Method of Testing Strength of a Standard Serum.

I will now give in brief outline the method of testing the strength of a standard serum so as to get absolute results. An actual example may be of interest.

Complement tested. Unit found to be $10/20 \times 1/50$, or 0.01 c.cm.

Antigen-complement mixture prepared by adding 1 c.cm. of antigen to about 20 c.cm. of saline, then adding $10/20 \times 1/50 \times 5/2 \times 25$, or 5/8 c.cm., of complement serum, and making up to 22½ c.cm.

This mixture had added to it 2½ units of complement per c.cm. To test the amount actually present 7/20, 8/20, 9/20, and 10/20 c.cm. were placed in tubes, made up to 1 c.cm. and ½ c.cm. sensitised emulsion added. The first two tubes showed slight haziness, the last two were clear, indicating that 9/20 c.cm. contained one unit, or 0.9 c.cm. two units, the amount required. (I may say that I am not certain that there is not a slight error here, tubes containing antigen not being easy to read off for complete hæmolysis; the error, if it occurs, is quite trivial.)

First approximation. The serum was tested by the technique already described, and found to give a reaction of 420000. Thus, 0.1 c.cm. of undiluted serum gave a complete reaction under the conditions of the experiment, whilst the same amount of a 1 in 2 dilution did not.

Second approximation. Dilutions of the serum of 1 in 1½, 1 in 1½, and 1 in 1½, were prepared. The first and second gave no hæmolysis, the last a trace of hæmolysis.

Third approximation. A dilution of 1 in 1½ was prepared. It gave no hæmolysis.

Lastly, the anticomplementary power of the serum was tested and found to be 0.125.

Thus the serum contains 1.625 units of reacting substance. If I were issuing this as a standard serum I should issue it as giving a complete reaction at 1 in 1½, a partial one at 1 in 2, and no reaction at 1 in 3; and these figures, I believe, would hold whatever technique were used. Such sera should be issued periodically by authority. If any experimenters would like to have them, in order to be able to compare their units with my own, I shall be pleased to send them to them on a small scale as opportunities allow.

Conclusions.

In this paper, therefore, I have attempted to show:—

1. That it is possible to prepare a standard Wassermann unit by the use of antigen prepared in a definite manner. I suggest that until further experience is obtained the absorption of two clear units of complement, tested in the manner described, shall be regarded as a standard unit, this being found to give good clinical results.

2. That antigen prepared in the manner described remains remarkably constant, and that if several specimens are prepared from different batches of similar ingredients, they will give constant results.

3. That syphilitic sera, prepared aseptically and free from foreign materials, remain constant for at least a month, and probably for much longer, at room temperature.

4. That the use of such sera affords an easy means by which any experimenter can obtain comparable results from time to time.

5. That the use of such sera, accurately standardised, will enable workers by any technique to obtain results which are comparable.

6. I suggest that the Wassermann reaction should be reported in terms of Wassermann units, either those which I have described or some modification thereof, the figures given by each laboratory being the same whatever the technique, and such as will indicate the number of times the serum is stronger than the weakest serum which will just give definite proof that the patient has syphilis.

TUBERCULOSIS SOCIETY.—Sir Malcolm Morris will open the winter session with an introductory address on "Past and Future of the Fight against Tuberculosis" on Monday, Oct. 28th, at 8 P.M. The meeting will be held at the House of the Royal Society of Medicine, 1, Wimpole-street, London, W., and is open to all practitioners of medicine.

A MATINÉE of one-act plays will be given at the New Middlesex Theatre, Drury-lane, London, W.C., on Friday, Nov. 8th, at 2 P.M., in aid of the Vanguard Farm for Disabled Soldiers and Sailors at Sutton Valence, Kent. Tickets may be obtained from Miss H. M. Ironside, 50, Lincoln's Inn-fields, London, W.C. 2.

A NEW TECHNIQUE OF HEART MASSAGE,

WITH A CASE OF RESUSCITATION.

BY T. C. BOST, M.D. WASHINGTON, D.C.,

TEMPORARY CAPTAIN, R.A.M.C.

With Remarks by A. NEVE, F.R.C.S.E.,

TEMPORARY MAJOR, R.A.M.C.; SURGICAL DIVISIONAL OFFICER.
WAR HOSPITAL, DARTFORD.

IN reviewing the literature of heart massage we find that this procedure has repeatedly been done, and in many instances with complete success; but in the career of any one surgeon, however long it may be, the opportunity will present itself but once or twice, if at all.

The first reported case was not until 1898 and the first reported complete success was as late as 1902 by Starling and Lane, so that even now from a clinical point of view heart massage may be considered of fairly recent origin and application. Green¹ in 1906 reviewed the literature and gave an abstract of 40 published cases. Many cases have since been reported, but from the leading medical journals² of many countries it would be difficult to collect more than ten successful cases in the last ten years.

Early Operation.

Judging by the reported cases complete success depends upon prompt operation, only 6 to 8 minutes after heart stoppage. Mollison's case³ made a good recovery after an interval of 13 minutes, but showed profound mental symptoms for several days. In view of modern physiological science and surgical skill, all will agree that heart massage should be done in cases of suspended heart action following an anæsthetic, which have failed to respond to the ordinary methods of resuscitation, and as these methods are in many cases of doubtful value they should not be relied upon. Schiff as early as 1874 demonstrated, by chloroforming dogs until the heart ceased to beat, that artificial respiration and stimulation by electricity were of no avail in restoring cardiac action, but that massage, directly applied, restored it after an interval as long as 11½ minutes; furthermore, that the shorter the interval of time that elapses before applying massage the higher the percentage of success.

The Methods Employed.

There has been a gradual evolution of methods of heart massage.

1. *The thoracic method.*—In this a flap consisting of the thoracic wall over the cardiac area is cut and turned back, the base being either inwards or outwards. The costal cartilages are cut through, the pericardium exposed, and sometimes opened. The proceeding is forcible and must accentuate shock. Many intercostal vessels and nerves are involved. Pneumothorax has occurred in several of the published cases, and it is not surprising that the successes were almost nil, and that the method has been abandoned.

2. *The abdominal route, subdiaphragmatic.*—It is a familiar fact that some pressure upon the heart can be effected from the abdominal side of the diaphragm, so it was a natural thought to apply such pressure when the heart's action was arrested during the progress of a laparotomy operation. When promptly applied the conditions were favourable to resuscitation (Gray, 1902; Igelsrud, 1904; Cohen, 1903; Sencert, 1905; Depage, 1905; Smith and Daglish, 1905; Ramsay, 1906). This method has probably been used at an early stage in many unpublished cases, and the promptitude has won success. It is also possible that some of these cases might have recovered without massage. It has been demonstrated that in a child whose thorax is small and tissues elastic compression is possible though difficult; but in the adult it would rarely be effective, as only the cardiac apex can be reached, and it slips away upward. Hence the need for the trans-diaphragmatic method to reach the base of the heart where the auriculo-ventricular nerve ganglia are situated.

Heart massage is a complex performance. In its lightest rhythmical form it may undoubtedly stimulate the cardiac nerves, but a gentle squeeze of the organ does more: it empties the blood from the flaccid, perhaps distended auricles into the ventricles, the blood current acts as the physiological stimulus to these, and then the coronary arteries supply fresh blood to the cardiac muscles; thus a

healthy circle is re-established, and is reinforced by the artificial respiration, which should be carried on the whole time.

3. The *trans-diaphragmatic abdominal* route has been several times adopted, probably only unsuccessfully because too late. It need not be condemned on the statistics hitherto available. As above pointed out, the successful cases of subdiaphragmatic massage were those in which an abdominal operation was being performed at the time of the heart failure. It was the facility and the promptitude which secured the success. The diaphragm was only incised in the late stages of the worst cases, as, for example, Green's second case, in which an hour after apparent death from diphtheritic syncope he incised the pericardium through the diaphragm, and by massage started a few contractions. What more could have been expected? or Maclaure's cases after tracheotomy and other measures carried out for 30 minutes?

The trans-diaphragmatic incision seems in these cases to have been approximately antero-posterior, splitting the muscle fibres and gaining direct access to the pericardium. There is some difficulty in executing this manoeuvre on account of the left lobe of the liver and the stomach; there is also some risk of injuring the musculo-phrenic artery and having concealed hæmorrhage; and the suturing of the opening in the pericardium and diaphragm is as difficult as it is also necessary.

Hence the advantage of the horizontal incision behind the left costal margin which we here describe.

Description of the New Technique.

The abdominal incision is made four inches long in the median line, extending from above the umbilicus well up into the xipho-sternal notch. The left costal cartilages are well retracted, bringing the anterior diaphragmatic insertion well into view. There should be a pillow under the waist. A two-inch incision, beginning one inch to the left of the median line, carried outwards behind the costal margin, cuts the fibres of the diaphragm near their insertion. A blunt instrument pushed in opens the pleural cavity, and the opening is rapidly dilated with two or three fingers of the right hand, so that the whole hand can then be passed into the thoracic cavity anterior to the pericardium. The hand is passed upward, the thumb behind the sternum and the fingers embracing the entire organ in the pericardium. The thumb compresses the right auricle and ventricle, and the base of the heart is effectively massaged. No vessels are injured in this incision, as the superior epigastric artery is internal to the incision and passes into the rectus muscle, and the musculo-phrenic branch enters the diaphragm through the cellular tissue behind the eighth or ninth costal cartilages and passes backwards, deeper than the incision. The liver and stomach, even if prominent, offer no obstruction to this route, nor is the pericardium in risk of being opened. During the massage the parts can be pressed round the wrist of the operator so that air is not sucked in, and there is no tendency to collapse of the lung.

Closure.—The incision is easily closed and made air-tight. The costal margin is retracted and the cut diaphragm pressed up while a continuous catgut suture is inserted by means of a strong curved needle and holder. While this is being done the assistant can make rhythmic pressure during inspiration relaxed during expiration so that any contained air may be expelled and no more be allowed to enter. The abdominal wound is then closed in the usual way.

Abstract of a Case.

Pte. M. P., aged 37, was severely wounded on Oct. 26th, 1917, both knee-joints being involved. There were prolonged treatment and several operations. By March, 1918, both knees were healed, the left knee ankylosed, and he was allowed up. A week later some vague shifting abdominal pains began to appear, with tenderness and some rigidity, first on right flank then on left, and an irregular temperature. He also had a cough. Diarrhoea alternated with constipation. A week later he had retention of urine, and the orderly officer passed a catheter; there was some pyuria and diminished quantity of urine. No casts were found. He was thin and losing ground, with a blood pressure of 155 mm. and leucocyte count 12,000. In consultation it was decided to perform laparotomy to determine the presence of any abdominal abscess, and the condition of the kidneys, some metastatic sepsis being suspected.

Operation.—On March 30th, after a preliminary hypodermic of atropine 1/100 gr. and morphia 1/6th, chloroform was slowly and carefully administered by the open method by an experienced anaesthetist.

Time-table.—11.45: Began anaesthetic. 11.55: Almost under. Anaesthetist asked the surgeon to wait a minute as the patient was not yet fully relaxed. 11.58: Respiration ceased, pupils dilated, and colour changed to waxy. No pulse could be felt. Artificial respiration at

once begun, with rhythmical traction of his tongue, and head of table lowered. 12.0: Strychnine and ether hypodermically. Auscultated, no heart sounds. 12.10: Artificial respiration pumps air well into chest, but nothing spontaneous. Eyes staring open, pupils dilated and insensitive. Captain Bost made a 4-inch epigastric incision, passed his gloved hand in, and pressed on the heart through the diaphragm. The heart felt quite flaccid and slipped upwards so that only the apex could be pressed, and there was no response. 12.15: Artificial respiration continued, and some rhythmical heart pressure first by Captain Bost, then by Major Neve. 12.20: The case appeared hopeless, but Captain Bost proposed to insert his hand into the thorax, and did so, incising the diaphragm as described above; he passed his hand up under the sternum, outside the pericardium to the base of the heart, which he could then completely grasp, and began slow pressure. 12.25: At first the organ was completely flaccid; after perhaps 12 seconds a sort of muscular twitch was felt, followed by a very feeble contraction, which in a few more seconds became strong and regular. 12.30: Pulse felt, colour returned, and massage stopped; injected pituitrin; artificial respiration continued. The diaphragm was sutured. A rapid exploration of the abdomen was made by Major A. Neve. There was some free clear fluid and no pus nor any inflammatory adhesions. The kidneys felt large. The wound was sutured and dressings applied. 12.45: Bandaging completed. Breathing slowly. Strong visible cardiac pulsation. 1.15: Back in ward. Blood pressure 145 mm. 1.30: Continuous proctoclysis was begun. He lay comatose.

March 31st: Still in same state, pupils medium size, sluggish. April 1st: Still same state; has had no convulsions. Has slight emphysema over left chest. Takes only 1 or 2 ounces of peptonised milk at the time, as he swallows badly. Pulse still strong and rapid. April 2nd: Emphysema had disappeared. He is more comatose. Died at 5.30 P.M., 77 hours after the operation.

Post mortem (April 3rd).—The laparotomy wound was well closed and quite clean; also the incision in the diaphragm, which was quite air-tight. There was no pneumothorax and the chest looked healthy except some septic metastatic foci at the base of both lungs. The pericardium and heart looked healthy. Both kidneys showed small calculi and pyelo-nephrosis. The left ureter was partly blocked by the pus and gravel at the bladder orifice.

REMARKS BY MAJOR NEVE.

The striking success of Captain Bost's procedure in this case as regards the resuscitation of the heart's action after 25 minutes' absolute cessation proves the value of efficient heart massage. Without that the man was already dead. It was clear to all the five surgeons who were present that we were dealing with a case of primary heart failure under chloroform narcosis, due to the toxæmia of the patient's disease.

We could carry on the respiration without his muscles, but not the circulation. Subdiaphragmatic massage was inefficient, because it did not stimulate the cardiac nerve ganglia at the base; but after incising the diaphragm and grasping the base of the heart, 10 or 12 gentle squeezes started regular contractions, and the strong apex beat became visible to all onlookers. We have discussed the technique elsewhere. The incision was one which Captain Bost had previously planned on a cadaver.

It is unfortunate that this method was not adopted a few minutes earlier, as the prolonged pause in the cerebral circulation was probably in part responsible for the onset of coma; but had the kidneys and lungs been healthy the patient might well have recovered.

Conclusions.

1. We consider that this case illustrates the unique value of heart massage, and that the human heart can be resuscitated after a variable length of time—in this instance after 25 minutes. Nothing else could have re-started the cardiac action in this case.

2. *Type of cases for massage.*—All cases of suspended heart action following an anaesthetic, regardless of theoretical etiological factors, after a certain interval. Cases of asphyxia should also fall within this group.

3. *Length of interval.*—This should probably vary with individual cases, but should rarely be done under five minutes (unless the abdomen be already open), and certainly after eight minutes, though a longer interval need not bar the operation. The simpler methods of resuscitation, such as artificial respiration, tongue traction, sharp percussion over the cardiac region, and inversion of the patient, should begin in the first minute, but not be uselessly persevered in to the neglect of more efficient measures.

4. Subdiaphragmatic massage may suffice, especially in children, and if very promptly undertaken. But if only the apex is reached and the heart remains unresponsive the diaphragm should be incised and the base of the heart be massaged without further delay.

5. That no surgeon, even if relatively unskilled, should be content to abandon a case without giving his patient the benefit of direct cardiac massage.

6. We claim that this new technique offers a simpler method of approach and is a decided improvement upon

all other ways of doing direct heart massage, as it involves less risk of hæmorrhage, trauma, and shock, and can subsequently be more quickly and satisfactorily closed.

We are indebted to Lieutenant-Colonel Bond for permission to publish this case.

References.—1. T. A. Green: THE LANCET, 1906, ii., 1708-1714. See also Cackovic: Arch. klin. Chir., 1909; abstract in Jour. Amer. Med. Assoc., 1909, lli., 1549.

2. Frazier: Journal Amer. Med. Assoc., 1911, lvi., 1448. Lambert: Austral. Med. Journal, 1911-12, N.S. i., 527. Wrede: Arch. klin. Chir., 1913, ci., 833. Weitz: Deutsch. med. Woch., 1915, xli., 338. Breitman: Trans. Internat. Med. Congress, 1913, Sec. v., Pt. 2, 264. A. R. Thomas: Journal Roy. Nav. Med. Service, 1918, iv., 91.

3. W. M. Mollison: Brit. Journal Child. Dis., 1917, xiv., 42.

A MODIFICATION OF WEBSTER'S TEST FOR THE PRESENCE OF T.N.T. IN URINE.

BY FRANK TUTIN.

(From the Department of Biochemistry and Pharmacology,
Medical Research Committee.)

IT has been shown by Webster¹ that T.N.T., when taken by the mouth, or otherwise absorbed into the system, is excreted in an altered form in the urine, where its presence may readily be detected. The urine to be examined is first extracted with ether, then acidified with a mineral acid and again extracted with ether. In the latter extract the presence of the azoxy-compound formed by metabolism from T.N.T. is readily shown by the development of a violet tint on the addition of alcoholic potash.

Possible Source of Error.

There is one possibility of confusion which, though it has probably been recognised by a number of workers, has apparently not hitherto been mentioned in published literature. Various purgatives (rhubarb, senna, cascara, &c.) contain substances (anthraquinone derivatives) which, when excreted in the urine, give under the conditions of Webster's test a red or reddish-violet colour, which might be mistaken for that produced by T.N.T. It is well known in medical practice that the urine of patients taking purgatives of this group will directly give a red colour with alkali, and this is rather loosely attributed to "chrysophanic acid." Chrysophanic acid is only one, and not the most important, of the substances concerned, and it seemed desirable to investigate the whole group from the point of view of their excretion and colour-producing properties, and to devise some modification of the T.N.T. test which would eliminate the possibility of confusion.

The results of this short investigation form the subject of this note. When I had completed it and had found that a slight modification of Webster's test made possible a clear distinction between the colour reaction due to T.N.T. and that due to any of the anthraquinone derivatives occurring in purgatives, I heard from Mr. Webster that he had himself come across the same possibility of error, that he had adopted the same modification of his test as that which I here suggest, and that he had found, like myself, that its introduction in any case sharpened and improved the T.N.T. reaction, whether anthraquinone derivatives were present or not.

My experiments were made firstly with the pure anthraquinone derivatives which occur in the different purgatives of this class, and secondly with doses of rhubarb root, since this drug contains all the known substituted anthraquinones present in the group.

The pure principles in question are rhein, aloë-emodin, emodin,² and chrysophanol ("chrysophanic acid"). They are all closely related chemically, the relation being briefly as follows: chrysophanol is a methyl-dihydroxyanthraquinone, aloë-emodin is the corresponding hydroxymethyl-dihydroxyanthraquinone, rhein the carboxylic acid yielded by the oxidation of aloë-emodin, and emodin is chrysophanol containing one additional, strongly phenolic

hydroxyl group. These substances were each administered by the mouth in 0.1 g. doses, and in each case the urine subsequently collected, when examined by Webster's method, gave a strong colour reaction which might easily have been mistaken for that produced by T.N.T. On further investigating these four samples of urine it was found that the rhein had been rapidly excreted unchanged, whilst the other three anthraquinone derivatives had each undergone more or less oxidation, the aloë-emodin being entirely, and the chrysophanol partially, converted into the corresponding carboxylic acid (rhein), whilst a portion of the emodin appeared to be oxidised to the corresponding trihydroxyanthraquinone carboxylic acid, a substance which has not hitherto been known. In all cases, however, it was found that an ethereal liquid could be obtained which yielded no colour with alcoholic potash if the extracts obtained from the acidified urine were washed with dilute aqueous sodium carbonate before being treated with the stronger alkali. It was, moreover, found that the azoxy-compound formed from T.N.T., which is the substance which yields the characteristic "Webster reaction," is not removed from ether by treatment with dilute aqueous sodium carbonate.

Description of Modified Test.

These results, therefore, indicate a method by which anthraquinone derivatives may be eliminated from the ethereal extract to be tested by Webster's method, and it is recommended that the test should be conducted in the following modified manner:—

The urine should first be extracted with two successive portions of ether. This treatment removes any T.N.T. which may be present from accidental contamination, and also chrysophanol. The urine is then acidified with hydrochloric or sulphuric acid and again extracted with ether. During these extractions the addition of alcohol is usually necessary to cause the separation of emulsions. The ethereal extract of the acidified urine must then be extracted twice with dilute aqueous sodium carbonate, washed with water, and then treated with alcoholic potash, when the characteristic violet colour will be produced if derivatives of T.N.T. were present in the urine. If anthraquinone derivatives were present the sodium carbonate extracts will have a reddish-violet colour.

The method as originally described by Webster, and the modified procedure given above were then applied to samples of urine from three people who had previously taken respectively (a) 0.01 g. T.N.T., (b) 0.01 g. T.N.T. + 1 g. rhubarb root, and (c) 1 g. rhubarb root. When following Webster's procedure all three samples gave a positive reaction, but after treatment with sodium carbonate (a) and (b) gave reactions due to T.N.T. only, whilst (c) gave no reaction. Moreover, the colour yielded by (a) after treatment with sodium carbonate was a much purer violet and appeared more intense than before this treatment. This was due to the fact that sodium carbonate removes from the ethereal extract small amounts of substances which give a yellow or brownish colour with alkali, and therefore mask, to some extent, the characteristic colour of the "Webster reaction." The employment of the modified test here proposed would therefore appear to be desirable on all occasions when examining urine for T.N.T., even when the possibility of the presence of anthraquinone derivative is known to be precluded.

In conclusion, the author wishes to express his indebtedness to the Wellcome Chemical Research Laboratories, who supplied the specimens of pure anthraquinone derivatives which have been mentioned.

THE death is announced of Miss Agnes E. Weston, G.B.E., the "Sailor's Friend," at the Royal Sailor's Rest, Devonport, at the age of 78.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL (UNIVERSITY OF LONDON).—The University Entrance Scholarship in Anatomy and Physiology (value £50) has been awarded to Miss A. M. Freeman.

THE NATION'S TRIBUTE TO NURSES.—A meeting in support of the Hon. Sir Arthur Stanley's appeal to the nation for £100,000 as a tribute fund for nurses was held in Belfast on Oct. 17th. It was addressed, among others, by Mr. Henry McLoughlin, of Dublin, organising secretary of the movement in Ireland. The money raised in Ireland is to be invested in four Dublin trustees, and the interest is to be used on behalf of Irish nurses. It was decided to appeal for funds in Belfast, and office-bearers were appointed.

¹ THE LANCET, 1916, ii., p. 1029.

² Emodin monomethyl ether, another constituent of rhubarb, was not separately investigated, since this substance always behaves exactly similarly to chrysophanol, unless it suffers demethylation, when, of course, it yields emodin.