CIRCULATING EOSINOPHILS IN CHILDREN IN HEALTH AND DISEASE

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At the present time the role of the adrenal cortex in disease is the subject of intensive investigation. The response of the adrenal gland to various forms of stress may be studied by measurement of changes in the circulating eosinophil count. The studies of Thorn et al. have provided a simple clinical method for determining the adrenocortical reserve in normal and Addisonian patients following the administration of ACTH. The decrease in the number of circulating eosinophils following test doses of epinephrine and insulin has also been used as an index of adrenocortical function. In the majority of these studies the determination of the adrenocortical reserve has been done in adults.

The present report is concerned with a comparison of the circulating eosinophil counts in a series of children including those in apparent health as well as those experiencing a variety of febrile and nonfebrile illnesses. In addition, the response of the circulating eosinophils to test doses of ACTH, epinephrine and insulin was studied.

Material and Methods

Venous or capillary blood may be used for measuring the circulating eosinophils. In the author's experience finger-tip blood was found to be practical and satisfactory. The eosinophil counts were determined using the Thorn modification of the Dunger method in which the eosinophils are stained bright red with an acetone-eosin stain while the other leukocytes are almost colorless. The Randolph phloxin stain may also be used.*

The white cell pipettes and special diluting fluid are placed in a tray of cracked ice for 10 min. prior to use. Blood is drawn up to the 0.1 mark, the diluting fluid to the 1.1 mark. The pipette is shaken gently at once for 30 sec. and replaced in the tray. The 0.2 mm. depth Levy counting chamber with Fuchs Rosenthal linear markings is filled and the eosinophils counted in the 16 large squares on each side of the chamber after 3 min. The final count is calculated by multiplying the total count in each chamber by the factor 3.125 and the average value used. It has been found that in a series of 8 duplicate determinations, the filled pipette may be stored at -20° C. or in the ice compartment of the refrigerator for at least 1 wk. with no change in the number of circulating eosinophils. At least 5 min. should be allowed for thawing and the pipette again gently shaken for 30 sec. before filling the counting chamber. It has been found that when the refrigerator is opened frequently, storage is not satisfactory. Gentle shaking consists of 1 shake/sec. Thawing should be done at room temperature and not by applying heat; the pipette should still be cold after thawing, never warm.

The "ACTH test" was done in the postprandial state, the last food having been given at 7 p.m. on the day prior to the test. Finger-tip blood was taken at 9 a.m. and 4 hr. after the administration of ACTH.

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* In differential smears the eosinophil count is not satisfactory unless the original number of eosinophils is more than 10%.

† The diluting fluid contains 10 ml. of 2% aqueous eosin solution, 10 ml. of acetone diluted with water to 100 ml.

408
In patients experiencing a febrile illness, daily eosinophil counts were determined through the convalescent period. The "epinephrine test" and the "insulin test" were done under the same conditions as the "ACTH test" with the exception that in the "epinephrine test" a 3 hr. interval was used. In the "ACTH test," 25 mg. of ACTH was injected intramuscularly. In the "epinephrine test" 0.3 cc. of 1/1000 solution was injected subcutaneously. In the "insulin test" 0.25 units of insulin/kg. body weight was injected subcutaneously.

A total of 351 circulating eosinophil counts were done on 75 children observed in the Pediatric Pavilion of The New York Hospital:

(a) 18 healthy children.
(b) 29 patients with acute febrile illnesses including 19 with active carditis, 7 with acute infections, 2 with disseminated lupus erythematosus and 1 with acute myeloblastic leukemia.
(c) 3 patients with mild febrile illnesses.
(d) 12 patients with nonfebrile miscellaneous diseases including Cushing's syndrome, adrenogenital syndrome, mild hypopituitarism, diabetes mellitus, diabetes insipidus, postencephalitic disease, an extrathoracic abscess, retrolental fibroplasia, chronic hemolytic anemia, cervical spine tumor with spastic paraplegia, rheumatoid arthritis and chronic osteomyelitis.
(e) 10 patients with various allergies including 6 with eczema, 2 with pansinusitis and 2 with eosinophilia of unknown etiology.
(f) 3 patients were studied before and after surgery; 2 patients had tonsillectomies and 1 patient had a laparotomy.

OBSERVATIONS

The range of circulating eosinophils for the children in apparent health was 109 to 339, which is well within the range of 80 to 500 given by Thorn et al. for their normal adults. The circulating eosinophil counts for the patients in the nonfebrile miscellaneous disease group and those with mild febrile illnesses also fell within the normal range, being 84 to 599 and 170 to 341, respectively. In the miscellaneous disease group the patients were all chronically ill and about half the patients had endocrine disorders. From these results it would appear that in the presence of chronic stress some degree of adaptation, in accordance with Selye's hypothesis, has taken place. The normal range in the circulating eosinophils in mild febrile illnesses may be attributed to the absence of severe stress in these patients.

The range in the initial counts for the children experiencing acute febrile illnesses was 0 to 97. In chart 1 the response of the circulating eosinophils in three of these patients is presented. It will be seen that the drop in temperature as the patients improved under antibiotic therapy was paralleled by a rise in circulating eosinophils to normal levels.

It is of interest that in 1907 the French investigator Lams stated that the eosinophils were an "index of convalescence." The prognostic significance of the circulating eosinophil counts in severe illness is illustrated by curve III in which the eosinophil counts in a patient with pneumococcal meningitis are presented. It may be noted that at the onset the eosinophil count was 0, indicating a normal adrenocortical reserve. This patient made a striking clinical recovery following penicillin-aureomycin therapy. In marked contrast is a recent report by Faloon et al. of a patient with Waterhouse-Friderichsen syndrome. Here, the initial count was 21, rising to 90 on the second hospital day, indicating a poor adrenal response to severe stress. These investigators gave supportive therapy with adrenocortical extract which lowered the eosinophil count to 6. It would, therefore, seem of prognostic importance to determine the circulating eosinophil count routinely in patients with acute febrile illnesses.
THE CIRCULATING EOSINOPHILS BEFORE AND AFTER SURGERY

CHART 2. Circulating eosinophils before and after surgery.

THE RESPONSE OF CIRCULATING EOSINOPHILS IN ACUTE FEBRILE ILLNESSES

CHART 1. Response of circulating eosinophils in acute febrile illnesses.

KATHARINE HAIN
Chart 2 illustrates the changes in the circulating eosinophils in a patient before and after laparotomy. The expected drop in the circulating eosinophils in patients with normal adrenocortical reserve was obtained 24 hours after surgery. The "ACTH test" on this patient before surgery was normal, indicating that he was a good surgical risk. As Roche et al.\textsuperscript{19} have recently stated, this finding is considered a good prognostic index. These authors also recommend the use of the "ACTH test" prior to surgery in order to evaluate the adrenocortical reserve before the severe stress of operation.

The range of the circulating eosinophil counts for the group of children with allergic manifestations was 393 to 2665. These values are well above the normal range, as would be expected. The changes in the circulating eosinophil count in a child with acute atopic eczema treated with ACTH are shown in chart 3. It will be seen that this patient exhibited the characteristic high eosinophil count observed in allergic states. Following administration of ACTH for 5 days there was a precipitous drop in circulating eosinophils which reached a low level of 18 but never dropped to 0.

It has been considered that there is an antagonism between the factors controlling the eosinophilia in allergic disorders and the normal factors responsible for the decrease in circulating eosinophils.\textsuperscript{1,2} This is reflected in the irregular response of the circulating eosinophils in allergic patients treated with ACTH or cortisone, or under stress. It is of interest that the eczema disappeared during therapy but returned gradually after therapy was discontinued.

In a previous publication,\textsuperscript{11} the response of the circulating eosinophils four hours following the administration of ACTH 25 mg. was shown for a group of 23 children, including normal subjects and patients with miscellaneous illnesses, as well as active and
in eight children with miscellaneous diseases using the "epinephrine test" and the "insulin test" are comparable to the results of Laragh and Almy and Recant et al. with adults, the drop in circulating eosinophils ranging from \(-30\%\) to \(-100\%\). These observations are comparable to those reported by Thorn et al. for adults. It is apparent that the adrenocortical reserve as determined by this test is normal in rheumatic children. In marked contrast are the observations of Thorn et al. in Addison's disease. They observed a decrease in the eosinophils following the administration of ACTH of \(-4\%\) or less. Almy et al. have recently reported comparable observations following the subcutaneous injection of epinephrine 0.5 cc. in Addisonian patients. The present author's results

**Chart 4.** Response of circulating eosinophils in acute rheumatic fever following ACTH therapy.

The mechanism responsible for the decrease in the eosinophil count following stress is obscure. However, the decrease apparently reflects the adequacy of the adrenocortical reserve.
CIRCULATING EOSINOPHILS IN HEALTH AND DISEASE

It has been shown in this presentation and by other investigators that the determination of the circulating eosinophil count is of diagnostic and prognostic significance. It appears that the circulating eosinophil count, provided that it is done under carefully controlled conditions, is a simple, practical clinical test of adrenocortical reserve.

**SUMMARY**

A total of 351 circulating eosinophil counts were done on 75 children.

The range of circulating eosinophils for 18 normal children was 109 to 359. In 12 patients with nonfebrile miscellaneous diseases the circulating eosinophil counts ranged from 84 to 599, and in three patients with mild febrile illnesses, from 170 to 341. A possible explanation for the fact that these counts fell within the normal range was discussed.

In 29 patients with acute febrile illnesses the initial circulating eosinophil counts ranged from 0 to 97. Serial counts during convalescence on three of these patients are presented and the prognostic significance discussed.

In 10 patients with various allergic manifestations there was a range of 393 to 2665. Serial counts on one case of acute atopic eczema treated with ACTH are presented. Serial counts on one patient before and after laparotomy are presented.

Results of the "ACTH test," the "epinephrine test" and the "insulin test" on a group of children with miscellaneous diseases are presented.

**REFERENCES**

Un total de 351 conteos de eosinófilos de la sangre fueron hechos en 75 niños. Los límites de los eosinófilos en 18 niños normales variaron entre 109 y 359 por milímetro cúbico de sangre. En doce niños con enfermedades diversas pero afebriles, el número de eosinófilos varió entre 84 y 599 y en tres pacientes con enfermedad ligera febril el número de eosinófilos osciló entre 170 y 341.

En 29 pacientes con enfermedades fébriles el conteo inicial de los eosinófilos varió entre 0 y 97. Conteos seriados fueron realizados durante la convalecencia en tres de estos pacientes y la significancia pronóstica es discutida.

En 10 pacientes con manifestaciones alérgicas diversas el promedio de los eosinófilos osciló entre 393 y 2665. El autor presenta datos de conteos seriados de eosinófilos en un niño con ecema atopico agudo tratado con ACTH y en un paciente antes y después de una laparotomía.

Se presentan los resultados del "ACTH test," "epinephrine test" y "insulin test" en un grupo de niños padeciendo de enfermedades diversas.
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