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FURTHER OBSERVATIONS ON THE DIAGNOSIS OF ANKYLOSTOMA INFECTION WITH SPECIAL REFERENCE TO THE EXAMINATION OF THE BLOOD.

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CONTENTS.

THE experience of the last few years in the Westphalian coal-field has shewn that the presence of *Ankylostoma* in a mine may become a matter of considerable industrial importance. Since it has been shewn that several of the metalliferous mines in Cornwall are thoroughly infected, the question of how far it may be present in, or spread to, other British mines has arisen in a practical form. When any large number of individuals have to undergo a medical examination for any such purpose it is of importance that such examination should be convenient at once for the examiner and for the examinee, that it should occupy as short a time as possible, and should, at the same time, be reliable. The diagnosis of the presence of *Ankylostoma* is commonly made by searching for the characteristic eggs in the faeces; and indeed a final diagnosis must rest in nearly every case on the results of this procedure, which is therefore not easily replaced by any other method when separate individuals are in question. But as applied to a large

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body of active working men this process has many disadvantages, and at the request of the Home Secretary an inquiry has been made into the practicability of other methods of examination[1].

The means of diagnosis at our disposal may be grouped under three heads :—

(1) General inspection of employees for cases of anaemia.
(2) Microscopical examination of faeces.
(3) Examination of the blood.

It will be convenient to examine each of these methods in order.

(1) *General Inspection.* From the point of view of Preventive Medicine, great emphasis must be laid on the fact that many, if not the majority, of the individuals who harbour the parasite in their intestines do not present any objective signs of disease, nor do they complain of any symptoms of illness. On the contrary, they will appear on ordinary examination, and will profess themselves to be, in perfect health. Yet it is these healthy "worm-carriers" who constitute the greatest danger of ankylostomiasis as a place disease; they have indeed greater powers than those who are actually ill of carrying infection from place to place, owing to their very healthiness and ability to work. Thus if one looks over a shift of men at Dolcoath, one sees comparatively few cases of obvious anaemia, even if the lips and conjunctivae are carefully examined and ruddy cheeks disregarded. If accurate haemoglobin estimations are made in these men, one finds an undue number of cases where the blood is on the lower limit of health (about 90 p.c. Hb.), and a certain number still lower (70 p.c. and upwards). But, though we have been mostly concerned with those who are really anaemic, we have found plenty of men with 95—105 p.c. Hb., examination of whose faeces shewed that they were infected. It is true that in any large collection of infected men a certain number of individuals will generally be found who are pale, complain of dyspnoea, and shew other signs of anaemia. But this is not invariably the case. At East Pool Mine (see below p. 451) I could not hear of any suspicious symptoms among the men at the time of my visit, nor could I find an underground worker who was anaemic on superficial examination. Yet *Ankylostoma* eggs were found in several samples of faeces, and there are reasons for thinking that some two-fifths of the men are probably infected.

It is, then, useless when searching for *Ankylostoma* in a mine to give any weight to the absence of cases of anaemia among the men,

[1] A short account of the results obtained has already appeared as a Parliamentary Paper [Cd. 2066], 1904.

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though the presence of such illness would of course be very suggestive.

(2) *Microscopical Examination of Faeces.* A mine may be examined for the presence of the worm by obtaining faeces from a number of the men and submitting these to microscopical examination. Results of a very definite character are thus obtained at once. There are, however, several practical objections to this method :—

(*a*) It must be remembered that the men are not under control in hospital, and that the samples are furnished by their goodwill alone. While paying the highest tribute to the willing way in which the great majority of the miners who have been asked to do so have assisted in the inquiry by performing what cannot be to them a pleasant task, I have no doubt that many refusals will often be met with. This is especially to be expected in places where there are no cases of actual illness in which the men's active interest may be aroused.

(*b*) In any case, it takes at least several days to obtain a sufficient number[1] of samples of faeces.

(*c*) There is a great opportunity for fraud, unless the stools are passed under supervision ; this is done in Westphalia, but would hardly be possible in this country.

(*d*) The microscopical examination is simple, and in most cases where eggs are present they are in such numbers that they are found at once. It is, however, necessary to search for a long time and on more than one occasion, before giving a definite verdict that eggs are absent.

(*e*) There is no doubt that a certain number of cases occur in which, though worms are present in small numbers (as proved by autopsy), the eggs are not found by direct microscopical examination of the stool. Nor are eggs found till about a month or six weeks after the larvae have entered the bowel. The results obtained by this method of examination are not therefore absolutely infallible.

Instead of obtaining stools directly from the men, one may collect

[1] What proportion of the total number employed underground constitutes a "sufficient number" is difficult to say. In most cases, however, where the worm has gained a footing in a mine, a large proportion—often nearly the whole—of the men are infected. The proportion, no doubt, varies with the suitability of the conditions (temperature, moisture, etc.) for the abundant growth and spread of the larvae; it will be lower in cool and dry than in hot and wet mines. If these conditions are not unfavourable, an examination of 10 per cent. of the men, taken at random, will probably give a very good idea of the frequency of infection. Scattered cases, however, might easily be missed in this way.

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portions of any faecal deposits which may be found underground. I have recently examined a large number of such specimens, and find that valuable results may be in this way obtained. Most of the objections mentioned above cease to apply when this method is used, but some other difficulties arise—

(*a*) In the first place it is a grave objection that the individual origin of each specimen is unknown.

(*b*) If circumstances are favourable, nearly all the *Ankylostoma* eggs present will have hatched out into larvae. The empty eggshells are practically invisible, and it is impossible to identify the larvae with certainty. A few dead eggs remain for a long time in such a condition that their nature is clearly seen, but they may be so few in number, in a stool which previously contained an abundance, as to require a very prolonged search to find them.

(*c*) Animals foreign to the human intestine enter the faecal deposits from the earth. Certain small nematode worms, which have their natural habitat in moist earth, are very often present; their eggs and larvae in some cases are not at all unlike those of *Ankylostoma*, and might easily cause confusion.

(*d*) It is not always an easy matter to obtain any number of specimens underground, and it is to be hoped that in the future it will be impossible.

(3) *Examination of the Blood.* Estimations of haemoglobin are often of great value in determining the presence or absence of an actual anaemia, allowing 90 p.c. of Hb. (on the scale of the Gowers-Haldane instrument) as the lowest limit which can be passed without comment.

The blood changes in those cases of *Ankylostoma* infection and of ankylostomiasis which were first examined in Cornwall have been already described in some detail[1], and it was shewn that in nearly every case a marked increase in the eosinophile leucocytes was present. This phenomenon seemed at once so frequent and so simple of demonstration that a further enquiry into the possibility of using it as a practical test on a large scale was thought to be desirable. Control examinations of the blood of non-infected miners were also necessary. The investigation has been limited to estimations of the *percentage* number of eosinophiles in dry blood films; any attempt to ascertain the *absolute* eosinophiles (which is doubtless the really important point) would necessarily remove the method from the sphere of simple practical hygiene. At each mine which was visited a number of men were examined, and a collection

[1] *Journal of Hygiene*, III. 1903, p. 111.

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of blood films made; at the same time specimens of faeces were, if possible, obtained from the underground workings. In this way a quantity of material could be obtained in a short time and examined at leisure in more suitable surroundings.

The data which have in this way been obtained are set out below; a short account of the conditions under which each group of men work precedes an account of the blood examinations and a summary of the evidence obtained from the examinations of faeces as to the presence of intestinal parasites. At the end of the detailed statement the figures are collected and compared; but the main result may be here anticipated. It is that the great majority of those who harbour *Ankylostoma* shew an eosinophilia, while non-infected miners do not.

A. Miners infected with Ankylostoma.

Dolcoath Mine, Cornwall.

The physical conditions of this mine have been already fully described: briefly, it is a deep, hot, wet, tin mine; faecal contamination previously very bad, but now much improved: Haldane, R. A. Thomas and myself have found *Ankylostoma* eggs in the faeces of every regular underground worker who has been examined, and there is every reason to suppose that practically everyone is infected. *Trichocephalus* is very common and a few have *Ascaris*.

i. *Men actually known to have eggs in faeces.* The majority of the differential counts of this group have already been published (this *Journal*, III. 1903, p. 128). Since that time[1] I have been enabled to examine films from a number of fresh cases. The whole number now amounts to 61 men; 51 of these shew an eosinophilia of more than 10 p.c., while only two are under 5 p.c.: average 17·8 p.c.

ii. *Underground workers at Dolcoath whose faeces have not been examined but who may be assumed to have Ankylostoma.*

(*a*) In 1902 twenty-two such cases were examined: most of the counts have been already given. They were mostly men who complained of some, but not extreme, symptoms of anaemia. Of these 20 were over 10 p.c.; average 19·7 p.c.

[1] This extension of the cases, and especially the periodical examinations of the blood in men under treatment, has been rendered possible only by a copious supply of films and estimations of haemoglobin for which I am indebted to Mr R. A. Thomas.

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(β) December, 1903: 24 men from the day shift, none of whom were obviously anaemic, taken at random in the "dry" (changing house): 16 over 10 p.c.; average 13·4 p.c. The detailed counts are as follows:—

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. J. G.[1]	20·6	25·4	2·6	45·8	3·6	2·0
J. J.	36·4	8·2	1·6	48·8	4·4	0·6
J. L.	26·6	17·4	1·4	48·4	5·6	0·6
J. S.	15·4	13·0	0·6	62·4	8·0	0·6
J. C. M.	26·4	19·2	3·4	41·6	8·2	1·2
C. M.	15·8	27·2	0·8	46·8	8·8	0·6
G. G.	28·4	18·8	2·4	40·4	9·6	0·4
C. B. W.	22·4	17·2	2·0	48·0	9·6	0·8
—. C.	17·6	10·4	2·4	58·4	10·0	1·2
J. H. S.	29·0	17·8	2·0	39·8	10·0	1·4
J. W.	17·2	20·8	0·8	50·0	10·8	0·4
F. C.	26·4	12·4	2·2	47·6	11·0	0·4
R. H. W.	15·4	10·6	1·4	60·0	11·8	0·8
F. P.	33·4	7·6	2·6	43·2	11·8	1·4
J. H.	21·2	8·8	1·6	54·8	12·0	1·6
W. H. G.	16·0	21·4	2·8	46·0	13·0	0·8
W. G.	14·8	15·8	1·6	53·8	13·2	0·8
J. V.	34·8	7·6	1·2	40·2	15·2	1·0
H. M.	27·6	16·0	4·8	35·4	15·4	0·8
F. P.	27·4	5·8	0	47·8	18·0	1·0
J. C.	22·2	20·4	0·8	34·8	21·6	0·2
E. J. B.	18·6	10·4	1·2	47·2	21·6	1·0
T. G.	11·8	6·0	0·8	48·8	31·0	1·6
A. M.	27·4	10·8	1·0	28·2	31·6	1·0

(γ) February, 1904: a similar series taken from 41 men of the night shift at random in the "dry": 36 over 10 p.c.; average 20·7 p.c. None of the men complained of any anaemic symptoms:

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
C. S.	31·4	6·2	1·2	56·8	3·8	0·6
—. H.	19·0	7·6	4·4	60·0	8·0	1·0
A. B.	25·8	6·6	0·8	57·2	8·6	1·0
J. W.	19·4	3·8	0·2	67·4	8·8	0·4
A. O.	32·4	5·6	2·2	49·2	9·2	1·4
R. S.	34·0	7·6	3·6	44·0	10·2	0·6
S. A.	24·2	9·0	4·4	50·4	11·0	1·0
—. S.	25·0	14·2	4·6	44·6	11·2	0·4
—. F.	18·4	3·2	1·8	64·0	12·0	0·6
J. H.	30·2	10·6	2·4	44·0	12·4	0·4

[1] The counts in these tables are all based on the classification of 500 leucocytes; in a few cases 1000 were enumerated.

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	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. P.	18·0	6·8	4·0	58·4	12·6	0·2
G. B.	36·0	5·2	0·8	43·0	13·8	1·2
J. U.	32·2	6·2	3·2	43·0	14·8	0·6
—. B.	16·6	4·2	2·0	62·0	15·0	0·2
P. C. B.	21·4	4·4	2·0	56·4	15·2	0·6
R. O.	26·4	8·8	1·2	46·8	16·0	0·8
W. T.	36·6	6·6	1·6	38·6	16·4	0·2
R. M.	34·0	7·0	1·4	39·8	16·8	1·0
W. P.	24·4	12·2	4·0	41·8	16·8	0·8
T. S.	24·8	5·6	2·0	49·2	17·6	0·8
E. I.	29·6	4·4	0·4	47·2	18·2	0·2
W. W.	31·6	4·6	0·8	43·8	19·0	0·2
J. T.	22·4	6·0	3·0	47·6	20·6	0·4
T. D.	32·6	7·2	2·4	36·0	20·6	1·2
S. C.	15·8	8·4	3·4	50·6	20·8	1·0
T. H. B.	27·0	8·8	0·6	42·0	21·2	0·4
F. P.	33·8	3·0	2·0	37·6	21·6	2·0
J. B.	26·0	5·2	3·0	42·0	22·2	1·6
T. W.	34·0	4·6	1·2	36·2	22·4	1·6
B. P.	31·2	4·6	1·2	36·0	25·0	2·0
R. M.	35·2	7·8	0·6	30·2	26·0	0·2
F. C.	19·4	5·0	2·2	45·4	27·8	0·2
J. C.	21·6	2·8	2·2	44·6	28·2	0·6
P. E.	23·6	6·2	2·4	37·6	29·6	0·6
R. O.	24·2	4·2	2·4	36·6	32·0	0·6
E. T.	16·2	5·4	0·8	44·0	33·0	0·6
T. C.	18·4	5·8	2·0	37·8	34·4	1·6
—. V.	26·2	3·4	0·6	30·8	38·2	0·8
J. C.	26·8	4·6	0·6	25·0	42·8	0·2
A. H.	23·8	5·4	2·4	24·4	43·8	0·2
A. E.	12·6	2·0	0·6	32·8	51·6	0·4

This series and the last (β and γ) contain four counts with low (3·6 to 5·6) percentages of eosinophiles. It has unfortunately not been possible to obtain faeces from these men, and they may not harbour the worm at all. But there is a probability that they do.

The next table summarises the figures obtained from this series of infected miners[1]:—

[1] At Dolcoath the total number of underground hands ("complement") is 717, of whom 148 have been examined = 20 per cent.

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Percentages of Eosinophiles.

	Cases	<1	1—	2—	3—	4—	5—	6—	7—	8—	9—	10—	15—	20—	25—	>30	Av. percentage
I. Known to be infected	61				2		1	1	1	1	4	18	15	10	3	5	17·8
II. Believed to be infected																	
(α) Dolcoath, 1902	22										2	5	7	3	0	5	19·7
(β) ,, Dec. 1903	24				1	1	1			3	2	9	3	2	0	2	13·4
(γ) ,, Feb. 1904	41				1					3	1	8	9	7	5	7	20·7
Total	87				2	1	1			6	5	22	19	12	5	14	18·5
Total of I. and II.	148				4	1	2	1	1	7	9	40	34	22	8	19*	18·2

* Of these, 12 are between 30 and 40 p.c., and 3 between 40 and 50 p.c. : the others are: 51·6, 56·2, 66·2 and 72·7 p.c.

B. Non-infected Mines.

a. Talke o' th' Hill, N. Staffs.; coal-pit: temperature at working face 72°—80° F. No history obtainable of any illness like ankylostomiasis: no cases of obvious anaemia seen. No traces of *Ankylostoma* or other worms found in faeces collected underground: faecal contamination not very obvious. Films obtained from 40 men: 38 were under 5 p.c.; average 1·9 p.c. Underground complement 480 = 8 p.c. examined.

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. F.	38·2	9·6	1·2	50·2	0·2	0·6
J. R.	29·4	5·6	0·8	64·0	0·2	0 [1]
W. D.	34·8	6·6	2·4	55·4	0·4	0·4
E. F.	25·2	7·2	2·8	63·6	0·4	0·8
I. F.	26·6	7·6	2·2	62·2	0·4	1·0
T. W.	12·8	2·6	1·0	82·6	0·4	0·6
W. E.	13·6	2·2	1·0	82·6	0·6	0 [1]
D. E.	29·6	4·8	2·6	61·8	0·6	0·6
J. W.	28·6	7·6	0·4	62·2	0·6	0·6
G. R.	28·8	6·6	1·4	62·4	0·6	0·2
W. B.	36·2	5·4	1·6	55·6	0·8	0·4
A. S.	26·6	9·8	3·2	59·0	0·8	0·6
J. F.	22·6	6·4	1·4	68·4	0·8	0·4
C. F.	30·8	8·2	1·8	58·0	1·0	0·2
W. S.	24·8	4·2	1·2	68·0	1·0	0·8
F. C.	25·4	3·8	1·8	67·0	1·0	1·0
T. W.	34·4	6·6	1·6	55·4	1·0	1·0
W. L.	53·2	8·0	1·2	35·8	1·2	0·6

[1] Mast cells present, but not seen in the 500 cells enumerated.

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	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. R.	28·0	7·6	5·8	56·4	1·4	0·8
W. P.	45·4	3·8	0·8	47·4	1·6	1·0
E. B.	43·4	8·4	3·0	43·0	1·6	0·6
W. G.	25·6	7·6	2·6	61·6	1·8	0·8
J. M.	29·0	4·4	3·2	61·0	1·8	0·6
T. W.	24·0	5·4	3·4	64·8	2·0	0·4
G. B.	24·0	10·4	5·2	56·2	2·2	2·0
A. F.	29·8	11·2	1·0	54·8	2·2	1·0
W. J.	48·4	5·6	2·0	41·0	2·2	0·8
A. N.	22·4	6·4	3·0	65·4	2·2	0·6
J. W. L.	35·0	8·4	2·4	50·4	2·6	1·2
G. W.	31·0	6·6	3·4	55·8	2·8	0·4
M. K.	23·6	5·6	3·2	64·2	2·8	0·6
A. L.	23·0	12·2	5·2	54·6	3·4	1·6
V. W.	36·4	5·8	1·6	52·0	3·4	0·8
A. D.	18·6	10·0	8·2	59·0	3·8	0·4
J. W.	27·6	4·0	0·6	63·2	3·8	0·8
J. W.	39·0	4·8	0·6	51·6	3·8	0·2
H. B.	26·6	10·8	4·0	54·2	4·0	0·4
H. F.	22·4	4·8	0·6	66·8	4·6	0·8
R. H.	28·6	13·4	6·2	46·0	5·0	0·8
E. T.	21·0	2·6	2·0	67·8	6·0	0·6

β. Snailbeach, Shropshire: lead and zinc mine; temperature 65° to 68° F. Nothing found or heard suggestive of *Ankylostoma*; 22 lots of faeces examined. No other intestinal parasites found. Faecal contamination very bad, and levels mostly wet, though the ladders and upper travelling roads were dry. Films from 42 men, 38 of which were under 5 p.c.; average 2·1 p.c. Underground complement 70 = 60 p.c. examined.

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
J. C.	8·6	12·0	3·0	76·4	0[1]	0[2]
W. P.	7·4	23·4	2·0	66·8	0·2	0·2
E. A.	15·2	11·2	3·8	68·8	0·4	0·6
J. E.	20·8	11·8	3·0	63·8	0·4	0·2
A. M.	15·0	10·2	3·4	68·8	0·4	2·2
R. P.	17·6	21·6	3·0	57·0	0·6	0·2
E. C.	11·2	20·2	1·6	65·2	0·8	1·0
G. P.	18·4	16·8	2·8	60·8	1·0	0·2
G. L.	36·6	15·4	2·8	43·0	1·0	1·2
G. H.	19·6	20·6	1·8	56·0	1·0	1·0
J. G.	19·4	11·8	1·4	66·0	1·0	0·4
J. B.	14·8	13·8	2·2	67·2	1·2	0·8
W. P.	24·8	11·0	2·4	60·2	1·2	0·4

[1] Eosinophiles present, though not seen in the 500 cells enumerated.

[2] Mast cells present.

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	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. M.	21·8	17·2	3·2	56·0	1·2	0·6
R. P.	18·2	15·0	0·6	64·0	1·2	1·0
F. B.	26·4	10·6	3·0	58·2	1·4	0·4
J. G.	22·0	16·6	0·2	59·2	1·4	0·6
W. B.	15·6	14·6	2·2	65·6	1·4	0·6
J. P.	16·0	19·0	4·0	59·2	1·4	0·4
M. R.	15·6	25·8	1·8	54·8	1·6	0·4
J. H.	15·2	27·4	3·0	52·0	1·6	0·8
W. H.	22·6	32·2	3·8	39·4	1·6	0·4
J. G.	15·2	21·8	3·0	57·4	1·6	1·0
J. H.	20·6	12·4	1·4	63·6	1·6	0·4
R. J.	15·2	14·0	3·0	65·2	1·8	0·8
T. P.	28·6	12·2	2·4	53·8	2·0	1·0
J. P.	23·4	10·2	1·0	63·0	2·0	0·4
I. B.	24·2	17·4	2·6	52·2	2·2	1·4
J. H.	9·6	21·6	2·4	63·0	2·2	1·2
J. R.	16·0	23·2	1·4	55·8	2·4	1·2
J. B.	15·6	17·2	1·4	63·2	2·6	0[2]
P. P.	24·0	16·8	1·0	55·0	2·8	0·4
E. P.	17·0	23·4	5·0	50·0	3·2	1·4
M. H.	38·2	14·6	0·6	42·4	3·4	0·8
A. P.	16·4	25·6	2·6	50·6	3·4	1·4
J. J.	15·0	19·6	1·4	59·2	3·6	1·2
T. S.	9·8	22·2	1·8	61·0	3·8	1·4
—. P.	6·8	19·2	3·0	66·6	4·0	0·4
E. P.	12·6	10·6	0·8	69·0	5·2	1·8
R. L.	39·6	13·2	2·4	37·4	6·0	1·4
W. H.	20·2	14·8	0·4	56·4	6·8	1·4
E. H.	17·8	23·8	1·0	49·6	7·2	0·6

γ. *Birchenwood, N. Staffs.*; coal-pit; temperature 72°—80° F. at face. Nothing found or heard suggestive of *Ankylostoma*; faecal contamination not extensive. 12 films, 9 of which were under 5 p.c.; average 2·7 p.c.

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
C. C.	18·4	10·0	2·8	66·8	0·8	1·2
S. B.	26·4	7·8	2·0	62·8	1·0	0[2]
F. C.	35·0	6·0	1·2	55·4	1·0	1·4
G. H.	37·2	6·0	1·0	54·2	1·0	0·6
A. S.	30·4	12·6	2·6	52·0	1·6	0·8
L. B.	25·2	6·6	1·2	64·4	1·6	1·0
M. C.	49·8	6·8	0·8	40·6	2·0	0[2]
S. W.	29·6	5·8	0·4	61·2	2·6	0·4
E. W.	35·6	5·8	1·8	53·2	3·4	0·2
I. C.	43·2	4·4	1·2	45·8	5·4	0[2]
J. K.	20·8	9·8	1·0	61·6	5·8	1·0
J. M.	27·8	7·2	0·6	57·6	6·0	0·8

[2] Mast cells present.

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δ. *West Kitty, St Agnes, Cornwall*; tin mine; shallow (110 fathoms) and quite cool. No history of anaemia etc. obtainable. Ten films, nine of which were under 5 p.c.; average 2·6 p.c.; the tenth case shewed 23·8 p.c. and on further examination abundant eggs of *Trichocephalus* and *Ankylostoma* were found in his faeces.

ε. *Surface workers at Dolcoath.* Though not strictly speaking miners, an examination of these men was made in order to exclude the Camborne climate and contact with Dolcoath ore as possible factors in the production of an eosinophilia. The men selected were tin-dressers, who only came in contact with the material after it had been passed through the stamps and had been roasted. Films 14, all of which were under 5 p.c.; average 2·0 p.c. There is no history of any of the purely surface workers at Dolcoath ever having had any anaemic symptoms.

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
M. M.	19·2	20·8	1·8	57·4	0·2	0·6
T. C.	20·0	20·4	1·4	57·4	0·2	0·6
W. W.	15·0	27·4	3·0	53·6	0·6	0·4
J. P.	27·4	11·8	3·6	56·0	1·0	0·2
J. R.	21·6	5·0	0·6	71·0	1·2	0·6
R. G.	7·0	4·4	5·4	81·6	1·2	0·4[1]
W. W.	16·8	25·4	1·6	53·8	1·4	1·0
J. C. P.	12·8	7·6	0·6	76·4	2·2	0·4
R. L.	42·0	12·0	2·4	40·0	2·4	1·2
J. C.	22·8	15·6	1·0	56·4	3·2	1·0
W. P.	35·0	18·6	2·2	40·4	3·2	0·6
W. H. R.	35·2	12·2	2·0	46·8	3·2	0·6
W. R.	19·8	16·2	3·4	55·6	4·0	1·0
R. P.	33·6	3·6	3·4	54·4	4·8	0·2

ζ. *Levant Mine, St Just, Cornwall*; tin, copper, and arsenic. A special interest attaches to this mine, which will perhaps justify a rather more detailed account of the results obtained. The present workings are to a large extent under the sea; the ventilation is very imperfect and the temperature very high, rising from 76° at the bottom of the downcast shaft (about 270 fathoms) to 90—93° in large areas of the deeper workings (300—320 fathoms). The level, ladders, etc. are wet and muddy and faecal contamination extensive. A considerable number of men have returned to work here in recent years from infected districts abroad, and I was aware that a few men from Camborne, who were actually known to harbour the worm, had been employed underground. I visited the mine, therefore, in the expectation that ankylostomiasis would be

[1] Considerable leucocytosis present from cystitis due to an enlarged prostate.

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found to be prevalent. Such, however, was not the case. No history of any suggestive illness among the men could be obtained: the mine has indeed a local reputation for being more healthy to work in than others in the neighbourhood[1]. From the underground workings 25 samples of faeces were obtained: these shewed the presence of numerous intestinal parasites (*Trichocephalus* in 24, *Ascaris* in 3, *Oxyuris* in 1) but no trace of *Ankylostoma*. Blood films were obtained from 41 men[2]; the differential counts of these gave the following figures:

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
W. D.	22·8	15·2	3·6	56·8	0·4	1·2
W. C.	31·2	15·6	0·8	51·6	0·4	0·4
W. S.	31·0	18·6	1·0	48·2	0·8	0·4
J. W.	29·8	10·0	0·4	58·8	0·8	0·2
H. M.	31·0	11·2	0·6	55·2	0·8	1·2
F. W.	23·0	19·0	2·6	53·4	1·0	1·0
—. W.	36·6	11·0	0·8	50·2	1·2	0·2
T. E.	29·0	7·6	0·4	61·0	1·2	0·8
W. T.	21·0	25·0	1·0	50·2	1·4	1·4
J. F.	42·2	7·6	0·4	47·4	1·4	1·0
J. T.	20·6	14·8	3·8	58·4	1·4	1·0
J. R.	32·6	8·8	0·4	55·8	1·6	0·8
J. H. T.	35·6	10·0	0·4	51·8	1·6	0·6
W. J. G.	35·4	6·8	0·6	54·8	1·8	0·6
H. J.	45·2	4·4	1·2	46·4	2·0	0·8
R. E.	25·4	8·0	0·6	63·6	2·2	0·2
T. M.	29·0	29·2	0·8	38·4	2·2	0·4
J. L.	30·0	10·6	0·8	54·6	2·2	1·8
W. T.	25·2	12·2	3·0	56·8	2·4	0·4
G. A. M.	33·6	12·0	2·6	49·0	2·4	0·4
R. W.	19·8	8·4	2·0	66·6	2·6	0·6
W. L.	34·4	18·4	1·8	42·2	2·6	0·6
J. R.	28·6	15·4	1·2	51·2	2·8	0·8
S. T.	40·0	8·6	1·2	46·0	2·8	1·4
R. O.	31·6	3·4	0·4	60·4	2·8	1·4
J. P.	35·8	8·6	1·0	50·4	2·8	1·4
W. F. M.	30·6	8·4	1·6	55·4	3·0	1·0
S. A.	15·6	17·8	3·4	59·6	3·0	0·6
—. T.	19·4	18·8	2·4	55·6	3·2	0·6
J. N.	48·8	10·2	0·2	36·6	3·4	0·8
B. P.	38·4	4·6	0	52·6	3·8	0·6
W. E. L.	39·2	6·8	0·8	48·8	3·8	0·6
F. U.	37·4	8·8	0·8	48·0	4·2	0·8
R. T.	36·4	10·0	0·4	48·6	4·4	0·2

[1] All these neighbouring mines (Botallack, etc.) have shut down some years since.

[2] Complement 478: examined 8½ per cent.

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	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
T. M.	32·6	14·6	2·8	44·4	4·6	1·0
J. E.	27·4	14·0	1·4	52·0	4·8	0·4
A. W. K.	16·6	30·4	3·2	44·6	5·0	0·2
R. H.	34·0	6·8	1·2	51·4	6·4	0·2
J. R.	21·0	7·8	0·6	61·4	8·4	0·8
H. T.	22·4	7·8	0·4	45·2	23·8	0·4
J. M.	21·8	8·0	0·4	42·0	25·6	2·2

Of these 41 men, 36 counts were thus less than 5 p.c.; of the rest two reached the very suggestive figures of 23·8 and 25·6. Samples of faeces were obtained by Dr C. S. Jago from the men with the four highest counts; and six weeks later I saw three of the men again and obtained further films. The results were as follows:

	p.c. of Eosin's	First Examination Stools	Second Examination Stools	Hb	p.c. of Eosin's
R. H.	6·4	*Trichocephalus*	——	104 p.c.	7·2
J. R.	8·4	*Trichocephalus & Oxyuris*	——	—	—
H. T.	23·8	*Trichocephalus & Ascaris*	*Trich. & Ascaris*	96	17·0
J. M.	25·6	*Trichocephalus*[1]	*Trich. & Ascaris*	105	18·4

No traces of *Ankylostoma* were found, and, since practically every underground worker in Levant seems to harbour *Trichocephalus*, the two highest figures were doubtless due to the *Ascaris* infection. The other two may be cases of *Trichocephalus* eosinophilia. I could find no other cause in R. H., who is a very robust lad.

The average for these 41 cases is 3·7 p.c.; without the two highest counts it is only 2·6 p.c.

Ankylostoma thus appeared to be entirely absent from a mine which seemed to be situated most favourably for its introduction and spread. The reason for this was, on further investigation, found to lie in the nature of the water which permeates the mine. Some of this flows in from the land and is ordinary spring water, but most of it is derived from the sea by leakage through the roof into the upper levels. Seven samples of water from different places were examined as to their content in salt. The results were as follows:

[1] Repeated searches failed to find any *Ascaris* eggs in this first sample; in the second they were very abundant.

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		NaCl per cent.
A.	210 fathoms level: dripping through from 190 ...	2·42
B.	210 further West standing water	2·44
C.	230 on North side	2·72
D.	230 on South side	2·28
E.	230 on East (landward) side	0·94
F.	278 taken from launder	1·8
G.	From pump in adit level close to surface	3·01[1]

Samples *A*, *B* shewed minute, and *C* and *E* rather larger traces of copper. No arsenic was present in any of them.

To compare with these, the salt in samples from some of the inland mines was estimated. The results were:

		NaCl per cent.
East Pool	200	0·009
,,	adit	0·018
South Crofty	Eastern engine ...	0·023
,,	Western engine ...	0·013
Dolcoath	375 Harriet ...	0·090
Silverdale	no. 6 pit	0·006
,,	no. 14 pit	0·004

We have previously (this volume, p. 86) shewn that less than 2 p.c. salt is sufficient to kill the larvae (especially when first hatched) of *Ankylostoma*, and I have since repeatedly confirmed this result. Such traces of copper as are present in the Levant water seem harmless to the larvae. It would appear then that this mine has escaped the disease from the fortunate circumstance that the roof was in times past left rather thinner than is altogether desirable.

The next table summarises these results and shews the distribution of 158 non-infected miners according to the percentage content of their blood in eosinophile leucocytes:

	Cases	<1	1—	2—	3—	4—	5—	6—	7—	8—	9—	10—	15—	20—	25—	>30	Av. percentage
III. (α) Talke o' th' Hill	40	13	10	8	5	2	1	1									1·9
(β) Snailbeach	42	7	18	7	5	1	1	2	1								2·1
(ζ) Levant	41	5	9	12	6	4	1	1		1				1	1		3·7
(ϵ) Surface workers at Dolcoath	14	3	4	2	3	2											2·0
(γ, δ) Other underground workers	21	1	8	3	4	2	2	1									2·7
Total	158	29	49	32	23	11	5	5	1	1				1	1		2·5

[1] Atlantic sea-water contains 3·4 p.c. NaCl.

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C. Partly Infected Mines.

Blood films were obtained from the men at two of the smaller tin-mines in the Camborne district. These mines are cool (62° to 68° or 70° F.) and not very wet, and, though there is a considerable exchange of men with Dolcoath, no cases of actual illness could be found. Indeed I saw several men who had been pale and short of breath while at Dolcoath and who had lost all their symptoms after coming to these mines: and this without any specific anthelmintic treatment. That this was not due to the mines being free from *Ankylostoma* was shewn by the discovery of the eggs in four out of 23 samples of faeces obtained at East Pool. These recoveries and the absence of illness are no doubt due to the unfavourable underground conditions which prevent the worm gaining a very firm footing; in this way repeated re-infections of the men are less frequent.

i. *East Pool and Agar United.* No illness. Twenty-three samples of faeces shewed, *Trichocephalus* 14, *Ascaris* 9, *Oxyuris* 1, *Ankylostoma* 4. Blood films obtained from 40 men (underground complement 223 = 18 p.c.) gave the following results.

These shew 14 cases under 5 p.c. and 17 over 10 p.c. of whom 3 were over 20 p.c. Careful inquiries were made of each man as to previous employment at Dolcoath: the four who had so worked are marked (*), and it is interesting to note that they all shew an eosinophilia of more than 10 p.c.

ii. *South Crofty:* a small cool tin-mine. No illness. No faeces obtainable as the mine had just been cleaned up. Twenty-two films obtained which gave the following results (underground complement 129 = 17 p.c.).

	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
T. S.	26·8	6·2	5·2	60·4	1·0	0·4
C. R.	29·4	11·0	3·8	52·8	1·4	1·6
W. H. M.	34·2	4·2	3·2	56·6	1·4	0·4
—. S.	19·0	5·0	5·8	68·2	1·8	0·2
L. H.	26·6	4·8	2·0	64·2	2·2	0·2
W. H. J.	25·2	5·6	2·8	63·4	2·2	0·8
W. J.	31·0	6·4	4·2	55·0	2·8	0·6
—. F.	26·0	5·0	5·8	59·2	3·2	0·8
W. S.	31·0	10·6	4·0	51·2	3·2	0 [1]
J. T.	18·6	3·0	4·2	70·8	3·4	0 [1]
E. L.	28·2	5·8	4·4	57·8	3·8	0 [1]
—. W.	27·6	9·4	11·2	47·4	4·2	0·2
E. H.	25·4	3·8	3·8	62·4	4·2	0·4
E. R.	21·0	9·6	4·4	60·4	4·4	0·2

[1] Mast cells present.

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	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
J. H.	23·4	5·0	2·2	63·4	5·2	0·8
J. C.	34·8	3·6	3·4	51·0	5·6	1·6
H. L.	31·2	12·0	3·6	45·0	6·2	2·0
S. J.	24·8	7·8	7·2	53·4	6·2	0·6
A. S.	29·8	5·2	4·4	53·8	6·4	0·4
A. J.	19·0	4·6	4·4	64·8	6·4	0·8
—. W.	16·8	8·4	5·2	61·4	7·0	1·2
—. C.	24·0	5·2	4·0	57·4	8·4	1·0
—. L.	21·8	11·2	11·0	46·6	9·0	0·4
*J. W.	21·6	8·8	5·8	53·4	10·4	0 [2]
—. W.	43·2	9·8	2·4	32·8	11·6	0·2
W. W.	24·2	6·0	2·2	56·0	11·6	0 [2]
H. J.	15·0	4·6	3·0	65·0	11·8	0·6
C. V.	27·2	4·6	3·4	51·4	12·6	0·8
—. H.	26·8	4·4	5·8	49·0	13·4	0·6
W. L.	12·4	9·4	10·0	53·6	13·6	1·0
W. G.	20·8	5·0	3·2	56·6	13·8	0·6
—. J.	23·4	4·0	1·2	53·4	17·0	1·0
F. N.	23·8	4·0	2·2	52·4	17·2	0·4
F. G.	19·4	2·0	1·0	60·4	17·2	0 [2]
*J. M.	31·2	5·2	3·2	40·6	18·4	1·4
—. K.	28·4	6·0	7·2	38·4	18·4	1·6
*J. C.	26·0	4·2	2·8	46·6	19·8	0·6
F. W.	8·2	4·4	3·4	61·8	21·8	0·4
W. G.	25·4	6·0	3·0	39·2	25·6	0·8
*W. W.	15·4	6·8	4·4	43·0	30·2	0·2
J. A. V.	35·2	7·6	5·4	50·4	0 [3]	1·4
W. J. L.	41·6	15·6	3·8	38·2	0·2	0·6
W. L.	31·0	4·4	2·8	61·0	0·4	0·4
W. W.	12·4	8·2	2·8	75·6	1·0	0 [2]
C. M.	26·4	6·2	2·2	63·2	1·8	0·2
W. P.	41·8	8·2	3·4	43·4	2·2	1·0
T. G.	24·4	6·2	6·8	60·0	2·2	0·4
W. G.	17·0	12·6	3·0	65·0	2·2	0·2
T. C.	24·8	2·8	2·2	66·4	3·0	0·8
W. R.	22·6	5·8	1·8	66·4	3·0	0·4
—. R.	33·0	5·8	3·8	53·2	3·6	0·6
J. H.	22·6	2·6	3·0	67·2	4·6	0 [2]
L. F.	34·2	19·2	10·4	29·6	5·4	1·2
—. N.	27·4	8·8	4·0	53·4	5·6	0·8
W. B.	32·6	4·2	0·8	55·8	6·2	0·4
—. H.	32·8	10·6	5·2	43·2	6·8	1·4
G. D.	44·2	7·8	3·8	36·4	6·8	1·0
W. T. M.	23·8	9·4	5·2	54·0	7·2	0·4
J. C.	23·6	3·0	3·8	51·6	16·4	1·6
J. O.	25·2	4·6	3·0	47·6	18·6	1·0
P. O.	22·4	2·2	1·8	47·2	26·0	0·4
[1]T. W.	20·2	4·2	1·8	44·6	27·4	1·8

[1] Worked at Dolcoath 7 years since, when he was pale and dyspnoeic: soon recovered in this mine.

[2] Mast cells present.

[3] Eosinophiles found.

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The prominent feature of the series for these two mines is the large number of cases which shew a low degree of eosinophilia. Comparing the figures with those from the two other series we find that, while of the infected miners 2·7 p.c. fall between 5 and 8 p.c. and of the non-infected miners 7·0 p.c., at these mines no less than 21 p.c. have eosinophile counts within these limits. This is probably due to the frequent infection with *Ascaris* which is present; the results obtained at Levant shew that *Trichocephalus* may probably be excluded. It has unfortunately not been possible to investigate these cases individually; and it is useless to speculate in the matter. There is no doubt that the high figures, in most instances at any rate, indicate *Ankylostoma*.

The blood counts from these two mines are not taken into consideration in the following discussion.

If we contrast the figures of the Dolcoath cases with those obtained for the series of 158 non-infected miners, the result is very striking (the figures are given as percentages of the total cases):—

Percentages of Eosinophiles.

	No. of cases	<1	1—	2—	3—	4—	5—	6—	7—	8—	9—	10—	15—	20—	25—	>30	Av. percentage
A. Infected	148	0	0	0	2·7	0·7	1·3	0·7	0·7	4·7	6·1	27·0	23·0	14·9	5·4	12·7	18·2
B. Not infected	158	18·35	31·0	20·25	14·6	6·3	3·2	3·2	0·6	0·6	0	0	0	0·6	0·6	0	2·5

The same figures are illustrated graphically in the accompanying chart, p. 454.

If these figures are examined it will be seen that among the infected cases there is a sudden increase in frequency at 8 p.c., while in the non-infected cases the curve has at this point practically reached zero. It is impossible to lay down any hard and fast rule as to what absolute number of eosinophiles per cubic millimetre of blood should be regarded as pathological; still less therefore can one define the corresponding point in percentage figures. From general experience one is justified in regarding any figure under 5 p.c. as being normal, though something must be amiss if a series of cases gives an *average* of 5 p.c.; above 10 p.c. one may say definitely that there is an eosinophilia. Between 5 and 10 p.c. cases are much more doubtful. The figures brought forward here indicate clearly that anything above 8 p.c. is to be regarded with suspicion, and seem to justify our placing the upper limit of the normal at 7 or 8 p.c. This figure is also in accord with general experience,

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though isolated cases of one sort and another have occurred in everyone's experience in which an eosinophilia of this degree has been explicable on no known ground. I would propose therefore, for the present practical

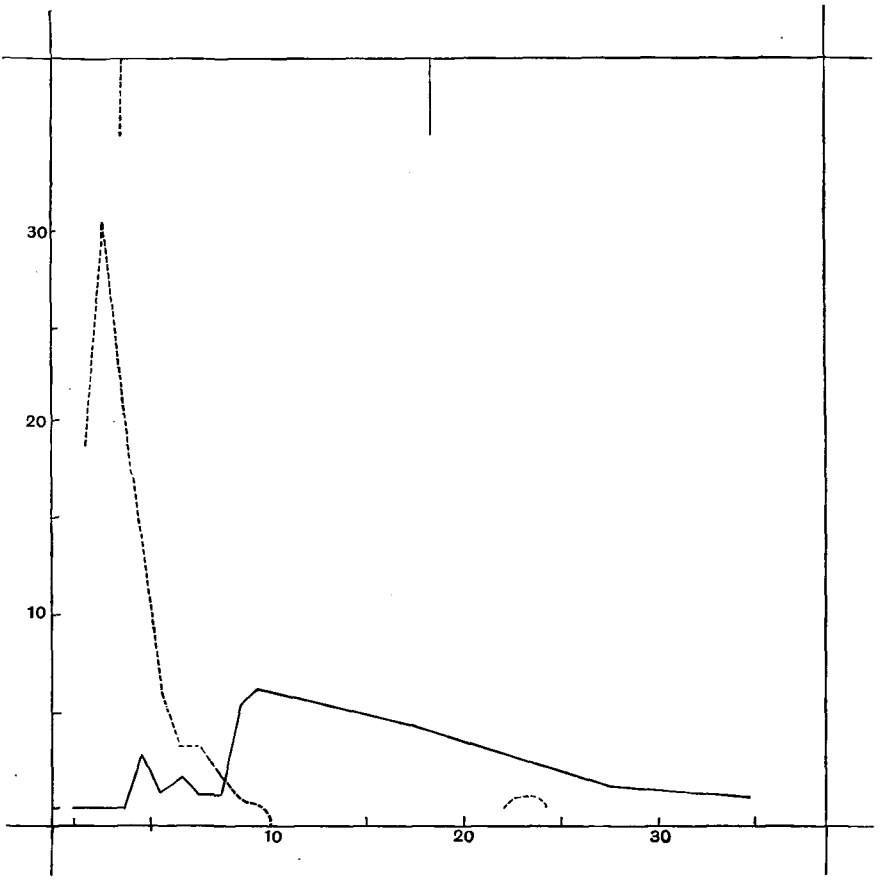

Fig. 1. The ordinates represent the percentage frequency of occurrence of each percentage of eosinophiles in the two series, the abscissae the percentages of eosinophiles. The continuous line represents infected, the interrupted line non-infected, miners.

purpose, to regard any figure under 5 p.c. as normal, numbers between 5 and 8 as doubtful, and any count of over 8 p.c. as extremely suggestive. On this basis the figures work out as follows:—

	No. of cases	under 5 p.c.	5—8 p.c.	over 8 p.c.	over 20 p.c.
Infected	148	3·4 p.c.	2·7	93·9	33·1
Not infected	158	91·1	7·0	1·9	1·3 p.c.

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If we make allowance on the one hand for those doubtful cases which are reckoned as infected (group A ii. β and γ, p. 441), and on the other hand for the two cases of high eosinophilia among the "non-infected" group for which a definite cause (*Ascaris* infection) was found, the figures become even more emphatic. And it is clear that the frequency of an eosinophilia in those infected with *Ankylostoma*, and its rarity among other miners, renders the method of examination by means of dried films one of considerable value. Among all the procedures of what may be called laboratory diagnosis of disease, there is not one which is not liable to those exceptions which occur in any other symptom or physical sign in every series of cases: there is in short no infallible method known—be it a Widal's reaction or an examination of the sputum for tubercle bacilli or of the morphology of the blood[1]—whereby we may put our penny in the slot and draw out a correct diagnosis every time[2]. Every such examination must be made with a knowledge of what it means, and interpreted in the light of adequate information as to both the individual case which may be in question and also the occurrence of similar changes under other circumstances. It will be necessary therefore to consider (1) methods, (2) circumstances which influence the eosinophilia of *Ankylostoma*, and (3) the other conditions in which an eosinophilia occurs. It will then be possible to arrive at a truer estimate of the value of figures which have been obtained.

I. *Methods.*

We are here for the time only concerned with the methods of making a differential examination of the leucocytes in dried blood-films.

(1) *Method of making films.* Those used in this inquiry have been made in three ways:—(1) by spreading the drop between two cover-glasses, (2) by smearing a drop on a slide with cigarette paper, and (3) by smearing a drop on the slide with the end of another slide. The latter method is, for purposes such as the present, by far the best. The films have, for the most part, to be made when and where the subjects can be best approached; in the case of metalliferous mines there is usually a "dry" (changing-house) which is warm and very dusty. In

[1] Even in medullary leukaemia the blood may at intervals be quite normal. The author has seen such a case.

[2] We are I believe indebted to Dr Otto Grünbaum for this happy expression of a truth which is often forgotten.

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coal-pits it is difficult to avoid taking the films underground; under circumstances such as these, with a very imperfect light and one's hands and belongings covered with mud and coal-dust, any method of using cover-glasses is out of the question. The combination of hurry and dirt requires something less fragile and I have found that the method of using two slides answers admirably. If films have to be taken underground it is well to avoid the face or the return air-ways: the air here will be so moist that the films take a very long time to dry. At the same time it is surprising what good specimens can be obtained even when a thin film is not dry for ten or fifteen minutes, and even then only when warmed over a safety-lamp: this slow drying results in an abundant coating of coal-dust, but the histological, if not the aesthetic, appearances in the stained film are all that are necessary, and often all that could be desired.

Slides have the further advantage that they are easier to clean than cover-glasses, and as the film is examined without mounting there is no trouble in using the same glass many times. I have found it convenient to carry the slides in ordinary envelopes, ten or a dozen in each. These can easily be carried about, and the slides when used are replaced in them. There is no need to keep the films apart; once dried they may safely remain in contact with one another. They must however be kept quite dry. Before visiting the mine, etc., each slide should have a small label affixed in which the subject's name etc. may be written when the film is taken.

Apart from considerations of practical convenience it is not clear that it is a matter of indifference which method is used. The cover-slip method gives probably the best results and is open to less theoretical objection than any process in which the blood is dragged along a slide. The method of cigarette paper seems to be thoroughly bad; a large number of the leucocytes are entangled in the paper, with the result that the differential count takes longer to make and one is unable to judge of the presence of a leucocytosis by looking at the stained film alone. Moreover it may be that the different varieties of cells are mopped up by the paper equally; this does not appear to be the case. It would seem that the neutrophile and eosinophile cells are taken up proportionately more than the others. The following figures shew the results of differential counts (500 cells) in two cases where simultaneous preparations were made by smearing the blood with cigarette paper and with another slide:

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		Mononuclear cells	Neutrophiles	Eosinophiles
A.	Cigarette paper	42·0	53·2	4·4
	Slide smear	32·6	60·8	5·4
B.	Cigarette paper	50·0	44·0	5·0
	Slide smear	37·8	52·6	7·6

The same objections hold, in the case of smearing with two slides, but I believe in a very minor degree. The larger cells must necessarily be to some extent separated from the smaller in this method if one attempts to make very thin films. Such films are however not advisable for the purpose of differential counts; not only are the white cells scattered over an area inconveniently large but many are destroyed. There is little doubt that the appearances in exceedingly thin films are less reliable than in somewhat more thickly spread preparations. In using two slides the thickness of the film can be nicely regulated at will, and if not too thin the differential count is probably as accurate by this as by any other method except those which make use of fresh wet preparations.

(2) *Staining.* For all practical purposes, no stain is at once so good and so convenient as a solution of eosinate of methylene blue in methyl alcohol (Jenner's stain). For the present series, a $\frac{3}{4}$ p.c. solution of Grübler's dry stain in Merck's methylalcohol has been used, staining for $2\frac{1}{2}$ minutes in a tube of stain; this may be used (with the occasional addition of a few drops of fresh solution) for at least 200 slides.

(3) *Examination.* Good films, well-stained, may after some experience be adequately examined with a $\frac{1}{3}$ inch or lower power, and the presence or absence of an excess of eosinophiles is seen at once. If a higher power is necessary, it is convenient to use an immersion, since it is then not necessary to mount the film. If an actual numerical estimation is wanted, a count of 500 is sufficient for practically all purposes; to count more than this is to strive after a precision which the method cannot possess. We have previously pointed out[1] that there is an error in the differential count of definite magnitude. The following figures shew the percentages of neutrophiles and eosinophiles in successive five hundreds on the same film in two cases:—

		A		B	
		Neutrophiles	Eosinophiles	Neutrophiles	Eosinophiles
1st	500	54·4	9·0	76·4	2·2
2nd	500	53·6	10·4	72·2	2·6
3rd	500	53·4	11·4	74·4	1·0
4th	500	50·0	10·8	76·2	1·2

[1] This *Journal*, III. 1903, p. 115.

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In both these cases care was taken that the whole 2,000 should be counted on as uniform a part of the film as possible. If the extreme margins of any (and especially smeared) films are counted, extraordinary and obviously unreliable figures are often obtained.

If no greater degree of accuracy than these figures shew is to be obtained by counting 500, it is interesting to inquire whether 200 would be sufficient. Except for those cells which occur in small numbers (eosinophiles and mast cells in normal blood), the results obtained from these shorter counts are fairly accurate:—

		A	B	C	D	E	F
200 counted	neutrophiles	45·0	68·0	37·0	44·5	52·5	58·0 p.c.
	eosinophiles	11·5	17·0	8·0	21·5	8·0	14·5 ,,
500 counted	neutrophiles	46·2	66·2	41·6	45·6	55·6	58·0 p.c.
	eosinophiles	15·0	18·6	8·2	19·8	9·8	12·0 ,,

II. *The Eosinophilia of Ankylostoma infection and ankylostomiasis and the conditions which influence it.*

(1) *Influence of the stage of the disease.* Previous observers have dealt almost entirely with the blood in those who are definitely anaemic, *i.e.* with the blood in ankylostomiasis. As far as I am aware no previous series of blood examinations of cases of *Ankylostoma* infection in persons who shew no symptoms of disease has been published. The phenomena exhibited by the leucocytes are not necessarily the same in the two classes. In our first paper[1] it was pointed out that the eosinophilia was most marked in cases in young persons which were of comparatively recent date and which did not necessarily shew any very severe diminution of the percentage oxygen capacity of the blood. Of such cases which we were fortunate enough to examine in the stage at which they shewed a distinct and high eosinophile leucocytosis comparable to that found in trichinosis, the following are good examples:—

	Age	History	Hb p.c.	Leucocytes per c.mm.	Eosinophiles per cent.	Eosinophiles per c.mm.
S. C.	23	1 month	80	56,000	66·2	37,000
E. J. T.	18	6 months	98	20,600	56·2	11,500

It was also pointed out that the numbers of leucocytes corresponded in a general way to the percentage of eosinophiles, though this phenomenon was not well marked until a definite leucocytosis of some 13,000 was reached. When however a stage of definite anaemia is

[1] This *Journal*, III. 1903, p. 121.

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reached, such leucocytoses seem to be far less frequent, and in many cases the leucocytes per unit volume are distinctly less than normal. Leucocytoses do however undoubtedly occur, and it would seem mostly in those who have reached a condition of anaemia very quickly. Thus both the following cases had only short histories of dyspnoea, etc.:—

	Age	History	Hb p.c.	Leucocytes per c.mm.	Eosinophiles	
					per cent.	per c.mm.
J. C.	17	6 months	50	44,000	72·7	32,000
N. S.	17	2 months	40	24,400	29·0	7,000

Of those who have reached a profound grade of anaemia many shew a diminution of the total leucocytes. B. K. Ashford and W. W. King[1] have recently described a number of such cases in a valuable series, in which counts of 2,000 to 4,000 were frequently found in cases which were extremely anaemic[2]. This diminution may be due to two factors: (1) *The dilution of the blood*: we have already shewn that this is the main cause of the diminution of the percentage haemoglobin content of the blood (vol. III. p. 112), and it is clear that the leucocytes per unit volume might be affected in a similar way. But there are at least two reasons for thinking that this factor cannot play any great part in concealing a leucocytosis. In the first place, leucocytoses may occur with marked anaemia. And, secondly, the blood always shews a strong tendency to restore its volume and percentage composition to the normal when any deviation is brought about by experiment or disease. A comparable example of this tendency is found in the normal leucocytic content of the hydraemic blood of chlorosis; though the blood is diluted some two or three times the leucocytes per unit volume remain about normal, and during cure the concentration of the blood may produce the appearance of a definite leucocytosis. Here the volume of the blood is altered beyond immediate cure, so that the efforts of the haemopoietic system can only reach the normal in so far as the percentage composition is concerned. From such considerations as these it does not seem

[1] *American Medicine*, VI. 1903, p. 391: some doubt is here thrown upon the accuracy of our observations relative to the existence of high eosinophile leucocytosis due to *Ankylostoma* because the authors have not been fortunate enough to meet with such cases. Ashford has however himself recorded a good example (7,200 eosinophiles in 18,000 total leucocytes), though he prefers to consider that it was due to a pneumonia of a somewhat hypothetical nature.

[2] The very low figures for the haemoglobin (7—12 p.c.) given here must be regarded with suspicion in the absence of any evidence as to the accuracy of the standardisation of the instrument used. I have recently found that in this part of the scale the Miescher-Fleischl apparatus gives results about 25 to 30 p.c. too low.

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probable that the hydraemia of ankylostomiasis would produce an apparent diminution in the leucocytes, but rather that the leucogenic tissues would proliferate to the degree necessary to maintain the number per unit volume at the normal or abnormal figure produced by the presence of the morbid agents. (2) The diminution of the total leucocytes may in the second place be due either to a cessation of the necessity for the reaction, or to a failure on the part of the marrow to produce it. There is little doubt that in time many individuals become practically immune to such worms as they may harbour. Several instances have been noted in Cornwall in which severe attacks of anaemia have passed off, leaving the miner with a normal Hb content and yet with abundant eggs in his stool. These cases especially occur where, by change of occupation, repeated reinfections are avoided, though they have also been found in those who have constantly been exposed to infection. Some of these shew low counts of both total leucocytes and of eosinophiles: on the other hand several shew high degrees of eosinophilia but no definite leucocytosis. But it would seem that the capacity of the marrow to keep up the eosinophilia may fail in those who are greatly reduced by long-standing anaemia or by intercurrent disease. Though we cannot deny that such diminution may be in part due to the dilution of the blood, yet this cannot be the whole explanation since the percentage of eosinophiles in many of these cases is also diminished[1]. Such results find a reasonable explanation in the partial exhaustion of that part of the leucogenic apparatus which has been chiefly stimulated, and the failure on the part of the individual to react, as shewn by a low percentage of eosinophiles, is with much justice regarded by Ashford as of unfavourable prognosis[2].

Ashford and King record 86 differential counts in 62 cases, all of whom were severely anaemic when first seen. Grouped in a similar way to our own figures, their results are given in the following table, together with 19 others previously recorded by Ashford[3].

	Counts	< 5 p.c.	5—8 p.c.	> 8 p.c.	> 20 p.c.
Hb under 50 p.c.	82	17 = 21 p.c.	15 = 18 p.c.	50 = 61 p.c.	11 = 13 p.c.
Hb over 50 p.c.	23	1 = 4	3 = 13	19 = 83	9 = 39
Total	105	18 = 17	18 = 17	69 = 66	20 = 19
Cornish cases	148	3·4 p.c.	2·7 p.c.	93·9 p.c.	33·1 p.c.

[1] Our own figures do not shew this clearly, but the number of cases of severe anaemia seen in Cornwall has been comparatively very small.

[2] *American Medicine*, VI. 1903, p. 391.

[3] R. C. Cabot, *Clinical Examination of the Blood*, ed. 4, 1903, p. 433.

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These results shew a frequency and intensity of eosinophilia considerably less than that found in our series. There are three factors which may be considered: (1) the degree of anaemia in the two series is altogether different: some 20 only of our Cornish cases had less than 50 p c. Hb. That this is the chief influence at work is rendered probable by the figures found by Ashford in cases which were to some extent cured; these correspond much more closely to our own results. But at the same time these improved cases are not necessarily comparable to ours, who were, except in a few instances, untreated men who had never suffered from any considerable anaemia, and in whom the worm was present in considerable numbers. (2) The people concerned are different in race, previous history, etc. It is impossible to assess the influence of this factor. They have doubtless in many instances haboured other intestinal parasites, so that it might be thought that their power of or need for an eosinophile reaction would have been thereby diminished. The Cornish miners, however, are infested with other worms to a degree which seems to be at least as great as that found in the tropics (see p. 449). (3) The worm concerned is different. All Ashford's cases are from Puerto Rico and are due to *Ankylostoma americanum*, Stiles. Until the factors of duration and degree of affection can be excluded we can only suggest that this may influence the intensity of the eosinophilia. The numerous cases scattered through recent American literature all apply to cases of anaemia and shew generally the same figures as those recorded by Ashford. It is, however, somewhat suggestive that the figures in those cases due to *A. duodenale* (of which a few have been imported to the United States) tend to be rather higher than those due to the other species. The cases are however too few to give any definite conclusion. It is very desirable that a study should be made of cases of infection by *A. americanum* apart from ankylostomiasis.

The conclusion may however be drawn that the eosinophile reaction is most constant and best marked in those who are not suffering from definite anaemia, that is, in just those persons who shew nothing which would suggest that they harbour the worm. For the purposes of practical hygiene this is a most fortunate occurrence.

(2) *Onset of eosinophilia after infection.* The period which must elapse between infection and the appearance of the increase in eosinophiles is necessarily very difficult to determine apart from direct experiment. The following circumstances occurring in a laboratory worker were however very suggestive, and in view of the lack of definite information seem to be worth recording.

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	Date	Hb p.c.	Total leuco-cytes per c.mm.	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
Nov. 10. First contact with any *Ankylostoma* material for a period of 11 months: during that time blood and stools had been repeatedly examined with completely negative results. On this date some infected faeces received from Cornwall.	30. x. 03	96	8050	26·0	6·2	5·0	59·4	3·0	0·4
	11. xii. 03	97	7800	17·6	15·0	2·8	53·6	10·4	0·6
	18. xii. 03	95	7000	19·8	14·8	2·4	52·8	8·2	2·0
Nov. 21. First contact with encapsuled larvae which had been bred in the laboratory at a low temperature. Blood not examined till Dec. 11. Stools repeatedly examined with negative results till Jan. 28, 1904, when a few eggs were found; they were found again on Feb. 3, but were always very few in number and many negative examinations were made.	2. i. 04	98	4500	29·4	10·8	4·2	47·8	6·8	1·0
	4. i. 04	98	7400	19·6	17·6	1·8	51·4	9·0	0·6
	1. ii. 04	94	9000	31·4	8·2	1·6	49·8	7·8	1·2
	12. ii. 04	101	7400	31·8	14·4	3·8	44·0	5·0	1·0
	8. v. 04	100	7900	16·4	10·6	6·6	59·2	7·0	0·2
	13. v. 04	—	—	30·2	11·2	1·6	49·4	7·4	0·2
On May 17, owing to an accident with a pipette, it was thought possible, though not likely, that some larvae had been swallowed. The blood was frequently examined during the next fortnight, but no material change was found. No eggs could be found on repeated searches. No examination of the blood was thereafter made for three weeks, when a well-marked eosinophile leucocytosis was found. Faeces searched regularly for eggs, but none were found till July 11; after this eggs were present in small numbers every day, though they could only be found with the greatest difficulty.	17. v. 04	101	7970	21·2	14·8	0·4	59·2	3·4	1·0
	31. v. 04	—	—	30·0	7·6	2·2	48·6	10·0	1·6
	22. vi. 04	97	15000	13·4	9·6	1·2	50·8	24·0	1·0
	27. vi. 04	103	9170	22·0	8·4	2·4	32·8	33·6	0·8
	4. vii. 04	104	13200	23·0	5·0	1·4	30·2	40·4	0

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A definite eosinophilia was thus found 20 days after the first possible contact with encapsuled larvae. No large amount of work with this material was done until Nov. 28 and the following days. No skin eruption was at any time present. As far as is definitely known the worms do not reach maturity for at least 30 days after infection, and in skin infection Looss has found an interval more than twice as long elapse before eggs could be found. In this case eggs were found 68 days after the first possible infection and 48 days after the eosinophilia was noted. Later on there was evidently a reinfection; eggs were found 55 days after the date on which this probably took place. Unfortunately the blood was not examined during a critical period of three weeks, but there was a definite rise in the eosinophiles 14 days after the probable infection, and 19 days before eggs could be found: a considerable eosinophilia with a moderate leucocytosis was present. The case also illustrates how the blood change may be present in a very marked degree when eggs are present in such small numbers that they would often be missed by the ordinary method of examination. During June and July some pain was experienced of a dyspeptic character but without any relation to the taking of food: there have been no other symptoms[1].

(3) *Relation of eosinophilia to treatment.* The effect of efficient treatment is uncertain and inconstant. The eosinophiles never seem to diminish quickly, and in many cases shew at first a rise. The following figures are from two cases which have been treated till no eggs were to be found in their stools.

			Differential counts						
	Date	Hb p.c.	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells	
J. S. 51	31. x. 02	48	13·4	7·4	6·2	56·2	16·0	0·8	Treated several times during 6 months
	15. xi. 02	43	10·8	5·6	3·4	61·0	18·0	1·2	
	vii. 03	64							
	3. xii. 03	92	13·4	14·4	1·4	55·4	14·8	0·6	No eggs found
	7. xii. 03	—	14·0	18·4	1·2	55·6	9·8	1·0	No eggs
	8. ii. 04	—	35·4	4·4	1·4	44·4	13·4	1·0	No eggs
R. C. 30	5. ii. 04	49	26·6	4·4	5·8	49·2	13·8	0·2	Treated 7. ii. 04
	20. ii. 04	58	16·0	7·6	2·8	62·4	9·8	1·4	
	22. iii. 04	72	31·0	9·0	2·4	55·6	2·0	0·0	No eggs
	29. iv. 04	90	42·2	6·0	1·6	37·0	12·6	0·6	

[1] The opportunity has been taken of shewing in this case that the fluid in blisters from burns and in the various stages of superficial skin infections contains no excess of eosinophiles though in the blood this variety was more numerous than the neutrophiles.

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The second case fell at one time to a normal figure, but afterwards shewed a recrudescence of the eosinophilia. The patient in this case had had symptoms for about 6 months only, while in the first case they had been present in a severe degree for some 4 years. We have not observed a case where the eosinophilia disappeared after treatment, and in many cases it undoubtedly remains for a considerable time. We have examined four men who had given up underground work some time previously on account of their anaemia, etc., and in whose stools no eggs could be found. They shewed an eosinophilia varying from 11 to 22 p.c., and are to be regarded as cases in which a natural cure has taken place after removal from any chance of reinfection, leaving however a marked eosinophilia.

Ashford and King have had the opportunity of following a number of cases till the worms were all expelled and the blood restored to an approximately normal condition. With regard to the eosinophilia they conclude that "there is a final return to normal after the patient is cured[1]." The figures given to illustrate this are however similar to those which we have obtained and by no means bear out the authors' conclusion:

	Before		After	
Case no.	p.c. Hb	p.c. eosin's	p.c. Hb	p.c. eosin's
VIII	45	12·5	70	7·5
LXV	22	12	75 circa	5
LXX	21	15	94	15

No definite conclusions as to the presence of worms after treatment can therefore be drawn from the degree of eosinophilia which remains, and this persistence must be particularly considered when using the blood-film method of examination. This method is I think practically valueless where a mixed lot of treated and untreated men are under examination. It is to be suspected that the degree and duration of the residuary eosinophilia would be greater in those who have been infected for a long period, but we have no figures which definitely shew this[2].

(4) *Influence of intercurrent disease, etc.* Intercurrent diseases which themselves produce more or less characteristic changes in the blood may influence the differential count either by concealing per-

[1] *loc. cit.* p. 394.

[2] A doubt was previously (this *Journal*, III. p. 127) expressed as to the validity of the evidence adduced by Ehrlich in support of his statement that an eosinophilia persists for a long time after expulsion of the worms. His statement is, it appears, correct, though the case cited by him does not shew it.

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centage eosinophilia by a large increase in the number of other varieties, or the diminution may be absolute and due to the presence of substances which are negatively chemiotactic to the eosinophiles. In many instances both of these factors would be at work. A normal absolute eosinophile count can on the contrary be raised to a percentage eosinophilia by a considerable diminution in the total leucocytes[1]. Our information on these points is very deficient. Leichtenstern[2] observed that the incidence of a lobar pneumonia reduced the percentage from 72 to 6, the figures rising again to 54 p.c. on recovery from the pneumonia. In the case of a Dolcoath miner (*Ankylostoma* eggs found, 45 p.c. Hb) we found in the film an obvious large leucocytosis with 77·4 p.c. neutrophiles and only 3·8 p.c. eosinophiles; ten days later the leucocytosis was much diminished and the neutrophiles were only 55 p.c., while the eosinophiles had risen to 15 p.c. The eosinophilia of his *Ankylostoma* infection was obscured at the time of the first examination by a neutrophile leucocytosis of undetermined origin[3].

It is somewhat remarkable that hardly any cases of these disturbances of the eosinophile count have been noted in the long series of blood examinations which have been made in infected miners, and which have included men suffering from pleurisy, miners' phthisis, tubercular peritonitis, carcinoma of stomach, etc. Factors such as time of day, period of digestion, etc., produce such small changes that for practical purposes they may be neglected. Far too much stress has been laid on the necessity of avoiding *e.g.* digestion leucocytosis in making differential counts. Not only is such leucocytosis very often absent in healthy people eating ordinary meals, but its magnitude is such that the error introduced is less than that inherent in the method. Practically, it is necessary to make a careful note of any abnormal conditions present[4] when taking the blood film, and if necessary make allowances for them. If an eosinophilia is obscured by a neutrophile leucocytosis, the abundance of leucocytes and the high percentage of neutrophiles will readily suggest the real state of affairs.

[1] This is actually seen in some anaemias.

[2] P. Ehrlich and A. Lazarus, *Die Anaemie*, Part I. p. 113.

[3] The most probable cause seems to be a latent carcinoma; the patient (aet. 51) has symptoms of gastric trouble.

[4] It is well to remember that trivial boils may give rise to a very considerable inflammatory leucocytosis.

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III. *States which are accompanied by an increase in the eosinophile leucocytes of the circulating blood.*

Since the rise of haematology a large number of conditions have been described in which an increase of eosinophiles has been observed. Such increase may be relative only to the number previously present, as for instance during the subsidence of a pneumonia. It is however proposed to summarize here only those conditions which cause an increase relative to the average normal quantity, and of such an order that about 10 p.c. at least are found. It is desirable that this should be done in order that we may be in a position to use the blood-film method of examination for *Ankylostoma* to the best advantage and interpret the results obtained in a proper manner. The extensive literature on the subject is in many parts rendered of little value for our present purpose owing to two circumstances. In the first place, an unfortunate prominence has always been given to positive cases: there are indeed very few conditions in which the frequency of occurrence of an eosinophilia has been worked out. It follows that in several abnormal states eosinophiliais commonly thought to be more frequently present than it really is. In the second place, especially in the older literature, adequate attention has not been paid to the possibility of the sporadic presence, among a series of cases of some disease, of certain individuals who are affected with some condition which, while giving rise to no obvious symptoms, may cause an eosinophilia. The condition above all others which thus requires to be constantly considered is the presence of intestinal worms.

The conditions, which are associated with an eosinophilia, may be grouped under four heads[1]:

(I) *Paroxysmal asthma:*

In true paroxysmal asthma a high eosinophilia (30—60 p.c.) has been frequently recorded[2], and some degree has been found in the asthmatical attacks occurring in emphysema. In true asthma some increase is said to be constant about the time of the paroxysms. I have examined a number of cases with negative results but in no instance could a secondary (pulmonary) origin for the asthma be strictly excluded.

[1] References to a few typical records are alone given. Many other references will be found in the text-books of Cabot, da Costa, Ewing, and Bezançon and Labbé, and in the memoirs referred to.

[2] J. S. Billings, *New York Med. Journ.* vol. LXV. 1897, p. 692: H. S. French, *Practitioner*, LXX. 1903, p. 307.

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(II) *Skin diseases:*

In pemphigus[1] and dermatitis herpetiformis[2], some degree (generally 10 to 20 p.c.) of eosinophilia is very frequent, but not constant. In other affections of the skin (chronic eczema[3], psoriasis[1], lupus[1], urticaria[4], etc.) high counts have from time to time been recorded. But it is exceptional to find an eosinophilia among any ordinary body of patients suffering from skin diseases. This is clearly shewn by the recent records of H. S. French[5]: of 90 cases, including most of the ordinary conditions, 13 shewed more than 5 p.c., and only 4 more than 10 p.c. I have examined a series of 11 cases of acute wide-spread urticaria: in no case did the eosinophiles reach 4 p.c.

(III) *Parasites:*

A. *Trematodes.*

(1) *Bilharzia haematobia.* Eosinophilia is very frequent and often of a high grade: A. C. Coles[6] 20 p.c., A. E. Russell[7] 23·8 to 33·6 p.c. I have found more than 20 p.c. at some period in the 5 cases which I have examined, and no clear case of active disease with normal eosinophiles seems to have been recorded. In one case a count of 47 p.c. fell to 5 p.c. when the patient finally ceased to pass any ova or blood[8].

B. *Nematodes.*

(2) *Ascaris lumbricoides.* High counts are sometimes met with (Solley 33 p.c.[9]): I have already mentioned (p. 449) two cases in adults with 23·8 and 25·6 p.c. But as a rule no marked increase is observed, and completely negative cases are recorded by Bücklers[10], Boycott[8], H. Limasset[11], etc.

(3) *Oxyuris vermicularis.* Bücklers has recorded a count of 16 p.c. in an adult: Limasset had four negative cases. I have examined

[1] J. Zappert, *Zeitschr. f. klin. Med.* XXIII. 1893, pp. 272—273.

[2] Laredde, *Annal. de Dermatol.* [3] IX. 1898, p. 1016.

[3] P. Canon, *Deutsche med. Wochenschr.* XVIII. 1892, p. 206.

[4] Ehrlich and Lazarus, *Die Anaemie*, Part I. Transl. by Myers, p. 150.

[5] *Guy's Hospital Reports*, 1903. It is very desirable that similar statistical records should be prepared for the other conditions in which eosinophilia occurs. Our information rests too much on the records of individual cases.

[6] *Brit. Med. Journ.* 1902, I. p. 1137.

[7] *Lancet*, 1902, II. p. 1540.

[8] *Brit. Med. Journ.* 1903, II. p. 1268.

[9] J. Ewing, *Clinical Pathology of the Blood*, ed. 2, 1904, p. 473.

[10] *Münch. med. Wochenschr.* 1894, p. 22.

[11] *Thèse de Paris*, 1901, p. 78: the whole subject of the occurrence of eosinophilia in worm infections is here reviewed.

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a series of 18 infected children: these shewed two with more than 10 p.c. (12·8 and 13·7), six between 5 and 10, and 10 with less than 5 p.c.[1] The conclusion is that while low grades are not infrequent, it is rare to find a high eosinophilia and quite common to find none.

(4) *Trichina spiralis.* Since the original discovery of the blood changes in this disease by T. R. Brown[2], a large number of cases have been recorded which shew the most extreme grades of eosinophilia; most of them afford good examples of a real eosinophile leucocytosis. The 21 cases collected by Cabot[3] average (first examinations) 16,000 (8,000 to 28,000) leucocytes with 32 p.c. (10 to 67 p.c.) eosinophiles, and a high degree is almost constant. A single negative case (0·5 p.c.) has however been seen by da Costa[4], and a probably negative one by Howard[5]. E. L. Opie[6] has recently contributed a valuable study of experimental trichinosis in guinea-pigs, in which the production of a haemal eosinophilia and of local accumulations which practically amount to eosinophile abscesses is well shewn.

(5) *Filaria.* The eosinophiles vary from 4 p.c.[7], through a number of cases shewing 7 to 20 p.c.[8], to an extreme figure of 70 p.c.[9] In *F. medinensis* A. Powell[10] records six cases from 4·75 to 12 p.c., average 7·6 p.c. I am not aware that any series of cases has been published from which the frequency and grade may be properly ascertained, but it seems that most cases run at about 7 to 12 p.c.

(6) *Trichocephalus dispar.* No clear case of any marked degree of eosinophilia has been recorded. P. K. Brown[11] finds an eosinophilia a "strikingly constant symptom" in every case of worm infection, and says "in no less than ten or twelve cases where the *Trichocephalus hominis* alone appeared, the percentage of eosinophiles rarely fell below 5." My own experience leads to the conclusion that it is very exceptionally, if ever, that the presence of this worm gives rise to any

[1] *Brit. Med. Journ.* 1903, II. p. 1268. [2] *Journ. Experimental Med.* 1898, p. 315.

[3] *Clinical Examination of the Blood*, ed. 4, 1903, pp. 434 ff.

[4] *Clinical Haematology*, 1902, p. 435: a local eosinophilia was found in the affected muscles.

[5] *Phil. Med. Journ.* IV. 1899, p. 1085.

[6] *Amer. Journ. Med. Sci.* CXXVII. 1904, p. 477.

[7] E. Bloch, *Deutsche med. Wochenschr.* XXIX. 1903, p. 511.

[8] A. C. Coles, *Brit. Med. Journ.* 1902, I. p. 1137; G. L. Gulland, *ibid.* p. 831; Vaquez, *C. R. de la Soc. de Biol.* LIV. 1902, p. 1425; J. A. Sicard, *ibid.* p. 1427; Calvert, *Johns Hopkins Hosp. Bull.* XIII. 1902, p. 133.

[9] Rembinger, *C. R. de la Soc. de Biol.* LIV. 1902, p. 1145.

[10] *Brit. Med. Journ.* 1904, I. p. 73.

[11] *Boston Med. and Surg. Journ.* CXLVIII, 1903, p. 585.

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eosinophilia. At Levant Mine (see p. 447) *Trichocephalus* was found in 96 p.c. of the samples of faeces examined, so that it may be assumed that almost every man was infected. Yet of 41 blood counts only 5 shewed 5 p.c. or more, and the only two of these which were above 10 p.c. were satisfactorily accounted for by the presence of *Ascaris*. In the remaining three cases (5·0, 6·4, 8·4 p.c.) the blood condition may have been due to *Trichocephalus*; on the other hand comparable counts (5·2, 6·0, 6·8, 7·2 p.c.) were obtained at Snailbeach (p. 445) where no evidence of the presence of any worms could be found. E. Becker[1] found 2 p.c. in a case of severe anaemia (Hb 35) which he attributed to the presence of *Trichocephalus*.

(7) *Anguillula stercoralis*. I can only find four blood examinations in pure *Anguillula* infections: Bücklers[2] found 13·5 p.c., P. K. Brown[3] 6·3 p.c., Pappenheim[4] 0·8 p.c., and R. P. Strong[5] 0·1 to 0·3 p.c.

(8) *Ankylostoma duodenale* and *A. americanum*. If we group together the Cornish cases (p. 460) with those recorded by Ashford (p. 460) we have in all 253, of which 82 p.c. shew over 8 p.c. of eosinophiles, 73 p.c. more than 10 p.c., and 27 p.c. more than 20 p.c.

C. *Cestodes*.

(9) *Taenia solium* and *T. mediocanellata*. Positive examples have been recorded by Bücklers (10·25 p.c.), Leichtenstern[6] (34 p.c.), and others. H. Limasset[7] counted 16 cases: five shewed at some period more than 5 p.c., but of these two only reached more than 10 p.c. (10·8 and 26·1). In Bücklers' six cases one was less than 5 p.c. and one more than 10 p.c. I have examined 8 cases: four were less than 5 p.c., three between 5 and 10 p.c., and one over 10 p.c. (13·0 p.c.). It would seem therefore that an eosinophilia is not common, and if present is usually of a low grade.

(10) *Echinococcus cysts*[8]. A high degree may occur: Achard and Clerc[9] found 40 p.c., C. S. Seligman and L. S. Dudgeon[10] 57 p.c., E. Bloch[11] 14·7 p.c. and Dargein[12] 12 p.c. On the other hand the reaction

[1] *Deutsche med. Wochenschr.* 1902, p. 468.
[2] *Münch. med. Wochenschr.* 1894, p. 22.
[3] *Boston Med. and Surg. Journ.* CXLVIII. 1903, p. 583.
[4] *Centralbl. für Bakteriol.* XXVI. 1899, p. 608.
[5] *Johns Hopkins Hosp. Reports*, X. 1902, p. 94.
[6] Ehrlich and Lazarus, *Die Anaemie*, Part I. Eng. Transl. 1900, p. 151.
[7] *Thèse de Paris*, 1901, p. 66 ff.
[8] Most of the cases are hydatids of liver.
[9] F. Bezançon and M. Labbé, *Traité d'Hématologie*, 1904, p. 623.
[10] *Lancet*, June 21, 1902. [11] *Deutsche med. Wochenschr.* XXIX. 1903, p. 511.
[12] *C. R. de la Soc. de Biol.* 1901, p. 969.

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often fails: H. Limasset (5, 4, 0·6 p.c.), Bezançon and Labbé (5, 4 p.c.).

(11) *Cysticercus cysts.* H. Limasset records 10 p.c., C. H. Achard and M. Loeper[1] 11 p.c., and I have seen a case of generalised infection of two years' duration which shewed 8 p.c.; P. Marie[2] (2 p.c.) and others have recorded negative cases.

(12) *Bothriocephalus latus.* The information available as to the leucocytes in infections with this important parasite is very scanty, and all the records apply to anaemic cases. Schaumann, in his classical monograph, found a decrease in the eosinophiles, while the elaborate studies of E. Rosenquist[3] include no mention of the matter. In J. Courmont's[4] case the eosinophiles once rose to 7 p.c. during recovery but were otherwise normal. It appears from the records of Courmont, J. Drivon[5] and others that *Bothriocephalus* is so common in the South of France, at Geneva (10 p.c.), and at St Petersburg (15 to 32 p.c. of autopsies) that, if any marked eosinophilia resulted from its presence, the fact would probably have been recorded. As far as our information goes, we must conclude that the presence of this worm does not cause an eosinophilia, but it is very desirable that the condition of the blood should be investigated in those who harbour the worm without suffering any ill effects from its presence. The profound anaemia which ensues in a few of the hosts may obscure the true leucocytic reaction to the parasite.

D. *Miscellaneous parasites.*

Pulex penetrans. F. Bushnell[6] found 8·2 to 19·3 p.c. in a case of malaria; this was apparently due to the presence of a "jigger" in the foot.

Balantidium coli. E. Ehrnrooth[7] found no eosinophilia in a case of chronic enteritis due to this parasite.

The presence of *Acarus, Pediculus,* the malarial parasite, *Trypanosoma,* the *Piroplasma* of the tick fever of Montana, etc. do not appear to give rise to any increase of eosinophiles, nor is any bacterial infection known which causes a similar blood change.

[1] *Bull. de la Soc. Méd. des Hôpitaux* (3), XVII. 1900, p. 867.
[2] *Ibid.* (3), XVIII. 1901, p. 1126.
[3] *Zeitschr. f. klin. Med.* XLIX. 1903, p. 193.
[4] *Journ. de Physiol. et Path. Gén.* V. 1903, p. 353.
[5] *Lyon Médical,* May 4, 1902.
[6] *Clinical Journal,* XXIII. 1903, p. 63.
[7] *Zeitschr. f. klin. Med.* XLIX. 1903, p. 321.

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(IV) *Miscellaneous and indeterminate conditions.*

Sporadic cases are within the experience of everyone, and are scattered throughout the literature, in which the eosinophiles have reached the upper limits of what may be considered to be normal or have been definitely increased to moderately or very high figures in the persons of those who present no morbid condition which can be said to account for the state of their blood. In other diseases some authors have so constantly found a figure at about 5 or 6 p.c. that there would seem to be necessarily some connection of causative value. In this way increased figures have been recorded with certain malignant tumors, osteomalacia, gonorrhoea, gout, syphilis, etc., and a more uniform (though small) increase has been associated with scarlet fever, chorea, general paralysis, etc. High figures have commonly been ascribed to the blood of children, and E. Horder[1] has recently described a remarkable eosinophilia of high grade (about 20 p.c.) which is present in all the native population at Pakhoi in South China. Some stress has been laid on the frequency of such cases in minimising the diagnostic value of an eosinophilia[2]; yet it is extremely exceptional in ordinary blood examinations in this country to meet with these cases. It may be stated quite definitely that malignant growths, gonorrhoea, etc. do not as a rule cause an eosinophilia, though in a few individuals, whose blood has been examined because they were suffering from these diseases, an eosinophilia has been found. It is probable that in these few cases there is a causal connection; even if this were definitely shewn to be the case it would be immaterial as far as the practical use of the blood conditions in the diagnosis of ankylostomiasis, trichinosis or the like is concerned. In normal children Zappert[3] found that the eosinophiles were distinctly increased in a number of cases: of 18 cases 6 were over 5 p.c. and one of these reached 14 p.c. Though subsequent observers[4] have found that in new-born children the eosinophiles rather often reach and exceed 10 p.c., yet in later years any such increase which we cannot attribute to some known cause seems to be at least infrequent[5]. Zappert did not take into consideration the possibility of the action of worms and it is hardly likely that all the children examined were free from intestinal parasites. In the same way it is necessary to

[1] *Journ. Trop. Med.* 1901, p. 285.

[2] J. Ewing, *op. cit.* p. 471.

[3] *Zeitschr. f. klin. Med.* XXIII. 1893, p. 244.

[4] A. O. M. Fehrsen, *Journ. of Physiology*, XXX. 1903, p. 326.

[5] *Brit. Med. Journ.* 1903, II. p. 1267: J. L. Morse, *Boston Med. and Surg. Journ.* CXLVIII. 1903, p. 573: A. Raybaud, *C. R. de la Soc. de Biol.* LVI. (1904), p. 540.

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exclude the action of known causes before attributing the increase of eosinophiles seen in the insane to their mental condition alone. The insane as a class are particularly prone to become infected with worms owing to their filthy habits, though it seems fairly clear that a moderate increase of eosinophiles accompanies some instances of several nervous and mental disorders[1]. In considering the remarkable eosinophilia which he finds to be universal among the natives in S. China, Horder, though recognizing the possible influence of leprosy and intestinal parasites, does not adduce any evidence that these factors can be excluded.

It is hardly necessary in the present connection to mention myelogenous leukaemia as a disease which is constantly accompanied by an absolute and usually by a relative, eosinophilia, since the blood-film is characteristic in so many other ways.

From this sketch of the occurrence of eosinophilia it may be concluded that it is of materially frequent occurrence with (1) true paroxysmal asthma, (2) dermatitis herpetiformis, (3) pemphigus, (4) *Bilharzia*, (5) *Trichina*, (6) *Ankylostoma*, and possibly with (7) *Filaria*; that it *may* occur with many skin diseases and with any worm (though *Trichocephalus* and *Bothriocephalus* are doubtful); and that one must be prepared to meet with occasional cases which do not fall under any of these heads.

Discussion of the results obtained.

My results shew that 94 p.c. of cases of *Ankylostoma* infection have an eosinophilia of more than 8 p.c. with an average of 18 p.c., and the preceding section indicates that there are comparatively few affections which give rise to figures which are comparable either in magnitude or frequency. As far as miners in active work are concerned, several of these diseases can be very easily excluded since the fact that the man is working is an adequate proof that he is not materially affected with *e.g.* trichinosis. Pemphigus, dermatitis herpetiformis and true asthma may all be described as diseases which are at once rare and likely to be mentioned by the patient. With *Filaria* and *Bilharzia* infection there is perhaps more danger; the latter is becoming com-

[1] *E.g.* chorea: Zappert (*loc. cit.*) records four cases with 8·7 to 19·5 p.c., and T. R. Brown twelve with 5 to 9 p.c. (*Medical News*, LXXXII. 1903, p. 1117). J. A. Capps (*Amer. Journ. Med. Sci.* vol. CXI. 1896, p. 650) records two instances of definite eosinophilia among 19 cases of general paralysis, but the question of worms is not considered.

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paratively common in this country though cases of latent infection are quite rare. Eosinophilia is not a pathognomonic sign of *Ankylostoma* infection or of anything else; but the method, if used with discretion and with an adequate knowledge of the necessary detail, can give results which reach a degree of accuracy which is surprising. Certain points must now be considered in the practical application of the method to technical diagnosis on a commercial scale.

The time occupied in making an examination of a mine by the blood-film method is certainly not more than that necessary to obtain and examine a corresponding number of specimens of faeces. It is true that the method requires more experience and skill than the direct microscopic examination of the stools, but sufficient familiarity with the necessary technique and with the microscopic appearance of blood corpuscles is not difficult to acquire. The preparation of the films alone is very simple, and they can be easily sent for examination to those who are more familiar with microscopical work. Under favourable circumstances it is possible to obtain blood films from 10 per cent. of 400 or 500 men in 20 minutes, and the preparation and examination of these specimens can be completed within 24 hours. The bulk of the specimens is small, and a large number can be carried in the pocket; they can, moreover, be kept in good condition for at least several months if immediate examination is for some reason inconvenient. The actual enumeration of the white corpuscles is laborious, each specimen taking about half-an-hour, sometimes much longer. In but few cases, however, is it necessary to do this and so find the exact percentage of eosinophile leucocytes; a rapid general examination will suffice to tell in nearly every instance whether they are present in normal or in definitely increased quantity. Positive results take a little longer (in microscopical examination) than in the direct examination of faeces, but negative results are reached much more rapidly. There is in this method no chance of fraud, since the specimens are obtained directly by the examiner from the subject, and there is little or no difficulty in persuading men to allow their fingers to be pricked.

There are, however, two serious drawbacks to the method. In the first place, as has been already mentioned, it is of very uncertain value in ascertaining whether an infected subject has been freed from the worms by treatment. Secondly, it cannot yield evidence of *Ankylostoma* infection of a character so positive as would justify the immediate administration of anthelmintic treatment. In every case an *absolute* diagnosis can only be made by finding eggs in the stools. But the

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method is not designed, nor is it proposed that it should be used, for this detailed examination of individual cases; it is rather a simple, and I think an accurate, way of investigating a large number of men easily and quickly to see if a suspicion of *Ankylostoma* is thereby raised of sufficient strength to justify the troublesome process of obtaining specimens of stools from a number of men. If specimens of blood from 10 or 20 per cent. of the underground men fail to reveal any cases of an increase in the eosinophile cells, it may be assumed that the mine is free from any extensive infection. If, on the other hand, any cases of eosinophilia are met with, the individual source of each blood sample is known; and further investigation of each positive case is then made to see whether the abnormality is due to the *Ankylostoma* or to one of the other causes of eosinophilia. It will be readily seen that the method is most superior to the primary examination of faeces in cases where there is no *Ankylostoma* infection.

The Leucocytes in infected and normal Miners.

The present inquiry has afforded an opportunity to collect information relating to the leucocytes other than the eosinophiles. The average differential counts for each of the groups of men dealt with in the earlier part of this paper are as follows[1].

A. *Infected*	No. of cases	Lympho-cytes	Inter-mediates	Large hyalines	Neutro-philes	Eosino-philes	Mast cells
Known to have eggs	61	18·7	7·4	3·5	51·9	17·8	0·68
A. Dolcoath, 1902	22	18·8	6·4	3·8	50·5	19·7	0·76
B. ,, 1903	24	22·9	14·3	1·7	46·8	13·4	0·91
C. ,, 1904	41	25·9	6·1	2·0	44·5	20·7	0·74
Total	148	21·1	7·9	2·9	49·1	18·2	0·73
Calculated after deduction of 15·7 p.c. eosinophiles		25·2	9·4	3·5	58·5	2·5	0·87
B. *Normal*							
C. Talke	40	29·4	6·8	2·4	58·8	1·9	0·67
C. Snailbeach	42	18·8	17·4	2·2	58·7	2·1	0·79
B. Levant	41	30·3	12·1	1·3	51·8	3·7	0·76
Other cases	35	26·5	10·5	2·4	57·6	2·4	0·57
Total	158	26·1	12·0	2·1	56·6	2·5	0·70

[1] The series which are marked *A* were examined with cover-glasses, *B* with the cigarette-paper method, *C* with slide-smears, and the rest by a mixture of all three methods.

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It would appear from these figures that, after making allowance for and deducting the excess of eosinophiles, the differential count of miners infected with *Ankylostoma* is approximately the same as that of similar normal persons. The infected miners have rather more neutrophiles and mast cells, distinctly more large hyaline cells, and fewer lymphocytes of all kinds. So little has been recorded about the occurrence and numbers of mast cells that they merit perhaps rather more extended mention, especially in view of their suggested association with eosinophiles.

It has not been uncommon to meet with statements that mast cells are not found in normal blood[1]; that they are only occasionally present[2]; and that "one-half per cent. is the maximum number in health[3]." These statements are calculated to convey an erroneous impression. The following figures shew the distribution of the mast cells by percentages in the series of cases which form the basis of this paper:

		Percentages of mast cells					
	No. of cases	0	< 0·5	0·5—	1·0—	1·5—	> 2·0
Infected	148	4·3	34·1	32·9	26·1	4·2	2·5
Normal	158	6·9	35·4	34·2	25·9	1·9	2·5

These figures are based on differential counts of 500 leucocytes in 17 cases out of 306 no mast cell was found in the first 500 leucocytes, but in every case one or more were soon discovered by further search. In a large number of films which I have recently examined with this point specially in view I have in no case experienced any difficulty in finding a mast cell. The conclusion to be drawn would seem to be that they are always present in normal blood.

In about 65 p.c. of cases they exceed Cabot's estimate of the maximum possible in health, and in 8 of the 306 persons 2 p.c. or more were counted. As was previously suggested by Haldane and myself[4], and has been recently pointed out by Goldhorn[5], the explanation of this discrepancy no doubt lies in a difference of method; Ehrlich's triacid mixture leaves the granules of these cells unstained, and, though the

[1] *E.g.* W. S. Lazarus-Barlow, *Manual of General Pathology*, ed. 2, 1904, p. 151.

[2] Following P. Canon (*Deutsche med. Wochenschr.* XVIII. 1892, p. 206) who failed to find any in 9 of 22 healthy persons.

[3] R. C. Cabot, *Clinical Examination of the Blood*, ed. 4, 1903, p. 66. P. Ehrlich and A. Lazarus, *op. cit.* p. 76.

[4] This *Journal*, III. 1903, p. 125.

[5] J. Ewing, *Clinical Pathology of the Blood*, ed. 2, 1904, p. 168.

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shape and tinctorial properties of the nucleus are characteristic, they are easily missed. Jenner's and similar stains bring out the blue-red metachromatic granules very clearly and render the cell very distinct.

That mast cells are somewhat increased in the presence of an increase of eosinophiles is rendered probable by the figures, though the differences are small. Of the infected cases 32·8 p.c., while of the normal cases only 30·3 p.c. reach 1 p.c. or more: the average for infected men is 0·73 p.c., for normal men 0·70 p.c.; but if allowance is made for the excess of eosinophiles the former figure is increased to 0·87 p.c.

The differential counts obtained for normal miners afford some basis for considering the effect, if any, of their mode of life on the leucocytes. The figures are widely different from those so often quoted from Ehrlich, who places the normal percentage of neutrophiles at 70—72 p.c., while in this series the average is but 57. There is little doubt that the former figure is too high; such a percentage may as a rule be taken to indicate the presence of a definite neutrophile leucocytosis. More recent determinations[1] give lower figures (60 p.c., 66 p.c.); the only accurate determinations made in this country with which I am acquainted are those of A. G. Phear[2], who obtained the following average figures for normal people—mononuclear 43·4, neutrophiles 54, eosinophiles 1·9, mast cells 0·7. These figures correspond very closely with our own, and lead to the conclusion that the high temperature, coal, tin, arsenic, lead, etc. underground do not cause any marked or definite alteration in the relative proportions of the different varieties of leucocyte.

[*Note.* The classification of the leucocytes adopted here has been previously discussed (vol. III. p. 115). The "intermediates" include non-granular[3] mononuclear cells, which are larger and have more cytoplasm and a less densely chromatic nucleus than the typical small lymphocyte, but which have not such large dimensions, such a pale nucleus, or such basophile cytoplasm as the typical large hyaline cell. It is no doubt a very mixed group; and there is some doubt whether the apparent numbers of this variety do not vary with the mode of preparation of the film and the idiosyncrasy of the observer's mood.]

[1] See Bezançon and Labbé, *Traité d'Hématologie*, p. 487.

[2] *Medico-Chirurgical Trans.* LXXXII. 1899, p. 331.

[3] Many of them shew the scattered, irregular granules, staining a metachromatic red with Jenner's stain, which have been recently figured by Ewing, *op. cit.* 1904, Plate III. and p. 123.

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Other Worm infections in Miners.

During the numerous examinations of faeces for the presence of *Ankylostoma* which have been made, results of some interest have been obtained with regard to the prevalence of other intestinal worms. Reference has already been made to the occurrence of *Anguillula stercoralis* in some half-dozen cases at Dolcoath (this vol. p. 98). Till recently the Dolcoath specimens were not examined specially for any worms except *Ankylostoma*, and it is to be regretted that much interesting material has in this way been lost. But of recent samples nearly all shew *Trichocephalus* and one or two *Ascaris*. In searching for these other eggs Stiles' plan of repeatedly shaking up the faeces with water and, after a few minutes, pouring off the supernatant fluid has been extensively used; it is very useful, since in some cases the eggs are very few. For *Ankylostoma* eggs it is not so valuable; they are generally very easily found without it, and they do not seem to settle so quickly or so completely as other eggs.

The results obtained are shewn in the following table:

Mine	No. of specimens	*Trichocephalus*	*Ascaris*	*Oxyuris*	*Ankylostoma*
Levant	25	24	3	1	0
East Pool	23	14	9	1	4
Snailbeach	22	0	0	0	0
Various coal-pits	28	0	0	0	0

No *Taenia* eggs were found in any case. There are we believe no figures published shewing the prevalence of the common worms among an ordinary English adult male population; but the figures of the Snailbeach lead-mine and the Staffordshire coal-pits probably represent approximately what is found among the ordinary population. There is at any rate no reason for supposing that the men in these mines should be less infected than those on the surface; at Snailbeach there is most abundant opportunity for coming in contact with faecal material. Most of the data which have from time to time been published have been recently collected by P. E. Garrison, B. H. Ransom, and E. C. Stevenson[1] from whose table the following figures are extracted:

[1] *Bull. No.* 13, *Hyg. Lab. U.S. Pub. Health and Mar.-Hosp. Serv.*, Washington, 1903.

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	Percentage of cases infected with				
	Trichocephalus	*Ascaris*	*Oxyuris*	*Taenia*	No. of cases
U. S. Gov. Asylum	10·8	0·4	0·8	0	500
Italy	38	30	4	7	73
India (Dobson)	4·4	10·5	15·4	1·4	1249
,, (Fearnside)[1]	7·3	36·1	—	—	200
Russia	5·0	5·8	7·1	14·5	600
Germany	19·8	16·5	12·4	0·3	2629

These figures can be taken only as rough indications of the frequency of infection. The mode of infection is such that everything depends on the precise habits of life of the persons investigated. Isolated instances of practically universal infection have been recorded: 90 p.c. of Japanese are said to have *Ascaris*, and a similar proportion have been found to harbour *Trichocephalus* in India, while 76 p.c. of Dobson's cases had *Ankylostoma*.

Judged even by a tropical standard, the prevalence of *Trichocephalus* and *Ascaris* at Levant and East Pool is remarkable; taking the two mines together, 79 p.c. of the men harbour the former and 25 p.c. the latter worm. The amount of infection at East Pool is such that the full data may perhaps be of interest:

Sample	*Trichocephalus*	*Ascaris*	*Oxyuris*	*Ankylostoma*	Earth nematodes and eggs
I	+	+	+		+
II	+	+			
III	+				+
IV	+	+			+
V	+	+			+
VI	+			+	
VII	+				
VIII	nil				
IX	nil				
X	nil				
XI	nil				
XII		+			+
XIII	nil				+
XIV	nil				+
XV	nil				
XVI	+	+		+	+
XVII	+	+		+	+
XVIII	+	+			+
XIX	nil				+
XX	+			+	
XXI	+				+
XXII	+				
XXIII	+	+			
Total	14	9	1	4	12

[1] *Brit. Med. Journ.* 1900, II. p. 541.

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Thus 15 out of 23 samples shewed the presence of some intestinal parasite, while in 6 instances two, and in three instances three were present, the total infections found amounting to 28 in 23 cases.

The figures are also given of the presence of the small nematodes which so frequently enter faeces from the earth; they are found about as frequently in cool non-infected mines such as Snailbeach as they are in the hot Cornish mines. They can be easily found in mud in these mines far from any faecal contamination, but they appear to flourish and multiply better in faeces, in which they often occur in immense numbers. Thus they have been noted at Levant in 7 out of 25 specimens, at East Pool in 12 out of 23, at Snailbeach in 14 out of 22.

Infection with *Ascaris* and *Trichocephalus* is believed on very satisfactory grounds to be direct, and to occur by the ingestion of the eggs themselves. *Taenia* of course requires an intermediate host, and I have not been able to find that cysticercus cysts are specially frequent among Cornish miners[1]. It is curious that *Oxyuris* should be so uncommon. It is evident that the thick shells of *Ascaris* and *Trichocephalus* are satisfactorily protective since they flourish in Levant where the water is sufficiently salt to prevent the introduction of *Ankylostoma*. There can be but little doubt that the prevalence of these parasites at Levant and East Pool is directly due to the filthy habits of the men: their absence at Snailbeach may be due to the lower temperature there (62°—68° instead of 70°—90° F.), since it is almost certain that the eggs must contain developed larvae before they will infect if swallowed.

[1] Pork is the chief meat eaten by the Cornish miners.

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