

9. The theory of "acidosis" is still incomplete. The modes of origin of "acetonuria" are complex, and are largely influenced by the amount of carbohydrate food assimilated.

10. For the solution of such difficult problems the coöperation of clinical physicians and experts in organic chemistry is essential.

Appendix.

Examples of errors and inaccuracies culled from textbooks on medicine and on urinary analysis.

1. Acetone gives a red colour with ferric chloride. This error occurs in Fagge, "Practice of Medicine," edited by Pye-Smith, 1888; and also in Roberts's "Treatise on Urinary and Renal Diseases," fourth edition, 1885. Gerhardt's test for acetoacetic acid was described in 1865.

2. Other substances (than acetoacetic acid)—e.g., formic, carbolic, and salicylic acids—give the same reaction in both fresh and previously boiled urine. For same read somewhat similar. No practised eye would confound the colours.

3. Both oxybutyric acid and acetoacetic acid react similarly with the ferric chloride test. This is not the case.

4. "Fehling's solution is reduced by acetone, but this test should be applied to the distillate from the urine." Acetone does not reduce the copper solution.

5. Rothera's nitroprusside test is true for acetone only. It is a much more sensitive test for acetoacetic acid.

6. Many drugs produce temporary diabetes. For diabetes read glycosuria.

7. "Large quantities of water are required (by the patient) to keep the sugar in solution, and for its excretion in the urine." Glucose is soluble in its own weight of water. The quantity of glucose in the blood of a severe case of diabetes is a fraction of 1 per cent.

Dublin.

TREATMENT OF SEPTIC WOUNDS, WITH SPECIAL REFERENCE TO THE USE OF SALICYLIC ACID.

NOTES BASED ON CASES AT THE MILITARY HOSPITAL, ENDELL STREET.

BY LOUISA GARRETT ANDERSON, M.D., B.S. LOND.,

CHIEF SURGEON;

HELEN CHAMBERS, M.D., B.S. LOND.,

PATHOLOGIST;

AND

MARGARET LACEY, B.Sc.,

RESEARCH ASSISTANT UNDER THE MEDICAL RESEARCH COMMITTEE.

THIS paper is based upon observations made upon approximately 1000 cases of septic wounds treated in the wards and operating theatres of the Military Hospital, Endell-street, during the period of six months from May to October, 1915. With the exception of a few cases from Gallipoli, all the men belonged to the British Expeditionary Force in France, and the majority were admitted to the hospital a few days after they were wounded.

While anaerobic infection was comparatively rare, septic infection was present to a varying degree in all the wounds. In order to test the effect of treatment on the bacterial growth in the wounds numerous agar cultures were made. The usual procedure has been to take cultures from the surface of the wounds, before and immediately after the dressings, each morning on successive days. After overnight incubation at 37° C. the relative number of colonies which developed on these cultures was noted. When wounds are irrigated with reagents such as hydrogen peroxide, weak solutions of perchloride of mercury, carbolic or boric acid lotion, there is often little difference to be noted in the number of colonies which develop on the cultures taken before and after the dressing or from day to day. For this reason the efficiency of many antiseptics when applied to wounds has been questioned, and it is evident that with reagents such as these the action of the lotion is often largely mechanical.

Many of the cases on admission were treated with hypertonic saline solution, either with continuous irrigation or with wet applications repeated two or three times a day. A preliminary test was made to determine the extent of bacterial growth which occurs in a nutrient medium containing varying quantities of salt. The organisms used were the staphylococcus pyogenes aureus and the bacillus coli

communis, and cultures were grown in a series of broth tubes containing from 0.5 to 12 per cent. sodium chloride. Quantitative estimations were made of the number of living bacteria added to the culture tubes and the number present after varying periods of incubation. With both micro-organisms proliferation occurred in 5 per cent. salt broth—i.e., in the strength of saline usually employed for surgical purposes; this was, however, much less rapid than in the lower salt dilutions. For example, in broth containing 5 per cent. saline staphylococcus pyogenes aureus increased after 24 hours incubation at 37° C. from 9 millions to 77 millions, and after three days to 708 millions. In broth containing 0.5 per cent. saline staphylococcus pyogenes aureus increased in 24 hours from 9 millions to 435 millions, and in three days to 1012 millions. In the 7 per cent. and 8 per cent. salt media multiplication was still further delayed. In the 10 per cent. and 12 per cent. salt cultures no proliferation occurred; the cultures of staphylococcus pyogenes aureus were still alive after 24 hours, but those of bacillus coli communis were sterile. It follows that when 5 per cent. hypertonic saline is applied to a wound the inhibition of growth due to the salt alone can only be very slight.

The majority of septic wounds heal rapidly if good drainage is provided and frequent dressings are applied. The choice of lotion seems immaterial provided the one selected is non-irritating and fresh infection is prevented. The ultimate recovery of the patient depends upon physiological processes, and if preference is given to any of the above reagents for routine treatment it would be to that which reinforces the physiological processes in the tissues of the wounds—viz., hypertonic saline solution.

In certain cases treatment with the so-called antiseptic lotions and hypertonic saline was not successful, and it was recognised that some improved method was required. The plan adopted was to select a few wounds which did not yield to ordinary treatment. These cases were made the object of a special investigation. Two antiseptic reagents were tried: (1) Eusol, as introduced by Professor Lorrain Smith and his collaborators¹; and (2) salicylic acid.

Treatment with eusol.—In eusol we possess a valuable and cheap antiseptic. In our experience the immediate effect of eusol is to sterilise the surface of the wound with which it comes in contact. Cultures taken directly after irrigation remain sterile. Numerous colonies, however, will develop on cultures taken after an overnight interval, and there is often no reduction of bacterial growth from day to day. The effect of the eusol is temporary only, because of the infection of the deep tissues. This is well recognised, and to meet the difficulty frequent application or continuous irrigation has been advised. In some cases, however, it is not easy to arrange for continuous irrigation, and whatever contrivance is adopted there is a tendency for the lotion to flow through certain channels to its exit, with the result that large areas of the wound do not get irrigated. In spite of these disadvantages, the clinical results obtained from eusol are very encouraging, and some cases have responded more rapidly to it than to other reagents. The following case illustrates its use:—

CASE 1.—Private, aged 19. A large abscess of the calf of the leg was opened; the pus grew staphylococcus pyogenes aureus. The cavity was irrigated with eusol and packed loosely with gauze soaked in eusol. Irrigation and the dressing were repeated twice daily, and each morning cultures were taken from the wound immediately before the irrigation. A series of cultures were thus obtained. From the first to the sixth day numerous colonies grew, and the cultures were indistinguishable from one another. On the seventh day there was a marked reduction in the number of colonies. On the eighth day only two or three colonies developed, and the subsequent healing of the wound was rapid. This series can be explained by the fact that free exudation from the abscess during the first six days diluted the eusol and washed it away from contact with the tissues. It was only when the exudation ceased that the antiseptic remained in contact sufficiently long for its action to be evident after an overnight interval.

In cases where eusol has not been a success the failure was apparently due to the fact that continuous treatment was impossible, and the effect of the antiseptic was transitory. Very little reagent is left in contact with the

¹ Brit. Med. Jour., July 24th, 1915; THE LANCET, Feb. 5th and 12th, 1916.

surface of a well-drained wound after irrigation with a watery solution. Treatment with salicylic acid in various forms was therefore tried, in some cases with conspicuous success.

Treatment with salicylic acid.—The examination of healing wounds shows that the presence of a certain number of bacteria need not be detrimental. In many instances rapid healing occurs in spite of their presence. Healing is usually not delayed unless exudation collects or the bacterial growth becomes sufficiently plentiful to liberate toxin or to produce ferments which digest the tissues. A continuous inhibition of bacterial growth may be more effective than the action of a powerful but transitory reagent. Salicylic acid is not such a powerful antiseptic as the hypochlorites, but it lends itself to continuous administration. Its properties as an antiseptic are well known, and it has recently been recommended by Sir William Watson Cheyne and his collaborators for use as a powder mixed with boric acid for a first field dressing. It is a light powder, feebly soluble in saline solution. If applied to a wound in a crystalline form it does not dissolve sufficiently freely to cause necrosis. Tested with a Ponder's film, salicylic acid is a positive chemio-tactic agent. It is also a lymphagogue.

The method has been to keep a saturated solution of salicylic acid in alcohol and to add a little of this to the last funnelful of saline solution with which the wound is irrigated in a proportion of 2-3 drachms to a pint. If applied in this way suspended in saline solution the crystals can be deposited over the surface and reach every part of the wound. They pass into solution slowly and exert a continuous bactericidal action. This method has the advantage that drainage-tubes can be used and free exit for discharge maintained. Dusting the wound with the dry powder has the disadvantage that the crystals float and do not reach deep crevices.

If the crystalline deposit reaches all parts of the wound where exudation is being discharged an immediate diminution occurs in the number of living bacteria on the surface of the wound. This decrease in the number of colonies occurs even when the cultures are made 24 hours after the last dressing, and this change in the bacterial flora is associated with a diminution in the amount of pus and usually with an improvement in the patient's general condition.

Salicylic acid may cause smarting, which usually subsides quickly, and in contact with blood it produces dark-brown acid hæmatin, which has an unpleasant appearance. These slight disadvantages do not, however, detract from its value as an antiseptic.

A thick paste of salicylic acid in sterile saline (1 gm. acid, 9 c.c. saline) has been used for the cut surfaces of long bones in septic amputations. In some cases the stumps have healed by first intention. In others slight sepsis occurred in the muscular flaps. In every case no infection of the bone marrow occurred.

The following cases illustrate the use of salicylic acid as an antiseptic dressing:—

CASE 2.—Private, aged 19. Admitted with septic wound of right knee-joint. The bullet had penetrated the joint and lodged in the outer condyle of the femur. The patient had been in hospitals in France for some weeks previously, and was in a very septic condition. The bullet had not been removed. The knee-joint was drained thoroughly and washed out twice daily with eusol. His condition improved, and sepsis subsided except in the neighbourhood of the outer condyle of the femur in which the bullet was embedded. At a second operation for removal of the bullet it was found that rarefactive changes had occurred leading to the formation of a considerable cavity in the bone, in the centre of which the shrapnel bullet lay. The walls of the cavity were scraped and cleaned with dry gauze and the space then filled with thick salicylic paste, and the external wound closed except for a small drainage-tube which was left in for 24 hours. Dry gauze dressing was applied externally. For the next three weeks no irrigation was employed, the gauze dressings only being changed. The temperature remained normal, and six weeks after the operation an X ray examination failed to show any trace of the cavity in the bone. He made an uninterrupted recovery.

CASE 3.—Private, aged 23. Was admitted with a compound fracture of the neck of the femur and necrosis of the separated head. After weeks of sepsis excision of the head of the femur was undertaken. For ten days following the operation the joint cavity, which was exceedingly septic, was

treated with eusol twice daily. The pain and position of the wound prevented more frequent dressing. As the sepsis did not improve eusol was discontinued and the cavity of the joint was filled with a mixture of salicylic acid and saline. Immediate diminution in the discharge and number of bacteria took place, and the patient entered on a slow but steady convalescence.

Salicylic gelatin.—Treatment with salicylic acid in a crystalline form has only been adopted for acute cases and for a short time. In the case of large wounds where the treatment was prolonged, it was thought desirable to diminish the quantity of the drug used. A gelatin medium was therefore made containing salicylic acid 2-4 per cent., in the hope that the viscosity of the mass would help to retain the reagent in the wound. This medium has been used for a large number of cases with considerable success.

The gelatin is prepared in the following way: 300 gm. of gelatin are added to 600 c.c. of freshly made normal saline solution. After melting in the steamer the medium is cleared with egg-albumin and filtered. It is divided into quantities of 100 c.c. and put into glass-stoppered bottles, which are then sterilised at 100° C. for three successive days. Special care must be taken with sterilisation as gelatin is liable to contain tetanus spores. When required for use a bottle is placed in warm water until the gelatin has melted and 2-4 gm. of pure salicylic acid are added. The acid must be added after sterilisation is complete and when the temperature is below 40° C. If the medium is subjected to prolonged heat after the acid is added the viscosity is lost. In 2 per cent. solution the salicylic acid dissolves completely and combines with the gelatin. In 4 per cent. solution some of the crystals remain in suspension. The fluid gelatin is poured into the crevices of the wound either through an irrigating funnel or directly from the bottle, and requires to be repeated daily.

In cases where the medium is retained in the wound it has often been noted that the bacterial flora will change when the treatment commences, pure cultures of streptococci being obtained, after an overnight interval, in wounds which previously grew a variety of organisms. The following cases illustrate the value of this treatment.

CASE 4.—Private, aged 32. Was admitted from a base hospital in France, where a flapless amputation had been performed through the lower third of the left thigh. The wound was very septic. Treatment with saline irrigation and later with strong solution of permanganate of potassium was employed for six weeks. He lost ground. Pus tracked up the muscles of the thigh. Operations were performed for opening sinuses, &c. He became emaciated and cachectic, and finally it was decided that further surgical interference could not be undertaken. At this stage treatment with salicylic acid gelatin was commenced and was applied twice daily. Local reaction was immediate. In a few days the pain ceased, the discharge diminished, and the temperature gradually subsided. Some days later an abscess was opened in the thigh, and after this he made an uninterrupted slow recovery.

CASE 5.—Private, aged 24. Admitted from a base hospital in France, where a flapless amputation had been performed through the middle of the left thigh. The bone was projecting and the wound was extremely septic. After six weeks' treatment with hypertonic saline solution a secondary amputation was done and large drainage-tubes inserted. Three days later the flaps became inflamed and septic. The trouble subsided rapidly under irrigation with peroxide of hydrogen and the application of salicylic gelatin introduced by means of an irrigating funnel.

Conclusions.—The conclusions to be drawn from these observations are:—1. The bactericidal action of many of the so-called antiseptics when applied to septic wounds is negligible. 2. The majority of wounds heal without the application of an antiseptic, provided free drainage is supplied and dressings are changed frequently. Hypertonic saline, in so far as it aids physiological processes, is preferable to many so-called antiseptics. 3. A strong antiseptic, such as eusol, can sterilise the surface of a wound with which it comes in contact, and, if applied continuously, gives excellent results. 4. Salicylic acid applied in a suitable form can often save cases when other methods have failed. It is particularly useful when dressings cannot be repeated at frequent intervals. 5. In all cases where recovery is delayed and the effect of the reagents of doubtful value the treatment should be controlled by making repeated cultures from the wound surfaces.