THE EXAMINATION OF BLOOD FILMS IN RELATION TO THE PREVENTION OF PLUMBISM AMONG SHIPBREAKERS

By A. E. FERGUSON and T. FERGUSON

From the Research Laboratory of the Royal College of Physicians, Edinburgh

CONTENTS

Introduction

The control of the lead risk among shipbreakers presents great practical difficulty. Measures for the prevention of plumbism applied successfully in other industries are here impracticable, with the result that the breaking up of a heavily leaded ship is almost invariably responsible for a number of cases of lead poisoning and much ill-health stopping just short of incapacity for work.

The work of the oxy-acetylene burner in shipbreaking involves inhalation of volatilised lead in greater or less degree. The lead is chiefly derived from paint or from red lead used as a filling agent. The type of plumbism met with in this industry is in comparison with others a more acute intoxication. Animal experiments by Tanquerel, Goadby and Blumgart have proved conclusively that lead is absorbed rapidly by the whole extent of the respiratory tract from the nasal passages downwards. Goadby demonstrated that when animals were confined in an atmosphere of lead dust toxic symptoms developed more quickly than when ten times as much lead was administered by the mouth.

References to the high incidence of lead poisoning among shipbreakers and to the difficulty of controlling the lead risk in the industry are to be found in many of the Annual Reports of the Chief Inspector of Factories and Workshops issued since the War. Thus, in 1924, Dr Middleton investigated the physical

https://doi.org/10.1017/S0022172400034641 Published online by Cambridge University Press

character and density of the fumes given off and concluded that they are particulate in character and may be present in considerable density, though not visible even in bright sunlight. During the years 1921–32 inclusive, 3578 cases of lead poisoning were reported to the Chief Inspector of Factories, and of these 693 were attributed to shipbreaking.

In view of the difficulty of controlling the causative fume and the high prevalence of plumbism, any prophylactic assistance which can be derived from medical examination of the workmen is specially valuable. Works doctors often find clinical examination inadequate for the early detection of cases of plumbism in the industry, and this research has been undertaken in the hope of finding some simple laboratory procedure which might supplement such clinical examination. Complicated technique is out of the question in field work, and this consideration rules out such aids as the quantitative estimation of lead excreted in the urine and total blood counts. Before the recent work of Jones made possible the estimation of reticulate cells in blood from examination of an ordinary film it even restricted the practical use of reticulocyte counts, with the specially prepared slides which they involved.

With these restrictions in view this investigation has been kept as uncomplicated as possible, and has been confined to ascertaining what useful evidence, if any, is obtainable from the examination of simple blood films. Films were taken at intervals of one month from one hundred burners, and after staining by Leishman's method, examined for the following points: the degree and type of punctate basophilia, the presence or absence of polychromasia, nucleated red cells and irregularity of the red blood corpuscles in size or shape, while a differential count was also made of the white cells. It was then attempted to correlate these findings with the symptoms presented at each clinical examination, and particularly to observe how the blood condition altered with the changing clinical picture from month to month.

As the work progressed it was found more practicable to discontinue the monthly examinations after five readings had been taken, and to concentrate on a more intensive study at weekly intervals of a smaller number of cases exposed to specially heavy lead risk. During this latter phase reticulocyte estimations were made in some cases. Other basic stains were used in the earlier months as well as Leishman's, but as they did not appear to have any marked advantage their use was discontinued.

The hundred burners forming the industrial population studied worked in two shipbreaking yards in Scotland. They represented all the workers employed in these two yards, and were in no way selected except that a particularly high incidence of lead poisoning had focused attention on the yards in question. Actually, rather more than half of the men had been off work from "lead poisoning" at one time or another before the investigation was set afoot, so that they represent a thoroughly heavily leaded population. The age distribution of the men and their duration of employment in the industry at the beginning of the research have been summarised in Table I.

The group is composed of young adults, and the duration of employment is for the most part short, a commentary on the undesirable nature of the work.

It was found that the risks involved fell into three categories which have been designated *A*, *B* and *C*. *A* represents the risk of shipbreaking a British war vessel, and is the greatest of the three: *C*, that of a battleship salved after some fifteen years' immersion in the sea at Scapa—easily the least dangerous of the three, while *B* represents the risk of work on a merchant vessel, liable to show more variation in lead content than the others, but with a risk somewhere between them, probably generally nearer *A* than *C*.

Table I

Age		Duration of employment	
15–20	3	Under 1 year	53
20–25	36		
25–30	31	1– 5 years	18
30–35	19		
35–40	8	5–10 years	22
40–45	3	10–15 years	7

In all 560 films have been examined. So far as possible the films were collected under similar conditions at the several examinations.

I. CHANGES IN RED BLOOD CELLS

(*a*) *Punctate basophilia*

Punctate basophilia was found to be present in every slide examined during the course of the investigation.

Following the description of punctate basophilia by Ehrlich (1885) and the recognition of its association with lead poisoning by Behrend (1899), Lutoslawski in 1902 reported that he had found ninety cases of punctate basophilia among 107 persons suffering from chronic lead poisoning. On the other hand, Biondi, at the Congress of Industrial Diseases in Milan in 1906, said he had not found punctate basophilia in the blood of persons suffering from severe lead intoxication. Russell (1915) gave the results of examination of a hundred cases of lead poisoning from the pottery district: 28 per cent. had no punctate basophilia. Oliver (1924) gives it as his opinion that punctate basophilia is present in 30–70 per cent. of cases of lead poisoning.

Sellers in 1926 published the results of examination of the blood of workers in various industries where a lead hazard was present, and his figures for punctate basophilia ranged from a 5 per cent. incidence in scrap lead workers to 88 per cent. in metal foundry workers (melting and drossing lead). He specifically mentioned a group of twenty-six oxy-acetylene burners employed by a firm of shipbreakers; 61·5 per cent. of the men had punctate basophilia. Sellers asserted that comparison as regards the lead risk could be made between factories engaged in the same or different kinds of industry by means of a sufficiently large number of blood tests, and that there was abundant evidence that the incidence of punctate basophilia in the different factories followed very closely the amount of danger incurred by the workmen. Lane (1931) declared that punctate basophilia was present in all workers exposed to a lead hazard—this opinion was based on the examination of about 4000 films from workers engaged in an electric accumulator works.

The cause and significance of punctate basophilia are not yet fully understood. While stippling is notably associated with lead poisoning it occurs also in other diseases, among

them pernicious anaemia, leukaemia, malaria and malignant cahexia. Opinions differ as to whether it ever exists in the normal subject: Key (1921) says that there is no punctate basophilia in normal adult blood: Sabrazès and his co-workers found it in healthy adults, as did also Teleky, while Hawes and Koenig have found it present in normal infants. Lane found punctate basophilia present to a slight extent in approximately half of 223 normal persons of no known lead exposure.

The frequent association of punctate basophilia with nucleated red cells led some observers to believe that the granules originated from fragmentation of the nucleus. This view is still held by a few haematologists (including Piney), but the weight of evidence is in favour of the cytoplasmic origin of the granules, as propounded by Pappenheim and Schilling Torgau, whose studies led them to the conclusion that polychromasia, punctate basophilia and reticulation, demonstrable by vital staining, were all due to the presence of basic staining protoplasm of youthful character, and all different expressions of substantially the same substance.

Key (1921) found basophilic cells of frequent occurrence in the blood of the mammalian embryo, the frequency decreasing with the age of the embryo. Brookfield (1928) confirmed the association of punctate basophilia with young cells in the human subject. Punctate basophilia is present classically where the bone marrow is excessively active: it never occurs in aplastic anaemia, but chiefly in toxic anaemias where the products of red cell degeneration are retained within the body (Price Jones). Gulland and Goodall (1925) regard punctate basophilia as a degenerative phenomenon occurring in young cells.

The scope of the present research does not afford an intensive enquiry into the cause of punctate basophilia, but several points have emerged which lend support to the theory that punctate basophilia is associated with an active marrow, and that it is the young cells that are—at any rate chiefly—involved. A record was kept of the number of nucleated red cells observed and the proportion of these showing punctate basophilia. Altogether 789 nucleated red cells were seen and of these thirty-two showed stippling (4 per cent.), while only 0·9 per cent. of all erythrocytes showed punctation. The films of the 100 workmen examined contained nucleated red cells at one time or another.

Punctate basophil counts of the 100 workmen at routine monthly examinations are summarised in Table II.

Table II. *Punctate basophilia among shipbreakers.*

	Thousands of basophils per million erythrocytes															
	–1	1–	2–	3–	4–	5–	6–	7–	8–	9–	–10	10–	20–	30–	40–	50–
May	4	9	8	12	5	10	9	7	2	2	68	18	2	2	0	0
June	1	6	5	11	11	10	8	5	8	3	68	14	5	0	1	0
July	1	1	4	12	16	15	9	5	10	2	75	16	3	3	1	1
Aug.	0	2	6	7	9	5	9	10	3	3	54	27	12	4	1	0
Sept.	1	7	11	11	9	9	13	9	4	3	77	15	5	1	0	1
Total	7	25	34	53	50	49	48	36	27	13	342	90	27	10	3	2

It will be seen that the counts most frequently met with fall between 3000 and 7000 per million. There are only seven under 1000, two of them falling below 500 per million, while at the other end of the scale they range up to a maximum of 62,000 per million.

These figures are generally higher than those recorded for other industries.

https://doi.org/10.1017/S0022172400034641 Published online by Cambridge University Press

Schmidt examined the blood of lead workers and non-lead workers. Of the latter 2 per cent. showed punctate basophilia, in no case exceeding 300 stippled cells per million. All lead workers showing symptoms exhibited punctate basophilia, and in 75 per cent. of cases stippled cells exceeded 300 per million. Schmidt was of opinion that the basophil count must reach 500 per million before it became of diagnostic significance. In his group of 100 reputed cases of lead poisoning from the pottery district Russell (1915) found that twenty-eight showed no punctate basophilia, forty-three had counts under 1000 per million, while only two exceeded 10,000, one being 15,000 and the other 25,000 per million. He found that the more convincing clinical cases were those with heavy punctate basophilia.

Reviewing the position in 1925, Aub, Fairhall, Minot and Reznikoff stated that their repeated daily examination of the blood during plumbism confirmed the observation of Meyer and Speroni that the granulation varies markedly in amount from day to day. Teleky regarded marked granulation as an index of rapid absorption of lead, but Aub and his co-workers observed marked stippling nine months after exposure had ceased and were not disposed to accept Teleky's view. Teleky and Schoenfeld declare that stippling is more intense in early than in severe plumbism. Oliver believes that some workers may exhibit a greater tendency to basophilia than others.

Sellers expressed the view that blood tests were of most value in the prophylaxis of lead poisoning (rather than in diagnosis), and, while unwilling to lay down an exact figure, regarded 500 stippled cells per million as representing a danger signal between lead absorption and lead poisoning. In his group of shipbreakers above referred to, 23 per cent. had more than 500 basophils per million. Lane considers small granule counts up to 3000 of little or no significance in a lead worker: they merely indicate exposure to lead. He agrees with Sellers on the value of average counts of groups of workers as indicating the degree of risk, and states that these averages are of more significance than individual counts, although the latter are useful in indicating new starters who are particularly susceptible to lead.

Table III shows the exposure risks for the various months. These risks (*A*–*C*) have been defined on p. 297.

Table III

	A	*B*	*C*
May	46	44	0
June	31	57	0
July	30	33	36
Aug.	22	34	42
Sept.	15	38	47

There has been a diminishing average risk throughout from May to September.

The figures in Table II demonstrate that, generally speaking, the height of the counts from month to month was remarkably constant despite the diminishing risk. In May, for instance, there were 76 per cent. falling under 10,000 per million, in June 77 per cent., in July 76 per cent. and in September 78 per cent. In August there was a notable fall to 55 per cent. though the risk then was less than in July, the more so since the August readings were taken within a few days of the workers' return after a holiday of at least ten days duration.

The occurrence of the annual holiday in August provided material for an interesting comparison not only between the August punctate readings as a group with those for July and September but also for a study of the effect of vacation with reference to groups of men exposed to the several risks.

Among men employed on risk *A* the average punctation before the holiday was 5000 per million as compared with 9000 after returning to work. With risk *B* the figures were respectively 8000 and 13,000 per million, while with risk *C* the averages were 11,000 and 13,000, the increase being relatively greatest in the case of the most severe exposure. The readings for men in group *C* must be interpreted in view of the fact that practically all of these men had been engaged on heavier risks during May and June and had on their transfer to group *C* shown a great increase in punctation at the July examination, recording then an increase which doubtless to some extent anticipated the rise shown after the holiday by the heavier exposure groups.

The majority of the August examinations were carried out five days after the men had returned to work, but about 25 per cent. were made on the first morning after resumption and it was found that, notably in the case of the higher exposure groups, the increase in punctation was greater then than among the men who had been back at work for five days.

Eleven of the cases are of special interest in so far as they were observed at approximately weekly intervals during a period while they were engaged in a heavy *A* risk (see p. 297). This risk occupied four weeks and its commencement was followed in some cases by a sharp rise in punctation, rapidly falling away and giving place to a trough of low punctation which continued during the heavy exposure, persisting with the appearance of symptoms of plumbism, to be followed on removal from intensive risk by a phase of higher punctation.

This increased wave of punctation following removal from a heavier exposure to a lesser has been frequently observed in the course of the investigation. Thus, among men who changed from an *A* risk to a *B* risk the average punctation rose from 5000 per million before the change to 10,000 at the succeeding monthly examination; with a change from a *B* risk to a *C* risk the average rise was from 6000 to 12,000, and with a change from an *A* risk to a *C* risk from 5000 to 12,000. It has to be borne in mind that these figures apply only to the monthly reading following the change and are not to be taken as inferring that over a long period punctation in the presence of a heavy risk is less than when the risk is smaller.

Table IV shows the influence of duration of participation in the industry on the count of punctate basophilia:

Table IV

Duration of exposure	Punctate basophils, thousands per million erythrocytes							
	–2·5	2·5–	5–	–10	10–	20–	30–	Total
Under 3 months	5	9	12	26	3	2	0	31
3 months–	6	15	31	52	7	5	2	66
6 months–	7	18	31	56	19	6	1	82
9 months–	2	7	21	30	13	1	1	45
1 year–	16	30	41	87	18	4	2	111
5 years–	6	32	33	71	22	5	3	101
10 years–	5	9	8	22	7	4	5	38

There is little difference in the height of the count reached in the several groups, though there is a tendency for workers in their first six months to have counts lower than with longer exposures. Very high counts are obtained most frequently among workmen of longest standing, though even in the highest group 58 per cent. of the readings fall below 10,000 per million.

The presence of punctate basophilia may be noted in the blood of new starters in this industry very soon after commencement of work. Indeed, a count of 14,000 per million has been recorded in the second day of employment, though this is exceptional. Counts in the region of 4000 or 5000 are, however, common within the first few days of starting work.

Table V sets out the incidence of symptoms among the men examined in relation to the height of punctate basophilia recorded at the examination at which the symptoms were noted.

Table V

Punctate count	Number examined	Number showing symptoms: Headache	Constipation	Abdominal pain	Anorexia	Blue line
–2500	50	7	8	7	5	10
2500–	113	21	31	22	17	37
5000–	173	23	38	32	25	54
–10,000	336	51	77	61	47	101
10,000–	90	16	15	23	14	25
20,000–	27	7	6	5	3	9
30,000–	15	2	5	4	4	1

These results are summarised on a percentage basis in Table VI.

Table VI

Punctate count	Percentage showing: Headache	Constipation	Abdominal pain	Anorexia	Blue line
–10,000	15	23	18	14	36
10,000–	18	17	26	16	28
20,000–	21	26	21	17	24

The incidence of symptoms tends to be slightly higher with increased punctation, though this is neither constant nor striking in degree. The number of workers showing a blue Burtonian line on the gums bears no significant relation to the height of punctation.

Even in the absence of variation in the risk involved, and in the continued absence of symptoms, the burner may show considerable variation in his punctate count from month to month.

(*b*) *Type of punctation*

Punctate basophilia has been described in the case records as being fine or coarse, according to the size of granules. The majority of the fine granules were just visible by the oil immersion lens and might easily be missed. Coarse

granules were up to about 1μ in diameter. There were many granules of intermediate size, and it was sometimes difficult to draw the dividing line between fine and coarse as regards an individual cell, but there was little difficulty in classifying the slide into the type which predominated—F, Fc, FC, Cf, C. Fine punctation is classically described as innumerable fine granules scattered uniformly throughout the cell. While this appearance was frequently met with, a smaller number of fine granules was more commonly seen, either situated eccentrically in a group or forming an incomplete chain round the periphery. Where the fine granules were few they were almost always marginally placed, although a few fine granules scattered irregularly through the cell were also seen, but infrequently. Sometimes the granules appeared to be adherent to the exterior of a shrunken-looking cell. Cells containing many fine granules scattered throughout almost invariably were polychromasic, frequently highly so. Coarse punctation consisted of one to four larger granules situated anywhere in the cell, although they too had a slight preference for the marginal position. Coarse and fine punctation frequently occurred in the same slide, but never in the same cell. The granules in any given cell were always of uniform size.

Fine punctation was that most commonly seen. It was the predominating type present in 80 per cent. of the films, while in fully half of these it was present alone. Fine and coarse were present in approximately equal numbers in 15 per cent., while in the remaining 5 per cent. coarse predominated, but its presence alone was of very infrequent occurrence.

Basophilic cells are seldom scattered uniformly throughout the field. They tend to be segregated in certain areas, leaving others almost clear, so that where the count was high a few fields might be seen where nearly every cell was punctate.

Table VII shows the distribution of the different types of punctation encountered in the examination of workers exposed to the several risks (p. 297):

Table VII

	Type of punctation present (%)				
Risk	F	Fc	FC	Cf	C
A	33	41	20	5	1
B	50	37	10	3	0
C	41	39	17	3	0

The value of Table VII is to some extent marred by the frequent changes of risk which the men have undergone, but it seems fairly obvious that, while there is rather more punctation of coarser type among men in group *A*, no reliable inference as to risk can be drawn from the type of punctation present in the blood film.

Table VIII deals with the type of punctation in relation to duration of participation in the industry:

Table VIII

Duration of employment	Type of punctation present				
	F	Fc	FC	Cf	C
Under 3 months	18	8	5	1	0
3 months–	29	24	9	2	0
6 months–	37	27	12	6	0
9 months–	14	24	6	1	0
1 year–	46	44	19	1	0
5 years–	46	39	13	5	0
10 years–	9	18	7	2	2

Punctation is finer among workmen of least exposure, though the differences between the groups are so small as to be of little practical importance. Very high punctate counts are usually predominantly fine in character, especially where the wave of punctation is of rapid development, as following a holiday or a change from a heavy exposure to one of less degree. On the other hand, cases where workers are heavily leaded and symptoms common (especially when associated with low punctation) tend to have the granules of coarser type.

(*c*) *Polychromasia*

Polychromasia is always present in the immature red cells of normal bone marrow and occasionally in the peripheral blood, where its presence becomes more prominent in all anaemic conditions associated with active red cell production. According to Brookfield it is a constant accompaniment of punctate basophilia.

Fully two-thirds of the films examined have been described as showing polychromasia in greater or less degree. The remainder were not entirely devoid of polychromasic cells and in assessing polychromasia for record purposes the general appearance of the film has been the criterion mainly adopted. It might perhaps have been more strictly accurate to substitute "Polychromasia +, ++ and +++" for the "−, slight and +" which have been used. About 60 per cent. of all the slides examined were highly polychromasic.

Polychromasia increases with exposure until the burner has been employed at the work for about a year. Thereafter its incidence tends to diminish slightly, but among men of upwards of five years standing there is a return to the early high incidence of polychromasia.

The degree of polychromasia is intimately related to the height of punctation. Table IX demonstrates this relationship:

Table IX

Polychromasia	Percentage of films showing punctate basophilia in thousands per million red cells					
	–2·5	2·5–	5–	10–	20–	30–
+	5	19	43	21	8	4
Slight	9	37	26	23	3	2
−	30	34	24	10	2	0

The least polychromasic slides are those of lowest punctation.

In general, the type of punctate basophilia present bears no significant relationship to the degree of polychromasia, though it has been frequently observed during the research that the individual cells most closely peppered with fine punctation showed the highest degree of polychromasia.

(*d*) *Reticulocytes*

The study of the reticulated cells is recommended by Key as a reliable indicator of the presence of young cells in the circulating blood. Some authorities, notably MacCord and his co-workers, and Jones (1933), have advocated the use of the reticulocyte count as an index of lead absorption as a substitute for the usual count of punctate basophilia.

Until recently this method had the disadvantage mentioned earlier of requiring the use of a specially highly treated slide, not always readily available for field work. Vital staining methods have, however, been applied to films from a series of burners subject to a specially heavy lead risk, and it has been found that there is a close correlation between the number of reticulocytes and the height of the count of punctate basophilia:

Table X

	August			September	
	12th	17th	25th	5th	14th
Reticulocytes (%)	3·8	2·8	1·6	1·5	2·3
Punctate basophils (per 1000 red cells)	12·4	8·5	3·8	4·2	8·6

These figures indicate the means of the readings on the dates in question. The films on August 12th were taken immediately after transfer to the intensive lead risk, work on which ceased on September 6th, *i.e.* the day after the fourth series of films. The reticulocyte curve showed a fall with the increase of risk and a rise on cessation of the very heavy lead exposure.

These findings are in accordance with those of Brookfield, who demonstrated in a series of cases being treated intravenously with lead that there was an intimate relationship between the reticulocyte, the stippled cells and the degree of polychromasia, and concluded that they were all different morphological expressions of the same substance.

(*e*) *Nucleated red cells*

Fifty-six per cent. of the films examined showed the presence of nucleated red cells, in the search for which roughly 80,000 red cells were examined in each film. Nucleated reds were found in at least one film from every case: 99 per cent. of them were of normoblastic type, the remainder of them being megaloblasts.

Table XI shows the incidence of nucleated red cells in relation to the height of the punctate basophil count.

Table XI

Punctate basophils per 1,000,000 red cells	Nucleated red cells			
	0	1–5	6–10	10+
Under 2500	30 (58%)	21	1	0
2500–5000	55 (47%)	60	2	0
Under 5000	85 (50%)	81	3	0
5000–10,000	67 (39%)	88	16	3
10,000–15,000	28 (44%)	31	4	1
15,000–20,000	13 (52%)	10	1	1
20,000+	17 (41%)	24	1	0

Nucleated red cells are seen most frequently in association with punctate counts in the region of from 5000 to 10,000 per million. Counts between 10,000 and 20,000 are apt to show fewer nucleated cells, while in the group of very high counts (over 20,000) normoblasts are again more frequent. Punctate basophilia were found four times as frequently in nucleated red cells as in all erythrocytes, and nucleated cells were slightly more frequent among slides showing marked polychromasia.

The occurrence of nucleated red cells bears no relation to duration of employment in the industry; they have been found as early as two days after the commencement of employment. Blair Bell, Williams and Cunningham have repeatedly observed nucleated red cells on the fifth day following the intravenous injection of lead.

(*f*) *Irregularity of size and shape of red cells*

Irregularity of size and shape of red cells was found in 15 per cent. of films examined. The irregularity generally affected size rather than shape, and cells of small size constituted the most common form of irregularity. Irregularity, when present, was nearly always associated with the presence of symptoms, or with a history of previous lead poisoning, or both: but by no means all cases presenting symptoms or a history of previous lead poisoning showed irregularity in the film.

II. CHANGES IN WHITE BLOOD CELLS

In striking contrast to the mass of literature on the subject of red cell changes in lead absorption is the almost complete absence of reference to the white blood cells. Such changes as have been noted in the literature have been either negative in character or so inconstant in occurrence as to be of little or no practical value. Several writers (*e.g.* Meyer) have pointed out that among workmen exposed to lead—as in the presence of many other toxic agents—there is apt to be a relative lymphocytosis. Biondi regarded eosinophilia and mononucleosis as of only slight relative importance in relation to plumbism. Brookfield noted a "tendency for the large mononuclears to show an increase from the normal 2 per cent. to about 5 per cent. of the total leucocyte count," and regarded this as being due to a stimulation of the reticulo-endothelial system; but he concluded that otherwise the findings as regards the leucocytes were quite negative. Blair Bell, Williams and Cunningham

found occasional evidence of relative lymphocytosis in patients treated by lead injections, and, fairly commonly, a slight increase in eosinophils, together with what they termed an increase of "streaky forms," but they summed the matter up by saying "there is nothing specific or definite in regard to changes seen in white cells, as there is in the red cells."

(*a*) *Neutrophil polymorphs*

The distribution of the proportion of neutrophil polymorphs found at the routine monthly differential counts of white cells is shown in Table XII.

Table XII

Percentage of differential count	Cases	Percentage of differential count	Cases	Percentage of differential count	Cases
20/25	1	45/50	44	70/75	41
25/30	1	50/55	71	75/80	11
30/35	9	55/60	91	80/85	4
35/40	17	60/65	97		
40/45	25	65/70	63		

There is lacking from the literature a standard distribution curve for normal subjects with which to compare this range, and haematologists differ widely in their definition of normal limits. Ehrlich's figure of 70–72 as the normal neutrophil percentage is generally regarded as too high. A mass of opinion (Medlar, Stitt, Oatway, and the recently published work of Price Jones) places the normal range at above 55–65 per cent., which is lower than Gulland and Goodall's 60–75 per cent., while still more recently Frimodt-Moller and Barton give 45–55 per cent. as the normal range and quote Von Bonsdorff's figure of 46 per cent. It is, therefore, difficult to draw any reliable conclusion from the polymorph distribution curve recorded in Table XII: probably it may be regarded as falling a little lower than normal, but, in any case it has not been found that the height of the polymorph percentage has, *per se*, any great significance.

Arneth counts were made on films from a few representative types of cases at each of the routine monthly examinations, and the results are summarised in Table XIII.

Table XIII. *Mean Arneth counts of workers showing varying degrees of exposure to lead.*

Case No.	Duration of employment at first examination	Previous history of lead poisoning	Risk at consecutive monthly examination	Mean Arneth counts I	II	III	IV	V	Condition during investigation
34	New starter	No	*AABBB*	2·2	25·3	51·5	18·2	2·8	No symptoms
35	New starter	No	*AACCC*	1·4	21·6	49·8	25·2	2·0	,,
99	3 months	No	*BBBBA*	0·6	16·0	41·8	34·8	6·8	Symptoms
23	3 months	Yes	*AACCB*	0·8	13·6	45·0	32·2	8·4	,,
64	4 months	No	*BBAAC*	1·4	17·6	43·4	33·2	4·4	No symptoms
11	8 months	No	*BBCCC*	1·6	22·8	46·2	25·4	3·8	,,
10	8 months	Yes	*BBCCB*	0·6	13·8	45·6	31·6	9·2	Symptoms
53	9 months	Yes	*BAABB*	0·2	14·2	41·2	38·2	6·2	,,
18	2 years	No	*BACCC*	0·6	15·4	47·2	30·4	6·4	No symptoms
32	3½ years	No	*ABAAB*	0·6	9·8	37·8	40·4	11·4	,,
79	7 years	Yes	*ABBBB*	0·6	8·6	40·0	37·4	13·4	Symptoms
52	10 years	Yes	*AACCC*	0·2	5·2	29·4	47·2	18·0	,,

The most striking feature of these results is the general shift to the right which they display; this is specially marked among workers with long exposure to lead. The Arneth count showed little variation from month to month, especially among the workers of older standing, and the shift to the right was noted at an early stage after the commencement of work in the industry as is evidenced by the following extract from the early record of Case No. 34, a new starter.

Table XIV

Month	Risk (see p. 297)	Arneth count I	II	III	IV	V
May	*A*	5	32	52	9	2
June	*A*	2	27	46	23	2
July	*B*	2	21	44	29	4

(*b*) *Eosinophils*

Table XV sets out the distribution of the proportion of eosinophils found at the routine monthly differential counts:

Table XV

Percentage of *differential count*	*Cases*	Percentage of *differential count*	*Cases*	Percentage of *differential count*	*Cases*
0–	165	3–	31	6–	7
1–	158	4–	8	7–	2
2–	94	5–	8	8–	1

These figures indicate that there is no high prevalence of eosinophilia among workers examined and a study of the individual case sheets shows that eosinophilia, when it does occur, is of no prognostic significance.

(*c*) *Basophils*

The proportions of basophil leucocytes found on differential count are summarised in Table XVI:

Table XVI

Percentage of differential count	Cases	Percentage of differential count	Cases
0–	420	2–	2
1–	51	3–	1

These figures, like the eosinophil readings, fall within normal limits and are of no special significance.

(*d*) *Lymphocytes and monocytes*

In the differential counts given in the case records lymphocytes are classified into large and small. Many cells of intermediate type were present, but lymphocytes were not described as large unless attaining to at least the size of a polymorph: frequently they were twice or thrice this size. The term "large lymphocyte" has been used to cover a certain range of cell type, the characteristic cell being typically lymphocytic, with a large deeply basophilic nucleus which often practically filled the cell. Other cells, again, had abundant

clear protoplasm and strongly resembled hyaline cells. They were frequently indented by red cells lying in apposition to them and often showed short pseudopodiae. Generally the protoplasm was structureless but occasionally it contained azure granules. The nucleus might be centrally or eccentrically situated, and might be indented on one or both sides, sometimes with production of a butterfly-like appearance suggesting that the cell was in process of amitotic division. In a few cells the nucleus was of still more complex shape.

The nucleus was always deeply stained and often presented a reticulate structure: occasionally a nucleolus was seen. In a few films there were seen cells of a loosely granular appearance without visible nucleus, and numbers of broken cells. Most of these were still recognisable but some were so degenerate as to beggar classification.

That the cells showing most increase were of lymphocytic origin was borne out by the presence of similar cells of all degrees of size from the normal small lymphocyte upwards. In a film from a worker of only three days exposure, where a count of 24 per cent. small lymphocytes was recorded more than half of these were larger than usual and the protoplasm more abundant. In a film from the same worker after 11 days exposure only about 8 per cent. of the 17·5 per cent. of small lymphocytes present could be described as of the usual size. By this time, too, enlargement of the lymphocytic nucleus had become a character of the film as distinct from a mere increase in amount of protoplasm, and in the films from workers of longer standing typically small lymphocytes were seldom seen so long as the worker remained well.

As "Monocytes" have been classified, in addition to cells of typical character, others of streaky appearance with complex nuclei somewhat resembling polymorphs but much larger in size and without definite granules. These are probably the same cells as were observed by Minot to be increased in poisoning by tetrachlorethane. Monocytes were found to account for less than 5 per cent. of all white cells in 81·3 per cent. of films examined: 17·1 per cent. of films fell between 5 and 10 per cent., while the remaining 1·6 per cent. gave monocyte readings between 10 and 15 per cent.

It is possible that in the case records the number of large lymphocytes has been slightly overstated and that of monocytes correspondingly understated, but it is felt that this is of little practical importance, since the purpose of the investigation is to find a method suitable for application by the works doctor, and precise differentiation between large lymphocytes and monocytes of the type described is admittedly a matter of great difficulty even for the expert haematologist. To overcome this difficulty it has been considered advisable, in discussing the practical application of the differential count, to combine the two types of cell, and the resulting figure, under the same large mononuclear lymphoid cells, is made the basis for the discussion which follows.

Table XVII sets out the proportion of the large mononuclear lymphoid cells in the differential count at the routine monthly examinations.

Table XVII

Month	Large mononuclear lymphoid cells, percentage in differential count											
	5–	10–	15–	20–	25–	30–	35–	40–	45–	50–	55–	60–
May	5	10	16	22	19	12	4	2	0	0	0	0
June	4	8	12	24	21	12	6	0	0	1	0	0
July	1	7	14	18	18	23	13	3	1	1	0	0
Aug.	2	3	5	12	23	10	17	7	7	7	3	2
Sept.	0	1	8	5	17	20	18	16	4	7	1	2
	12	29	55	81	98	77	58	28	12	16	4	4

When these figures are considered in conjunction with the falling risk from month to month it is apparent that there is an increase in these large cells corresponding fairly closely with the decline in risk.

Table XVIII. *Relationship between risk and proportion of large mononuclear lymphoid cells at routine monthly examinations.*

Month	Risk			Percentage of large mononuclear lymphoid cells		
	A	*B*	*C*	5–	25–	45–
May	46	44	0	53	37	0
June	31	57	0	48	39	1
July	30	33	36	40	51	2
Aug.	22	34	42	22	57	19
Sept.	15	38	47	14	71	14

It is found that the height of the large cell figure is related to the incidence of symptoms; and this relationship is much closer than that prevailing in the case of punctate basophilia. Table XIX shows the number of cases examined, grouped according to large cell count, with the number of workers in each group showing symptoms or the presence of a Burtonian blue line on the gums.

Table XIX

Percentage of large mononuclear lymphoid cells	Number examined	Number with				
		Headache	Constipation	Abdominal pain	Anorexia	Blue line
5–	41	13	16	11	7	11
15–	136	30	34	38	29	45
25–	175	18	34	23	18	39
35–	86	14	16	9	10	24
45–	28	1	2	1	0	8
55–	8	1	1	0	1	3

The relationship is brought out more clearly in Table XX, where the number of groups has been reduced and the incidence of symptoms shown as a percentage of the workers in each group:

Table XX

Large mononuclear lymphoid cells	Percentage of workers with				
	Headache	Constipation	Abdominal pain	Anorexia	Blue line
5–	24	28	28	20	32
25–	12	19	12	11	24
45–	6	8	3	3	31

With the notable correlation in respect of symptoms there is an absence of any relationship between the large cell count and the presence of blue line on the gums.

The relative increase in the proportion of large cells begins to appear very soon after commencing work in the industry, and while the element of individual variation plays some part, the average reading generally shows the total of monocytes and large lymphocytes to be approximately equal to the small lymphocytes before the end of the first week, while by the end of the second week the large cells usually outnumber the small in a ratio of fully 2 to 1. This ratio is subsequently maintained so long as the individual remains well: it is sometimes very much exceeded, notably where a reading follows passage from a heavy lead risk to one lighter. Many instances of this suggest themselves, especially where the risk has changed from *A* to *C* (see p. 297), and again, in the readings taken during August, just after the annual holiday. This latter factor explains why the proportion of large cells appears to be even higher in August than in September, though in the latter month fewer men were exposed to an *A* risk. The high upward swing of the large-cell curve after such a diminution of risk generally follows closely upon the change of exposure which causes it, though in cases where the previous exposure to lead has been exceptionally severe and long-continued the sharp rise may be delayed for a few weeks. In the case of the post-holiday rise, return to a major risk was speedily followed by a drop in the proportion of lead cells, though in the presence of a *C* risk the figure may remain high for some considerable time.

It has not been possible to ascertain how long the excess of large cells persists after cessation of exposure to lead: this probably depends on the extent to which the worker is "leaded." The proportion of large cells gradually falls away and after a month the small lymphocytes have been found to be as numerous as the large, even in the case of men who had been exposed to an *A* risk: with a *C* risk the fall may be more rapid.

Experience shows that for practical purposes the most useful guide to the workers' condition is the ratio prevailing between the large mononuclear lymphoid cells and the small lymphocytes. A fall in this ratio while the man is at work is to be regarded as a grave warning of impending disaster and an indication for the immediate removal of the man from the risk.

The eleven cases already referred to are of special interest in the illustration of this point.

Thus Case No. 92 in May gave a ratio of large lymphocytes and monocytes to small lymphocytes of only 10·5 : 23·5 following a severe attack of lead poisoning a few weeks previously. He was then on a *B* risk, and by the following month the ratio had improved slightly to 12·5 : 19. In July the improvement was much more marked (30·5 : 8·5), and on July 31st, following his holiday, the ratio was 33 : 6·5. On August 11th he was transferred to an *A* risk and the following day his ratio was found to be 33·5 : 5·5. On August 17th it was 28 : 4, and on August 25th 25 : 15. He remained free from

symptoms, but on September 5th his ratio had fallen to 17 : 15·5. He was removed from the *A* risk on the following day and examination on September 14th showed a marked improvement in the ratio to 41·5 : 7·5. With this improvement he stated that he felt much better in general health.

Case No. 90, too, had been off work on account of lead poisoning shortly before the date of his first examination, though in his case recovery had been more complete, as evidenced by his ratio 30 : 8·5. He was on an *A* risk and at the following monthly examination his ratio had fallen to 18·5 : 12. In view of his history he was transferred to a *B* risk and the ratio improved in July to 20 : 6·5. On July 31st, a few days after his holiday, it was as high as 47·5 : 6·5. On August 14th he was transferred to an *A* risk and on August 17th his ratio was 40·5 : 17·5. By August 25th it had fallen to 28 : 14 and on September 5th there was a sharp drop to 17 : 30·5. He was removed the following day to a *B* risk, but when seen on September 14th complained of headache and abdominal pain, with deterioration of his general condition. By this time, however, his ratio was again rising and his symptoms had disappeared when he was seen a fortnight later.

Case No. 91 had been engaged in the industry for four months when he was first examined, and had not suffered from lead poisoning. He had no symptoms, and his ratio was 32·5 : 11·5. He was on a *B* risk. In June he complained of headache and his ratio had fallen to 21 : 21. In July he was better though still continuing his *B* risk and his ratio had risen to 35·5 : 13·5. On July 31st, after his holiday, his ratio was 49 : 6, and on August 11th he was transferred to an *A* risk. The following day his ratio was 33·5 : 7, on August 17th it was 31 : 9. On August 25th it was rather lower at 19·5 : 8, and on September 5th he was found to be showing clinical deterioration. He complained of headache with constipation and his ratio had fallen to 10·5 : 16·5. The following day he was transferred to a *B* risk and on September 14th his symptoms had largely cleared up though he did not feel as well as he had done a month previously. His ratio was now 20·5 : 12 and on September 30th, along with marked clinical improvement, had risen to 28 : 11.

When first seen Case No. 98 had been employed as a burner for six months. He was on a *B* risk and gave no history of lead poisoning. He had no symptoms and his ratio was 28 : 7. In June he was off work on account of a foot injury, and when seen in July had a ratio of 30 : 6. On July 31st he was free of symptoms and his ratio was 37 : 11·5. On August 11th he was transferred to an *A* risk, and the following day his ratio was found to be 26 : 7. On August 17th it was 32·5 : 5 and on August 25th 25 : 9. He was next examined on September 5th when he was still free from symptoms but his ratio had fallen steeply to 15·5 : 28. He was transferred to a *B* risk the following day, but three days later had to lie off work on account of headache and colic.

The examinations afford numerous similar records amply establishing the value of the ratio in relation to clinical condition: it is now proposed to discuss

briefly this and the other findings in relation to the prevention of plumbism among shipbreakers.

III. Discussion

Previous investigators have agreed that any help which examination of the blood can give in the control of lead poisoning is to be derived solely from the red cells. Changes in the white cells have been dismissed unanimously as trifling in amount, inconstant, unspecific and of no practical value. Regarding red cell changes there is no such unanimity. Almost all the authorities have looked to punctate basophilia as the source from which help was most likely to be derived, though a few have insisted on the importance of such factors as total red cells and haemoglobin estimations and irregularity in size or shape of the cells in the estimation of clinical condition.

The attitude to punctate basophilia has varied widely. Nearly all authorities are agreed that its presence in any considerable amount is to be regarded as suggestive of lead absorption, though there is still dubiety about the height of the punctate count which may be accepted among lead workers as without grave significance. Lane regards any figures under 3000 punctate cells per million as being of little importance, though earlier observers considered a very much lower figure as the permissible limit. Sellers and Lane are inclined to regard average height of punctation among large groups of workers as indicating the degree of lead risk to which they are exposed, and some physicians have advocated exclusion from industry of workers whose punctate basophil count reached high levels of varying degree, even in the absence of clinical symptoms. Recent work has rather tended to throw doubts on the acceptance of these views. Gehrmann (1933), discussing the prevention of lead poisoning in industry, advocates, *inter alia*, careful and frequent medical examination, each examination consisting of search for subjective and objective signs of lead absorption, including complete blood examination, with a careful search for stippled cells. He considers the presence of punctate basophilia to indicate lead absorption, but thinks that the height of the punctate count is in no way indicative of the degree of absorption. R. Jones (1933) has pointed out that severe cases of plumbism of long duration with marked secondary anaemia may show very few basophilic cells till they are taken away from their exposure and effectual treatment results in a start being made towards recovery, and that in fact the percentage of reticulocytes may be below normal while the illness is most severe (as may also be observed in cases of pernicious anaemia). Böttrich (1932) made the same statement regarding punctate basophilia in cases of plumbism of long standing, and Davidson *et al.* (1933), investigating outbreaks of lead poisoning from the consumption of contaminated water, were unable to show any close parallelism between the incidence of punctate basophilia and the degree of contamination of the water, or the amount of lead excreted in the urine.

In considering the results of the present investigation it has to be borne

in mind that the lead risk of the shipbreaker is much more acute than that generally met with in industry. It may be that the problem studied here is radically different from that in other fields, such as the pottery or electric accumulator industries, and it may be that measures of medical control applicable to these industries are inapplicable to shipbreaking, and *vice versa*. Here, for instance, it has been found that every film examined showed the presence of punctate basophilia, and if this has no quantitative significance obviously any examination for punctation is of little or no value in the industry. It has now been found that in shipbreaking the height of the punctate count is not necessarily related to the development of clinical symptoms of plumbism. It is not uncommon to find a fall in punctation along with the development of clinical symptoms, while recovery from an attack of lead poisoning is frequently associated with a high wave of punctation. Nor does punctation increase with an increase in risk, for many instances have been noted of a great increase in punctation following a holiday or transfer from a heavier risk to a lighter. At the same time, there has been observed in some cases a more transitory rise in punctation for the few days immediately following transfer from a lesser risk to a greater, this being followed by a sharp fall in the continued presence of the heavier risk. In this connection it is of interest to recall the words of Russell in 1915: "I have often looked but without success for a case to illustrate the theory that the marrow reacts actively to small doses of lead and throws out punctate red blood cells, but if the dose is increased above a certain quantity it becomes paralysed and the basophil cells disappear from circulation. This is known to happen in chronic experimental lead poisoning, as was shown by Naegeli and Lutoslawski, and with other poisons Schmidt got similar results."

It has been pointed out that the type of punctation present offers little assistance, while polychromasia and reticulocyte counts have been found to correspond fairly closely with the counts of punctate basophilia. Nucleated red cells have been seen in association with widely varying clinical conditions, while irregularity of size and shape has been noted particularly following a breakdown in health. It appears to be a late manifestation, possibly of some value in assessing compensation claims but little or no help from the viewpoint of prevention, with which this investigation is primarily concerned.

In considering the white blood cells, a study of the granulocytes has been found to yield little of practical importance. There is no significant eosinophilia and the shift to the right which has been observed in the Arneth counts occurs early and in workers still comparatively well, though it attains its most striking degree among heavily-leaded burners of long standing.

Much more help has been derived from a study of the lymphocytic picture. Price Jones (1933) states that the large lymphocyte is generally accepted as a younger form of the small lymphocyte, and in this research it has been found that a relative excess of large lymphocytes is developed very soon after starting work as a burner. This excess is well marked after two or three weeks

in the industry, and so long as it continues to be a feature of the blood picture there seems little reason to apprehend any serious breakdown in health. The increased ratio of large lymphocytes to small appears to be of the nature of a defensive reaction. Biondi in 1922 gave it as his view that the hypothesis of a mechanism of humoral defence would probably have to give way to an immunity obtained through histogenesis.

Workers may differ in the ratio which they display under similar conditions of exposure, and it is difficult to lay down a hard and fast line of demarcation between safety and danger. It has been found in this research that so long as the ratio of large lymphocytes (plus monocytes) to small lymphocytes exceeds 2 : 1 the worker is not likely to develop symptoms. In the rare instances where symptoms are present under such conditions they are almost invariably of slight degree and seldom necessitate removal of the workman, though it may be desirable to transfer him to a lesser risk for a period. Any fall below this level is to be regarded as an indication for intensive supervision even in the absence of symptoms. With a ratio as low as 1 : 1 the worker ought certainly to be excluded from the industry; if symptoms have not already developed by that time their appearance is imminent. In practice the difficult cases are those with ratios falling between 2 : 1 and 1 : 1, and in these cases a decision as to exclusion may turn on the clinical condition of the workman, the presence of symptoms indicating removal, or on a fall in the ratio from one examination to another. Such a fall, though of only slight degree, is to be regarded as a grave warning.

The frequency of examination will depend chiefly on the severity of the risk involved. In relation to shipbreaking, it is suggested that the routine examination for risks *A*, *B* and *C* (see p. 297) might well be made at intervals of one, two and four weeks respectively, though in the case of the two minor groups it may be necessary in cases of special difficulty to introduce weekly observations.

Routine blood examinations cannot replace careful clinical supervision, but they can provide the physician with an instrument capable of anticipating clinical collapse. The determination of the ratio between large lymphocytes and small, now advanced as a preventive measure, does not imply any complicated technique. Its general application would help towards a reduction of the risk of lead poisoning which is at present so serious in the shipbreaking industry.

ACKNOWLEDGMENTS

We desire to express our thanks to Dr J. C. Bridge, H.M. Senior Medical Inspector of Factories, for his help in the preparation of this report, and to the Staff of the Laboratory for technical assistance.

REFERENCES

AUB, FAIRHALL, MINOT and REZNIKOFF (1925). Lead poisoning. *Analytical Reviews of General Med., Neurol. and Pediatr.* **4**.

BEHREND (1899). *Deutsche med. Wschr.* **25**, 254 (Vereins-Beilage No. 42).

BELL, WILLIAMS and CUNNINGHAM (1925). The toxic effects of lead administered intravenously. *Lancet*, ii, 793.

BIONDI (1922). Plumbism. *Internat. Labour Office Review*, **6**, 278. Geneva.

BLUMGART, H. L. (1923). Lead studies. VI. Absorption of lead by the upper respiratory passages. *J. Ind. Hyg.* **5**, 153–8.

BONSDORFF, A. VON (1927). Den vita blodkroppbildens betydelse vid lungtuberkulos før bodømande av sjukdomens aktivet och prognos. *Tuberkulose Laegemode, Copenhagen Transact*, p. 12.

BÖTTRICH (1932). Die Bedeutung der basophil getüpfelten roten Blutkörperchen, speziell für die Begutachtung von Bleikrankheiten. *Zbl. f. Gewerbehyg.* XIX. Jahrg. N.S. **9**, 3–28.

BROOKFIELD, R. W. (1928). Blood changes occurring during the course of treatment of malignant disease by lead, with special reference to punctate basophilia and the platelets. *J. Pathol.* **31**, 277.

DAVIDSON, L. S. P. *et al.* (1933). Lead poisoning in the north-east of Scotland. *Lancet*, ii, Aug. 12.

EHRLICH, P. (1885). Zur Physiologie und Pathologie der Blutscheiben. *Charité-Ann.* **10**, 136.

FRIMODT-MOLLER, C. and BARTON, R. M. (1933). A study of the differential count and sedimentation test in tuberculosis with a suggestion for an index figure summing up the information derived from them. *Tubercle*, **14**, 529.

GEHRMANN, G. H. (1933). Lead poisoning in industry. *Amer. J. Pub. Health*, **23**, 687.

GOADBY, K. W. (1909). A note on experimental lead poisoning. *J. Hygiene*, **9**, 122–33.

GULLAND and GOODALL (1925). *The Blood.* Edinburgh: Green.

HAWES, J. B. (1909). A study of reticulated red blood corpuscles by means of vital staining. Its relation to polychromatophilia and stippling. *Boston Med. and Surg. J.* **161**, 493.

JONES, PRICE C. (1933). *Blood Pictures.* Bristol: John Wright and Sons.

JONES, R. (1933). Estimation of basophilic cells (reticulocytes) in blood by examination of ordinary blood films. *U.S. Pub. Health Rep.* **48**, No. 633. Washington.

KEY, J. A. (1921). Studies on erythrocytes, with special reference to reticulum, polychromatophilia and mitochondria. *Arch. Int. Med.* **28**, 511.

KOENIG, H. (1910). Blutbefunde bei Neugebornen. *Fol. Haematol.* **9**, 278.

LANE, R. E. (1931). The rôle of punctate basophilia in the control of industrial plumbism. *J. Ind. Hyg.* **13**, No. 8.

LUTOSLAWSKI, quoted by RUSSELL (*infra*).

MACCORD, CAREY P. (1928). A new test for industrial lead poisoning. *Bull. U.S. Bur. of Labour Statistics*, No. 460. Washington.

MEDLAR, E. M. (1928). The leucocytic formula in the tuberculous considered as a reaction to damaged tissue. *Tubercle*, **9**, 218.

MEYER, E. and SPERONI, D. (1906). Ueber punktierte Erythrozyten. *Münch. med. Wschr.* **53**, 796–7.

MEYER, S. (1931). Ueber Blutveränderungen bei gewerblichen Schädigungen, *Arch. f. Gewerbepath. u. Gewerbehyg.* **2**, 526–57.

OATWAY, W. H. (1930). A correlation of the leucocytic interpretation of Medlar with clinical findings in tuberculosis. *Amer. Rev. Tub.* **21**, 786.

OLIVER, T. (1924). Lead poisoning. Sources, symptoms and treatment. *Industrial Health* (Kober and Hayhurst), Section 9, p. 421.

PAPPENHEIM, A. (1919). Morphologische Haematologie. II. *Fol. Haematol.* **24**, 86.
PINEY, A. (1928). *Diseases of the Blood.* London: Churchill.
RUSSELL, J. (1915). Basophilia in lead poisoning. *J. State Med.* p. 359.
SABRAZÈS, J., BOURRET and LEGER (1900). Les hématies à granulations basophiles dans le saturnisme expérimental et clinique. *J. de physiol. et de path. gén.* **2**, 941–6. Paris.
SCHILLING TORGAU (1911). Arbeiten über den Erythrocyten. *Fol. Haematol.* **11**, 572.
SCHMIDT (1907). *Arch. f. Hygiene*, **63** (quoted Russell, *supra*).
SCHOENFELD, J. (1921). Zur Frühdiagnose der Bleivergiftung. *Zbl. f. Gewerbehyg.* **9**, 3–7.
SELLERS, A. (1926). *A Report on the Value of Blood Examination in the Control of Lead Poisoning.* Private Report to Chief Medical Inspector of Factories.
STITT, E. R. (1927). *Practical Bacteriology, Blood Work and Animal Parasitology.* London: Lewis.
TANQUEREL: *vide* MEILLERE, G. (1903). *Le Saturnisme*, **1**, 89. Paris: Doin.
TELEKY, L. (1919). Die Frühdiagnose der Bleivergiftung. *Schrift. a. d. Gesamtgebiet der Gewerbehyg.* **5**, 1–27.

(*MS. received for publication* 2. VIII. 1934.—Ed.)