TROPICAL EOSINOPHILIA: AN ÄETIOLOGICAL INQUIRY.

By Captain E. A. A. Ritchie, M.B., B.S.Lond., M.R.C.S.Eng.
Royal Army Medical Corps.

INTRODUCTION.

The existence of a disease-entity characterized by cough, sputum, increasing loss of
weight and massive eosinophilia, has been recognized in India by the term "Tropical Eosino-
philia." In this paper I shall record the case-report of an African native who was kept
under observation for a period of sixteen weeks in an attempt to discover the obscure äetiology
of this interesting tropical condition.

OBSERVATIONS.

In his original paper, Weingarten [1] described a series of eighty-one cases occurring in
Indians and in Europeans domiciled in India. He regarded the disease as peculiar to certain
parts of India. Conceivably, the condition is peculiar not only to India but to other tropical
and sub-tropical countries. In Weingarten's series the disease affected males in the ratio
of 8:1, the age-incidence being 25-45. The course of the disease was chronic but benign.
The medical literature accessible to me in my peripatetic career offers scanty reference to
this condition; a single reference reads as follows: "Tropical non-parasitic Eosinophilia;
obscure; may be transient; sometimes familial" [2].

CASE PROTOCOL.

The present case was studied in an adult African male from Tanganyika serving with the
East African Forces. Precise ages are not obtainable in African subjects so that this soldier's
age would be in the 25-30 group.

Onset.—The presenting symptoms were acute febrile onset, with cough, purulent sputum,
retrosternal pain and weakness. Clinically, the conjunctivae were inflamed; in the chest,
breath sounds were absent while added sounds were generally present; in the abdomen, the
spleen was enlarged two fingers'-breadth (not tender). There was no generalized lymph
adenitis.

Febrile periods (one to five weeks).—Evening rises of temperature with increasing signs in
the chest continued for a week. At this stage bronchopneumonic consolidation was detected
and per-oral sulphapyridine started; the temperature fell to normal within twenty-four
hours. A total dosage of 17 grammes was given in five days, then discontinued. After a period
of six days the temperature rose again to 99° F. On the ninth day the exhibition of sulphap-
pyridine was repeated; on the next day the patient was afebrile. The drug was continued for
eight days making a further dosage of 34 grammes. At this stage the clinical signs had im-
proved considerably—breath sounds were audible and reduction in added sounds; sputum
diminished in amount. Chest X-ray showed resolution of patchy consolidation in the left
base and in the right mid-zone. A bout of diarrhoea then occurred: the stools yielded
negative results; the patient responded to routine treatment. The patient now continued
afebrile.

Period of Apyrexia: (sixth week—onwards).—Clinically the chest was clear. A second
X-ray was not deemed necessary particularly in view of the short supply. In the abdomen
the spleen was no longer palpable. Physically, the patient felt stronger and had obviously
 gained in weight (scales not available). The finding of a rising eosinophil count led to
regular estimations and the genesis of the "eosinophil curve" is recorded graphically (Chart
I). In the course of a search for "focal sepsis," the dental condition was found productive
and the patient sent to the Dental Officer who reported as follows: "Local chronic peri-
donitis due to traumatic occlusion and absence of both lower central incisors. These teeth
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will be progressively extruded so are best left to do so rather than extract. I have scaled tartar and applied 10 per cent chromic acid.”

It is of interest that in certain East African tribes in Tanganyika, Uganda and Kenya the permanent lower incisors are removed by the parents at or just prior to puberty, that is, after the second dentition for the lower central and lateral incisors—that for the central incisors being at the age of 7 [3].

When only the central incisors are removed occlusion may result—as in this instance (see sketch); when central and lateral incisors are extracted a permanent gap persists. Unaware of these tribal customs the Dental Officer thought the missing teeth were unerupted.

Sketch of Dental Formula.—(A) Receding gingival line with pockets of pus; (B) Exposed incisor root; (C) Absent central incisors.

Chart I.—Circulating eosinophils in the peripheral blood-stream.

Treatment of the Eosinophilia.—Included arsenotherapy (substituted by antimony tartar emetic on one occasion when an arsenic preparation was not available), courses of Filix mas (to observe the effect on intestinal helminths, present—it was thought—but undetected), and ascorbic acid 150 mg. daily. Arsenical preparations used included N.A.B. 0.45 gramme and 0.6 gramme intravenously; “sulphostab” 0.45 gramme intramuscularly; and “mapharsen” 0.06 gramme given intravenously.

After five injections of arsenicals, the eosinophil count had fallen to 17 per cent of the total W.B. count. At this stage two intramuscular injections of “pentnucleotide,” 1 c.c. and 3 c.c., were given to observe the effect on the eosinophil/neutrophil ratio (see Chart I).
Points Noted.—(1) The failure of sulphapyridine to affect the rising eosinophil tide during the acute febrile stage (see Chart I). (2) The initial specificity of arsenotherapy and in particular N.A.B.—it was regretted that further supplies of this preparation were not available for a complete assay. (3) The greater eosinophil response to pentnucleotide. It was noted
that the eosinophil level rose while the neutrophil fell; this effect was not immediately checked by the exhibition of two further injections of mapharsen. (4) The eosinophilia in the febrile stage is accompanied by a neutropenia; when the eosinophil level declined the neutrophil climbed (see Chart II).

Discharge to Unit.—At the end of sixteen weeks the patient was returned to unit. There was marked increase of weight, abatement of symptoms of cough and weakness; the patient felt quite fit for his military duties. The blood picture of leucocytes was reflected as shown: Total white count = 11,900, with eosinophilia = 36 per cent and neutropenia = 29 per cent.

Investigations.

Blood Film.—Initially, during rises of temperature, routine blood slides were taken for malarial parasites with negative results.

Blood slides for microfilariae were not included in our investigations in view of the uniformly negative results achieved by Weingarten who made quite extensive searches for these organisms in diurnal/nocturnal blood films, in the sputum, urine and faeces of his cases.

Chest X-ray.—Here included (see p. 179), shows a picture consistent with bronchopneumonic consolidation.

Sputa Tests.—Five consecutive sputa tests were negative for the M. tuberculosis.

B.S.R.—Apparatus was deficient to implement this investigation.

Blood Counts.—Recorded graphically on Chart II.

Urine.—Yielded a trace of albumin, nil in the deposit; the albumin disappeared in later specimens.

Stools.—Concentrated specimens were repeatedly examined for helminths with nil result.

Sternal Puncture.—Findings are tabulated below (ninth week):

<table>
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<tr>
<th>Cellular types</th>
<th>Per cent</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>24</td>
<td>20–50</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>7.5</td>
<td>2–10</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>2</td>
<td>2–12</td>
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<tr>
<td>Eosinophils</td>
<td>7</td>
<td>0–4</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>3</td>
<td>0–1</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>2.5</td>
<td>0–1</td>
</tr>
<tr>
<td>Premyelocytes</td>
<td>1</td>
<td>1–8</td>
</tr>
<tr>
<td>Myeloblasts</td>
<td>1</td>
<td>0–3</td>
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<tr>
<td>Lymphocytes</td>
<td>1</td>
<td>2–4</td>
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<tr>
<td>Monocytes</td>
<td>26</td>
<td>5–20</td>
</tr>
<tr>
<td>Erythroblasts</td>
<td>5</td>
<td>0–5</td>
</tr>
<tr>
<td>Megaloblasts</td>
<td>1</td>
<td>0–3</td>
</tr>
</tbody>
</table>

Total nucleated cells = 198,000/c.mm. Myeloid/Red cell ratio = 1.4:1.

The Pathologist reported as follows: "No significant deviation from normal eosinophilia. No evidence of an eosinophilic aleukæmia."

Kahn Blood Test.—I regret not having submitted a blood Kahn in the early stages in view of the treatment of the condition by arsenotherapy. There was nothing in the clinical findings to indicate this test at the outset; later, after N.A.B. had been given, the value of the test was vitiated.

Discussion.

Differential Diagnosis.—Before establishing this diagnosis, the more commonly occurring diseases were excluded in addition to the following:

(a) Pulmonary tuberculosis, which was simulated by wasting, evening rises of temperature, cough and sputum; against this diagnosis were the rapid physical and clinical improvement, the negative sputa and X-rays, the characteristic rising eosinophil count, with coexisting depression of the neutrophil count and the absence of tachycardia and clubbing of the nails.
(b) Eosinophil leukaemia was a possible diagnosis in view of the blood count and early splenomegaly; the sternal puncture was an essential diagnostic aid.

(c) Asthma cum helminths: the early bronchial symptoms of somewhat explosive nature suggested the tentative diagnosis of bronchial asthma which is associated with a raised eosinophil count during periods of attacks; in Africans, the combination of bronchial asthma with helminth infection would account for a higher eosinophil count. Neither of these postulates was established. It is patent that in dealing with indigenous populations exposed to helminth infections of divers forms at an early age the possibility of a concomitant helminth infection must be borne in mind. I incline to the view that, in African subjects, eosinophilia 10 to 12 per cent of the total white count represents a normal deviation as compared with the figure of 1 to 4 per cent in European patients.

(d) Other conditions with a raised eosinophil count include infestation with ankylostoma, dracunculus, clonorchis (5 to 10 per cent); filaria and paragonomiasis (10 to 20 per cent); Loa loa (up to 60 per cent); bilharzia and trichinosis (20 to 60 per cent) [4]. These conditions do not present the other clinical features seen in tropical eosinophilia.

(e) "Ascaris pneumonia," in which an atypical pneumonia occurs due to infestation with the ascaris and accompanied by a raised eosinophil count, required exclusion. I have seen such cases of sulphapyridine-resistant pneumonia in Africans which cleared up completely after the exhibition of the appropriate anthelmintic. Manson-Bahr makes the following interesting notes on this condition: "Although ascaris pneumonia is not often diagnosed in man its presence has been suspected in West African negroes. In experimental animals heavily infected with ascaris larva, death takes place from pneumonia after four to five days. The larva, in their wanderings through the lung capillaries, must give rise to considerable disturbances. The experiment of Koino, a Japanese investigator, must be mentioned. He swallowed 2,000 ripe human ascaris eggs. Six days later he was attacked by a definite pneumonia with dyspnoea, cyanosis, a pyrexia of 104°F and a fever which lasted seven days. The sputum was profuse from the eleventh to sixteenth day and contained ascaris larvae, of which 202 were counted. The liver was enlarged and there was congestion of the conjunctivae. Ascaris infection is usually associated with eosinophilia but this is by no means so reliable as was formerly considered. During the invasion stage, when the larva are resident in the lungs, there is a very definite eosinophilia but this diminishes as the worms enter the intestinal canal" [5].

(f) Yet another rare possibility was that condition described by Loeffler [6], in which radiographic pulmonary infiltration was accompanied by moderate leucocytosis and eosinophilia clinically; there was little disturbance of the physical health.

Etiology.—(1) Predisposing causes:

(a) Nutritional factors. May become operative if coexistent with other aetiological factors hitherto unknown. It has been observed that many natives of Africa and/or India are or were suffering from diseases due to vitamin-lack, e.g. beri-beri, pellagra, osteomalacia. Others were border-line subclinical cases, not displaying the florid clinical picture. In the Army, however, these deficiencies are not likely to arise.

(b) Allergy might play some part in the causation of this condition but there is not sufficient evidence to invoke it.

(c) Endocrine imbalance as a factor appears to be too hypothetical.

(d) Hereditary familial characteristic.

(2) Exciting causes:

(a) Infection. The disclosure of a septic focus in the dental condition may be significant, particularly as African subjects are generally free from dental sepsis by virtue of their habit of post-prandial dental toilet with a special "green-stick."

Septic foci in the tonsils, gall-bladder or appendix in Africans are also rare; the prostatic crypts as a nidus of infection (due to previous urethritis) can be dismissed on the grounds of rarity in this disease of tropical eosinophilia—relatively speaking—compared with the recent frequency of urethra-prostatitis.
(b) Disturbance of metabolism. Whether such a factor could induce changes in the blood picture through the medium of the bone-marrow it is premature to decide, considering the little disturbance of the marrow as reflected by the sternal puncture findings.

Conclusions.

The condition known as tropical eosinophilia occurs in tropical and subtropical climates. It can prove incapacitating when the eosinophil count is rising accompanied by fever, weakness and pulmonary infection. The acute febrile episode can be controlled by the exhibition of arsenotherapy, after which the patient improves physically pari passu with a decline in the eosinophil count. The eosinophil count may rise later to a figure above normal without any deterioration of the physical condition of the subject. Whether the condition remains symptomless it is difficult to say without the help of follow-up case-records (always a tedious procedure with Service personnel).

Summary.

The progress and course in an African subject presenting the clinical picture of cough, sputum, loss in weight and massive eosinophilia are here recorded. An infective aetiological basis superimposed on a familial history is put forward. Treatment with arsenicals is recorded graphically.

Acknowledgments.

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Bibliography.

[5] Ibid., 1940, 804.