been found sequestered in the partially destroyed cartilages. Infected areas are met with here in close proximity to normal tissue, and more organisms have been found at the extreme limits of the affected and damaged areas than in the centre of fibrous degenerated tissue. One of the difficulties attendant on subsequent operations on joints, especially excision, is the secondary suppurations which undoubtedly arise from these loculi containing remnants of the original infection.

*Wounds Entirely Healed but Breaking Down after
a Long or Short Interval.*

Many wounds have been examined belonging to this class; they are frequently wounds involving bone, often with very slight bone involvement and no fracture. Histological and bacteriological examination give the same findings, whilst the penetration of the bacteria into the bone extends a considerable distance either side of the original lesion. These wounds break down again after trivial injury or over-exercise. A histological examination of tissue excised near such wounds shows the infection mainly at the junction of the normal and fibrous tissue. The outcome of bacteriological observations on a large series of wounds of latent infection, together with histological examination of excised tissue, points to the physiological action of anaërobic bacteria rather than to general systemic toxæmia as the underlying cause of the persistent infection. The most persistent organism is the *B. sporogenes*, which is in itself of low pathogenic power. It can, however, survive for a long time and in culture tubes, when associated with streptococci or organisms of the *coli* group, and undergoes cyclic development, spores forming and germinating slowly but persistently, with the result that the material becomes ultimately entirely digested. In cases heavily infected with the *B. sporogenes* persistent local oedema has been observed. Histologically, minute general thrombosis of vessels in the immediate vicinity of the wound is common; the thrombus may even spread up through the smaller vessels and project into the larger. Histological examinations of these cases show that the "splash" effect produced in the soft tissues by the velocity of the projectile extends over a considerable distance, that numerous radiating cracks in the tissue occur which become the seat of hæmorrhage. The blood clot formed contracts, associated with the discharge of serum from the wound, coincidentally the bacteria make their way into the cracks, doubtless by capillarity, and subsequently become shut off from the main wound cavity by fibrous tissue and remain latent. There is some indication that this fact has an important bearing on the practical question of the movement of wounded men. It certainly has a very practical bearing on the deep infection of the wounds.

Summary.

In summarizing my observations on wounds in home hospitals from 1915 to the present time it appears—

1. That the mass infection has diminished progressively, but that
2. The persistence of anaërobic bacteria has not undergone similar qualitative reduction.
3. That by the use of the two antiseptics of which statistics have been available (bipp and hypochlorite) no great diminution in anaërobic flora has been effected.
4. That latent infection as opposed to persistent infection is of great importance in "subsequent operations," and that latent infection is determined by the treatment of the case in the first week of the injury, possibly in the first three days.
5. That in latent infection organisms are found in close proximity to healthy tissue and therefore in a region likely to become the site of an incision in a subsequent operation.
6. That bone fragments split off at the original injury invariably become sequestra, probably due to the proteolytic action of the bacteria rather than to destruction of blood supply.
7. That of the various methods which have so far been made use of in the immediate treatment of wounds, immediate excision of the lacerated tissues is apparently the only one that has produced a marked diminution in the anaërobic flora of the wounds.

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NOTES ON VIBRION SEPTIQUE.

BY

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THE following is a brief account of the anaërobic organism known variously as the *Vibron septique* and the bacillus of Gohn and Sachs; the name *B. oedematis maligni* has also been used for it.

The conflicting accounts of early writers and the very real difficulty due to the close symbiotic association of widely differing species of anaërobic has obscured our knowledge of this type. *Vibron septique* is very easily passed over in mixed culture, so that its presence has often escaped the notice of workers dealing with wound infections. I propose to use the name *Vibron septique*, under which I include the bacillus of Gohn and Sachs; *B. chauwei* is an allied type, but is a different organism.

The name *Vibron septique* is here applied to a group of strains which are in complete agreement with each other in (a) morphology; (b) cultural characters, including the reactions upon various sugar media; (c) pathogenicity and reaction in the animal body. They do not, however, fall into one group upon the agglutination reaction.

From the trend of modern research it is becoming clear that in many cases the organisms responsible for any given pathological condition must be looked upon as a series of very closely allied types, which can in certain instances be separated from each other by various slight *differentia* and notably by the agglutination reaction. It may eventually be useful to subdivide the group into subgroups, possibly with specific names. It is proposed to deal with the agglutination reactions of *Vibron septique* in another publication. In general, it may be said that in working with anaërobic it is premature to conclude that a strain represents a separate species because it produces specific agglutinins.

The following is a list of the strains studied:

1. *Vibron septique*, Pasteur Institute strain.
2. *B. R.*, Pasteur Institute strain.
3. *V. septique*, strain "Amatzi"; derived from blood culture; from Dr. Weinberg.
4. *V. septique*, strain "Cairny"; from fatal case of gas gangrene.
5. *V. septique*, strain "Summers"; blood culture from case of gas gangrene.
6. *V. septique*, strain "Dynes"; from fatal case of gas gangrene.
7. *V. septique*, strain "Prior"; from case of gas gangrene.
8. *V. septique*, strain "Alexander"; from hæmorrhagic blister fluid in a case of gas gangrene.
(Strains 4 to 8 were supplied by Captain Stokes.)
9. *V. septique*, strain "J. I."; from case of gas gangrene isolated by Miss Hempl.
10. *V. septique*, strain "James"; from case of gas gangrene.
11. *V. septique*, strain "Brissons"; from case of gas gangrene.
12. *V. septique*, strain 141; from case of gas gangrene.
13. *V. septique*, strain 133; from case of gas gangrene.
(Strains 10 to 13 were supplied by Captain Henry.)
14. *V. septique*, strain 227; from wound of patient forty-nine days after wounding; no symptoms of gas gangrene.
15. *V. septique*, strain 145; from wound of patient seven days after wounding; no symptoms of gas gangrene.
16. *V. septique*, strain "Jerral"; from wound of patient without symptoms.
17. *V. septique*, strain "Bedford"; amoebic abscess of brain; material from Captain Armitage.
18. *V. septique*, "Milk" strain, isolated from milk.
19. *V. septique*, "Milk Con." strain, isolated from milk.
20. *V. septique*, strain "George A."; from case of gas gangrene developing upon operative treatment of a healed wound.
21. N. I., *V. septique*; strain isolated by Miss Hempl from wound of patient without symptoms of gas gangrene.

The following were studied for comparison:

22. *B. chauwei*; from case of black quarter; from Sir John McFadyean.
23. *B. chauwei*, culture isolated by Dr. MacIntosh from Rauschbrand muscle from Denmark.
24. *B. oedematis*, strain "Jolly"; from Dr. Weinberg, from case of Dr. Dalyell.
25. *B. oedematis*, strain "Delombre"; from Dr. Weinberg.

I have much pleasure in expressing my cordial thanks to the many colleagues to whom I am indebted for material from cases in their charge, or who have most generously placed their cultures at my disposal. My thanks are due to Dr. Roux, Dr. Weinberg, Dr. MacIntosh, Miss Hempl, Captain Armitage, N.Z.M.C., and Sir John McFadyean. I am quite especially indebted to Captain A. Stokes, D.S.O., R.A.M.C., and to Captain Henry, R.A.M.C., for much valuable material and for kind co-operation during the course of the work.

Morphology.

The *Vibron septique*, like many anaërobic, has a rather wide range of variation in morphology according to the circumstances in which it develops.

Typically, in a young culture in meat medium it appears as a Gram-positive rod of varying length considerably thinner than

B. welchii and in size closely resembling *B. sporogenes*; spores are formed with great freedom, and may be found at any stage of development. They may be centrally placed, and in short rods; they may occupy practically the whole extent of the organism, producing barrel-shaped or clostridial forms. The spores are, however, very frequently subterminal or even terminal; the shape of the fully developed spore is often oblong rather than oval, the ends being slightly flattened.

When grown on inspissated serum the appearance may be extremely varied—club-shaped individuals, bulbous, deeply staining types, filaments and the “navicular” or “citron” forms described later may all be present as well as the rods and spores already mentioned. In Noguchi tubes containing fresh tissue these “citron” and club-shaped individuals may also appear.

Apart from these forms just mentioned there is nothing very characteristic in the morphology of *Vibrio septique* in culture which would distinguish it from other anaerobes.

Motility.

In young (twenty-four hour) cultures and in the freshly taken oedema fluid of recently dead animals the organism is motile.

Cultural Reactions.

The cultural reactions are as follows:

Colony.—Surface colonies are semitransparent and rather delicate; the edges may be crenated, and there may sometimes be a tendency to form flat or branching outgrowths; woolly filaments of the tangled thread type are not formed, and the colonies do not grow down into the medium. Surface colonies

Broth.—In plain nutrient broth the growth is rather feeble; the medium becomes turbid in twenty-four to forty-eight hours and, later, the growth sinks to the bottom of the tube. In glucose broth the growth is very vigorous, and the sinking of the organisms is very striking; this occurs after about thirty-six to forty-eight hours of incubation. There is often a lag of about twelve to eighteen hours during which growth may fail to appear, even when a very vigorous proliferation is about to occur within the next twelve hours.

Meat.—In this medium there is vigorous growth and considerable formation of gas. A vivid pink colour is produced which varies in exact hue according to the constituents of the medium (the colour is darker in heart muscle and brighter in skeletal muscle, etc.); after a time the bacteria sink down so that the fluid above the meat becomes as clear as before inoculation. The colour may gradually fade from the meat on exposure to air. There is no blackening and no putrefactive odour, and the meat does not become soft and friable. Meat covered with paraffin is a very good medium for the cultivation of this organism.

Inspissated Serum.—*Vibrio septique* grows freely on this medium in an anaerobic jar; there is no liquefaction, not even the faintest pitting of the surface after weeks of incubation. The morphological range of the bacillus on inspissated serum is very great—club-shaped individuals, deeply staining oval or bulb-shaped types, “citrons,” and filaments may all occur. Spores are formed very readily on this medium, and a sealed culture may be left on one side for more than a year without any apparent loss of vitality. The subcultures then made show no abatement of vigour and retain their pathogenicity for laboratory animals.

Alkaline Egg Fluid.—The medium becomes uniformly opaque without the formation of a clot.

FIG. 1.—*Vibrio septique*, twenty-four to forty-eight hour meat culture. Mag. 1,500.

FIG. 2.—*Vibrio septique*, Noguchi tube culture, showing rods, spores, and a “citron” type. Mag. 1,500.

FIG. 3.—*Vibrio septique*, from muscle of guinea-pig. Post-mortem specimen; “citrons” and club-shaped type are shown. Mag. 1,500.

FIG. 4.—*Vibrio septique*, from liver of guinea-pig, showing “citrons,” oval and bulb forms. Mag. 1,500.

require good conditions of anaerobiasis; a serum agar or glucose serum agar medium is favourable to growth. On salicin agar with or without serum the colony is larger, and while it retains its rather translucent character the whole appearance is more robust. Plates should be dried before spreading, as there is a certain tendency for *Vibrio septique* to grow in a uniform surface film instead of in discrete colonies. Good surface colonies can be obtained by stroking a loop dipped in the inoculum over three or four serum agar slopes in succession; one of the slopes generally yields clean discrete colonies which can be picked off.

Deep Colonies.—These have a transparent or semi-transparent appearance; the centre is not very compact, and the edges show coral-like branchings.

Characters in Milk.—When grown in milk, either in an anaerobic jar or in paraffin-covered media in an ordinary incubator, acid is produced, and, finally, after three to seven days, there is clotting, with or without the production of gas. If the sowing has been large and the culture is growing very vigorously the acid and clot reaction may be more rapid and the production of gas more obvious, but the delayed reaction is the more frequent, especially in recently isolated strains.

Noguchi Tubes.—A broth or glucose broth tube into which a piece of fresh liver or kidney, taken under sterile precautions from a rabbit or guinea-pig, has been dropped forms a most excellent medium for the growth of *Vibrio septique*. The citron forms occur in this medium and they afford a useful diagnostic feature.

Sugar Reactions.—These are quite definite, and are set out in the accompanying table; *B. welchii* (one type only), *B. oedematiens*, and *B. chauveii* are also shown for comparison. The medium for these tests may be casein digest broth, to which is added the requisite sugars in concentrations of 1 to 1.5 per cent.; litmus or the alkaline egg fluid, as described by Henry, may be used as indicators. The readings should be made at forty-eight to seventy-two hours. This medium can be used sealed with liquid paraffin. Serum litmus agar slopes made up with the desired sugars can also be used with success but require a good anaerobic apparatus.

Pathogenicity and Animal Reactions.

Vibrio septique is pathogenic for guinea-pigs, pigeons, rabbits, and mice; all the strains dealt with have retained

Table of Cultural Reactions.

Name.	Meat.	Milk.	Inspissated serum.	Glucose.	Levulose.	Galactose.	Saccharose.	Maltose.	Lactose.	Inulin.	Salicin.	Mannite.	Dulcife.
<i>Vibrio septique</i> ...	Gas: pink colour; no blackening	Acid: clot after 3 to 6 days	No liquefaction	+	+	+	-	+	+	-	+	-	-
<i>B. welchii</i> ...	Gas: pink colour; no blackening	Acid: rapid clotting with evolution of gas	No liquefaction	+	+	+	+	+	+	*	-	-	-
<i>B. oedematiens</i> ...	Gas: pink colour at first, then bleached	Acid after 4 to 6 days; very slow clotting	No liquefaction	+	+	-	-	+	-	-	-	-	-
<i>B. chauveii</i> ...	Gas: no blackening	Acid: clot after 3 to 6 days	No liquefaction	+	+	+	+	+	+	-	-	-	-

* Variable according to type.

their pathogenicity for these animals, some of them during years of culture under laboratory conditions. There is a certain variability in virulence, due in part to the conditions of growth. The most virulent cultures are twenty-four hour growths in glucose Noguchi tubes, glucose broth cultures of the same period come next, and ordinary broth is the least favourable medium for inoculation into animals.

The infecting dose for the particular type of laboratory animal used must be ascertained.

In some cases 0.1 c.cm. of a twenty-four hour glucose broth culture, or even less, will kill a 300 gram guinea-pig in twelve to eighteen hours; 0.5 c.cm. to 1 c.cm. is generally a lethal dose for a 300 gram guinea-pig, and the minimal lethal dose can be ascertained if desired. A sublethal dose of a virulent culture may be withstood by a guinea-pig without any symptoms, whereas a very slightly higher dose or even the same dose in another animal of corresponding weight will produce death with the typical lesions. Sublethal doses in guinea-pigs do not appear to produce any reaction. I have in no instance observed the recovery of an animal that had shown any symptoms of infection as a result of the injection of this organism. The occurrence of extensive oedema with subsequent recovery, which is so striking a feature of the reaction of guinea-pigs to sublethal doses of *B. welchii*, is absent when *Vibrio septique* cultures are used.

Post-mortem Appearances.

These are as follows:

There is an extensive blood-stained oedema, and a considerable amount of gas is developed in all the muscle tissue involved. The muscles affected have a characteristic deep red colour. There may be a collection of fluid in the peritoneal cavity and in the pericardium; this is not as a rule very evident in guinea-pigs which have died in twelve to twenty-four hours, but is a very well-marked appearance in rabbits which have succumbed to the infection after twenty-four to forty-eight hours. The suprarenal bodies may show a variable amount of redness, but this is not so regular nor so marked as in guinea-pigs which have died from infection with *B. welchii*.

There is no putrid odour. The pale digested appearance of the infected muscles so frequently seen in *B. welchii* infections is not seen with *Vibrio septique*.

B. oedematiens in guinea-pigs produces a gelatinous oedema quite colourless, with little or no gas; the muscles involved are pale pink in colour.

Microscopical Appearances.

The microscopic appearances are as follows:

Film preparations stained by Gram's method, made from the muscle of an animal which has died of infection by *Vibrio septique*, show rods and the characteristic citron or navicular forms. They are of very varying length; they have a pale granular appearance, and generally contain a deeply staining portion at one end of the body or at both. Sometimes the granular part may take up the stain with somewhat greater intensity, but there is always a differentiation between the granular part and the deeply staining points. These "citrons" are stages in a type of spore formation that takes place only in the animal host or in the presence of live tissue or in serum. This is not the only type of spore formation which takes place in the host, the ordinary method whereby the spore arises in the rod also occurs. In addition to the "citrons" large club-shaped types which appear to be swollen rods occur—these are not very frequent in muscle; oval or bulb shaped, deeply staining forms, often in short chains, may also be present. It should be noted that if the infection has run a very rapid course and if the post-mortem examination has followed immediately upon the death of the animal the "citrons" and spores may not have been formed at all or may be present only in small numbers. "Citrons" also occur in infections with *B. chauvei*, but are not known in any other type of anaerobic infection. It should be noted that *B. chauvei* has not so far been recorded as infecting man.

Films made from the peritoneal surfaces of the liver show a greater or less number of long snaky chains and filaments. These long filaments are characteristic of a *Vibrio septique* infection; they are not found in infections with *B. welchii* nor with *B. oedematiens*. Mice and rabbits show the filaments quite as clearly as guinea-pigs. The citron, club, and bulb forms can be found in the liver as well as in the infected muscle.

Vibrio septique produces septicaemia, and the heart blood taken with aseptic precautions and inoculated into paraffin covered meat medium yields good cultures.

"Vibrio Septique" in Mixed Culture.

Vibrio septique growing with *B. sporogenes* or in mixed culture derived from wounds is extremely difficult to recognize, and even when its presence is suspected it may be a very tedious and lengthy process to unravel it from the other anaerobes present by growing on selective media and plating, etc. The injection of such a mixed culture, either grown in glucose broth for twenty-four hours or from a meat culture, into a guinea-pig or mouse will afford the post-mortem picture described above, and moreover the cultivation of the heart blood in meat medium will often give a pure culture of *Vibrio septique*. Should this heart blood culture not be pure at the first passage the predominant organism will certainly be *Vibrio septique*, and plating or a second animal passage will then purify the strain.

Vibrio septique in these mixed injections into guinea-pigs will outrun both *B. sporogenes* and *B. welchii*, and the animal usually dies of a *Vibrio septique* septicaemia, even when both the above mentioned anaerobes are present in the culture inoculated.

Such a mixed culture destined for injection into an animal should, however, always be freed from *B. welchii* by growing for two or three days in milk and then heating to 80° for ten to fifteen minutes; the heated material should be inoculated into meat medium and (after subculture into glucose broth if desired) then injected into the animal. In mixed culture the dose should be 1 to 1.5 c.cm. for a 300 to 400 gram guinea-pig and 0.25 to 0.5 c.cm. for mice.

Vibrio Septique in Wounds.

Vibrio septique, like other pathogenic anaerobes, may be present in wounds both of recent date and of long standing without causing any symptoms in the patient. It may, on the other hand, be responsible for a serious or even fatal case of gas gangrene. These acute infections usually occur within a few days of wounding, but may arise at any time, especially after operation. One of the strains here studied was obtained from a gas gangrene condition arising from the operative treatment of a wound healed for over two years, but which still contained a very small pocket of pus in the scar tissue.

In an active infection with *Vibrio septique* the organism may be present in the discharge from the wound, in muscle, in the fluid from haemorrhagic blisters, in the skin near the wound, and possibly in the blood stream. A careful examination of films from the muscle, or from the blister fluid, should any have been formed, or from the discharge, may show among other organisms the characteristic "citrons" and deeply staining oval or bulb types; rods with or without spores, will also be present, but cannot be distinguished from other bacilli. The worker should familiarize himself with the *Vibrio*

septique types as they appear in guinea-pigs, as the recognition of "citrons," etc., in the films direct from the patient affords a valuable and very rapid diagnosis. The injection of the fluid from haemorrhagic blisters or other exudate into a mouse or guinea-pig will produce the characteristic appearances if *Vibrio septique* is present, and cultures should be made at the same time in meat.

If the animal test is not available more time should be spent upon the examination of films, as that may afford an immediate indication of the presence of the organism; demonstration of the organism in culture even under favourable conditions would not provide a definite diagnosis

FIG. 5.—*Vibrio septique*, from liver of guinea-pig, showing long filaments, etc. Mag. 1,000.

FIG. 6.—*Vibrio septique*: "citrons" from haemorrhagic blister fluid of patient suffering from gas gangrene. Mag. 1,500.

for some days. The absence of citron forms, etc., must not be regarded as evidence that *Vibrio septique* is not present in the wound. *Vibrio septique* appearing in a wound showing an active condition of gas gangrene should be considered as a serious finding, whether accompanied by *B. welchii* or alone.

SUMMARY.

1. *Vibrio septique* is a saccharolytic organism clotting milk in three to seven days, without putrefactive or digestive reaction on meat or inspissated serum. It is a strict anaërobe.

2. Spores are readily formed upon all media. They are oval in shape, and central or subterminal in position.

3. The organism is pathogenic for man. It is also pathogenic for laboratory animals (rabbits, mice, pigeons, and guinea-pigs) both in pure culture and when mixed with other anaërobics.

4. In the animal body the lesions are a blood-stained oedema and deep red colour of the infected muscles. The organism also infects the blood stream.

5. Characteristic morphological types of the organism are found in the muscles; these are "citrons," club and bulb-shaped forms, as depicted in Figs. 2-4, and 6. On the peritoneal surface of the liver long snake-like filaments and chains are formed; these are specific to the *Vibrio septique* type among the pathogenic anaërobics at present known.

6. The citrons and also the deeply staining oval or bulb types may be met with in muscle tissue and in the fluid from haemorrhagic blisters in man in cases of active infection with this organism. This affords an immediate and valuable diagnosis, but a failure to find these types does not constitute evidence that the case is free from an active infection with *Vibrio septique*.

APPENDIX.

*Casein Digest Medium.*¹

To a 2-litre flask containing 1 litre of tap-water add 20 grams of anhydrous sodium carbonate. Transfer the flask when boiling to a water-bath and add 200 grams of casein, dusting this in gradually to avoid the formation of lumps; then place the mixture in a large Winchester quart bottle, allow to cool down, and add 3 grams of pancreatin with 15 c.cm. of chloroform. Incubate at 37° C. for five days, shaking vigorously from day to day to break up the crusts that have formed, then add 3 more grams of pancreatin and incubate for ten days longer. After fifteen days' digestion in all the mixture is treated with 400 c.cm. of N/1 HCl, steamed for thirty minutes to drive off the chloroform, and then filtered. The filtrate is treated with 120 c.cm. of N/1 NaOH, and its reaction is adjusted to PH = 7.3, using either the hydrogen electrode or phenol-sulphonaphthalein as an indicator in a Marriott scale. The resulting stock broth is diluted with two parts of 0.5 per cent. NaCl in tap-water before use, the reaction being again adjusted if necessary.

The sugars required can be added to this.

*Serum Agar Sugar Medium.*²

Ordinary agar 75 c.cm., sterile serum 25 c.cm., litmus solution 5 c.cm., to which 1 gram of the required sugar has been added and sterilized by steaming. The medium is made up as for ordinary serum agar.

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TREATMENT AND PROPHYLAXIS OF MALARIA.

BY

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A good many articles on the subject of the treatment of malaria have appeared recently in medical journals,¹ evidently because many men suffering from this disease have been invalidated to Europe as the result of the war. A certain amount of apprehension must be felt as to the after-effects of some of the lines of treatment advocated. Time and experience can alone settle the questions raised, but, as a contribution to the subject, I desire to draw attention to a memorandum I wrote for the P.M.O., H.M. Forces in India, in 1901, on the use of hypodermic

injections of quinine in malaria. The method (which was described in a review of the memorandum published in the BRITISH MEDICAL JOURNAL of March 29th, 1902, p. 793) has stood the test of time and experience. Since writing that memorandum (about seventeen years ago) I have had no reason to deviate one iota from the dicta I then laid down. Other medical men who have made independent observations on these statements of mine have corroborated them.

As I have had uniformly good results from this treatment, I think it will be useful to give a summary of it, for it seems to have dropped out of mind. I must in the first place strongly insist that the technique for the hypodermic injection must be carried out as laid down, otherwise grave results may occur. It must not be thought that quinine injections can be given hypodermically in the same free and easy way as a hypodermic injection of morphine. In the second place, I wish to make it clear that I do not recommend intramuscular injections, but hypodermic, that is, below the *cutis vera*, and above the fascia of the muscles.

Requirements.

1. An all glass 20 m hypodermic syringe with stout needles, thoroughly sterilized.
2. Saline solution 0.5 per cent., sterilized.
3. A wide-mouthed test tube about 3 in. long, sterilized.
4. Carbolic oil 5 per cent. and some cotton-wool.
5. Pure quinine bisulphate 4 grains.
6. Spirit lamp.

Method of Subcutaneous Injection.

Prepare the patient's flank between the iliac crest and the last true rib by cleansing with soap and water, and then smearing with carbolic oil on wool (I do not like tincture of iodine if it can be avoided).

(a) Put the 4 grains of quinine bisulphate into the sterilized test tube.

(b) Fill the syringe with the 0.5 per cent. saline solution; squirt this into the sterilized test tube to dissolve the quinine powder.

(c) Heat the quinine solution in the spirit flame till it comes to the boiling point.

(d) Fill the syringe with this boiled quinine solution.

(e) Dip the needle into the carbolic oil.

(f) When the solution cools down to about 100° F., pick up between finger and thumb of left hand (with carbolized cotton-wool intervening) a good lump of the *cutis vera* in the flank; plunge the needle in up to the hilt (eyelet downwards) into the subcutaneous tissue; sweep the point of the needle from side to side through the connective tissue, describing the arc of a circle, thus breaking down any small trabeculae, and freeing the point of the needle from any fat globule it may be in, and then inject all the solution into the space thus formed; withdraw the needle quickly; massage the flank with the carbolized cotton-wool to disseminate the fluid as much as possible.

If the above directions are carried out properly, I guarantee that the patient does not feel the uncomfortable sensation of burning or pain; and, strange as it may appear, many of my patients never know when the injection has begun or when ended; in fact, the only remark they make is that they felt me pinching up their skin!

The injection is to be given—the method described being strictly observed on each occasion—once daily for five consecutive days in alternate flanks. In addition, $\frac{1}{2}$ grain arsenious acid should be taken by the mouth, and also 5 grains (only) of quinine well diluted, in the early morning daily; the arsenious acid and the quinine should be continued for a month.

The treatment described is all that is required for an uncomplicated case of malaria, but the complications of malaria may be manifold, such as congested liver and disordered action of stomach and bowels, with loss of appetite and constipation. Measures for the treatment of these conditions on ordinary lines should be taken, but must be regarded as adjuncts to what I call the specific treatment by hypodermic injections of bisulphate of quinine.

For chronic relapsing cases of malaria, with enlarged spleen and liver, the same specific treatment is undertaken, but the five hypodermic injections are repeated every fortnight (together with local treatment of the "ague cake" spleen, by counter irritation producing a mild splenitis, etc.) till the spleen or liver becomes normal.

An important point to which I wish to draw attention is not to overdose the patient with quinine by the mouth, thereby upsetting the digestion and ruining any benefit he