of the dose above 5 mg., were noted.

Corticosteroids have been said to have significant effects on the quality as well as the quantity of the leukocytes. Pituitary adrenocorticotrophic hormone (ACTH) evokes a leukocyte response in man and animals.¹ Dougherty and White² have shown that ACTH injected in various mammals produces an absolute lymphopenia provided the adrenal cortex is intact. Daughaday, Williams, and Daland³ have shown similar responses in man, indicating that a single intramuscular injection of ACTH will result in an absolute and relative polymorphonuclear leukocytosis and a lymphopenia also relative and absolute. Eosinopenia was also observed. Hudson,⁴ experimenting with guinea pigs, suggested that the reduction of eosinophils was probably due to lack of discharge of the eosinophils from the bone marrow under the influence of corticosteroids.

Nowell,⁵ using culture techniques, indicated that prednisolone apparently prevented the lymphocytes from undergoing mitosis without interfering with mitosis itself.

It is therefore clear that the use of corticosteroids in any form is likely to

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TABLE I. Steroid dosage*

Total 48 hour dose	No. of subjects
2.5- 5 mg.	15
10 -15 mg.	17
20 -30 mg.	21
35 -45 mg.	11
50 -60 mg.	8
65 mg.	1
80 mg.	1

*Taken as a total dose, 8:00 A.M. every 48 hours; range, 2.5 to 80 mg.

TABLE II. Variability and range in total white cell count

Day-on steroids:	8 hours after administration of total dose
Day-off steroids:	24 hours after administration of total dose
Day-on 9,675	Range 5,000-17,550
Day-off 10,153	Range 4,850-18,000

TABLE III. Cellular distribution

Type of cell	Per cent	
	Day-on	Day-off
Segmented cells	82.2	46.5
Lymphocytes	15.8	46.0
Eosinophils	1.1	5.0
Monocytes	0.1	2.0
Basophils	0.3	0.2

have a profound effect on the cell distribution and perhaps the total number of circulating leukocytes.

Children suffering from chronic steroid-dependent asthma, who require long-term corticosteroids, present a special problem. They are subject to concurrent illness in no less degree than their normal peers. Consequently, it becomes of paramount importance to know what effect their maintenance steroid therapy has on the quantity and quality of the white cells if this laboratory procedure is to have any meaning in the diagnosis of complicating pathology, especially the occurrence of infection. Even more so is it necessary to know what effect steroids have when administered on an alternate-day basis (the total dose being given at 8:00 A.M. every 48 hours).

PROCEDURE

Seventy-four subjects took part in the study. There were 26 females and 48 males. Their age range varied from 6 to 15 years. They were all chronic, perennial asthmatics who had been on an alternate-day regimen of corticosteroid therapy for many months prior to this study.

All the counts were performed by the same technician in order to avoid any possible bias that might have been present if different technicians had done the counting and the differential. All counts were performed between 2:00 and 3:00 P.M. on the day-on and day-off steroids. This was done to avoid any possible circadian effects or any changes that could possibly be accounted for because of food ingestion or any other variable that might be time-related.

The prednisone (which was the steroid administered to all children) was given at 8:00

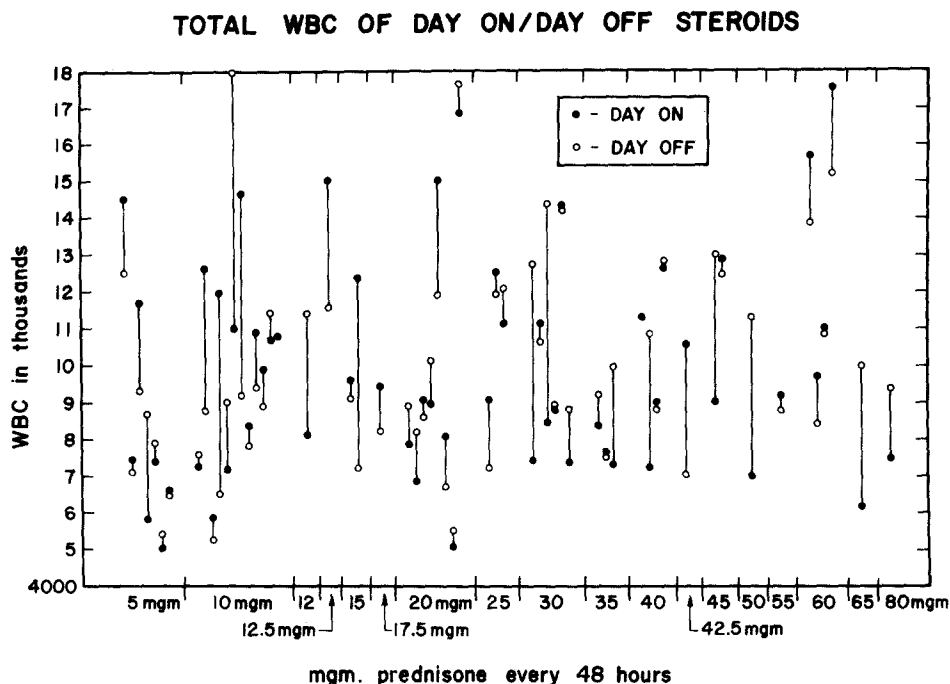


FIG. 1. Distribution of the total white cell count (all cells) on the day-on and day-off prednisone (57 children).

A.M. as a total dose for the succeeding 48 hours, the dose level being determined by degree of asthma control achieved in the face of full activity.

The initial day-on count thus allowed 6 to 7 hours for any steroid effects to become apparent. The next count was done 24 hours after the day-on count, each subject having thus received no further steroids for 24 hours prior to the second count.

All subjects were on oral bronchodilators, and these remained unchanged on either the day-on or the day-off. If the changes noted were due to such medications, they should have been the same on either day. No stat medications (epinephrine, isoproterenol, rectal or intravenous aminophylline) were given for 24 hours prior to the blood count on either day.

All children were clinically free of asthma or any other pathology when the counts were done.

RESULTS

The number of subjects at various increments of prednisone are noted in Table I. Fifty-three subjects were on 30 mg., or less every other day, 11 were in the 35 to 45 mg. range, and 8 were between 50 and 60 mg.; 2 subjects were at higher doses.

Total white cell count

The variability and range in total white cell count are shown in Table II. It will be noted that there was essentially no difference between total white cell counts on either day, in the majority of subjects both the day-on and day-off having almost the same range. It is of interest to note that 52 of the subjects (67.6 per cent) showed a variation in total counts of 3,000 or less, half of them being no different to within 1,000 cells. Thirteen subjects (20.3 per cent) had an

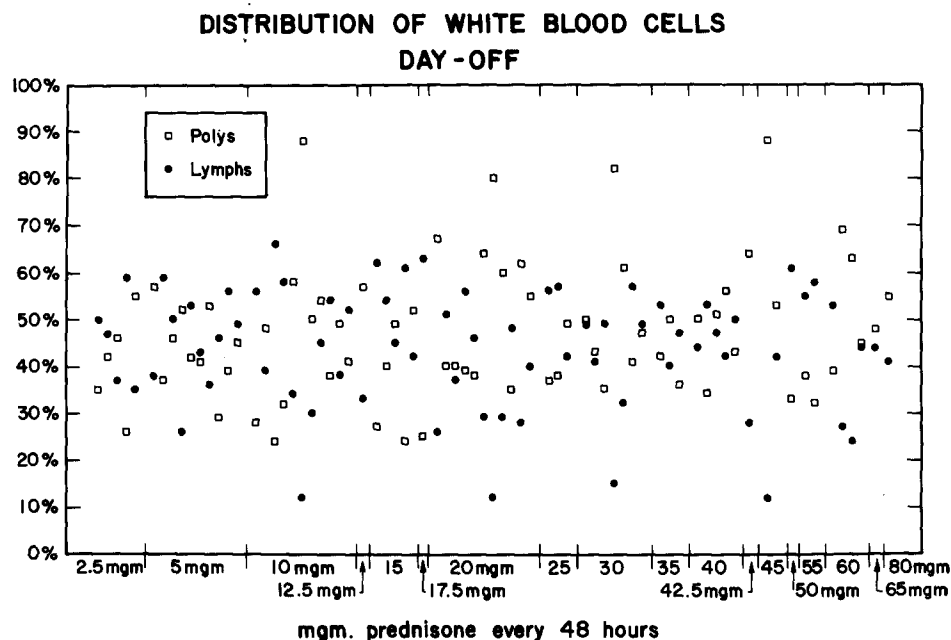


FIG. 2. Distribution of the polymorphonuclear leukocytes and lymphocytes on day-off steroids (74 children).

increase of more than 3,000 on the day-on when compared to the day-off, while 9 had an increase above 3,000 on the day-off when compared to the day-on.

Fig. 1 illustrates the individual variation in 57 of the children in relation to total dose (17 subjects were omitted for the sake of clarity, but all show the same distribution). There is no evidence that the total count is dependent on the prednisone dosage.

Cellular distribution

The distribution of cells, however, shows a marked change on the day-on when compared to the day-off steroids. Table III outlines the changes noted in the various leukocyte types. The polymorphonuclear leukocytes show a marked increase that is both absolute and relative, accompanied by an equally marked decrease in lymphocytes that is also relative and absolute.

Examination of Figs. 2 and 3 (which graphically display the polymorphonuclear leukocyte and lymphocyte percentages on the day-off and day-on, respectively) indicates that in large part the change occurs to the maximal degree at dosage levels of 10 mg., or greater, every other day. There is a tendency for the differences between the 2 cell systems to approach that found on the day-off at 5 mg. and less.

The eosinophil counts show the expected drop on the day-on, and it was of interest to note the same change in the monocytes. Basophils apparently showed no differences, but the very small numbers of these cells make this interpretation open to question.

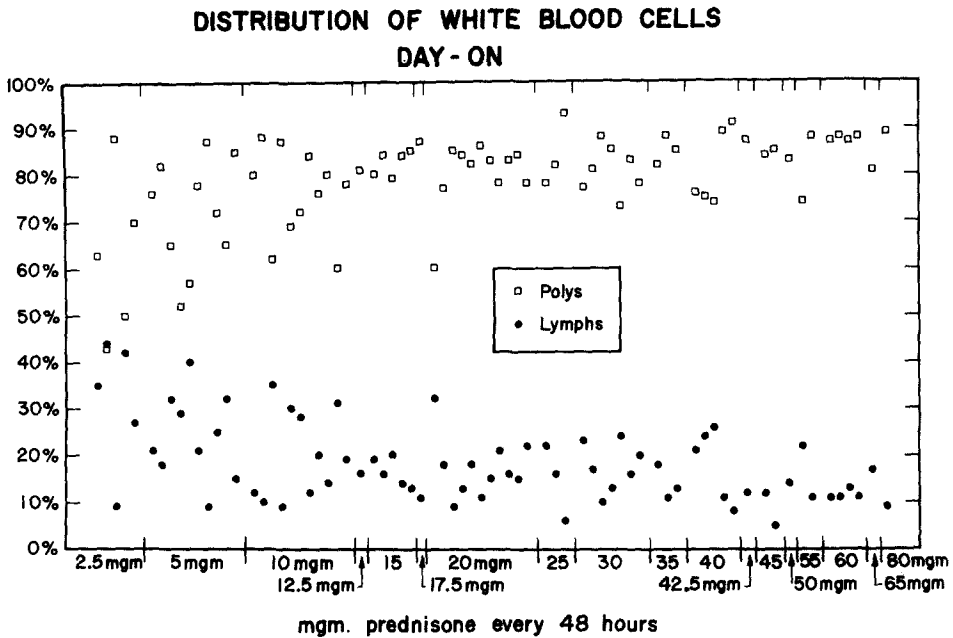


FIG. 3. Distribution of polymorphonuclear leukocytes and lymphocytes on day-on steroids (74 children).

COMMENT

In general terms this study has demonstrated that in these subjects the majority have shown no significant change in the total white cell count no matter what the dose level of prednisone was (within the 2.5 mg. to 80 mg. range). This finding is contrary to the accepted view that corticosteroids affect the total white cell count. The fact that 13 subjects did show significant increases on the day-on is counterbalanced by 9 subjects who showed very similar changes on the day-off and hence reflect individual responses of a minority of the children.

It is highly unlikely that these changes are due to cell destruction or increased production, although the underlying mechanisms were not studied. Lymphocytes are destroyed by corticosteroids in certain animals but not in man. The rapid changes noted (24 hours in this study but probably far sooner, as changes in eosinophils occur within 3 hours) indicate a probable homeostatic mechanism that mobilizes polymorphonuclear leukocytes from the storage compartment in the microcirculation and causes emigration of lymphocytes into reticuloendothelial storage sites. The decrease in eosinophils may be based on a prolongation of mitosis and retention in the bone marrow, and hence reduced entry of such cells into the circulation as well as removal to storage sites outside the circulation.¹

Whatever the mechanisms involved, the findings in this study indicate that it is essential to establish a baseline count and distribution of the leukocytes in all children who are likely to be on prolonged alternate-day prednisone therapy for asthma (and probably for any disease that requires similar therapy) if com-

plicating pathologic processes develop that require a white blood cell count and differential as an important facet of diagnosis. Baseline counts should be done during a quiescent phase of the illness for which steroids are being given, as well as in the absence of any other complicating pathologic process, of which infection is likely to be the most important. It is true that the majority of subjects in this study showed no changes in total count, but the real differences noted in a sizable minority (32.4 per cent) indicates that each child must have individual baseline and differential counts performed.

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