VALUE OF HAEMATOLOGY IN DIAGNOSIS OF CHRONIC PLUMBISM

BY

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Lead poisoning has been recognized since 200 B.C., when clinical symptoms were first described by Nikander (Major, 1945). Jaundice as a symptom was noted by John Huxham in 1759, and from that time it became perhaps the most common form of recognized industrial and accidental poisoning. During the past 30 years, owing to the improvement in industrial hygiene and to surveillance by factory inspectors and industrial medical officers, there has been a great decrease in the incidence in this country, and rarely does a clinical pathologist see the blood changes characteristic of chronic lead poisoning (Browning, personal communication, 1950). Therefore I feel that it is of value to report the following findings.

The Factories Act, 1937, Section 66, which deals with the notification of lead poisoning, leaves the diagnosis in the hands of the medical officer without any definite directions other than: "Every medical practitioner attending on or called in to visit a patient whom he believes to be suffering from lead poisoning contracted in any factory shall forthwith send addressed to the Chief Inspector of Factories . . . a notice . . ." Several medical practitioners to whom I have spoken on the subject interpret this as meaning that in the absence of findings such as Burtonian line, wrist-drop, colic, or encephalopathy one does not notify workers as being unfit because of their working conditions. The haematological findings set out below may perhaps give further guidance on the diagnosis of chronic plumbism, especially, for example, on the variations in the punctate basophil count, and provide a basic standard for the purposes of notification. Under the present regulations cases without clinical symptoms cannot be notified as lead poisoning, but a "toxic anaemia," recognized as such, would lead to further investigations, "toxic anaemia" being defined as any dyshaemopoietic disturbance.

Occupational Environment

Two sets of lead workers from separate factories were examined. The first (Group A) were employed in the following processes in the manufacture of lead paint: grinding, processing, paint-mixing, and dispatching of the products. It was in this group that the gross anaemias occurred in spite of the fact that the employees wear masks, have the extra allowance of milk daily—provided by regulation in the knowledge that high calcium diets prevent gross lead absorption (Tompsett, 1937)—and obey the elementary hygienic regulations appertaining to their trade.

The second group (B) work in a factory which manufactures lead ingots for use in printing works and lead for electricity cables, and also recovers lead from scrap (mainly from old batteries). There is no white lead processed in this concern. In this factory the atmosphere is kept damp by constantly flowing water on the floors, and highly efficient fume extractors are fitted over all furnaces and vats.

Methods

Standard methods were used for all the investigations, carried out by only two operators in order to eliminate, so far as possible, personal variations. Absolute haematological values were estimated, using Wintrobe tubes centrifuged at 3,000 r.p.m. for 30 minutes and calculated from the packed cell volume. Punctate basophilia estimations were calculated from a differential count on 3,000 red cells. As there has been much discussion on the variability of these estimations (Whitby and Britton, 1933; McFadzean and Davies, 1949) the following staining method was used. Films were dried in air, flooded with undiluted stain (Leishman) for one minute, diluted with twice the volume of buffered distilled water, pH 7, and allowed to stain for 10 minutes, then rinsed with the same buffered distilled water and dried in air. All films were stained with the same batch of stain. The films were examined microscopically, using a 2-mm. objective and $\times 8$ eyepiece. The haemoglobin was estimated, using an "EEL" photoelectric colorimeter calibrated with the Gibson-Harrison standard (B.D.H.) of 16 g. haemoglobin per 100 ml. Reticulocyte counts were done as recommended by Dacie (1950), and the red-cell fragility test was a modified method of his technique.

Haematological Findings

The gross haematological findings are set out in Tables I and II. If no abnormality was noted at the preliminary full blood count and examination of a stained film, reticulocyte counts and red-cell fragility tests were not made.

TABLE I.—Group A

Case No.	Age	Occupation	Years Occpd.	Date	100% = 16 g%		R.B.C. mill.	P.C.V. %	M.C.V. μ^3	M.C.H. $\mu\text{g.}$	M.C.H.C. %	Retics. %	Punctate Basophilia %
					Hb	g. %							
1	28	New worker		7/11/50	86	13.8	4.3	38	88	32	36		Nil
2	50	Paint mixer	4	7/11/50	86	13.8	4.2	31	74	33	44		"
3	39	Grinder	15	20/10/50	56	9.0	3.4			26		1.5	2.4
				2/11/50	59	9.4	3.4	30	88	28	31		3.1
				12/1/51	71	11.4	4.0	37	92	28	31	1.0	0.05
4	50	Grinder	16	7/11/50	64	10.2	3.5			30		3.3	3.2
				24/11/50	68	10.9	4.7	34	72	23	32	3.0	2.0
				12/1/51	74	11.8	4.4	39	88	27	30	1.2	0.4
5	50	Processor	5	7/11/50	85	13.6	4.6			30		1.2	0.23
				7/11/50	78	12.5	4.1	28	68	30	44		0.2
				23/1/51	83	13.3	4.7			28			0.3
6	43	Grinder	20	20/10/50	80	12.8	4.3			30		2.0	0.03
				7/11/50	95	15.2	5.0	41	82	30	37		0.06
				23/1/51	84	13.4	4.4			30			0.5
7	34	Dispatch	5	20/10/50	63	10.1	3.6			28		1.2	0.26
				7/11/50	75	12.0	4.6	41		28	30		
				23/1/51	79	12.6	4.1			30			0.14
8	52	Processor	25	20/10/50	61	9.8	3.9			25		5.5	5.0
				7/11/50	61	9.8	4.0	38	95	24	26		3.4
				12/1/51	71	11.4	4.7	38	81	24	30	10.0	1.3

TABLE II.—Group B

Case	Years in Lead	Occupation	Hb %	R.B.C. mill.	W.B.C.	Retic. %	Stippling %
A	2/52	Scrap sorter	78	4.2	14,400	1.5	Nil
B	4½	Moulder	80	4.1	9,600	1.0	0.2
C	3	Carpenter	86	4.9	7,800	1.2	0.5
D	3/12	Blast charger	75	5.3	13,600	2.0	0.45
E	3	Scrap sorter	73	3.8	9,000	1.6	0.25
F	6/52	Labourer	83	5.1	6,600	1.2	Nil
G	4	Electrician	86	5.0	6,000	1.0	0.062

Punctate basophilia were present to a varying degree, but did not appear to be related to the duration of exposure or the type of work (Fig. 1).

Hypochromic Anaemia.—It has been recognized by various observers that the hypochromia is common whilst exposure is heavy, and is usually accompanied by stippling (Lane, 1938; Kemp, 1947), without which it is impossible to state the cause of the anaemia. The red-cell count should be taken as a guide to the general health of the worker, and if anaemia is present it would be wise to remove him from exposure to toxic agents.

FIG. 1.—Showing stippling of red cells.

No obvious abnormality was found in the differential counts of these men save in a new entrant to the factory (see Table II) who complained of colicky abdominal pain one morning whilst at work and had an acutely inflamed appendix removed shortly after. This emphasizes the importance of an open mind when dealing with industrial workers. Taleky (1946) states: "I have seen about a dozen appendicectomies performed on lead-poisoned persons because lead was not recognized in the occupation. On the other hand, one sees appendicular abscesses diagnosed as lead poisoning because the patient was a lead worker."

Red-cell Fragility.—Variations in red-cell fragility have been reported in cases of lead absorption (Whitby and Britton, 1933), but in my series (Group A) the quantitative fragility curves (Fig. 2) were altered in parallel with the increase in the basophil count, and showed varying

FIG. 2.—Quantitative fragility curve.

degrees of decreased fragility. In no case did we find an increased fragility even to a slight degree. An average normal curve and a curve taken from a case of familial acholuric jaundice are incorporated in the graph for comparison.

Marrow Findings.—Case 3 was admitted to hospital because of a minor accident, and he allowed a marrow puncture to be performed from the iliac crest. The films were stained in the usual way. The total nucleated count was 100,600 (proerythroblasts 2%, early normoblasts 6%, normoblasts 12%, punctate normoblasts 7.5%, neutrophil myelocytes 5.5%, eosinophil myelocytes 1%, metamyelocytes 5.5%, eosinophils 1.5%, monocytes 1%, lymphocytes 12%, segmented polymorphs 46%). Basophilic stippling of the erythrocytes in this marrow was found to be 28,000 per million erythrocytes. The peripheral blood picture is that dated November 2, 1950. A normoblastic hyperplasia of the marrow was demonstrated along with stippling of normoblasts and erythrocytes as observed by other workers (Leitner, 1949), but no evidence of increased karyorrhexis was seen (Kienlé, 1943).

Other Haematological Findings.—Polychromasia, anisocytosis, and poikilocytosis were observed in the blood pictures of those showing the most severe anaemias. The reticulocyte count was repeated on several occasions along with the basophilic count, with which it appeared to have a direct relation. The mean corpuscular volume was low or normal in most cases.

Urine

Lead estimations were carried out on the urine of six workers in Group A showing punctate basophilia. Table III shows that those with the greatest haematological changes had the most lead in their urine. The estimations were repeated on the three cases showing abnormally high volumes after an interval of three months away from risk of lead absorption, and blood pictures were repeated at the

TABLE III

Case No.	Lead in Urine (mg./litre)	
	24/11/50	15/2/51
3	0.21	0.05
4	0.38	0.1
5	<0.1	—
6	<0.1	—
7	<0.1	—
8	0.57	0.07

same time (January 1, 1951). Although the urinary lead content had fallen to what may be regarded as normal limits, the blood pictures had not shown much improvement, particularly in haemoglobin level (Table III).

Other Findings

The only patient in Group A not wearing dentures had a definite blue line on his gums in the characteristic manner, about 1 mm. from the gum margin, along with a fairly extensive dental sepsis.

Case 8, when seen on January 12, 1951, showed clinical evidence of mild jaundice along with a reticulocyte count of 10%, serum bilirubin 1.6 mg. per 100 ml., and Coombs test nega-

FIG. 3.—Showing blue line on gums.

tive. His jaundice did not deepen, and had disappeared at the end of a further three weeks: this was perhaps the manifestation of a mild haemolytic crisis, the only one noted during this investigation.

Discussion

A relation was noted between the degree of punctate basophilia and the decrease in red-cell fragility in this series, contrary to the usual views in the literature (Whitby and Britton, 1933). The results of the present study suggest that there is still a definite risk of occupational anaemia in the lead worker in this country, although there would appear to be no direct relationship between duration of exposure and the degree of toxic effect found; one may therefore presume that personal idiosyncrasy to lead exposure plays a large part. It should be noted that in the factory employing the Group B workers, in whom there was no lead poisoning, the floors are subject to constant spraying with water. This supports the observations of Rodier (1948) that miners engaged in working processes where the atmosphere was damp were less liable to lead intoxication; he took as his standard for lead intoxication a basophilia of 0.25 per thousand erythrocytes. Faure (1949) surveyed lead miners in Morocco, and stressed that not one of the wash-house men was affected; plumbism was here taken to be present if one or more basophilic red cells were present in 10 microscopical fields. The demonstration that all the workers in Group A showed evidence of intoxication suggests that other cases may be present in similar factories throughout the country. None of these workers had been notified as a case of lead poisoning before this investigation, as none had shown any obvious clinical symptom resulting from their occupation. It suggests that a stricter haematological control of those who work in contact with lead should be observed, using the evidence of a hypochromic anaemia and the presence of punctate basophilia, with or without decreased fragility, as diagnostic aids. It is necessary to keep in mind the other causes of punctate basophilia, such as phenylhydrazine poisoning in the treatment of polycythaemia, cirrhosis of the liver, haemolytic anaemias, etc., but the differential diagnosis should present no gross difficulty in the presence of collateral evidence and a routine haematological investigation.

The men state that when they are paid as piece-workers their main aim is to do as much as possible in the shortest time. In so doing they find that the wearing of masks and the taking of full precautions cuts down their output, and therefore the temptation to be careless in such matters is great. It would seem reasonable to suggest that further prophylactic measures could be taken by (a) abolishing piece-work in the lead industry; (b) notification of and removal from exposure of those workers showing toxic manifestations; and (c) exercising stricter haematological control of the lead industry, especially by the punctate basophilic count.

Summary

Blood pictures in two groups of lead workers are presented for comparison and observation.

The presence of punctate basophilia does not appear to be related to type of work or duration of exposure.

Decreased fragility curves were demonstrated in those patients more severely affected.

A hyperplastic normoblastic marrow is described.

Estimations of total lead in urine revealed that the patients showing gross haematological changes had the highest urinary lead levels.

A plea for stricter ruling on haematological control of lead workers is tentatively put forward, and abolition of piece-work in the lead industry is suggested as a further preventive measure.

Addendum

Since this work was completed 16 further lead workers have been examined, and two showed what may be regarded as characteristic features of chronic plumbism.

Case Y.—R.B.C., 4,300,000; Hb, 77% (12.32 g.); M.C.V., 92 μ^3 ; M.C.H., 28.65 $\mu\mu\text{g}$; punctate basophilia, 0.5%; reticulocytes, 5%; red-cell fragility decreased (90% at 0.3 saline, 10% at 0.25 saline). This worker was thought to have chronic plumbism.

Case Z.—This man, a worker in lead for six years, complained of a yellowish tinge developing in his skin since January, 1951; three months previously he had complained of abdominal pain. His general practitioner sent him to the laboratory for investigation, and the haematological findings were as follows: February 26: Hb, 63% (10.08 g.); R.B.C., 3,700,000; W.B.C., 9,200 (polymorphs 85%, eosinophils 1%, lymphocytes 14%); five punctate normoblasts seen in peripheral blood film; punctate basophilia, 5.9%; reticulocytes, 12%; Coombs test, negative; van den Bergh indirect, 1.5 mg. per 100 ml.; red-cell fragility 90% at 0.3 saline, 10% at 0.45 saline. Marrow puncture revealed a hyperplastic normoblastic marrow, with neutrophil polymorphs 19.5%, small lymphocytes 2.5%, monocytes 1.5%, metamyelocytes 4.5%, myelocytes 5%, eosinophil myelocytes 1%, erythroblasts 1%, normoblasts 45%, karyorrhectic normoblasts 4%, normoblasts showing punctate basophilia 16%. This patient had a blue line on his gums (Fig. 3).

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BACT. COLI IN INFANTILE DIARRHOEA

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Following the earlier suggestions of Beavan (1944) and Bray (1945), the isolation of certain serological strains of *Bact. coli* from the faeces of infantile diarrhoea has been reported from the United Kingdom by Giles and Sangster (1948), Giles *et al.* (1949), Taylor *et al.* (1949), and Kirby *et al.* (1950); from France by Buttiaux *et al.* (1951); from Germany by Braun and Henckel (1951); from Sweden by Laurell *et al.* (1951); from Australia by Williams (1951); and from the United States of America by Neter and Shumway (1950).

Attention has been focused primarily upon epidemic outbreaks, especially among the newborn, in whom these organisms have been found with remarkable consistency.