and night, in winter weather. Most of the cases of bronchopneumonia and many of the lobar forms in feeble infants did not do well under this management, which was discontinued after several months' trial. The aim is now to have a steady supply of fresh, outside air delivered into a ward that has been moderately warmed, which has proved more satisfactory.

If better results are to be obtained in the hospital treatment of pneumonia in infants, efforts must be made in two directions: 1. We must try to have them admitted earlier. 2. Patients must be promptly discharged as soon as resolution has taken place. If home treatment is impossible, the baby should be sent to the hospital when the disease is first recognized, before bad feeding, poor air and faulty hygiene have lessened the chances of recovery. Dispensary doctors, social workers or visiting nurses can do effective work in this direction. If the baby is moribund, with few hours to live, it had better be kept at home rather than have the last moments made uncomfortable by transit. Some of my patients were in this condition when admitted. A very wide experience has taught me that sick infants, especially those having pneumonia, should not be retained in hospitals any longer than is necessary to get over the acute symptoms. If kept too long, there is constant danger of relapses and reinfection. While this can be guarded against by careful nursing in small, well-ventilated wards, as a rule the babies recover much quicker outside of an institution. It is most difficult to avoid various secondary and cross infections in weak infants who are collected together in one place. My plan is to remove these infants from the hospital as soon as the acute symptoms have subsided and board them out in private homes in the country under the constant supervision of a doctor and nurse who are paid for this work. Only in this way have I been able to prevent many relapses, and make permanent the work of cure in babies who have been sent to the hospital from homes of ignorance and poverty.

51 West Fifty-First Street.

ABSTRACT OF DISCUSSION

DR. F. C. NEFF, Kansas City: In the paper Dr. Chapin spoke of the importance of the feeding in these infants with pneumonia. During the past two years I have had occasion to employ wet nurses in the feeding of certain infants suffering from pneumonia, babies that had previously done perfectly well on the bottle. Because of the seriousness of pneumonia in infancy, I believe that breast milk increases the chances of a favorable outcome.

Egyptian Medicine.—The Egyptians were probably the most healthy people of history. Herodotus spoke of them as the healthiest nation, and Diodorus said that from the king to his humblest subject the mode of life in Egypt seemed as if ordered by the physician rather than the lawyer. The Egyptians stayed off disease by a reverent attention to the vitality of the body. They were the first people to master the question of antiseptics. By cassia, frankincense, and myrrh they preserved the body from microbes of dissolution. But whether it was that their vitality shielded them during life from notable microbic attack or some other reason prevailed, they confined their use of antiseptics to the preservation of the dead from dissolution and not the living from disease.—G. T. Wrench: Lord Lister, His Life and Work.

THE ETIOLOGY AND TREATMENT OF OZENA

A PRELIMINARY REPORT *

HENRY HORN, M.D.

SAN FRANCISCO

Just before the outbreak of the European war in July, 1914, Guggenheim of St. Louis, Murray of Minneapolis, Glogau of New York, and I embraced the opportunity to study, in the private laboratory of Hofer of Vienna, his work on the etiology of ozena.

His positive statements that the *Coccobacillus foetidus ozaenae* of Perez was the true and only etiologic factor in this disease, and his enthusiasm over the results of treatments by vaccines under Kofler in Chiari's clinic led us all to the determination to investigate this matter on our return to America.

As is well known, the superficial observation which is afforded the onlooker in a large clinic, where a series of cases — perfectly familiar to the experimenters, but new to the observer — is shown, is extremely unsatisfactory, and any personal conclusions are therefore unfair to the series under observation. The brilliant cases are shown, the poor cases usually slighted. Even daily observations of crust formations and degree of fetor vary greatly with different observers, and the detailed report of cases made by Hofer does not convey the same impressions as a similar but smaller series would to the personal observer.

To read the articles which Hofer has published, one would conclude that all the work has been a steady progression toward the desired end. Such is not the case, because in conversation with him, and with others in Vienna, who are familiar with his work, many difficult obstacles have had to be surmounted.

It is not fair, therefore, to the general medical public and to the specialists of America, to give the impression that the millenium in the treatment of ozena has arrived, that the isolation of the etiologic organism is easy and that the preparation of the vaccines is a matter of routine. Such is far from being a true statement of the case, and any one who empirically treats all cases of ozena with vaccines made from subcultures of strains furnished by Hofer is doomed to bitter disappointment.

It is the object of this paper to sound a note of warning and to make some suggestions, which are the result of constant experimentation along these lines during the last twelve months.

If we can presently put into the hands of the medical public a specific for this dreadful disease, it will almost rank in value with the discovery of the antitoxin of diphtheria.

True, it is not a matter of saving life; but those of us who have treated the victims of this most disgusting of all diseases which afflicts otherwise normal individuals know that the gratitude of these patients for a restoration from their former social ostracism is as great as the gratitude of the mother whose child is restored to health.

In debating this subject let us ask ourselves the following questions:

1. Is the Perez bacillus the true and only cause of ozena?

* Read before the Section on Laryngology, Otology and Rhinology at the Sixty-Sixth Annual Session of the American Medical Association, San Francisco, June, 1915.

2. Has not the undoubted cure of certain cases with vaccines made from the Perez organism and the undoubted failure to cure in other cases, clinically similar, weakened our concept of the clinical entity of clinical ozena?

3. Is it not possible that cases of ozena clinically identical may be cured by several different vaccines?

4. Shall we not have to revise somewhat our clinical classification of ozena?

5. Is the information already at hand sufficient to enable us to produce a successful vaccine?

A close analysis of the literature, already put out by Hofer, would seem to indicate that the questions just enumerated have all been answered. Such is not the case. During our laboratory work with Hofer he constantly reminded us that the isolation of the organism was an exceedingly difficult task; that it had taken him several years to gain his present results, and that many of his vaccine experiments for one reason or another had been failures.

It is also possible that in the short time which we spent in his laboratory many essential details were overlooked.

First, then, it seemed logical to repeat some of his principal experiments on rabbits with the cultures furnished by him, and I present for consideration a series of rabbits' heads prepared in Kaiserling solution and mounted in glycerin.

The necropsies were made as soon after death as possible, usually within two or three hours. Animals which had to be killed were struck across the base of the skull in order to obviate any congestion of the nose due to the administration of chloroform or ether. The heads were first skinned and the skull sawed through exactly in the median line, so that the saw split apart the two upper incisor teeth. The lower jaw was not saved. The skull was opened like a book and usually one nostril was found completely closed by the septum while the other side was free. The closed side was opened with a sterile knife, and any bacteriologic examination could then be made without fear of contamination.

The method of dosage was as follows: An ordinary agar slant was freely inoculated with a platinum loop of pure culture of the growth to be experimented on. This was incubated for twenty-four hours, and then 10 c.c. of sterile physiologic salt solution added and the growth brought into a suspension. The dosage was taken from this suspension and injected into a vein of the ear.

EXPERIMENTS WITH RABBITS

RABBIT 1.—Hofer's original cultures, Strain M. Oct. 17, 1914, Injection 1, 0.5 c.c. of live culture. October 23, Injection 2, 1.5 c.c. of live culture. October 30, rabbit killed.

Necropsy.—General necropsy negative. The anterior turbinate on each side distinctly but slightly congested as compared with the posterior turbinates.

RABBIT 3.—Hofer's original cultures, Strain M. In this experiment the pure cultures were transferred directly to the given amount of water and injected as follows: Oct. 23, 1914, Injection 1. One loop of pure culture added to 5 c.c. of water, and 1 c.c. of this suspension injected. October 27, Injection 2. Two loops of pure cultures added to 5 c.c. of water, and 1 c.c. injected. November 4, Injection 3. Three loops of pure cultures added to 5 c.c. of water, and 2 c.c. injected.

Necropsy.—Nov. 23, 1914, general necropsy negative. Anterior turbinate congested with small strings of whitish pus throughout. In left anterior turbinate, collection of whitish pus pockets. No marked atrophy. From this pus a polymorphous gram-negative organism was obtained which

answered all the microscopic characteristics of the Perez bacillus but gave no distinct odor. Agar slants inoculated with heart blood of this animal remained sterile after twenty-four hours' incubation.

RABBIT 5.—Weight, 3,195 gm. Hofer's original cultures, Strain M. Nov. 20, 1914, Injection 1. Six loops from original pure cultures in 1 c.c. of water, and injected. November 25, weight 2,860 gm. Loss, 335 gm. in five days, marked loss of appetite. Rabbit has marked snuffles; does not move about. Apparently quite ill. Injection 2: Agar slant inoculated freely from original cultures and grown for twenty-four hours. One c.c. added and emulsion made. This entire emulsion used as injection. November 27, weight, 2,620 gm. December 17, rabbit has regained some appetite and runs about cage. Still very thin. December 23, 5 c.c. of water added to subculture grown on agar through four generations. Injection 3: 2 c.c. of the foregoing injected. Feb. 23, 1915, rabbit died. Very thin, large ulcerations on hind legs and around rectum.

Necropsy.—General necropsy negative. Marked atrophy of posterior turbinate with deposits of pus. Anterior turbinate congested, somewhat atrophic.

RABBIT 9.—Hofer's original cultures, Strain G. Five c.c. of salt solution added to twenty-four-hour growth on infusion agar. Dec. 16, 1914, Injection 1: 2 c.c. of the foregoing. December 30, rabbit died.

Necropsy.—Rabbit very thin. Entrance to nose blocked with pus. Necrotic areas in lobes of ears. General necropsy negative. Intense congestion in anterior turbinates. Very little free pus. Posterior turbinates dark brown.

RABBIT 10.—Cultures isolated by Dr. Klenk, Minneapolis. Five c.c. added to twenty-four-hour growth on plain agar. Dec. 15, 1914, Injection 1: 2 c.c. of the foregoing injected. December 15, rabbit died twelve hours after injection.

Necropsy.—General necropsy negative. Anterior turbinate intensely red and congested, with dark red patches in middle turbinate. Posterior turbinate red and angry looking, with small area of intense congestion. Blood taken from heart and grown in Rosenau's glucose and agar tubes shows many small colonies of gram-negative, small fairly constant cocci.

RABBIT 7.—This rabbit was injected with killed organisms of the original Hofer strain for the purpose of producing an agglutinating serum. Five c.c. of salt solution was added to twenty-four-hour growth on agar and killed by heating in water bath to 68 C. for one hour. Dec. 7, 1914, Injection 1: 2 c.c. of the foregoing. December 17, Injection 2: 3 c.c. December 23, Injection 3: 4 c.c. Jan. 2, 1915, rabbit died.

Necropsy.—General necropsy negative. Both anterior turbinates at anterior and posterior pole intensely congested. Middle portion pink. Posterior turbinates somewhat atrophic. Some free pus in nose.

RABBIT 6.—Experiment exactly the same as in Rabbit 7. Nov. 27, 1914, Injection 1: 1.5 c.c. of the foregoing killed organisms. Immediately after injection, the rabbit showed evidences of lung embolism or infarct and seemed about to die, lay on side, was unable to stand. Partial recovery after several days. December 7, rabbit killed. Very thin, congestion of the left lung. Eyes almost closed with pus. Some secretion in nose. Nose, right side: Anterior turbinate pinkish, very dry, no secretion. Posterior turbinate dark brown, no secretion. Left side: Posterior turbinate intensely congested and filled with fresh blood clot. Posterior end of the anterior turbinate intensely congested and filled with blood clot.

COMMENT

Other series of rabbits were inoculated with killed cultures exactly after the method employed by Hofer, but up to the present time, I have been unable to obtain an agglutinating serum.

The rabbits did not lose weight during these experiments, and the appetite remained good. Various changes were made in the dosage, length of time between injections, etc., but the serum obtained would agglutinate neither with Hofer's original cultures nor

with the cultures made from undoubted clinical types of ozena.

We can only conclude then, that the intravenous injection of live cultures in very large doses will kill rabbits in from twelve to twenty-four hours, the only necropsy finding of any consequence being the selective action of the organism on the mucous membranes of the turbinate bones of the nose.

In smaller doses, intense congestion, first of the anterior turbinate and later of the posterior turbinate, can be brought about. If this process is allowed to continue, pus forms in and about the turbinated bodies, finally entirely blocking up the nares.

In some of the rabbits which withstood the large doses for a comparatively long time, marked atrophy of the turbinates was noted. The amount of congestion seems to vary with the size of the dose and the virulence of the strain. Thus, in Rabbit 10, prepared from a strain isolated in America and from which comparatively few subcultures had been made, the greatest effect was seen.

Naturally, this series is far too small on which to base other than confirmatory evidence. Many side lines of experimental study presented themselves, and these are now being carried on.

DETAILS OF THE WORK

With the exception of a short article by Guggenheim, nothing has appeared to my knowledge in English concerning these investigations, so that it might be well briefly to review the details of Hofer's work before we pass to the therapeutic use of the vaccines.

The subject of the etiology of ozena has been worked on for years by different observers in various parts of the world. As is well known, the disease is far more common in Europe than it is in America. The international investigation which was started two years ago by Mayer fell flat in the United States, probably because the men saw so few cases that they had very little interest in the subject.

Every specialist, however, has one or more such cases a year, and as a usual thing, a general lack of knowledge on the subject, combined with the general pessimistic view of the results of treatment, causes him to slight or probably not treat the case at all. Such an attitude is now no longer defensible. In properly prepared vaccines we have a potent factor in our hands for vast improvement. We can promise not only that the odor will disappear but also that the formation of crusts will be reduced to a minimum.

In this paper all other forms of atrophic rhinitis, syphilis, tuberculosis, etc., will not be mentioned. We are dealing only with the typical clinical picture of ozena, which is familiar to all rhinologists.

Stripped of all unnecessary details, the method of isolation is as follows:

A crust is taken from the nose, preferably at the anterior end of the middle turbinate. This is dropped in a bouillon tube and incubated for exactly twelve hours. This period of incubation is a very important point, for it has been found that a lesser period does not give the organisms time to grow, and an incubation of more than twelve hours causes such an overgrowth of the accompanying organisms that isolation of the Perez bacillus is impossible.

At the end of twelve hours, one drop from this bouillon tube is spread over from three to five agar Petri dishes. These are incubated for twenty-four hours, and then the separate colonies are fished and transferred to agar slants.

In fishing for the colonies a great deal of experience and judgment is necessary, those conforming to the characteristics of the staphylococcus, *Micrococcus catarrhalis*, streptococcus, *Bacillus proteus* and other well-known forms are not transferred. There is nothing characteristic about the colonies. They are usually small, moist and transparent.

After twenty-four hours on agar slants, a characteristic odor is usually developed by which the organism can be fairly well identified. There is also nothing characteristic of the slant growth, the pure culture looking much like ordinary staphylococci. The presence of a marked odor is very variable. It is not the marked sickening odor of ozena in the patient, but a milder, though still characteristic odor.

The final test of agglutination, which Hofer says is simple, has not proved so, either in my hands, or in the hands of several trained bacteriologists.

I have followed out exactly the technic of Hofer, as well as several other details suggested by bacteriologists who have been interested in my work, but so far I have been unable to secure any satisfactory agglutinating serum even in very small dilutions.

The cause of this failure I am unable to explain. It is possible that the subcultures which were made from the original Vienna strains were so attenuated that they had no effect on the rabbit. Agglutinating serums prepared from our own cases are now being experimented with, but so far no definite conclusions can be drawn.

The injections of these organisms into the rabbit and their subsequent recovery from the nose I have been repeatedly able to carry out, and these experiments seem free from criticism.

TREATMENT

This, then, brings us to the most important part of the subject, namely, the treatment. One fact stands out without question, and has been proved so often that it needs no support. Cases which clinically would be classed as true ozena have been vastly improved temporarily and possibly permanently by the administration of several of the stock vaccines on the market, which usually contain the Friedländer bacillus, *Micrococcus catarrhalis*, pneumococcus and streptococcus.

This may raise two points: 1. Is ozena possibly a mixed infection? 2. Are there certain types which cannot be clinically differentiated and of which the Perez bacillus is not the etiologic factor? It would also seem possible that some of our many failures are due to the fact that the growth of the various extraneous organisms in the nose are for the moment more important than the Perez bacillus and that perhaps our results would be better if we preceded the treatment by the use of a stock mixed vaccine, to be followed in turn by a vaccine made from the Perez organism or possibly, as we are now considering, a combination of the Friedländer bacillus, *Micrococcus catarrhalis*, pneumococcus and streptococcus, with a vaccine made from the mixed strains of the Perez bacillus.

In this paper I am not going to quote histories of cases treated with the stock mixed vaccines. I am, however, going to report a few cases in which the Perez vaccines were used which tend to show, although they do not prove, the great value of this remedy in the treatment of ozena. What I do particularly want to show are the sources of error which may creep in and which are to be avoided.

The detailed report of Hofer's cases would lead one to suppose that there is nothing more to be desired.

My experience in America and the experience of two or three others leads us to suspect that either we are not in possession of full details or that our technic has not been developed to the highest possible point.

It should also be remembered that in the series of unbroken successes which Hofer reports, nothing is said of the possibility of recurrence after the treatment has been stopped. Judged by our small experience, this is something which must be very carefully considered but which does not in any way mitigate against the value of the treatment. In other words, my position is this, that although I admit the fact that the investigations of Hofer are practically free from criticism, I am not at all certain that cures from the vaccines as used by him will prove to be absolute and permanent.

In spite of the fact that the preparation of autogenous vaccines in these cases is a very difficult thing, it will probably prove that this is the only method by which we can be certain of a good result. Hofer himself mentions this fact in his last article, but very truly adds that in clinical practice this is an impossibility. He also makes the point, which we have also proved to our satisfaction, that in cases which clinically are undoubtedly ozena, we are unable to isolate the Perez bacillus, but an administration of the stock Perez vaccine will either cure or greatly improve the case. This simply proves that there are certain bacteriologic conditions over which we at present have no control.

The method of administration of the vaccines as worked out by him in his last article is of great importance and covers the ground so completely that I have nothing of value to add.

Most of the vaccines used by him in his clinical work are made from seven or eight different strains, to which has been added one strain of the Perez bacillus which occurs normally on the mucous membrane of the nose of dogs.

The various strains vary extraordinarily and are difficult to preserve. They must be carefully protected from heat and light. For the best results, careful watch must be made for the constitutional symptoms, which are less marked with old vaccines than with those freshly prepared.

The clinical manifestations are the best guide to dosage, and a period of at least one week should intervene between injections. The dose varies with every vaccine and every patient. An initial dose of 50 million, doubling until the proper constitutional symptoms develop, is about correct.

The general reactions are rise of temperature, loss of weight, malaise and vomiting. The local reactions are redness and swelling around the injection and swelling of adjacent glands. Symptoms referable to the nose are coryza, free discharge from the nose, sensations of heat and fulness over the bridge from the mucous membrane.

These local reactions in the nose are what we should endeavor to produce if the full effect of the vaccine is desired. As a usual thing, the patient is instructed not to douche the nose until it becomes absolutely necessary; in this way, a good idea of the amount of improvement can be gained.

Notes should be kept on: (1) the intensity of the odor; (2) condition of the accessory sinuses; (3) condition of the crusting, and (4) the improvement in subjective symptoms.

The improvement is usually noted by the patient after the first dose. The parents notice the improve-

ment in the degree of odor. The crusts blow out more readily, and the feeling of tightness across the forehead is improved. From five to fifteen injections are considered necessary for a complete cure, and the patient must be carefully watched for a relapse, when the treatment should again be instituted.

I give below a few typical case histories which show the undoubted beneficial effects of the vaccines. None of these patients do I consider cured, but the marked improvement warrants one in continuing treatment.

CASE HISTORIES

CASE 1.—M. G., woman, aged 19, family history negative, had odor and discharge from nose for thirteen years. Both nasal spaces very large with great atrophy. Large greenish foul-smelling crusts over entire nose, especially at anterior end of middle turbinate. Ethmoids opened. Six months' treatment with ordinary autogenous vaccines without improvement. Dionin treatment of no avail. A proprietary mixed nasal stock vaccine used three months without any improvement. Starting April 1, 1915, Perez vaccine of mixed strains used for twelve injections with vast improvement. Some slight crusting and slight odor still perceptible. Subjective improvement well marked. Patient well satisfied. Cultures from nose demonstrated Perez bacillus in typical form.

CASE 2.—M. Z., woman, aged 32, Hungarian. Typical ozena since childhood. Treated for years in European clinics without improvement. Typical ozena, fully developed atrophy, horrible stench. Perez bacillus demonstrated. Two injections of 100 million caused odor to almost entirely disappear. Patient lost from sight.

CASE 3.—S. P., woman, aged 27, German, first seen in 1912, family history negative. Typical ozena with pansinusitis. Treatment for three years by surgical means. All sinuses opened, including right Killian with great improvement. Odor and crusts would not improve. Pus condition 50 per cent. better. Stock mixed vaccines used over period of months as well as autogenous vaccines with slight success. Principal complaint, blinding headaches and odor. Treatment with autogenous vaccine of Perez bacillus showed immediate and profound improvement. No odor at any time, no crusts, headaches entirely gone. Patient washes nose once a week, formerly twice a day. Case considered cured.

CASE 4.—J. M., boy, aged 9 years, Spanish, complained of frontal headaches and odor and crust blocking from right side. Examination of mother shows typical ozena, brother two years younger also typical ozena. Has always played with dogs. Examination of right side reveals profound atrophy, greenish crusts on middle turbinate, odor foul. Left side free. Perez bacillus isolated in pure culture. Treatment over three months with a proprietary mixed nasal vaccine shows some improvement but odor always the same. Perez vaccine, mixed strains begun April 10 and continued to present time. Some improvement in odor, great improvements in crust formation. Headaches gone. Still under treatment. The improvement with the Perez vaccine greater than with any previous form of treatment.

CASE 5.—H. M., boy, aged 8 years, brother of J. M. History exactly the same. Nasal condition clinically identical except the left nostril is involved. Could not isolate the Perez organism. Even very small doses produce violent headaches, high temperature, vomiting and malaise for several days. Improvement slight, if any. Probably Perez bacillus not the only organism involved. Still under observation.

CASE 6.—M. deV., girl, aged 16 years, of Italian parentage, had negative family history. Odor very disagreeable to family. Headaches especially in frontal region. Right side large greenish foul-smelling crust blocking entire nostril. Perez organism not yet isolated. Marked improvement after second injection. Treatment for three months. Improvement very marked. Crust almost gone. Odor disappeared. Just returned after two weeks' absence with marked odor. Patient still under treatment.

CONCLUSIONS

I think we are in a position to admit the following facts:

1. The *Coccobacillus foetidus ozaenae* Perez, as isolated by Hofer, has answered all the bacteriologic requirements necessary to establish its identity as the etiologic factor in ozena.

2. The isolation of this organism is attended with considerable difficulty.

3. The production of agglutinating serum in rabbits is an exceedingly difficult task.

4. The preparation of autogenous vaccines in every case is very difficult, if not impossible.

5. At present mixed vaccines made from various strains of Perez bacillus is the most practical method of treatment which is now available.

6. It may be necessary to precede or combine with the treatment the vaccines made from the organisms which are usually present in combination with the Perez bacillus.

7. It may be possible that there may be two or more types of ozena bacteriologically different but clinically identical.

209 Post Street.

ABSTRACT OF DISCUSSION

DR. W. T. CUMMINS, San Francisco: I can discuss Dr. Horn's paper only bacteriologically. I had the opportunity a year ago of hearing a paper on ozena in Vienna, and I made several interrogations relative to the bacteriologic side of it. I must confess that a certain amount of skepticism was engendered at that time, but at least a part of it has disappeared since knowing of Dr. Horn's work and hearing his paper. There is one rather inharmonious point, I might say, in the lack of agglutination in Dr. Horn's work compared with that of Dr. Hofer. It is rather remarkable if they have the same organism. We know that some organisms are not capable of producing agglutinins in the animals injected. The rabbits injected by Dr. Hofer showed agglutination, and if Dr. Horn had used a larger number of animals it is possible that some agglutination might have been demonstrated.

There is one point that engendered a certain amount of skepticism in my mind, although it may not be important, and that is the subject of pleomorphism. There are certain organisms that are pleomorphic, and it is said that this organism may be rod-shaped or coccoid. This condition is noted with a few intestinal bacteria. It seems that this organism of ozena belongs to the Friedländer group, to which the bacillus of rhinoscleroma is presumed to belong. There is one very strong point indicating the specificity of this organism, and that is the localized reaction in the nose after intravenous injection in rabbits. Dr. Horn's specimens certainly show well-marked nasal lesions indicating selective bacterial activity. I must say that the technic is quite laborious, and I agree with Dr. Horn and the other gentlemen who have worked it out that the ability to detect the odor, and the tedious fishing of colonies from the original plates require an unquestionably long time. I am glad to state that my original skepticism has been somewhat modified, but I still possess a certain degree of it relative to the etiologic position of this organism in ozena.

DR. GEORGE H. WILLCUTT, San Francisco: I had the opportunity in Vienna of seeing some of the work done along this line by Dr. Kopfler in the Chiari Clinic. I can agree with Dr. Horn that many cases were not benefited; in fact, only about 50 per cent. showed any improvement, and in that 50 per cent. there were many relapses. The bacteriologic examinations made by Dr. Hofer showed the *Bacillus mucosus*, *sarcinae*, and the *Coccobacillus foetidus ozaenae*, and at that time he was not sure that the condition was due to the coccobacillus alone. He made a suspension, as Dr. Horn has very well explained, and began his injections with

about sixty millions, increasing the amount weekly until he reached about six hundred millions. Following the injections he would at times find local reactions and also a general reaction occasionally. One of the local signs Dr. Horn failed to mention was the increase of the odor in a number of cases. The odor was markedly increased in some cases after the first injection. The pharyngitis which is usually present in these cases showed improvement before the nasal condition, and after one or two injections disappeared in most of the cases. Kopfler injected some patients fifteen or twenty times, while others showed some improvement after a few injections, and control examinations made two or three months later showed improvement in the local condition, the crusts having disappeared; there was more discharge from the nose and the mucous membrane was more normal. However, 50 per cent. of the patients treated did not show a cure.

DR. WILLIAM R. MURRAY, Minneapolis: The etiology of ozena is a subject that has been of great interest to the medical profession for many years. Lowenberg, Fraenkel, Paulson, Hajek, Abel, Perez, and others have described micro-organisms which they have considered the cause of ozena. The importance of this subject was emphasized in 1911 when an international collective investigation of ozena was begun under the direction of Prof. Alexander of Berlin. This committee is engaged in studying the researches of Perez, who in 1899 described an organism which he believed to be the cause of ozena. Perez's findings have recently been confirmed by Hofer of Vienna.

A year ago I obtained a culture of the Perez bacillus from Dr. Hofer and what work I have done, in association with Dr. Larson, university bacteriologist, has been in connection with the use of a Perez vaccine and an effort to confirm the laboratory findings of Hofer. We have examined, bacteriologically, thirty-eight cases of atrophic rhinitis. Crusts were planted in broth and on agar plates. In no instance was the bacillus of Perez isolated. Agglutination tests were made in thirty-four cases. The serum was tested out in dilutions of 1:100. There was not one frank positive agglutination reaction obtained. Twenty-four rabbits were injected intravenously with cultures from the crusts of patients. Fifteen of these rabbits died. At necropsy a streptococcus, staphylococcus, bacillus of Lowenberg, proteus, pyocyanus and coli bacillus were isolated. The Perez bacillus was not obtained either from the heart's blood or the nasal mucosa. The bacillus of Perez, obtained from Hofer, was injected intravenously into a number of rabbits. It was found to be nonpathogenic for adult rabbits. The bacillus was not found in the nasal passages. Seven suckling rabbits were injected with the same organism and the Perez bacillus was isolated from the heart's blood and nasal mucosa. The organism, which had thus passed through a young rabbit, was found to be pathogenic for adult rabbits. At necropsy it was found that the nasal mucosa was highly injected. It was ascertained, however, that the nasal cultures were positive only in those cases in which the heart's blood was positive.

Our bacteriologic evidence against the Perez bacillus being the cause of ozena is: (1) in thirty-eight cases examined, we were not able to isolate the Perez bacillus; (2) in thirty-four cases, we were not able to obtain an agglutination reaction (3) of twenty-four rabbits injected with mixed cultures from crusts, none showed the Perez bacillus.

Clinically about twenty cases of atrophic rhinitis were treated with vaccines (Perez). Of these cases, twelve (true ozena cases characterized by advanced bilateral atrophy, large greenish crusts and a fetid odor) were observed for a period of from three to eight months. Vaccines, obtained from two strains of the Perez bacillus, were administered at intervals of seven days in doses from 50,000,000 to 500,000,000. In a few of the cases there was clinical improvement, the odor disappearing, the crusts becoming smaller and more easily expelled and atrophic pharyngitis showing improvement. Other cases did not show any objective or subjective evidence of improvement, and in no case could it

be considered that a cure was effected or that there was a permanent disappearance of crust formation.

DR. HENRY LEWIS WAGNER, San Francisco: I would like to ask whether the infarcts had been found in other parts of the body, and where, if other animals had been utilized outside of rabbits? The first man who made a bacteriologic examination of ozena, did so in a laboratory under my supervision in the University of Witzbach, and he then discovered the polymorphous condition of the germ; but in those days—it is now practically twenty-seven years ago—the condition now recognized was not understood, and I am very much interested and have followed it, although I personally have remained rather skeptical. There were a woman and two children, boys I think, in our clinic, but I recall that one boy only showed the characteristic sign of malodor; the mother as well as the other boy showed no sign whatever of the so-called ozena odor, and I think certainly there is no question that the mother as well as one boy should not be included. I have seen these children, and certainly there is no question that all three of them have been benefited.

DR. H. W. LOEB, St. Louis: It seems to me that while work is being done at present, we are still up against the same proposition, whether or not the organism discovered is saprophytic or pathogenic. I should like to ask Dr. Horn if he discovered crusts in the rabbit's nose, and also if he has been able to isolate the Perez bacillus from the nasal discharge. Looking over the various developments in the treatment of ozena in the past twenty years, it seems to me that after all we have achieved more by relieving the nose of the discharge and of the consequent saprophytic changes than by any other plan of treatment. I feel, however, that while we must remain somewhat skeptical, we should be thankful that Dr. Horn was able to make a positive reaction in the mucous membrane of the rabbits.

DR. HENRY HORN, San Francisco: I think that the discussion has brought out the point which I made, that the value of the treatment will be determined by our personal experience. Any one who has read the last article of Hofer in the *Archives of Laryngology* would say that it was exceedingly optimistic. This is the general impression concerning his work, and his enthusiasm during our stay in his laboratory was pronounced. Dr. Willcutt was in Vienna during preliminary stages of this work and he knows that Hofer had just as many obstacles to overcome as we have. In reply to Dr. Loeb's question, I can say that in all the rabbits injected with the original Hofer cultures we recovered the Perez bacillus in the nose. We also recovered it in the heart's blood by the Rosenau method. Regarding the pus in the nose, I have seen a large collection of pus pockets, but no crusts have been seen. I have never noticed odor in the nose of a rabbit, and I do not think that Hofer claims this; but he does claim crusting and atrophy. The point that Dr. Loeb made, that the removal of the saprophytes is a long step toward a cure, is undoubtedly true, and is exactly the point I made. As far as I can see, in the twelve cases I have handled, I have seen as good results with stock nasal vaccine as from the Perez vaccine. As regards the infarcts, I have seen none. Hofer claims there are no changes at necropsy other than the local change in the nose.

Leaders in Rural Sanitation.—It is conceded that among rural people leadership is notably lacking; there is no organization which can be relied on and no idea of social responsibility. Who then can lead in a movement for betterment? The county health officer and the doctor. It is within the authority of the health official to demand certain requirements in the interest of public health and for the protection of the individual. Health work touches intimately the family life in every phase; and it is so personal in many aspects that one with authority like the health officer, or with influence such as the physician has, can teach acceptably and by practical application just what the farmer, his wife and children need to know.—Oscar Dowling. *The American Journal of Public Health*, May, 1915.

A NEW METHOD FOR THE PROPHYLACTIC APPLICATION OF TETANUS ANTITOXIN *

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It has become a fact well established by both clinical and experimental observations that, in the large majority of cases, administration of tetanus antitoxin at the time of, or shortly after, infection by tetanus spores will prevent the development of tetanus. The almost uniformly successful results obtained for a number of years in cases of Fourth of July injuries in the United States have proved conclusively the value of the prophylactic use of tetanus antitoxin.

The present European war has, however, emphasized another phase of the tetanus problem which demands consideration. The routine administration of antitetanic serum to all wounded soldiers is now a fairly general practice both in Germany and in France. In spite of this, owing to the conditions governing the care of the wounded in war, cases of tetanus continue to occur (1) in those soldiers in whom the prophylactic injection has been accidentally omitted, and (2) in those in whom the injection of antitoxin has been delayed until one, two or even more days have elapsed after injury. The occurrence of isolated cases of tetanus in these two groups has tended, in the minds of many European physicians, to cause doubt as to the efficacy of prophylaxis against this disease.

To overcome the delay in administration, it was evident early that some more simple method of application of antitoxin was desirable. The subcutaneous injection of liquid antitoxin, immediately following an injury, manifestly is not a procedure that can always be carried out.

Methods previously proposed to meet this objection, the powdered antitoxin of Calmette, the local applications of liquid antitoxin advocated by Suter, and the rubbing into the wound of antitoxin salve as recommended by Bockenheimer, for reasons which will be discussed in a later article, did not appear to be satisfactory.

Accordingly, after experiments with various methods of local application, the following was found to fulfil best the requirements: Liquid antitoxin was poured on pads of sterile absorbent cotton in such amounts as to render the cotton uniformly moist but not wet enough to drip. These pads were then dried for twenty-four hours in a moderate heat (from 40 to 45 C., 104 to 113 F.). A previously sterilized evaporating dish or earthenware mortar, covered with a double layer of filter paper, was found satisfactory for this purpose. Drying in vacuum did not appear to give any advantage. The dried antitoxin cotton became a stiffened mass, resembling dried paper pulp. This was weighed and then divided into pieces which by weight would represent definite quantities of antitoxin; for example, if the entire mass contained twenty units of dried antitoxin, one twentieth by weight would represent about one unit.

The experimental proof of the efficacy of this method will be described more in detail in a later communication. It is sufficient here to note that when the prepared cotton was bound on freshly made

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