rectal region as described above, though I have succeeded a number of times in blocking limited areas for operation on painful lesions involving the anal margin.

A brief recital of the case referred to will perhaps be of interest here:

Patient.—On Feb. 27, 1906, I was called to see Mr. J. B., aged 23, whom I found in bed.

History.—For several years he had been a sufferer and supposed his trouble was merely the ever-popular "piles."

Examination.—I found three well-developed internal hemorrhoids situated well up in the anal canal, an exquisitely painful fissure with its external "sentinel pile," and, as was to be expected, a spasmodic and hypertrophied sphincter.

Operation.—I advised the patient that a general anesthetic would be necessary. He consented, but his dread of it was so great that I determined first to attempt the operation by blocking the nerve supply of the entire region. This was done on the following day, after the manner outlined above, with complete success, and with practically no pain. The sphincter was divulsed, the internal hemorrhoids ligated and removed, the fissure curetted and incised, and the "sentinel pile" amputated. The patient left the hospital in six days.

The method is certainly a rational one and I shall not hesitate to resort to it in suitable cases.

Following are some of the advantages which, from personal experience, I feel warranted in claiming for local anesthesia in rectal surgery:

1. It is simple, safe and effective.
2. It eliminates the dangers and discomforts of general anesthesia.
3. Pain at the time of operation is usually absent and always so slight as to be easily borne.
4. Postoperative pain is less by far than after the old methods.
5. Time required for the operation is greatly reduced.
6. Confinement to bed is rendered a matter of expedience, rather than necessity.
7. The period of detention from business is diminished fully one half.
8. Under this method the hospital becomes a convenience and luxury rather than a dreaded essential.
9. It is a thoroughly reliable means of affording relief in many cases which would otherwise be unsuitable for operation.
10. It robs these operations of their terrors and makes it possible to reclaim this work from the hands of the "no knife" advertisers.

I hope I will not be misunderstood if, as a final thought in this connection, I say a word or two of caution. The method is simple, but its successful employment demands thorough familiarity with the anatomy of the rectum and anus, discriminating knowledge of the various types of pathology to which they are subject, and no small degree of operative dexterity. Patients afflicted with anorectal diseases are uniformly, perhaps also peculiarly, nervous and apprehensive, and the very thought of operation is sometimes sufficient seriously to embarrass even the most skillful efforts in that direction. An air of confidence, gentleness of manipulation and rapidity of execution are of the utmost importance if success with the method is hoped for.

The field of application of the methods above described is, of course, by no means restricted to the anorectal region. I have repeatedly employed them in minor surgical operations, such as excision of superficial tumors, removal of ingrowing nails, amputation of fingers, etc. I am profoundly convinced that it is a duty we owe our patients to spare them general anesthesia whenever it is possible to do so, and that we should welcome and faithfully test all methods looking to this end.

THE SPIROCHAETA PALLIDA (TREPONEMA PALLIDUM) IN SYPHILIS.*

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An immense amount of work has been done in the last eleven months on the etiology of syphilis, work that very probably will mark an epoch in our knowledge of that scourge of the human race. It seems worth while to review briefly what has already been accomplished.

HISTORICAL REVIEW.

Lassar calls attention to the fact that more than twenty-five causes of syphilis have been described during the last thirty years. As early as 1837, Donn described a parasite found in syphilitic ulcers and named it *Vibrio lineola*. In 1902, Bordet and Gengou found spirochetes in chancres and throat lesions, but discontinued their researches when they did not find the organisms constantly.

Early in 1905 Siegel observed actively motile flagellate bodies in enormous numbers in the blood of several syphilitics and named them *Cytorrhycetes luis*. Schaudinn had earned a reputation in the study of protozoa, malarial parasites, trypanosomes, etc., and he was appointed by the Imperial Board of Health in Berlin to investigate Siegel's work. He called to his aid Hoffmann, an expert syphilologist, and in April, 1905, they published the description of a very delicate spiral organism which they had found in all of 26 cases of primary and secondary syphilis. The *Cytorrhycetes luis* was not mentioned at all in their reports. Since then a few investigators have found it, many have failed, and some say that it must be an artefact.

Schaudinn and Hoffmann named their organisms *Spirochaeta pallida*, and a larger one which they found associated with it they called the *Spirochaeta refringens*. This has been found only on the surface of syphilitic lesions, in various other ulcerated surfaces and smegma from healthy men and women.

Hoffmann, in one communication, reports finding the pallida constant in over 300 cases of syphilis, and he has never found it in non-syphilitic material.

LESIONS IN WHICH THE SPIROCHETES HAVE BEEN FOUND.

In the primary sore, the pallida has been found very frequently. Especially in non-ulcerated chancres, and in the upper layers of the lesion there may be very few, so the scraping should be thorough. Many say that the deeper the scraping or section the more the spirochetes. They are also found in the juice from enlarged glands. Smears from mucous patches usually show many pallida, refringens and other spiral organisms, as, e. g., the *Spirochaeta Vincenti*. Scrapings and blood from condylomata of the anus and splenic blood show them; but in the peripheral blood of syphilitics with active lesions they are rarely found. Blood and serum from skin lesions occasionally shows the pallida and shows the refringens only when the skin is broken. It has been suggested that the eruption is a true embolic process, the spirochetes being distributed by the blood stream.

The pallida has been found sometimes in enormous numbers, in almost all the organs of congenitally syphilitic children, in macerated fetuses, in a child of 6 and in the fluid of syphilitic bull. It is suggestive that the liver, which receives most of the blood coming directly from the placenta, generally contains more spirochetes than any other organ. The pallida has been found in small numbers in the placenta. Pallida and refringens

* Read before the Cooper Science Club, San Francisco, April 2, 1906.

have been found in late secondaries and have been reported found in tertiaries in a very few instances. All the authorities cast doubt on these reports and deny their accuracy, especially when the lesion is ulcerated and the observer inexperienced.

Typical pallida have been found in the primary and secondary lesions in monkeys and apes inoculated from man and from syphilitic monkeys.

Control examinations have been made of material from various venereal and other ulcerating lesions, and most of the observers report not finding the pallida. Kiolomenoglou and von Cube have found in various non-syphilitic lesions, breaking down carcinomata, etc., the pallida, refringens and many atypical forms which can not be classified with either. Schaudinn saw the specimens and admitted the presence of more than two species, but maintained with Hoffmann that all spirochetes found in non-syphilitic conditions can be differentiated from the pallida, either morphologically or tinctorially. Hoffmann has found the refringens in ulcerating carcinoma, and lately Rumpf reports finding spirochetes constantly in carcinoma. He describes these as being coarser and thicker than the pallida, with blunt ends and staining blue with Giemsa. Rosenberger describes many spirochetes in 76 per cent. of specimens taken from the buccal mucous membrane and the tartar of the teeth. Most of these resembled the refringens; some were pale, but a little too thick for the pallida; others resembled the *Spirochaeta Vincenti*, and another variety was very delicate, very long, faintly staining and irregular in shape. All had pointed ends. In non-syphilitic lesions, Siebert has seen spirochetes just as delicate as the pallida.

Only the pallida have been found in sections of syphilitic lesions, and it has not been found in sections of carcinomata and other lesions which showed spirochetes in their discharges.

Mercurial treatment does not cause a rapid disappearance of the pallida or the refringens, as was at first reported. Care must be taken that the refringens which only may remain is not mistaken for the pallida.

CLASSIFICATION.

The question very naturally arises, What is the spirochete and what is its relation to other spiral organisms? The clearest answers to these questions can be found in an article by R. Blanchard.¹ He submits the following classification:

- I. SPIROBACTERIA: Vegetable in origin.
Genera: *Spirosoma*, from nose and mouth.
Vibrio, the comma bacillus, etc.
Spirobacillus.
Spirillum, from stagnant water.
- II. TRYPANOSOMIDAE: Protozoa.
Genera (a) *Spirochaeta*.
Species: *Spirochaeta* in stagnant water and tartar of teeth.
Spirochaeta Obermeieri.
Spirochaeta of African tick fever and possibly of Texas fever and other diseases of this kind.
Spirochaeta refringens (Schaudinn, 1905).
Spirochaeta pallidula (Castellani) found in parangi or yaws.
Spirochaeta Vincenti.
Spirochaeta in dysentery.
Spirochaeta constantly found in stomachs of dogs.
Spirochaeta found in surfaces of ulcerating neoplasms.
Spirochaeta in smegma and in ulcers.
- (b) TREPONEMA: (Schaudinn) (syn. *Spirochaeta spiro-nema*).
Species: *Tr. pallidum* (Schaudinn).
- (c) TRYPANOSOMA:
Species: *Tr. Gambiense* (Dutton) sleeping sickness. There are many other species usually transmitted by insect bites.
- (d) TRYPANOPLASMA: Four species found in fishes.

DESCRIPTION OF THE SPIROCHAETA PALLIDA.

The *Treponema* or *Spirochaeta pallida* is described as being extremely delicate, weakly refractile, spiral or corkscrew-shaped, with three to fourteen bends which

are more acute than in any other spirochete, resembling the edge of a saw. Both ends are pointed, which is very important to notice, as it will generally enable one to exclude little shreds of elastic tissue which are often beautifully coiled. The length is 4 to 14 mm.; the breadth immeasurable; it has a rotary motion forward and backward, and it may bend slightly in the middle. A vibratile membrane and flagella have been suspected by many, but as yet have not been clearly defined. The ultramicroscope shows segments and what may be a nucleus. Multiplication is by longitudinal division. It is very refractory to stains, and the pink color obtained with Giemsa is supposed to differentiate it from other spirochetes. Metchnikoff and Roux point out that this can not be depended on and cite an instance. They found in the primary sore of a monkey a delicate pallida, typical in all but that it was stained clear blue. They inoculated a chimpanzee from this monkey, and later obtained spirochetes identical morphologically, but staining a pale rose with Giemsa from the same bottle. The writer has seen in a specimen taken from the gums of a non-syphilitic young man with pyorrhea alveolaris delicate spirochetes with long wavy curves which stained pink with Giemsa. Other thicker spirochetes in the specimen were stained blue.

The refringens is thicker, flatter, the curves are fewer and longer; ends may or may not be pointed; it is also motile, bending on its own axis or stretching out into almost a straight rod, and it may be caught by the fixing agent in any irregular position. It is easier to stain than the pallida and takes the blue of Giemsa.

The *Spirochaeta pallida* does not pass through an unglazed porcelain filter, and this may explain the findings of Klingmuller and Baermann, who got no results after inoculating themselves with filtered syphilitic virus. Schaudinn placed the pallida with protozoa after studying two parasites found in the blood of the stone owl. These appear in the stomach of the *Culex pipiens* as trypanosomes and spirochetes.

TECHNIC.

Mucous patches, condylomata, chancres and ulcerating surfaces should first be lightly scraped so as to get a little blood-tinged serum. The scrapings usually show no *S. pallida* and may show irregular forms of the refringens. Skin lesions should be well washed with absolute alcohol, a small incision made in the skin and the slide touched only to the drop of blood. Blister fluid may show spirochetes. Flexner finds that the pallida appears only after the vesicant has acted for many hours, and concludes that the spirochetes are not in the lymph spaces or they would appear sooner.

Enlarged glands should be aspirated with a large needle and powerful suction so that small pieces of white gland-substance may be found when the contents of the syringe are washed. These particles may contain spirochetes in enormous numbers. Blood should be taken carefully to avoid contamination from skin lesions and mixed with 10 parts of 0.3 per cent. acetic acid. Centrifugalize, make smears of the sediment and stain. Always make several specimens, as there are often very few organisms and these have a tendency to be all in one place.

Material to be examined unstained should be mixed immediately with a little normal salt solution and the cover-slip may be sealed. The pallida is very difficult to find this way, and the light must be well regulated. So many stains have demonstrated the pallida that I can not begin to describe them here. The Giemsa or azur stain is the surest and is easily used. The other

1. La Semaine Médicale, Jan. 3, 1906.

SOME OF THE SECTION OFFICERS.

1.—T. H. WEISENBURG, Philadelphia. Secretary Section on Nervous and Mental Diseases. 2.—WHARTON SINKLER, Philadelphia. Chairman Section on Nervous and Mental Diseases. 3.—WALTER L. BIERRING, Iowa City, Iowa. Secretary Section on Pathology and Physiology. 4.—CHARLES S. BACON, Chicago. Chairman Section on Obstetrics and Diseases of Women. 5.—LEWIS H. TAYLOR, Wilkesbarre, Pa. Chairman Section on Ophthalmology. 6.—THOMAS F. REILLY, NEW YORK CITY. Chairman Section on Pharmacology and Therapeutics.

SOME OF THE SECTION OFFICERS.

7.—W. J. BUTLER, Chicago. Secretary Section on Diseases of Children. 8.—DENSLOW LEWIS, Chicago. Chairman Section on Hygiene and Sanitary Science. 9.—W. SOHIER BRYANT, New York City. Secretary Section on Laryngology and Otology. 10.—W. C. HOLLOPETER, Philadelphia. Chairman Section on Diseases of Children. 11.—ROBERT F. WEIR, New York City. Chairman Section on Surgery and Anatomy.

stains are liable to be erratic, giving good results in one specimen and none in others. The Hastings stain, diluted the same as for blood films and used for 6 to 24 hours, has made the prettiest specimens in my collection; but I generally use the Giemsa in a 1:15 dilution, as its results are more uniform, it acts more quickly and the diluted stain keeps very well. The specimens are first hardened, 5 to 60 minutes, in absolute methyl alcohol and then left in the dilute Giemsa 1 to 15 hours.

Goldhorn uses a stain which acts in a few seconds and is said to give beautiful and uniform results. If this be true, it is the stain *par excellence*, as the searching of the specimens is often so tedious that one would gladly save time in the staining.

The Levaditi stain is probably the best for sections and is a modification of Ramon y Cajal's stain for nerve fibers. Several observers have traced their failures in not finding spirochetes in sections to delay in fixing the tissue. They conclude that a specimen is useless six hours after removal. This agrees with the fact that syphilis is so seldom contracted from fomites and cadavers.

PERSONAL OBSERVATIONS.

Ten cases of primary, secondary, tertiary and congenital syphilis and 8 controls have come under my observation. The following is a summary of the primary case:

CASE 1 (by courtesy of Dr. Peck).—Patient was a young man with a chancre on sheath of penis, much indurated and covered with a hard crust. This was softened, scraped, and smears showed no spirochetes after long and careful search. This chancre was excised, sectioned and stained by Dr. Oliver and myriads of pallidæ found. This case demonstrates the value of scraping deeply before taking smears.

The following were secondary cases:

CASE 2.—Man, aged 40, had large condylomata around anus. He had had some treatment. Smears from unwashed surface showed many of the refringens type, no pallidæ. Some spirochetes of pallida type were found, but midway in thickness between pallida and refringens.

CASE 3.—Man, aged 30, had extensive condylomata. Smears taken superficially showed many spirochetes of the pallida type; some of the refringens type. Pallida is frequently bent about the middle.

CASE 4.—Boy, aged 18, had very severe infection, condylomata, mucous patches, large tonsils, extensive skin eruption. Superficial scrapings from condylomata showed few of the refringens type; deep scrapings showed many pallida; mucous patches showed as many as six pallidæ in a field. Twenty injections of mercuric chlorid caused no diminution in the number of spirochetes of either type. The tonsils were removed with the guillotine, and juice from the depths contained no spirochetes of any kind. This was after about thirty injections, and it would be interesting to find if mercury causes a disappearance of the pallida in the tissues when it does not affect those on the surface of the body.

CASE 5.—Man, aged 35, had wart-like condylomata around anus. Few spirochetes of the pallida type were in smears. Ulcer at angle of mouth showed spirochetes of the refringens type and mouth spirillæ. This man had treatment for about four months.

CASE 6.—Woman, aged 25, had large chancroids of vulva, which appeared about same time as secondaries from previous infection. Smears showed spirochetes of both types and long, delicate threads, resembling those found in noma. These occasionally seem to have a tendency to form spirals and loops. Mucous patches in the mouth showed spirochetes of both types.

CASE 7. (by courtesy of Dr. Schmoll).—Superficial smears from mucous patches showed myriads of spirochetes of both types and a few spindle-shaped bacteria, described by some writers as associated with spirochetes.

The following is a summary of a late secondary case:

CASE 8 (by courtesy of Dr. Krotoszyner).—Typical punched out leg ulcers appearing two years after the primary sore. One specimen out of six showed a few typical spirochetes of both types. This case shows that one must take several specimens.

The following is a summary of a tertiary case:

CASE 9.—Patient was a woman. There were typical specific ulcers of legs. No spirochetes of any kind found.

The following is a summary of a case of congenital syphilis:

CASE 10 (by courtesy of Dr. Porter).—Infant, aged 4 months. The mother was syphilitic and the child had a mucous patch on tongue and snuffles. Swab from nose showed pallidæ.

The following were control cases:

CASE 11.—Pus was taken from large ulcerating carcinoma of the jaw. There were myriads of spirochetes as delicate as the pallida but irregularly twisted. Some were very long and straightened out into threads with a curve here and there.

CASE 12.—Epithelioma of hand. Discharge showed a very delicate spirochete resembling the pallida.

CASE 13.—Young man with no history or evidence of syphilis had marked pyorrhea alveolaris. Smears from gums showed at least two varieties of spirochetes, one of which resembled the refringens.

CASE 14.—In stomach contents from case of gastric cancer no spirochetes of any kind were found.

Two chancroids, one of penis and the other of the vulva, a vaccination pustule and pus from tubercular sinus showed no spirochetes.

CONCLUSIONS.

The spirochete was found in 7 out of the 10 cases of undoubted syphilis. Its absence in the smears from the chancres and one condyloma may be due to the smears having been taken too superficially. The tertiary ulcers were entirely negative. This agrees with the findings of other observers. The controls were negative except the carcinoma, epithelioma and pyorrhea alveolaris. These showed what may be several varieties of spirochetes, most of which are very delicate; some as delicate as the pallida, but none of them had the regular sharp bends. Occasionally one is seen which would puzzle an expert. They probably are saprophytes, as they can live in pus. The pallida soon disappears from pus. If the pallida is proved to be the cause of syphilis, doubtful lesions will be examined as sputum is now, but the diagnosis probably will never be as sure, especially in lesions in the mouth, or on the genitalia where other spirochetes are normally found. Even with the circumstantial evidence against the *Spirochaeta pallida*, its discovery now, in a doubtful skin lesion or genital ulcer would be a good point in the diagnosis. A great deal will depend on the experience of the observer, and to become skilled will take a great deal of time and patience, as the specimens are often few and far between. The *Bacillus lepræ* has been accepted on less evidence than has been brought forward for the *Spirochaeta pallida*.

It is dangerous to depend too much on morphology, and it has been suggested that the spirochete is a stage in the life-cycle of a protozoan; perhaps the Siegel flagellate and the *S. refringens* may be another stage of the same organism.

Some of the most significant facts pointing to the pallida being the cause of syphilis are:

1. Its practically constant presence in syphilitic lesions in their various stages.

2. Its constant absence in non-syphilitic lesions, contrary findings being doubted especially when the difficulties in diagnosis are considered; and the fact that the observers are all beginners in this field.

3. Its presence in the organs of congenital syphilis and in the placenta.

4. The fact that only the pallida has been found in the deep tissues of syphilitics.

5. Its presence in syphilitic monkeys and in the secondaries of apes even after passing the virus through these animals.

6. The retention of syphilitic virus by the unglazed filter, showing that the causative organism is not ultra-microscopic.

7. The presence of most spirochetes in the most infectious lesions.

8. The fact that the *Spirochæta pallida* seems to be morphologically more distinct as a species than the other spiral organisms.

9. The fact that it seems to be more highly differentiated as a parasite and soon disappears when removed from living tissues.

It would seem now that there is some analogy between dourine (mal de Cadéras) and syphilis. The former is a disease of horses and asses met with in the Mediterranean countries, transmitted by coitus and caused by the *Trypanosoma equiperdum*, which can pierce a healthy vaginal mucous membrane.

Much work remains to be done especially in the study of sections where there is not the confusion of secondary infections.

We may hope some day to understand the mysteries of hereditary syphilis.

The pallida has not yet been cultivated, and this is not likely to be easy of accomplishment on account of its marked parasitic tendency. It is significant, however, that the trypanosomes have lately been cultivated on human blood with 5 per cent., each, of sodium citrate and sodium chlorid. When this is done, we may hope for immunizing and curative sera which will cause the name of Schaudinn to be placed with those of Jenner, Behring and Pasteur.

City and County Hospital.

Special Articles

THE PHARMACOPEIA AND THE PHYSICIAN.

CHAPTER XXIII.

DRUGS ACTING LOCALLY ON THE SKIN AND MUCOUS MEMBRANES.

Local Anesthetics and Anodynes.

The introduction of cocain marked a decided advance in the production of local anesthesia.

Previous to that, freezing the part by immersion in a mixture of salt and snow, or shaved ice, or by spraying with ether or other volatile liquid, was used, and while a procedure of this kind does produce complete anesthesia, the pain experienced during the freezing and thawing greatly exceeds that which would be caused by such a simple operation as opening an abscess or the removal of a small foreign body, such as a splinter or piece of glass, when readily accessible. It is because of the inherent dread which the average person has of the surgeon's knife, that he will undergo suffering akin to that with which he is familiar, rather than endure a lesser one which seems dreadful because it is unfamiliar.

It is also true that the injection of cocain sometimes causes more pain than the operation for which it is given would, and, since surgical operations have become so much more common than they were formerly, many adults willingly bear the brief, sharp pain of a simple incision, rather than resort to cocain, which has come into a certain disrepute because of the abuse of it by its victims, the majority of whom have become such through the use of supposedly harmless nostrums pretending to be valuable remedies for hay fever and other minor affections.

Cocain, which is benzoyl ecgonin, shows a certain chemical analogy to atropin and aconitin, which resemble it somewhat in their action on sensory nerves, and it is also related to phenol through the benzoyl group, since benzoic acid differs from phenol only by having a COOH group in place of the OH of the phenol. The anesthetic action of phenol is second only to that of cocain.

Aside from the systemic effect, which we need not fully detail here, cocain paralyzes sensory nerve endings with which it comes in contact and even nerve trunks when in sufficient concentration; if the solution is sufficiently dilute and the action not too long continued, the nerve endings rapidly return to normal (the nerve trunk more slowly), when the application is discontinued and the cocain removed by absorption into the general circulation, or evacuated.

When a fairly strong solution, 3 per cent., is injected into the area about a nerve trunk, or an even weaker solution, 2 per cent., within the nerve sheath, both sensory and motor paralysis occur in about fifteen minutes, affecting, of course, the entire distribution of the nerve; the effect lasting for some hours after intraneural injection.

Since aqueous solutions are not absorbed from the unbroken skin, they must be injected beneath the epidermis, at least, in order that they may come into actual contact with the nerve ends.

When the solution is injected deeply into the muscular tissue the greater part of it passes into the general circulation and is lost so far as local action is concerned. To avoid this, it is better to inject the solution between the layers of the skin, at the same time limiting the circulation in the part as much as possible by compressing the blood vessels, preferably with a rubber band or other tight bandage.

Practically, the same object may be achieved by the use of a solution of the alkaloid of the suprarenal gland immediately preceding the injection of the solution of cocain. The injection of the solution of suprarenal alkaloid (epinephrin, adrenalin or one of the other trade preparations) causes a local vasoconstriction that in turn prevents the rapid absorption of the cocain solution into the general circulation, and also prevents, for the time being, the excessive hemorrhage that is so objectionable in minor operations. When it is necessary for the solution of cocain to diffuse through a part, a moment should elapse after the injection before applying the constricting bandage.

The combined use of suprarenal alkaloid and of cocain has proved to be of particular advantage in the eye and in the nose. One reason, and probably the most weighty one, is to be found in the fact that normal mucous surfaces have a tendency to absorb cocain very rapidly.

When cocain is applied to mucous membranes, either in powder or in solution, it causes its local effects for a short time and is then absorbed, producing its systemic action. Herein lies one of the chief sources of danger of the many so-called hay-fever remedies, which virtually consist of cocain with some diluent powder, such as sugar of milk, and are intended to induce and to continue the truly terrible cocain habit.

Owing to the brief action and rapid absorption, frequent repetition is necessary to secure relief in "colds" and the user is peculiarly liable to become addicted to the habit which, in its baneful effects, is not exceeded perhaps, in the whole range of drug addiction, not even excepting alcoholism. As a matter of fact, many of the so-called hay-fever nostrums are intended primarily for supplying those who are already victims of the habit and who would find difficulty in buying the drug under its real name. This practice may be said to constitute a disgraceful example of the lack of control of the nefarious nostrum traffic by the law.

We should be particularly careful to warn patients and others against the insidiousness of this type of self medication that our skirts may at least be kept clean in connection with this one phase of the evil.

Cocain in solution is readily decomposed on boiling, but if the solution be made with sterile, cold water there will be little cause to anticipate sepsis from its injection, with the usual precautions. The solution may be sterilized, however, by heat-