There were three tracheotomies (including one emergency laryngotomy) and eleven haemorrhages necessitating ligation of the external, and three of the common carotid. These three latter are all living, and apparently not suffering any discomforts as a consequence of this operation.

NOTE ON FLAVINE, SODIUM DESOXYCHOLATE, AND QUININE AS A MOUTH-WASH.

BY

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In the estimation of the value of chemical substances at present employed as antiseptics in the mouth and throat there is a sharp division of opinion as to the advisability of employing antiseptics in the treatment of infections where the chemical is brought in contact with such a delicate structure as the mucous membrane. Any chemical which would act as a bactericidal agent, which at the same time would not destroy the life of cells and inhibit phagocytosis, and which could be applied to such a delicate surface as the mucous membrane without causing an irritant action, would satisfy a long-felt want in mouth and throat treatment.

I have in the course of the last ten months examined a series of substances comprising the principal antiseptics, washes, lozenges, pastilles, etc., in common use.

Neufeld has shown that bile salts have a solvent action on pneumococci, but not on other bacteria. Bile salts also dissolve completely leucocytes, spermatozoa, amoebae, spirochaetes, and trypanosomes.¹ Mair has brought evidence to show that scarlet fever is due to a pneumococcus-like organism which is also bile-soluble,² and has indicated that there is reason to believe that "trench nephritis" is due to a similar bile-soluble diplococcus. Mair found that the solvent action on pneumococci of sodium desoxycholate was ten times as powerful as sodium cholate or the commercial sodium taurocholate.³

These bile-soluble diplococci show also a special sensitivity to solutions of quinine, and there is evidence that a combination of desoxycholate and quinine has a much greater bactericidal effect on them than can be accounted for by a mere summation effect.

A solution with the following formula:

Quinine hydrochloride	...	...	5 grams.
Sodium desoxycholate	...	...	40 "
Glycerin	...	...	250 c.cm.
Water	...	...	to 1,000 "

has been in use in the form of a fine spray for the throat and nose in cases of scarlet fever for some months, with results so far satisfactory that they show that the treatment does no harm, and that septic throats clear up with it at least as rapidly as with any other form of treatment.

Messrs. Allen and Hanburys are now preparing tablets containing:

Sod. desoxycholate	...	...	gr. 1
Quin. ethyl. carb.	...	...	gr. 1
Ol. menth. pip.	...	...	m. 30
Glycyrrhiz. ammon.	...	...	gr. 2

Also with flavine 1 in 1,000.

The quinine desoxycholate solution has a considerable bactericidal effect also on other cocci which are not bile-soluble, and in the strength used it appears to have no irritant effect on the mucous membrane.

The method employed to test the value of the preparations checking the development of bacteria were all carried out in the same month; only one test was made in twenty-four hours. The mouth was first rinsed thoroughly with distilled water, and after thirty minutes the saliva was expectorated from the mouth into a sterile test tube, and then a loopful inoculated into nutrient agar and plated. At the end of an hour another test was made in the same manner. These tests were used as controls. Immediately after the second control the substance to be tested was rinsed thoroughly over the mouth, and then tests made in the same manner every half-hour up to the fourth hour. Plates were incubated for twenty-four hours

and counts made. The most favourable results were obtained from a solution containing:

Desoxycholate	...	...	2 per cent.
Quinine	...	...	0.25 per cent.
Flavine 1 in 2,000.	...	...	

Judging from the chemical action of the desoxycholate and quinine tablet, it should be an excellent treatment for infected throats, as in the strength used in these tablets all the pneumococci strains are easily destroyed without causing any irritation on the mucous membrane. This pathogenic group alone is giving more trouble than any other strains to be found in the mouth and throat. Again, amoebae are very easily cleared out of the mouth with sodium desoxycholate and quinine in the strength used in these tablets, as I have found in cases of pyorrhoea caused by amoebae.

In the solutions containing desoxycholate and quinine and flavine the bacterial count, even after four hours, was in most cases considerably lower than the control before treatment, whereas with the more irritating antiseptic solutions the count rises rapidly after the initial fall until it reaches a figure in excess of the normal. I consider this secondary rise in the number of bacteria to be a useful indication of an irritant effect on the mucous membrane. The same difference is seen in comparing the effects of the 1 per cent. carbolic and the desoxycholate and quinine tablets. The latter do not show the same reduction in the number of bacteria as the corresponding solutions, possibly because the effect in the mouth is somewhat localized. At the same time the effect on the throat of the slowly dissolving tablet should be greater than that of a mouth-wash, as the swallowing of the saliva in which the tablet has dissolved keeps up a continuous action on the mucous membrane of the throat.

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ACRIFLAVINE PASTE AS A DRESSING FOR INFECTED WOUNDS.

BY

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Owing to the limited supply of acriflavine we have been using this reagent at Leicester in the form of a cream or paste, somewhat on the lines of the B.I.P. method recommended by Rutherford Morison, which has given good results in certain cases. Thorough and efficient surgical treatment of the wound is still a necessary preliminary, but the results so far obtained with acriflavine paste as an adjunct to such surgical treatment are sufficiently encouraging to justify a wider trial.

I speak of such injuries as lacerated wounds of soft tissues, compound fractures of limb bones, and of septic cavities in bones associated with osteomyelitis, which often resist repeated efforts at sterilization by scraping out, and the removal of foreign bodies and bony sequestra. It is these heavily infected, profusely suppurating wounds as we see them at the base hospitals that seem to be especially benefited by packing with acriflavine paste after preliminary surgical sterilization and drainage. Amputation wounds have also been treated by leaving a quantity of the antiseptic material between the lightly sutured flaps where the amputation has had to be carried through infected tissues.

Several different forms of cream or paste have been tried:

1. Acriflavine soap paste is made by neutralizing stearic acid with sodium carbonate in the proportion of 1 part of sodium carbonate to 1½ parts of stearic acid with the addition of 0.1 per cent. of acriflavine. The soapy compound so prepared is canary yellow in colour and firm in consistence.

2. Acriflavine gelatine is made by heating French gelatine in water with the addition of acriflavine 0.1 per cent. The consistence of the jelly is determined by the amount of water added.

3. Acriflavine starch mucilage is made by adding boiling water to starch with the addition of 0.1 per cent. of acriflavine; one part of starch to 10 of water forms when cold a thick mucilage. This form of dressing has been found useful for large granulating surfaces, such as flush amputation stumps, in which the absence of sticking is very helpful.

Of these the acriflavine stearate soap paste has been chiefly used so far, and may possibly be increased in antiseptic strength with advantage. No doubt a better basis in which to incorporate the antiseptic will be devised. It will be useful to say a word about the results from the clinical and bacteriological points of view.

Clinically.

The wound is first surgically cleansed, and if highly infected may be dried and swabbed out with acriflavine spirit or watery solution and is then packed with the acriflavine paste. It is either left open with a top dressing of acriflavine gauze or it is closed by suture partly or entirely. If there are grounds for thinking that the infection may be inhibited by the antiseptic paste, aided by the preliminary mechanical sterilization, and especially if the state of the surrounding tissues will allow of coaptation of the sides of the wound without undue tension, it is closed. A wound so treated when examined two or three days later should, if progressing favourably, show an absence of any inflammatory peripheral zone, though there may be some slight redness and swelling about the skin edges and suture lines; there should be an absence of general malaise or evidence of toxic absorption. The cavity of the wound will contain a quantity of the canary yellow creamy substance, some of which will have exuded on to the gauze. In favourable circumstances—as, for instance, in the case of a cavity left in the head of a tibia after the removal of a shrapnel bullet with the debris of an abscess cavity and a quantity of bone—suture of the skin over the cavity so packed resulted in primary union of the soft parts, and the gradual consolidation of the bony cavity beneath. In other cases, where closure of the soft parts by suture has not been possible or only partially successful, time has been gained by reduction in the size of the wound. Where a wound so packed has been left open it can be refilled with the acriflavine paste at subsequent dressings, or irrigation with the watery solution and plugging with acriflavine gauze may be used. A considerable number of wounds have been treated with the paste, and while only a limited number have been so circumstanced in regard to the condition of the tissues and the arrest of the infection as to close primarily under one application of the paste, yet quite a number have improved during treatment, and post-operation flares, if present, have been less violent.

Bacteriologically.

It seems clear that, as in the case of B.I.P., wounds packed with acriflavine paste or soap are not sterilized in the bacteriological sense. Clinically the infection is inhibited or arrested, but organisms are still found in the discharge from the wound. There are, however, certain encouraging facts about the canary yellow coloured pus which collects in, or oozes from, such wounds when not closed. In the first place there is distinct evidence that many of the cells are living phagocytes and not dead pus cells; thus:

(a) If a drop of such pus be examined on a slide in normal saline with the addition of 1 per cent. watery iodine solution, a considerable number of the cells will show the mauve-coloured iodophil exudation which I have already described¹ as a delicate indication of functional activity in leucocytes. Dry films showing the same glycogen reaction may be fixed and stained in iodine vapour and mounted in iodine gum.

(b) A little powdered carmine is mixed with a drop or two of pus from the wound, thinned, if necessary, with normal saline. This is incubated for an hour in a plasticine cell. After the removal of the plasticine the incubated cells are examined in normal saline and 1 per cent. watery iodine solution. A number of the cells will have ingested the carmine grains.

(c) A dry film of the same pus from a wound in which the virulence of the infection had been inhibited by the

acriflavine paste, when stained with carbol. methylene blue gave evidence of active phagocytosis by the polymorph leucocytes, many of which contained cocci.

These three tests, each confirmatory of the others, may be used to test the relative non-toxicity to leucocytes of acriflavine, Dakin's solution, B.I.P., or any other antiseptic. Non-toxicity to phagocytes is of equal importance with bactericidal capacity in antiseptic reagents, and the relative non-toxicity of acriflavine is a matter of great importance.

I have already drawn attention² to the fact that sterilized rice starch grains previously mixed with B.I.P. are taken up by some of the leucocytes in a wound packed with that substance, but these starch grains so ingested, together with other free grains, are colourless and not blue. It has been suggested, probably rightly, that the absence of any iodine starch reaction in a wound treated with B.I.P. previously mixed with starch is due to the fact that the protein substances, either bacterial or leucocytic, seize upon the nascent iodine and prevent it reaching the starch grains. It is interesting to find that phagocytes from wounds dressed with acriflavine starch emulsion also ingest starch freely, though there can be no question of iodine action in this case.

From what I have seen of wounds treated by acriflavine in the casualty clearing stations in France and the base hospitals in England I think it will be found that a strength of 1 in 2,000 watery solution is better than a stronger solution for continuous application. How far the method of paste application is suitable for fresh wounds after initial surgical sterilization must be a matter for trial at the front. The non-toxicity of acriflavine, both local and general, seems however to be a point in its favour. It also does not give a shadow with x rays when the paste is packed in a wound.

Doubtless some surgeons who begin by applying acriflavine either in watery solution or as a paste to the surfaces only of infected wounds without efficient surgical sterilization will be disappointed with the results, for acriflavine, like all other antiseptic applications, will not reach the recesses of wounds when applied to the surface only; the reagent must be conveyed to the deepest parts, as Dakin's solution is conveyed by Carrel's tubes, or it must be applied thoroughly by the surgeon when the wound is freely exposed under an anaesthetic. Chemical sterilization must be the handmaid of surgery, and cannot take the place of drainage and mechanical sterilization by surgical means.

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ACUTE OSTEOMYELITIS OF THE FRONTAL BONE: OPERATION: RECOVERY.

BY

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THE gravity of this condition is so well known to and dreaded by those who are familiar with the surgery of the nasal accessory cavities that no excuse is necessary for bringing forward a case in which recovery took place. I will only anticipate by saying that the outlook of the patient was as bad as could be, that surgical intervention was adopted almost as a forlorn hope, and that the pluck and cheerfulness of the sufferer was one of the outstanding and bright features of an otherwise anxious and distressful situation.

History.

Mrs. T., aged 35, was taken ill with "influenza" during the first ten days of September of 1916. She suffered from intense pain in and around the left eye, and over the left frontal region. The temperature had varied from 99° to 100° in the morning to 103° to 104° at night.

I saw her at her home in Surrey on the evening of September 10th, and noted the following conditions: The left upper eyelid was intensely red and oedematous so that she could not open the eye. Chemosis of the conjunctiva in its outer half. There was slight oedema over the region of the left frontal sinus, and it extended outwards to the parotid region, over the left malar region, and as far downwards as the left angle of the jaw; but none of these regions were congested, and hence they were in striking contrast with the hyperaemia and oedema of the left upper eyelid. Deep pressure over the region of the frontal sinus