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Review Article

A Review on Eosinophil count at different conditions

Obeagu,Emmanuel Ifeanyi[1] and Obeagu, Getrude Uzoma[2]

[1]Diagnostic Laboratory Unit,Department of University Health Services,Michael Okpara University of Agriculture,Umudike,Abia State,Nigeria.

[2]Department of Nursing Science,Ebonyi State University,Abakaliki,Nigeria.

*Corresponding author: *emmanuelobeagu@yahoo.com*, *obeagu.emmanuel@mouau.edu.ng*

Abstract

The eosinophil granulocyte is a leucocyte characterized by the presence of relatively large round granules with an affinity for acid dyes such as eosin. These granules are contained in the cytoplasm of the cell and usually they do not overlap the nucleus. The granules are relatively large, round with well defined boarders and stain a brilliant reddish orange. In the intra-uterine life, leucocyte production occurs in the spleen, lymphoid tissue, liver and sometimes bone marrow. Before birth, the bone marrow progressively takes over the granulocyte production. The maturation of eosinophil granulocyte actually ranges from the development of specific granules to loss of basophilia of cytoplasm, ripening of the segmented nucleus and finally development of motivity and ability to act as phagocyte. Mitotic division during maturation occurs up to this myelocyte stage where it is most active. The metamyelocyte is not capable of mitosis.The rate of production of mature eosinophils in the bone marrow is influenced by a number of factors e.g. ACTH (Adrenocortico-thropic hormone) and corticosteroids, which causes marked eosinopenia of the peripheral blood. When this occurs, release of mature eosinophils from the bone marrow is inhibited but no accumulation of mature forms is demonstrable.

Keywords: Eosinophil, Morphology, Production rate, Functions, Life span,Eosinophilia,Eosinopenia.

Introduction

In clinical examination, importance is often attached to abnormally high or abnormally low value of the number of eosinophils circulating in the blood. This applies especially to changes in the numbers of eosinophils in the course of certain diseases like parasitic infection and allergic reactions, or during the administration of drugs.

In our locality, eosinophila is not uncommon feature even in healthy subjects. A recent study (Ukaejiofo *et al.*,1979) showed the 95% confidence interval for eosinophil by the differential count in the healthy adult Nigerian male of higher socio - economic class to be 11±1%. This represents a figure much higher than the frequently quoted Caucasian normal values. The reason for this is probably because of the endemicity of parasitic infection in our environment due to fifth and dense vegetation. So in our hospitals, eosinophil count is frequently requested to monitor response to allergic conditions and in patients under treatment for parasitic infections. We have therefore decided to study further the viability of eosinophils in stored blood taken into sequestrene as an anticoagulant.

Several factors have been shown to affect the normal values of blood eosinophil count. These are diurnal variation, age sex and geographical distribution. There is normally considerable diurnal variation in the eosinophil count, and differences amounting to as much as 100% had been recorded. The lowest counts are found in the morning (8am -12pm) and the highest is at night (midnight–4am) (Dacie and Lewis,1985). This finding was investigated by (Unrbrand, 1958), who also confirmed that the number of eosinophils fall from morning to noon, rises in the course of the afternoon, and night, reaching a maximum at about midnight to 4am, and then falls to the original value.

The reasons for this variation, apart from the stress are as follows.

1.It was found that the excretion of adrenocotical steroids in the urine shows regular 24 hours variation, it being minimal during sleep and maximalin in the morning, (Pincus, 1943). The course of the variation therefore supports the view that the number of eosinophils, not only during stress but also under normal condition, is regulated wholly or in part by adrenocortical steroids.

2.The variation might be related to light, (Archer, 1963) however, this was not at all clear.

3.(Cunningham, 1975) observed age and sex difference in children. According to him children under 10 years of age had substantially higher average value than those previously reported for adults. Peak values for boys occurred at 8-10 years, ($p<0.01$) and for girls, at 6-8 years ($p<0.05$). On the average, boys had higher eosinophil count than girls ($p<0.05$). the values being given as $0.180x10^9/L$ respective. Some authors had gone further to compare the methods for eosinophil count. According to (Discombe, 1946), it is quicker and more accurate to determine the eosinophil count of blood in a haemocytometer using a special diluting fluid, than to do a differential count using stained films.

(Randolph and Stanton, 1945) had earlier claimed that the differential count method has a large margin of error and therefore not suitable for the enumeration of eosinophils in the peripheral blood.

Several other authors (Rud, 1947; Spier and Meyer, 1949) also confirmed that the direct count method is preferable because the indirect procedure involves a greater variation in cell counts and is impractical especially when the eosinophil counts are low. However, clumping is often observed in the direct count method if blood is exposed to air for a considerable length of time (Spier, 1952). On the other hand, (Ukaejiofo *et al.*, 1978) recommend the differential (indirect) method, provided the film was made by an experienced hand, and more than one hundred cells surveyed. Most authors have failed to investigate the rate of degeneration of eosinophils in stored below. Storage above twenty four hours at non temperature may equally affect both the morphology and eosinophil numbers.

Morphology and staining characteristics of the eosiophil

The eosinophil granulocyte is a leucocyte characterized by the presence of relatively large round granules with an affinity for acid dyes such as eosin. These granules are contained in the cytoplasm of the cell and usually they do not overlap the nucleus. The granules are relatively large, round with well defined boarders and stain a brilliant reddish orange.

The cytoplasm has a faint sky blue tinge. The nucleus stain somewhat less deeply than that of the polymorphonuclear neutrophil and usually has two connected segments, rarely more than three. The mature eosinophil is slightly larger than the mature neutrophil, its average diameter being about 9-16µ (De Gruchy, 1973).

Production and maturation

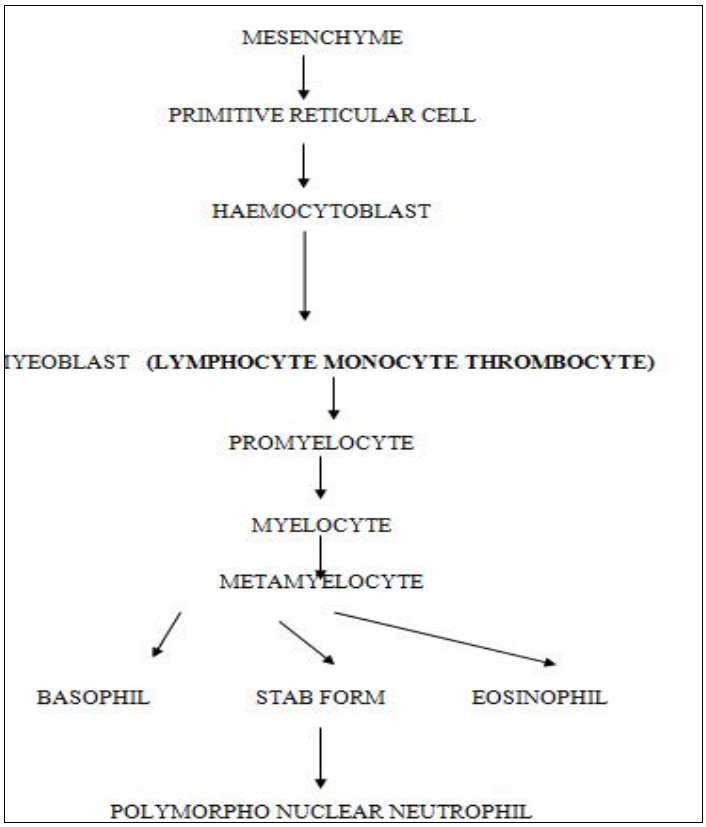
In the intra-uterine life, leucocyte production occurs in the spleen, lymphoid tissue, liver and sometimes bone marrow. Before birth, the bone marrow progressively takes over the granulocyte production. On attaining adult life, granulocyte production occurs mainly in the bone marrow while lymphocyte and monocyte production occur in other collection of lymphoid tissues. All blood

cells regardless of their site of origin are derived from the primitive reticulum cells or the undifferentiated stem cells produced from the mesenchymal cells of the reticuloendothelial system. This gives rise to haemocytoblast which in the bone marrow has the ability to differentiate and develop into the granulocytic series and also to lymphocytic tissues.

The most early recognisable precussor of all granulocyte is the myeloblast. This gives rise to a sequence of promyelocyte, myelocyte, metamyelocyte, stab cell and mature granulocyte. Specific granulation into neutrophils, eosinophils or basophils starts from the myelocyte stage. The myeloblast is about 15-20µ in diameter (Willis, 1945). The cytophasm is non-granular, deep blue in colour and posses a perinuclear halo. It may show pointed or rounded tag. The nucleus is round and occupies almost all the cytoplasm and stains reddish purple. It has fine structure and contains two to six well defined pale blue nucleoli. It is peroxidase negative. The promyelocyte is similar to myeloblast but the cytoplasm of the former contains some granules that stain purplish red. The cytoplasm is large than in myeloblast and it is peroxidase positive. The nucleus may still contain nucleoti but has begun to close up. The chromatin strands are coarser, the myelocyte is about 11-18µ (Dougherty, 1976), has increased cytplasmic nuclear ratio and stains from light-blue to pink. The mature myelocyte has predominantly pinkish cytoplasm and it is peroxidase positive. The nucleus is reduced in size, round and oval in shape. The metamyelocyte has a pinkish cytoplasm containing specific granules. The nucleus is slightly indented and has coarse chromatin. The stab form is smaller than the metamyelocyte. Its cytoplasm stains pink and it also contains evenly distributed purplish granules. The nucleus assumes U-shape (De Gruchy, 1973). The final stage of maturation is the eosinophil granulocyte. It is about 16µ in diameter and has its cytoplasm characterized by the presence of large, round and distinct granules which stain eosinophilic.

The maturation of eosinophil granulocyte actually ranges from the development of specific granules to loss of basophilia of cytoplasm, ripening of the segmented nucleus and finally development of motivity and ability to act as phagocyte. Mitotic division during maturation occurs up to this myelocyte stage where it is most active. The metamyelocyte is not capable of mitosis.

Eosinophils develop mainly in the bone marrow. Evidence of eosinophil; leucopoiesis developing elsewhere is confined to pathological states.



Developmental stages of polymorpho-nuclear granulocytes.

Production rate

The rate of production of mature eosinophils in the bone marrow is influenced by a number of factors e.g. ACTH (Adrenocortico-thropic hormone) and corticosteroids, which causes marked eosinopenia of the peripheral blood. When this occurs, release of mature eosinophils from the bone marrow is inhibited but no accumulation of mature forms is demonstrable (Archer, 1957).

When administration of corticosteroid is stopped, there is a rapid and marked increase in mature eosinophils in the bone marrow, followed after about 24 hours by a rise and even a transitory eosinophila of peripheral blood. At this time the marrow eosinophila declines and in two or three days the status is back to normal. When the histamine content of circulating blood is raised, and maintained high, an increase in circulating eosinophis is easily demonstrated. This has been done by intravenous drip infusions (Archer, 1963) and by use of hisfamine release compounds (Fernex, 1968). In these circumstances the bone marrow eosinophils gradually increase and a steady state is reached.

If however a glucocorticoid is then given, there is a reduction in circulating eosinophil and also in blood histamine. In clinical atopy, a somewhat similar condition may arise with raised blood eosinophils so long as the patient is suffering active and prolonged reaction between antigen and antibody.

Life span (kinetics)

Estimates of the time spent by eosinophils in blood have until recently been based on the changes in blood eosinophil counts following treatment with glucocorticiods or ACTH. These studies led to an estimate that eosinophils spent from a quarter of an hour to several hours in blood. Almost every study has indicated that the life time of the eosinophil in blood is shorter than that of neutrophil. Recently, two new methods for the estimation of the life span of eosinophils have been used. Radioisotope labels and transfusion of pelger-Huet anomaly cells. The radioisotope studies of the eosinophils are far confined to the rat. (Foot ,1963, 1965) used continous intraperifoneal administration of tritrated thymidine. By this means labeled eosinophils first appeared in circulating blood three days after the infusion commenced. He calculated that the half-life in the blood eosinophils is 8 to 12 hours and in tissue, the half-life was about 22 hours. (Rasumussen *et al.,* 1967) also investigated rate after injection of tritrated thymidine, but after one single intraperifoneal administration rather than by infusion. The results were somehow different, giving a half-life in blood for eosinophils of about 17 hours with a maximum of 24 hours. Labeled eosinophils appeared 36 hours after injection which was roughly half the time found by Foot made comparable study of rats after single intraperitoneal injection of titrated thymidine, but recorded a longer time the life span of eosinophils in the circulating blood.

These authors calculated the half-life in blood to be about two days. The probable life-span of eosinophil in tissue was found to be about the same; that is from two to four days. The eosinophil myelocyte turnover and maturation time were found to be about three days and 8 to 12 hours respectively. In the dog, a study of eosinophil in the blood was made by (Carper and Hoffman ,1966). They used pelger Huet anomaly cells obtained from a dog with this trait, and transfused them into a normal compatible bitch. They found that eosinophils disappeared from the circulation with a half life of about half an hour, and neutrophils with a half-life of 4.8 hours. (Dale *et al.*, 1975) studied the kinetics of 51-chromium labeled eosinophils in 6 patients with idiopathic hper-eosinophilic syndrome. The kinetics of these cells were compared with the G51 labeled neutrophils of 9 normal subjects. The patients studied consistently showed that autologous labeled eosinophils transiently left the circulation pool in the first 3 hours after infusion re-entered the circulation pool and then disappeared from the circulation with a mean blood half-life of 44 ± 2.0 hours. In contrasts, the neutrophils of normal subjects left the circulation progressively with an estimated blood half-life of 12.4±2.o hours. However these data suggest that the leucocytosis of hypereosinophilic syndrome may be due to the presence in the blood of an increased number of cells with a relatively long blood half-life. It may seem right to conclude therefore that the eosinophils have a shorter blood half-life than neutrophils and that it probably lies between 1 and 24 hours, most likely about 6 hours, the time spent in the tissue to which eosinophils may from blood is longer, from one to several days.

Functions

Eosinophils are phagocytic but unlike the neutrophils, their numbers decrease in the peripheral blood during acute bacterial infection. An eosinophalia on the other hand does occur in a Varity of allergic conditions and infestation with certain parasites and to antigen-antibody complexes. Local tissues accumulations of eosinophils are also found in respiratory mucosa in such conditions like Hay fever and Asthma. Eosinophils are also seen in tissue that is undergoing inflammation, especially when most cells degranulation is a feature.

The process for the assemblage and orderly, and there is a stimulus called chemotaxis that is responsible for this. This chemotaxis is caused by Histamine which has been found to attract eosinophils in man and animal (Archer, 1963, 1965; Fernex, 1968). There is also an evidence that antigen-antibody complexes are chemotaclic for eosinphils and that these leucocytes phagocytes particles of this nature. However, not all antigen-antibody conjugates attract eosinophils because the complexes formed are too small (Archer, 1965).

When inflammation results from the interaction of antigen and antibody, or when it involves the degranulation of most cells, hisfamine is usually released. (Lichtenstein and Osler, 1964) showed that

histamine release by this reaction is an active multistep response. When histamine is released, eosinophils are attracted to the tissue counteract the effects of the mediators of inflammation namely histamine, 5-hydroxy tryptamine and bradykinin.
(Archer *et al*., 1962) demonstrated that eosinophils delayed the onset of histamine induced broncho-span in guinea pigs. It was than concluded that at least two of the three characteristic properties of histamine can be antagonized by eosinophils; increased capillary permeability and constriction of smooth muscle.

The blood eosinophilia associated with parasitic infestation occurs as a result of relatively chronic process when there is tissue damage. Free living nemafodes in the bowel seem to be irrelevant with regards to the eosinophil in circulating blood unless damage to the bowel wall occurs. The eosinophil leucocyte is thus seen to have an important function in the inflammatory response. This function is the limitation of the effects of at least some of the chemical mediators of inflamation.

Normal values

Eosinophil count has continued to attract the attention of many authors, and there are various values of total and differential eosinophil count given by them. The Caucasian values obtained by (Discombe, 1946) in a study he carried out on 60 healthy adult caucassian was given as 0-$0.2x10^9$/L.

(Muehroke et al., 1952;Rud, 1947) in their study on healthy adult cavcassians, gave their value as $0.4\text{-}0.44x10^9$/L for total eosinophil count; and 1-6% for differential eosinophil count.

Others like (Uhrbrand, 1958; Dacie and Lewis, 1985; De Gruchy, 1973; Wintrobe *et al.*, 1974), gave their results as shown in the table below. A lot of work had also been carried out on healthy African subjects to determine their eosinophil level. The results obtained showed higher values than those from their caucassian counterparts.

(Forbes, 1941) in a study on Negro workers in mississsipo. Found the average differential eosinophil count to be 3.5%. (Roland Moore, 1985) in a study on non pregnant women in Nwanza, Tanganyika, found the mean total eosinophil count to be $0.711x10^9$/L, and differential count to be 11.5%. In another study on indigenous people of East Africa he found the mean total eosinnophil count to be $0.669x10^9$/L, and the differential count to be 11.1%.

Haematological observation in East African students population, furthermore found the total eosinophil count to be 0. 450 (±2SD) and differential count to be 9% (±2SD).

In Nigeria, some important studies on the normal values of eosinophils had been performed.Ukaejiofo *et al*.(1979) published the value of differential eosinophil count as 11±1%. From their study on healthy adult Nigerians.

Eosinophilia

This is the absolute increased in eosinophil above the normal range 0.04-0.4x10^9/L (Dacie and Lewis, 1985). It has been found in the following conditions:-

Parastic infection:

Eosinophilia occurs in all helminth infection, and it is of definite diagnostic value in infections with hookworm, tapeworm, threadworm, trchuria, filarial etc. the cell commonly forms about 20% of the total leucocyte count, and is exceptional cases may be as high as 60% (Okelo, 1979).

Allergic disease

In bronchial as time, food sensitivity, hay fever, urticaria etc, the eosinophils of the blood may number from 10 to 60% of the total leucocyte (Arnoldson and Helander, 1958).

Skin disease

Any infection or irritative condition of the skin such as penphigus, dermatitis, psoriasis etc may give rise to eosinophilia. The amount of eosinophila appears to bear some direct relation to the intensity of the infection and d the extent of the skin effected (Whitby and Britton, 1969).

Acute infection

In most acute infections, for example scarlet fever, it is usual for eosinophil to be diminished in the acute stage to return to the blood during recovery and to be definitely increased during convalescence. These changes are of some prognostic value. In rheumatic fever, eosinophilly if associated with cholera, an eosinophilia of as much 10% may be found in the acute stage (Whithy and Britton, 1969).

Eosinophilia is also recorded in disease conditions such as leukemia, lupus erythematosus, Hodgkins disease, ulcerative colitis, eosinophilic granuloma etc. some drugs like chlorpromazine pitocarphine, phosphorus, camphor, copper sulphate sodium salicylate, digitalis etc (Romano and Geiger, 1936) can cause blood eosinophils are produced by animals as a protection against foreign protein. It was also suggested that the function of eosinophil is to neutralize or antagonize the effects of histamine (Archer, 1959). The eosinophil increase is therefore due to chemotaxis caused by the liberation of histamkine in any allergic reaction and it is a protective reaction. Eosinophils are not source of histamine rather they are antagonistic to histamine.

The eosinophil which follows an acute fever may be the result of stimulation of bone marrow by the protein products set free during the process of inflammation; this again may be an allergic phenomenon. So long as inflammatory process is in existence, eosinophil production is depressed, but once the acute toxic stage is over, then the marrow is able to react to the stimulus of the protein products.

Eosinopenia

This is a decrease in the absolute number of eosinophils below normal e.g. below 0.04-1x10^9/L (Dacie and Lewis, 1985) and occurs in stress situations like shock, surgery, severe burns, blood loss, electric shock. Eclampsia, labour and severe infection. It is also seen in Cushing's syndrome after the administration of cortisone or ACTH.

It has been found that eosinopenia of the peripherial blood and spleen which is usual in acute infection and uremia, or after ephedrine and adrenalin administration, insulin hypoglyoaemia; is probably due adrenal cortical stimulatin (Godlowski, 1948). Eosinopenia is of prognostic values in surgical operation in that it indicates increased adrenecortical activity when no such reduction in eosinophil occurs; the inference is adrenocortical insufficiency which may be associated with severe symptom of shock.

The phenomenon of eosinopenia depends partly upon inhibition of release of eosinophil from the

marrow and partly increased destructive by the cells of the reticulo-endothelial system (Esselier and Dimity, 1954).

Conclusion

The eosinophil granulocyte is a leucocyte characterized by the presence of relatively large round granules with an affinity for acid dyes such as eosin. These granules are contained in the cytoplasm of the cell and usually they do not overlap the nucleus. The granules are relatively large, round with well defined boarders and stain a brilliant reddish orange. In the intra-uterine life, leucocyte production occurs in the spleen, lymphoid tissue, liver and sometimes bone marrow. In the intra-uterine life, leucocyte production occurs in the spleen, lymphoid tissue, liver and sometimes bone marrow. Before birth, the bone marrow progressively takes over the granulocyte production. On attaining adult life, granulocyte production occurs mainly in the bone marrow while lymphocyte and monocyte production occur in other collection of lymphoid tissues. All blood cells regardless of their site of origin are derived from the primitive reticulum cells or the undifferentiated stem cells produced from the mesenchymal cells of the reticuloendothelial system. Eosinophils are phagocytic but unlike the neutrophils, their numbers decrease in the peripheral blood during acute bacterial infection. An eosinophalia on the other hand does occur in a Varity of allergic conditions and infestation with certain parasites and to antigen-antibody complexes. Local tissues accumulations of eosinophils are also found in respiratory mucosa in such conditions like Hay fever and Asthma. Eosinophils are also seen in tissue that is undergoing inflammation, especially when most cells degranulation is a feature.

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