The effect of small doses of mercury in modifying the number of the red blood corpuscles in syphilis : a study of blood-counting with the hématimètre / by E.L. Keyes.

THE EFFECT

OF

SMALL DOSES OF MERCURY

IN

MODIFYING THE NUMBER OF THE RED BLOOD CORPUSCLES IN SYPHILIS;

A STUDY OF BLOOD-COUNTING

WITH THE

HÉMATIMÈTRE.

BY

E. L. KEYES, M.D.,

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WITH TWO WOOD-CUTS.

[Reprinted from the American Journal of the Medical Sciences, for January, 1876.]

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ERRATA.

Page 12, fourth line from top, *for* "0.0006 mm.," *read* "0.006 mm."

" 14, sixteenth line from top, *for* "20 syphilitic," *read* "21 syphilitic."

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The value of mercury in the treatment of syphilis is recognized quite generally in the profession, but the most varied views are held as to the best method of using the remedy. Some practitioners advocate the old method, a prompt, brilliant course to induce salivation, hoping, alas, vainly! to strangulate the disease. Many, a majority indeed, believe in the value of numerous, interrupted, short treatments, not pushed to salivation; while others maintain that the best course to secure a patient from serious trouble, early or late in the disease, is to give mercury unremittingly during a long series of months.

To this last class I have always belonged, and my observation, now extending over ten years, fortified by the larger and longer experience of my friend and partner, Prof. Van Buren, leads me to hold to my position still, until another course can be proved to be more beneficial to the patient, or this one can be shown to do him harm.

The position is this, that syphilis is most surely controlled—most often cured, as far as any future evidence of its existence is concerned—by the unremitting use of small doses of mercury, continuously given during not less, and very often more than two years, the quantity being barely enough to keep down the symptoms and not enough to make the patient physically conscious of taking any medicine at all; the drug being pushed if necessitated by symptoms, and iodide of potassium being used when required.

I believe it to be a rule, to which there are very few exceptions, that a patient in fair general health with syphilis treated in this manner from

the period of his first eruption, and attending, meantime, to hygienic laws, will have but one general eruption (the first, and perhaps that will not be fully generalized), will have no *serious* lesion subsequently, and will be and continue to be in as good or better health after his treatment than before. To this rule, of course, there are exceptions, but they are not numerous.

In reading a paper by Liègeois,[1] I was first apprised of the fact that small doses of sublimate, administered to healthy men or animals, caused them to increase in weight. Larger doses, of course, were followed by loss of weight, and, naturally, still larger ones were fatal.

I came to accept this statement as a fact, without seeking to demonstrate it by personal experiment, because I had *clinical* proof in many of my syphilitic patients, whom I watched slowly gain in weight and strength, while under the prolonged use of minute doses of mercury.

I was familiar with the well-known results of the examinations of syphilitic blood made by Ricord and Grassi, and with the wide-spread prejudice, partly due to these experiments, that mercury reduced the proportion of red blood corpuscles, while iodide of potassium increased it early in syphilis. Yet clinical experience with small doses of mercury spoke loudly against this view, and I could not honestly heed the purely scientific warning of Grassi.

In 1874, in a very interesting article containing the tabulation of many careful experiments, Wilbouchewitch[2] arrived at the following conclusions concerning the blood in the early days of syphilis :—

1. Small doses of mercury, when given to a syphilitic patient, increase the number of red blood corpuscles at first, and slightly diminish the number of the white globules.
2. The long-continued use of small doses of mercury gives the same results which mercury in large doses yields in animals; namely, diminution of the red blood corpuscles, diarrhœa, etc.
3. It is, consequently, important to know when to discontinue treatment, and this can only be determined by counting the blood corpuscles.
4. It is necessary, in treating syphilis, to give mercury until the red corpuscles begin to diminish in number, then to cease in order to allow them to increase, to return to mercury when the number of red cells again diminishes under the influence of syphilis—and so on indefinitely.

On reading this article attentively, it became clear to me how M. Wilbouchewitch, while counting the blood corpuscles of his patients conscien-

[1] Des Résultats cliniques et scientifiques obtenus avec les Injections sous-cutanées de sublimé à petites doses dans l'étude de la Syphilis : Gaz. des Hôp., 88, p. 347, 89, p. 350, 1869—noticed by me in a Report on Syphilis, N. Y. Med. Gaz., Feb. 26, 1870, p. 150.

[2] De l'Influence des Préparations mercurielles sur la Richesse du Sang en Globules rouges et en Globules blancs—Archives de Physiologie, 4 and 5, 1874, p. 508.

tiously, might, by a faulty interpretation of his facts, have arrived at the above conclusions.

1st. All his patients, each with chancre, some with an early eruption, were treated in a hospital (Midi), taken away from their ordinary mode of life, and associated with sick people amid the depressing surroundings of hospital existence, with the sad picture of syphilitic eruptions, such as they saw around them, constantly on their minds as in prospect for themselves.

2d. Of the ten cases from which the conclusions of the paper were drawn, five received (each) a little over $\frac{1}{8}$ gr. of corrosive sublimate four times a day from the commencement (4 centigrammes daily), the other five got $\frac{3}{4}$ gr. of protiodide of mercury twice daily (10 centigrammes a day)—surely in neither case a very small dose.

3d. The falling off in red corpuscles commenced at varying periods—after from 5 to 24 days of treatment, a mean for the ten cases of exactly eleven days—and yet the author does not seem even to suspect that, possibly, his patients are being over-dosed.

4th. In five cases only is mention made of the weight of the patients. These lost, respectively, over $2\frac{1}{5}$, $2\frac{1}{5}$, $3\frac{1}{5}$, $3\frac{1}{5}$, $3\frac{1}{5}$ pounds, and that in a very few days. It seems impossible that even a careless observer could have drawn any conclusion from a patient who lost $3\frac{3}{10}$ pounds in 20 days of mercurial treatment in a hospital (Case III.), except that either the hospital injured him or that his treatment was excessive, yet neither of these ideas seems to have occurred to M. Wilbouchewitch. It would have been extraordinary had there been an increase of red blood cells above the general standard in these cases.

5th. In five of the ten cases the blood was counted again at periods varying from eight to nineteen days after the patient had left the hospital and discontinued treatment. In each case the number of red cells had increased, and it is but fair to infer that the patients had also gained in weight under their improved hygienic surroundings—but upon this point the author is silent.

It seems, therefore, that it is upon an erroneous interpretation of facts that Wilbouchewitch has built his theories and formulated his scientific laws for the treatment of syphilis. The above analysis of his facts seems to me to destroy the value of his premises and to make his conclusions worthless.

Wilbouchewitch also killed a few rabbits with large doses of mercury.

In the "Report of the Edinburgh Committee of the British Medical Association, by J. Hughes Bennett,"[1] there are fourteen carefully tabulated records of experiments made upon dogs, by giving them different forms of

[1] Researches into the Action of Mercury, etc., on the Biliary Secretion, 2d ed., London, 1874.

mercury in varied doses. The experiments were carried on solely with a view to determine the action of the substance employed upon the liver, yet, incidentally, a close study of the tables yields the following important information—of which, however, the Committee took no note.

Corrosive sublimate, blue pill, or calomel was given, but whatever mercurial was used, the dog invariably lost weight when a large dose of the mineral was administered, whether kept up for a short period ($1\frac{3}{5}$ gr. sublimate during 1 day, loss $\frac{1}{4}$ pound) or for a long one ($19\frac{1}{2}$ gr. sublimate during 13 days, loss $7\frac{1}{4}$ pounds, p. 29).

Absolutely, the only instances in the report where a *gain* in the weight of the dog is noted, are two. In both, comparatively small doses of corrosive sublimate were employed, from $\frac{1}{6}$ gr. daily to $\frac{1}{3}$ gr. twice a day—and a continuance of the latter large dose for more than 48 hours caused a loss of about 6 pounds in one case, while the same dog, suffering from an artificial fistula in the abdomen, had increased in weight over three ounces in four days under the administration of $\frac{1}{6}$ gr. corrosive sublimate twice a day, and had held what he gained until the dose was increased (p. 51). The other animal (p. 49) took four grains of corrosive sublimate in twelve days, and gained about the same amount. These are the only dogs of the series in which a gain in weight is noted, and they each had abdominal fistula. They alone took reasonably small doses of mercury.

Upon the data set forth above I undertook to investigate the effect of mercury upon the blood This paper is a record of the results obtained.

The Hêmatimètre.—A special instrument is necessary in order even to approach accuracy in an estimation either of the quantity or number of cellular elements contained in a given volume of blood. Chemical methods, those yielding the often-quoted estimates of Andral and Gavarret, of Becquerel and Rodier, those of Hittorf, Erlenmyer, Marchand, Nasse, Zimmermann, and others, can only be approximative. Grassi's method[1] was chemical like that of Andral, but deserves particular mention as being the first scientific effort (1844) to determine the effect of syphilis, and of the use of mercury and of iodide of potassium in this disease, upon the proportion of red corpuscles in the blood.

All the methods of actually counting the blood cells which are found referred to by writers on this subject (those of Hirt, Lorange, Marfels, Moleschott, Vierordt, Welcker, Mantegazza, etc.), whether they were for counting the red or the white cells, had the defect of not accurately establishing the count for a given volume of blood. The dilution of the blood

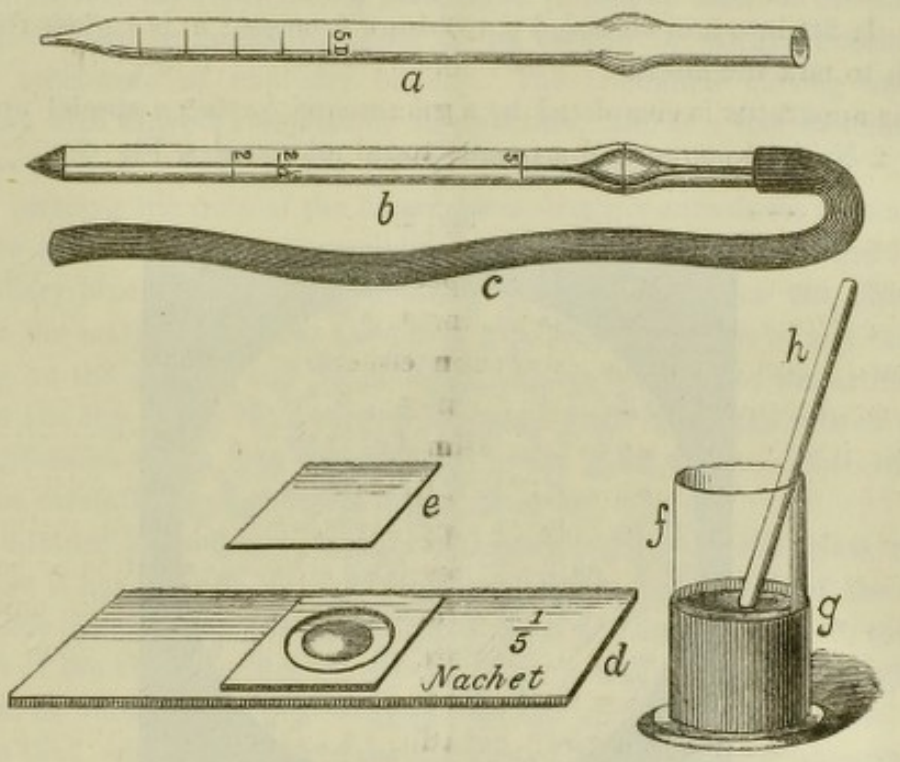
[1] Referred to by MacCarthay, Du Diagnostic et de l'Enchaînement des Symptomes syphilitiques. Thèse de Paris, 1844, and rather fully in Ricord's Leçons sur le Chancre, 2d Ed., Paris, 1860, p. 185.

was known, and the superficies included in the count more or less accurately established; but the thickness of the layer of blood counted was a more or less variable factor. Many of the attempts formerly made were undertaken to establish, approximately, the relative proportion between the white and red corpuscles rather than to determine the absolute number of red corpuscles contained in a given volume of blood.

The first recorded instance of which I am aware wherein accuracy was aimed at in estimating the exact volume of blood counted, was that of Cramer,[1] and a cubic millimetre of blood was adopted as the unit of volume. The process was a rough one.

In 1867, Potain made a positive step in advance in this direction by devising an ingenious set of instruments, requiring, however, considerable skill and care in their management, which allowed him, by the use of a special mathematical formula, to arrive at an easy estimate of the number of red corpuscles in a cubic millimetre, by counting a small portion of diluted blood.

Fig. 1.



Malassez[2] gave Potain's method to the world and wrote (and is still writing) extensively upon the subject of blood-counting. The instrument

[1] Nederl., Lancet, 1855, referred to by Hayem Gaz. Hebd., May, 1875.

[2] Comptes Rendus de l'Academie des Sciences, Dec. 1872; De la Numération des Globules rouges du Sang, Thèse de Paris, 1873; Nouvelle Méthode de Numération des Globules rouges et des Globules blancs du Sang, Archives de Physiologie, 1874, 1. p. 291.

described and used by Malassez is somewhat complicated, and not free from the accusation of possible inaccuracy. I shall not describe it, as a much more simple and exact apparatus exists. I refer to the hématimètre of Hayem and Nachet, recently described (with plates) by the former gentleman.[1]

This is the instrument which I have used.

Fig. 1, represents all its essential parts except the microscope. A few words will suffice to describe them.

a, is a graduated glass pipette, each line on the tube marking off a capacity of 100 cubic millimetres, 5 D therefore indicates 500 cubic mm.

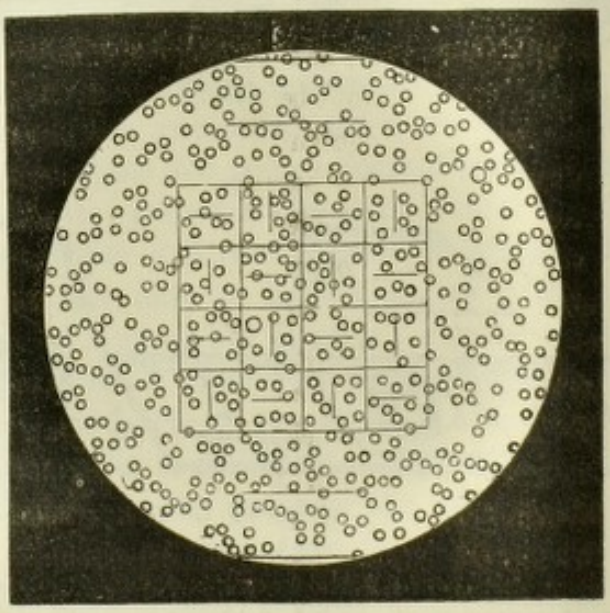
b, is a smaller capillary pipette graduated to 2, $2\frac{1}{2}$, and 5 cubic mm.; the operator takes the rubber tube *c* into his mouth to facilitate the entrance of blood into the pipette by suction.

d, is a glass slide upon which is cemented a glass cell with a circular opening 1 centimetre in diameter, the depth of the cell being exactly $\frac{1}{5}$ mm.; *e*, the covering glass to fit over the cell. A drop of fluid is represented in the cell.

f, is a small glass cup to receive the blood and artificial serum for mixing. It fits into a brass stand *g*, to insure firmness; *h*, is a glass rod with which to mix the fluids.

The apparatus is completed by a microscope having a special eye-piece (No. 2 Nachet) containing a quadrilateral micrometer, Fig. 2.

Fig. 2.



The large square of the micrometer is further divided into sixteen smaller squares, while each smaller square contains a line drawn half way across it to facilitate the counting.

[1] De la Numération des Globules du Sang, Gaz. Hebd , May 7, 1875, p. 291.

Manner of using the Instrument.—The ocular above described, being adjusted to a microscope, the draw-tube is so arranged that for a given objective (No. 2 Nachet is suitable) a side of the square micrometer in the eye-piece measures accurately $\frac{1}{5}$ mm. upon a stage micrometer. The depth to which the draw-tube has been pushed in is then scratched upon the tube so as to be readily arranged in a moment, and the microscope is ready for use.

I have always adopted as a standard of dilution 1 to 250, as this scatters the corpuscles sufficiently to make them easy to count. The actual process is as follows :—

The pipette *a*, is filled to the mark 5 D, with the diluting fluid, which is at once emptied into the glass cup *f*. The pulp of the finger of the patient whose blood is to be tested should be deeply pierced with a glover's needle having a triangular cutting point. The blood should not be driven forward into the finger by pressure before the puncture. A string should not be tied around the finger. A round sharp needle should not be used. Repeated experiments, with needles and knives upon myself, which lack of space forbids my reproducing here, have proved to me that the above suggestions must be heeded in order to be certain of always obtaining uniform specimens of capillary blood. The triangular cutting needle does away with Hayem's objections to puncture,[1] and is a less formidable instrument than the knife in the eyes of the patient.

After piercing the pulp of the finger quick firm pressure down the finger will force out a large drop from the puncture. This must be sucked into the capillary pipette without delay, lest it coagulate. When the pipette is full to the mark 2, its point should be rapidly wiped clean of any blood adhering on the outside, and the contents at once blown into the artificial serum in the cup *f*. A little suction back and forth clears the tube of any blood corpuscles which may have adhered to the glass within. Both tubes should be carefully washed before being put away.

The mixture should now be thoroughly agitated with the glass rod, and before it has time to settle, a drop is placed in the middle of the cell on the slide *d*, care being taken that the drop is not large enough to touch any part of the circumference of the cell (Fig. 1, *d*). The covering glass *e*, should be immediately placed upon the cell. Should the drop be too large, so that, when the thin glass is adjusted, it spreads out enough to touch the circumference of the cell and to be partly sucked up beneath the covering glass and top of the cell, the latter must be wiped and a new drop placed within it. Finally a small drop of water or saliva is applied to the edge of the covering glass, under which it circulates around the top of the cell, serving to hold the cover in place and prevent the evaporation of any part of the drop within.

[1] Loc. cit., p. 294.

The slide thus prepared is placed under the microscope. In a few moments the counting may begin, the blood corpuscles will have all settled to the bottom of the cell, and a picture similar to that shown in Fig. 2 will be seen on looking through the microscope. The counting should not commence until all the corpuscles are upon the same plane and can all be focused together. It is better to count each of the sixteen squares and write down its number separately, so that in counting the square beneath it, should there be any doubt about counting a given corpuscle lying upon the line, a glance at the number recorded for the square above may remove all doubt. Many corpuscles will be found lying upon the outside lines bounding the large square. I have adopted the rule of rejecting all those lying upon the upper and right-hand outside lines (of the large square) and counting all those lying upon the lower and left-hand outside lines.

After having thus obtained the number of red corpuscles situated within the large square, it becomes easy by a simple equation to find the number in a cubic millimetre. A single count, however, exposes to sources of error, and in order to approach more nearly to exactness, I have uniformly counted the number contained in the large square in five different portions of the field (sometimes ten), and have taken a mean of the whole number of counts as the standard.

The computation is as follows: The glass cell on the slide is $\frac{1}{5}$ mm. deep. The eye-piece micrometer marks off $\frac{1}{5}$ mm. square, therefore, the count of red corpuscles (or white as the case may be) must indicate the number contained (in the dilution used) in $\frac{1}{5}$ mm. cube. But $\frac{1}{5}$ mm. cube is 1-125th of a cubic mm., therefore, the number counted must be multiplied by 125; and the blood was diluted by adding 250 parts of fluid to 1 of blood (2 cubic mm. to 500 cubic mm.), therefore the product above obtained must be again multiplied by 251 to get the number of corpuscles in a cubic mm. of pure blood. Instead of multiplying twice, a single multiplication by the product of 125×251, 31375, will give the same result.

Letting $x =$ the mean of 5 counts; the equation then is simply: The number of red corpuscles in a cubic mm. of blood $= x \times 31375$.

Fluid used to dilute blood for counting.—I experienced great difficulty in obtaining a good fluid for diluting blood, which time would not alter. All of those proposed are serviceable while fresh, but none of them will keep when a pipette is dipped into it daily. Bacteria, when present even in small numbers, make the count very uncertain, because the motion of the little rods causes the corpuscles to move about the field and to run together into groups, and as each corpuscle in the large square counts for 31,375 in the final result, it becomes at once apparent that anything making it difficult to avoid counting a corpuscle twice or tending to distribute them unevenly is disastrous to accuracy.

Round and oval-celled cryptogamic growths in a diluting fluid are also objectionable, since some of their cells are apt to be counted as blood corpuscles and *vice versa*. The artificial serum of Malassez (1 vol. of solution of gum acacia sp. gr. 1020, and 3 vols. solution of equal parts of sulphate of soda and chloride of sodium of same density) is open to this objection; and, besides this, has the defects of distorting the corpuscles in shape and disolving them after a few hours.

My friend Dr. L. A. Stimson, to whom I am indebted for much valuable assistance in experimenting to obtain a proper fluid, brought me, in the month of May, from Paris, an ounce of Schultze's iodized amniotic liquid of the cow. This makes a homogeneous mixture with blood, but contracts the red corpuscle somewhat, and after the bottle has been dipped into a few times with the pipette, my ounce, at least, was swarming with bacteria. The same criticism applies to the fluid of ascites, and the clear serum from a hydrocele of the tunica vaginalis. Iodine, carbolic acid (pure or impure), salicylic acid, iodate of calcium, carbonic acid, sulphurous acid—none of these, unless added in a strength destructive to the blood corpuscle, is able to prevent the rapid development of bacteria in either of the two fluids above mentioned.

In searching for a good fluid, Dr. Stimson and myself tried a variety of saline solutions, but failed to find perfection in any of them. Finally it occurred to me that healthy urine containing blood, often shows the blood corpuscles perfectly preserved in size and shape on the day following that on which the specimen was voided. Knowing that a proper fluid must have a specific gravity of about 1020 in order not to distort or dissolve[1] the corpuscles, I experimented with healthy urine of that sp. gr. The specimen I used was neutral, sometimes very faintly alkaline (phosphatic, not ammoniacal), and answered admirably. But urine will not keep long even when filtered, especially if it is contaminated by having a pipette dipped into it. Bacteria will appear in it very promptly, and as it is inconvenient to get a fresh specimen of urine to use each day, I undertook to prepare a permanent urinary fluid. This was finally accomplished, and I give the result, omitting the steps by which it was reached.

Take urine, neutral, slightly phosphatic, easily obtainable after eating, about 1020 sp. gr., and make of it a saturated solution with borax. Clouds of earthy phosphates are thrown down. Filtration yields a clear, alkaline fluid sp. gr. about 1030. Add one-half volume of water, or enough to reduce the sp. gr. to 1020, and the fluid is ready for use.

This fluid retains its brilliancy for a long time,[2] although daily contami-

[1] Too light a fluid, water for instance, dissolves the corpuscles so quickly that not one of them can be found on putting the mixture prepared with it, immediately under the microscope. Too heavy fluids distort the corpuscles and cause them to collect into heaps.

[2] Mould appeared upon it after two months.

nated by the pipette; no bacteria or confervoid growths appear. It makes a homogeneous mixture with blood, and preserves the color of the corpuscles. The latter become perfectly spherical, are slightly, but uniformly contracted (measuring 0.0006 mm.). They are perfectly preserved for a number of hours, after which some of them begin to dissolve.

The above is a good fluid, and has no poisonous properties. The following is very much better, but the corrosive sublimate may make it objectionable to some.[1]

Take of urine, neutral or slightly alkaline, sp. gr. 1020, a sufficient quantity, filtered. Add gr. v of corrosive sublimate in powder for each ounce of urine. This will throw down dense clouds of amorphous urates, so fine that ordinary filter paper will not remove them. After standing, the urates deposit, and the clear fluid above may be easily decanted. Reduce with water to sp. gr. 1020.

The result is a limpid, sparkling, acid fluid which remains clear no matter how often contaminated with the pipette, and does not seem to allow of the growth of any form of vegetation. It makes a perfect mixture with blood. It bleaches the red corpuscles quickly, and very slightly, but uniformly, increases their size. They retain, however, their flattened, bi-concave, disk-like shape, and do not become dissolved after standing more than twenty-four hours—beyond which time no test was made.

Estimation of the accuracy of the Hématimètre.—Theoretically the method of enumerating the blood corpuscles with the instrument of Hayem and Nachet is absolutely accurate; practically it is not so. This is largely due to the minuteness and infinitely vast number of the objects counted. It would be folly to try to calculate the number of red corpuscles in the human body, for when obtained, the figures would give no more idea to the ordinary mind of what the number really is, than would the word infinite.

For example—to reduce the whole matter to figures which can be easily understood—the population of the entire earth is estimated at considerably under 1,500,000,000. The *hématimètre* shows that one cubic mm. of pure blood of a male adult in good health, holds on an average 5,000,000 red blood corpuscles. But a cubic millimetre does not furnish a very accurate idea to the mind. A centimeter is better, it is of appreciable size, something over the third of an inch (exactly .39371 inch). A cubic centimeter is equal to 1000 cubic millimetres, and, therefore, contains 5,000,000,000 red blood corpuscles—a number of distinct red cells (not to count the white corpuscles) in each cubic third of an inch of blood, more than three times greater than the population of our entire globe.

This vast number of cells is probably undergoing daily and hourly

[1] It is a strange coincidence that I should have found mercury the best preservative for blood corpuscles.

variation to a slight extent. Wilbouchewitch noticed a very marked increase after meals. I endeavoured to avoid this source of error by counting my patients between the hours of 9 and 12 in the morning. In my own case there was a marked diminution after being up most of the night with a patient—a loss fully recovered from on the next day. In counting the same drop of diluted blood, it is rare for any two counts to be exactly alike, and for this reason I have always taken the mean of 5, often 10, counts, to approach more nearly to accuracy. This seems more necessary when we consider that each separate corpuscle counts for 31,375 in the final result—but yet, after all, 30,000 is a small matter when compared with the infinite number of these little cells. I have found it prudent also not to count very near the edges of the drop on the slide—where the corpuscles are apt to collect together unevenly.

In the same drop on different counts carefully made (mean counts of 5, not single counts), I have sometimes found a difference in the final result of as much as 200,000 to the cubic mm. Therefore, I cannot look upon this method, although followed out with conscientious care, as being absolutely accurate, nor should I consider a few counts, taken alone, of any value whatsoever. But relatively, I believe it to be very reliable, and if, in a great number of counts in different cases, the testimony of the figures should be largely in one direction, and the counting had been conscientiously performed, I should consider their evidence unimpeachable.

Of course for accurateness of results, to compare with those of another observer, the glass cells must be absolutely equal in depth. That this is generally so I doubt not—but it is not always so. There is a difference in depth of about $\frac{1}{50}$ mm. between my cell and one in possession of Dr. Stimson. There is a uniform difference of about 10 per cent. in the count of the same blood in the different cells. This is undoubtedly due to the fact that the depth of the cells is measured (they are ground after being cemented) with a sharp-pointed instrument, which might readily make an error of nearly $\frac{1}{50}$ mm. on account of inequalities in the surface of the glass.

Each cell, however, is absolutely accurate in itself, and the *relative* results obtained by it are (relatively) accurate; therefore, any series of observations made with one and the same cell, possesses positive value, whether the actual numbers accord with the results of observers using other cells or not.

All the counts contained in my tables were made with a single cell, whether counted by Dr. Stimson or myself. Absence of error was still further secured by getting Dr. Stimson to make many of the counts for me, he knowing neither the patient nor his previous count. In the experiment upon myself, where I took mercury for a fortnight, Dr. Stimson made all the counts of my blood, ignorant of what experiment I was the subject.

I have certainly taken every honest scientific precaution in my experiments, always counting (or having counted for me) the blood as soon as

it was drawn, and recording the figures in a book, one after another, without order, attached to the name of the patient and referring to his case in my note book, and entirely disconnected from any previous count. I entered upon the investigation as a searcher for truth, and came out convinced but astonished. After collecting together the scattered counts and arranging them into tables, I was infinitely surprised at the *uniformity* of the result; not at the *result*, for, candidly, that I expected, but at its wonderful uniformity. Had I manufactured the figures myself I could not have done more to sustain the statement: that mercury, in small doses long continued in syphilis, increases the number of red corpuscles in the blood, and maintains them at a high standard in a majority of all cases.

Tabulated experiments, with remarks.—I have carefully counted the blood 101 times (5 to 10 counts each), not including a great number of counts to settle side issues of various kinds. A record of the blood of 27 individuals is contained in the following tables, of which 6 were apparently sound, 20 syphilitic. My first recorded count was on June 5, 1875; my last for this article, Oct. 26, 1875. Most of the patients were in affluent circumstances, many of them spending the greater part of the summer out of town; 3 hospital cases only were counted for comparison. The circumstances, therefore, are favourable for rather high counts.

The cases will be grouped into tables and considered as follows:—

I. *Average of red blood corpuscles in 1 cubic mm. of blood of the healthy adult male.*

II. *Effect of small doses of mercury upon the blood early in syphilis.*

III. *Effect of the long-continued use of small doses of mercury upon the blood in syphilis.*

IV. *Effect of mercury in excess upon the blood in syphilis.*

V. *Effect of mercury combined with the iodides upon the blood in syphilis.*

VI. *Effect of mercury, in hospital, upon the blood in syphilis.*

VII. *Effect of small doses of mercury upon the blood in individuals not syphilitic.*

No special attention has been given in these experiments to the white blood corpuscles, or to the effect of iodide of potassium alone; both very valuable subjects for investigation. In some cases of late syphilis counted, but not included in this report, the iodide of potassium, used alone, seemed very active in its power of increasing the number of the red blood cells. The counts taken of women are not included in the report, as the number of cells they possess seems to be naturally somewhat lower than that of men, and my object has been to establish a just comparison between the results obtained from healthy men and adult males with syphilis who had been for a longer or shorter period under mild mercurial treatment. None of the cases (except the hospital ones) were selected, but all were taken as they came along, at least such as could be induced to allow themselves to be counted, and such as the hurry of morning office hours gave time to count. I have avoided multiplicity of figures and of details as much as

possible in the following tables. Figures are perplexing to the eye and wearisome to the mind.

I. *Average of red blood corpuscles in* 1 *cubic mm. of blood of the healthy adult male.*—To obtain a healthy standard for comparison, I made, with the help of Dr. Stimson, 33 examinations of 5 or more counts each. The conditions were most favourable for a high standard. The time was summer, the individuals all in flourishing health. Of the five whose blood was counted, Dr. Stimson was just from Europe, in the full flush of health, and during the period of counting, passed most of his time in the country. For myself, I was in excellent health, and during July was in the country for four days and five nights of each week, in full relaxation of mind and body, doing no work harder than fishing. Of the other three individuals counted, one was a full-blooded gentleman living in the country, two others, young physicians, one in town, one in the country. Two out of the five are six feet tall, and weigh about 200 pounds each ; a condition seemingly favourable to a high count.

TABLE I.

	No. of red corpuscles in 1 cubic mm.	REMARKS.
Dr. Stimson, average of 14 counts,	5,068,793.	Counts extended from June 5th to September 15th. Taken at all hours of the day, before and after meals, to get an average.
Dr. Keyes, average of 14 counts,	4,815,040.	Inclusive, from June 5th to July 22d ; also taken indifferently at all hours of the day.
Dr. ——, 3 counts,	5,045,063.	Lives in country ; fat, young, well.
Dr. ——, 1 count,	4,706,250.	Not fat, but in good health ; living in town.
Mr. ——, 1 count,	5,697,700.	Large, fat, beyond middle age ; healthy ; lives in country.
Average 33 counts,	4,990,550	

The above table is derived from exceptionally good sources. As for the number of blood corpuscles, I believe that each man is a standard to himself ; but it was necessary to get a general average of good health to use as a standard of general comparison for patients not well, and those under the influence of mercury for a long time when first counted, as their own natural standard in health could not be known.

The above estimate, of nearly 5,000,000 blood corpuscles for the cubic mm., I believe to be a high average for Americans in the neighbourhood of New York during the summer and autumn.

To compare the above result with that obtained by other investigators, Hayem[1] places the mean at about 5,000,000, more or less, for the blood of the finger of the healthy adult male. Vierordt established as a mean for his own blood something over 5,000,000. Welcker estimated it at 4,600,000 ; Cramer at 4,726,000. Malassez gives the lowest, placing the number at something less than 4,500,000 ; but he is not very definite upon the subject of healthy average, being more interested in his writings in a description of the instrument and in considerations of diseased blood.

In the most extreme cases of anæmia (excepting only two cases) Hayem

[1] Loc. cit., p. 295.

never counted less than 3,000,000. In this respect my experience has been similar to his.

II. *Effect of small doses of mercury upon the blood early in syphilis.*—The following five cases all had early syphilis. The chancre was seen and treated upon all except patient *e*, whose primary lesion occurred four months before commencing treatment. The protiodide of mercury in granules, gr. $\frac{1}{6}$ each, was used in every case (except *e*), and, as every man's capacity for mercury varies, each patient was ordered to commence with one granule after each meal, and to increase by one granule each day (not each dose) on every fourth day, until there was some evidence of irritation produced by the mercury, when the dose was to be immediately reduced to one-half, and there held until further notice. In the table a double line ═══ indicates that below that point mercury was taken.

TABLE II.

	No. of red corpuscles in 1 cubic mm.	REMARKS.
Patient a.		
June 21,	3,457,525.	Chancre and indurated glands. Patient thin, delicate; goes to country for summer. Tonics, etc.; no mercury.
July 2,	4,564,062.	Appetite good; mind easy; gain in weight and strength.
July 20,	4,516,900.	Health fair; continue tonics and cod-liver oil.
Sept. 4,	5,283,550.	Fat and well; chancre healed, indurated epitrochlear gland, erythema of fauces; commence mercury.
Sept. 18,	5,327,475.	Three and up to six granules; average gr. j protiodide daily; slight mucous patches on lips, tongue, and throat; no eruption; appetite excellent.
Patient b.		
Aug. 20,	4,586,025.	Chancre healing; commencing roseola; no fever; epitrochlear and post-cervical glands indurated; commence mercury.
Sept. 13,	4,636,450.	Reached six granules ten days ago, since then three daily; roseola.
Oct. 2,	4,863,125.	Slight relapse of roseola, some pains in joints; takes five granules daily.
Oct. 26,	5,396,500.	Roseola and pains gone; mucous patches on tonsils and anus; patient fat, in excellent health and spirits; has recently been taking four granules a day.
Patient c.		
Aug. 28,	4,863,125.	Health good; lives in country; infecting chancre now ten days old; to commence mercury.
Sept. 3,	5,200,975.	Five granules a day with a little iron.
Sept. 22,	6,168,325.	Has gained six pounds in two weeks by change of residence in the country; takes six granules.
Oct. 5,	5,606,125.	Has come to town to work; lost weight; erythema of fauces; faint mucous patches.
Oct. 26,	5,208,250.	Mind depressed, appetite poor; osteocopic pains; plentiful mucous patches; no eruption, fear of which keeps him terribly anxious; looks well; takes six granules daily.
Patient d.		
Sept. 7,	5,127,665.	Chancre eight weeks ago; mercury for nineteen days; eight granules were reached; now four are taken; mucous patches; has had faint roseola.
Patient e.		
Sept. 20,	5,484,350.	Chancre four months back; abundant mucous patches and post-cervical glands; no eruption; probably has been taking mercury, but is not certain; to take three grains of blue pill daily with chlorate of potash.
Oct. 2,	5,578,875.	Mucous patches nearly well.

These cases do not call for much comment: *a* improved greatly under his tonics and hygiene, and still further under a mild mercurial; *b* gained over 800,000 in his count while taking a mild mercurial continuously for ten weeks; *c*, under splendid hygienic surroundings, after taking mercury for twenty-five days, showed an increase in his count of over 1,300,000, corresponding to the clinical expression of improvement denoted by six pounds gain in weight in two weeks; but afterwards, under the depressing influence of poorer hygiene, hard work, and the anxiety caused by the fear of a general eruption, he lost his extra weight, and the gain in corpuscles fell off to only a little over 300,000 above his first count This man was taking mercury continuously for two months, and, according to Wilbouchewitch, should have fallen off largely from his first count.

a, *b*, *c* were first counted before they had taken any treatment—one was delicate, the other two very healthy, yet they all marked below 5,000,000, the healthy standard. Notwithstanding this they all reached above 5,000,000, protected by hygiene and mercury from the depressing influence of advancing syphilis.

d and *e* were not counted until they had taken mercury for some time, and both of them when counted reached above the healthy standard.

III. *Effect of the long-continued use of small doses of mercury upon the blood in syphilis.*—From the following table I have felt obliged to exclude all patients who had taken any of the iodides, making of these latter a special group. I have, therefore, only three patients to offer as examples of the harmlessness—or rather the advantage—of the long-continued use of small doses of mercury alone in syphilis.

TABLE III.

	No. of red corpuscles in 1 cubic mm.	REMARKS.
	Patient f.	
June 7,	5,333,750.	Chancre July, 1874. Has taken average of 1½ gr. protiodide of mercury daily for eleven months; has occasional mucous patch.
Oct. 22,	5,220,800.	Continued above dose until six weeks ago; since then has taken nothing.
	Patient g.	
June 11,	5,647,500.	Chancre in December, 1874. For six months has averaged 1½ gr. protiodide of mercury daily; syphilitic rheumatism and mucous patches.
Oct. 8,	4,699,975.	Continued mercury until three weeks ago, when he was thrown from a carriage. He is just out of bed from his injuries, and has lost seven pounds in weight.
	Patient h.	
Oct. 4,	5,020,000.	Chancre eighteen months ago; mercury ever since; average gr. j protiodide daily; latterly ⅔ gr. daily.
Oct. 26,	5,208,250.	Continues at same dose; looks and feels well; small elevated papular patch on leg.

To crystallize out the facts from the above cases, it may be added: None were large men; none were naturally robust; one was lymphatic, and not very strong; one belonged to a phthisical family; one had only

a short time before recovered from prolonged sickness with an angular curvature of the spine. Yet all, after prolonged use of small doses of mercury for respectively eleven, six, and eighteen months, showed a blood count above the healthy average, and, clinically, were in excellent health; further, *e* lost 100,000 after ceasing his mercury for six weeks; *g* lost 1,000,000 and 7 pounds weight from accidental causes, during the period of loss taking no mercury; *h*, having no drawbacks, maintained his average.

IV. *Effect of mercury in excess upon the blood in syphilis.*[1]—The patient who furnishes the following table lived in the country, visiting me in consultation with his physician. He was a large man, fairly nourished, with a late syphilitic lesion (ten years from chancre) threatening an important function. During his treatment an effort was made to produce mild salivation—the effect of which was, on the whole, somewhat beneficial. He took a mixed treatment.

TABLE IV.

Patient i.

	No of red corpuscles in 1 cubic mm.	REMARKS.
June 9,	4,627,818.	For some time past has taken gr. xl of iodide of potassium t. i. d., and ʒss inunction twice daily of 20 per ct. oleate.
June 20,	4,391,500.	Inunction of ʒiss of oleate daily, and gr. ij iodide, t. i. d. Manifest improvement in health, appetite, and the function threatened; no iodism or ptyalism; ordered to push
July 8,	5,333,750.	inunction; add $\frac{1}{12}$ gr. of biniodide of mercury to internal dose of ʒj of iodide of potassium three time a day.
Aug. 28,	4,398,775.	One month ago diarrhœa and slight ptyalism came on and lasted till one week ago. Patient was greatly depressed at the time; now feels better; takes gr. $\frac{1}{12}$ biniodide of mercury, and gr. xlv iodide of potassium, t. i. d.; no inunction.

Had it been possible to see this patient when salivated and count his blood then, instead of one week after his recovery, I cannot doubt, that his count would have been below 4,000,000. As it was he lost about 1,000,000 by the excessive use of mercury.

V. *Effect of mercury combined with iodides upon the blood in syphilis.*—In this list, which naturally furnished the largest number of patients, it would be fair to expect frequent exceptions to the rule that mercury increases the number of the red corpuscles in syphilis, because so many of those patients who need prolonged treatment late in the disease, become more or less cachectic and broken in general health. I have been, however, surprised at the good showing these patients have made. Only 2 of the 9 cases (*j* and *r*) averaged, on the whole number of counts, below 5,000,000, the normal standard, and this among patients with old syphilis collected at random.

[1] Patient *s*, Table VI., is another example of excess in mercury.

Table V.

	No. of red corpuscles in 1 cubic mm.	Remarks.
Patient j.		
June 9,	3,478,078.	Lymphatic, pallid, cachectic. Chancre three years ago; ecthyma on legs; papulo-squamous eruptions on scrotum. Has been taking a mild mixed treatment of late.
July 8,	4,190,150.	Eruption better; has been taking gr. $\frac{1}{12}$ biniodide of mercury and gr. iv iodide of potassium, t. i. d.
July 23,	4,258,165.	Eruption nearly well; has continued biniodide at $\frac{1}{12}$ grain.
Aug. 20,	4,307,344.	Eruption well; iodic acne. Has taken gr. $\frac{1}{24}$ biniode and gr. x iodide of sodium.
Sept. 8,	3,934,425.	Constipation; appetite poor; intense pain in anus at stool. I find fissure of anus and divulse the same.
Sept. 23,	3,733,225.	Fissure well: general condition gradually bettering: takes gr. $\frac{1}{16}$ biniodide of mercury, and gr. x iodide of potassium, t. i. d.
Patient k.		
June 10,	4,944,700.	Chancre ten months ago. Has taken mercury ever since, and lately some iodide. Is over-worked—run down; has ulcerated throat; is taking gr. $\frac{1}{16}$ bichloride of mercury.
July 16,	5,647,500.	In country since last visit. Feels and looks better. Continue mercury, adding gr. v iodide of potassium, t. i. d.
Sept. 4,	4,549,375.	Iodide disagreed. Patient got an attack of diarrhœa with bloody passages, and stopped everything for a time. Is now taking gr. $\frac{3}{5}$ protiodide of mercury daily.
Patient l.		
June 22,	4,894,500.	Tall and thin, not anæmic; lost 25 pounds during past few years since he became syphilitic. Has been under mixed treatment; has large painful node. Has taken gr. xv potass. iod. t. i. d., but no mercury for four months past. Is gaining in weight. To take gr. v more of the iodide of potassium and $\frac{1}{24}$ gr. bichloride of mercury at a dose.
June 29,	5,183,150.	Is now within fifteen pounds of full weight Node less tender.
Patient m.		
July 10,	4,473,075.	Recently taking Donovan's solution. Chancre and eruptions four and a half years ago. Six months of mixed treatment a year ago. Papulo-squamous patches and ulcers on scrotum.
July 24,	4,392,500.	Ulcers have healed under gr. $\frac{1}{16}$ biniodide of mercury, and gr. v iodide of potassium, t. i. d.
Aug. 21,	5,020,000.	Small ulcerated gumma of penis. Health excellent. Has been taking gr. $\frac{1}{12}$ biniodide of mercury, gr. vijss iodide of potassium, t. i. d.
Oct. 10,	6,193,425.	Health splendid. Ulcer of penis well. Has been taking same medicines at doses of gr. $\frac{1}{12}$–gr. x. Is five pounds heavier than full weight in ordinary health.
Patient n.		
July 31,	5,195,700.	Chancre three and a half years ago; mercury ever since, with intervals of rest, recently. One small scaly patch on lower extremity. Patient desires to keep under treatment, as his wife is pregnant with her first child. Takes gr. $\frac{1}{16}$ biniodide of mercury, gr. iv iodide of potassium, t. i. d.
Aug. 20,	5,020,000.	Has taken recently gr. $\frac{1}{3}$ protiodide of mercury, t. i. d., and a little inunction of 5 per cent. oleate.
Oct. 7,	6,092,925.	Just returned from the country in excellent condition. Takes gr. $1\frac{1}{3}$ protiodide of mercury daily.

	No. of red corpuscles in 1 cubic mm.	Remarks.
	Patient o.	
Aug. 20,	4,612,125.	Syphilis several years' standing. Has taken a vast amount of iodides for syphilitic hemiplegia, mania, etc. Physical condition and appetite at present fair; has been taking gr. $\frac{1}{30}$ of the biniodide of mercury, and gr. xxvij of the iodide of sodium, t. i. d.
Oct. 4,	5,547,500.	Has continued medicine steadily, improving in physical appearance.
	Patient p.	
Aug. 27,	6,444,515.	In magnificent physical condition. Has taken mercury continuously for nearly three years, and continues to take it until his wife, who is pregnant with her first child, shall have been delivered. Is taking gr. v iodide of potassium, gr. $\frac{1}{12}$ biniodide of mercury, t. i. d.
Sept. 17,	6,226,350.	Has reduced iodide of potassium to $2\frac{1}{2}$ grains at a dose.
	Patient q.	
Sept. 22,	4,712,525.	Large man, not anæmic. Chancre twelve years ago; no treatment for many years; threatening of carious disease of bones of the nose and of paraplegia. To take mixed treatment of biniodide of mercury gr. $\frac{1}{10}$, iodide of potassium gr. vijss.
Oct. 22,	5,400,000.	Improvement undoubted, especially of nose.
	Patient r.	
Sept. 22,	4,888,125.	Old syphilis; general condition fair; persistent mild tuberculo-ulcerative lesion. Has been taking inunctions, with gr. $\frac{1}{10}$ biniodide of mercury and gr. v iodide of potassium, t. i. d.
Sept. 28,	4,555,650.	For one week has taken gr. xx iodide of potassium, and gr. $\frac{1}{40}$ bichloride of mercury, t. i. d. Eruptions worse.

Not considering any effect the iodides might have had, it will be noticed in these 9 cases, that 7 of them, when first counted, ranged below the normal standard of 5,000,000. That it was not the mercury which produced this effect must be evident upon a careful perusal of the table.

Patients *j*, *k*, *l*, *m*, *o*, *r*, were suffering from a continuation of symptoms of syphilis which treatment had not been able to remove, were more or less blighted by the disease. Patient *q* belonged to the same class, but had taken no mercury for nearly twelve years, and indeed, gained over 600,000 in his count by taking mercury for a month.

The two patients who counted high were in perfect health, and both were continuing treatment simply from fear that, if they did not, some trouble might arise which would affect their pregnant wives and involve their children. One had a small scaly patch, the other absolutely nothing as an evidence of syphilis; and patient *p* made the best count I ever obtained from any one, and had been taking mercury continuously for three years. The other patient reached over 6,000,000 after taking mercury almost uninterruptedly for three and a half years.

Patients *m*, *p*, and even *q*, therefore, speak loudly in favour of the prolonged use of mercury.

Patients *j* and *r* were severe, inveterate cases of disease, and poor specimens of the effect of treatment clinically, as well as microscopically.

k counted low at first, because pulled down by overwork. He reached over 5½ millions at one time, and fell again after diarrhœa with bloody stools.

l reached over 5,000,000 on gaining back a few pounds he had lost.

m, depressed at first under a new outburst of disease, reached above 6,000,000 by three months of mercurial treatment.

o touched 5,500,000 while under observation.

In short every patient of the nine had a general average above 5,000,000, except *j* and *r*.

VI. *Effect of mercury, in hospital, upon the blood in syphilis.*—The blood of the following patients was counted to make a short study of the difference between hospital and private patients. Three cases were selected in the Charity Hospital: one salivated, just admitted; one an old case, in the hospital for two years; one, a new case, with chancre just getting well when admitted.

TABLE VI.

	No. of red corpuscles in 1 cubic mm.	REMARKS.
	Patient s.	
June 13,	3,990,900.	Salivated for fifteen days, ten of which in hospital.
June 20,	3,335,162.	Eats but little; salivation improving.
June 27,	4,516,900.	Salivation nearly well, eating well.
	Patient t.	
June 13,	3,081,025.	Chancre five years ago; rupia and ulcerations. Has been two years in hospital; ℥ij iodide of potassium, t. i. d., lately; no mercury for six months.
June 20,	3,670,875.	Has taken $\frac{1}{16}$ gr. biniodide of mercury, and gr. xv iodide of potassium for a week.
June 27,	3,592,333.	Very positive improvement in ulcers; same treatment.
	Patient u.	
June 13,	4,612,125.	Young man; chancre two months ago; ten days in hospital; roseola; no treatment as yet.
June 20,	4,216,800.	Has taken ¼ gr. protiodide of mercury, t. i. d., for a week; roseola disappearing; suppurative peri-adenitis threatening in the groin.
June 27,	4,551,888.	Same treatment; roseola gone; suppuration averted in the groin.

This table tells its own story:

s entered salivated. His count increased after he began to eat.

t debilitated by disease and hospitalism, showed a wretched count. His improvement under observation, I think, was largely due to the greater quantity of good air he got by going out of doors in the pleasant June weather; yet I certainly believe the mercury helped him.

u, if counted daily, might for a time have furnished figures like those given by Wilbouchewitch, yet possibly better, in spite of his threatening bubo, because his dose of mercury was so small.

VII. *Effect of small doses of mercury upon the blood of individuals not syphilitic.*—The material for this table was derived from two sources.

Patient *v*, a young man, badly frightened by an ulcer on the penis the nature of which, when first seen, could not be positively pronounced upon, insisted, for his own peace of mind, upon being treated until the time for the eruptions had passed. He was, therefore, by his own will and consent, put upon mercury, and made the subject of observation. He turned out to have no syphilis, much to his own and my satisfaction.

I made myself the subject of experiment to fill the table.

TABLE VII.

	No. of red corpuscles in 1 cubic mm.	REMARKS.
Patient v.		
June 6,	5,365,125.	Has averaged gr. j protiodide of mercury daily for four months. Has gained in weight: feels perfectly well.
June 27,	5,302,375.	Has gradually diminished dose, taking lately gr. $\frac{1}{3}$ daily.
Myself.		
Sept. 10,	4,775,275.	Just from the country, perfectly well. To take $\frac{1}{5}$ gr. protiodide mercury three times a day for two weeks.
Sept. 20,	5,572,200.	
Sept. 24,	5,175,875.	Up greater part of last night with a patient; no appetite for breakfast.
Sept. 25,	5,562,062.	Slept well and was abundantly hungry for breakfast.

Patient *v* ranked far above average after taking mercury for four months, during most of which time he was perfectly well, for his chancroid healed kindly; but the result, in his case, was partly due to his living a more regular life, which his chancroid frightened him into.

As for myself, I started at about my healthy average (see Table I.), and gained over 700,000 in two weeks. I made no change whatever in my mode of life, and took the extra precaution to get Dr. Stimson to make my count on each occasion, he being ignorant what manner of experiment I was subjecting myself to. My loss by one night's watching was made up by the next night's rest.

Conclusion.—From what has been written, it seems fair to conclude that—

1. 5,000,000 red blood corpuscles in the cubic mm. is a full, high average for the adult healthy male. Anæmia very rarely goes below 3,000,000; fine conditions of physical health reach above 6,000,000. In ordinary seasons, in the city, 4,500,000 would indicate a fair state of health. (Table I.)

2. Mercury decreases the number of the red cells when given in excess, especially in hospitals (Wilbouchewitch). (Tables IV. and VI.)

3. Syphilis diminishes the number of red corpuscles below the healthy standard. (Table II., first counts.)

4. Mercury in small doses continued for a short or for a long period in syphilis, alone or with the iodide of potassium, increases the number of red corpuscles in the blood, and maintains a high standard of the same. (Tables II., III., and V.)

5. Mercury in small doses acts as a tonic upon healthy animals, in-

creasing their weight (Liègeois, Bennet's report, above referred to). In larger doses it is debilitating or fatal.

6. Mercury in small doses is a tonic (for a time at least) to individuals in fair health, not syphilitic. In such individuals, it increases the number of the red blood corpuscles. (Table VII.)

210 Madison Avenue, New York, Nov. 15, 1875.