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different degrees of subdivision in the erythrocytes:

1. One can use the McCord technique - the so-called Basophilic Aggregation Test, which involves all of the erythrocytes which contain basophilic material - stippled cells, basophilic erythrocytes, and some, at least, of the reticulocytes. McCord has described the technique and has given the limits of its significance on a quantitative basis.

2. One can use any of the methods that have been described for staining the erythrocytes, and any of the procedures advised by various observers for obtaining quantitative or semi-quantitative estimates of the numbers.

The most important thing is to develop data in one's own hands, from his own use of the method selected, and to put the procedure on as uniform and quantitative a basis as his skill and facilities will permit.

In counting the numbers of stippled erythrocytes one must first have excellent microscopic equipment, must develop a very good and uniform method of making and staining the films, and must spend enough time on each film to determine the numbers of "stippled" erythrocytes (not those that are basophilic but those that have distinct granules, whether coarse or fine) in relation to the total numbers of erythrocytes seen. The best means of expression is that of numbers of "stippled" erythrocytes per million erythrocytes. In arriving at this estimate, we find it necessary to count not less than fifty fields in which the erythrocytes are distributed evenly without overlapping.

I attach herewith a description of the procedure which we usually use. We sometimes use Wright's stain instead of that described, and it works satisfactorily if one checks the stain carefully, from time to time (certainly every new batch), with a film (or films) of known character, with reference to the numbers of stippled erythrocytes thereon.

As I have indicated, the entire procedure is a poor one for the purpose. Something like half of the films obtained (one per man) from any group of exposed men - unless their exposure is of the grossly dangerous type that results in frequent cases of lead poisoning - will give normal results at any time you choose to look at them. The high results are not necessarily indicative of danger, and the low results give no real assurance of safety. The best that one can say is that the average value of all of the findings from a specific group of men will give some clue to the severity of the exposure of the group as a whole, as compared with the findings from a group that is not subjected to any exposure to lead, or with those from groups whose exposure to lead is clearly much greater or much less severe. That is to say, the method will differentiate groups, to some

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extent, in accordance with the severity of their exposure, but its application to the individual man is very untrustworthy.

There is one feature of the phenomenon that is of some significance. If a man who has been giving low results begins suddenly to develop an increase of a progressive character in the numbers, one had better look out. Even this, however, is not specific evidence of increased lead absorption, since normal individuals, for no reason which one can find, have showers of stippled erythrocytes in their peripheral blood from time to time. People vary in this respect, some tending to be very stable and others labile, with reference to their hematopoietic response to non-specific stimuli. Indeed the more one studies this phenomenon, the more unreliable it is found to be in relation to lead absorption.

I must say an additional word of caution on a matter of medical technique. If I had to accept the medical responsibility for a group of men whose occupation involved dangerous exposure to lead, without having the facilities that would enable me to bear that responsibility in accordance with sound modern medical knowledge and technique, - and thank God or good fortune that I'm not in that position, although I did have such serious responsibilities, before we investigated and developed really satisfactory methods and principles - I would depend less upon the non-specific laboratory findings based on hematological changes, and more upon what I could find of prodromal and incipient signs of lead intoxication, in my handling of the situation. I would use the laboratory findings, since they would help, but I would never allow them to alter my clinical judgment in any instance in which I suspected that intoxication was impending or in which I found it in an early stage. In my opinion, the dependence of a well trained and capable physician, in such a situation, upon the findings of a technician in a hematological laboratory, borders on criminal negligence or malpractice, in these days of knowledge on these matters. Some clinicians, like Elston Belknap, say they depend on "stippling" to guide them. Do not be deceived; they do nothing of the kind. They know that the exposure in their plants is under reasonably good control, and that serious disability is not to be expected among the men under their supervision, if they keep their clinical eyes open. If the "stippling" warns them that a man needs special attention, they give it, and act accordingly. If it fails to warn them, as unfortunately it sometimes does, they have a relatively mild case of lead poisoning to deal with. Fundamentally, Belknap, who is a better clinician than many, depends upon his clinical judgment. If it coincides with the laboratory findings, all is well and easy; but if the two do not agree, he acts on his clinical judgment. He denies this, but I am quite sure it is true, nevertheless.

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In general, the figure of 8 to 12 stippled erythrocytes per fifty microscopic fields (by our technique this is about 600 to 1000 stippled erythrocytes per million erythrocytes) is commonly regarded as the point of differentiation between safe and dangerous absorption. It is as good a rule of thumb as any, but as I said before, if you apply this rigidly, you take men out of work who are in no danger at all, and you leave men at work whose danger, however slight it may be, is imminent.

I have taken much more time than I can afford to say these things in a letter, which I have said in the literature, notably in the report of the Committee on Lead Poisoning of the APHA, and also in the work edited by Frank Patty, Industrial Hygiene and Toxicology, published by Interscience Publishers, Inc., which, incidentally, will come out in a new edition before many months. However, I have spent so much of my life in an effort to get decent methods of medical control into the lead trades, that it seems a bit late to economize.

I trust that your questions have been answered in sufficient detail to be of assistance to you.

Cordially yours,

Robert A. Kehoe, M. D.

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March 9, 1955

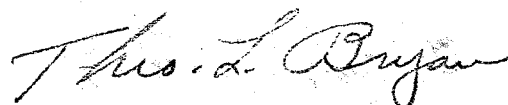
Dr. Robert Kehoe
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Dear Dr. Kehoe:

In checking of blood smears of men that work around lead fumes in the smelting, etc., the problem has been raised as to the number of fields and the approximate number of cells that should be checked to determine the percentage of stippling. Another problem is whether or not basophilic red cells are counted. The last question is what do you consider the upper limits of normal of stippling and basophilic red cells?

I would appreciate your time and consideration in this matter.

Sincerely,



Theodore L. Bryan, M.D.

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