# THESIS ON THE BLOOD IN SKIN DISEASES

## WITH SPECIAL REFERENCE TO THE

## OCCURRENCE OF EOSINOPHILIA.

BY

EDWARD. W. M<sup>c</sup>CORMICK, M.B., Ch.B. ProQuest Number: 13905432

All rights reserved

INFORMATION TO ALL USERS The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 13905432

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved. This work is protected against unauthorized copying under Title 17, United States Code Microform Edition © ProQuest LLC.

> ProQuest LLC. 789 East Eisenhower Parkway P.O. Box 1346 Ann Arbor, MI 48106 – 1346

## CONTENTS

Section 1. Introduction Historical Outline and Leading Facts about Eosinophiles and Section 2. **Basophiles** Classification of Skin Diseases in which Eosinophiles occurs Section 3. Blood Changes in Skin Diseases Section 4. Section 5. Notes of Cases Section 6. Significance of Eosinophilia in Dermatology Summary and Conclusions Section 7. Section 8. Bibliography, Charts and Diagrams

SECTION 1.

# INTRODUCTION

~

j

요즘 문화 영향은 동안을 수

## INTRODUCTION

Eosinophilia and its connection with certain dermatoses has been well known, but the subject has seldom been investigated in its entirety. It is a symptom which has too often been taken for granted. There has been a great deal of work done lately on the subject of anaphylaxis and protein sensitisation, and a symptom which is common to it and certain dermatoses is eosinophilia. It may seem a far cry from the violent reactions of serum sickness and the distressing symptoms of asthma to the relatively quiet efflorescences of dermatitis, but there is netwertheless a symptom common to both of these in eosinophilia, Moschowitz (1) in a paper discussing the relationships of certain dermatoses and anaphylaxis says—" A feature common to all these diseases we have mentioned, and one to which attention has not been drawn, is this; they are all associated with eosinophilia." This increase of eosinophiles, both locally and in the blood, may link up these conditions in some way. Writers on the subject state that this eosinophilia is the expression of the agent, or even the agent itself in the production of the diseases.

During the winter of 1924-5 it was my good fortune to be house physician to the skin wards of the Western Infirmary, Glasgow, under the late Dr. Wylie Nicol. My interest had been aroused in the subject of haematology, and I began to make some observations on the blood of a number of skin cases. The first few results happened to be encouraging, and so during the rest of my time I made a detailed examination of the blood of every patient admitted to the wards, as well as many of the cases seen in the dispensary. A great deal of the work showed nothing abnormal, but the results are all recorded here and their bearings on the aetiology of skin diseases is discussed. Sometimes in Dermatology, though not very often, the blood is studied as a part of the routine examination, but as yet very few orderly attempts have been made to study this subject from the aspect of the blood. In the course of my work I have examined a series of over a hundred cases. Not all of these have shown marked changes, but the results, whether positive or negative, are recorded in full later in this thesis. The conditions in which eosinophilia is

seen are classified, the changes discussed and my conclusions drawn from them It will be my endeavour to show that certain anaphylactic conditions which show an eosinophilia are allied aetiologically to certain skin diseases. I hope to throw some light on the nature of that aetiological factor.

I am indebted to the late Dr. J. Wylie Nicol, Prof. J. Goodwin Tomkinson and Col. D. J. Mackintosh for their kindness and forbearance and for their permission to record these results.

.,

被推到一些公司 计内容存取通行 人名

 (สายการณ์และ 1.5 และเกณะการณ์ สายุ เล่าร่างการณ์ แสรงการ (การณ์ที่ เสร็จที่สุรรุษการการการ กละเหน่าไป, การสองการณ์ พระประเทศ ตั้ง (การพูมิ2) ก่าวส่วนเป็นสูงขุณ มีผล และสมบัตร์ไหน่ง สุรภาณาการ (กละเหน่า การณ์ พระประเทศ และการณ์ และสาย การสอง ไฟส์ สายการณ์สูงใหญ่และไม่สาย (กละเหน่า การณ์ พระประเทศ สร้าง)<sup>115</sup> (การประเทศการส่วนสายการสองการสายได้ สุรภาณาสาย (กละเหน่า ร่าง การสารณ์และการทางสายสายการสายใจกละการสาย การไป (การประเทศ การประเทศ (กระเทศ แกรมายการการสำนารการทางสายสาย สายการสาย การไป (การประเทศ)) (การณาและ การสายการใน (การการทางสายสายใจกละการสาย การไป (การประเทศ))

unestanti, provi de cons**ette cella de cons**erva en esta data a sebre de cara conserva da nome de contre e de conserva esta sebre de conserva esta consette da la france a connom y constructiones que de la conserva da conserva da conserva esta conserva da la france da conserva da conse nom y constructiones que de la conserva da conserva da conserva da conserva da conserva da conserva da conserva

e o gale fa good was been ger a restance en

이 이야 한다. 이 이 이 이 가지 않는 것을 생<sup>수를</sup>

to and a state where the

# SECTION 2.

# (a) HISTORICAL OUTLINE

# (b) LEADING FACTS ABOUT EOSINOPHILES AND EOSINOPHILIA

(c) LEADING FACTS ABOUT BASOPHILES

## 2. HISTORICAL OUTLINE

## EOSINOPHILIA

In 1773 Hewson (1a) first discovered leucocytes in the blood. It was not until 1846 that Wharton Jones (1a) differentiated the leucocytes, describing them as nucleated types and granular types. The latter he divided into fine and course varieties—the polymorph and the eosinophile. In 1878 this was confirmed by Rindfleisch. (1a) In 1878 Erhlich, (1a) by his researches on various stains and dyes on the leucocytes classified them according to their affinity for basic, or neutral dyes. Sherrington (1) Gulland (2) and others subsequently discussed these findings and, with their own researches the basis of the present classification of leucocytes was formed.

The first workers who connected eosinophilia with the skin were Kanthack and Hardy. (3) They were the pioneers of research work on this subject and their papers were published in 1892. I propose to describe in detail their experiments as far as they affect Dermatology, since they have a definite bearing on some of my own observations recorded later in this thesis. They used Zieglers chambers for most of their work. This chamber consisted of two cover-slips cemented together, a thin circle of tin-foil being placed between them. Two small holes were placed at either end and the cavity was filled with a broth culture of bacilli. These were placed in various parts of the body and the cells which were attracted to the vicinity were carefully noted.

1 Placed under the skin.—Eosinophiles were seen in enormous numbers, not only in the chambers but also in their vicinity. They took from  $7\frac{1}{2}-9\frac{1}{2}$  hours to appear.

2 Experimental Blistering.—Blisters were produced experimentally by Liquor Epispasticous. It was found that mostly polymorphs were attracted to the spot, but eosinophiles were present in varying numbers according to the individual. They ranged from 6%-45%. They then go on to explain how the eosinophile attacks bacteria. It applies itself to the bacteria and "excretes" its granule substance. Then the large hayaline cell injests the organisms now presumably dead.

3

Hankin and Kanthack (4) were the first to connect the oxyphile cell and bacteria. They stated that the resistance to the growth of organisms in the body was due to the production of a substance in the cell which they called a "defensive proteid." In 1893 Zappert (5) assembled cases from the literature and added some cases of his own. Gulland (6) in 1894 referred to the degeneration of eosinophiles. These cells, he said, are in constant brownian movement and as they die they become sluggish and lose their clear outline. The nucleus dies by chromatolysis. He then refers to a paper by Heidenhain (7) which states that the granules are ranged radially to the atrosphere, the smallest being the nearest to it. This arrangement was very clearly seen in a film from a case of dermatitis exfoliativa which I examined, in which there were a few eosinophile myelocytes present. The concentric distribution was very plain, the granules at the periphery being almost twice the size of those next to the atrosphere.

It was Leredde (10) in 1898 who first called attention to the presence of eosinophiles in certain dermatoses. H. S. French (8) in 1902 made an examination of the blood in skin diseases. In these conditions he found that eosinophilia was not nearly so constant a symptom as he had formerly thought. In 1909 (9) he made a classification referred to later in this thesis. He placed eosinophilia under three headings. 1.—Asthma. 2.—Parasitic conditions. 3.—Bullous dermatoses. Thus connecting up anaphylaxis helminthiasis and dermatology.

During the next twenty years little was done in relation to this subject. It was not until lately that three interesting papers dealing with the matter were published. These appeared in 1912, 1915 and 1924 and will be referred to fully in a later section.

4

and the second second

# LEADING FACTS ABOUT EOSINOPHILES AND EOSINOPHILIA.

The eosinophile cell is so called on account of its being an oxyphile cell which has a marked affinity for acid dyes, in particular eosin. (Erhlich (14) 1878). In size the eosinophile cell of the blood is slightly larger that its brother the polymorph. It varies from 10-14u. It can be recognised unstained by its relatively large size and its highly refractile granules. The granules are arranged in concentric fashion round the atrosphere, the smallest next to it and the largest at the periphery. Heidenhain (7)Buchanan (11). These granules are highly refractile whether stained or unstained. The cell substance is faintly basophile in reaction and stains a weak blue. It consists of a fine rectangular meshwork. The nucles is bi-lobed or tri-lobed, mostly the former, and is usually "spectacle-shaped," the two lobes being joined by thin bands of chromatin. It does not stain so deeply or show such a definite chromatin meshwork as that of the polymorph.

With regard to percentage, Gruner (12) says that in every hundred leucocytes we may expect to find one eosinophile. Gulland and Goodall (13) say that the normal is up to 4%. Eosinophilia may be said to be present when four or more eosinophiles are seen in every hundred leucocytes. And this percentage has been taken as normal. In myelogenous leukaemia there is usually an increase, but this form of eosinophilia will not be discussed, except in relation to basophilia.

#### BASOPHILIA.

I propose to deal shortly with basophiles, since I have found that they are closely connected with eosinophiles.

## HISTORICAL OUTLINE.

Erhlich (14) in 1878 was the first worker who differentiated basophiles from other leucocytes. He found they contained granules which were well stained by methylene blue. He called them "Y" granules.

In 1880 Westphal found basophiles in tumors, in tuberculous

and syphilitic ulcers, and in certain skin diseases. Later, Unna (16a) found the same and described them in cases of urticaria.

Cannon (15) in 1892 found them increased in twenty cases of skin diseases and says that they were slightly more increased when eosinophiles were present.

In 1896 Gilchrist (16) found basophiles — the "mastzellen" of Erhlich — increased in a case of urticaria in a child. He also found they were increased in a case of artificially produced weals. (Urticaria factitia). He states that the whole corium as well as the blood vessels were full of these cells. The interesting fact was that the eosinophiles were increased as well, in even larger numbers.

Da Costa (17) in 1905 found mast-cells increased in helminthiasis along with Eosinophilia.

## MORPHOLOGY.

The structure of these cells is simple. They have a tri-lobed nucleus. poor in chromatin; and indistinct cell substance, faintly basophiles; and large irregular shaped granules which stain deeply with basic dyes. These granules are characteristic and are refractile when stained, but are not seen in the fresh specimen. Their size is slightly larger than the Eosinophile, 9-12y. Their percentage in the blood is small. Gruner says that there are '47% present in the blood of 60% of the population, and that they are most numerous after meals.

terms of the second second

and a subserving a second second of the second s An and the second sec

# SECTION 3.

# CLASSIFICATION OF SKIN DISEASES IN WHICH EOSINOPHILIA OCCURS



## 3. CLASSIFICATION.

In classifying the conditions in which Eosinophilia is found. French [(3) sect. II] divided them under three headings. Firstly, asthma: secondly, parasitic conditions; thirdly, bullous dermatoses. It is interesting to note that the connection between eosinophilia and the bullous dermatoses was mentioned as early as 1909. In the last group French included pemphigus, dermatitis herpetiformis and erythema bullosum. Da Costa (4) in 1905 gave a classification of diseases found in conjunction with epsinophilia. In his first group he includes skin diseases, and finds eosinophilia in I. dermatitis herpetiformis, eczema, erythema multiformae, herpes (?) lupus (?) pemphigus, prurigo, psoriasis and urticaria. (To include all these conditions is over-generous. Certainly herpes and lupus can be omitted). II. Helm-IV. Post febrile conditions. inthiasis. III. Diseases of the bone. V. VI. Myelogenous leukaemia. With the passing of time and the Asthma. gaining of knowledge this classification has become considerably modified.

"Diseases of the skin may be divided for certain purposes into two groups—the first where the cutaneous manifestations can be shown to be the direct result of a specific parasite .... and the second where the eruption is a manifestation of a reaction which may not have been adequately explained." (MacCormac) (1).

Gruner (2) in his book on the biology of the blood cells states that—"The first question of interest and the most simple to decide upon is that of the factors which bring about eosinophilia and eosinopenia in the blood stream."

These two sentences have guided me. In the first place I set out to discover the conditions in which eosinophilia was found. Then, with these facts at my disposal I set about correlating the conditions. Eosinophilia was found in two types of diseases. Firstly in skin diseases and secondly as a result of anaphylactic reactions. In the case of the former I was at once struck by the frequency with which one found eosinophilia in vesicular or bullous lesions. This group was the largest and the cells were found with most constancy here. In the non-bullous variety eosinophiles were also found but they were not so numerous, with the exception of one disease, namely dermatitis exfoliativa, in which they were present in large numbers. However, attention will be drawn later to the fact that this condition is closely allied to bullous lesions. In the second group, anaphylactic reactions, eosinophilia is also found, but it is not so constant a symptom as it is in certain of skin diseases.

## THE SKIN GROUP.

I have divided this section into two sub-divisions. Firstly, those diseases in which the lesion is characterised by the bleb, bulla or vesicle. This embraces such conditions as penphigus, dermatitis herpetiformis bullous dermatitis or vesicular eczema, and urticaria. In the second sub-division I place the non-bullous conditions, such as exfoliative dermatitis, eczema, scabies, erythema multiformae and urticaria.

## THE ANAPHYLACTIC GROUP

In this group are included a diversity of conditions and it seems at first sight almost fantastic to class together such diseases as asthma, serum reactions and helminthiasis. But though their symptoms are vastly different yet in their cause they all bear a marked relationship to one another.

It will be seen that urticaria is a member of every group. It is found as an anaphylactic skin reaction; it may show vesicles or it may be non-bullous. I have noticed that asthmatical subjects develop urticarial rashes frequently. It is one of the most prominent symptoms of serum sickness and almost invariably eosinophilia is seen when it is present.

There are many ways in which the members of these skin groups can be correlated. Cranston Low (5) says that dermatitis herpetiformis is allied in many ways to the urticarias and the pemphigus group. Bullous dermatitis has been seen to turn into a chronic form of eczema and vice versa. Szarka (6) in a paper on dermatitis exfoliativa says that it is a severe form of pemphigus. He states definitely that he regards these three diseases as identical. I have seen psoriasis turn into the more serious condition of exfoliative dermatitis, and both conditions when treated overzealously with various ointments may exhibit a severe dermatitis superimposed on the original condition. This I have found to be characterised by an increase in eosinophiles. I was very impressed by the fact that asthma is constantly associated with a chronic form of dry eczema. Meltxer (7) said that asthma should be classified among the phenomena of anaphylaxis. Burwinkle (8) says that asthma, psoriasis and eczema are associated. In discussing asthma and urticaria Czerny and Strumpel (9) group them together under the heading of the "exudative diathesis." Goldschmidt (10) has stated that certain of his laboratory workers who were associated with, and subsequently infected with ascarides developed a form of anaphylaxis which was characterised by attacks of spasmodic asthma and eczema. This is of interest as it proves the relationship between helminthiasis and anaphylaxis,

It will be seen from these remarks that there is a very close connection between all the diseases mentioned, and though the manifestations of them are very varied yet I hope to show later on that they are closely connected by a condition common to them all — eosinophilia.

# SECTION 4.

BLOOD CHANGES IN SKIN DISEASES

## 4. BLOOD CHANGES IN SKIN DISEASES.

In this, the most important section of this thesis, I shall take the changes in the blood in Dermatology as a whole first. (Section A). Then I propose to describe the various diseases and their haematological peculiarities individually. (Section B).

Historically, it is interesting to note that Leredde (1) in 1902 first drew attention to eosinophilia in Dermatology. There are three papers to which I have given special attention: Schamberg and Strickler (4) in 1912; Engman and Davis (2) in 1915; and Towle and Swartz (3) in 1924. All have written interesting articles on this subject.

To these conclusions I have added my own contributions. Over a hundred cases of skin diseases passed through my hands and in every case a searching blood examination was made. These cases are all described in detail in Section 5, but I have used my results both collectively and individually where necessary in this section.

## Section A. LEUCOCYTOSIS.

In my own series I found leucocytosis in the acute cases. In dermatitis exfoliativa, dermatitis herpetiformis and bullous dermatitis there was a marked increase. In a severe case of scabies it was moderate. Ten out of sixteen cases of acute eczema showed slight leucocytosis.

Engman and Davis (2) report an increase in 88 cases out of 227. In 15 it was decreased, with a relative increase in the lymphocytes. These latter were mostly present in cases of seborrhoeic dermatitis. 20 cases of syphilis were included in this series. Towle and Swartz (3) found an increase in six conditions—scabies, impetigo, erythema multiformae, dermatitis exfoliativa, dermatitis herpetiformis and pemphigus. Schamberg and Strickler (4) do not give accurate details of the white cell count in each case, but they record that in most conditions where a marked abnormality of the cells was seen, there was an accompanying leucocytosis.

#### SUMMARY.

Leucocytosis in acute cases was increased. In chronic cases it was either normal or decreased, mostly the latter.

## POLYMORPH LEUCOCYTOSIS.

In my own cases the polymorphs were nowhere increased. In a few they approached normal, but the majority of the counts showed a decrease. This decrease was at the expense of an increase of the lymphocytes and eosinophiles,

Engman and Davis (2) examined 276 cases. 140 of these were normal, while 125 showed a decrease and 11 an increase. A decrease in these cells was particularly marked where other cells were increased. Towle and Swartz (3) out of 136 cases found no increase in any instance. Schamberg and Strickler (4) give details of 12 cases. Of these, 10 was decreased, one was normal and one was increased. French (5) gives an account of 4 cases, two of which were normal, while two showed a decrease,

#### SUMMARY.

The polymorph leucocytes are usually decreased. Out of 458 examinations, the percentage of 143 was normal, 12 were increased and 303 were decreased.

## LYMPHOCYTOSIS.

Of the cases which I examined all showed an increase except one which was normal, but this was combined with an Eosinophilia of 55%. None showed a decrease. The increase was most marked in a case of lupus vulgaris.

Engman and Davis (2) cite 275 cases, of which 117 showed an increase. The small lymphocytes were increased where the large mononuclears were decreased. According to Towle and Swartz (3) lymphocytosis was most seen in scabies, impetigo and erythema multiformae. It was marked in lupus vulgaris, at the expense of the large mononuclears. Schamberg and Strickler (4) examined 9 cases, 5 showed an increase, 3 were normal and one was decreased. One of these was very low, only 4%. But this case showed an eosinophilia of 50%. Their average was 28%, which must be regarded as high. French (5) records 4 cases, one was normal and one showed a decrease at the expense of the eosinophiles, while none showed a decrease.

#### SUMMARY.

444 cases were examined. 50% showed an increase, and these were mostly in chronic cases.

## EOSINOPHILIA.

Out of the 97 cases I examined 21 showed an increase, my average being 195%. The highest percentage recorded was 22% in a case of bullous dermatitis. The highest average percentage was seen in dermatitis exfoliativa where in two cases, the eosinophile count remained up over a period of four months. The counts in each case were taken repeatedly over this period

Engman and Davis (2) examined 250 cases. Of these, 71 were increased giving an average of 28%. Towle and Swartz (3) examined 126 cases, 35 of which showed an increase. Their average was 20%. Zappert (6) quotes 168 cases from the literature, his average of increase over these being 9.5%. Schamberg (7) examined 24 cases. 16.18% showed an increase.

#### SUMMARY.

APPROXIMATELY 20% OF SKIN CASES SHOW AN EOSINOPHILIA OF SOME DEGREE.

## LARGE MONONUCLEARS.

In my own series I found that the mononuclears were mostly normal. In a few cases they were increased at the expense of the small lymphocytes.

Of 272 cases examined by Engman and Davis (2) 108 were increased. Towle and Swartz (3) state that there is a decrease in mononuclears in lupus vulgaris.

#### **BASOPHILES**.

In the investigations of most of the workers mentioned before, these cells have been ignored. In my own series counts of 3% and 2% are recorded in two cases of dermatitis exfoliativa and 1.5% in dermatitis herpetiformis. In a case of vesicular eczema a count of 1% was seen during the acute stage. This fell to 5% as the disease decreased, and it was synchronous with the fall of a high eosinophilia.

Michelson (8) found an increase in a case of dermatitis exfoliativa, while Engman and Davis (2) found the same in two cases. Pollitzer (9) records an increase of 4.5% in bullous eczema. Fox (10) quotes 3.15% in pemphigus, while Schamberg (11) found 3% of these cells in urticaria papulosa, and 2% in pemphigus.

## Section B. DERMATITIS EXFOLIATIVA.

In two of my cases the average percentage of eosinophiles taken repeatedly over a period of four months, was  $12^{\circ}4\%$  and  $12^{\circ}8\%$  respectively. The highest percentage recorded was 18%, occurring in each case. Leucocytosis was present — 9,800 and 10,500. The basophilia was as high as 3% in one case, and  $1^{\circ}5\%$  in the other.

Engman and Davis (2) examined 4 cases. All showed a Leucocytosis; eosinophilia was normal in one case, increased in 3, and the highest count recorded was 33.6%. These cases all showed a lymphocytosis. Basophilia was seen in 2 cases where there was eosinophilia.

Towle and Swartz (3) cite 7 cases. In 6 there was a high eosinophilia. All showed an average leucocytosis of 12,000. Fordyce (12) had one case in which the leucocytosis was as high as 30,000 with a marked eosinophilia rising to 30%. Michelson (8) also gives one case which had a leucocytosis of 9,600 with no eosinophilia but a basophilia of 2%.

#### SUMMARY.

Out of 15 cases the average leucocytosis was about 10,000. Eosinophilia was a constant feature in 14 out of 15. It rose as high as 30% and was usually found to be about 12%. Basophilia was mentioned to to be increased in 5 cases.

## DERMATITIS HERPETIFORMIS.

Two cases of mine were examined. The leucocytosis in one case was 9,400. Eosinophilia was 9% and 17%, the highest percentage recorded being 21.5%. There was a basophilia of 1.75% in one case, and in the other it was absent. These cases, however were not seen in the most acute stage. It was my misfortune to have contact with them only when they were emerging into convalescence.

Engman and Davis (2) record 27 cases. They found leucocytosis in 4 out of 14, and eosinophilia in 13 out of 27, Their highest count was 24%. Basophilia was noted in 5 cases, 4 of these being seen with eosinophilia. Towle and Swartz (3) examined 14 cases. Their average leucocitic was 14,700. Eosinophilia was seen in 9 cases. Eosinophiles were also found in the tissues. Schamberg and Strickler (4) collected 13 cases from the literature. The highest was that recorded by Bushnell and Williams of 717%. All these cases showed a leucocytosis. The average differential count was polymorphs 37.5%; lymphocytes 28%; eosinophiles 21.6%. Zappert (6) assembled 24 cases, his average eosinophilia being 16%. Oliver (13) cites a case where the lesion began as a vesicular one and then became bullous. This case showed a leucocytosis of 8,200 after nine months' duration. Gilchrist (20) found eosinophiles in the exudate of this disease, while Klausner and Kreibich (28) and Heuch record finding them in herpetic blebs in large numbers.

#### SUMMARY.

This series covers 71 cases. 61 of these showed eosinophilia. The average increase ranged from 10% to 15%. Leucocytosis, though not so prominent a feature as in the former disease was still present. Eosinophiles were seen in the exudate and blebs in increased proportions.

#### PEMPHIGUS.

Engman and Davis (2) report 8 cases. Leucocytosis was seen in 5 of these. The highest percentage recorded was 74%, just before death. Basophilia was seen in one of these cases, along with eosinophilia. Towle and Swartz (3) examined 12 cases. They found eosinophilia in 10 out of the 12; their average leucocytosis was 1,500.

Zappert (6) drew 36 cases from the literature. These showed an average eosinophilia of 14%. He examined 5 cases of his own. His eosinophile counts were 33%, 14<sup>15</sup>%, 29<sup>28</sup>%, 6% and 3%, during convalescence. His average therefore, is 20<sup>6</sup>%. Schamberg and Strickler (4) collected 6 cases from the literature. Detailed accounts of three observers are given :—Fox; polymorphs 60<sup>5</sup>%, lymphocytes 21<sup>75</sup>%, mononuclears 3<sup>15</sup>%, eosinophiles 9<sup>1</sup>%. Leredde; polymorphs 49%, lymphocytes 35%, eosinophiles 16%. Schamberg; polymorphs 60%, lymphocytes 20%, mononuclears 2%, eosinophiles 18%.

Stanziale (14), Andry (15) and Bowen (16) record cases of 28%, 15<sup>2</sup>4% and 6% respectively. Winfield (17) examined one case of 13%. Coe (18) reports cases showing from 10% to 15%. One fatal case had 6%.

Cranston Low (19) records 7 cases :--

|     | Polymorphs | Lymphocytes       | Eosinophiles |               |
|-----|------------|-------------------|--------------|---------------|
|     | 69.5       | 18                | 12.2         |               |
| · 🛉 | 40         | - 45              | 15           | · .           |
|     |            |                   | 20.27        |               |
| -   | 53.8       | 35 <sup>.</sup> 4 | 8.8          |               |
|     | 56.8       | 27.9              | 7.8          |               |
|     | 59.6       | 27.9              | 11.2         | Basophiles 3% |
|     | 45         | . 4               | <b>50</b>    | -             |

## SUMMARY.

The average eosinophilia was 20% out of all these cases. Leucocytosis was increased as well as the lymphocytes, but these latter were increased at the expense of the polomorphs.

## BULLOUS DERMATITIS.

A peculiarly interesting case of my own showed on admission the following differential counts :--polymorphs 65%, lymphocytes 20%, eosinophiles 12%, mononuclears 2%, basophiles 1%. The eosinophile count rose in seven days to 20%, fell in eight days to 8%, and three weeks after the commencement of the disease it was down to 4%. The leucocytosis on admission was 11.600, falling in a week to 9,000. Two other cases were examined of less severity and widespread distribution than the above. One of these, involving abdomen, back and arms showed an eosinophilia of 125%, falling in a week under treatment to 7%, and in fourteen days to 2%, or normal. The other case involved the legs only and was resistant to treatment. The eosinophile percentage remained level, and with a fresh outbreak rose from 4% to 7%.

Schamberg and Strickler (4) examined 2 cases. Their average eosinophilia was 167%. They report that bullous eruptions show a high initial percentage which falls as the condition improves, only to reappear with a fresh outbreak. Pollitzer (9) also examined 2 cases. Detailed counts show an increase in the polymorphs of 44% and 45%; lymphocytes 175% and 215%. Eosinophilia was 385% and 335% respectively; the leucocytosis in one case was 9,500. In one case the eosinophilia fell in two days from 335% to 205%, and in seven days it was as low as 4%. Thereafter it ranged from between 2% and  $6\frac{1}{2}$ %, rising just before death to  $74^{\circ}/_{\circ}$ .

Pultz (10) discovered an eosinophilia in one of his cases but does not give full details of it. Pultz, however, connected the eosinophile with the basophile. Both were seen in the vesicles he examined, sometimes in large quantities and even when the blood percentage was not high. Both types were seen in artificial vesicles. The summary of his paper states that vesicular skin eruptions show a definite eosinophilia and mast cell increase, with a relationship between the two types of cell.

#### SUMMARY.

7 cases have been recorded here. Leucocytosis is seen to be well marked. Eosinophilia is relatively high, falling as improvement takes place. In the following section I am going to discuss these cases in detail, when the significance of the counts will be seen.

## ECZEMA.

I examined 47 cases of eczema. 16 of these were acute cases and 7 were cases of impetigo. Most of them, in particular the acute cases, showed a slight leucocytosis. 20 of the chronic cases showed a relative lymphocytosis. Only in those cases where there was a vesicular formation was eosinophilia present in any marked degree.

Engman and Davis (2) examined 25 cases. In 5 of these they found a leucocytosis, while slight lymphocytosis was seen in most. Eosinophilia was present in 8 cases, and basophilia along with eosinophilia was observed in 7. All these cases were acute. Of the chronic cases 12 were examined, Leucocytosis was seen in 6, eosinophilia in 6, basophilia in conjunction with eosinophilia in 3. Towle and Swartz (3) had 28 cases. None of these showed any vesicular characteristics. It is stated that no special cellular change of the blood was seen. Zappert (6) collected 29 cases from the literature. His average eosinophilia over these was 475%. In three cases of his own, of which he gives little detail, the average eosinophilia was 975%, 5'66% and 4'7%.

French (5) gives details of 4 cases :--

| Polymorphs | Lymphocytes              | Eosinophiles     | Distribution              |
|------------|--------------------------|------------------|---------------------------|
| 74         | <b>20</b> <sup>.</sup> 2 | 5 <sup>.</sup> 8 |                           |
| 71         | 16 <sup>.</sup> 5        | 13:5             | extensive and widespread  |
| 67         | 28 <sup>.</sup> 5        | 5                | involving buttocks & legs |
| 59         | <b>28</b> <sup>.</sup> 5 | 6                | involving the trunk       |

It is worthy of note that the highest count was seen in the most widespread case.

Schamberg and Strickler (4) quote 3 cases of Cannon's (20). One case which involved the legs only had 5% eosinophilia. One involving the whole body had 14'19%. Another case of generalised pruritis had 10'3%. One chronic generalised case showed 23'1%, while two extensive cases of their own showed a differential count as follows:— polymorphs 74% and 46%, lymphocytes 19'4% and 44%, eosinophiles 6'6% and 10%.

#### SUMMARY.

The results here are striking. Eosinophilia occurs markedly when a large area of skin is affected. I have noted that it decreases as the surface area affected becomes smaller. Cannon states that eosinophilia is proportionate to the extent, intensity and chronicity, rather than to the form of the dermatoses.

#### **PSORIASIS**.

17 cases of my own were examined. 5 of these were widespread eruptions and showed a definite eosinophilia. The rest, of less severity, showed a normal count. Nearly all of these cases showed lymphocytosis, while the highest eosinophilia seen in any of them was 10%.

Engman and Davis (2) examined 13 cases. 4 showed leucocytosis, 10 lymphocytosis, eosinophilia was seen in one and basophilia in 2. Towle and Swartz (3) examined 23 cases. They state that they did not find much change in these, although 6 of them showed an eosinophilia. They add that the increase in eosinophiles is only seen where the disease is widespread.

Schamberg and Strickler (4) give details of 4 cases :---

| Polymorphs | Lymphocytes       | Eosinophile        | s Distribution              |
|------------|-------------------|--------------------|-----------------------------|
| 61         | 34.3              | 4.2                |                             |
| 54         | 40 <sup>.</sup> 5 | 5 <sup>.</sup> 5 e | xtensive                    |
| 54         | 40.1              | 5.9 。              | on the body                 |
| 50         | 43.4              | 6 <sup>.</sup> 6 e | extensive and long duration |

They examined 15 other cases of less extensive distribution and of short duration. All of these showed a normal eosinophile count. There was a marked tendency for the lymphocytes to be increased in all their cases. They quote 3 cases of Cannon's showing an eosinophilia of 25%, 475% and 10% - 17%. They also quote 25 cases of Zappert's, his average over these being 4.5%. Zappert (6) treated 2 cases showing an eosinophilia of 9.88% and 5.23%.

## SUMMARY.

Here again the agent causing the disease seems to have little effect on the blood cells, as I have previously stated. The more widespread the disease the higher the eosinophilia. Lymphocytosis is almost universally present, pointing out the chronic character of the condition.

## URTICARIA.

I examined 5 cases of urticaria. Of these 3 showed slight eosinophilia while the other 2 were normal.

Engman and Davis (2) record 11 cases. Eosinophilia in conjunction with basophilia was seen in 3 cases, leucocytosis in 2. Schamberg and Strickler (4) had one case only. This was widespread and showed the following count ;—polymorphs 70%, lymphocytes 23%, eosinophiles 7%. Zappert (6) had 6 cases and the average eosinophilia only amounted to 3%.

Hallam (21) examined papularurticaria in children. His differential counts show slight eosinophilia, but he includes this under "sensitization diseases." He says the condition is anaphylactic.

#### SUMMARY.

Urticaria may well be included amonst those conditions of anaphylactic origin. These cases which I examined were not of a severe nature, nor were they of widespread distribution. For this reason the results were not striking.

## SCABIES.

Of my own cases 3 were examined. One was very extensive, the count being :--polymorphs 70%, lymphocytes 22'4%, eosinophiles 6'6%. The other 2 cases were not severe. The eruption was limited and the eosinophilia normal. Slight lymphocytosis was seen in every case.

Towle and Swartz (3) examined 10 cases, in which they found no marked change in the eosinophiles. The extent of the eruption in their cases is not given; 2 which had abundant pus infection showed a leucocytosis also a slight lymphocytosis. Schamberg and Strickler (4) report 47 cases. 38 of these, or 80%, showed eosinophilia of 5% and over. The maximum was 19%; the average was 7%. They state that those cases which showed no increase were the ones in which the eruption was scanty. Kolmer (22) gives details of 18 cases. His average was 6%. Normal controls on cases of the same age averaged 2%. His figures for the eosinophilia in six of these cases were as follows :—6.61%, 5.33%, 3%, 5% 9% and 5.79%.

## SUMMARY.

The eosinophilia is relative to the extent of the affection. Lymphocytosis is present in chronic cases.

#### IMPETIGO.

7 cases of my own were examined. No change was seen except slight leucocytosis.

Towle and Swartz (3) examined 25 cases. They report that leucocytosis with slight lymphocytosis was seen in most of these. Eosinophilia was only discovered in 4 cases.

SUMMARY. Results are indefinite.

## ERYTHEMA MULTIFORMAE.

I examined 2 cases, but no change was found. This may have been due to the fact that my cases were not of a severe variety.

Engman and Davis (2) examined 5 cases and slight eosinophilia was observed in one. Towle and Swartz (3) had 20 cases. They record that eosinophilia is fairly increased in some of the cases; there is no leucocytosis and they state this as a toxin disease. Zappert (6) examined 2 cases. He found eosinophilia in both— $4^{.75\%}$  and  $4^{.27\%}$  respectfully.

## SUMMARY.

Slight eosinophilia may be found. Towle and Swartz (3) say that this is a toxin disease caused by some foreign protein.

## LUPUS VULGARIS.

3 cases of mine were examined. Eosinophilia with slight leucocytosis and lymphocytosis was seen in every case. A noted feature of these cases was the sudden increase of eosinophilia after an injection of tuberculin. In corroboration of this Ewing (23) records eosinophilia after injections of tuberculin. He observed a lymphocytosis primarily, followed by an eosinophilia. Da Costa (24) quotes cases of eosinophilia after tuberculin injections. Andre and Courmont (25) observed eosinophilia after injections of haemolytic sera. Engman and Davis (2) had 2 cases, both of which showed a leucocytosis. One case having a bullous eruption contained 28,000 per c.c. Lymphocytosis was relatively high at the expense of the polymorphs. Eosinophiles were increased and there was a slight basophilia. They give details of one case; — white cell count 28,000, polymorphs 395%, lymphocytes 435%, eosinophiles 16%, basophiles 15%.

## SUMMARY

The protein of the serum is supposed to act as a toxin which causes the eosinophiles to appear in the circulation.

## MISCELLAEOUS.

Engman and Davis (2) examined 11 cases of dermatitis seborrhoeica. Leucocytosis was present in 7 of these, some lymphocytosis was seen; eosinophilia was present in 3 cases, and basophilia in conjunction with eosinophilia in one. 3 cases of my own were investigated. 2 showed no change: the other, which involved the whole of the body, showed 5%, falling to normal in six days after treatment.

Schamberg examined a case of prurigo which had an eosinophilia of 21%, dropping to 26% after the subsidence of the disease under treatment.

5 cases of lichen planus, and 2 cases of pityriasis rosea were examined. The blood in both these conditions showed no change. One interesting case of epidemorysis bullosa was investigated :—red blood corpuscles 4,660,000; white blood corpuscles 12,200; haemoglobin 65%; colour index 7. A differential count was of normal proportions.

#### GENERAL SUMMARY.

The results and investigations given in this section range over nearly 500 cases of skin disease. Leucocytosis is more pronounced in acute cases than it is in chronic cases, Polymorphocytosis is almost everywhere decreased. Lymphocytosis is present in roughly 50% of all cases, but it is most marked in the chronic types.

Eosinophilia taken over all the cases and not from specially selected ones is found in 20% of all dermatoses. This average has been taken over 668 cases collected from the literature and includes my own series of 97 cases. Eosinophilia is a constant symtom of dermatitis exfoliativa, dermatitis herpetiformis. pemphigus and bullous dermatitis. It is also a fairly constant feature of those diseases which involve a large surface area.

Basophiles are not much referred to and we can derive very little information from the literature and my cases, except that they are mostly seen in conjunction with, and have some relation to the eosinophile.

The eosinophile is seen as a tissue cell in most bullous conditions where there is a high blood eosinophilia.

e (e). **Beste state e** an Arene a see of shurder were the dwe e on the state of the

general and de la sectar de la completa de la sector de la Completa de la sector de la sector

网络小学教育学校 法法律保险公司

and a service state to a service of the service of

# SECTION 5.

# NOTES ON CASES

and the second state

## 5. NOTES OF CASES.

## DERMATITIS EXFOLIATIVA.

This disease is known to be one of the most serious of all skin affections. It is characterised by a generalised dermatitis and profuse scaling of the whole of the body. It was my good fortune to see two of these cases and follow them from the initial stages to their convalescence. The condition may be divided into two types. The primary type, which arises without any connection to any other skin disease; and the secondary type which succeeds some other condition such as psoriasis, seborrhoeic dermatitis or dermatitis herpetiformis.

My first and worst case was of the primary type. The other was of the secondary variety, following on psoriasis. It is curious to note that these cases occurred in men, both were miners, and both had spent most of their working life underground and up to their knees in water.

The blood examination in both cases showed remarkable characteristics. There was eosinophilia ranging from 10% to 20%; basophiles were present, 5% to 4%; and both showed a leucocytosis of between 10,000 and 12,000.

#### A. CLARK.

<u>History</u>. This man had had no previous skin disease. He was a miner and an alcoholic. He was ill four months and was discharged at the end of that time improved though far from well.

<u>General Condition</u>. During the whole of his illness this patient ran a temperature ranging from normal to 101° f. He had a mild attack of nephritis during the third month of the disease; this is a complication which sometimes arises and is due to the inability of the skin to act as an excretory organ, thereby throwing extra work on the kidneys which they cannot deal with properly. This condition cleared up quickly under appropriate treatment and after this a distinct improvement was noticed in the skin. The only other symptom of note, and one not usually mentioned, was his large appetite.

Blood Examination. The initial blood count was as follows— Haemoglobin 70%; white blood corpuscles 10,040; colour index '72.

The white cell count was repeated at intervals but it was found to be constant between 10,000 and 11,000.

|              | 22<br>Oct | 27<br>Nov | 11<br>Dec | 7<br>Jan | 27<br>Jan | 26<br>Feb | Average            |
|--------------|-----------|-----------|-----------|----------|-----------|-----------|--------------------|
| Polymorphs   | 70        | 70        | 62        | 66       | 54        | 51        | 62 <sup>.</sup> 16 |
| Lymphocytes  | 18        | 14        | 16        | 14       | 18        | 27        | 16 <sup>.</sup> 16 |
| Eosinophiles | 6         | 10        | 18        | 12       | 14        | 17        | 12.8               |
| Basophiles   | 4         | 4         | 2         | 4        | 2         | 2         | 3                  |
| Mononuclears | 2         | 2         | 2         | 4        | 2         | 3         | 2.5                |

Films were taken at regular intervals and were found to have a high eosinophile percentage throughout. The basophiles were also abnormally high, and on three occasions they reached 4%. Another feature was the amount of platelets seen. These were of a much larger size and were stained deeper than those of normal blood. The eosinophiles were normal in size and shape, but some of them showed vacuoles present in the substance, and several of them were found burst with the granules scattered in the vicinity of the free nucleus. This is an artefact caused by the spreading of the film, but nevertheless it demonstrates that these cells have an increased fragility, a fact referred to by Hardy, as mentioned earlier in this thesis.

It is worthy of note that the percentage of eosinophiles did not fall even though the general condition of the patient was greatly inproved towards the end of his stay in the wards. He was discharged at the end of four months, but he still had a fair amount of hyperaemia of his skin and was still scaling. On discharge his eosinophile percentage was 12.5%.

#### G. WALKER.

<u>History</u>. This patient was also a miner. He had had erysipelas in 1917 and had suffered from psoriasis for many years. He had this condition for a month previous to his admission.

<u>General Condition</u>. He was referred to us by his doctor who had been treating his psoriasis with chrysarobin ointment. We first saw him on a Monday with a severe dermatitis of his legs and arms. He was given treatment, but appeared on the following Wednesday exhibiting a typical dematitis exfoliativa and was at once admitted to the wards. His was not so severe a case as the previous—secondary cases like this never are—and at the end of three months he was greatly improved. An increase in the appetite was also noticed.

<u>Blood Examination</u>. On admission his white cell count was 17,000 per cm. In a week it had fallen to 11,400. His eosinophile percentage remained

between 10% and 20% throughout the course of the disease; the basophiles were not so numerous as in the previous case but were still relatively high. There was a marked similarity in the blood picture of the two cases.

|              | 5                 | 20   | 30                | 11  | 27   | 7   | 20  | 5   |                    |
|--------------|-------------------|------|-------------------|-----|------|-----|-----|-----|--------------------|
|              | Dec               | Dec  | Dec               | Jan | Jan  | Feb | Feb | Mar | Average            |
| Polymorphs   | 52                | 58   | 50                | 60  | 56   | 53  | 42  | 56  | 54 <sup>.</sup> 9  |
| Lymphocytes  | 36                | 25   | 20 <sup>.</sup> 5 | 25  | 30   | 30  | 38  | 26  | 28 <sup>.</sup> 25 |
| Eosinophiles | 10 <sup>.</sup> 5 | 14.2 | 18                | 11  | 11.2 | 12  | 17  | 16  | 13.9               |
| Basophiles   | ·5                | 1    | 1                 | 2   | 1.2  | 2   | 1.2 | •5  | 1.15               |
| Mononuclears | : 1               | 1.2  | 1.2               | 2   | 1    | 3   | 2.2 | 1.5 | 1.72               |

The marked rise of the eosinophiles on the 30th December, 1924 to 18%, was synchronous with a dermatitis superimposed upon his exfoliative condition and caused by the application of a weak chrysarobin ointment which, however, proved too strong for his skin. Soothing treatment was applied and ten days later the eosinophiles had fallen from 18% to 11%. The basophiles then rose to 2%, and it is interesting to note that a rise in basophiles is seen in an inverse ratio to a fall in eosinophiles. Platelets were increased in size, were more numerous and were stained deeper than normal. The patient was discharged after three months with an eosinophilia of 16%.

#### SUMMARY.

(a) Dermatitis exfoliativa exhibits a characteristic blood picture.

(b) Two cases were examined and showed an eosinophilia which ranged between 10% and 20%. This was maintained for over three months in each case.

(c) An increase in basophiles was also recorded and was also found to be constant.

(d) Platelets were increased in size, staining deeper than normal and seeming to be more numerous.

(e) Leucocytosis of between 10,000 and 12,000 was present in both cases, but was higher at the beginning of the disease.

(f) Eosinophilia and basophilia varied inversely to one another.

## DERMATITIS HERPETIFORMIS.

Two cases of this condition were seen and examined. Unfortunately they were dispensary cases. They were both convalescent and no chance was offered to me to carry out any extensive investigations. The first case had been ill for four months when I first saw it. At this stage it showed a leucocytosis of 9,400. Its average eosinophilia was 9% and it was slowly improving under treatment.

|              | 2<br>Feb | 10<br>Feb         | 3<br>Mar          | 26<br>Mar | Average |
|--------------|----------|-------------------|-------------------|-----------|---------|
| Polymorphs   | 57       | 60 <sup>.</sup> 5 | 50                | 66.5      | 66      |
| Lymphocytes  | 32       | 28 <sup>.</sup> 5 | 35                | 30.5      | 18.2    |
| Eosinophiles | 9'5      | 8.2               | 12 <sup>.</sup> 5 | 6         | 9       |
| Basophiles   | ·5       | 1.2               | 1                 | 0         | .75     |
| Mononuclears | 1        | 1                 | 1.2               | 2         | 1.75    |

The other case was very similar, but its white cell count was normal. This case on my first examination showed an eosinophilia of 21.5%. One month later this had fallen to 12.5%, and an interesting fact is that the last count I was able to make on it six weeks after my first examination still showed 17%, and this was present even though the rash had practically disappeared.

| Polymorphs   | 47.5 | 56                | 51 <sup>.</sup> 25 |
|--------------|------|-------------------|--------------------|
| Lymphocytes  | 28   | 29 <sup>.</sup> 5 | 28 <sup>.</sup> 75 |
| Eosinophiles | 21.5 | 12.2              | 17                 |
| Basophiles   | 0    | ·5                | •5                 |
| Mononuclears | 3    | 1.2               | $2^{\cdot}5$       |

## BULLOUS DERMATITIS.

This disease is naturally classed among the bullous lesions. It is characterised by the presence of vesicles or blebs forming on the skin. They arise from a simple papule which becomes enlarged. Fluid appears in the centre and forms a vesicle. This breaks down and a crust forms which on removal, shows a red, raw, inflamed area of skin.

#### ANDERSON.

This man was admitted on the 23rd February and was dismissed on the 26th March 1925. During that time he suffered from an acute vesicular condition involving practically the whole of his body. He showed a most perfect rise and fall of eosinophilia coincident with the state of the disease.

These cells averaged 14% of the leucocytes on admission. They rose steadily during the first week until his condition began to improve. On the 1st March they reached 22%. Then he started to get better and it was interesting to observe how the improvement took place and at the same time the eosinophilia grew less and less.

The basophiles were entirely absent while the eosinophile percentage was high, but they reappeared in the circulation when the eosinophiles began to fall.

The area affected was widespread, practically the whole of the body was covered.

In this case I also took the opportunity of examining the contents of some of the vesicles. I prepared the specimens and stained them both with Lieshman's stain Papenheim's stain and by Gramm's method. The results were extremely interesting. Polymorphs were present in all stages of degeneration, many of them showed distinct vacuolation, while others contained bacilli which they had injested. A few, but not many, of the polymorphs were normal. The eosinophiles were almost as numerous as the polymorphs, all of them were vacuolated—some slightly. but most of them in an extreme degree while others, which had been burst in the preparation, showed their granules scattered around the vicinity of the nucleus. In no case were any bacilli seen in these cells; they only contained the vacuoles, some showing one or two, some as many as half-a-dozen or more. There were numerous basophiles present, but not as many as there were eosinophiles. Relatively, however, they were more numerous. They did not show any peculiarity, except that several of them were found exploded like the eosinophiles. This is a characteristic referred to by Hardy and mentioned earlier in this thesis. Several large epithelial cells were seen, with weakly staining basophile protoplasm and a large metachromatic nucleus. Bacilli of all types were found in the skin, as well as staphlococci and streptococci. The latter were more numerous and were first seen in a slide stained with Lieshman's stain. This was corroborated in the film stained by Gramm's method. The rest of the contents was made up of epithelial debris and unrecognisable, disintegrated cells.

|              | 24  | 25                | 27  | 1  | 2                 | 3                 | 5                | 9   | 12  | 14                | 16  | 20   | 25        |
|--------------|-----|-------------------|-----|----|-------------------|-------------------|------------------|-----|-----|-------------------|-----|------|-----------|
|              | Feb | Feb               | Feb |    |                   |                   |                  | Ma  | rch |                   |     |      |           |
| Polymorphs   | 65  | 55                | 51  | 43 | 52 <sup>.</sup> 5 | 60                | 68               | 62  | 58  | 54                | 53  | 65.5 | <b>66</b> |
| Lymphocytes  | 20  | 25                | 24  | 33 | 32                | 25 <sup>.</sup> 5 | 16               | 28  | 33  | 36 <sup>.</sup> 5 | 38  | 28   | 20        |
| Eosinophiles | 14  | 18 <sup>.</sup> 5 | 22  | 22 | 13                | 11                | 12               | 8   | 5   | 6                 | 6   | 4.2  | 2         |
| Basophiles   | 5   | 0                 | 0   | 0  | 0                 | 0                 | •5               | 1.2 | 1   | 1                 | •5  | 0    | ·5        |
| Mononuclears | ·5  | 1.2               | 3   | 2  | 2 <sup>.</sup> 5  | 2.2               | 3 <sup>.</sup> 5 | •5  | 3   | 3                 | 2.2 | 2    | 1.2       |

A differential count of the contents of one of the vesicles was as follows: Polymorphs 42%; Lymphocytes 15%; Eosinophiles 37%; Basophiles 25%; Mononuclears 35%. It is interesting to contrast this with the differential count of Pollitzer, who recorded a similar case and made a like count of the vesicles. His figures were: Polymorphs 3%; Lymphocytes 22.5%; Eosinophiles 74%; Mononuclears 5%. He also draws attention to the vacuolation of the eosinophiles and their increased fragility.

#### BOLTON.

This was the case of a man who had a vesicular rash on his abdomen, back and arms. None was seen on the face, legs or head. The condition was of shorter duration than the previous case, lasting only a fortnight, when the patient was discharged almost free of any trouble. The initial percentage of eosinophiles on admission was 125%. This fell in ten days to normal. For one week the disease was obstinate to treatment, eosinophiles remaining about 7%. But with the start of improvement the sudden drop resembled a "crisis." The percentage of basophiles is again seen inversely to to the eosinophile percentage.

|              | 19                | 20                | 21                | 26  | 1   | 8          |
|--------------|-------------------|-------------------|-------------------|-----|-----|------------|
|              | Apr               | Apr               | Apr               | Apr | May | May        |
| Polymorphs   | 42.2              | 50 <sup>.</sup> 5 | 55                | 61  | 45  | <b>5</b> 0 |
| Lymphocytes  | 40                | 36                | 32 <sup>.</sup> 5 | 30  | 50  | 43         |
| Eosinophiles | 12 <sup>.</sup> 5 | 10                | 9                 | 7   | 2   | 3          |
| Basophiles   | 1.2               | 0                 | •5                | •5  | 1   | 2          |
| Mononuclears | 3.2               | 3 <sup>.</sup> 5  | 3                 | 1.2 | 2   | 2          |

#### CHEVERINGTON.

This woman had a typical vesicular condition which was limited to her legs. The eruption when seen at first was slight. There was a rise in eosinophiles as the condition became worse, during the first few days. The disease reached its height in one week, when the eosinophiles were also at their highest percentage. Coincident with improvement after the first fortnight there was again a sudden drop in their percentage.

|              | 8         | 13                | 22   | 4    | 11   | 18   |
|--------------|-----------|-------------------|------|------|------|------|
|              | Nov       | Nov               | Nov  | Dec  | Dec  | Dec  |
| Polymorphs   | <b>56</b> | 63 <sup>.</sup> 5 | 61.2 | 51.2 | 59   | 62   |
| Lymphocytes  | 37        | 27:5              | 29   | 40   | 33.5 | 31:5 |
| Eosinophiles | 4         | 5                 | 5    | 7    | 6    | 3    |
| Basophiles   | •5        | •5                | 2    | •5   | 1    | 1.2  |
| Mononuclears | 2.2       | 3.2               | 2.2  | 1    | •5   | 2    |

#### SUMMARY.

From these cases we can draw interesting conclusions.

(a) In vesicular dermatitis eosinophilia is present, In a widespread case it rose as high as 20% and over.

(b) Eosinophiles were present in large numbers in the vesicles, but were not germicidally phagocytic.

(c) Eosinophiles form vacuoles in their substance, but whether this is due to their injesting a toxin, or whether the vacuoles contain an antitoxin is uncertain.

(d) Basophiles have also chemiotactic properties, but those cells which were seen were haemic cells and not the basophile tissue cell described by Unna.

(e) The eosinophilia varies correspondingly with the surface area involved.

(f) The eosinophiles and basophiles vary inversely to one another.

## ECZEMA.

47 cases in all were examined. 31 of these were men, 16 were women. Of the whole 16 were acute cases, there were 7 of impetigo, and 24 were chronic cases.

There was very little change seen in the blood of these cases. White cell counts were made in 15 cases. The average was 7,500, a very slight increase. Differential cell counts were done in all cases with disappointing results, the only characteristic feature of them all being the relative lymphocytosis seen in the chronic cases. Here the lymphocytes were increased at the expense of the polymorphs. In none of these cases was there any evidence of eosinophilia

## **PSORIASIS**.

17 cases were examined. 6 were men and 11 were women. 5 cases, or approximately 30%. showed eosinophilia.

This condition is a common skin disease, characterised by red patches covered with thin silvery scales. It is regarded as a dry seborrhoea by Norman Walker, thereby connecting it with dermatitis exfoliativa and dermatitis herpetiformis which he also says are forms of seborrhoea. Here again the surface area involved seems to influence the height of the eosinophile percentage. The sites which the disease selects for attack are the elbows, the knees, and the scalp. When it affects these positions only the eosinophilia is not usually high, but when there is a large area involved more eosinophiles are seen.

#### GILLIES.

This man came in with a typical psoriasis involving the trunk, scalp, face, arms and one leg. The other leg had been amputated in 1914. He showed a 10% eosinophilia on admission. It is a matter of conjecture, but probably a certainty, that this percentage would have been higher if he had had his other leg, for even the stump was covered with the disease. He was a troublesome patient, and discharged himself from the wards after a fortnight's treatment and before he was cured.

| 10                        | 17  | 24  |
|---------------------------|---|---|
| Feb                       | Feb   | Feb   |
| <b>4</b> 6 <sup>.</sup> 5 | 57 <sup>.</sup> 5                                     | 58  |
| 41                        | 32  | 31  |
| 10                        | 10  | 9   |
| •5                        | 0   | 1   |
| 2                         | •5  | 1   |
|                           | 10<br>Feb<br>46 <sup>.</sup> 5<br>41<br>10<br>.5<br>2 | $\begin{array}{cccc} 10 & 17 \\ Feb & Feb \\ 46^{\circ}5 & 57^{\circ}5 \\ 41 & 32 \\ 10 & 10 \\ 5 & 0 \\ 2 & 5 \end{array}$ |

#### GUTHRIE.

This was the case of an old lady aged 78, who had extensive patches on her elbows, knees and in her scalp. She had suffered from psoriasis for years, but had had no other skin disease. After three weeks treatment the condition was very much improved, but her eosinophilia, though not of a high percentage, had not fallen as one would have expected.

|              | 8   | 15                | 22  |
|--------------|-----|-------------------|-----|
|              | Feb | Feb               | Feb |
| Polymorphs   | 60  | 58 <sup>.</sup> 5 | 58  |
| Lymphocytes  | 34  | 35                | 37  |
| Eosinophiles | 4   | 5                 | 4   |
| Basophiles   | 0   | 0                 | 0   |
| Mononuclears | 2   | 1.2               | 1   |

#### LARKIN.

This was the case of a young girl of 21. The disease was fairly generally distributed but was not of a severe type. She stayed ten days in the ward and only two counts were secured.

| Polymorphs   | 55 | 59  |
|--------------|----|-----|
| Lymphocytes  | 38 | 24  |
| Eosinophiles | 5  | 6   |
| Basophiles   | 1  | •5  |
| Mononuclears | 1  | 2.2 |

#### FERRIER.

This case was that of a man 56 years old. He had a long standing history of skin disease. For years he had suffered from chronic eczema and lately this had changed to a condition which was unrecognisable to the doctor who had been treating him outside. He was admitted to the ward with that puzzling condition known as eczemo-psoriasis. The eczema cleared up in seven days but the psoriasis was more obstinate to treatment. As the severity of the condition diminished and the surface autolysis became decreased, so the eosinophilia was reduced. He was discharged after three weeks with his skin condition cured and his eosinophile percentage normal.

|              | 25           | 26                      | 3   | 7                 | 14                |
|--------------|--------------|-------------------------|-----|-------------------|-------------------|
|              | Feb          | Feb                     | Mar | Mar               | Mar               |
| Polymorphs   | 52           | 49                      | 55  | 56 <sup>.</sup> 5 | 62 <sup>.</sup> 5 |
| Lymphocytes  | 39           | 42.5                    | 36  | 36                | 29                |
| Eosinophiles | 6            | <b>5</b> <sup>.</sup> 5 | 6   | 4.2               | 3                 |
| Basophiles   | ·5           | 0                       | 1   | 2                 | 2                 |
| Mononuclears | $2^{\cdot}5$ | 3                       | 2   | 2                 | 3.2               |

#### HYNDMAN.

This case, a man, showed a typical distribution of psoriasis, involving the elbows, knees and scalp. The condition was long-standing and most obstinate. A noted feature of this ease was the high lymphocytosis which reached 45.5% in one count.

|              | 3   | 10                | . 17        |
|--------------|-----|-------------------|-------------|
|              | Apr | Apr               | Apr         |
| Polymorphs   | 54  | 49.5              | 25          |
| Lymphocytes  | 40  | 45 <sup>.</sup> 5 | 42.2        |
| Eosinophiles | 5   | 4.2               | <b>5</b> .5 |
| Basophiles   | 1   | •5                | 0           |

#### SUMMARY.

Not all cases of psoriasis show eosinophilia; only in those which are severe and widespread may we expect to get any degree of eosinophilia. The height of the eosinophilia is never very great and is dependent on the area involved.

## URTICARIA.

In my classification, this condition comes under every heading. It may be bullous or non-bullous, and is a disease caused by the reaction of the body to some noxious substance, otherwise an anaphylaxic reaction. At the same time, it may be bullous on one part of the body and non-bullous on another. It is sometimes associated with conditions such as asthma and serum reaction, but no matter which form it may take and with what it may be connected, if the condition is widespread, eosinophilia is present.

#### E. W. McC.

I have always been unable to take oatmeal in any form whatever. On the 16th February I started taking a plate of porridge every morning and four or five oatcakes with every meal. In a week a rash appeared, a typical non-bullous urticarial rash. Before I started this I had taken a control examination of my blood, in which I found the eosinophile percentage was 15%. After three days the rash became spread over the whole of my skin and I decided that the cause of science as such was too irritating to be continued. The eosinophiles which had risen up to 5% remained up for a few days, but by the time the rash had completely gone they were normal again.

|              | 16₋<br>Feb | 24<br>Feb   | 27<br>Feb | 9<br>Mar | 16<br>Mar | l wk. later | 3 wks. later |
|--------------|------------|-------------|-----------|----------|-----------|-------------|--------------|
| Polymorphs   | 51.5       | <b>5</b> 0  | 54        | 57.5     | 60        | 55          | 58           |
| Lymphocytes  | 41.2       | 43          | 39        | 36.5     | 34        | 40.2        | 31.2         |
| Eosinophiles | 1          | <b>3</b> .5 | 5         | 4        | 2         | 2           | 8            |
| Basophiles   | 2          | •5          | 1         | 0        | 0         | 1           | 0            |
| Mononuclears | 4          | 3           | 1         | 2        | 4         | 1.5         | 2.2          |

Three weeks later I again yielded to temptation and indulged in a single plate of porridge. Within twenty-four hours I had an extremely irritating rash all over my body and legs. This sudden appearance of urticaria was due to the fact that I had once again become sensitised to oatmeal. I took films of my blood at once and found that eosinophilia had risen as high as 8%. In one week's time this had fallen to 2%.

#### NEIL.

This was a case in which urticaria was present in both forms bullous and non-bullous. The patient was a boy of four and a half years old, and had had a similar attack six months previously. A searching enquiry failed to reveal any definate cause. It is interesting to note that his grandmother had suffered from spasmodic asthma for twenty years and had had a dry eczema intermittently for about the same period. The patient had large bullae, about the size of a split walnut, on his legs, while his back showed typical urticarial weals. A differential count of his blood was made on two occasions, with the following results—

| Polymorphs    | 54  | 58                |
|---------------|-----|-------------------|
| Lymphocytes * | 36  | 33 <sup>.</sup> 5 |
| Eosinophiles  | 7   | 6                 |
| Mononuclears  | 3.2 | 2.2               |
| Basophiles    | 5   | 0                 |

It was not possible to get any more films as he was a private patient and objected to "treatment."

#### SERUM REACTIONS.

#### RICKFORD.

This was an extremely interesting case of a man who had angioneurotic oedema of his face and lupus vulgaris on his hands. He had a tuberculous history and had suffered from alopecia four years previously. The oedema was chronic and had been intermittent over a period of fourteen years. His blood on admission showed a slight leucocytosis of 9,000, and 7% eosinophiles.

It was in this case that I first found that injections of tuberculin had some effect on the blood. He was being treated with Koch's Old Tuberculin and for some time he showed no reaction. But afterwards this became fairly severe and the injections were stopped. I examined a film of his blood immediately after a severe reaction when his temperature was 104° f. Eosinophilia of 10% was seen ; this had fallen in two days to 6%.

After this I had no further opportunity of examining his blood as the injections were stopped. His blood count before the injections was as follows: Haemoglobin 75%; red blood corpuscles 5,140,000; white blood cells 9,500; colour index, 8.

|              |     |                           |    | after injection<br>with<br>severe reaction | 2 days later |
|--------------|-----|---------------------------|----|--|--------------|
| Polymorphs   | 54  | 58                        | 57 | <b>6</b> 0 <sup>.</sup> 5                  | 58           |
| Lymphocytes  | 36  | <b>3</b> 3 <sup>.</sup> 5 | 35 | 27   | 33.5         |
| Eosinophiles | 7   | 6                         | 7  | 10   | 6            |
| Mononuclears | 3:5 | 2.2                       | 1  | 2.2  | 2            |
| Basophiles   | 5   | 0                         | 0  | 0  | 5            |

It will be seen that before the injections this man had 7% of eosinophiles. At this time he came under the Urticarial section. But after the tuberculin injections had increased his eosinophilia and he could be classed under the Serum Reactions.

#### McAULAY.

This man had a folliculitis barbae, which is immaterial to the case. The important point is the treatment he was receiving. He was being given injections of anti-staphlococcal vaccine. After every injection his eosinophile percentage rose and this was accompanied by a mild anaphylaxic reaction, his temperature rising to 103° f. Shivering and headaches occurred and on one occasion vomiting.

The man was dismissed cured, but though the method is known, the explanation is not. Most authorities would say that the emulsion of dead bacteria developed an anti-toxin in his blood which dealt effectively with the infection. However, from the experiments that have since been made, I think it more probable that it is the plain horse serum and not the dead germs held in suspension which was the reason of his improvement. The body regarded the serum as a foreign protein element. The eosinophiles were mobilised and their presence effected the cure.

|              | 28  | 3   | 5                 | 9    | 12   | 14    | 17  | 20   | 25                | 2 <b>6</b> | 27 |
|--------------|-----|-----|-------------------|------|------|-------|-----|------|-------------------|------------|----|
|              | Feb |     |                   |      |      | -Mare | :h  | •    |                   |            |    |
| Polymorphs   |     | 56  | 63 <sup>.</sup> 5 | 61.5 | 51.2 | 61    | 60  | 59   | 65 <sup>.</sup> 5 | 57:5       | 61 |
| Lymphocytes  |     | 37  | <b>27</b> .5      | 29   | 40   | 32    | 33  | 38.5 | 29                | 35.2       | 30 |
| Eosinophiles |     | 4   | 5                 | 5    | 7    | 5     | 4.2 | 6    | 5                 | 4          | 6  |
| Basophiles   |     | .5  | .5                | 2    | •5   | 1.2   | 1   | 0    | 0                 | 1          | 0  |
| Mononuclears |     | 2.2 | 3.2               | 2.2  | 1    | ·5    | 1.2 | 1.2  | •5                | 2          | 3  |

#### MILLER.

This man had a chronic eczema. It was thought to be of streptococcal origin; at least, streptococci were found in his skin on examination. They were probably a contamination.

The point of interest here is that the patient's treatment consisted of injections of anti-streptococcal vaccine. After his first two injections he showed a moderate reaction in both and a rise in the number of his eosinophiles. After the third injection there was no reaction and his eosinophilia was unaffected. The condition of this patient on leaving the hospital was disappointing.

| 6 | 11                | 12  | _13   | 15  | 17  | 26  | 28 | _3   | .9   |
|---|-------------------|---|---|---|---|---|----|--|--|
|   |                   |   | -Febru  | iary–   |   |   | ·e | - Mar  | Mar  |
|   | 57 <sup>.</sup> 5 | 67 <sup>.</sup> 5   | 53.2  | 51  | 66  | 55  | 58 | 57 <sup>.</sup> 5                                      | 55   |
|   | 34                | 24  | 38  | 40  | 25  | 37  | 35 | 34   | 34 <sup>.</sup> 5                                      |
|   | 5 <sup>.</sup> 5  | 5   | 6   | 7   | 65  | 5.2   | 5  | 5  | 6.2  |
|   | 3                 | 1.2   | 0   | •5  | 1   | 1   | 0  | 1  | 2  |
|   | 1                 | 2   | 2.2   | 1.2   | 1.2   | 1.2   | 2  | 2.2  | 2  |
|   | 6                 | 6 11<br>57 <sup>.</sup> 5<br>34<br>5 <sup>.</sup> 5<br>3<br>1 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |    | $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$ |

## TUBERCULIN INJECTIONS

Besides the case of Rickford, which has been quoted above, the blood of two other cases after tuberculin injections were examined.

#### EVANS.

This was a young girl of fifteen with lupus vulgaris of the face. Injections of Tuberculin were given of increasing strength, and the blood was examined at regular intervals over a period of four weeks. The graph given at the end of the paper shows the steady rise of the eosinophile percentage.

|              | 8<br>Feb          | 16<br>Feb    | 19<br>Feb | 24<br>Feb | 27<br>Feb | 5<br>Mar         |
|--------------|-------------------|--------------|-----------|-----------|-----------|------------------|
| Polymorphs   | 68 <sup>.</sup> 5 | 65           | 67        | 70.2      | 68        | 64               |
| Lymphocytes  | 26                | <b>28</b> .5 | 26        | 23        | 26        | 28.5             |
| Eosinophiles | 1                 | 2.2          | 3.2       | 4         | 4         | 5 <sup>.</sup> 5 |
| Basophiles   | •5                | ·5           | 0         | •5        | 0         | 0                |
| Mononuclears | 4                 | 3.2          | $2^{.5}$  | 2         | 2         | 0                |

#### DARMODY.

This case was that of a woman of twenty-one who was also having tuberculin injections. Her count was taken over a period of four weeks and shows a resemblance to that of the former case. The lymphocytes are worthy of notice. They increased markedly as well as the eosinophiles, but at the expense of the polymorphs.

|              | 8   | 16              | 24               | 27                        | 5   |
|--------------|-----|-----------------|------------------|---------------------------|-----|
|              | Feb | Feb             | Feb              | Feb                       | Mar |
| Polymorphs   | 73  | 73 <sup>°</sup> | 70               | 55                        | 55  |
| Lymphocytes  | 23  | 21              | 25               | <b>3</b> 9 <sup>.</sup> 5 | 36  |
| Eosinophiles | 2   | 0               | 2 <sup>.</sup> 5 | 4                         | 5   |
| Basophiles   | 0   | •5              | 0                | •5                        | 1   |
| Mononuclears | 2   | 3.2             | 2.2              | 1                         | 2.2 |

#### DRAKE.

This lady was a private patient and was receiving injections at the West London Hospital for rheumatoid arthritis. The injections given were in the nature of protein shocks. They caused an increase in the eosinophiles as is seen in the table. Each count was taken 24 hours after the injections. The reactions after them was severe and combined with an acute urticaria. It was on account of this that I was consulted. The counts unfortunately had to be discontinued as the patient enquired at the hospital whether they were essential to the cure of her condition.

| Polymorphs   | 54   | 54 |
|--------------|------|----|
| Lymphocytes  | 39.5 | 40 |
| Eosinophiles | 4    | 5  |
| Basophiles   | •5   | 0  |
| Mononuclears | ·2   | 1  |

Another case of a similar nature was examined after these same injections. An irritating urticaria was present, covering nearly the whole of the body, and combined with severe anaphylaxic symptoms. A slide of the blood was taken (only one) and this showed the following differential count-Polymorphs, 70.5%; Lymphocytes, 22.5%; Eosinophiles, 7%.

#### SCABIES.

Three cases were examined but only one was of an extensive nature. The count in this instance was as follows—Polymorphs, 70%; Lymphocytes, 22.5%; Eosinophiles, 6.5%. The other two cases were not so widespread, the eruption only appearing on the hands and arms. However, they were both of long duration, having been present for several weeks, and lymphocytosis was the characteristic feature.

## IMPETIGO.

This condition was examined in seven cases, mostly children. Nothing of a marked nature was seen in any of the cases. In two of them there was a slight leucocytosis of about 9,000. It is doubtful, however, as to whether any true leucocytosis was present, as it must be remembered that the average normal number of leucocytes is higher in infancy and childhood than during adult life. The counts of 8,400 and 9,000 may therefore be taken as normal.

## ERYTHEMA MULTIFORMAE.

Two of these cases passed through my hands and were examined. The results were disappointing. Definitely no change was seen despite the fact that other observers describe an eosinophilia.

## LUPUS VULGARIS.

Four cases were examined and the change in these was noted to be lymphocytosis. Three of these cases were treated by injections of tuberculin and the results of these are recorded above. The other case, which was treated in a different manner, only showed lymphocytosis.

## SEBORRHOEIC DERMATITIS.

Three cases were examined. Two showed no change. The third case, a woman of thirty-three, had a widespread eruption over the whole of her body. Treatment happened to be very successful and in a week the rash had nearly disappeared. The differential counts were exactly what one would expect, the falling of the eosinophilia to normal being synchronous with the improvement in the condition. A high basophilia was seen in the first count; leucocytosis was 7,500 and was unaffected.

|              | 20                | 23                | 26   |
|--------------|-------------------|-------------------|------|
|              | July              | July              | July |
| Polymorphs   | 63                | 67                | 67   |
| Lymphocytes  | 29 <sup>.</sup> 5 | 28 <sup>.</sup> 5 | 31   |
| Eosinophiles | 5                 | 3                 | 1    |
| Basophiles   | 2.2               | 1.2               | 1    |

## EPIDERMOLYSIS BULLOSA.

#### RUTH DRURY.

This very rare but interesting disease was seen in a young girl of twenty. She had been in the wards two years previously for the same complaint. This condition is stated to be an hereditary one and a relation of the urticarial family. Bullae were present over the whole of the patient's body. They appeared everywhere, sometimes for no reason at all; while at others they were attributable to some slight knock, or to the irritation of her clothes. The bullae ranged in size from that of a small pin-head vesicle to a bleb, the largest being the size of a plum. This is definitely a bullous disease. When I first saw the condition my expectations were aroused and I was fully assured that an eosinophilia would be present. Despite the disappointment the details are interesting and are herewith recorded.

The blood picture on admission showed a leucocytosis of 12,200, and in two weeks 11,400. The red blood cells were normal—4,660,000—and the haemoglobin was 65%, giving a colour index of '7, which is low. A differential count showed a lymphocytosis, but practically no increase in the eosinophiles.

| Polymorphs   | 64.2                     | <b>60</b> <sup>.</sup> 5 | 61 <sup>.</sup> 5 |
|--------------|--------------------------|--------------------------|-------------------|
| Lymphocytes  | <b>28</b> <sup>.</sup> 5 | 35                       | 37                |
| Eosinophiles | - 4                      | 2:5                      | 1                 |
| Basophiles   | 0                        | •5                       | 0                 |
| Mononuclears | 3                        | 1.2                      | ·5                |

weeks.

2

The contents of the bullae were examined on two occasions. These bullae which were examined were produced experimentally. A sharp knock was given to the patient's skin and the bullae formed in three to four hours. Its contents were then taken and examined. One of the bullae thus formed was haemorrhagic. An examination of the contents showed a differential count as follows:—

These counts were taken once every week over a period of three.

| Polymorphs   | 44                | 46 |
|--------------|-------------------|----|
| Lymphocytes  | 39 <sup>.</sup> 5 | 34 |
| Eosinophiles | 14.5              | 20 |
| Basophiles   | 1.2               | 0  |
| Mononuclears | •5                | 0  |

The red blood corpuscles were normal, but in one slide a nucleated red cell was seen. In the other, one solitary giant cell was seen. The eosinophilia in the bullae is extremely high, much higher than the blood eosinophilia. This supports the view that the eosinophile is as much, if not more, a tissue cell than a circulating cell. All the eosinophiles seen in this examination showed the vacuolation and fragility which has been described often before.

## LICHEN PLANUS.

Three cases were examined but showed normal counts in every instance,

## PITYRIASIS ROSEA.

Two cases were examined and no change was seen.

## HERPES ZOSTER.

Two severe cases were examined. No haematological change was seen.

## THE EOSINOPHILE AS A TISSUE CELL.

This section would not be completelwithout reference to the presence of eosinophiles in the tissues. At an earlier stage I quoted the work of Kanthack and Hardy (1). Their work proved that eosinophiles were attracted to certain cases of local inflammation. In particular they were attracted to experimental blisters in numbers varying from 6% to 45%. Gilchrist (2) found eosinophiles in experimental weals, the cells appearing in 45 minutes. He also found them in the exudate of dermatitis herpetiformis.

I have examined the vesicles in certain of these conditions and in every case where there has been a blood eosinophilia of any marked degree there has also been a tissue eosinophilia. The vesicles in one of my own cases of bullous dermatitis were found to be full of these cells, and most of them were found to be in a degenerated state. A peculiar characteristic of these cells was the presence in their protoplasm of large vacuoles. The eosinophile, in the presence of the presumed toxin, is an explosive cell, and some of them seen in this case were burst, the nucleus being set free in the serum and surrounded by the coarse oxyphile granules. Various vesicles of urticarial eruptions were examined and showed eosinophiles in the exudates in increased numbers and in a similar swollen state.

## VACUOLATION OF EOSINOPHILES.

The presence of vacuoles in the eosinophiles has been referred to above. They were seen as circulating cells in cases which had shown a high and continued eosinophilia count. In one case of dermatitis exfoliativa they were numerous, and as many as six vacuoles were seen in the protoplasm: the average number was 2 or 3. In these cases many of the eosinophile cells were burst, while other varieties seen in the film were intact. This artefact had taken place in the spreading of the film, but it demonstrates that the cells possess an increased fragility. Another feature that I noted was that the granules of the eosinophile had become larger and look "water-logged" in those instances where the cell was vacuolated.

# SECTION 6.

# SIGNIFICANCE OF EOSINOPHILIA IN DERMATOLOGY

and the second secon

٠

•

and the second second

# 6. SIGNIFICANCE OF EOSINOPHILIA IN SKIN DISEASES.

The knowledge of the physiology of the eosinophile is not very profound. As Gruner (1) says with regard to this matter—" Speculation is rife, but facts are few."

It is increased psysiologically after food, in pregnancy, during childhood, after the injection of certain drugs, and during convalescence of fevers.

As a diagnostic factor it is of use in some conditions. In helminthiasis, scarlet fever and certain forms of leukaemia the presence of an increased percentage of eosinophiles is valuable. Certain anaphylactic conditions—asthma, hay fever, urticaria, protein "shock," and serum reactions all show a certain amount of it. It is known to be present in some skin diseases. These will be discussed in detail later.

#### THE EOSINOPHILE AS A RESULT OF A PROTEIN TOXIN.

It has been stated that eosinophilia occurs physiologically after food. Rous (2) found that by feeding dogs on large quantities of meat their eosinophile percentage was raised. He accounts for this increase by the fact that the large increase of ingested protein had a chemiotactic influence on the eosinophiles. It is fast becoming an accepted fact that eosinophilia is a reaction of the blood to a foreign protein.

W. D'Este Emery (3) and Cowie and Calhoun (4) both say that the essential cause of anaphylaxis is a protein toxin.

It has been found that injections of Koch's Old Tuberculin cause eosinophilia. Besides the extractive substances this tuberculin contains Peptone Salts as its base.

Herrick's (5) experiments on the subject are very interesting. He first of all made an aqueous solution of ascaris lumbracoides and sensitised a rabbit with it. Subsequent injections caused a blood eosinophilia. He then isolated the protein of this extract and his injections caused practically the same results, thus proving that it was the protein, *per se*, in the extract which was the causative agent. He then states that these facts have a definite connection with asthma.

#### EOSINOPHILIA AND ASTHMA.

The connections between these two conditions was noted as early

as 1889, when Muller (26) found eosinophiles in the sputum of asthmatics. In 1890 Fink (26) found eosinophiles in the blood, thereby proving that eosinophilia was both a local and a haematological symptom in asthma. Later Towle and Swartz (17) made the statement that a feature common to both asthma and anaphylaxis was eosinophilia.

Burwinkle (6) associated asthma, psoriasis and eczema. Meltzer said that asthma should be classified among the phenomena of anaphylaxis. Towle (31) associated asthma with hay fever, urticaria and asthma, stating that they are anaphylactic and that one may expect eosinophilia in these cases reaching 20%.

Emery (7) states that serum disease of anaphylactic origin often occurred with a history of asthma.

Goldschmidt (8) found that laboratory workers who dissected ascarides suffered from anaphylactic symptoms combined with asthma. Periodic attacks of this latter condition persisted sometimes for more than two weeks after the workers had ceased dealing with the worms.

Billings (9) records a case of asthma combined with swelling of the face and arms—angio-neurotic oedema—and a marked excess of eosinophiles in the blood, the highest count being 53.6%.

Herrick (10) records an eosinophilia in a case of asthma of 72'5%. Basophiles were not seen in this count. Four months later the eosinophilia had dropped to 7%, but the basophiles had risen to 3%. It is interesting to note once again this persistent inversity between eosinophiles and basophiles.

It will be seen from the foregoing that there is a large amount of evidence connecting eosinophilia, asthma and anaphylaxis. Eosinophilia is a symptom of both, and there must therefore be something between the two conditions which is common to each of them.

## EOSINOPHILIA AND ANAPHYLAXIS.

One of the most important contributions which has been brought forward is the relationship of eosinophilia to the phenomenon of anaphylaxis. Eosinophilia has been found to be a constant and marked accompaniment to the reactions of anaphylaxis. Those cases of anaphylaxis which I have examined have all shown some degree of eosinophilia.

Moschowitz (11) in 1911 was the first observer who drew attention to this relationship. After quoting from a large quantity of literature he said "A feature common to all these diseases we have mentioned—and to which attention has not been drawn—is this :— they are all associated with eosino-philia. The increase in the blood and the local manifestations must bear some relation to anaphylaxis."

Towle (12) says that anaphylactic shock shows eosinophilia for 24 hours or longer. Cowie and Calhoun (13) say that where there is no eosinophilia there is no anaphylaxis; while Ravitch and Steinberg (14) state that eosinophilia is a marked accompaniment of anaphylaxis and concomitant in many, if not all cases, and it is a commonly accepted fact, that anaphylaxis is caused by a protein which is foreign to the system. Towle states that certain skin diseases are so often seen in conjunction with anaphylaxis that they can be taken, *per se*, to indicate that phenomenon.

# THE EOSINOPHILE AS AN INDICATION OF TOXIC CONDITIONS.

Leredde (15) in 1898 was the first observer to call attention to the presence of eosinophiles in certain dermatoses. His view was that they were an indication of a toxic condition.

With those workers who say that the eosinophile is a direct result of a toxic condition, I disagree. Eosinophilia in dermatology to my mind is a secondary result in a primary protein toxic condition. As has been stated, the diseases in which eosinophilia is seen are mostly of long duration and very grave. Dermatitis herpetiformis, pemphigus and dermatitis exfoliativa are three diseases which are amongst the most severe in Dermatology. They involve the whole surface area of the skin, they are all of long duration, two of them are of a bullous nature, and all show a high and constant eosinophilia.

The action of these conditions on the organism, and the way in which eosinophilia is caused is doubtful. Theories, however, are not lacking. Engman and Davis (16) seem to regard the eosinophile as a tissue cell which is called into the blood by certain stimulations, such as the presence of a parasite or certain toxins. Other agents (they do not state whether parasite, bacteria, toxins or fungi) act on the skin more than on the internal organs, thus producing a protein substance which in its turn creates an eosinophilia. With this theory I am not altogether in agreement. Eosinophiles are admittedly tissue cells, but they are certainly not called into the blood from the tissues by the causative agent. The converse is what actually happens. The eosinophiles are called from the blood into the tissues by a protein substance which, in my opinion, has been formed by the autolysis of the skin caused by the skin lesion. Towle and Swartz (17) also regard eosinophiles as tissue cells rather than as a circulating element. In pemphigus they say that the causative agent acts on the skin, and though not in itself a parasite, it exerts the same influence as a parasite. In dermatitis herpetiformis the agent acts more on the skin, producing a protein toxin which causes eosinophilia. Here again my remarks made in the preceding paragraph apply. The eosinophile is mobilised by a protein toxin, but this toxin is not the causative agent of the disease, as Towle and Swartz state, but comes from the products of autolysis of the skin.

## THE EOSINOPHILE IN RELATION TO THE EXTENT OF THE DERMATOSES.

I have found that in most of my examinations the extent of the disease is in relation to the height of the eosinophilia. In all those conditions which involve the whole body—dermatitis herpetiformis, dermatitis exfoliativa and pemphigus—there is, in my cases, a consistently high count. And if a condition of less severity than those quoted is present, such as psoriasis, or eczema, or urticaria and happens to involve the whole of the body then I have invariably found eosinophilia present.

Towle and Swartz (17) stress a point with regard to the extent of a lesion. Where it is widespread they say that eosinophilia should most certainly be looked for. They ask three questions—Are these conditions related? Are they of toxic origin? If they are, what is the nature of the toxin?

When a lesion is severe and extensive, we may expect a moderate amount of eosinophiles. Rackeman (18) in discussing the question says that Erhlich's conception of eosinophilia is that it occurs wherever there is epitheilial or cellular destruction, and that it is the reaction to a native protein broken up inside the body.

Cannon (19) says that the eosinophilia is proportionate to the extent rather than to the form of the disease. And here we have the answers to the three questions put by Towle and Swartz. Firstly, the conditions are related in one respect— namely, that they are all eruptions which effect the whole of the surface area of the body. Secondly, owing to the large amount of skin area involved, a toxin is produced by the surface autolysis which is eosinotactic. Thirdly, the toxin is of a protein origin.

## BULLOUS CONDITIONS,

As has been shown, eosinophilia is present in severe bullous conditions of Dermatology, such as dermatitis herpetiformis, pemphigus, and I have included amongst this group acute bullous dermatitis, or, as some might call it, vesicular eczema. I wish to deal with this latter consideration here. Pollitzer (20) quotes a case which is very similar to one of my own. Pultz (21) also records a case but does not give much detail except to say that there was a decided eosinophilia.

I am inclined to regard acute bullous dermatitis showing a high eosinophile count as a separate entity, and to segregate it from the muck-heap of Dermatology commonly known as eczema.

Dermatitis exfoliativa is a severe generalised infection. The whole of the skin of the body is affected. A high eosinophilia is to be expected and I have always found one. This condition is held by Szarka (22) and supported by Knoepfelmascher (23) and Lainer (24) as well as by Wieland (25) to show that dermatitis exfoliativa is really a severe form of pemphigus. Certainly the blood picture in the two diseases is very similar, so I have regarded the former as being in this class.

## NON-BULLOUS CONDITIONS.

The knowledge gained from the examination of the blood in other forms of dermatitis merely tells us that the larger the area of skin involved the higher the percentage of eosinophiles will be. When a large area of skin is affected the evidence seems to be that a protein toxin is set loose, causing eosinophilia. The question which arises is whether this toxin derived from the skin is similar to the toxin which causes certain anaphylactic conditions such as asthma and urticaria. The only similarity they have is eosinophilia.

## THE EOSINOPHILE AS A TISSUE CELL.

However, the eosinophile has been proved to be a tissue cell as well as a circulating cell. It has been found in the blood of asthmatics, but it has also been found in the sputum of asthmatics. Muller and Fink (26), Opie (27) has found it actually entering the lumen of a bronchus. I have found eosinophiles in the bulla and vesicles of acute dermatitis. Gilchrist (28) has found them in experimental weals and in the exudate of dermatitis herpetiformis. Ravitch and Steinberg (29) quote the finding of eosinophiles in herpetic blebs in large quantities. Stokes (30) found large collections of eosinophiles at the site of the bites of flies.

This is to my mind proof that the agent which attracts the eosinophiles in all these conditions is of a similar nature. The fact that serum will cause eosinophilia, whether plain horse serum, a vaccine in suspension in a serum, or even anti-diphtheric toxin, seems to be significant. There is a large amount of serum present in bullous conditions to attract the eosinophiles; and even in non-bullous diseases, where the area affected is large, there must be a considerable amount of serum in the subcutaneous layers of the skin which will also attract these cells.

Something in the serum, when it is called out pathologically, attracts the eosinophiles. This something is stated by most authorities to be of a protein nature. It is not a normal inhabitant of the body. It is a foreign toxin.

To sum up, the significance of eosinophilia in Dermatology is clinically and aetiologically of small importance. It tells us that there is a certain amount of protein toxin being absorbed from the skin. That this product is harmful is proved by the fact that eosinophilia in other conditions, as well as in skin diseases, is a pathological condition. It tells us that there is a large area of skin involved. It is a marked accompaniment of asthma and anaphylaxis and these conditions are caused by an agent which is of a protein variety. The eosinophile cell itself has been seen as a tissue cell which is influenced by chemiotactic agents. probably also of a protein nature.

(a) Developing the second of the second sec second se

# SECTION 7.

# SUMMARY AND CONCLUSIONS

## 7. SUMMARY AND CONCLUSIONS.

When a skin lesion is severe and extensive, an accompanying eosinophilia is to be expected.

Bullous lesions usually show a high percentage of eosinophiles in the blood during the acute stage; this falls as the disease subsides and rises with a fresh outbreak.

Bullous dermatitis or vesicular eczema, if severe and widespread, will show eosinophilia and as such should be regarded as a separate entity in Dermatology.

Eosinophiles have nothing to do with the "causa causans" of skin diseases. Their appearance is purely symptomatic.

The evidence is all in favour of their being a "toxin" cell. In no case were they found to be bactericidal, nor have any of the recent observers suggested this.

The eosinophile is also a tissue cell. It is seen in large numbers in the skin, in the vesicles and in the discharges from the skin. It is present in the skin in greater proportions than in the blood.

When the eosinophile comes into contact with noxious material it developes vacuoles in its substance. The granules become swollen and the whole cell increases in size. The "fragility" of the cell is increased.

These vacuoles are either the product of an osmosis or a secretion. They have either ingested a toxin or secreted an anti-toxin. Owing to their increased fragility the obvious presumption would be that they have secreated an anti-toxin for liberation.

Inversity of the basophiles and eosinophiles often occurs. When the eosinophilia has fallen the basophiles appear to be increased in the circulation. Nothing has been gleaned as to the physiology of the basophile.

Eosinophilia is a pathological condition produced by the presence in the body of foreign proteins. It may occur both as a tissue and a circulating cell. When present in skin diseases it is the expression of the haematological system against the noxious proteins released by surface autolysis. The eosinophile cell is a "toxin" cell only.

# SECTION 8.

# BIBLIOGRAPHY

## 8. BIBLIOGRAPHY.

## SECTION 1.

#### 1. MOSCHOWITZ. New York Med. Journ. Vol. XCIII, 1911, p.15.

## SECTION 2.

1. SHERRINGTON. Proc. Roy. Soc. No. 55, 1894.

la Quoted and discussed by SHERRINGTON, No. 1.

2. GULLAND. Journ. of Psysiol. Vol. XIX. May 1895, p.385.

3. KANTHACK and HARDY. Journ. of Physiol. Vol. XVII. 1894-5,

pp.81-119.

4. HANKIN and KANTHACK. Proc. Camb. Philos. Soc. Vol. 7, pt. 2.

5. ZAPPERT. Zeit. f. Klin. Med. Bd 23, p.227. Quoted by 5a, EWING.

5a EWING. Clinical Pathology of the blood. London 1904, p.163.

6. GULLAND. Journ. of Physiol. Vol. XVII, 1894.

7. HEIDENHAIN. Quoted by Gulland. Journ. Psysiol. Vol. XIX, 1895.

8. FRENCH. B.M.J. April 30th, 1902.

9. FRENCH. Guy's Hosp. Gazette. Dec. 25th, 1909, p.533.

10. LEREDDE. Ann. de Dermat. et de Syph. 1898, 35 IX, p.1106.

11. BUCHANAN. Liverpool Medico-Clin. Journ. Jan. 1908.

12. GRUNER. Biology of the blood cells, p.249.

13. GULLAND and GOODALL. The blood. Edinburgh 1925, p.92.

- 14. EHRLICH. Zeits. C. Klin. Med. Bd. I, 1880, p.553.
- 15. CANNON. Deutsch. med. Wochenschir, 1892, Vol. XVIII, p.206.

16. GILCHRIST. Bull. Johns. Hophkins. Hosp. 1896. Vol VII. No. 64, p. 141. 16a. Quoted by above, No. 16.

17. DA COSTA. Clinical Haematology, London 1905, p.217.

## SECTION 3.

1. MACCORMAC. B.M.J. Oct. 24th, 1925.

2. GRUNER. Biology of the Blood Cells. Chapt. VI, p.263.

3. FRENCH. Guy's Hosp. Gazette. Dec. 25th, 1909, p.533.

4. DA COSTA. Clinical Haematology. London, 1905, p.256.

5. CRANSTON LOW. Ananphylaxis and Sensitisation, pp.74-76.

6. SZARKA. Monotssch f Kinderheilk, May, 1926, p.255.

7. MELTZER. Journ. Amer. Med. Ass'n, 1910, Vol. 55, No. 12, p.102.

8. BURWINKLE. Winer Medizinsche Wochenschrift, 1910, p.420.

9. CZERNY and STRUMPEL. Medizinsche Klinkert, VI, p.885.

10. GOLDSCHMIDT. Munchen med. Wehnsehr, 1910, Vol. 57, p.1991.

## SECTION 4.

- 1. LEREDDE. Ann. de Dermat. et de Syph. 1898, 35 IX, p.1106.
- 2. ENGMAN and DAVIS. Journ. of Cutan. Dis. Vol. XXXIII, No. 12, Feb. 1915, p.73.
- 3. TOWLE and SWARTZ. Journ. Derm & Syph, May, 1924, p.554.
- SCRAMBERG and STRICKLER. Journ. of Cut. Dis. Vol. XXX, Feb. 1912. No 2, p.53.

5. FRENCH. Guy's Hosp. Reports, 1904, LVII, p.81.

6. ZAPPERT. Ztchr. f Klin. Med. 1893, XXIII, pp.227-308.

7. SCHAMBERG. Journ. Cut. Dis. Feb. 1912.

8. MICHELSON. Archives of Dermat. & Syph. Vol. II, No. 5, Nov. 1920,

9. POLLITZER. Journ. Cut. Dis. April 1911, Vol. XXIX, No. 4.

- 10. OTTO PULTZ. Archiv. fur Dermat. v Syph, Vol. CXI, No. 1, 1912, p.19
- 11. SCRAMBERG. Quoted by Schamberg and Strickler.
- 12. FORDYCE. Archives of Dermat. & Syph. Vol. II, No. 5, Nov. 1920,

p.571.

p.571.

13. OLIVER, Archives of Dermat, & Syph. Vol. II, No. 5, May, 1920, p.404

14. STANZIALE. Quoted by Schamberg and Strickler.

,,

- 15. ANDRY
- 16. BOWEN.
- 17. WINFIELD. Journ. Cut. Dis. Dec. 1908, Vol. XXVI, No. 12, p.574.
- 18. COE. Amer. Med. 1902, p.1092.
- 19. CRANSTON LOW, Brit. Journ. Dermat. 1909. p.135.
- 20. CANON. Deutsch. Med. Wehnschr, 1892, XVIII, p.206.
- 21. R. HALLAM. Brit. Journ. Dermat. & Syph. March, 1927, p.95.
- 22. KOLMER. Journ. Cut. Dis. June, 1911, Vol. XXIX, No. 6.
- 23. EWING. Clinical Pathology of the blood, London, 1904, pp.156-7 & 172,
- 24. DA COSTA. Clinical Haematology. London, 1905, p.257.
- 25. ANDRE and COURMONT. Folio Haematologica, 1904, p.389.
- 26. JOHNSON. Journ. Cut, Dis. Vol. XXX, p.96, 1912.
- 27. GILCHRIST. Bull. John's Hopkins Hosp. 1896, Vol. VII, No. 64, p.141.
- 28. RAVITCH and STEINBERG. Journ. Cut. Dis. Vol. XXXIII, No. 8,

Aug. 1915, p.580.

(Quoting Klausner and Kriebich Folio Haematologica, May, 1913).

## SECTION 6.

- 1. GRUNER. Biology of the Blood Cells, p.253.
- 2. ROUS. Journ. Exper. Med. 1908, p.537.
- 3. W. D'ESTE EMERY. B.M.J. Nov. 4th, 1911.
- 4. CALHOUN. Arch. Int. Medicine. Vol. XXIII, Jan. 1919, p.69.
- 5. HERRICK, Arch. Int. Medicine, Vol. II, 1913, No. 2, p.165.
- 6. BURWINKLE. Winer. Medizinsche, Wochenschrift, 1910, p.420.
- 7. EMERY. B.M.J. Nov. 4th, 1911.
- 8. GOLDSCHMIDT. Munchen med. Wochensehrift, 1910, Vol. XII, p.1991
- 9. BILLINGS. N.Y. Med. Journ. May, 22nd, 1897.

- 10. HERRICK. Journ. A.M.A. Vol. 57, Dec. 2nd, 1911, p.1836.
- 11. MOSCHOWITZ. N.Y. Med. Journ. Vol XCIII, 1911, p.15, et seg.
- 12. TOWLE. Archiv. Dermat. & Syph. Vol II, No. 5, Nov. 1920, p.531.
- 13. COWIE and CALHOUN. Arch. Int. Med. 23, Jan. 1919, p.69.
- 14. RAVITCH and STEINBERG. Journ. Cut, Dis. 1915, Vol XXIII,

pp.578-582.

- 15. LEREDDE. Ann. de Dermat. et de Syph. 1898, 35, IX, p.1106.
- 16. ENGMAN and DAVIS, See Sect. 4, No. 2.
- 17. TOWLE and SWARTZ. " " No. 3.
- 18. RACKEMAN. Arch. Int. Med. Oct, 1919, No 22, p.517.
- 19. CANON. Deutsch. Med. Wehnschir, 1892, Vol XVIII, p.206.
- 20. POLLITZER. See Sect. 4, No. 9
- 21. PULTZ. ., " No. 10
- 22. SZARKA. Monatssch f Kinderheilk, May, 1926, p.255.
- 23. KNOEPFELMASCHER. Quoted by Szarka, see 22 above.
- 24. LAINER.
- 25. WIELAND,
- 26. FINK. Beitrage zur Keuntnis des Eiters. Dissent, Bonn 1890.
- 27. OPIE. Journ. Amer. Med. Soc. Vol. CXXVII, No. 3, March, 1904, p.477.
- 28. GILCHRIST. Bull. John's Hopkins Hosp. 1896, Vol. VII, No. 64, p.141. (Journ. Cut. Dis. 1908, p.122).
- 29. RAVITCH and STEINBERG. Journ. Cut. Dis. Vol. XXXIII, No. 8, Aug. 1915, p.581.

(Quotes Klausner and Kriebich, Folio Haematologica, 1913).

- 30. STOKES: Journ' Cut. Dis. 1914, Vol XXXII, p.751 & 830.
- TOWLE. Arch. Dermat. & Syph. Vol II, No. 5, Nov. 1920, p.531.
   STAUBLI. Evgebuisse der Inn. Med. v. Kinderheilkinde, 1910, 6, p.193.





