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INDUSTRIAL ACCIDENTS AND HYGIENE SERIES

A NEW TEST FOR INDUSTRIAL LEAD POISONING

THE PRESENCE OF BASOPHILIC RED CELLS IN LEAD POISONING AND LEAD ABSORPTION

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U. S. BUREAU OF LABOR STATISTICS

NO. 460 WASHINGTON APRIL, 1928

A NEW TEST FOR INDUSTRIAL LEAD POISONING[1]

A Nontechnical Statement of the Problem and a Summary of Principal Findings

The danger of lead poisoning is so widespread in industry and the action of lead as an intoxicant is so insidious that any method by which the early effects following lead exposure may be detected prior to any disability would be of the greatest worth wherever lead is a hazard.

In the past the diagnosis of lead poisoning has generally depended upon the presence of definite and easily recognizable symptoms, with the result that the disease has become well established before measures to correct the condition are instituted. Therefore the incidence of lead poisoning remains high, notwithstanding the fact that the mode of entry of this toxic substance into the body is well known, that the distribution of lead after absorption is well established, and that the factors influencing the absorption, deposition, and excretion of lead are fairly well understood. This is due to the fact that there has been lacking any suitable index of lead absorption among workers who are exposed to the hazard but who have not developed obvious manifestations of the disease.

A simple laboratory method which would reveal the degree of lead absorption in the individual and thus permit the institution of preventive measures before actual lead poisoning has taken place would be of great value in the prevention and control of the disease. Such a test was proposed in a preliminary report by McCord, Minster, and Rehm in 1924,[2] the proposed test being based on the appearance in the blood stream of immature red cells. The present report is based upon a continuation of the preliminary study, and the purpose of the investigation is to determine the extent of usefulness of this test in detecting lead absorption and lead poisoning in workers and others, and as a measure of the extent of the lead hazard in different occupations and industries.

[1] Collaborating in this work are Dorothy K. Minster, A. B.; William Paul, B. S.; Elizabeth M. Schwebel, Ch. E.; H. G. Higginbotham, M. D.; Alfred Friedlander, M. D.; Charlotte Wiedemer, M. D.; Susie Friedlander, A. B.; all members of or consultants to the Industrial Health Conservancy Laboratories.

[2] "Basophilic aggregation test in lead poisoning," by C. P. McCord, D. K. Minster, and M. Rehm, in Journal of the American Medical Association, May 31, 1924, vol. 82, p. 1759.

The report includes a technical description of the production of the immature red cells, of the technique followed in making the blood counts, and an account of the clinical and laboratory materials utilized. The study includes the examination of more than a thousand persons, some of whom were exposed to lead while other groups were used as controls in checking the results of the tests.

Following is a brief summary of the conclusions reached as a result of the study, a more complete statement of the results being carried at the end of the report.

The number of immature red cells in the blood which contain basophilic substance—that is, substance which is stainable by certain dyes—is increased above normal limits in various pathologic states, including lead intoxication, benzol and arsenic poisoning, certain types of anemias, at times in acute infections, and in many other conditions; but in a person exposed to lead and in the absence of other conditions presenting high basophilic red cell counts such a condition may be accepted as indicative of lead absorption or lead poisoning.

Cases of definite lead poisoning ordinarily present basophilic red cell counts ranging from 7,000 to 50,000 per cubic millimeter of blood, although the counts, rarely, may fall below 7,000 or may exceed 100,000. It is possible that very high basophilic red cell counts—that is, in excess of 50,000—may be present without symptoms of clinical lead poisoning, but cases of poisoning are prone to develop among a group presenting such high basophilic red cell counts.

Workers exposed to lead who present basophilic red cell counts in excess of 6,000 to 7,000 should be regarded, in the absence of other conditions productive of such increased counts, as potential lead-poisoning cases and as such should be subjected to treatment.

The use of this test has revealed not only an extensive absorption of lead among workers in those industries and those departments with a known lead hazard, but also among office workers, clerks, etc., in these industries who in the past have commonly been considered as unexposed. This is especially true if the lead hazard is present in the form of lead dust.

The basophilic red cell counts do not, however, stand in any constant relation to the hemoglobin percentage, to the total red or white count, or to the late effects of lead poisoning, such as wrist drop.

IMPORTANCE OF LEAD POISONING

Lead poisoning continues to be the outstanding severe occupational disease in the United States. Although the report of Hoffman [3] indicates a diminishing death rate from lead poisoning, it should not be maintained that the incidence of this disease has reached negligible numbers. For many reasons mortality statistics are of little value in a study of lead-poisoning incidence. One outstanding reason is that rarely does a lead-exposed worker die of lead poisoning which is uncomplicated and typical. The im-

[3] U. S. Bureau of Labor Statistics Bul. No. 426: Deaths from lead poisoning, by F. L. Hoffman. Washington, 1927.

mediate cause of death is usually some chronic lesion to which lead absorbed over a long period may have contributed, but the physician in making out the death certificate is prone to place emphasis on the apparent cause of death, such as the nephritis, the cardio-vascular diseases, etc., without associating lead as a primary producing factor.[4] Lead mortality rates are so low as to serve only remotely as an index of lead morbidity. For every single death from lead not fewer than 50 cases of nonfatal lead poisoning are believed to occur. On this basis, Hoffman's [3] figure of 142 deaths in the United States registration area in 1924 (the latest figures available) would indicate a yearly minimum of 7,100 lead-poisoning cases in this same area. In Ohio alone, since the application of the occupational disease act (July 1, 1921) up to January 1, 1927, 907 cases of industrial lead poisoning have been reported, including 37 deaths. Eight hundred and forty-two of these claims entailed awards from the State fund for compensation and medical care of $287,760, together with a loss of 277,112 days.[5] To this number of cases of clinical lead poisoning occurring in Ohio, and those estimated for other portions of the registration area, must be added the larger number of cases of "lead absorption" common to both industry and the general population.

A circumstance favorable to the perpetuation of a high lead poisoning morbidity rate grows out of the fact that most diagnoses are dependent upon the actuality of plumbism, rather than upon the detection of the lead-absorption stage preceding lead poisoning. Much confusion now exists as to the relation between "lead absorption" and "lead poisoning." "Lead absorption" has come to be accepted by some as synonymous with "mild lead poisoning," reserving the term "lead poisoning" for the profound lead episodes, such as encephalitis. This interpretation has led to evasion in reporting such cases in some States requiring the reporting of "lead poisoning," but not specifying "lead absorption." More nearly exact definitions of several commonly used terms are as follows:

I. *Lead ingestion without absorption.*

Lead may enter the alimentary tract without concomitant absorption and leave the body in the feces in the same amounts. No absorption, no symptoms, no lead in the urine, no blood changes.

II. *Lead absorption.*

Lead may enter the body through any portal and be retained for indefinite periods without subjective manifestations. The quantity of lead so absorbed may be sufficient to produce lead poisoning under conditions favoring its development, such as acidosis. Obviously, lead poisoning is always preceded by a stage of lead absorption, but lead absorption is not always followed by lead poisoning. In this stage lead may be demonstrated in feces and urine. Blood changes may occur. A lead line may be present in lead absorption.

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[3] U. S. Bureau of Labor Statistics Bul. No. 426: Deaths from lead poisoning, by F. L. Hoffman. Washington, 1927.
[4] U. S. Bureau of Labor Statistics Bul. 120: Hygiene of the painters' trade, by Alice Hamilton, M. D. Washington, 1913.
[5] Industrial Commission of Ohio. Division of Safety and Hygiene. Special Bulletin No. 1. Columbus, Ohio, 1927.

III. *Lead poisoning, or lead intoxication.*

When absorption of lead is associated with any symptoms commonly accepted as characteristic of lead poisoning, lead absorption has passed over into clinical lead poisoning.

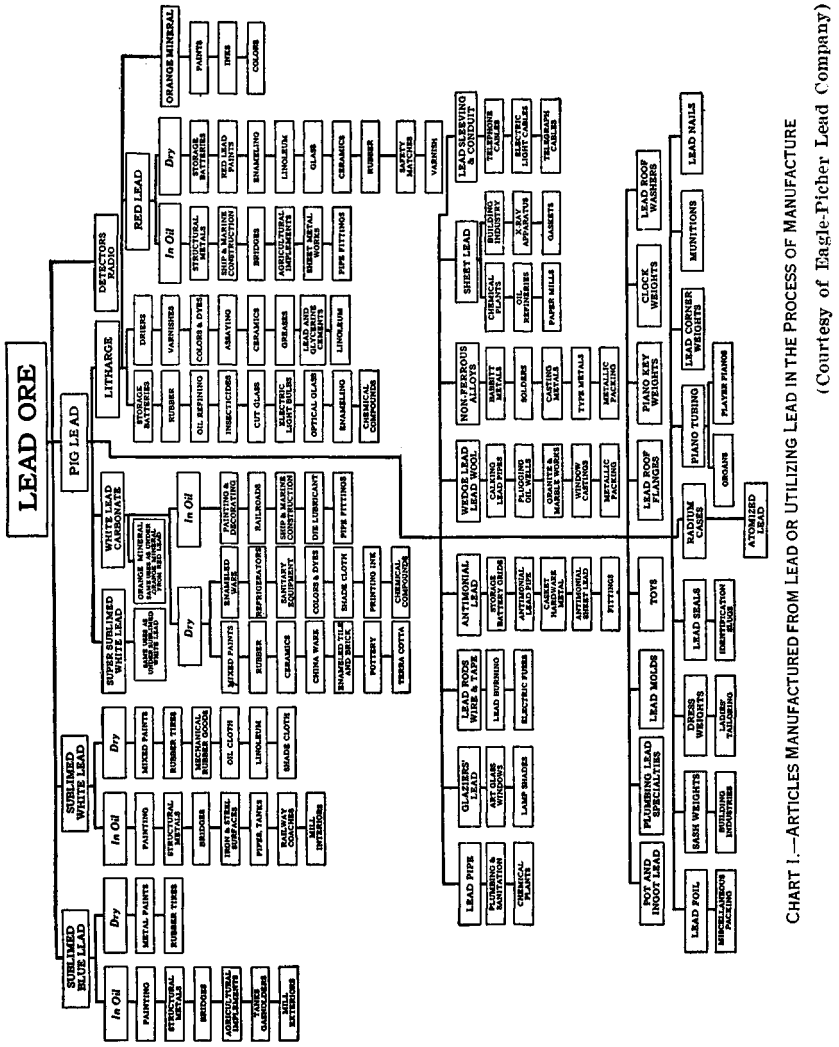

CHART 1.—ARTICLES MANUFACTURED FROM LEAD OR UTILIZING LEAD IN THE PROCESS OF MANUFACTURE

(Courtesy of Eagle-Picher Lead Company)

Obviously, lead absorption is to be recognized as a necessary stage between lead exposure and clinical lead poisoning. If control has failed in the elimination of exposure, the next point of attack is during the stage of absorption, when the worker is still at work and free from symptoms. Every person absorbing lead in any appreciable amounts is a potential case of lead poisoning. Given a sufficient exposure, there is in all likelihood no freedom from susceptibility to lead absorption or lead poisoning. However, lead is not

equally absorbed by all persons equally exposed and equal absorption of lead by a group of workers does not lead to similar responses, either as to severity or as to the time of manifestations among the different individuals. Because of these circumstances it becomes highly desirable to have available some simple laboratory procedure through the application of which lead absorption and the fluctuation of the rate of lead absorption in the individual may be detected.

Such a test was proposed in a preliminary report by McCord, Minster, and Rehm, in 1924.[2] This proposed test is based on the appearance of immature red cells in the blood stream. This present report is based upon a continuation of the preliminary study. The purpose of this investigation is to determine the extent of usefulness of this test as previously employed and as subsequently modified, as: (*a*) A quantitative index of lead absorption, (*b*) an index of imminent plumbism, (*c*) an index of actual lead poisoning, (*d*) a measure indicative of the extent of the lead hazard in particular processes or industries.

IMMATURE RED CELLS

The production of red blood corpuscles (erythrocytes) is, in normal adult human life, a bone marrow function. The endothelium lining the sinuses of bone marrow is the tissue from which the primitive red cells spring. Prior to their entry into the blood stream, these cells undergo a series of modifications such as the acquiring of hemoglobin and the loss of nuclei. The bone marrow remains the site of this maturation. Under normal conditions, the blood stream, though intimately in contact with these developing erythrocytes does not dislodge them until maturity is attained. It is improbable that the delivery of developed red cells is in anywise dependent upon any activity of the cells themselves, such as ameboid movement, although the quality of adhesion of immature red cells as described by Key[6] may be a factor of red cell retention in bone marrow. The growth pressure arising from a growing tissue confined in an unyielding environment finds least resistance in the blood stream and thus leads to extrusion of the more mature red cells lying at the periphery of developing masses. These erythrogenetic centers commonly present the least mature cells at the center with movement outward as maturation progresses. Through such controlled processes as here briefly described, an orderly steady flow of formed red cells is secured for normal life.[7]

When, however, the bone marrow or other portions of the body are subjected to abnormal circumstances this well-balanced delivery of red cells into the peripheral circulation is upset and cells not yet mature may find their way, in large numbers, into the general circulation. A stimulation of the bone marrow only slightly in excess

[2] "Basophilic aggregation test in lead poisoning," by C. P. McCord, D. K. Minster, and M. Rehm, in Journal of the American Medical Association, May 31, 1924, vol. 82, p. 1759.

[6] "Studies of erythrocytes, with special reference to reticulum, polychromatophilia, and mitochondria," by J. A. Key, in Archives of Internal Medicine, November, 1921, vol. 28, p. 511.

[7] "The pathological physiology of blood cell formation and blood cell destruction," by C. K. Drinker, in Oxford Medical Looseleaf, Vol. II, p. 509; "Studies of living human blood cells," by F. R. Sabin, in Bul. of the Johns Hopkins Hospital, September, 1923, vol. 34, No. 391, p. 277; "Experimental bone marrow reactions: III, Polycythemia, normoblasts, and erythrocytic hyperplasia of the bone marrow produced by gum shellac," by G. L. Muller, in Journal of Experimental Medicine, May, 1927, vol. 45, No. 5, p. 753.

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of normal may be met by an increased delivery of red cells in a state of essential maturity. An increased stimulus, however, leads to a delivery of cells progressively less mature, until under the most direful conditions if any cells at all enter the blood stream they may be so little removed from the endothelium as to possess no hemoglobin.

The stimuli to which bone marrow responds are numerous, but the mechanism through which response is secured is uncertain in some circumstances. When hemorrhage occurs, immature red cells are immediately found to be in the blood stream and continue to appear until the emergency no longer exists. In divers anemias, immature cells commonly are detectable. The absence of immature cells under such conditions is an unfavorable aspect.

Ultra-violet irradiation induces a similar response. Neoplasms involving the bone marrow may effect an abnormal blood picture through pressure. Rarely, a quickly generated leucocytosis has as a concomitant immature red cells in the blood stream.[8] Elvidge[9] has secured an outpouring of immature red cells following intravenous injections of quartz particles. Lehmann[10] produced similar results with calcium carbonate, coal, and cement dust administered through inhalations. Paul, Friedlander, and McCord[11] found that benzol, long known to exert an action on bone marrow, led to altered blood pictures because of the extrusion of unripened blood cells from the bone marrow. Similar results were obtained by Muller[8] with colloidal silver, india ink, shellac. Lead is also capable of inducing a marked increase in the numbers of immature cells in the peripheral blood (McCord, Minster, and Rehm[2]). It thus appears that among other stimuli, bone marrow may respond to (*a*) physiologic stimulation, (*b*) pressure stimulation, and (*c*) toxic stimulation.

CHARACTERISTICS OF YOUNG ERYTHROCYTES

Such young red cells as may be found in the peripheral circulation have qualities or markings that serve to distinguish them from mature cells.

The nucleated red cell is characteristic of marked immaturity.[12]

The immature cell is more resistant to heat distortion than mature cells.[13]

The young cells are usually larger than the older cells in the same preparation.[14]

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[2] "Basophilic aggregation test in lead poisoning," by C. P. McCord, D. K. Minster, and M. Rehm, in Journal of the American Medical Association, May 31, 1924, vol. 82, pp. 1759–1763.

[8] "Experimental bone marrow reactions: III, Polycythemia, normoblasts, and erythrocytic hyperplasia of the bone marrow produced by gum shellac," by G. L. Muller, in Journal of Experimental Medicine, May, 1927, vol. 45, No. 5, p. 753.

[9] "Foreign particles, the reticulo-endothelial system and anemia," by A. R. Elvidge, in Journal of Pathology and Bacteriology, 1926, vol. 29, No. 4, p. 325.

[10] "New experimental investigations on the value of basophilic granulated erythrocytes in the early diagnosis of lead poisoning," by H. Lehmann, in Archives of Hygiene, 1926, vol. 96, p. 321, abstract in Journal of Industrial Hygiene, February, 1927, vol. 9, No. 2, p. 34.

[11] "Basophilic material in benzol poisoning," a preliminary report, by W. D. Paul, A. Friedlander, and C. P. McCord, in Journal of Industrial Hygiene, May, 1927, vol. 9, No. 5, p. 193.

[12] "Properties of young erythrocytes in relation to agglutination and their behavior in hemorrhage and transfusion," by R. Isaacs, in Archives of Internal Medicine, February, 1924, vol. 33, p. 193.

[13] "Resistance of immature erythrocytes to heat," by R. Isaacs, B. Brock, and G. R. Minot, in Journal of Clinical Investigation, June, 1925, vol. 1, p. 425.

[14] Biffi. H.: In Bul. Soc. Med. Ann., 1908, vol. 79, p. 8. (Quoted from Key.)

The immature cells are more resistant to crenation than more mature cells.[6]

The hemoglobin content is less in developing cells.[6]

A tendency appears to exist among premature cells to adhere one to another, and to white cells.[6]

The incompletely developed cell consumes oxygen, while the adult erythrocyte consumes none or much less oxygen.[15]

The specific gravity of immature red cells is less than that of adult cells.[16]

Seyfarth[16] believes that immature red cells are given to poikilocytosis more readily than mature cells.

Immature red cells contain basophilic material.[6]

BASOPHILIC SUBSTANCE IN IMMATURE RED CELLS

With any cells having so many distinguishing markings as indicated above, it should prove readily possible to devise some test to detect their occurrence.

Of all these characteristics of young cells, the presence of basophilic substance appears to be most constant, and the one that lends itself best to the demonstration of immature cells.

The exact nature of basophilic material is not known. It is vaguely described as a lipoidal derivative of the cell nucleus, as a rest of the primary protoplasm, as a product of nuclear pyknosis. Earlier it was thought that this substance was peculiar to blood corpuscles. Subsequently, it has been shown to have a wide distribution in body tissues. In the case of red blood cells, it is a constituent only of immature cells and of the pathologic, misbuilt types of cell such as is found in hemolytic jaundice.[16] Prior to birth, a period exists in which all red blood corpuscles in the fetal circulation are basophilic.[17] At birth the percentage of basophilic substance in the red cells of human beings is still far above the normal for adults. This number quickly falls during the first 10 to 15 days of post-uterine life and by the end of the first month of life the basophilic containing cells in the peripheral circulation are scant.

Seyfarth,[16] who describes basophilic material under the term "substantia granulo filamentosa," outlines the morphology of basophilic-containing cells as follows:

> Vital stained bone marrow of the embryo and the newborn and smears made during life (by sternum puncture) of the marrow of man and animals show that the earliest form of red cell, the hematocytoblast, which contains absolutely no hemoglobin, shows no perceptible substantia granulo filamentosa. As soon as the slightest amount of hemoglobin is perceivable in the protoplasm of the cell one can see the first appearance of the vital granules always situated very close to the nucleus. Other erythroblasts show larger or smaller vital granules, but always in close proximity to the nucleus. Again in other

[6] "Studies on erythrocytes, with special reference to reticulum, polychromatophilia, and mitochondria," by J. A. Key, in Archives of Internal Medicine, November, 1921, vol. 28, p. 511.

[15] "Oxygen consumption of human erythrocytes," by G. A. Harrop, in Archives of Internal Medicine, June, 1919, vol. 23, p.745. (Quoted from Key.)

[16] "Experimentelle und klinische untersuchungen über die vitalfarbbaren erythrozyten," by C. Seyfarth, in Folia Haematologica, Band 34, Heft 1 zu 7. April, 1927 (Archiv).

[17] "Reticulation and age of red blood corpuscles in normal and anaemic mice," by S. B. De Aberle, in Anatomical Record, March, 1927, vol. 35, No. 1, p. 30 (abs.). See also footnote 16.

cells having a smaller nucleus it is not possible to see any protoplasm as usually seen in these early forms. This protoplasm is obscured by a heavy wall of substantia granulo filamentosa clothing the nucleus. In some of these cells it is possible to notice a slight excrescence of hemoglobin from the substantia. Other erythroblasts that have smaller nuclei and, therefore, are older forms, show a zone of hemoglobin about the wall of the substantia. In the riper erythroblasts and in the normoblasts the zone of hemoglobin is broader while the wall of substantia about the nucleus becomes a little lighter, broader and less compact. At this time the granules and threads are discernible. Most of the normoblasts show a smaller nucleus surrounded by a wall of substantia that shows many gaps. And, later, one sees forms that look like the serrations of a broken crown sitting on the nucleus * * *. As the cell ripens, this wall of substantia becomes lighter, smaller granules are seen and also thread forms. These break up to small granules spread mostly at the margin of the cell, and when most of the substantia has disappeared there are left only these fine granules at the margins. The end result is a red cell fully ripe and free from all vitally staining substance.[18]

When basophilic material is present it may be observed in a variety of forms, some of which are undoubtedly the result of physico-chemical manipulation and do not represent native states of this substance. Polychromasia, reticulated cells, punctate stippling, substantia granulo filamentosa, basophilic aggregations, mossy cells, etc., are but different stages or phases or modifications of the same mother substance. It is very difficult to determine which of these forms, if any, represents the native form. Seyfarth maintains that the unstained blood as seen in the dark field presents reticulation, and that the diffuse polychromasic granulation is a solution product brought about in the fixation and staining. This author further maintains that so rigid are these reticulo-granular formations that after cellular disruption by hypotonic stains these networks may float away intact, and that manually these networks may be uncoiled under the microscope.

For the purpose of this work, the terms commonly used in connection with the basophilic content of red cells are employed as defined hereinafter.

Polychromotaphilia or *Polychromasia* as applied to red cells is descriptive of a diffuse but discrete distribution of basophilic material throughout the greater portion of the red cell. When such cells are stained with Wright's type of stain these cells appear grayish, bluish, or purplish, and are commonly less translucent than other red cells in the same preparation. Between the origin of the primitive red cell in the endothelium, after the first appearance of hemoglobin, and the nonnucleated adult cell, practically any stage of development may be accompanied by polychromatophilia. There are some reasons to believe that every red cell passes through a stage in which polychromasia may be exhibited. There are other reasons to believe that polychromasia is present only when the maturation is speeded up beyond natural rates. Polychromasia is evidence of regeneration of red cells and commonly is regarded as a beneficent phenomenon.[19] When this polychromatophilia results from a toxic irritation of the bone marrow in the absence of a physiologic need for additional cells in the blood stream, this beneficence may be questioned.

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[18] Our translation; for exact language see original text.
[19] "The pathological physiology of blood cell formation and blood cell destruction," by C. K. Drinker, in Oxford Medical Looseleaf, vol. 2, p. 509.

Basophilic reticulation is that intracellular arrangement of basophilic substance in which a network or skein exists. This network may occupy the entire cell or be limited to the periphery or the central position of the cell. This form has given rise to the term "reticulocyte" and the condition in which it exists is termed "reticulosis." Some doubt is justified as to the existence in a native state of reticulation. When a stain of the Wright type is applied to a fixed blood smear, polychromasia, if such exists, is brought into visibility. No reticulocytes, however, are thus brought into view. Since this stain is capable of staining basophilic substance as shown by the polychromasia, and since basophilic reticulation is of the same origin, the absence of the latter suggests that this condition does not exist. When, however, a slide preparation is stained by any of the well-known suitable vital or semivital methods, especially if the red cells become hemolyzed in the process, reticulation is readily observable and polychromasia is then not in evidence. It appears tenable that reticulation at times at least may be a creation rather than a native state of basophilic substance. We have on this account avoided the terms "reticulocyte" and "reticulosis." Of this, Key[20] states—

> polychromatophilia and reticulum occur normally in all young red blood cells.

In the next paragraph, however, in referring to his earlier publications, he states—

> * * * the reticulum is formed by the union of this basophilic substance (polychromatophilia) with a supra vital stain.

Cupp[21] has shown that in the animals studied by him all red cells in the peripheral circulation are reticulated. Cupp's reticulation is, however, probably not composed of basophilic material. It is possible that the basophilic reticulation is but a rearrangement of polychromatophilic granules around the elements of the network of Cupp's reticulation.

Punctate stippling is a third form of basophilic material in red cells. This form is probably never seen in bone marrow cells, although chemical manipulation may create a picture simulating this condition. In the peripheral circulation it is characterized by the presence within the red cell of multiple minute discrete clumps of a material having the staining reactions of basophilic material. That punctate stippling is not a result of staining, as is believed to be true for reticulation, may be demonstrated by the examination of fresh untreated blood.[6] Punctate stippling is to be associated with young red cells, and represents a young cell that has been harmed. The source of the stipples is probably the polychromatophilic cell. It is thus a preformed condition denoting degeneration, or at least representing a pathologic state. Punctate stippling is thus not an

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[6] "Studies on erythrocytes, with special reference to reticulum, polychromatophilia, and mitochondria," by J. A. Key, in Archives of Internal Medicine, November, 1921, vol. 28, p. 511.

[20] "Lead studies: Blood changes in lead poisoning in rabbits with especial reference to stippled cells," by J. A. Key, in American Journal of Physiology, September, 1924, vol. 70, p. 86.

[21] "On the structure of the erythrocyte," by C. D. Cupp, in Anatomical Record, 1915, vol. 9, p. 259.

index as to numbers of immature cells, but possibly of numbers of pathologic or degenerating immature cells.

Basophilic aggregations is a term introduced by McCord, Minster, and Rehm [2] descriptive of the various forms of basophilic material as found in red cells that have been laked, thus removing the hemoglobin and bringing the basophilic material into greater visibility. Through variations in technical procedures as to tonicity, time, and acidity it has proven possible to produce divers forms of basophilic substance within the cells from the same blood specimen. These include fragmentation, combined reticulation and granulation, coarse stippling and fine stippling, wreaths or bands at the periphery, balls of clumped basophilic substance at the center of the cell, œdematous red cells with distended reticulum, etc. These are not artifacts in the common use of that term, but are artifactitious so far as geometric form is concerned.

Whatever be the significance of the various geometric forms of basophilic substance, its presence in red cells in numbers above normal is the surest and earliest indication of bone marrow response to toxic or physiologic stimulation.

METHODS OF DETECTING BASOPHILIC MATERIAL

Consideration of the relative merits of the many procedures available for the demonstration of basophilic material can not be included in this publication. Reference is made again to the work of Key [22] for a comprehensive presentation of methods and literature. Our data in this respect are limited to a description of the methods we have used most satisfactorily, and others in common use.

WRIGHT'S STAIN

This widely known method of staining is suitable for the demonstration of punctate stippling and polychromatophilia. Reticulation is not brought out by this procedure. The technique of staining, and the characteristics of cells so stained, are too well known to call for additional comment.

ROBERTSON'S METHOD FOR THE COUNTING OF RETICULATED CELLS [23]

A saturated solution of brilliant cresyl blue was made up in normal salt solution. This was kept as a stock solution. When a count was to be made, a small quantity of it was diluted eighty times [24] with normal salt solution and

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[2] "Basophilic aggregation test in lead poisoning," by C. P. McCord, D. K. Minster, and M. Rehm, in Journal of the American Medical Association, May 31, 1924, vol. 82, pp. 1759.

[22] "Studies on erythrocytes, with special reference to reticulum, polychromatophilia, and mitochondria," by J. A. Key, in Archives of Internal Medicine, November, 1921, vol. 28, p. 511; "Lead studies: Blood changes in lead poisoning in rabbits with especial reference to stippled cells," by J. A. Key, in American Journal of Physiology, September, 1924, vol. 70, p. 86.

[23] "The effects of experimental plethora on blood production," by O. H. Robertson, in Journal of Experimental Medicine, August, 1917, vol. 26, No. 2, p. 221.

[24] "Since doing this work, a second saturated solution of cresyl blue has been made up, using a different stock of the dye, which went into solution to a considerably greater extent than the first. The result was that a 1:80 dilution of this saturated solution was much too strong a staining fluid. It was found necessary to dilute to 180 for satisfactory staining. It is apparent, therefore, that each saturated solution of cresyl blue has to be tested beforehand for its optimum staining dilution. This is a very simple matter and needs to be done only once."

mixed with blood in a pipette for counting white cells in the proportion of one part of blood to twenty parts of cresyl-blue solution. The mixture was shaken in the pipette for 5 minutes. The cells were thus equally distributed as well as stained. They were counted at once in fresh preparations, which were sealed with vaseline to prevent disturbances due to drying. At least 1,000 red cells were counted at each test. When the numbers of reticulated cells were less than one in a thousand, 10,000 red cells were counted. In the latter case, only the first 1,000 were counted individually, the field being the unit of count for the remaining 9,000.

CUNNINGHAM'S METHOD FOR THE COUNTING OF RETICULATED CELLS[25]

In this study it was found that permanent preparations could be made by combining a vital with a Wright's stain. The reticulation is as clear, if not clearer, than by the older methods, and the Wright's stain retains all its differential qualities, except the polychromatophilia, which is not present. The ease and simplicity of this method brings the study of reticulated erythrocytes within the scope of routine blood examination.

The technique is divided into two stages, first, a small drop of a 0.3 or 0.5 per cent aqueous or alcoholic solution of brilliant cresyl blue is placed on the end of a clean slide or the center of a cover glass, smeared around over an area 1.5 centimeters in diameter with the aid of a match or glass rod and permitted to dry. After this is dry there may be a narrow margin of thick stain which should be wiped off with a damp cloth, leaving a central, uniform area. These slides or cover glasses may be prepared in large quantities, and if stacked side by side in a box and kept dry the stain will not deteriorate. The second stage consists of taking a drop of fresh blood on a clean cover slip and dropping it face down on one of the areas of dried stain. If the cover slip is clean the blood will quickly spread to the edges. The stain goes into solution almost instantly. (This preparation may be observed as a vital stain.) The cover glasses, or slide and cover glass, are now pulled apart as in making an ordinary blood smear and are permitted to dry. Smears may also be made by placing the drop of blood directly on the dried stain and spreading it with a cigarette paper or another slide. On drying, the blood turns a dirty greenish blue color. The slide cover glass is then stained with Wright's blood stain. Too vigorous washing causes the reticulum to lose some of its stain. The preparation is dried in the usual manner and when mounted in Canada balsam keeps at least four months and probably much longer.

The reticulum is stained a deep or light blue, depending on its density, and gives a striking picture in its contrast with the pink protoplasm of the cell as shown in the accompanying illustrations. Various types of reticulation are easily seen from the heavy skeinlike material to knotted granular particles connected by delicate blue threads and finally the separate granules which resemble stippling seen with Wright's stain alone. The nucleated erythrocytes in human blood usually have many fine threadlike blue staining filaments around or radiating from the nucleus. There is no polychromatophilia seen. Whether the reticulation has replaced the polychromatophilia or not is a question requiring further investigation. The examination of many smears certainly suggests this as a possibility.

FRIEDLANDER–WIEDEMER METHOD OF ENUMERATION OF BASOPHILIC RED CELLS[26]

Two collaborators in this present study have previously published a counting method, as follows:

After cleansing the finger or the ear of the subject in the usual manner, and pricking, blood was drawn into the leukocyte tube of any good hemocytometer up to 0.5. Brilliant cresyl blue solution (0.25 per cent) in normal saline solution was then drawn in until the mixture of blood and stain reached point 11

[25] "A method for the permanent staining of reticulated red cells," by T. D. Cunningham, in Archives of Internal Medicine, October, 1920, vol. 26, No. 4, p. 405.
[26] "Basophilic aggregation in the newborn," by A. Friedlander and C. Wiedemer, in American Journal of Diseases of Children, December, 1925, vol. 30, pp. 804–809.

on the counting tube. The tube was shaken for about three minutes; then a drop was expressed on the ruled counting slide. With a D D Zeiss high dry lens, counts and computations were made as for leukocytes, the figure derived representing the total number of basophilic red cells per cubic millimeter.

In such a preparation the basophilic substance commonly presents itself as two or three coarse granules, with or without a few reticulating strands interwoven.

THE BASOPHILIC AGGREGATION TEST

The simple method used by McCord, Minster, and Rehm [2] in testing for imminent lead poisoning or lead absorption permits the collection of large numbers of blood specimens without difficulty, and without

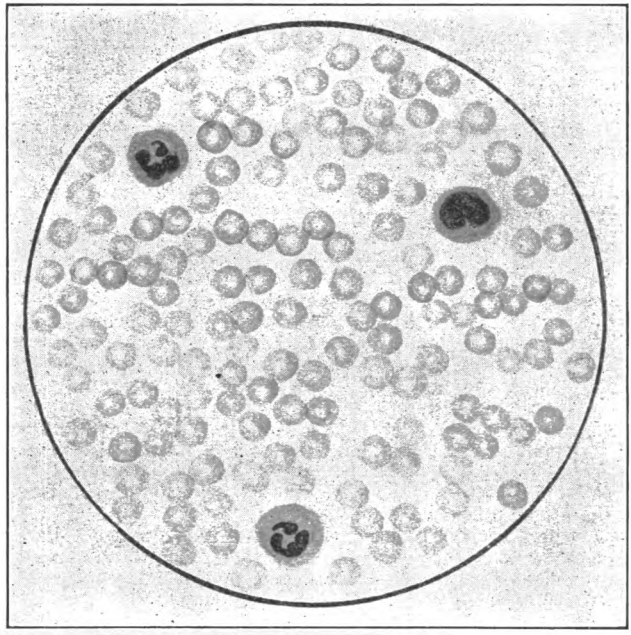

FIG. I.—DIAGRAMMATIC REPRESENTATION OF A FRESH BLOOD SMEAR

the necessity for any apparatus. In this procedure a blood smear, approximately three times the thickness of that in common use for differential counts, is made on a glass slide. This smear is unfixed and is air dried. Staining is secured by a dilute, acidulated methylene blue or by hypotonic saline methylene blue, or through the use of dilute Manson's methylene blue. Staining is carried out for 10 minutes. Overstaining does not occur. The excess stain is dashed off and the slide is dipped in distilled water as few times as are necessary to remove the remaining stain. The slide is allowed to dry in air. Examination is made with an oil immersion lens, without any cover slip.

[2] "Basophilic aggregation test in lead poisoning," by C. P. McCord, D. K. Minster, and M. Rehm, in Journal of American Medical Association, May 31, 1924, vol. 82, pp. 1759–1763.

Microscopic examination presents the usual red cells only as faint shadows (Fig. II), except for the periphery which may be distinct. The white cells stain deeply and the various types may be differentiated. If there are red cells containing basophilic material, this material stands out sharply as coarse granules or as combined granules and network. (Figs. IV and V.) This staining method appears to bring into greater visibility the very diffuse basophilic material seen in polychromatophilic cells.

If the blood smears so stained are of approximately the same thickness, a counting, for several fields, of the cells showing basophilic aggregation affords a rough quantitative estimate as to the excess

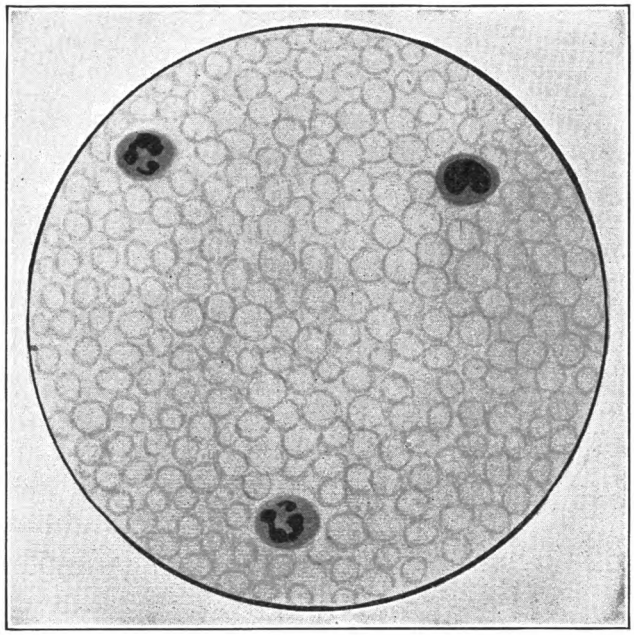

FIG. II.—DIAGRAMMATIC REPRESENTATION OF A FRESH BLOOD SMEAR WITH CELLS LAKED WITH HYPOTONIC SALINE

All red cells are enlarged and delineated only by periphery. No basophilic substance in cells. Characteristic of normal blood.

over normal. The normal person may, by this method, show only one or two basophilic cells in an entire slide, while in lead poisoning every microscopic field may present 10 or more basophilic red cells.

CLINICAL AND LABORATORY MATERIALS UTILIZED IN THIS WORK

The conclusions reached in this investigation are derived from the results of the examinations of over a thousand persons (1,045) to determine the number of basophilic-containing red cells found in the blood stream under a variety of conditions. The actual number of tests made are far in excess of 1,000, for in some instances as many as

30 tests were made on a single person. These persons may be divided into the following groups:

Control I.—One hundred and forty-five persons without any exposure to lead were tested to establish the range of normal numbers of basophilic red cells. This group included no persons known to be abnormal in any way. It included persons of all ages, both sexes, several races. The tests were made over a period of months embracing all seasons and at such times as were likely to detect the influences of physiologic processes, such as eating, sweating, etc. The range of normal limits accepted by us is stated and discussed in a subsequent section.

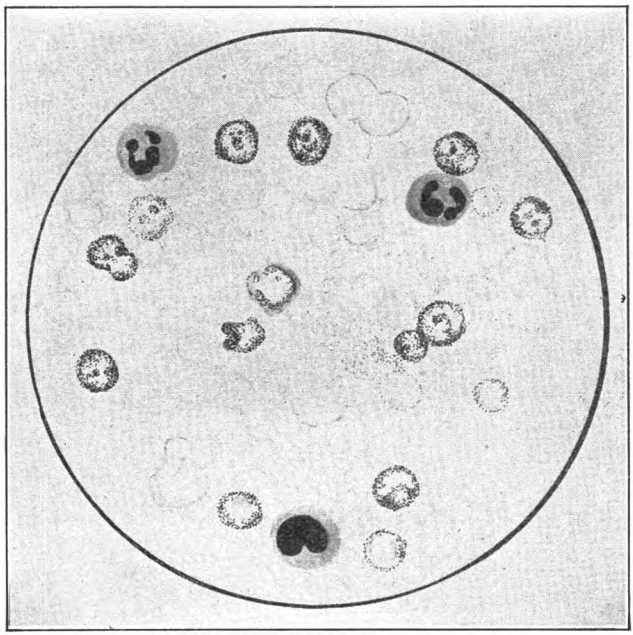

FIG. III.—DIAGRAMMATIC REPRESENTATION OF A FRESH BLOOD SMEAR WITH CELLS LAKED WITH HYPOTONIC SALINE

Many cells contain basophilic substance. Characteristic of blood in lead poisoning, severe anæmias, hemolytic icterus, etc.

Control II.—A second control group was made up of more than 100 patients found in a general hospital. In this phase of the work emphasis was placed on a study of anemias, leukemias, pregnancy, the newly born, premature births, the influence of ultra-violet irradiation, infections, acute and chronic. The data derived are far too diversified and extensive to permit of inclusion here in detail. The trend of the entire results establishes that there are many physiologic and pathologic conditions besides lead intoxication in which numbers of basophilic red cells far exceed normal limits. These conditions are such that with one exception little conflict is to be anticipated in the application of these methods to the early detection of lead absorption. The one exception is benzol poisoning, which is closely asso-

ciated with lead poisoning through the extensive use of both of these toxic substances in the painting industry.

Control III.—A third control group of 200 persons were patients in a tuberculosis sanatorium. This group was selected because the preliminary study suggested that this common infectious disease might so often be positive as to jeopardize the worth of this method in the control of lead poisoning. The results show that only after

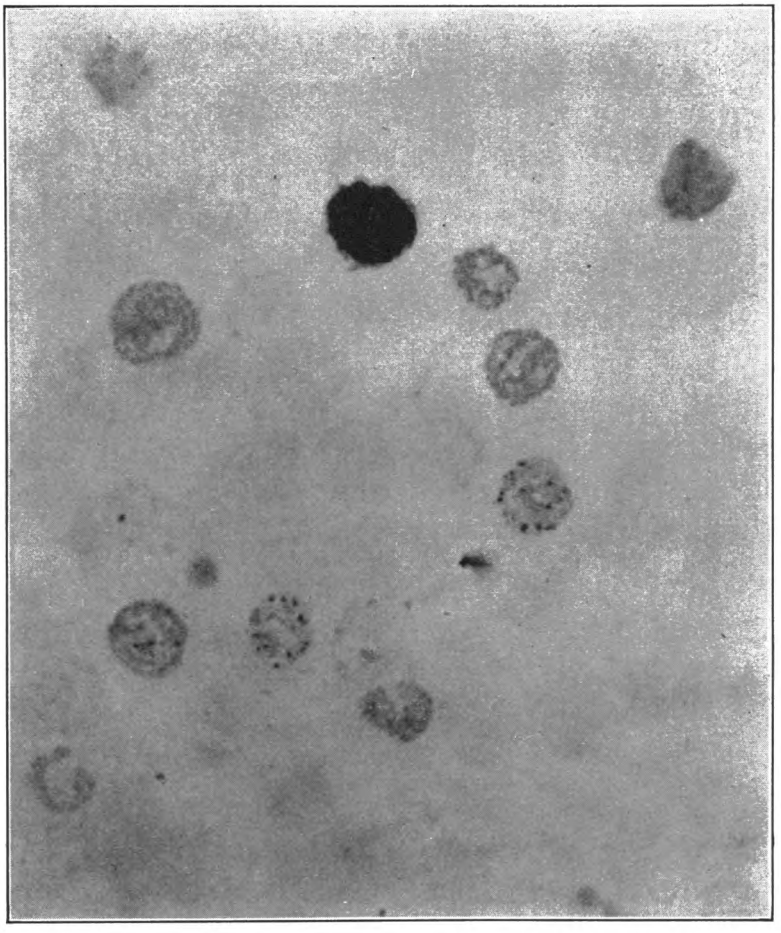

FIG. IV.—MICROPHOTOGRAPH OF LAKED BASOPHILIC RED CELLS IN BLOOD OF LEAD POISONING CASE
Laked normal red cells may be faintly seen as shadows

hemorrhage (possibly also tuberculous peritonitis) do counts approximate the high counts seen in rarer diseases, such as pernicious anemia or lead poisoning.

IV. *Lead exposed.*—This study included various groups of lead workers in seven industrial plants, representing divers types and different degrees of lead hazards. The total number of workers, including persons subsequently reappearing as lead poisoning cases, was 550. The group included white lead manufacture, lead founding, storage battery manufacture, red lead manufacture, newspaper

composition, spray painting, brush painting, and soldering. The various occupations represented in these groups were:

House painters.
Spray painters.
Solderers.
Linotypers.
Hand composition workers.
Stereotypers.
Pasters.
Battery chargers.
Battery assemblers.
Battery-grid molders.
Lead-oxide mixers.
Corrosion workers.
Water grinders.
Oil grinders.
Lead packers.
Lead-pipe makers.
Solder makers.
Office workers in lead industries.
Maintenance groups in lead industries, including crane operators.
Buckle molders.
Red-lead workers.
Tanbark workers.
Dry-kiln tenders.

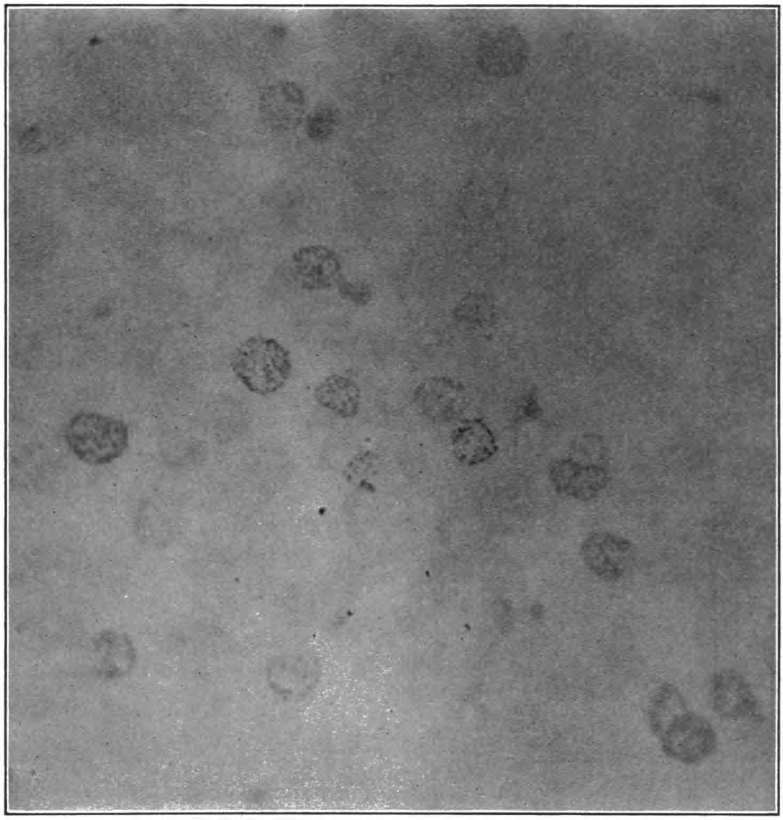

FIG. V.—MICROPHOTOGRAPH OF LAKED BASOPHILIC RED CELLS IN BLOOD OF LEAD POISONING CASE

Laked normal red cells seen faintly as shadows

A subsequent section is given over to the discussion of findings from this group.

A listing of the articles manufactured from lead or utilizing lead in the process of manufacture (with the exception of organic lead compounds) is shown in Chart I.

V. *Lead-poisoning cases.*—Fifty cases of clinical lead poisoning were included in this study. The significant findings are discussed in a separate section.

VI. *Animal experiments.*—In addition to studies made on human beings, experimental observations have been carried out on rabbits, dogs, cats, monkeys, guinea pigs, chickens, goldfish, etc. A portion of this animal study has already been published in connection with a study on the influence of benzol and its homologues on basophilic red cell production.[11] These animal studies establish precisely that an intake of lead is quickly followed by the appearance in the blood stream of abnormal numbers of basophilic red cells.

BASOPHILIC RED CELLS IN NORMAL PERSONS

A traditional figure of 0.8 per cent is widely accepted as representing the basophilic cell incidence among normal adults. Isaacs[27] states—

> In health, while the number of these corpuscles in the peripheral blood vary around 1 per cent, increases to 2 or 3 per cent may take place without evidence of disease.

Vogel and McCurdy[28] suggest as normal figures for basophilic cells 5 to 10 per cent for infants and 0.5 to 2 per cent for adults. Krumbhaar[29] furnishes a table of normal reticulated cells for man and other animals, as follows:

Species	Range (per cent)
Man	0.1–0.8
Monkey	.0–.8
Dog	.1–1.4
Cat	.0–.4
Guinea pig	1.0–4.0
Rabbit	.6–2.8
Mouse	1.0–6.0

This author cites Cathola and Dannay as finding in children, after the fourth day of life less than one cell per thousand. Stitt[30] records not more than 1 reticulated cell per 500 as the normal limit for healthy adults.

Some authors in commenting on the normal occurrence of basophilic cells use the word "rare." If, however, we extend Isaacs' upper normal figure of 3 per cent to a person presenting a total red count of 5,000,000 per cubic millimeter, we derive 150,000 reticulated cells per cubic millimeter, which is far from "rare." At best it is to be recognized that the normal basophilic count is not standardized. The slide methods (usually Cunningham's or Robertson's) such as have led to these enumerations offer many sources of error. Few persons

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[11] "Basophilic material in benzol poisoning," a preliminary report, by W. D. Paul, A. Friedlander, and C. P. McCord, in Journal of Industrial Hygiene, May, 1927, vol. 9, No. 5, p. 193.

[27] "Effect of Röntgen ray irradiation on red blood cell production in cancer and leukemia," by R. Isaacs, in American Journal of Medical Science, January, 1926, vol. 171, No. 1, p. 20.

[28] "Blood transfusion and regeneration in pernicious anemia," by K. M. Vogel and U. F McCurdy, in Archives of Internal Medicine, 1913, vol. 12, p. 707.

[29] "Reticulosis—increased percentage of reticulated erythrocytes in the peripheral blood," by E. B. Krumbhaar, in Journal of Laboratory and Clinical Medicine, October, 1922, vol. 8, No. 1, p. 11.

[30] "Practical bacteriology, blood work, and animal parasitology," by E. R. Stitt. Philadelphia, P. Blakiston's Son & Co., 7th ed.

would attempt to derive the total white-blood count by counting in relation to 1,000 red cells and expressing the total in relation to the total or normal red count. Nicholson [31] has questioned the accuracy of differential counts made by slide methods because of uneven distribution. In the case of immature cells, Key,[6] has pointed out a tendency to cohesion and adhesion to white cells thus jeopardizing any even distribution throughout the slide surface. Seyfarth [16] states:

> In the grown, healthy person there are from 0.1 per cent to about 0.2 per cent of vitality stained erythrocytes in the peripheral blood. This count is also given as normal by Naegeli, Morawitz, and others. Higher figures, as some of the previous workers have stated, could not be substantiated in counting 50 healthy, rested, abstinent men. Cunningham stated in 1919 that he obtained counts about 0.8 per cent in normal persons. Roessingh's counts of 30 healthy individuals were from 0.4 per cent to 1.8 per cent, but these figures are too high. He used the Widal and Abrami method of centrifuging his blood, but did not realize that the vitally stained cells are found mostly in the upper layers.
>
> In full grown animals I have found the following average figures of vitally stained erythrocytes in the peripheral blood; these were counted at the Leipzig abattoir. In the horses, cattle, sheep, and hogs there were hardly any vitally stained cells to be seen. The cat showed 0.1 to 0.2 per cent; the dog, 0.2 to 0.5 per cent; the guinea pig, 0.5 to 5 per cent; rats, 3 to 5 per cent; mice, 4 to 6 per cent; rabbits, 3 to 8 per cent. In the younger animals we obtained the highest counts.

Our own examinations of normal persons for basophilic red cells have yielded results better in keeping with Seyfarth,[16] Naegeli, Moravitz, Stitt, Cathola, and Dannay.

In 145 normal persons, repeated counts rarely exceeded 5,000 basophilic cells per cubic millimeter of blood. By far the greater number were below 1,000 such cells. In the spring months in some persons considerably exposed to sunlight the normal count mounts to a maximum of 20,000 per cubic millimeter and may remain high during the summer. We believe this is due to additional ultra-violet irradiation from sunlight. Artificially produced ultra-violet rays stimulate a prompt formation of basophilic red cells far in excess of normal. According to Krumbhaar [29] the usual oil immersion lens field contains approximately 200 red cells. In our thicker slide preparations about 600 cells are then present. If our figures were in accord with Isaacs' concept of from 1 to 3 per cent as normal, we would, assuming only 1 per cent of such cells, expect to find six basophilic cells in an average field. This has been true in no instance for normal adults.

As utilized by us the chamber counting method has yielded as a normal basophilic count a maximum of 5,000 per cubic millimeter, with some temporary increases up to 20,000 per cubic millimeter as a spring and summer seasonal variation. By the slide method of basophilic aggregation normal persons have never presented (except

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[6] "Studies of erythrocytes, with special reference to reticulum, polychromatophilia, and mitochondria," by J. A. Key, in Archives of Internal Medicine, November, 1921, vol. 28, p. 511.

[16] Experimentelle und klinische untersuchungen über die vitalfarbbaren erythrozyten," by C. Seyfarth, in Folia Haematologica, Band 34, Heft 1 zu 7. April, 1927 (Archiv).

[29] "Reticulosis—increased percentage of reticulated erythrocytes in the peripheral blood," by E. B. Krumbhaar, in Journal of Laboratory and Clinical Medicine, October, 1922, vol. 8, No. 1, p. 11.

[31] "A combined diluting and staining fluid for differential leucocyte counts in the counting chamber," by D. Nicholson, in Journal of Laboratory and Clinical Medicine, March, 1927, vol. 12, No. 6, p. 548.

in the seasonal variation) more than 1 cell per average field. The average count for normal individuals is approximately 500 per cubic millimeter. Although counts up to 5,000 may be accepted as within normal limits for a particular individual, this may be indicative of a pathologic condition for an individual who when normal would not exceed the average of 500. As possible exceptions to our statements as to normal counts we record the following physiologic or near-physiologic states in which higher counts have been observed by us or by others: Pregnancy, newborn, profuse sweating, after arsenic or iron medication, high altitudes, exposure to ultra-violet rays or X rays; possibly also the intake of foods effect slight variations.

BASOPHILIC RED CELLS AS AN INDEX OF EXPOSURE TO LEAD

Five hundred and fifty lead workers have been examined from one to thirty times for the presence of basophilic red cells in the blood. The types of industry and the divers trades presenting the lead hazards have been mentioned in a foregoing section. Wherever a lead hazard exists some but not all the exposed workers exhibit basophilic red cells in excess of normal. This is shown in Table I, in which the results from the testing of groups of workmen selected at random are arranged in the order of previously accepted degree of hazard.

In this table the types of processes have been divided into eight zones according to the degree of exposure to lead. In Zone I fall the workers without known exposure. In Zone II fall the workers whose exposure is remote, such as automatic solder machine tenders, etc., through the increasing severities of exposure to Zone VIII, where workers are exposed directly and grossly to lead dusts. It will be noted that the average number of basophilic red cells for each zone increases as the severity increases—863 per cubic millimeter in Zone I, 1,233 per cubic millimeter in Zone II, to 24,800 per cubic millimeter in Zone VIII.

TABLE I.—*Number of basophilic red cells in workers, arranged according to an already established degree of hazard, by zone*

Zone I: Industrial workers without known exposure to lead (control)		Zone II: Remote exposure to lead, such as in tin-can manufacture		Zone III: Exposure such as office workers in lead industry.		Zone IV: Molten lead workers		Zone V: Red-lead makers, painters		Zone VI: Wet or oil lead grinding		Zone VII: White-lead corrosion workers; battery pasters		Zone VIII: Workers exposed to lead dust; white-lead packers	
Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood	Period of exposure	Number of basophilic red cells per cmm. of blood
3 years	800	33 years	1,000	22 years	400	24 years	2,400	2 months	3,200	13 years	3,600	30 years	1,200	9 years	68,600
8 years	2,400	8 months	600	23 years	1,600	20 years	2,600	6 months	800	8 months	600	1 week	4,000	8 years	1,200
2 months	400	1 year	400	6 years	200	10 years	1,400	8 years	2,000	5 months	3,400	1 week	600	17 years	2,800
6 months	200	10 months	200	16 years	2,000	20 years	400	20 years	4,600	12 years	4,800	11 years	2,400	4 years	4,400
1 month	400	8 months	1,600	16 years	600	20 years	800	19 years	4,000	1 year	800	21 years	1,800	21 years	4,800
8 months	200	8 months	200	21 years	400	2 years	1,200	3 years	6,200	29 months	5,800	5 years	3,800	12 years	12,400
11 years	400	10 months	1,200	39 years	1,200	18 years	1,200	2 months	29,000	8 years	8,600	2 years	1,200	4 years	18,000
11 years	200	8 months	200	7 years	200	20 years	400	3 months	4,200	5 years	10,000	2 years	9,200	4 months	92,000
7 years	1,800	1 year	200	3 years	1,200	18 years	1,000	7 years	3,200	8 months	5,400	3.5 years	9,200	12 months	3,200
3 months	2,200	11 years	4,600	5 years	1,400	15 months	600	7 years	1,800	24 years	600	14 years	18,200	1.5 years	1,400
36 years	3,400	6 months	1,800	8 years	800	14 years	800	30 years	1,600	5 months	7,000	13 years	6,800	1 year	1,800
1 month	600	1 year	800	9 years	400	25 years	600	3.5 years	3,200	16 years	1,000	6 years	26,200	8 years	61,600
31 years	800	8 months	2,600	1 year	400	15 years	1,000	19 months	2,200	2.5 years	200	6 years	15,800	8 years	70,400
25 years	600	4 years	3,000	1 month	1,400	20 years	1,200	19 years	3,000	2 months	800	18 months	54,600	5 weeks	4,600
12 years	600	1 year	600	6 years	600	27 months	4,800	6 years	800	3 months	3,200	3 months	6,000		
7 years	400	8 months	400	17 months	6,600	15 years	2,400	1 year	200	5 months	4,800	8 months	7,600		
26 years	200	8 months	200	15 years	4,000	21 years	3,000	2.5 years	5,000	4 months	9,600	3 years	9,200		
5 years	400	10 months	600			7 years	3,800	9 years	200	7 years	44,800	4 years	20,400		
4.5 years	600	1 year	1,000			1 year	1,600	21 years	1,000	1 month	600	7 months	22,400		
3 years	200	9 months	800			13 years	1,800	13 years	6,800	23 years	2,800	1 year	2,400		
24 years	600	6 years	4,400			5 months	3,600	3 months	600	3 days	600	10 years	800		
18 years	1,600	3 years	1,200			7 years	4,200	1 month	1,400	1 year	2,600	2 years	4,200		
		21 years	800			7 months	4,200	1 month	1,200			2 weeks	3,800		
		30 years	1,200			17 years	6,600					3 years	12,400		
Average	863		1,233		1,376		2,150		3,747		5,527		10,175		24,800

From this specimen table, which is characteristic of the entire group, it appears also that the length of exposure to the hazard has very little to do with the percentages of basophilic red cells present. Only during the first few days of exposure in cases of marked susceptibility is time an essence. It may not be maintained that a year's service in a work place having a minor lead hazard is equal in danger to 20 days in a work place having a severe lead hazard. In our experience many workers exposed to minor lead hazards may work over periods of years without presenting either signs or symptoms of lead absorption or lead poisoning. Gradual accumulation of lead may take place to the threshold of lead poisoning, but this is far from being a regular occurrence. The extent of the lead hazard to which the worker is exposed, rather than the duration of exposure, determines the probability of lead poisoning.

It is from the individuals who present basophilic red cells in excess of 6,000 per cubic millimeter that clinical cases of lead poisoning are apt to arise, regardless of the hazard zone into which they have been arbitrarily placed.

The total harm produced by lead upon exposed workers is not represented by the number of clinical cases of lead poisoning. It is believable that small quantities of lead repeatedly absorbed exact a toll from the health and length of life of the workers even in the absence throughout life of any clinical lead poisoning. Prevention of frank lead poisoning is not sufficient. Control should be extended to embrace lead absorption. If positive tests for an excess of basophilic red cells be accepted as evidence of lead absorption, then any abnormally high basophilic red count in a lead worker should command attention without waiting for actual complaints.

All data have been analyzed to determine the influence of the age of the worker on the numbers of basophilic red cells. No such relation was established.

Many of the persons presenting high basophilic red-cell counts, while remaining at work, were none the less cases of lead poisoning. Commonly, these persons present some of the following lesser characteristics of plumbism—anemia, low hemoglobin, Burtonian line, joint pains, muscle cramps, headaches, constipation, anorexia, etc. Under treatment and supervision there is no necessity for the removal of these mildly involved workers from all employment. On the other hand, others may evince no signs of lead absorption other than the presence of basophilic cells in large numbers until without warning they suddenly become acutely and severely ill with lead poisoning. Undoubtedly, quantitative determinations of lead in urine under such circumstances would lead to the recognition of imminent poisoning, but no dependable methods of urinalysis are available for quick routine application in lead industries. Given sufficient exposure while at work, enough lead may be absorbed in one day to provoke lead poisoning. This necessitates in some industries examinations at such short intervals as two weeks. Since urinalysis for lead routinely requires a period represented by days, this otherwise excellent procedure is at present impractical.

At the time of counting basophilic red cells other blood examinations were carried out as follows: Total red count, hemoglobin, total white count, differential white count, Cunningham count of reticu-

lated cells, basophilic aggregation tests. No constant relation was established between the percentages of basophilic red cells and the total red count, total differential white count or hemoglobin. A basophilic count far in excess of normal (e. g., 50,000 per cubic millimeter) is compatible with a hemoglobin of 110 per cent and a red count of 5,500,000. A relative lymphocytosis is frequently associated with a high basophilic count but either may occur without the other.

Punctate stippling stands in no regular quantitative relation to the basophilic material brought out by the methods that we have employed.

In those industries utilizing lead in some of its various forms, some departments will obviously present a greater lead hazard than others. In newspaper composition the linotype room, if equipped with electric heating devices and completely inclosed heating chambers, manifestly affords less opportunity for plumbism than the stereotype room. In white-lead manufacture the corrosion room work is far more hazardous than, for example, "buckle casting"; kiln drying and emptying is commonly more dangerous than pulp grinding. In storage-battery manufacture the pasting of grids represents the outstanding danger point, while the lead hazard is almost negligible in the electric charging room.

At present the accepted test as to the extent of the hazard or as to the efficacy of protective measures is found in the number of lead-poisoning cases that arise. Since the number of actual cases does not represent the totality of harm from lead, this test, which is accepted as a measure of the hazard, is fallacious, for in departments in which no cases arise the inference is that no hazard exists, yet appropriate tests may show that every worker is absorbing lead. The data of Table I suggest that a relation exists between the number of basophilic red cells in the blood of workers and the severity of the hazard. If this is true, a procedure becomes available for the testing of the efficacy of devices protecting the worker against lead poisoning and will permit the grading, with relative certainty, of various types of work as to the extent of the lead hazard. Further, to prove this method of graduation, we have applied these tests to specific departments in two lead-using industries. The results are shown in Table II.

TABLE II.—*Basophilic red cell counts in the workers in two lead-using industries, by department*

Basophilic red cell count for individual workers	Estimate of hazard	Type of work
Daily newspaper plant: Linotype department—Linotypers without previous hand work within 20 years		
400 400 200 200 600 400 1,200	Electrically heated inclosed lead pots. Exposure to metallic lead but little evidence of dust.	Linotype work.
Average for group..... 485		

TABLE II.—*Basophilic red cell counts in the workers in two lead-using industries, by department*—Continued

Basophilic red cell count for individual workers	Estimate of hazard	Type of work
Daily newspaper plant: Linotype department—Linotypers with previous hand work within 20 years		
1,400 1,600 1,600 2,000 600 400 400 200	Similar to above, except for previous greater exposure in hand work. No cases.	Linotype work.
Average for group..... 1,025		
Daily newspaper plant: Composing room—Hand composition		
2,800 1,200 1,000 600 800 600 1,000 400 1,200 1,200 200	This work involves direct handling of type, and some open casting of type. No cases.	Usual hand composition.
Average for group..... 1,000		
Daily newspaper plant: Stereotype department—Stereotyping		
1,200 4,800 2,400 3,000 3,800 1,600 1,800 3,600 4,200	Molten lead hazard with small quantities of dust present. No cases.	Stereotype composition work, with additional hazard of heated printing inks.
Average for group..... 2,933		
White-lead factory: Office workers		
600 800 1,200 1,400 800 400 400 1,400	Low. No cases.....	Office work in white-lead factory, well isolated from factory. Little communication between this building and adjacent factory building.
Average for group..... 875		
White-lead factory: Corrosion room—Take-out		
2,600 11,000 7,800 4,600 12,400 3,800	Hazardous. Many workers presented signs of lead poisoning.	Work involves emptying of corrosion pots. Hazard from dust. Hazard from pulp lead.
Average for group..... 7,033		

TABLE II.—*Basophilic red cell counts in the workers in two lead-using industries, by department*—Continued

Basophilic red cell count for individual workers	Estimate of hazard	Type of work
White-lead factory: Corrosion room—Setting group		
3,400 7,200 4,800 2,800 4,600 1,000 800 1,000 200 600 4,200	Some hazard. Handling of buckle lead. Source of known cases of plumbism.	Some lead dust from repeatedly used tanbark. Some shifting of this group to other jobs.
Average for group..... 2,616		
White-lead factory: Molten metallic lead department		
2,400 200 6,200 600 1,800 800 1,000 1,800 5,200 1,000 1,200 2,600 3,800 1,800 1,800 2,200 3,000 200 2,000 4,000 400	No known cases of lead poisoning from this department.	Lead pipe molding. Solder molding. Lead at low temperatures only.
Average for group..... 2,095		
White-lead factory: Dry kiln room—Dry lead packing		
61,600 68,600 1,800 1,400 70,400 22,400 4,600	Extremely hazardous. Clinical evidence of lead poisoning.	Hopper tending. Barreling dry white lead. Kiln-room work. Dust everywhere.
Average for group..... 32,971		
White-lead factory: Shipping department		
600 3,800 2,600 2,200 2,200 1,400	Some exposure from pulp lead, outside containers. Shipping room near molten-lead room.	Much handling of metallic lead and containers of white lead.
Average for group..... 2,133		

TABLE II.—*Basophilic red cell counts in the workers in two lead-using industries, by department*—Continued

Basophilic red cell count for individual workers	Estimate of hazard	Type of work
White-lead factory: Water grinding		
2,600 600 2,800 600 44,800	Few cases of lead poisoning originate in this department or in the oil grinding department. Carelessness a considerable factor.	Grinding of lead pulp after corrosion, prior to drying in kiln room.
Average for group..... 10,280		
White-lead factory: Recovery room		
9,600 4,800 3,200 1,800	Workroom very foggy. Brass pouring in this department. High temperatures of molten lead.	Reclaiming work. Handling of dross and metallic lead. Some blow-torch work.
Average for group..... 4,850		

Although no cases of clinical lead poisoning have appeared in any department of the newspaper plant referred to in Table II, the results from the examination of workers in various departments for basophilic material in the blood suggest that stereotype work is more hazardous than hand-composition work and that hand-composition work affords a greater hazard than linotype composition with inclosed electrical heating devices. This classification based on blood examination alone confirms the commonly accepted opinion as to the relative hazard in the newspaper plant departments.

In the white and molded lead factory a number of danger points or dangerous departments are apparent from our examination as well as from actual experience as to the source of clinical lead cases. It is obvious that corrosion work constitutes a greater hazard than work in the molten-lead department. Our figures here show an average of 2,095 basophilic red cells for the molten lead group as against 7,033 for the corrosion room "take-out" group. This again bears out the belief as to the relative hazards of these two departments. White lead in dry form, such as found in barrel packing and in kiln-room work, affords a high degree of lead hazard as again shown by our figure of 32,971 basophilic red cells.

In this same factory it was also possible to locate through routine blood examination for basophilic material unsuspected danger points; for example, the office boy in the works manager's office, which is set apart from factory work, proved to have a high count of basophilic red cells. Observation established the fact that foremen and workers from the factory daily tracked lead into this office, and this was stirred up by the office boy's ineffectual daily sweeping.

For the best application of this method of grading the hazards, tests on a considerable number of workers in any department are desirable. The larger the number of workers examined, the more accurately will the average number of basophilic red cells show the true magnitude of the hazard. In determining the degree of hazard

by this method, known ambulatory cases of plumbism should not be included. In Table II, under "Water grinding" the count from one known case of plumbism is included. As a result this type of work is made to appear more hazardous than the "take-out" work in the corrosion room. This is not true.

In Table II, under "Shipping department," it appears that an average of 2,133 cells per cubic millimeter obtained. This suggests that this work is as hazardous as "molten-lead work," which department averaged 2,095. In this particular factory this, undoubtedly, is a true representation of the facts, because the shipping department and the molten-lead department are adjacent, without separating walls. The lead hazard is therefore about the same in these two departments.

In "corrosion work" those men who place buckles of lead into corroding jars and later build up the tiers of such jars on beds of tanbark are far less exposed than the group who later tear down these stacks and empty out the corroded lead. The relative hazards are shown by comparison of the "setting group," which averaged 2,616 basophilic red cells per cubic millimeter, as against the figure of 7,033 for the "take-out" group.

In the newspaper plant the older linotypers presented a slightly higher count than the younger men. All previous work had prompted the belief that in adult years age alone was not a factor in the basophilic red-cell count. Further inquiry established that nearly all of these older men had in previous years performed "hand typesetting," which is known to be a more hazardous type of lead work.

Our total results, of which the tables presented are but specimens, suggest that through the routine examination of lead-exposed workers the degree of hazard and unsuspected danger points may be established. This method affords a simple procedure for the recognition of lead absorption by groups. Although not infallible, this method promotes the hygienic control of the lead hazard in the absorption stage.

BASOPHILIC RED CELLS IN CLINICAL LEAD POISONING

From fifty cases of lead poisoning under our supervision we have made the following observations with reference to the occurrence, duration, and significance of basophilic red cells:

Clear-cut clinical cases of lead poisoning almost invariably present large numbers of basophilic red cells. The range more often encountered was from 7,000 to 50,000 per cubic millimeter. (See Case Group X.) However, counts up to 96,000 were not unusual. The higher counts may not be interpreted as an index of greater severity of the disease.

Long standing sequelæ of lead poisoning, such as wrist drop or other neuro-muscular lesions, need not necessarily be associated with an increase of basophilic red cells, although one case of double wrist drop, following lead poisoning about 10 years previous, did present a high count. We are not certain that this is evidence of retained lead from his earlier known involvement, owing to the fact that he is still employed in a lead industry, although in a department apart from any definite lead hazard. (See Case 18, P.)

Clinical lead poisoning habitually arises in industry among those workers who on previous examinations have presented high basophilic counts or counts that show increases on successive tests, although within the range of normal. (See Cases 39, B. and 12, R.)

We have observed two patients who within a three-year period have suffered from lead poisoning of severe character four or more different times. During the first portion of this mentioned period we were utilizing only the slide method. The oft-repeated tests revealed a high basophilic aggregation count of from 4 to 6 per microscopic field. Whenever for any reason, such as infection or overwork, the normal régime of either of these two men was upset clinical lead poisoning was prone to appear; but at the time of the disabling episodes the basophilic red cells did not apparently increase. In other words, the amount of lead harbored by these men over periods of months was sufficient to provoke lead poisoning—given a condition of reduced alkalinity or comparable changes in the blood and tissues.

Many of our cases were treated with alkalies following the treatment outlined by Aub.[32] Although symptoms and some signs readily disappeared, the number of basophilic red cells remained high. This we feel is explicable inasmuch as alkali treatments lead to a deposition of lead primarily in bony tissues where the contact with bone marrow may not be terminated. (See Cases 20, C. C.; 36, F. G. H.) There its restricted toxic action may lead to a continued outpouring of premature red blood cells, even though no other lead action is manifest. The use of milk in a lead industry as a preventive measure in part limits the absorption of lead from the intestinal tract; in part leads to the deposition of lead in a relative harmless form in bony tissues, because of its calcium content. However efficacious milk may be in warding off clinical plumbism through this latter action, it does not prevent the appearance of basophilic red cells.

Alkali treatment resulting in apparent cures without subsequent deleading treatment will lead to the appearance of basophilic red cells for an indefinite period. This evidence of retained lead suggests that in the termination of treatment with only an apparent cure the way is paved for a recurrence of clinical plumbism at a subsequent time. Our experience with basophilic cells as an evidence of retained lead suggests in some instances that in the course of months these cells may gradually disappear in the absence of further exposure. This may mean that the retained lead slowly has been eliminated. On the other hand, in a few ancient cases of lead poisoning we have administered acids in the hope of liberating residual lead. Under such circumstances we have been able to detect at times increased numbers of basophilic cells. In Table II we noted that linotype operators who earlier had engaged in the more hazardous occupation of hand typesetting averaged higher as to basophilic cells than did operators who had done no handwork previously. This suggests that some lead may be stored indefinitely in the absence of deleading treatment. The use of such medicaments as KI or NH_4Cl in the treatment of acute lead poisoning appears to increase the basophilic count transiently; but eventually such treat-

[32] "Lead poisoning," by J. C. Aub, L. T. Fairhall, A. S. Minot, and P. Rezinkoff. Baltimore, Williams & Wilkins Co., 1926.

ment will lead to the essential disappearance of basophilic red cells from the blood stream. (See Case 39, B.)

A number of cases are now excerpted pertinent to one or more assertions made in the preceding paragraphs.

CASE 36, F. G. H.

First seen October 14, 1926; white; age, 57; house painter for 30 years. Came to us on account of loss of strength, beginning eight weeks previously; loss of 18 pounds weight in 7 weeks. Suffers from nausea and dizziness. Additional questioning established further pertinent information as follows: The vomiting of practically all food, constipation, copper taste in mouth, low-grade intermittent abdominal pain, sleeplessness, very severe cramps in calves of legs with some cramps in other muscle groups, joint pains in knees, wrists, and fingers, and continuous thirst.

Our examination led to these findings: Body generally flabby as to musculature, except over abdomen which was rigid; stooped as to posture; unsteady as to gait; tremors in all parts of the body. Patient easily exhausted. Temperature, 98.8. Pulse, 116; after exercise, 140; irregular. Respirations, 36; blood pressure, 148/86. Extremities emaciated, with muscles apparently atrophic. Reflexes diminished; marked weakness in extensor group of muscles of both hands. Hand grips without force. Skin flabby but not colored. Pallor.

Eyes present an arcus senilis. Pupils react to light but not to accommodation. An ulcer was present on nasal septum. The mouth presented many missing teeth, gross pyorrhea, calcareous deposits with purple areas in diseased gums, suggesting exaggerated lead lines. The less diseased gums exhibited a definite lead line.

Cobbler's chest. Heart examination revealed a systolic murmur, tachycardia, slightly irregular. The abdomen was rigid, particularly over epigastrium. Tenderness on pressure over stomach.

Routine urinalysis was negative, save for a trace of sugar. Gastric lavage and analysis established a free HCl of 48 and a total acidity of 66.

The examination of the blood when first seen established hemoglobin, 75 per cent; red blood count, 3,960,000; white blood count, 7,600; differential—polymorphonuclears, 59; small lymphocytes, 34; large lymphocytes, 6; eosinophils, 1. Marked polychromasia and punctate stippling. Basophilic red cell count, 28,600 per cubic millimeter of blood. Basophilic aggregations averaged 8 per microscopic field. A diagnosis of lead poisoning was made and alkali treament instituted at his home. On November 5, 1926, basophilic red cells were 19,200. His basophilic aggregation test averaged 5.7 per microscopic field.

By December 29, 1926 (two and one-half months after first examination), this patient was entirely free from complaints. His teeth had been removed or repaired; weight and strength regained. He was certified for work on January 3, 1927. His basophilic red count was then 42,000 per cubic millimeter; the white blood count, 8,600; Hemoglobin, 85 per cent; the basophilic aggregation test averaged 6 cells per field.

On April 8, 1927, after patient had been discharged for four months, another examination of the blood was made with results as follows: Hemoglobin, 85 per cent; red blood count, 4,700,000; white blood count, 10,000; differential—polymorphonuclears, 67; small lymphocytes, 24; large lymphocytes, 8; transitional, 1. Basophilic red count, 40,000. Basophilic aggregation test, 11 per field. Patient declined deleading treatment. In the ensuing months no symptoms have reappeared.

This case is cited for three purposes—(*a*) to point out the usual range of basophilic red cell counts in lead poisoning; (*b*) to point out the perpetuation of such cells after apparent cure by alkalinization; (*c*) to show the limitation of the slide method (b. a.) for quantitative purposes. Although unreliable for precision work, any such high numbers per average microscopic field should always be regarded as significant.

CASE 18, P.

White; Hungarian; white-lead worker; age, 47. Presents ancient double wrist drop, which originated in 1917 as a result of lead poisoning when working in corrosion department. Now engaged in outside work on tanbark pile. No complaints beyond partial loss of use of hands. Examination of blood shows: Hemoglobin, 75 per cent; white blood count, 13,600; differential—polymorphonuclears, 55; small lymphocytes, 45; eosinophils, 0; transitionals, 0; basophilic red cell count, 18,200. Basophilic aggregations, 4.8 per average field. This case suggests the possibility of retained lead throughout a period of 10 years.

CASE 20, D. C.

White; male; age, 60. Janitor in storage battery factory. Began work at the factory in September, 1926. At first was placed on lead grid piling. Later mixed lead oxides and still later did janitor work with gross exposure to lead oxide dusts. After these months of hazardous work, patient suddenly developed typical lead colic, with unusually severe constipation, muscle cramps, pallor, nausea, with a slight degree of meningeal irritation. In a hospital he was given alkali treatment, together with appropriate measures for pain, constipation, etc. At this time patient's blood findings were: Hemoglobin, 65 per cent; red blood count, 4,240,000; white blood count, 14,200. Basophilic red cell count was 28,000. Basophilic aggregation averaged 6 per field.

After six weeks patient was ambulatory and free from complaints. His blood at that time contained: Red blood count, 4,700,000; white blood count, 8,500; differentials—polymorphonuclears, 65; small lymphocytes, 26; large lymphocytes, 4; transitionals, 4; eosinophils, 1. The basophilic red count was then 20,000, with basophilic aggregations 6 per average field. Ten days later this patient was at work (not lead work). At that time his basophilic red count was 28,000. Two months later patient's blood was again examined. The basophilic count remained the same, 28,000. Patient agreed to deleading treatment, but before this could be carried out he developed an acute infection involving the respiratory tract and various joints. After this passed his basophilic red cell count was within normal limits and has so remained.

This case is cited because of the persistence of basophilic cells after the disappearance of symptoms and the disappearance of these cells after an infectious process.

CASE 12, R.

White; male; age, 20. After working for three months as a paster in the manufacture of storage battery plates, he developed characteristic lead poisoning and was sent to a local hospital. Between two and three weeks after entering upon this employment this man's blood presented 1 basophilic aggregation per average microscopic field. Three weeks later this average had increased to 6 per field. During the intervening period patient suffered from mild manifestations suggestive of lead poisoning, such as nausea, vomiting, slight pallor. He continued to work although taking alkalis. Two weeks later the routine testing revealed about the same number of basophilic red cells. The routine test for the next two-week period again established an excess of basophilic red cells. These warning prodromata continued until at the end of the third month of exposure this patient developed a mild respiratory infection. Immediately an acute lead poisoning in severe form was precipitated. At that time the basophilic aggregation test averaged 12 to 15 cells per microscopic field. Tests were made at one week intervals for three weeks, all of which ranged from 5 to 8 cells per average field. Patient fully recovered and left this type of employment.

This case is cited to point out our recognition of the imminence of lead poisoning as evidenced in increasing numbers of basophilic red cells, and its precipitation at the time of a respiratory infection. This patient should have been removed from hazardous work at the end of his sixth week of employment.

CASE 39, B.

White; male; age, 25; worked with molten lead. In August, 1925, this man suffered from acute lead poisoning. He lost but one week from work, although the evident lead poisoning was noteworthy for a much longer period. Beginning with September we noted an increasing amount of basophilic material on successive tests:

October 7, 1925	++++
November 5, 1925	+++++
November 19, 1925	++++++++++

Patient, by this time, was suffering from disabling lead poisoning, calling for treatment. However, by January 5, 1926, patient had become deleaded through the use of ammonium chloride, so that for a period his routine tests showed:

January 25, 1926	++
February 12, 1926	++
March 5, 1926	Poor slide.
March 30, 1926	++
April 16, 1926	++
May 6, 1926	+++
May 20, 1926	++++
June 4, 1926	++++

Thus again reaching the danger zone for clinical lead poisoning.

This case is cited to show the mounting numbers of basophilic cells following exposure.

CASE 48, T. A.

Male; white; age, 66. Suffered from lead poisoning in January, 1924. At that time he was a mixer of lead oxides. He lost two weeks' time from work. His condition was complicated by preexisting chronic bronchitis, myocarditis, and hypertrophic arthritis. He was completely deleaded through the use of ammonium chloride.

On resumption of work he was given the job of plant carpenter and plumber, which was without severe exposure to lead. One day, while at work, patient became thoroughly drenched while repairing a broken pipe and worked throughout the day with wet clothing. He developed pneumonia or some severe respiratory infection. He was treated at a general hospital and completely recovered. In May of the same year patient again became disabled, suffering from myocarditis, bronchitis, arthritis, senility, etc., but without evidence of lead poisoning. Nevertheless he filed a claim for compensation. Various examinations at hospitals failed to disclose any proper reason for the acceptance of this condition as directly attributable to lead. In this instance no basophilic red cells beyond normal numbers were detectable.

This case is cited to bring out the possible field of usefulness of these described tests in the discrimination between lead poisoning and conditions simulating this disease.

CASE GROUP, X

We made the following test as to the efficacy of basophilic red cell counts as an index of lead poison or imminent lead poisoning.

Eighty-five examinations were made on 85 workers in a white-lead and metallic-lead products factory. In this number 11 workers presented basophilic red cell counts in excess of 7,000 cells per cubic millimeter of blood. The exact figures were:

Corrosion worker	7,800
Do	11,000
Do	12,400
Do	7,200
Kiln-room worker	61,600
Do	68,600
Dry white lead packer	70,400
Do	22,400
Scrap-lead furnace tender	18,400
Furnace dross skimmer	32,000
Water grinder	44,800

With this evidence alone, the names of these workers were presented to the plant industrial physician (who had not participated in our examinations) with the request that these men be carefully examined for lead poisoning. This physician reported that 9 of these 11 men were either previously known ambulatory cases or else proved to have clinical evidence of lead poisoning. Our own clinical examinations established evidence of lead poisoning in 9 of these 11 workers. In 1 of this group of 9 the patient was free of complaints at this time but had suffered from severe lead poisoning about two years previously.

This group is cited in the belief that in basophilic red cell counts alone, made on lead-exposed workers, there is suggestive evidence of lead intoxication or marked lead absorption whenever the count is in excess of 6,000 to 7,000 per cubic millimeter of blood.

SUMMARY

Examinations as to the occurrence of basophilic red cells in the blood have been carried out on more than 1,000 persons (1,045), representing (*a*) normal persons, (*b*) pathologic states other than lead poisoning, (*c*) lead-exposed workers, and (*d*) clinical lead poisoning.

The results derived and conclusions formed are now summarized:

(1) The number of basophilic red cells found in 145 normal adults was commonly less than 1,000 per cubic millimeter of blood. In a few persons believed to be normal the count exceeded 1,000, but was less than 5,000. Possible exceptions are to be found in several physiologic states, viz, in the newborn, in pregnancy, when in high altitudes, after considerable exposure to sunlight, especially in springtime, after X-ray exposure, after profuse sweating, after iron or arsenic medication, and possibly slight variations are to be associated with food intake. In the physiologic states to which the worker is likely to be subjected the basophilic red cell count does not exceed 20,000 per cubic millimeter.

(2) The number of basophilic red cells is increased above normal numbers in the following pathologic states: Lead intoxication, benzol poisoning, arsenic poisoning, in all types of anemia in which there is regeneration, hemolytic icterus, following hemorrhage, leukemias, at times in acute infections, in neoplasms involving the bone marrow, and in polycythemia.

(3) In the absence of other conditions presenting high basophilic red cell counts a high basophilic red cell count in a person exposed to lead is accepted as indicative of lead absorption or lead poisoning.

(4) Mounting numbers of basophilic red cells in workers exposed to lead is indicative of imminent clinical lead poisoning.

(5) Frank cases of lead poisoning almost invariably present basophilic red cell counts in excess of 7,000 such cells per cubic millimeter of blood. Rarely do the counts exceed 100,000. The usual range is from 7,000 to 50,000.

(6) Treatment with alkalies leading to a cessation of symptoms is not necessarily followed by the disappearance of basophilic red cells.

(7) Treatment with substances leading to the excretion of lead is followed by the diminution and disappearance of excessive numbers of basophilic cells.

(8) The number of basophilic red cells present in lead poisoning or lead absorption does not stand in any constant relation to hemoglobin percentage, total red or white count, differential white count, or preformed punctate stippling.

(9) Sequelæ of lead poisoning, such as wrist drop, do not stand in any constant relation to basophilic red cell counts.

(10) Very high basophilic red cell counts, such as 60,000 to 80,000, may be present without the actual signs or symptoms of clinical lead poisoning. From the members of any group presenting such high

basophilic red cell counts, clinical cases of lead poisoning are prone to arise.

(11) Lead-exposed workers presenting basophilic red cell counts in excess of 6,000 to 7,000 should be accepted, in the absence of other conditions productive of such increased counts, as lead poisoning prospects and should be subjected to lead eliminating treatment or alkali treatment with subsequent lead eliminating treatment. This is especially desirable if successive examinations reveal progressive increases in the number of basophilic cells.

(12) The counting method utilized in this work for the enumeration of basophilic red cells is more accurate than the slide method for basophilic aggregations.

(13) The slide method as utilized for the approximation of the numbers of basophilic red cells is not sufficiently accurate to permit of calculation in terms of numbers of basophilic red cells per cubic millimeter of blood. This method, however, is a dependable method for the recognition of small numbers or large numbers of basophilic red cells. By this method the examining physician may recognize workmen who are approaching dangerous degrees of lead absorption.

(14) The application of these methods suggests that in lead industries many workers commonly regarded as unexposed, such as office workers, clerks, etc., actually may also absorb much lead and thus become potential cases of lead intoxication. This is especially true if the hazard of lead is in the form of dust.

(15) Basophilic red cell counts made on all workers in various large departments of an industry with a lead hazard, afford a possible index of the degree of the lead hazard of the departments and permits of comparison of the degree of hazard between several departments.

LIST OF BULLETINS OF THE BUREAU OF LABOR STATISTICS

The following is a list of all bulletins of the Bureau of Labor Statistics published since July, 1912, except that in the case of bulletins giving the results of periodic surveys of the bureau only the latest bulletin on any one subject is here listed.

A complete list of the reports and bulletins issued prior to July, 1912, as well as the bulletins published since that date, will be furnished on application. Bulletins marked thus (*) are out of print.

Conciliation and Arbitration (including strikes and lockouts).

*No. 124. Conciliation and arbitration in the building trades of Greater New York. [1913.]
*No. 133. Report of the industrial council of the British Board of Trade on its inquiry into industrial agreements. [1913.]
No. 139. Michigan copper district strike. [1914.]
No. 144. Industrial court of the cloak, suit, and skirt industry of New York City. [1914.]
No. 145. Conciliation, arbitration, and sanitation in the dress and waist industry of New York City. [1914.]
No. 191. Collective bargaining in the anthracite coal industry. [1916.]
*No. 198. Collective agreements in the men's clothing industry. [1916.]
No. 233. Operation of the industrial disputes investigation act of Canada. [1918.]
No. 255. Joint industrial councils in Great Britain. [1919.]
No. 283. History of the Shipbuilding Labor Adjustment Board, 1917 to 1919.
No. 287. National War Labor Board: History of its formation, activities, etc. [1921.]
No. 303. Use of Federal power in settlement of railway labor disputes. [1922.]
No. 341. Trade agreement in the silk-ribbon industry of New York City. [1923.]
No. 402. Collective bargaining by actors. [1926.]
No. 448. Trade agreements, 1926.

Cooperation.

No. 313. Consumers' cooperative societies in the United States in 1920.
No. 314. Cooperative credit societies in America and in foreign countries. [1922.]
No. 437. Cooperative movement in the United States in 1925 (other than agricultural).

Employment and Unemployment.

*No. 109. Statistics of unemployment and the work of employment offices in the United States. [1913.]
No. 172. Unemployment in New York City, N. Y. [1915.]
*No. 183. Regularity of employment in the women's ready-to-wear garment industries. [1915.]
*No. 195. Unemployment in the United States. [1916.]
No. 196. Proceedings of the Employment Managers' Conference held at Minneapolis, Minn., January 19 and 20, 1916.
*No. 202. Proceedings of the conference of Employment Managers' Association of Boston, Mass., held May 10, 1916.
No. 206. The British system of labor exchanges. [1916.]
*No. 227. Proceedings of the Employment Managers' Conference, Philadelphia, Pa., April 2 and 3, 1917.
No. 235. Employment system of the Lake Carriers' Association. [1918.]
*No. 241. Public employment offices in the United States. [1918.]
No. 247. Proceedings of Employment Managers' Conference, Rochester, N. Y., May 9–11, 1918.
No. 310. Industrial unemployment: A statistical study of its extent and causes. [1922.]
No. 409. Unemployment in Columbus, Ohio, 1921 to 1925.

Foreign Labor Laws.

*No. 142. Administration of labor laws and factory inspection in certain European countries. [1914.]

Housing.

*No. 158. Government aid to home owning and housing of working people in foreign countries. [1914.]
No. 263. Housing by employers in the United States. [1920.]
No. 295. Building operations in representative cities in 1920.
No. 368. Building permits in the principal cities of the United States in [1921 to] 1923.
No. 424. Building permits in the principal cities of the United States in [1924 and] 1925.
No. 449. Building permits in the principal cities of the United States in [1925 and] 1926.

Industrial Accidents and Hygiene.

*No. 104. Lead poisoning in potteries, tile works, and porcelain enameled sanitary ware factories. [1912.]
No. 120. Hygiene of the painters' trade. [1913.]
*No. 127. Dangers to workers from dust and fumes, and methods of protection. [1913.]
*No. 141. Lead poisoning in the smelting and refining of lead. [1914.]
*No. 157. Industrial accident statistics. [1915.]
*No. 165. Lead poisoning in the manufacture of storage batteries. [1914.]
*No. 179. Industrial poisons used in the rubber industry. [1915.]
No. 188. Report of British departmental committee on the danger in the use of lead in the painting of buildings. [1916.]
*No. 201. Report of committee on statistics and compensation-insurance cost of the International Association of Industrial Accident Boards and Commissions. [1916.]
*No. 207. Causes of death, by occupation. [1917.]
*No. 209. Hygiene of the printing trades. [1917.]
No. 219. Industrial poisons used or produced in the manufacture of explosives. [1917.]
No. 221. Hours, fatigue, and health in British munition factories. [1917.]
No. 230. Industrial efficiency and fatigue in British munition factories. [1917.]
*No. 231. Mortality from respiratory diseases in dusty trades (inorganic dusts). [1918.]
No. 234. Safety movement in the iron and steel industry, 1907 to 1917.
No. 236. Effect of the air hammer on the hands of stonecutters. [1918.]
No. 249. Industrial health and efficiency. Final report of British Health of Munitions Workers Committee. [1919.]
*No. 251. Preventable death in the cotton-manufacturing industry. [1919.]
No. 256. Accidents and accident prevention in machine building. [1919.]
No. 267. Anthrax as an occupational disease. [1920.]
No. 276. Standardization of industrial accident statistics. [1920.]
No. 280. Industrial poisoning in making coal-tar dyes and dye intermediates. [1921.]
No. 291. Carbon-monoxide poisoning. [1921.]
No. 293. The problem of dust phthisis in the granite-stone industry. [1922.]
No. 298. Causes and prevention of accidents in the iron and steel industry, 1916 to 1919.
No. 306. Occupational hazards and diagnostic signs: A guide to impairments to be looked for in hazardous occupations. [1922.]
No. 339. Statistics of industrial accidents in the United States. [1923.]
No. 392. Survey of hygienic conditions in the printing trades. [1925.]
No. 405. Phosphorus necrosis in the manufacture of fireworks and in the preparation of phosphorus. [1926.]
No. 425. Record of industrial accidents in the United States to 1925.
No. 426. Deaths from lead poisoning. [1927.]
No. 427. Health survey of the printing trades, 1922 to 1925.
No. 428. Proceedings of the Industrial Accident Prevention Conference, held at Washington, D. C., July 14–16, 1926.

Industrial Relations and Labor Conditions.

No. 237. Industrial unrest in Great Britain. [1917.]
No. 340. Chinese migrations, with special reference to labor conditions. [1923.]
No. 349. Industrial relations in the West Coast lumber industry. [1923.]
No. 361. Labor relations in the Fairmont (W. Va.) bituminous-coal field. [1924.]

Industrial Relations and Labor Conditions—Continued.

No. 380. Postwar labor conditions in Germany. [1925.]
No. 383. Works council movement in Germany. [1925.]
No. 384. Labor conditions in the shoe industry in Massachusetts, 1920–1924.
No. 399. Labor relations in the lace and lace-curtain industries in the United States. [1925.]

Labor Laws of the United States (including decisions of courts relating to labor).

No. 211. Labor laws and their administration in the Pacific States. [1917.]
No. 229. Wage-payment legislation in the United States. [1917.]
No. 285. Minimum wage laws of the United States: Construction and operation. [1921.]
No. 321. Labor laws that have been declared unconstitutonal. [1922.]
No. 322. Kansas Court of Industrial Relations. [1923.]
No. 343. Laws providing for bureaus of labor statistics, etc. [1923.]
No. 370. Labor laws of the United States, with decisions of courts relating thereto. [1925.]
No. 408. Laws relating to payment of wages. [1926.]
No. 434. Labor legislation of 1926.
No. 444. Decisions of courts and opinions affecting labor, 1926.

Proceedings of Annual Conventions of the Association of Governmental Labor Officials of the United States and Canada.

*No. 266. Seventh, Seattle, Wash., July 12–15, 1920.
No. 307. Eighth, New Orleans, La., May 2–6, 1921.
No. 323. Ninth, Harrisburg, Pa., May 22–26, 1922.
No. 352. Tenth, Richmond, Va., May 1–4, 1923.
No. 389. Eleventh, Chicago, Ill., May 19–23, 1924.
No. 411. Twelfth, Salt Lake City, Utah, August 13–15, 1925.
No. 429. Thirteenth, Columbus, Ohio, June 7–10, 1926.
No. 455. Fourteenth, Paterson, N. J., May 31 to June 3, 1927.

Proceedings of Annual Meetings of the International Association of Industrial Accident Boards and Commissions.

No. 210. Third, Columbus, Ohio, April 25–28, 1916.
No. 248. Fourth, Boston, Mass., August 21–25, 1917.
No. 264. Fifth, Madison, Wis., September 24–27, 1918.
*No. 273. Sixth, Toronto, Canada, September 23–26, 1919.
No. 281. Seventh, San Francisco, Calif., September 20–24, 1920.
No. 304. Eighth, Chicago, Ill., September 19–23, 1921.
No. 333. Ninth, Baltimore, Md., October 9–13, 1922.
No. 359. Tenth, St. Paul, Minn., September 24–26, 1923.
No. 385. Eleventh, Halifax, Nova Scotia, August 26–28, 1924.
No. 395. Index to proceedings, 1914–1924.
No. 406. Twelfth, Salt Lake City, Utah, August 17–20, 1925.
No. 432. Thirteenth, Hartford, Conn., September 14–17, 1926.
No. 456. Fourteenth, Atlanta, Ga., September 27–29, 1927.

Proceedings of Annual Meetings of International Association of Public Employment Services.

No. 192. First, Chicago, December 19 and 20, 1913; Second, Indianapolis, September 24 and 25, 1914; Third, Detroit, July 1 and 2, 1915.
No. 220. Fourth, Buffalo, N. Y., July 20 and 21, 1916.
No. 311. Ninth, Buffalo, N. Y., September 7–9, 1921.
No. 337. Tenth, Washington, D. C., September 11–13, 1922.
No. 335. Eleventh, Toronto, Canada, September 4–7, 1923.
No. 400. Twelfth, Chicago, Ill., May 19–23, 1924.
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No. 360. Time and labor costs in manufacturing 100 pairs of shoes, 1923.
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*No. 121. Sugar prices, from refiner to consumer. [1913.]
*No. 130. Wheat and flour prices, from farmer to consumer. [1913.]
No. 164. Butter prices, from producer to consumer. [1914.]
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No. 369. The use of cost-of-living figures in wage adjustments. [1925.]
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*No. 331. Code of lighting: Factories, mills, and other work places.
No. 336. Safety code for the protection of industrial workers in foundries.
No. 350. Specifications of laboratory tests for approval of electric headlighting devices for motor vehicles.
No. 351. Safety code for the construction, care, and use of ladders.
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No. 378. Safety code for woodworking plants.
No. 382. Code of lighting school buildings.
No. 410. Safety code for paper and pulp mills.
No. 430. Safety code for power presses and foot and hand presses.
No. 433. Safety codes for the prevention of dust explosions.
No. 436. Safety code for the use, care, and protection of abrasive wheels.
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*No. 162. Vocational education survey of Richmond, Va. [1915.]
No. 199. Vocational education survey of Minneapolis, Minn. [1916.]
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No. 161. Wages and hours of labor in the clothing and cigar industries, 1911 to 1913.
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*No. 190. Wages and hours of labor in the cotton, woolen, and silk industries, 1907 to 1914.
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No. 421. Wages and hours of labor in the slaughtering and meat-packing industry, 1925.
No. 422. Wages and hours of labor in foundries and machine shops, 1925.
No. 435. Wages and hours of labor in the men's clothing industry, 1911 to 1926.

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No. 442. Wages and hours of labor in the iron and steel industry, 1907 to 1925.
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No. 446. Wages and hours of labor in cotton-goods manufacturing, 1910 to 1926.
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