The Clinical Estimation of the Alkalinity of the Blood: A Criticism and a Commentary

by "Scrutator"

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Among the factors which compose the environment of a cell in the human body as we would suppose, could be of greater importance than the chemical reaction of the fluid medium in which that cell lives. One sense of the importance of this reaction is increased rather than diminished by the knowledge of the fact ascertained by physiologists that during life this reaction is invariably alkaline in its nature that, indeed, in the world appear to be compatible with the continued existence of the cell. It must, therefore, be of the first importance for physiologists to ascertain what are the variations in the degree of this alkalinity which are compatible with health. The pathologists to inform themselves to what extent variation outside this health limit either themselves produce, or are produced by, the inherent processes of disease. Notwithstanding this seeming importance, however, it subject
is one which has received but scant attention in comparison with that which has been devoted to the study of the variations in the cellular elements of the blood or in some of the chief constituents of these cells, e.g., haemoglobin. This defect is especially observable in English scientific literature, Jeffries' being the only English writer who has treated the subject at all fully. The present writer has, during the last 3 years, devoted considerable attention to the variations in the alkalinity of the blood in disease, to the methods by which these can be clinically estimated, and has taken occasion to make himself acquainted with the Continental literature bearing upon the subject. He has come to certain conclusions regarding these methods, the results which they have already afforded or are likely in the future to afford. The present Essays is intended as a criticism upon these methods, a commentary upon their results.

On attempting to estimate the alkalinity of the blood by the ordinary chemical methods employed for other fluids e.g. by adding an acid by titration till a neutral reaction is reached, we are confronted by certain initial difficulties. These are due in part to the physical character of the blood and in part to its chemical composition. The fact that the blood is a highly albuminous fluid forbids the employment of a mineral acid, being also of a somewhat thick consistency the thorough admixture of the acid demands some trouble though this has been done the red colour of the blood is apt to interfere with the precise determination of the ind. reaction. Further, the blood is not a homogenous but consists of particles, the corpuscles, suspended in a fluid, the plasma. The determination of the alkalinity of the whole blood must include both these elements. Now by the separation of the corpuscles it has been found that these contain more alkali than
the serum (ladoso).—Any method, therefore, which does not ensure thorough breaking down of the compounds, with consequent liberation of the alkaline salts herein contained, cannot give accurate results.

The peculiar chemical composition of the blood presents even greater difficulties. It must be borne in mind that the blood is not by any means a simple chemical solution but, on the contrary, consists of a highly complex mixture of substances in various and varying combinations.

Of these, two, the bicarbonate of soda or di sodic phosphate (Na₂HPO₄) and are chiefly responsible for the alkaline reaction. But in both these salts nearest still present an atom of hydrogen, replaceable by metal. Yet both react as alkaline to ordinary reagents. Hence the curious paradox which has been explained by Drouin (2) that the blood is chemically an acid but acts as an alkaline solution to ordinary chemical reagents. He has estimated

(2) Drouin, Hémo. alkalinétique et hémo. acédimétique. Thése, Paris, 1892
This 'acidity' by a special method of titration finds that it fluctuates just as the alkalinity does. Apart from this the colored reagent added is employed to show when the neutral point is reached, has a considerable influence upon the result obtained. Thus we find that monobasic salts of phosphoric acid are acid to litmus but neutral to phenol red. Bisulfate salts of the same acid are alkaline to litmus but neutral to phenol red. Now as such salts are normally present in the blood to which we obtain will obviously depend on whether we employ litmus or phenol red as indicator. In addition to this CO₂ is always present in the blood but when liberated by the addition of another acid it escapes as a gas or affects litmus feebly if at all. In the case of diisobutyl phosphate on the other hands the phosphoric acid liberated is able to act upon litmus as acid. Hence a blood the alkalinity of which is chiefly due to phosphate of soda
will give an apparently lower alkalinity than one in which the alkalinity is chiefly due to the bicarbonate.

It does not exhaust the list of difficulties that have been specially insisted upon by Meyer(3) that we have no right arbitrarily to select a certain reagent, e.g., litmus, to exclude from the category of acids all substances which fail to give a red reaction with it. Thus some alcohols, some amidic acids, some amides are chemically acids but do not react as such to litmus. These may be present in the blood. Some of the higher fatty acids, also, when liberated are insoluble in water and therefore cannot affect the litmus.

When we consider these objections we might at first be tempted to abandon any attempt to gauge the alkalinity of the blood as in the nature of things impossible. The physical difficulties, however, can, as we shall see, be overcome by suitable methods, while, as

(3) Meyer, Archiv. f. exper. Path. u. Pharmak. xvii, 1883
regard the chemical doctrine it must be said that many of them are rather theoretical than practical. For although it be true that blood is in one sense an 'acid' fluid in that it contains many salts which replaceable hydrogen atoms, yet we find that these salts which give what we commonly understand by an alkaline reaction predominate greatly over the others. Now what we wish to obtain is a quantitatively not a qualitatively result. That is to say, the blood reacting like litmus as ordinary alkaline solutions do we can ascertain not, perhaps, to the presence or absence of what particular substances fluctuations in this alkalinity are due but yet to what degree the fluctuations themselves occur. Our results will be comparative, not absolute. The mixture of different substances in blood in the blood always yielding a balance in favour of alkalinity to litmus by our methods should be able to show us whether this balance
is disturbed if so, whether in the direction of increase or of diminution. The substances which, while chemically acids, do not react to litmus are not likely to be present in the blood in such quantity as materially to affect our results.

Let us ask, then, what methods we have at our disposal for estimating the total alkalinity of the blood, and shall confine ourselves to methods of clinical applicability. Obviously we cannot justify demands upon such a method too great accuracy. Like all clinical methods it must needs be more or less of a compromise between accuracy and simplicity, but it should be able to inform us of fluctuations in the degree of alkalinity of the blood with as much accuracy as we can inform ourselves of fluctuations in the amount of their Haemoglobin. We shall now proceed to consider the available methods of how they answer the requirements. All other methods
Luntz (Centralblatt für die med. Wissenschaften, 1867) was one of the first to estimate the alkalinity of the blood. He employed titration by means of phosphoric acid. This method demanded too much blood to be available for clinical purposes. The same criticism applies to the method of Lassar (Archiv f. d. gesammte Physiol. Bd. 68) who employed tartaric acid instead of phosphoric. Liebig (Berichte der deutschen chem. Gesellschaft, 1, 48, 1858) devised a method for showing the alkaline reaction of the blood by means of plates of plaster of Paris impregnated with calcium. When a drop of blood was placed upon the plate the plasma soundtrack it changed the calcium to lime—the corpuscles remaining on the surface where they could be wiped off without obscuring the results. Obviously this method really gave an indication of the alkalinity of the plasma out of the total blood of the red corpuscles, which as we have seen, are rich in alkaline and not blood plasma. Besides it could not show to what degree
alkalinity of the plasma existed. After this we find Renzi(4) employing this method to estimate variations in the alkalinity of the blood in droezer but as he was guided solely by the intensity of the blue colour produced by different bloods his results are certainly not accurate. Lépine(5) or Canard(6) was the first who made extensive observations in man using the titration method but employing comparatively large quantities of blood. It was not until a decade ago that Landois(7) introduced a method which required only easily obtainable quantities of blood. As this is the type of titration method now in use it deserves a word of description. The principle of the method consists in preventing coagulation of the blood by a neutral salt and while all the alkali present is neutralized by titration with tartaric acid, litmus paper being employed to show the 2nd reaction. Solution of sulphate of soda is accordingly prepared. To this a 2.5 per cent. of tartaric acid is added in

(4) Renzi; Virchow's Archiv. Pp. 102, 1885
(5) Lépine; Gazet. Med. 1879
(6) Canard; Thése, Paris 1878
(7) Landois; Real Encyclop. III, 1885.
graduated amounts. Thus flu. I will contain
\[
\frac{10}{100} \text{ acid} \quad \frac{20}{90} \text{ acid} \quad \text{or up to } \frac{10}{100} \text{ sulph.}
\]

Equal quantities of one of these solutions of
blood are sucked up into a fine pipette,
mixed in a watch glass, Reachin tried with
brownie litmus paper if still alkaline
the next strongest solution is taken down
till result is neutral. This method has
been largely employed by von Jakob, who
shown the blood will emulsiphile glasses of
peiper. 9 who found the latter unnecessary.

It has found its most recent advocate
in Brownin 10 whose thesis constitutes the most
comprehensive monograph on the alkalinity
of the blood which has yet appeared. 11 He
slightly modified the method of Landois, using a
normal salicylic acid sol. to mix with the sulphate

of soda solution, with a drop of he placed in the
first fluid, 1 drop acid & 9 of sulphate, the 2nd
receives 2 of acid & 8 of sulphate or up to the 16th

(8)  von Jakob; Zeitschrift f. klin. Med. xiii. 1888
(10) Brownin, op. cit.
An equal amount of blood is then added to each glass or rapidly titrated delicate litmus paper being used to determine in which glass the reaction of the mixture is neutral. This method is all the whole simpler than the original one of Landor's quite as accurate.

And all these methods have the drawback of being somewhat elaborate demanding for their proper application a considerable amount of blood, if apparatus of practice on large amount of time. It was, however, to be desired that a simpler method might be found. Such a method Harecraft or Williamson believed to have discovered in 1888 or described it in the Proceedings of the Roy. Soc. of Edin. for that year. Since then this method has received favourable notice in various standard works dealing with clinical methods (1884 von Jakob's Clinical Diagnos. 3rd Ed. 1894 Finkelstein's Clinical Manual) and is advised for employment on account of its simplicity. To present with according
started his observations by the use of this
method, he employed it in nearly 500 cases of
disease & believes that he is able to
demonstrate conclusively that it is
entirely unreliable & undeserving of any
place in clinical methods of investigation.
In order to make clear the reasons for his
condemnation a brief description of the
method must first be given.
The method of St. George's Hospital, London, depends
on the fact that if a drop of blood be
placed upon the surface of a neutral
stained litmus paper the stain prevents
the corpuscles of the blood from entering
the interstices of the paper while the plasma
is able to soak in on wiping away the
drop the blue colour due to its alkalini-
ity of the plasma is distinctly seen under
faulted by the red colour of the corpuscles.
The fact that the alkalinity of the blood
could be demonstrated in this manner
was pointed out some years ago by Jung
by Hülser.
It occurred to Hagcaft Williamson that by heating litmus papers with different strengths of a solution of acid, then soaking the paper thus obtained, one would get a series of graduated strength, one of which would just be neutralized by the alkalinity of normal blood—all the papers more strongly acid than this could remain unaltered on wiping away the drop of blood. While all the less acid papers would exhibit a blue reaction, which would be the more strongly marked the less acid the paper. The method of preparing the papers is detailed in detail in the original Communications of its authors above referred to.

This method seems at first sight to be a great advance upon the titration procedures. It has the undoubted merit of simplicity; it can be carried out with great rapidity. Hagcaft stated that by its means, he had found the reaction of the blood to vary as greatly as that of the urine.*

* See quotation in von Jakob's Clinical Diagnosis - English translation of 3rd ed.
Specimens of acidified glass litmus papers prepared for testing alkalinity of blood according to method of Haycraft-Willkomm.

No. 1: meat acid paper.
Hence it would seem to answer every require-
ment. The writer started his investigation
with the use of this method under the belief
that it really possessed all these advan-
tages. He prepared papers according to the
general directions of Maycracht Williamson.
He found it simpler, however, to get neutral
litmus papers ready glazed and to treat these
with different strengths of acid. The glaze is
not thereby sufficiently removed to prevent the
blue colour left on wiping away the drop
of blood from being distinctly seen. Sulphuric
acid was used to impregnate the papers—a
series of 10 being prepared. The first, a strongest
paper, was soaked in a normal solution of
sulphuric acid, no II was soaked in (1/2)H2SO4,
no III in (1/3) H2SO4, and so on up to $\frac{1}{2}$ which
was the weakest of the series. (Examples
of the papers employed have been pasted in a different
side of the paper) it was found by experiment
that normal blood reacted to $\frac{1}{2}$ all the
papers above this were unaffected while all below gave a blue reaction. By placing the papers in a row in a small letter clip they could be dipped rapidly into a drop of blood, the drops wiped off in the same order. The highest paper which gave a distinct blue colour was noted. This represents the alkalinity of that particular specimen of blood. The standard having been already determined by experiment with normal blood. Of course the results afforded can only be approximate as there is a considerable difference between, say, $\frac{1}{2}$ and $\frac{1}{3}$ sulphuric acid solution.

But in this respect the method would not compare unfavourably with the titration method of Landor's. Nor did the writer find that there was much force in the objection - the only one he has hit to be seen advanced against this method - that there is difficulty in determining exactly which is the paper which just gives a blue reaction with the drop of blood.
| Date | Name | Age | Sex | Race | B/P | Temp | Hb | WBC | RBC | Hct | S.G. | Diabetes | Glycosuria | Albuminuria | Nitrites | Phosphate | Pus Cells | Casts | Albumin | Glucose | Remarks |
|------|------|-----|-----|------|-----|------|----|-----|-----|-----|-----|---------|------------|------------|-----------|---------|-----------|----------|--------|---------|---------|---------|-------|
| 1/8  | Wilson | 32  | M   | Black| 110 | 98.7 | 6.5| 18  | 24  | 912 | 9.2| Normal  | Trace      | Trace      | Trace     | Trace   | Trace     | Trace    | 92%     | Trace  | Nxd. 3000 | 60    |
| 1/8  | John  | 24  | M   | Black| 110 | 98.7 | 6.5| 18  | 24  | 912 | 9.2| Normal  | Trace      | Trace      | Trace     | Trace   | Trace     | Trace    | 92%     | Trace  | Nxd. 3000 | 60    |
| 2/8  | Mary  | 32  | F   | White| 110 | 98.7 | 6.5| 18  | 24  | 912 | 9.2| Normal  | Trace      | Trace      | Trace     | Trace   | Trace     | Trace    | 92%     | Trace  | Nxd. 3000 | 60    |
| 2/8  | Jane  | 24  | F   | White| 110 | 98.7 | 6.5| 18  | 24  | 912 | 9.2| Normal  | Trace      | Trace      | Trace     | Trace   | Trace     | Trace    | 92%     | Trace  | Nxd. 3000 | 60    |
In the contrary he made a large number of observations in diseases of all sorts. He was almost invariably able to say definitely to which paper the blood first reacted. A sample table of some of these observations is given opposite. It was only later, on coming to compare the results with those of other authors obtained by the titration method, that it was found that, while in many diseases the results coincided, in others marked discrepancies occurred. It will be noticed in the table that all the cases of anaemia shown, by Haycraft's method, an alkalinity distinctly above that of normal blood. Indeed this was a fact which very early impressed itself upon the writer. He found it true of all anaemias—simple, pernicious, chlorotic, leucocytæmia. All showed by Haycraft's method an alkalinity decidedly—often, apparently, excessively—above the normal. Now if there be one fact on which all those who have employed the
titration method are agreed it is this — that in anaemia the alkalinity of the blood is below the normal. Often, indeed, to a very marked extent. (See von Jakob, Reiper, Brodin, already quoted) Only in a few cases of pure chlorosis, i.e. of reduction of the haemoglobin only, was the alkalinity found — as estimated by titration — to be normal or in excess. How, then, is this contradiction in the results yielded by the two methods to be explained? Why should the alkalinity of the blood in anaemia as estimated by Haycraft, Williamson's method be found to be distinctly increased, while when estimated by Landor's method it is found to be equally distinctly diminished? Both results cannot be correct. One or other method must be faulty, must be, therefore, unreliable to be rejected. Which is it to be?

It might at first be asserted that the results of the two methods are not comparable because
Will be in town 2 to 5 shortly.

Yes, I believe it is a good idea to liberalize our policies.

The changes to the legal system are officially effective from now.

The species differ significantly from each other. In the case of the species, the differences are more pronounced.
In searching for another explanation it struck us that the waxy condition of the blood in anaemia might be at the root of the mystery. Obviously a waxy fluid will diffuse through the plaæe or the surface of the craft's papers more rapidly than a more viscous one. If the acid waxes thus be neutralised in a given time the waxy fluid will appear more alkaline than the more viscous liquid even although the actual amount of alkali contained in both be identical.

This alone at once explains why an anaemic blood should, when examined by the plaæed paper method, be found to be apparently more alkaline than a blood which is normal.

It remained to put this explanation to the test of experiment.

Our first one had to determine whether, say, a 'normal' acid paper was, or was not, just neutralised by a 'normal' alkali solution, and if so, if an acid by an alkaline solution. Heycraft believed, apparently, that this was so for he says
if the blood in any given case just reacts to \( \frac{x}{10} \) acid we know that this will just be neutralised by \( \frac{x}{10} \) alkali, as we know the amount, say of \( Ca(OH)_2 \), contained in such an alkali solution we can easily calculate the amount of alkali contained in the blood in terms of \( Ca(OH)_2 \). Then he makes the significant addition — "This is, perhaps, not absolutely true, for probably the blood plasma does not percolate so readily into the litmus paper as does a water solution of an alkali; in this case, however, the error will be uniform" (quoted in von Johk's Clin. Diagnosis). Prof. Harecraft has evidently never put the question to the experimental test. Had he done so he would doubtless have found, as the writer has done, that, so far from, say, an \( \frac{x}{10} \) alkali soln. just neutralising a paper impregnated with \( \frac{x}{10} \) acid soln., such a paper gives a distinctly blue reaction even with an \( \frac{x}{10} \) alkali solution! If, then, one takes a comparatively viscous alkali
solution. For this purpose the writer employed a solution of caustic soda in glycerine - one finds that the result is quite different. If, for example, one adds to 50 cc neutral glycerine 1 cc normal soda solution, it will be found to react to about paper No. III. If 20 cc of distilled water be then added to this alkalised glycerine the paper again tested it will be found that a more acid paper will now react; that is, although the solution is really more dilute than before yet apparently it is more alkaline, a paradox which is evidently to be explained only by the more rapid and thorough percolation into the paper of the more wearable solution. No further proof of the great influence which the consistency of the fluid exerts as a factor in determining to which paper it will react is, we think, necessary. To return now to the blood. It will be at once evident, in the light of the above experiments, that the diffusive power of the drip, as determined by its greater or less viscosity, is a much
true potenta factor in determining to which of 
Wagner's methods will 
react than in the greater or lesser amount 
of alkali which it contains. Inasmuch 
as his viscosity is an unconstant 
irreducible quantity we are compelled select 
antly to conclude that the method is 
ndefined of all reliability therefore of all practical 
utility it should no longer be recommended 
ks of clinical reference. We have given 
the evidence on which we have come to this 
Conclusion in some detail as we considered 
his last right when employed in the destructive 
criticism of the work of a physiologist of 
some repute. 
This method, which promised so much, having 
failed us, we are driven back upon the 
employment of the clinical determination 
of the alkalinity of the Blood, of one of the 
titration methods— that is, practically, the method 
of Lindóis or Brown's modification of it. 
It must be realised however, that this method 

gives the alkalinity of the blood as a whole, not that of the plasma only. Now we do not know that the amount of alkali contained in the corpuscles is likely to be of much importance to the tissues generally which only come into direct contact with the plasma. Hence it does not tell us what which we especially wanted to know, i.e., the degree of alkalinity of the fluid medium in which the cells are bathed. For in this all. The titration method will only give prep results, even as regards the total alkalinity of the blood, if properly carried out. It has been known for some time that the alkalinity of the blood just began to be investigated, but the alkalinity diminishes rapidly after the blood is withdrawn from the vessels, probably owing to the formation of a form of lactic acid during clotting. In order to obviate this source of fallacy it has hitherto been supposed to be necessary to carry out the titration as rapidly as possible.
alkalinity before any acid has had
time to form. Those who do this seem to
forget that the blood is mixed with sulphating
soda solution with the express object of pre-
venting coagulation. Further, Lowry has
shown that unless the blood be titrated slowly
so that the body temperature are the red corpuscles
are not broken down the total alkalinity
is therefore not detected, the contents that.
previous results have given too low an estimate
in some cases not much above that of the
serum alone owing to all the red corpuscles
not having been attacked. Tilia then,
for, can only tell us definitely what is the
alkalinity of the blood as a whole that has
much of this is due to alkali contained
in the corpuscles that much to alkalis
dissolved in the plasma. Furthermore, it can only
give us reliable information even upon this
one point when carried out will the precautions
urged by Lowry, is then performed slowly at
the body temperature.

"Lowry; Archiv. für die gesamte Physiol. Bd. 58. 1894"
We may turn now to the second part of our subject, the consideration of the results which the above method of determining the alkalinity of the blood has afforded. Before drawing any conclusions as to the alterations of the alkalinity due to disease we must, of course, make ourselves acquainted with the variations which occur under physiological conditions. Now the first point we would desire to emphasize regarding the alkalinity of healthy blood is its great constancy. This has been found by every method of the earliest days and reported by it in his investigations. Quantitatively, the alkalinity of healthy blood is about equal to that of 270 mg NaOH per liter. This constancy is the more remarkable when one reflects upon the varying amount of alkaline substances constantly entering the bloodstream. The only
Circumstances in which it is especially altered are during the ingestion of food or after severe muscular work. The alkalinity is considerably increased in the former condition, decreased as the result of the latter. The increase after meals is synchronous with the appearance of the "alkaline tide" in the urine. The latter is to be regarded as the expression result of the former. The increase of the alkalinity is probably to be explained, in large part at least, by the absorption of considerable quantities of alkaline salts from the food. In part, however, it may be due to the discharge into the circulation of sodium carbonate or bicarbonate resulting from the production of hydrochloric acid in the secreting cells of the stomach from sodium chloride. The hypothesis advanced not long ago by Bence Jones of the existence of this periodical increase of alkalinity is not...
it necessary to see that observations on the same case are always taken at the same time in relation to food. Otherwise the results might be fallacious.

The effect of severe muscular work is to cause a fall in the alkalinity of the blood, this being probably due to the production of considerable quantities of lactic acid by the metabolism of the muscles.

Turning our attention now to the condition of the blood in disease we find that the constancy above referred to is maintained in a remarkable manner. There are comparatively few diseases in which the alkalinity of the blood is appreciably altered. The balance of alkalinity, therefore, is not easily disturbed. By what mechanism this balance is maintained we know not, but this we know, that it is a remark-
rises much above the mean the excess appears to be promptly excreted by the kidney. In the reverse direction, however, the mechanism does not seem to work so well. Considerable quantities of acid products can accumulate in the blood without being got rid of. Hence reduction of alkalinity is very much more frequently found in disease than increase. One may, indeed, have an increased alkalinity of the blood, but perhaps one exception never found as the result of disease. Nor here are many marked conditions in which one could not expect a priori to find any alteration in the alkalinity of the blood. This expectation is usually found to be justified. There are, however, in which form what we already know of their pathology some such alteration might naturally be looked for. Amongst the latter are (1) all diseases associated with profound alterations of the general metabolism e.g. all fevers.
(2) all diseases of the blood itself, (3) some special toxic states e.g. Anaemia, jaundice, advanced diabetes, (4) some so-called 'diabetic' conditions e.g. bout Rheumatism. Now as a matter of fact, as far as our observations have hitherto gone, the above list includes practically all the diseases in which any marked alteration in the alkalinity of the blood has been found to occur. We shall consider, briefly, each group individually.

(1) Speaking generally, one may say that fever as a protest that it is accompanied by a diminution in the alkalinity of the blood. This diminution is very constant, but not invariably, as found to be closely proportionate to the height of the fever but not to its duration. It is most probably occasioned by the entrance into the circulation of imperfectly oxidised metabolic products of an acid nature.
which are laid hold of by the alkaline salts in the blood are neutralised. We do not know, however, that any of the general symptoms of fever can be ascribed to this diminished alkalinity nor that it would be at all advisable to make it the basis of any special line of treatment. For the former it is a choice of two evils since the acid products cannot, apparently, be at once eliminated; it is better that they should be neutralised although the reduction in the alkalinity of the blood is, perhaps, unfavourable to tissue vitality. It has been shown by Castellini and Caravaggi that alkaline liquids stimulate the protoplasmic movement of the yeasts while liquids poor in alkaline seem to render them torpid. It is interesting to collate with this the further fact observed by Todaro that an increased alkalinity of the blood artificially produced renders animals much more resistant to organisms. The bearing of these observations upon

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Castellini Caravaggi; Gaz. degli Ospitale 1893

Todaro; Centralb. f. Batte. u. Parasitenk. Fel. 1895
the pathology of fever is obvious.

(2) If we have stated in an earlier part of this Essay that in almost all the Anaemies the alkalinity of the blood is reduced. This is true of simple anaemia, pernicious anaemia, steatorrhoea (also in cancer). The causes of the reduction are probably several. Seeing that as has already been stated, the red cells contain a considerable quantity of alkali, any reduction in their number must of itself entail a corresponding reduction in the total alkalinity of the Blood. This explanation of the reduced alkalinity of anaemia is supported by the fact that in case of pure chlorosis (i.e. where there is reduction of haemoglobin while red cells remain of normal number) the alkalinity of the Blood is not reduced - may indeed be increased (Reiper), this being the only form of anaemia not accompanied by a lowered alkalinity. Von Jacksch (14) has found that in anaemia there is an increased amount of

(14) von Jacksch: "Uber Anaemia Acidemica": Deutsch. med. Wochenschrift 1898
wric acid present in the blood. He attributes this to deficient oxidation of the tissues. This is, doubtless, another cause of the diminished alkalinity. On the other hand, Spies (1) has shown that lactic acid is present in the blood in anaemia. It is also possible that in anaemia the blood is really more watery than normal, the saline constituent being reduced just as the cellular elements are. Here again we could point out that the diminished alkalinity of the blood cannot be made a reason for the administration of alkaline remedies in anaemia. Iron & Arsenic are both drugs which tend to reduce the alkalinity of the blood, yet the utility of both in anaemia is undoubted. The mineral acids are probably more helpful than alkalies.

(3) In all the toxic conditions mentioned above the alkalinity is also diminished. In jaundice this is probably to be attributed to the presence of bile acids in the blood. In anaemia reduction occurs, partly to a marked extent. This is no more noticeable as renal disease is not found per se to lead to

any reduction of the alkali of the blood. Its presence is an additional argument, were one needed, against the ammonia theory of anaemia but to what toxic substance it is due is unknown. In diabetes the alkalinity tends to be low but is always specially reduced if coma supervenes. Its occurrence is to be accounted for by the entrance into the blood of free butyric acid. It is worthy of remark that some clinicians e.g. Neumay, administer alkaline carbonates to their diabetic patient, as a matter of routine. This fact, as a fort, will be subject of keeping up the alkalinity of the blood to the normal standard.

(4) We come finally to certain "diabetic" conditions in which the investigation of the alkalinity of the blood is of peculiar interest: we refer to gout and rheumatism. In the former the alkalinity of the blood is stated to be more reduced than in any other disease. We have had no opportunity of observing a case ourselves but this is just that the known
presence of excess of uric acid in the blood seems
lead us to expect. On the other hand the old acid-
thesis of acute rheumatism leads to the determination
of the alkalinity of the blood in that disease a peculi-
ary interest. Is the alkalinity reduced? The reply is
definitely or almost unanimously in the neg-
avive. Peppe, in J. Phil. Trans. have all failed
to find any reduction with their results the ob-
servations of the present writer agree. This
is corroborated by the results of special anal-
yses. Farrow (Draper's system, m.s.ed.) having
failed to find any uric acid in the blood in
acute rheumatism, while Salomon has failed
to demonstrate the presence of lactic acid.
In chronic articular rheumatism in rheu-
matic arthritis the alkalinity would appear
to be sometimes reduced but this may be due
to accompanying anaemia.
we may refer lastly to the effect of drugs on the
reaction of the blood. These bring out very
clearly the existence of the regulating mech-
anism. It has been found almost impossible
to affect permanently the reaction of the blood by the administration of alkaline or acid substances by the mouth. Hoffmann fed pigeons on substances yielding only an acid ash but found that alkalies were retained in order to form bases with the acids in the blood. This seems even when pure acid is administered than would suffice to neutralize all the alkali in the body. Lassar (16) for only slight effects from the administration of even large quantities of acids. Alkalies this results have been confirmed by those of other observers. A few alkalies called "alkalies" such as phosphoric or arsenic have been found to produce some diminution in the alkalinity - probably by lessening tissue oxidation. In carbonic acid poisoning a considerable reduction occurs from the same reason. In this case the presence of considerable quantities of lactic acid in the blood has been demonstrated (Auer.)

The comparative inability of means of drugs to influence the reaction of the blood is remarkable and constitutes all the therapeutically rather disappointing.

Summary

In closing, briefly summarise the results of our investigation, we have seen that the clinical determination of the alkalinity of the blood is rendered difficult alike by physical and chemical considerations. That the existing methods have been devised with the object of overcoming these difficulties. That these methods are for practical purposes only two in number—the titration method (Kendrew) and the phenolphthalein paper method (Haycraft-Williams). We believe that we have been able to show that the second of these 2 methods is worthless for this reason—that the reaction it yields is very largely dependent upon the viscosity of the blood examined as a result of extreme inconstancy. Of this we claim to have furnished practical experimental proof. We therefore urge that the method should be discarded and recommendation discontinued. That there is therefore available for the clinical determination of the alkalinity of the blood the titration method alone, troublesome rather...
ambrous though it be. That the results afforded by this method can apply only to the alkalinity of the blood as a whole then, only when the titration is carried out slowly at the body temperature, are these results reliable. We are thus left in ignorance how much of the alkali in any given case is contained in the blood cells and how much in the plasma.

But the clinical application of this method has brought into prominence one striking fact regarding the alkalinity of the blood——its constancy. That this constancy tends to be maintained both in health and in disease is apparently the result of a regulating mechanism by which alkali is retained or excreted as required. The alterations in disease are practically always in the direction of diminishment, induced probably by the entrance of acid substances into the circulation. Thus we have Lactic Acid present in Lycoglycaemia, Co. poisoning, in, Urine Acid in Gout and Anaemia, Pyruvic Acid in Diabetes.
That in addition to these conditions the alkalinity is reduced in anaemia, in all febrile conditions and in all anaemia, with the exception of chronic in which the alkalinity is normal or even increased. The reasons for the reduction in these different diseases are briefly discussed. That all these exceptions in which processes, like those which are physiological, are not accompanied by appreciable alterations in the alkalinity of the blood, lead us to the fact, owing in large measure to the existence of the regulating mechanism already referred to, we are practically unable materially to influence the reaction of the blood by the administration of drugs.

As the number of available observations by different observers is now fairly large, and nearly every known disease one is entitled to conclude that still much more will be made out by existing methods. On reviewing the practical results of the in-
acquired one is bound to confess that they are rather meagre. These results certainly throw wide lights, even if of a negative character, on some pathological questions but as regards direct clinical bearing it is we think, evident that the information to be derived from the estimation of the alkalinity of the blood in any given case is hardly commensurate with the expenditure of time trouble which that estimation entails.