the growth. The crayon of solid CO₂ is trimmed to a diameter corresponding to that of the growth. The application is made with firm pressure, and continued until a narrow ring of the healthy tissue around the base of the growth is white and frozen by conduction from the centre. Properly carried out in this way there should never be a failure in dealing with a common wart. In the reaction that ensues a blister is formed under the base of the wart, causing it to be thrown off. Twelve cases were treated in the series under consideration; 9 were completely cured, 2 are still under treatment, and 1 ceased attending. There was no reason to think that these last would not be equally successful under further treatment.

Naevi.

The 105 cases presented 129 naevi for treatment, which were made up as follows:

Capillary ...	...	...	...	85
Cavernous ...	...	...	...	32
Capillary and cavernous (mixed) ...	...	...	...	5
Stellate ...	...	...	...	1
Lymphatic ...	...	...	...	2
Port-wine marks ...	...	...	...	4

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Distribution:

Head and neck ...	...	...	...	61
Arms ...	...	...	...	10
Thorax ...	...	...	...	21
Abdomen ...	...	...	...	16
Pelvis ...	...	...	...	6
Perineum and genitals ...	...	...	...	6
Legs ...	...	...	...	9

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Of the 85 capillary naevi, no less than 74 were cured by a single application of solid CO₂ lasting, on an average, forty seconds; 6 cases had two, 2 had three, and 2 had four applications; while 1 case was incompletely cured after three attempts and was finally finished off by electrolysis.

Of the 32 cavernous naevi, 20 were cured by one application, 4 had two, and 2 had three applications; 6 cases were incompletely cured or not benefited, and finally dealt with by electrolysis.

In all cases in which the capillary and cavernous varieties were coexistent the capillary part was treated by CO₂ and the rest by electrolysis. Of the whole series, 12 had finally to be dealt with by electrolysis. The stellate naevus and the two lymphatic naevi were all cured by a single application of CO₂.

At the time of writing, the cases of "port-wine mark" are still under treatment. These cases require much time whatever the mode of treatment employed, but I am convinced that in CO₂ we have a remedy better than any hitherto known, except perhaps radium, as I have seen equally good results from both. All the cases I have treated with CO₂ are doing exceedingly well, and the outlook is very hopeful. It is noteworthy that in treating cases of this kind the first application seems to have little or no influence in reducing the depth of colour, even after waiting three weeks. After the second application the effect is very marked, and may be sufficient.

It will be seen from the above results that, taking capillary naevi as they come, no less than 87 per cent. have been cured by a single application, and I venture to say that with greater experience an even higher percentage would be obtained were I starting a similar series again. As might be expected, the results in treating cavernous naevi were not so good, but even here the proportion cured by a single application was as high as 63 per cent.

Higher percentages of cures are, of course, possible and obtained by other methods, such as electrolysis and the cautery, but it must be remembered that with these a general anaesthetic is always necessary. No anaesthetic, local or general, is ever necessary with carbon dioxide, as the application is practically painless and of only a few seconds' duration. I have had children who never cried or moved during the application; this is, of course, exceptional, but it does show that the process cannot be a very severe one.

REFERENCE.

¹ *Lancet*, December 4th, 1909.

THE CLINICAL ESTIMATION OF "ACIDOSIS."

By A. E. BARNES, M.B., M.R.C.P.,

MEDICAL REGISTRAR, ROYAL INFIRMARY, SHEFFIELD; MEDICAL TUTOR,
UNIVERSITY OF SHEFFIELD; LATE RESEARCH SCHOLAR,
BRITISH MEDICAL ASSOCIATION.

THE subject of acid intoxication is becoming daily of greater importance, it being more generally recognized as a terminal condition in a large number of diseases. Although it usually proves fatal, yet the occasional brilliant success which follows properly applied therapeutic measures must render welcome any means by which the condition may be recognized before it has reached a stage beyond hope of recovery. It seems desirable, therefore, to record some of the routine methods which have been made use of in the work of the Practical Medicine Laboratory of the University of Sheffield during recent months, from which results of considerable interest have been obtained. No originality is claimed for the methods here described. It is well recognized that acidosis may exist for years without any marked effect upon the general health, but, whilst at any time the acidosis may increase to such an extent as to become a positive danger and demand urgent treatment, yet the means at our disposal for knowing when that danger is imminent are as yet incomplete.

To remedy this defect it is necessary that a large number of cases should be examined and followed up for prolonged periods. It is therefore essential that such methods of examination should be used as will, whilst giving a good general idea of the state of metabolism, not be too complicated for general clinical use. The first requirement is a method which will show approximately the amount of organic acid in the urine. It has been assumed that in diabetes the β oxybutyric acid is the factor which requires measurement, and various methods have been devised to do this. All of them, however, are either difficult to carry out or require expensive apparatus. The usual method of estimating the quantity from the difference between the values obtained for dextrose by titration and polarization respectively involves not only expensive apparatus, but the assumption that all the difference is due to the above acid—an assumption which seems somewhat unsafe in view of the fact that many cases of severe diabetes give a definite reaction for laevulose when tested by Seliwanoff's method. The other methods of extraction by ether are very tedious, and even that with the best apparatus (Lind's) is stated to require seven hours for complete extraction.

To obviate these difficulties we have used a modification of Folin's method for determining the total organic acidity of the urine. In this method all the organic acids are estimated together, including, therefore, uric and hippuric as well as the fatty acids. The latter, however, are so small in quantity that they may be neglected.

Method.

1. Take 20 c.cm. of urine. Dilute with water and add some crystals of neutral potassium oxalate and a few drops of alcoholic solution of phenolphthalein. Titrate with decinormal caustic soda solution until a definite red tinge appears. The number representing the total acidity is obtained as follows:

$$\frac{\text{C.cm. of } \frac{N}{10} \text{ caustic soda solution used}}{20 \text{ (c.cm. of urine)}} \times \text{Total number of c.cm. urine passed during 24 hours.}$$

The total acidity for twenty-four hours thus expressed in units of decinormal soda is due to acid salts and to organic acids not combined with alkalis or ammonia.

2. The titration is now carried a stage further by adding to the same urine mixture 2 c.cm. of previously neutralized commercial formalin. (The neutralization is easily done by adding phenolphthalein followed by dilute alkali until a pink colour appears.) In a few seconds the pink coloration of the mixture disappears. This is due to the fact that the ammonia present in the urine in combination with acids has united in a condensation reaction with the formaldehyde as hexamethylenetetramine. Thus the acid which was previously combined with this ammonia base has been set free, causing the disappearance of the pink colour. Further titration is now carried out with the same decinormal caustic soda solution until the pink colour reappears. The number of cubic centimetres of decinormal caustic soda solution used in this further titration represents the acidity of the urine which has been neutralized by the ammonia, and this is the factor which we require to determine the organic acids; it will be called the "ammonia acidity." Each cubic centimetre of decinormal caustic soda solution used in this second

titration represents 0.0014 gram of nitrogen in the form of ammonia.

3. The next step is to ascertain the "mineral acidity." This is obtained as follows: 20 c.cm. of urine are placed in a platinum crucible, dried and ashed, great care being taken to prevent the contents rising beyond a dull red heat. The mass is then dissolved in distilled water, and titrated with either decinormal acid or alkali as required. All the ammonia and organic acids have been driven off by the heat, leaving only the mineral bases and acids. The mineral acidity is then easily calculated by the following formula:

$$\frac{\text{No. of c.cm. of } \frac{N}{10} \text{ alkali (or acid) used}}{\text{No. of c.cm. of urine used (20)}} \times \frac{\text{Total No. of c.cm. of urine passed in 24 hours}}{\text{hours}} = \text{Mineral acidity.}$$

In a normal urine the residue is acid, and the mineral acidity then gives a number expressed in cubic centimetres of decinormal alkali, and is marked in *plus* quantity; in cases of acidosis the ash is alkaline owing to the acids in the blood having combined with bases in the blood in accordance with the tendency of the blood to maintain its normal reaction, but the result in terms of decinormal acid solution is still called mineral acidity, but expressed in *minus* quantities.

These estimations having been made, we are now able to calculate the organic acidity in terms of decinormal soda solution, according to the following formula:

$$\text{Ammonia acidity} + \text{total acidity} - \text{mineral acidity} = \text{organic acidity.}$$

The method is really quite simple. The only expensive part of the apparatus is the platinum crucible, but in cases of acidosis, where the ash is alkaline, a nickel crucible may be substituted; and, as a matter of fact, considerations of economy have compelled us to use a nickel crucible in our experiments.

By this method we can detect any perversion of ammonia or alkali excretion, and as it shows at once if the body is being drained of alkalis to any marked extent, it gives direct control of the most dangerous factor of acidosis (alkali starvation). It is desirable to estimate also the nitrogen content of the urine, and for this we have used the Kjeldahl method. By so doing we can obtain the ammonia-nitrogen coefficient, and see how the nitrogen distribution has been disturbed by the acidosis.

It may be objected that the Kjeldahl method is too cumbersome for general use, but it is so accurate and inclusive of all nitrogenous bodies that it demands a place in clinical medicine. In fact, in severe cases of diabetes it is absolutely indispensable, for it is now recognized that the nitrogen balance is of much greater importance than the sugar content from the point of view of prognosis and dietetic treatment. Given the apparatus and the place to accommodate it, we have found it only slightly more troublesome than the tricky aërometric determinations.

An estimation of the phosphorus excretion in the form of phosphates (reckoned as P_2O_5) is of value in showing how the basic phosphates are drained from the blood. The body seems to hold to its phosphorus salts until the very last, and any abnormal excretion is usually a sign of danger.

We have tried these methods in a variety of cases. The normal organic acidity is equivalent, according to Voegtlin, to about 300 units, the normal ammonia-nitrogen coefficient being 3 to 5 per cent.

A case of cirrhosis of the liver with ascites, albuminuria, and gouty tophi gave the following figures: Quantity of urine 752 c.cm. Total acidity 176, ammonia nitrogen 0.2422 gram, mineral acidity 26, phosphates 1.69 gram, total organic acidity 375 units, total nitrogen 6.316 grams, ammonia-nitrogen coefficient 3.8 per cent. The acidosis is thus very slight, the ammonia-nitrogen coefficient not being disturbed. Up to six weeks later this man has had no clinical symptoms of toxæmia, his symptoms being mechanical (ascites).

Another man, with cirrhosis of the liver and ascites complicated with nephritis, gave the following figures: Quantity 454 c.cm., acidity 289, ammonia 0.6610 gram, mineral acidity -45, organic acidity 760, total nitrogen 6.356 grams, ammonia-nitrogen coefficient 10 per cent. There is here a definite acidosis, but we cannot say how much the ammonia increase was due to the liver insufficiency or to production of acids. After large doses of sodium bicarbonate the figures were: Quantity 482 c.cm., acidity 108, ammonia 0.5060 gram, mineral acidity -86.76, organic acidity 556.71, total nitrogen 7.155 grams, coefficient 7.07 per cent. As the phosphates and chlorides gave very low figures, we concluded that there was a retention of salts, including the alkalis, and that all attempts to treat the acidosis would be useless. This was the case, for the man died in coma two days after the last examination, and for twenty-four hours had complete suppression of urine.

Another earlier case of cirrhosis had severe ascites, which recurred after paracentesis; there was much emaciation and slight oedema of the legs. The ammonia coefficient was

5 per cent., and he recovered so much that he was able to return home. Unfortunately this was before we began to determine the organic acids.

In diabetes some interesting results have been obtained. In this disease we have come to recognize that the deprivation of carbohydrates is not the only factor in treatment. Some authorities, in giving a prognosis, lay more stress on the relation of nitrogen intake to output than on the sugar excretion. There is no doubt that the attempt to remove glycosuria by dieting is apt in some cases to produce coma, whilst in others the results are most beneficial. As coma is due to acidosis we ought, by estimation of the organic acids in the urine, to be able to separate these two classes of cases in time to prevent coma. To the surgeon these facts are of interest, as it is not unlikely that the fatal results of operations on diabetics are seen when the effect of the operation has been to increase the organic acid or diminish its excretion beyond the danger line, near which line it may have been hovering for some time. The recognition of these cases would save the surgeon from operating on absolutely hopeless cases. We have been able to follow one case of diabetes after a severe operation.

Mr. Miles Phillips, of the Jessop Hospital, Sheffield, kindly sent us specimens of the 24-hourly urine of a case of early carcinoma uteri in a fat glycosuric patient. On admission it had been found that there was 4 per cent. of sugar in the urine, but by a partial restriction of carbohydrate this had been reduced to 2 per cent. Before the operation it was only possible to obtain a 24-hour specimen for one day, but this urine gave the following data: Quantity 1,931 c.cm., acidity 621, ammonia 0.773 gram, mineral acidity -193, organic acidity 1,367, total nitrogen 16.49 grams, ammonia-nitrogen coefficient 4.6 per cent. As we knew that the organic acid could rise to above 4,000 units without coma we felt justified in saying that there would be no very great danger in the operation from the point of view of acidosis. For a few days after operation we were able to obtain 24 hourly specimens as the urine was removed by catheterization. The following are the figures obtained:

Date.	Quantity.	Acidity.	Nitrogen as Ammonia.	Mineral Acidity.	Organic Acidity.	Nitrogen.	Co-efficient.	Phosphates.
11th ...	1931	621	0.773	- 193	1367	16.49	p. cent. 4.6	—
14th*...	—	—	—	—	—	—	—	—
15th ...	1050	903	0.933	- 73.5	1643	16.75	5.5	4.25
16th ...	965	458	1.0132	- 28.95	1216	13.78	7.3	2.581
17th ...	965	299	1.0402	- 0	1041	12.00	8.6	1.582
18th ...	852	340	0.9338	- 17	1020	11.92	8.6	1.789
21st ...	908	295	0.5021	- 376	1030	9.2797	5.4	0.6719

* Vaginal hysterectomy.

This case was undoubtedly, from the purely clinical point of view, a suitable case for operation, for it was not a severe case of diabetes. It furnishes, however, some indications, although not evidence which is truly scientific, as to the manner in which operation may affect a diabetic very seriously. For the first twenty-four hours the patient took no food of any kind. Yet we see that there was a large nitrogen excretion. The phosphates were also markedly increased. The urine was loaded with urates, and a quantitative estimation by the rough and ready method of Sicuriani gave 2.4 grams of uric acid. The coincident increase of phosphate and of uric acid was interpreted as an index of leucocyte destruction, and this was confirmed by the occurrence of slight pyrexia. As the ammonia coefficient was hardly increased, it was concluded that it was not an increase of organic acid which was depriving the body of the basic phosphates of the blood. As it is probable that in acidosis some of the acid is excreted in combination with the basic phosphates, this increased excretion due to the operation may deplete the body of phosphorus, and aid in the production of coma. It is of interest to note that "septic" operations are notoriously more dangerous than aseptic ones, and an increased drain of phosphates might supply a simple explanation. The excretion of phosphates afterwards became subnormal, particularly on the 21st, when sodium bicarbonate had been given. Although after the operation the urine became free from sugar, there was still an increase

in the organic acidity above the normal. We have unfortunately no exact data as regards the food taken, but the gradual diminution of nitrogen coincidentally with the ingestion of more food, is an index that in this case nitrogenous metabolism was in a good condition, and that the patient was able to recuperate somewhat from the starvation incident to a severe operation. The fall in ammonia with the accompanying fall in mineral acidity was the result of giving sodium bicarbonate. As an example of a moderately severe case of diabetes we give the following data from a middle-aged woman who was on a diet almost free from carbohydrate.

Quantity 3,635 c.cm., acidity 981, ammonia 1.323 gram, mineral acidity 54.5, organic acidity 1,563, phosphates 3.44 grams P.O., total nitrogen 20.7195, ammonia-nitrogen coefficient 6.3 per cent.

As a contrast to this, take the following figures from the case of a young man who on a less restricted diet was passing exactly the same amount of urine:

Quantity 3,635, acidity 1,163, ammonia 3.56 grams, mineral acidity -181, organic acidity 3,944, phosphates 3.88, total nitrogen 17.78 grams, ammonia coefficient 20.06 per cent.

Some cases of diabetes have been followed for weeks, and interesting results have been obtained, which will be communicated in a joint paper with Dr. Arthur Hall.

In order to obtain figures for the changes occurring during starvation, a case of rectal "feeding" was examined:

The patient, a woman aged 30, had apparently a gastric neurosis, and one day, after severe retching and vomiting, had a slight attack of haematemesis. She was admitted and fed exclusively per rectum for seven days, at the end of which the following figures were obtained: Quantity 511 c.cm., acidity 183, ammonia 1.234 gram, mineral acidity -15, organic acidity 1,131, phosphates 0.82 grams, total nitrogen 4.57 grams, ammonia-nitrogen coefficient 26.7 per cent. This at once raised the question of pregnancy, but we were unable to decide with certainty as a vaginal examination was refused. Nothing could be felt from the abdomen, and there were no other indications of pregnancy.

The patient subsequently got quite well. The above cases afford illustrations of the general applications of this method, which in our opinion provides a rough estimate of several factors which are very important in the treatment of many conditions, and has the great advantage of being applicable to ordinary clinical work by a man with the usual training of a modern medical student. A vast field of work is open to the ordinary worker in such conditions as cirrhosis of the liver, eclampsia, pernicious vomiting of pregnancy, the effects of narcosis, many cases of so-called neuroses (which may, as in one described by Voegtlin, be accompanied by an acidosis due to some unknown fatty acid), rheumatoid arthritis (also sometimes accompanied by an acidosis), and the acute infections. Cases of marasmus in infants promise to afford very interesting results in view of recent Continental work. In fact, they seem to open the door for the admission of recent work in metabolism to the practice of the general physician.

It may be objected that the methods here described are not accurate. This objection applies especially to the method of ammonia determination, which was first published by Malfatti; it has been used also by other workers, and has been tested by Macpherson¹ against the Folin method. He found that it gave slightly higher results, and this may be due to the fact that it estimates at the same time the amino acids. The method of determining the organic acids has been adopted for original research on metabolism at the Johns Hopkins Hospital,² and has given satisfactory results. It has given results in our experience which accord with clinical observation, and is so easily applied that we draw attention to it in the hope that some highly qualified chemist may test its accuracy, and either condemn it or show that it gives results sufficiently accurate for clinical purposes.

I have great pleasure in thanking the medical staff of the Infirmary for permission to use their cases, and Dr. Hall for kind help in preparing this paper.

REFERENCES.

¹ Macpherson, BRITISH MEDICAL JOURNAL, March, 1909. ² Reports from the Laboratories of the Johns Hopkins Hospital, July and August, 1907.

Memoranda: MEDICAL, SURGICAL, OBSTETRICAL.

LOCAL INJECTIONS OF STRYCHNINE IN NEURITIS.

I DESIRE in all humility to ask for a trial of the following simple treatment for neuritis—namely, the injection twice daily of $\frac{1}{100}$ gr. of strychnine in about 20 minims of sterilized water along the course of the affected nerve. The "cure" never in my experience takes longer than four weeks.

London, E.C.

GEORGE H. R. DABBS, M.D.

TREATMENT OF RINGWORM.

THE several antiseptics advocated for outward application in cases of ringworm are far from satisfactory, the prolonged duration of the disease proving their inefficiency. In dealing with the numerous cases of pediculosis in our fever wards we always employ the essential oil of sassafras, which, without exception, we find acts as a specific in such cases. When both pediculosis and ringworm occurred in the same scalp, it was noticed that the latter disease also reacted favourably to this preparation. This led me to test the possible usefulness of the oil for ordinary cases of ringworm, and so far the results have been most happy. The hair is cut closely around in order to identify the patches, the application of the oil being made twice a day by means of a camel-hair brush. This is continued for a few weeks, as the case indicates. No irritation is produced, while the preparation is most pleasant to use. Not only is the spread of the infection prevented, but that the fungus is being destroyed with certainty is recognized in two or three weeks, by commencing development of fine hairs.

In country practice, where treatment by α rays is impracticable, this method will, I venture to think, prove a valuable addition to the several means recommended by various authorities.

E. LYNN JENKINS, M.B., B.Sc.,

Medical Officer, Isolation Hospital, Hinckley and District.

CASE OF COMPLETE INVERSION OF THE UTERUS: REDUCTION AND RECOVERY.

MRS. H., aged 24, a primipara, was delivered with forceps at 7 p.m. on December 2nd, 1909, after a tedious labour, presentation being occipito-posterior. Delivery with forceps was easy, no severe traction being required. I waited expecting the contractions which would expel the placenta, and meantime used no undue traction on the cord nor pressure on the fundus. After an hour and twenty minutes contractions began, and increased in violence every minute, and latterly were extremely violent. The placenta began to be extruded, was finally expelled, and was followed by a hard mass and much haemorrhage. I placed my left hand on the abdomen, and found the uterus gone. I grasped the neck of the mass between my knitted fists and controlled the bleeding very largely. The patient was blanched and gasping, and the situation was alarming in the last degree. I sent for the assistance of my nearest colleague, and, pending his arrival, held the bleeding in check. I tried to separate the edges of the placenta where it was still undetached, and was astonished at the very close incorporation of placenta and uterus. Presently my colleague, Dr. Mackay, arrived. I requested him to sluice the mass with biniodide solution (1 in 1,000), and then to detach the placenta. He experienced the same difficulty, and remarked upon the extremely close adhesions. I still held the mass firmly by the neck and plugged the sinuses with my fingers as the difficult and tedious detachment of the placenta proceeded. When it had been finally accomplished as well as we could do it, the uterus was well washed with biniodide solution. My colleague gave chloroform. I squeezed the organ into a smaller volume as a first step and then tried reduction by inverting the fundus. It was almost at once evident that that method would not succeed for two reasons: (1) the tissue of the uterus was too friable and would not bear the pressure of the fingers; (2) it formed a very unnecessary bulk in passing the os.