

of a film. The mixture was incubated for 24 hours and then a film prepared and a culture made on agar.

Film of acriflavine	1/90,000	in serum	showed	good growth.	
"	"	1/30,000	"	"	no obvious growth.
"	proflavine	1/30,000	"	"	good growth.
"	"	1/10,000	"	"	no obvious growth.

The cultures on agar showed that all the staphylococci were not killed by 1/10,000 acriflavine or proflavine, although the colonies, which were fewer in numbers in the stronger dilutions, did not appear for two or three days, except in the cases where the films showed obvious growth. This effect of retarding the appearance of the growth was very noticeable in all the bactericidal experiments, and is clearly to the credit of the antiseptic. I find, therefore, with Dr. Browning, that acriflavine acts better in serum than in broth, but not in such extremely dilute solutions.

3. The effect of a large volume of antiseptic on a small volume of infected pus.

*Experiment.*—One part of infected defibrinated blood was mixed with 9 parts of antiseptic. After 15 minutes 20 c.mm. of the mixture were added to liquid agar, which was then shaken and sloped.

Streptococci in acriflavine	1/15,000,	no growth.
"	proflavine 1/4000,	growth equal to that in the control.
"	" 1/1000,	considerable reduction in the number of colonies, but not complete sterilisation.

The effect of 1/1000 acriflavine and proflavine on the staphylococcus and a coliform organism was hardly appreciable, but 1/500 killed considerable numbers, especially of the staphylococci.

In a similar experiment with a particular sample of pus acted on by acriflavine 1/100 for 16 hours, 20 c.mm. of the mixture added to agar gave a growth of a coliform organism equal to that given by the control.

4. Regarding the toxic effect of the antiseptic.

In opsonic preparations containing 1/1500 acriflavine, I found evidence of phagocytosis after 15 minutes' incubation, but I also found marked agglutination in the mixture which made it impossible to prepare satisfactory films. It seems possible, therefore, that the phagocytosis was more apparent than real, and that the organisms merely adhered to the phagocytes and were not ingested.

In order further to test the toxicity on cells, I employed Fleming's emigration tubes, using four parts of blood and one of antiseptic in saline. From time to time I examined the specimens on a warm stage. I noticed the character of the clot was dependent on the amount of antiseptic present, the meshes being coarser and the fibrin filaments thicker in the stronger dilutions. Amoeboid movements of the leucocytes were quite apparent for an hour in 1/1500 acriflavine. Within three hours, however, all movement in the 1/1500 specimens had ceased. In a second experiment there was after five hours no movement to be detected in the 1/16,000 specimens and only very sluggish movements of a few leucocytes in the 1/32,000, while the activity in the 1/64,000 was considerably reduced. After 16 hours, on careful searching, very slight movement of one or two leucocytes was still detected, but most of the leucocytes had taken on the appearance typical of the action on them of acriflavine—i.e., they became spherical, staining faintly yellow, the nuclei becoming very well defined. On the other hand, the controls were very active at the end of 16 hours and still showed amoeboid movements at the end of three days. Some of the specimens which were mounted showed less evidence of emigration, especially those in the stronger antiseptic, than direct observation in the earlier stages led one to expect, but careful watching showed that the leucocytes in these fell more freely out of the clot into the serum.

The specimens containing 1/1000, 1/2000, and 1/4000 acriflavine could not be removed from the emigration tube owing to the contents coagulating, a fact which seems inconsistent with the absence of injurious effect on the tissues. Proflavine has distinctly less effect than acriflavine. For example, some movement was detected in the 1/2000 dilution after five hours. On more than one occasion it was very noticeable that in the proflavine specimens there was a very free growth of bacilli after a few hours. This was in striking contrast to the case of the controls and the acriflavine specimens.

5. Compatibility of acriflavine with other antiseptics.

It is rapidly precipitated by Dakin's solution, also by mercuric chloride.

#### Conclusions.

1. Acriflavine is, as regards both its antiseptic and toxic properties, more potent than proflavine.

2. Acriflavine has a very marked bactericidal inhibiting action on streptococci and a less marked on staphylococci,

but on some other organisms its effect is practically insignificant.

3. Its action is therefore strikingly selective.

4. It has a marked but slow toxic action on the tissue.

5. This toxic action of acriflavine is not so great that it should not make when used in dilute solution (say 1/4000) an efficient application in a dressing for a wound infected with streptococcus or staphylococcus.

6. It should be applied after the wound has been thoroughly cleansed by washing, first with a rapidly acting antiseptic lotion, such as Dakin's solution, and then by a normal saline.

## Clinical Notes :

### MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

#### A CASE OF DIPHThERIA PRESENTING UNUSUAL MULTIPLE PARALYSES, WITH RECOVERY.

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THE following notes relate to a patient recently under my care. The paralytic sequelæ were unusual.

A girl, aged 9½ years, was admitted on May 27th, 1917. Her illness began on the 24th with sore-throat and vomiting, and she was said to have been "delirious." Previous infectious diseases were measles and chicken-pox. A throat swab taken before admission had proved positive for *B. diphtheriæ*. Temperature on admission 99·8° F., pulse-rate 150, respiratory rate 36. Antidiphtheritic serum (B. W. and Co.), 12,000 units, injected subcutaneously.

The patient was fairly well nourished, but pale and toxic in appearance. Tongue thickly furred, breath characteristically malodorous. Throat much injected, fauces œdematous. Tonsils completely covered with false membrane, as were also the uvula and most of the soft palate. Altogether the right throat showed the greater involvement. There was an accompanying bilateral anterior cervical adenitis, more marked on the right side. Heart sounds accelerated, soft and somewhat indeterminate in character. Pulse rapid, soft, and compressible. Lungs—there were evidences of general pulmonary catarrh. Kidneys—haze of albumin in urine.

May 28th: Throat little different; pallor extreme. 12,000 units additional serum subcutaneously. 29th: Throat condition practically unchanged. 10,000 units additional serum orally. An alkaline diuretic, diaphoretic mixture was administered. 30th: As the throat was not yet clear of membrane 10,000 units serum given orally.

June 2nd: Exhaustion marked and outlook ominous. Heart labouring considerably; its action irregular, beats poor in quality. Whisky and strychnine exhibited. 5th: Patient had developed palatal paralysis. Nasal speech pronounced, soft palate immobile, palatal reflex lost. Slight difficulty in deglutition, but no regurgitation of fluids by nose. 13th: Right internal strabismus present, causing double vision. 15th: Urine—albumin free. There was paralysis of the right levator palpebræ superioris, producing ptosis. 26th: Right internal strabismus gone. 27th: Right ptosis gone. 29th: There was loss of power of accommodation. Letterpress blurred and she could not see clearly. Pupils equal but slightly dilated.

July 2nd: It was observed that she had deviation of the tongue to the right on protrusion. 7th: There was distinct right facial paralysis. Right face expressionless and immobile. Lips pendant on the same side. She was unable to whistle or puff out her cheeks. 9th: Palate still immobile. 15th: Speech returning to normal. Palate less immobile. 16th: Sight normal. 20th: Speech normal. Palate freely mobile, reflex active. 26th: Face normal. 28th: Allowed up. 29th: The tongue was protruded in the middle line.

August 18th: Dismissed well on sixty-seventh day of illness and sixty-fourth day of residence.

It will be seen that the subject of the above notes presented six distinct and different diphtheritic palsies, representing a toxic neuritis of the several nerves involved. In order of occurrence the muscles affected were: palatal, right external rectus, right levator palpebræ superioris, both ciliaries, right lingual, right facial.

The palatal palsy was bilateral. It appeared on the thirteenth day of illness and lasted for 45 days. In consideration of the early serious and complete faucial involvement this abnormally lengthy persistence was doubtless largely contributed to by local myositis. Its presence for so long was certainly an index of the severity of the original lesion. The condition represents a toxic neuritis of the glosso-pharyngeal nerve.

The right internal strabismus was noticed on the twenty-first day of illness and was absent 13 days thereafter. Neither the date of appearance nor disappearance is particularly unusual, as the diphtheritic toxin shows a ready enough proclivity for causing abducent neuritis comparatively early, but the affection seldom persists for any length of time.

The palsy of the right levator palpebræ superioris appeared on the twenty-third day and continued for 12 days. Oculomotor neuritis producing ptosis is decidedly rare complicating diphtheria.

The loss of power of accommodation was comparatively late in its onset—namely, the fifty-fourth day of illness. This loss may manifest itself as early as the third week, although more usually during the seventh or eighth. The disability remained with her for 17 days, a somewhat short period for third nerve neuritis causing cycloplegia.

The tongue affection observed on the fortieth day of illness provides, perhaps, the most unusual feature of this case. According to most writers, actual involvement of the tongue *per se* is either discredited or considered extremely rare. If this condition is observed in conjunction with facial palsy its interpretation may be simple, for, "owing to the fact that the lips are drawn to the sound side, the tongue, when protruded, looks as if it were pushed to the paralysed side, but, on taking its position from the incisor teeth, it will be found to be in the middle line."<sup>1</sup> Such an explanation does not appear sufficient in this instance, as the tongue affection was noticed five days before the appearance of any facial involvement, and persisted three days after the facial musculature had returned to normal. If this tongue manifestation be conceded independently of the more or less concomitant facial palsy it would represent a concurrent neuritis of the right hypoglossal nerve.

The facial paralysis was present on the forty-fifth day and persisted for 19 days. This type is rare and does not ordinarily appear until the later weeks of convalescence.

Noteworthy features, then, were the multiplicity and comparative rarity of the palsies exhibited, together with the consistently right-sided character of the phenomena observed. This latter feature was in conformity with expectations, based on the grosser initial lesion of the right throat. Although post-diphtheritic palatal and ocular (external rectus and ciliary) affections are not uncommon, coincident involvement of upper eyelid and face muscles is very rare, whilst an independent tongue lesion is most unusual.

### A CASE OF PUERPERAL SEPTICÆMIA SUCCESSFULLY TREATED WITH INTRAVENOUS INJECTIONS OF COLLOSOL ARGENTUM.

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IN the treatment of sepsis the problem to be dealt with is how most efficiently to weaken or destroy the infective organisms with the least damage or reduction of vitality to the patient's tissues. The intravenous injections of salvarsan and its many substitutes in syphilis have suggested possibilities in other diseases, of which the present case is, I think, an illustration. Until a number of cases have been published, and an opinion formed from them, it is difficult to know quite how far to go. Several times lately I have treated desperate cases of septicæmia with intravenous injections of eusol. In each case there has been marked improvement, but in each case the injections were left until all other treatments had proved unavailing and were too late, and I determined, should occasion arise again, to start earlier. The result in this case having been markedly beneficial would seem to make it worth publication.

<sup>1</sup> Osler: The Principles and Practice of Medicine, p. 1020.

Mrs. A, aged 20, was admitted to the Princess Christian Hospital on August 8th, 1917, with the following history. She was delivered of a live child by forceps one week previously; child weighed at birth 8½ lb. The delivery was quite easy, forceps being applied to the head low down for delay in the second stage. There was a moderate-sized perineal tear, which was repaired. The perineum became septic and the stitches were removed. When admitted to hospital her temperature was 104° F., pulse 128, respiration 30. She was seen by the house surgeon, Dr. H. Maxwell Quackenbos. She had had two rigors. There was a thin sanious discharge from the vagina, a small ulcer over the perineum, and slight abdominal tenderness. She was given a purgative and the bowel washed out. Placed in the Fowler position for seven hours daily and given hot vaginal douches of lysol; also a mixture containing hexamine, acid sodium phosphate and bromide, and a dose of polyvalent serum, which was continued every day until a vaccine had been made. The next morning her temperature was normal, but in the evening it rose to 105°, and she had a rigor.

On the following day, the 10th, she was given an anæsthetic. The perineum and vagina were well swabbed out with iodine, the uterus curetted with a flushing curette, and packed with gauze soaked in collosol argenti. Her pulse before the operation was 148, her respiration 32. After the operation her temperature and pulse fell a little, but the temperature continued to rise each night to between 104° and 105° and she had rigors at intervals. Blood taken from the median cephalic vein grew a pure culture of the streptococcus, from which a vaccine was made. The vaccine was commenced on August 15th.

It was obvious at this time that the patient was losing ground, so she was given 20 c.cm. of collosol argenti into a vein. This was followed by a profound rigor and a certain amount of collapse, but the next day her general condition was much improved, the temperature had fallen to normal, and the pulse at 6 A.M. was counted at 80. The temperature rose, however, again at night, but continued at a lower range. The dose of collosol argenti, 20 c.cm., was repeated four times at intervals of a couple of days, and was followed on each occasion by a profound rigor, but, although the patient was ill, the picture had changed and she was obviously improving and in no immediate danger. She began, however, to relapse, developed a thrombosis in the external saphenous in the middle of the right calf, and her pulse returned to between 120 and 130.

On Sept. 7th the condition again became serious and a blood culture gave a growth of pure streptococcus. A further 20 c.cm. of collosol argenti were given, followed, as before, by a severe rigor; the temperature fell, and the next day remained at the normal. The general condition and appearance instantly improved, and in a couple of days she appeared to be out of danger. The temperature has since remained normal, and she has put on flesh, regained a healthy appearance, and left the hospital in excellent condition.

There has been a trace of albumin in the urine at times, but the injections of silver have up to the present caused no irritation of the kidneys and no pigmentation of the skin.

A septicæmia in which pure streptococci circulate in the blood and grow without forming local foci is undoubtedly a dangerous condition. Serum, even in very large doses, has not in my experience proved altogether satisfactory. Vaccines have seemed better in their action, but the result still uncertain. In the cases in which I have used intravenous injections the patient has always been better the next day. The general improvement in condition has been every time noted to be apparent, both to the patient and friends. On two, if not three, occasions on which the picture was almost desperate before the injection the day following the patient was caught reading the paper.

Whether or no this case would have recovered on other lines of treatment it is impossible to say, but three deductions may be made. 1. That the direct introduction of antiseptics into the blood stream in cases of septicæmia seems always to be beneficial. 2. That 20 c.cm. of collosol argenti every 48 hours produced no untoward effects. 3. That the injections should be commenced before the patient's strength is exhausted.

Weymouth.

LITERARY INTELLIGENCE.—Messrs. Cassell and Co., Limited, announce for early publication new and enlarged editions of Treves and Keith's "Surgical Applied Anatomy" and of Candy's "Manual of Physics"; the former has been revised by Professor Keith, assisted by Dr. W. Colin Mackenzie; and the "Manual of Physics" by the author.