adding phenol is a drawback, and now recommend the following method: Incubate the agar serum for about two hours at 37° C. Then a 30 per cent. solution of peptone is taken, and 4 c.cm. of it is mixed with 2½ minims of phenol (measured) for each ounce of the peptoned agar serum. No precipitate will be found in this peptone solution.* It is then poured into the agar serum, and mixed up with it, when the colloidal solution remains perfectly clear. It is unnecessary to incubate further. It is best to use the patient's own serum, as it contains some appropriate antibody, more or less.

When a case has been thoroughly examined, the diet, etc., arranged, and any endocrine defect attended to, first try intravenous injection of peptone (5 per cent.) up to 2½ or 3 c.cm.; if after a time, say four to five weeks, but little improvement is found, carefully and slowly introduce into the vein peptoned agar serum (½ c.cm. up to 3½ or 4 c.cm.) when, in many cases, excellent results will be obtained.

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THE FIXATION OF ANTISEPTICS BY DRESSINGS AND TISSUES:

ITS IMPORTANCE IN WOUND TREATMENT, WITH SPECIAL REFERENCE TO ACRIFLAVINE.

BY

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THE application of an antiseptic to infected tissues by means of wet dressings ought to be regulated by a knowledge of several factors. These comprise principally, of course, the relative toxic effects of the drug on the tissues and on the pathogenic organisms, and the influence exerted on antiseptic action by the presence of exudate. But it is also of importance to know the extent to which dressings and the tissues may fix the chemical substances employed, since upon this will largely depend the amount of antiseptic remaining free to act upon the organisms disposed at or near the surface of the wound. The latter point is dealt with in the present communication, and it is shown that with a certain class of antiseptics, to which acriflavine belongs, the capacity of the cotton dressings to absorb the drug must be taken into account in determining the strength of solution which is to be employed.

Experiments to measure the absorptive capacity of gauze for acriflavine, phenol, and mercuric chloride were carried out by soaking swabs of absorbent gauze of average size (5 grams) in measured amounts of solution of determined strengths. The swabs had been previously well washed in distilled water and dried. After soaking for various periods the swabs were removed from the solutions and as much fluid as possible was allowed to drain away in the course of a minute. Then an estimation was made of the concentration of the substance in the fluid expressed by firmly wringing out the swab, and also the concentration remaining in the fluid residue in which the gauze had been soaked. When fixation of the antiseptic by the gauze had occurred the amount which was subsequently given off when the swab was soaked in distilled water was also determined.

In the first instance the behaviour of gauze when treated with solutions of sodium chloride, mercuric chloride, and phenol was investigated. Quantitative titrations were carried out in each

instance according to standard methods; silver nitrate being used for sodium chloride, potassium iodide for mercuric chloride, and bromine water for phenol. The same procedure was followed in each case, and the sodium chloride experiment will alone be dealt with in detail. A 5-gram swab, previously autoclaved and sterilized at 25 lb. pressure for two hours, was placed in a beaker containing 100 c.cm. 0.85 per cent. NaCl solution, and allowed to soak for one hour. It was then removed and allowed to drip into a beaker for one minute before being wrung out into a second beaker. (It should be noted that from a 5-gram swab dripping wet some 35 c.cm. of fluid can be expressed, while approximately 6 c.cm. of water are firmly held.) The swab was found to have no affinity for the sodium chloride. Similar results were obtained when a swab was soaked in mercuric chloride 1 in 1,000 for one hour, or in 4 per cent. phenol for forty-eight hours.

The absorption of acriflavine was estimated by comparing in uniform test-tubes the tint of 5 c.cm. of the expressed fluid, or the residue, with a series of standards consisting of 5 c.cm. of the following strengths, 1 in 1,000, 1 in 2,000, 1 in 3,000, down to 1 in 10,000, 1 in 20,000, 1 in 30,000, down to 1 in 100,000, in 0.85 per cent. saline. The disturbing effect of fluorescence was overcome by adding 0.3 c.cm. strong hydrochloric acid to each tube. In this way a brownish-yellow colour was obtained which could be easily matched. When kept in the dark the depth of colour of the solutions remained constant for about a fortnight. The results were in sharp contrast to those with the previously mentioned substances. Thus on soaking a 5-gram swab in 100 c.cm. 1 in 1,000 acriflavine solution—that is, about three times as much fluid as the gauze will hold without dripping—there was a rapid absorption for the first three minutes, when the concentration of the dye in the residue was reduced to 1 in 1,200, and to 1 in 1,600 in the fluid expressed from the swab. The gauze thereafter continued to absorb at a much reduced rate until the saturation point was reached in about twenty-four hours, when the residue and the fluid expressed from the swab were both reduced to a concentration of 1 in 1,800.

In view of the active absorptive power of the gauze for acriflavine it appeared that if a number of swabs were successively soaked in a limited quantity of the solution, the antiseptic property of the latter would rapidly become reduced to a low level. As the procedure was one likely to be followed in actual practice when wounds were being treated with the antiseptic it was decided to carry out quantitative experiments. Nine 5-gram swabs were soaked successively in 500 c.cm. acriflavine 1 in 1,000 for periods of three minutes; each swab on removal was allowed to drip into the fluid for one minute. After the removal of the sixth swab the concentration of the residual fluid had fallen to 1 in 1,300, and after the ninth to 1 in 4,000. The first, third, and ninth swabs were placed in Petri dishes for twenty-four hours in a cool place in order to allow of maximal fixation of the antiseptic and to prevent evaporation. These swabs were then wrung out into separate beakers. (There was little difference in the concentration of the dye obtained at the beginning and the end of wringing of each swab.) The fluid wrung from the first swab was of strength 1 in 1,400, from the sixth 1 in 2,000, and from the ninth 1 in 4,000. Therefore the concentration of flavine in the fluid wrung from the last swab is such as has a powerful antiseptic action. When six swabs were simultaneously soaked for three minutes in 250 c.cm. 1 in 1,000 acriflavine—nearly the minimum amount of fluid capable of efficiently soaking such a number of swabs—the residue was reduced in strength to 1 in 3,000, and the fluid expressed from the swabs after ten minutes contained slightly less than 1 in 3,000.

A marked impoverishment of antiseptic property of the available fluid occurred when six swabs were simultaneously soaked for three minutes in 250 c.cm. of 1 in 2,000 acriflavine. The residue was reduced to a strength slightly in excess of 1 in 20,000 and the fluid wrung from the swabs to about 1 in 30,000.

The experiments were then repeated with a 5-gram swab soaked in 100 c.cm. of a 1 in 5,000 solution of acriflavine, since this strength has been frequently recommended for use with gauze swabs. After three minutes the concentration in the residue was reduced to 1 in 9,000, and that in the fluid wrung from the swab to between 1 in 10,000 and 1 in 20,000. The saturation point of the gauze was approximately reached after soaking for twenty-four hours; then both the residue and the fluid wrung from the swab showed a concentration slightly greater than 1 in 20,000. When six 5-gram swabs were soaked successively in a solution of 500 c.cm. of acriflavine 1 in 5,000 for periods of three minutes each the residue was found to be reduced to a concentration of 1 in 100,000, which is approximately the limit at which antiseptic action takes place. When six swabs were added simultaneously to 500 c.cm. of acriflavine 1 in 5,000 and allowed to soak for three minutes the residue was reduced to a concentration of 1 in 20,000, and the fluid wrung from the swabs to rather less than 1 in 30,000. Accordingly, when a number of swabs are soaked either successively or simultaneously in an amount of 1 in 5,000 solution of acriflavine, which is double that sufficient to saturate the swabs with fluid, the available antiseptic becomes reduced nearly to an ineffective level.

A gauze swab saturated by soaking for about seventy-two hours in three successive portions of 100 c.cm. of acriflavine 1 in 1,000, and afterwards wrung out and dried, holds the dye with considerable firmness. But when a swab so treated was then soaked for twenty-four hours in 100 c.cm. of 0.85 per cent. saline the concentration in the fluid was 1 in 6,000. A similar experiment carried out with a swab saturated in acriflavine 1 in 5,000 imparted to the fluid a concentration of the drug of 1 in 20,000.

In order to form some estimate of the capacity of the tissues to fix the various antiseptics experiments were carried out with minced ox muscle. The tissue was left in running water for twenty-four hours to remove haemoglobin and other soluble

* The 30 per cent. peptone solution may be made by heating peptone in saline at about 90° C. for a considerable time, shaking up, adding 0.5 per cent. phenol, allowing to stand for a few days and filtering. If necessary it can be obtained clear and sterile from Martindale (10, New Cavendish Street, W.1) in any amount, however small.

material which might interfere with the transparency of the fluid to be tested. The washed tissue in amounts of 5 grams was soaked for a definite time in 100 c.cm. of the various solutions (mercuric chloride, phenol, or acriflavine) and the concentration of drug remaining in the solutions estimated. After soaking 5 grams of the treated muscle in 1 in 1,000 mercuric chloride for twenty-four hours the antiseptic could not be detected in the fluid. Five grams of minced muscle after soaking in 100 c.cm. of 4 per cent. phenol for twenty-four hours reduced the strength to approximately 3.7 per cent. A solution of acriflavine 1 in 1,000 was reduced in strength after one hour to 1 in 1,200, and after twenty-four hours to 1 in 1,400, and a solution of acriflavine 1 in 5,000 fell in an hour to a concentration of 1 in 8,000 and in twenty-four hours to 1 in 10,000. Thus, as measured by such methods, the amount of antiseptic which is fixed by the tissues is in the case of acriflavine much the same as that fixed by gauze; phenol, although not fixed by gauze, is markedly fixed by tissue, whereas mercuric chloride is very powerfully fixed by the latter.

Conclusions.

1. In the treatment of wounds with an antiseptic such as acriflavine allowance must be made for the considerable affinity of cotton dressings for this class of antiseptic. (On the other hand, phenol and mercuric chloride have practically no affinity for cotton.)

2. The concentration of the acriflavine solution should be such that after the gauze has satisfied its affinity for the antiseptic there is still a sufficient concentration left free to act in the tissues. It follows, therefore, that the swab must be applied dripping wet and not wrung out. Quantitative experiments have been carried out by soaking gauze swabs in approximately three times the amount of solution which can be taken up, and estimating the concentration of the antiseptic in the fluid expressed. It has been found that after three minutes' soaking in 1 in 1,000 acriflavine solution the fluid expressible from the gauze contains 1 in 1,600 of the antiseptic, and even after twenty-four hours' soaking the fluid expressed contains 1 in 1,800. When a 1 in 5,000 solution is employed under similar conditions the fluid expressed from the gauze after three minutes' soaking contains 1 in 9,000 of the dye, and after twenty-four hours' soaking the fluid expressed contains 1 in 20,000. The above concentrations employed according to this procedure have been shown to give a dressing which is very satisfactory for treating septic infections without inhibiting healing.¹

3. When a lesser proportion of the solution is used, or when swabs are soaked successively in the fluid, there is great danger in the case of the 1 in 5,000 concentration that the amount of antiseptic available may be reduced to an ineffective level.

4. Experiments on the fixation of antiseptics by tissues have shown that minced and washed muscle, while it absorbs mercuric chloride very actively, has a definite though much less marked affinity for phenol and acriflavine, the last being absorbed to a slightly less extent than by gauze.

I have to thank Dr. C. H. Browning for his criticisms and suggestions in the course of the work.

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CURVATURES OF THE SPINE FOLLOWING ENCEPHALITIS LETHARGICA.

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IN addition to the characteristic attitudes which are so frequent a sequel of the disease, encephalitis lethargica in young patients is occasionally followed by definite localized spinal curvatures. Only these definite curvatures are here considered. They have their origin in abnormal muscular contraction, and in this respect differ from all other forms of spinal deformity; for spastic conditions such as hemiplegia and spastic diplegia do not give rise to spinal curvatures.

Five examples of the condition have come under my observation: in four the symptoms of the preceding illness were characteristic of encephalitis lethargica; in the fifth

the initial symptoms, although probably due to that disease, were of a somewhat anomalous nature. All the cases were in children or young adolescents.

Antero-posterior Curvatures.

Perhaps the most striking and characteristic deformity, seen in two cases, is an arched curve of the cervical spine, convex backwards, which carries the head forwards; the arch of the curve may be of so high a grade as to bring the chin into firm contact with the front of the chest. It is clearly evident that this posture is not due to a mere falling forwards of the head by its own weight, but is brought about by a contraction of the anterior and antero-lateral muscles of the cervical spine, which can be felt as firmly contracted muscular masses on each side of the neck; the sterno-mastoids remain perfectly lax. On attempting to bend the head still further forwards, and thus increase the curve, the posterior spinal muscles are found to contract. Thus the head is held in its new posture by the combined action of the muscles at the front and the back of the spine. A lateral view of this deformity, with the strongly arched neck and powerfully contracted muscles, presents so unusual an appearance as to suggest the designation of "pony neck." By steady manual pressure the resistance of the muscles can be overcome in a few moments, and the deformity partly or completely reduced. The passive raising of the head is accompanied by the appearance of a deep depression in the neighbourhood of the seventh cervical vertebra; this is due to the pivotal movement backwards of the cervical spine as a whole upon the rest of the spinal column.

Another type of deformity is a curve convex backwards in the dorsal region—a dorsal kyphosis. By this curve an inclination forwards of the upper part of the body is brought about, somewhat resembling that seen in the cognate condition of paralysis agitans; but the curvature is of a more localized character than that seen in paralysis agitans.

Lateral Curvatures.

Lateral curvatures may occur in any region of the spine, causing very diverse deformities; they are associated with rotation, but are not accompanied by regular compensatory curves such as are seen in scoliosis. The curvature may be localized to a few vertebrae, but is never angular.

The deformities produced may be extreme; in one case a lateral curve of the cervical spine brought the ear into firm contact with the top of the shoulder, the curvature being caused by a unilateral contraction of the prevertebral cervical muscles, the sterno-mastoid and trapezius remaining unaffected.

General Characters of the Curvatures.

Notwithstanding their diverse character, the curvatures present certain features in common. In all of the observed cases, examination led to the belief that they were caused by a contraction of a section of the prevertebral muscles; a bilateral contraction causing an antero-lateral curve, and a unilateral contraction bringing about a lateral curve. By traction and pressure the curves may be partly or completely straightened out, but as time goes on the vertebrae tend to become wedge-shaped and distorted, as shown by skiagraphic examination; reduction is thus rendered more difficult and incomplete.

The curvatures are associated with a hypertonus of the muscles of the limbs and the uncurved portion of the spine; the tendon reflexes may be increased; clonic movements may be present, and, occasionally, deformities of the limbs. The mental condition may be fairly good.

Pathology.

In all of the observed cases the contraction of a special muscle group was found responsible for the curves—namely, that of the prevertebral muscles. The explanation of this phenomenon is probably to be found in the tendency of encephalitis lethargica to attack the mid-brain, the substantia nigra, and the lenticular nucleus—that is to say, those regions of the brain that preside over the postural reflexes and automatic muscular movements of the body. Owing to the damage sustained by these regions there is an impairment of the highest and most