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.

REFERENCES.

¹ BRITISH MEDICAL JOURNAL, February 3rd, 1917. ² Ibid., December 23rd, 1916.

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

and lower half of the frontal bone was very painful. The mucous membrane of the left nasal cavity was swollen, deeply injected, and pus was visible in the anterior cleft of the middle meatus. The appearances in the right nasal cavity were normal.

The patient complained of dull headache, there was no vomiting, the pulse was 94, and her temperature was 102.4°.

It was obvious that the patient had an acute suppurative inflammation of the frontal sinus, and arrangements were made to bring her by motor to London next day.

Operation.

On September 11th, at 5 p.m., I opened the frontal sinus through an incision immediately below the line of the eyebrow, and terminating internally just above the internal canthus. On elevating a small disc of bone from the anterior wall of the sinus pus and air bubbles escaped. The whole anterior wall was removed; it was red, soft, and infiltrated with pus. The mucous membrane was intensely oedematous, and was wiped out—not curetted—with small gauze swabs. It was now seen that small points of pus made their appearance in the diploic spaces, which had been exposed on the boundaries of the sinus cavity, and I was forced to the doleful conclusion that osteomyelitis of the frontal bone had commenced, and that probably our intervention would prove to be "too late."

A loose wick of gauze was placed in the sinus, fomentations applied, and the patient returned to bed.

After-History.

The following are the chief points in the after-history and treatment of the illness:

September 13th. Some oedema of right upper and lower eyelids noticed. Free discharge of pus from the left frontal sinus and considerable oedema of fronto-parietal region. Oedema of left eyelid remains as before operation, and there is considerable proptosis of the eye.

September 18th. Opened an abscess in the orbit and evacuated 2 drachms of pus. Oedema of fronto-parietal region remains the same and free discharge of pus from the original incision in the eyebrow continues.

Since the first operation on the sinus this has been irrigated morning and evening with normal saline and hydrogen peroxide solutions, and it was possible to pass the cannula between periosteum and bone as far as the hair line—that is, as far as the oedema of the soft parts extended. In spite of the gravity of the local condition the temperature never rose above 100°, but usually attained that degree in the evening. Headaches were frequent, but were controlled by a combination of aspirin, salicylate of quinine, and codeia. The patient was cheerful, her mental condition remained good, and she took her food and slept fairly well.

Bacteriology.—The organisms found in the pus at the first operation were *Staphylococcus aureus*. There is also a small number of Gram-negative bacilli of coliform type. These, however, are relatively insignificant. Both organisms have been obtained in pure culture. No vaccines were used.

October 5th. During the past two or three days a painful swelling has appeared in the left breast. To-day, under local anaesthesia, I evacuated 4 drachms of thick greenish-yellow pus. This complication seemed to forebode evil and the possibility of further dissemination of infection, but the mammary abscess quickly healed and our fears proved to be groundless.

Time went on, and in spite of twice-daily irrigations of the sinus and of the subperiosteal cavity over the left frontal bone, the discharge of pus remained very profuse; the patient was not making headway, her sleep was not restful, and she was losing flesh.

Her husband was summoned from France and the pros and cons of an extensive operation for removal of the affected region of the frontal bone laid before him. He assented to this proposition, which was shared by Dr. Lack and myself.

October 23rd. A median incision was made in the forehead from the line of the hair to the inner end of the original incision in the eyebrow and a transverse incision from the upper end of the first and beyond the hair line to the temporal region. The scalp was turned outwards, and revealed a sad state of affairs.* The whole of the left frontal bone presented an inflamed and partially necrosed condition. Loose portions of bone were

removed, and in two places the adherent and inflamed dura mater came away with the bone, together with subjacent cortical substance of the brain. As much of the infiltrated and necrosed bone was removed as seemed advisable. A curved and multi-perforated drainage tube was placed around the borders of the bone wound and the scalp replaced and sutured in position. Fomentations were applied four-hourly for three days, and then replaced by ordinary dry dressings.

The patient made a rapid recovery, and returned home under the care of her local medical attendant on November 4th.

Three weeks later I was called down to see her, and found she was suffering from an acute attack of facial erysipelas, which had started from the internal angle of the original incision over the sinus. Once more she made an uninterrupted but somewhat slow recovery. Since then I have removed one or two small sequestra which have worked their way down to the incision in the eyebrow, but the patient is now well and the picture of good health.

REMARKS.

1. In my own personal experience this is the only case of acute osteomyelitis of the frontal bone complicating acute frontal sinus suppuration that I have seen recover, although I know that a few others have been recorded—for

example, one patient was shown by Mr. Mollison at the Laryngological Section, Royal Society of Medicine, May, 1917, and the photograph of yet another patient was exhibited who had survived thirteen operations for the relief of the condition. The instance I record also illustrates another curious experience which is generally agreed upon—namely, that an extensive operation may save the life of a patient when the osteomyelitis complicates an acute suppurative inflammation of the frontal sinus which hitherto has not been operated upon; whereas, when the frontal bone becomes infected after, and as a result of an operation on the frontal sinus, the issue is practically always a fatal one in spite of the most extensive operations for the removal of the infiltrated bone.

2. It may be asked why at the first operation, and seeing that the frontal bone diploë were infected, I did not proceed at once to a more extensive removal of the bone. My answer is that the disease had existed only for some ten days, and I hoped that by freely opening the frontal sinus and providing for subsequent drainage the diploë bordering on the sinus might recover, and even if they did not do so the infected area might become delimited in the course of a few weeks, and involve less traumatism in its removal than if I had proceeded at once to an extensive operation. Furthermore, with such an acutely infective condition I was anxious not to expose more healthy tissue than the immediate necessities of the case demanded.

3. Opinions vary as to whether the complication is more likely to follow operation on an acute or chronic empyema of the sinus. In my own practice I have had three cases which terminated fatally, and have seen several others in consultation, but in all of them the complication has set in after operation on a chronic suppurative inflammation.

4. With regard to the method of exposing the frontal bone, I should not use the median forehead incision again because it leaves a noticeable scar. In a more recent case I laid bare the infected region by a transverse incision commencing in the middle line beyond the hair, and passing downwards and outwards to the temporal fossa, then directly forward to the outer angle of the eyebrow, where it joined the frontal sinus incision below the line of the eyebrow. The included portion of the scalp was then turned upwards and inwards towards the middle line. The small incision in the exposed portion of the temporal fossa healed by immediate union, and is no longer easy to detect.

FIG. 1.—Osteomyelitis of skull resulting from septic infection of the diploë after operation on the frontal sinus. The patient died after nine months of suffering, and after numerous operations for the removal of abscesses in different regions of the body. a, Sequestra; b, longitudinal sinus; c, left frontal sinus (anterior wall removed). This was the first recorded case in which the sequence of osteomyelitis as a complication of nasal sinus suppuration was detected (vide BRITISH MEDICAL JOURNAL, 1889). Surgeons interested in the subject are advised to read Dr. Dan McKenzie's monograph on the subject (*Journ. Laryngology*, vol. xxviii, 1913).

*The nature of the lesion can best be illustrated by reference to the illustration of a more extensive and fatal case.

5. When osteomyelitis complicates an operation on the frontal sinus it usually makes its appearance as a non-inflammatory oedema in the soft parts which cover the margin of the bony wound, and this sign is still more ominous if an area of oedema appears at some distance from the wound in the sinus. A coincident rise of temperature may be noted. If such a swelling be incised no pus escapes, but the wound does not heal and suppuration soon makes its appearance, while the oedema spreads still further.

The only treatment of any value in such case is to expose the frontal bone very freely and to remove its whole thickness involving a liberal area of healthy bone around the inflamed region. Delay and hesitation are unpardonable, while fomentations, incisions in the oedematous areas, or the administration of vaccines only betray the ignorance of the surgeon as to the grave condition of his patient.

6. As to the cause of the complication, my impression is that it is due to two details in faulty technique: (1) When the sinus is opened and the diploic spaces in the margin of the bony wound are exposed, infective material is introduced into them by curetting the walls of the sinus with a small sharp spoon. The diseased and pus-infected mucous membrane should be wiped away gently with small sterile swabs. (2) The lips of the wound in the soft parts should be left widely open and only the lightest packing placed in the sinus cavity. Since adopting these precautions I have experienced no anxiety in any of my cases.

It may not be out of place to state that opening an acute or chronic empyema of the frontal sinus by the intranasal method does not exclude the possibility of osteomyelitis of the frontal bone, for at least one case has already occurred, the details of which may be studied in the *Journal of Laryngology*, June, 1917, p. 186.

A NOTE ON THE ASSOCIATION OF HERPES ZOSTER WITH ARSENIC.

BY

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It is well known that arsenic administered in large quantity may have a harmful effect on the nervous system, both central and peripheral, and from time to time cases of herpes zoster have been recorded which have been ascribed to arsenic. Hutchinson was one of the first observers to point out this association.

Herpes zoster is looked upon commonly as being secondary to some change, either haemorrhage or inflammation, in the posterior root ganglia of the spinal nerves, but it has been recognized for a long time that the lesion is not confined to these ganglia. For instance, in some cases the cerebro-spinal fluid has been found to contain a well-marked lymphocytosis, pointing to involvement of the meninges, and in others the occurrence of Kernig's sign has suggested that the posterior roots have not escaped the inflammation.

Many cases of herpes zoster have been described which have been associated with, or followed by, a generalized vesicular eruption, and Dr. Parkes Weber¹ has recently summarized some of these. It has been suggested that herpes zoster is a modified and localized form of varicella, but the evidence of this is by no means conclusive. On many occasions the apparent connexion between these two diseases has been noted. There can be little doubt, however, that some of the cases were examples of a generalized shingles, but in others true herpes zoster appeared to have been produced from contact with a patient suffering from varicella, and vice versa.

The following case is of interest, as it relates both to the question of the association of arsenic with herpes zoster and also to the question of generalized herpes zoster:

A naval officer, aged 54, was seized during January, 1916, with an attack of multiple adenitis, together with paresis of the lower limbs and retention of urine. Except for the fact that he had spent twenty-three years in India there is nothing in his history which appears to have any bearing upon his illness.

He was a stout man of close on 15 st. in weight. On admission to Haslar on February 25th, 1916, he was found to

have almost complete paraplegia of the upper motor neurone type. The lymphatic glands in his cervical, pre-auricular, axillary, and inguinal regions were markedly enlarged and somewhat tender. There was no palpable enlargement of the spleen. The red cells were 4,500,000 and the white cells 3,000 per cubic millimetre. Of the latter, 50 per cent. were polymorphonuclears, and there were 2 per cent. of eosinophiles. The colour index was 0.77. His systolic blood pressure was 150 mm. of mercury. There were no visible haemorrhages. The Wassermann reaction of his serum was negative (Fildes). The cerebro-spinal fluid was not examined.

The connexion between the glandular enlargement and the paraplegia was not very evident, nor indeed was the nature of the adenitis. We were unable to obtain the consent of the patient to the removal of a gland. There was no evidence that the mediastinal glands were involved. Towards the end of March his general condition, other than that of the glands, had improved considerably. Treatment by liquor arsenicalis was commenced, and he continued with it until May 9th, 1916, when he went on convalescent leave.

On July 5th, 1916, he was readmitted, looking and feeling much better. He was able to walk quite well. The condition of the glands appeared to be about the same as when he was last seen. He told us that he had been taking the medicine throughout. On July 10th an eruption of herpes appeared on the right side of his abdomen. It assumed considerable dimensions, and covered roughly the area of skin corresponding to the eighth, ninth, and tenth dorsal segments of the cord. The eruption was not preceded by any pain but it was associated with pain when it was fully developed. By this date he had been taking 15 drops of Fowler's solution daily since March 23rd, a total of some 1,600 drops, or, roughly, 15 grains of arsenic. The eruption rapidly became generalized, vesicles appearing over the face, body, and limbs; the eyelids were considerably swollen. After a short time the eruption healed in the usual manner, and on July 28th the patient was discharged to his home. The condition of the glands was not materially altered. The temperature was normal throughout, except during the time when he was suffering from herpes.

REFERENCE.

¹ *British Journal of Dermatology*, March, 1916.

The Croonian Lectures

ON

ADAPTATION AND DISEASE.

DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS,
LONDON, JUNE 26TH, 1917.

BY J. G. ADAMI, M.D., F.R.S.,
TEMPORARY LIEUT.-COLONEL C.A.M.C.

LECTURE IV.

THE PHYSICO-CHEMICAL BASIS OF IMMUNITY AND
EVOLUTION.

(Abstract.)

In the previous lectures it had been shown that the studies upon pathogenic bacteria and upon immunity proved conclusively the existence of direct adaptation of a definite order, both in the lowest and in the highest forms of life. To the academic biologist such a suggestion of a direct action of external agencies as a prime cause of variation is as shocking and improper as would be the suggestion of a risqué story to some dear, modest elderly maiden lady. And yet it is along these lines that medical research is surely leading us.

Believing that we are in the right, where is it that the biologists have gone wrong? It was suggested that the

Photograph taken to show enlargement of glands and healing herpes on July 26th, 1916. A few of the generalized vesicles can be seen.