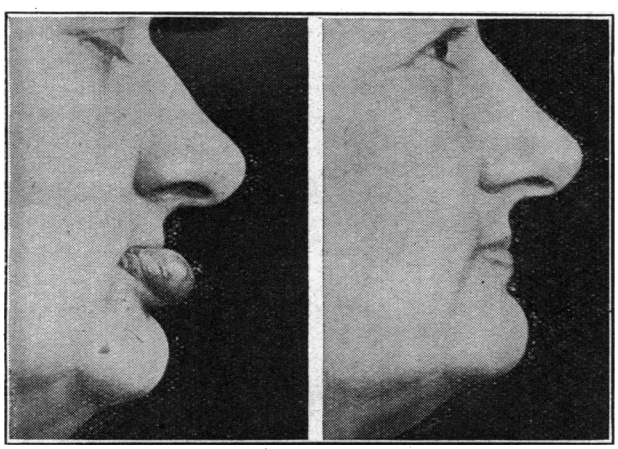
the untoward sequelae from diathermy, such as interference with the epiphysial growth, damage to the eyes, or epilation, that may result from radiotherapy. The superficial nature and delicate endothelium of the large capillary angioma tempted me to treat a few with a flat-button electrode of 7 mm. diameter. Cosmetic results were excellent, and the method was less tiring than treatment from beneath by the insulated needle, but a low-intensity current must be used to avoid overheating the tissues, with subsequent sloughing and scar formation. The latter method is undergoing further trial with electrodes of various diameters.

Cavernous Angiomata.—These are generally situated deeply and are covered by healthy skin or mucosa, little or no blemish being left after treatment. Some of my best results were obtained in these cases (see illustration),



Photographs showing cavernous angioma of lower lip before and after treatment with the insulated needle.

the response often being dramatic. With care the tissues and configuration of the area—apart from the deep scarring in the tumour—may be returned to normal. Some of the cases had been treated by irradiation previously, and in these diathermy was used carefully because of the danger of sloughing of the irradiated tissue.

Port-wine Stains.—These present a problem best left to the plastic surgeon. In the one case treated there were obvious capillary overgrowths in parts of the stain. The recorded case responded well and the patient was delighted with the result, but the treatment was an arduous and difficult undertaking. The lesion involved the right side of the face and both eyelids, and great care was needed to avoid scarring and resultant contractures. The port-wine portion of the stain remained almost entirely unaffected by the treatment.

The two *capillary lymphangiomata* occurred in the tongue. They were considerably reduced in size and showed marked improvement after four treatments with the needle electrode. Neither case has required further attention for the past two years.

The *cystic hygroma* was a small one situated in the left supraclavicular fossa. It disappeared completely after a single treatment by the needle electrode four years ago, and there has been no recurrence. Because of the remarkable power of growth which these tumours possess, treatment at the onset is advocated.

In the present series there was only one case of *cirsoid aneurysm*, and it involved the left superficial temporal artery. The main artery was ligated and the remaining secondary varicosities were treated with the diathermy needle electrode on four occasions. The tumour disappeared entirely, and when the patient was examined two years later it had not recurred.

I have had no experience of the treatment of the angiomata involving a whole limb, and I very much doubt if this method of treatment could be applied with success. Fortunately these extensive lesions are rare.

Summary

A series of 82 patients with angiomata have been treated with diathermy, and these have been followed up for one year after treatment. All forms of angiomata, except the port-wine stain and angiomata involving a whole limb, may be treated with a specially insulated needle. This method is simple and safe, and gives a cosmetic result which is comparable with that of other methods of treating capillary angiomata, and is superior to them in the treatment of cavernous angiomata. The preparation of the special needle and the way to use it are described.

I wish to thank Mr. Wilfred Hynes, our plastic surgeon, for his great help and criticisms, and for allowing me to treat patients under his care. I am also grateful to Mr. H. Blacow Yates and Dr. E. R. A. Cooper for the help they have given me.

REFERENCES

Aiken, D. (1944). *Lancet*, **2**, 212.
Ribbert, V. A. (1898). *Virchows Arch.*, **151**, 381.

USE AND INTERPRETATION OF THE FANTUS ESTIMATION OF URINARY CHLORIDE

BY

W. H. TAYLOR, B.M., B.Ch., M.R.C.P.

(From the Department of Biochemistry, Radcliffe Infirmary, Oxford)

Since its advocacy by Marriott (1947), the ward test of Fantus (1936) for estimating urinary chloride ion concentration has been widely used in clinical practice. This communication describes experiments which have been made to determine its reliability, and records circumstances in which interpretation of the test in the normal fashion would lead apparently to mistaken conclusions about the electrolyte requirements of certain patients.

Methods

Fantus Test.—The method described by Fantus (1936) was used. It is essentially a modification of the Mohr (1856) titration. To 10 drops of urine a drop of 20% potassium chromate solution is added. With the same dropper, silver nitrate solution (29 g. per litre) is added drop by drop until a permanent and distinct colour change to red-brown occurs. The number of drops thus required is taken as a measure of the content of chloride in grammes of NaCl per litre.

Volhard Titration.—The method described by Peters and Van Slyke (1932) was used.

Results: (a) Anions Estimated by the Test

It is usual to estimate chloride ions in urine by a method involving their precipitation as silver chloride in acid solution, as in neutral or alkaline solution other silver compounds may be precipitated and render the

estimation inaccurate. The Fantus test is, of course, carried out in neutral solution, or nearly so, depending upon the *p*H of the urine. The extent to which the formation of other compounds renders the test unreliable must therefore be determined. This was done by the addition of various anions in the form of the solid sodium or ammonium salts to 10 drops of urine and then performing the test.

Of the anions commonly present in urine, sulphate, phosphate, and bicarbonate were without effect upon the result of the test. Urates, however, did affect the result, and the magnitude of this effect must be assessed. The normal daily excretion of urates in urine is 0.1–2 g. (Harrison, 1947) measured as uric acid, and the normal urinary volume is 1–1.5 litres. The normal concentration of uric acid in urine could therefore vary from 0.007 g./100 ml. to 0.2 g./100 ml. Uric acid is known to form monobasic and dibasic salts with cations, and, assuming that one molecule of silver nitrate reacts with one of uric acid, then one drop of the 2.9 g./100 ml. silver nitrate solution used in the Fantus test is equivalent to one drop of 2.8 g./litre uric acid solution, or to 10 drops of a 0.28 g./litre solution. At the most, therefore, the amount of urate present in 10 drops of urine used in the Fantus test would utilize 0.7 drop of the silver nitrate solution. If the di-silver urate were wholly formed, 1.4 drops would be utilized.

Carbonate ion was also found to interfere with the test. The amounts normally present in urine are small, but in urine which has stood for some time, especially if infected, urea is converted into ammonium carbonate, and this may cause an appreciable error. It was found that the Fantus test result may be increased by up to 2 g./litre if the urine is allowed to stand for 24 hours at room temperature. The presence of silver carbonate in the reaction mixture at the end-point of the Fantus test can often be demonstrated by the addition of a mineral acid to the filtered precipitate. There is an effervescence of carbon dioxide, which can be detected by the usual tests. It is important, therefore, always to perform the test upon a fresh urine specimen.

There are other factors which could potentially affect the result of the Fantus test. The chromate ion is only stable in the *p*H range 6.5–9 (Vogel, 1939). In more acid solutions the reaction

$$2CrO_4^{--} + 2H^+ = 2HCrO_4^- = Cr_2O_7^{--} + H_2O$$

occurs. The tendency of this would be to reduce the chromate ion concentration and delay the appearance of the end-point in an acid urine. A further factor which may be of significance in a urine containing large amounts of ammonium ion—that is, when infected or in acidosis—is the ability of silver ions to form the argentammonium ion $(Ag(NH_3)_2)^+$. This factor would again tend to increase the number of drops of silver nitrate solution used.

(b) Error in Performance of the Test

The accuracy of the test depends also upon producing drops of equal volume from a dropping pipette with rubber teat. The ability to do this depends in turn on the experience of the observer. Thus, two biochemists and three technicians who were accustomed to using dropping pipettes made many estimations on the same urine specimen, giving results shown in Table I.

Three house officers and two medical students, unaccustomed to using the method, gave a rather wider scatter (Table II).

TABLE I

Correct Urinary Chloride Concentration (g./litre)	No. of Drops of $AgNO_3$ Used	No. of Readings
1·9	2	10
	3	2
8·5	8	3
	9	9
4·0	7	4
	8	8
	9	1
4·5	4	1
	5	7
	6	1
4·5	4	2
	5	6
	6	1

TABLE II

Correct Urinary Chloride Concentration (g./litre)	No. of Drops of $AgNO_3$ Used	No. of Readings
8·5	6	2
	7	2
	8	5
	9	2
	10	1
5·7	5	2
	6	1
	7	7
	8	2
6·2	6	1
	7	4
	8	13
	9	4
4·0	6	1
	7	6
	8	3
4·0	5	2
	6	5
	7	2
	8	1

These results afford an illustration of the inability of the test to give reproducible results even in the hands of the more experienced manipulators, and the decreased reliability with those less experienced. The urine containing 4 g. NaCl/litre was markedly alkaline and contained much carbonate ion, giving high Fantus test values which illustrate well the points made in the preceding section.

It should be noted, however, that the smaller the amount of chloride ion in the urine the less will be the inaccuracy caused by drops of unequal size, as fewer drops will be needed.

(c) Effect of Errors in Practical Use of Test

In 62 urine specimens the results obtained by the Fantus test were checked by the Volhard titration. The Fantus test was in each case performed by the same observer on urines which had stood for not longer than four hours, so that errors due to the formation of ammonium carbonate and to inexperience with a dropping pipette were minimal. The results are given in Table III.

TABLE III

Volhard Titration g./litre	No. of Urines Tested	No. of Fantus Test Results Giving Error of	
		1–2 g./litre	2–3 g./litre
0–1	26	8	2
1–2	5	0	0
2–3	3	1	0
3–4	8	4	0
4–5	3	0	1
5–6	5	2	0
6–7	5	3	1
7–8	2	1	0
8–9	1	0	0
9–10	3	1	1
10–11	1	1	0

The largest error is 2–3 g./litre, and this occurred in 5 out of 62 estimations (8%). An error of 1 g./litre or over occurred in 26 out of 62 estimations (42%).

From a statistical point of view these specimens show a preponderance of urines containing little chloride ion. The natural accuracy of the test is greater in these urines, so that the results expressed show the test in as favourable a light as possible.

(d) Interpretation of the Results of the Fantus Test

Marriott (1947) considers that " in concentrated urine, with a specific gravity of more than 1020, less than 3 g./litre (of chloride measured as NaCl) suggests (salt) depletion." Black (1950) considers that a urinary salt concentration of less than 5 g./litre indicates the need for increasing salt intake. He makes the reservations that the urine must be reasonably concentrated, that there must be no disease of the suprarenal glands, and that the Fantus test may fail to show salt deficiency in the presence of acidosis. Marriott also mentions that during intravenous saline therapy there may be an adequate concentration of chloride ion in the urine although the body is still salt-deficient.

There are patients, however, in whom such an interpretation of the Fantus test may be misleading : first, those in whom there is hyperchloraemia and hypernatraemia but a urinary chloride ion concentration of less than 1 g./litre in a concentrated specimen ; and, secondly, those with hypochloraemia and hyponatraemia yet with a high urinary chloride concentration and symptoms of salt deficiency but with no evidence of Addison's disease. This second group may be subdivided into those (mentioned by Marriott) in whom saline transfusion is being carried out and those in whom there is no such therapy.

During the past year 12 patients of the hyperchloraemia group have been noted in the Radcliffe Infirmary. They consist of 6 fatal cases of head injury, 1 non-fatal case of perforated peptic ulcer (post-operative), 1 fatal case of carcinoma of the oesophagus (post-oesophagectomy), 1 fatal case of fat embolism (post-traumatic), 1 fatal case of diabetic coma, 1 fatal case of meningitis and lung abscess, and 1 fatal case of post-operative partial gastrectomy. The cases with head injury have been reported in some detail in a separate communication with other workers (Higgins *et al.*, 1951).

The biochemical findings in the following patient are fairly typical.

Case Report

A man aged 57 with a 20-year history of epigastric pain characteristic of peptic ulceration developed the symptoms of pyloric stenosis. Seven months previously he had had an attack of renal colic, but a subsequent intravenous pyelogram had shown good concentration of the dye and no calculi in the kidneys. The blood-urea concentration was 33 mg./100 ml. After a period of preparatory medical treatment, a Billroth I partial gastrectomy was performed. Post-operative progress was stormy, with recurrent haematemesis and a persistently low blood pressure. Two weeks after the operation a hypostatic chest infection with rise of temperature developed, and the patient died.

For the first two days after operation fluid balance was maintained mainly by intravenous transfusion ; a total of 1,140 ml. (2 pints) of blood, 1,140 ml. (2 pints) of 0.9 g./100 ml. saline, and 1,700 ml. (3 pints) of Ringer–Locke solution was given. By mouth, 1,140 ml. of water was given. The measurable urinary output totalled 1,730 ml. (61 oz.) and the stomach-tube aspirations 1,250 ml. (44 oz.).

Thereafter for five days an average oral daily intake of 2,850 ml. (5 pints) of water or 50% milk in water was given. Aspirations averaged 1,140 ml. (40 oz.) daily, and collectable urine 910 ml. (32 oz.) daily. During the last three of these days a total of 3,410 ml. (6 pints) of 5% glucose solution and 1,140 (2 pints) of 0.9 g./100 ml. saline was given.

At this stage, on the seventh day after operation, the plasma chloride ion concentration was 700 mg. NaCl/100 ml. (or 120 mEq/litre) and blood urea 176 mg./100 ml. The urine, of specific gravity 1015, was completely free of the chloride ion. Treatment was designed to reduce this high chloride level. Over the next four days an average oral intake of 2,840 ml. of milk, water, and glucose was given with 1,700 ml. of 5% glucose solution intravenously daily. The only sodium chloride received was in the milk. The aspirations averaged 1,360 ml. (48 oz.) daily and the measurable urine 1,140 ml. (40 oz.). The plasma chloride levels fluctuated as follows: 690, 700, 790, and 650 mg./100 ml. (118, 120, 135, and 111 mEq/litre) over the next four days. The serum sodium level on the last of these days was 162 mEq/litre (372 mg./100 ml.) and the plasma bicarbonate 15 mEq/litre (35 vols./100 ml.). The blood urea, after rising to 417 mg./100 ml., fell to 271 mg./100 ml. Throughout this time the urinary chloride concentration varied between 0 and 0.4 g./litre, as measured by the Volhard method. The urinary urea concentration on two occasions was 2.6 and 3 g./litre. Fantus test estimations made by the nursing staff usually gave urinary chloride concentrations of 0–1 g./litre and 1–2 g./litre, although on two occasions misleadingly high values were obtained—2–3 g./litre and 3–4 g./litre.

At this point, 11 days after the operation and five before death, chloride ion was passed for the first time and the urinary concentration rose to 4.5 g./litre. However, chest infection developed and the patient became febrile and generally more ill. It proved impossible to give more than 1,700 ml. (3 pints) of fluid by mouth daily. Blood, glucose solution, hypotonic saline, and sodium sulphate were given intravenously in addition. The patient's condition deteriorated steadily and he died 16 days after the operation.

At necropsy there was thrombosis of several mesenteric veins, causing gangrene and perforation of the colon at a point near the recto-sigmoid junction. Uraemic ulceration of the large and small bowel and bilateral pulmonary congestion and oedema were also found. The coronary arteries were atheromatous, with narrowing of the lumina. There was no significant renal disease, macroscopically or microscopically.

Comment

Had this patient been given intravenous saline therapy during the period of hyperchloraemia and hypernatraemia, as the urinary chloride tests would have indicated, it seems likely that the plasma sodium and chloride levels would have risen even higher.

During the same period 10 patients falling into the second, or hypochloraemic, group were noted. Six were receiving intravenous saline transfusions post-operatively, and four not. Three of the six were children. One, a boy of 11 years subjected to investigative laparotomy, passed 7.5 g. NaCl/litre in a urine of specific gravity 1012 when his plasma chloride level was 87 mEq/litre (510 mg./100 ml.) and his serum sodium level 128 mEq/litre (297 mg./100 ml.). Another child of 8 weeks, following Ramstedt's operation for pyloric stenosis, passed 5.4 g. NaCl/litre in his urine on a day when his plasma chloride level was 82 mEq/litre (480 mg./100 ml.) and he appeared clinically to be salt-deficient. Of the three adults, two were post-abdominal operation cases and one was in diabetic hyperglycaemic coma.

The remaining four all suffered head injuries severe enough to keep them unconscious for several days.

Despite the maintenance of an adequate milk, water, and glucose intake, and an adequate urinary output, they developed unmistakable signs of salt deficiency. One man aged 84, for example, was thought to have had a cerebral thrombosis causing him to fall and sustain a head injury. Five days later the normal skin turgor was lost, the intraocular tension was diminished, the cheeks were hollowed and sunken, and the tongue was dry and wrinkled. His urine was found to contain 7.8 g. NaCl/litre and his serum sodium ion concentration was 130 mEq/litre (300 mg./100 ml.) and plasma chloride ion concentration 82 mEq/litre (480 mg./100 ml.). No intravenous fluids had been given. These four patients responded slowly to Ringer–Locke solution by mouth. Had the Fantus test been performed and interpreted in the usual way, this fluid would have been denied them, as they would not have been considered salt-deficient.

Discussion

The foregoing results pose two separate problems : first, the accuracy of the Fantus test as a measure of urinary chloride ion concentration ; and, secondly, the value of that concentration as a guide to sodium and chloride ion requirements in disease.

Assuming for the time being that the urinary chloride concentration is of some value, it is important that the Fantus test should give a fairly accurate result for values from 0 to 5 g. NaCl/litre, over which range it is going to provide a basis for Na and Cl therapy. Although, for reasons given above, the natural accuracy of the test is greater at lower urinary chloride concentrations, the values obtained under conditions approximating to the best still show an undue amount of error. A urine containing less than 1 g./litre ought not to be estimated as containing 2–3 g./litre as it was in 2 out of 26 cases. In the hands of less practised persons, such as house officers and nursing staff, an error of this magnitude might occur more frequently. In the case described for example, such urines were twice estimated as containing 2–3 g./litre and once as containing 3–4 g./litre. It is surely indefensible that such results be used as a basis of treatment, especially when the Volhard estimation is in itself so easy and accurate and involves the use of only two solutions, a pipette, a burette, and a conical flask.

The usefulness of urinary chloride estimations may be questioned on a number of grounds. In the first place, sodium is probably the most important ion maintaining extracellular fluid volumes, and urinary chloride ion variations are of use only in so far as they reflect changes in urinary sodium ion concentration. This they may fail to do in acid (Black) or alkaline urines, for example.

Secondly, their usefulness is considerably diminished if they do not reflect the need of the body for sodium ions. The schemes of treatment given by Marriott and by Black assume that they do reflect this need, with the exceptions stated. There is considerable evidence to support this, particularly in the salt-depleted states produced in the Tropics (Marriott) or by forced sweating (McCance, 1936) in otherwise normal individuals. In most patients in whom problems of fluid balance arise in hospital this relationship between urinary chloride concentration and the body's requirement of sodium ions still holds good, but exceptions arise. Those quoted in this paper have all come to light in a hospital of 842 beds in one year. The hyperchloraemic group is discussed more fully elsewhere, where it is argued that the primary disturbance is inability of the kidneys to excrete the chloride ion. An intravenous saline transfusion or oral salt intake will then produce high plasma chloride and sodium levels. Use of the urinary chloride concentration as a guide to therapy would lead to precisely this state of affairs and run the risk of oedema, particularly of the lung bases.

The hypochloraemic group of patients, who pass a urine of relatively high chloride concentration while receiving saline transfusion, are most interesting and need characterizing further. Again, only the minority of patients so treated behave in this way.

The remaining group of patients lose both sodium and chloride ions spontaneously and become progressively salt-deficient. They behave as though they had Addison's disease, and appear to differ essentially from the transfusion group, who may not pass chloride ions in the urine prior to transfusion. Again, it is apparent that use of the urinary chloride concentration would lead to treatment quite the reverse of that required.

Other workers have recently criticized the value of urinary chloride tests. Wilkinson *et al.* (1950), after investigating sodium and chloride balance post-operatively, remark : " It is a corollary of the hypothesis we have advanced that determinations of urinary chloride afford no reliable guide to the requirements of salt and water during the immediate post-operative period, excellent though they are in other circumstances." Spencer (1950) similarly remarks : " Chloride determinations on the urine are sometimes valuable guides to diagnosis and treatment, but they do not necessarily reflect the balance of chloride and sodium in the body." He then goes on to quote examples from the literature.

The conclusions seem to be (*a*) not to use the Fantus test if a more accurate method is available, and (*b*) never to rely on a urinary chloride estimation alone as a basis for salt therapy, but to take into account also the clinical signs and the plasma chloride (or, better, sodium) concentration.

Summary

The errors and reliability of the Fantus test have been investigated.

Its use may lead to serious error in urinary chloride estimations, especially in the hands of inexperienced persons.

The urinary chloride concentration may not be an accurate guide to salt therapy. Examples where this is the case are given.

I wish to thank Dr. V. Smallpeice, Professor L. J. Witts, Mr. A. Elliot Smith, and Mr. J. C. Scott for permission to use the case records of patients under their care, and the staff of the Biochemistry Department for performing the blood analyses in the case described. My thanks are also due to the technical staff, house officers, and medical students who performed the experiments mentioned in Section B, and to Mr. J. R. P. O'Brien for advice and encouragement.

References

Black, D. A. K. (1950). *British Medical Journal*, **1**, 893.
Fantus, B. (1936). *J. Amer. med. Ass.*, **107**, 14.
Harrison, G. A. (1947). *Chemical Methods in Clinical Medicine*, 3rd ed. Churchill, London.
Higgins, G., Lewin, W. S., O'Brien, J. R. P., and Taylor, W. H. (1951). *Lancet*, **1**, 1295.
Marriott, H. L. (1947). *British Medical Journal*, **1**, 245, 285, 328.
McCance, R. A. (1936). *Lancet*, **1**, 825.
Peters, J. P., and Van Slyke, D. D. (1932). *Quantitative Clinical Chemistry*, vol. II. Baillière, Tindall and Cox, London.
Spencer, A. G. (1950). *Lancet*, **2**, 623.
Vogel, A. I. (1939). *Quantitative Inorganic Analysis*. Longmans, Green and Co., London.
Wilkinson, A. W., Billing, B. H., Nagy, G., and Stewart, C. P. (1950). *Lancet*, **2**, 135.