

to prognosis. The plate, of course, often misses a growth that is observed in the broth. We have not encountered a case which has recovered (nonserum cases) with more than 15 colonies of pneumococci in 1 cc. of blood, and we have seen only 1 case with 15 colonies recover. In their early monograph on pneumonia, Avery, Chickering, Cole and Dochez² have spoken of these phases of blood culture work and it is interesting that in their group of nonserum treated cases with pneumococcus in the blood stream there were no recoveries where more than 15 colonies were found. The positive blood culture cases that recover must be those in which the colonies are very few; at least, this has been our experience. Fatal cases, however, may occur where only a few pneumococci are present. Further observations pertaining to this particular phase of blood culture work should be of considerable value and Koch³ has informed us of an interesting study, now in press, correlating the blood culture findings and prognosis. The positive blood culture group is an important one, because the severity of the disease in any community bears a close relationship to the number that have a bacteremia. As Topley⁴ remarks, the positive blood culture is an index of the severity rather than an accurate index of the presence of the organisms in the blood. Further, one is well able to agree with his statement that "the prognostic significance of a positive blood culture is one of the best attested facts which have emerged from the bacteriologic study of this disease." Any therapeutic measure that is to be considered in pneumonia must lower the mortality in this group of cases.

Dextrose has been given in adequate dosage during the past 2 years, and from the mortality figures in Table 2 there can be no other conclusion reached than that this method of therapy has failed. While we have seen symptomatic improvement frequently following the use of intravenous dextrose, and in some instances an almost dramatically favorable response, yet we are forced to admit that these good results were never seen in the positive blood culture cases where the pneumococcus count has been above 15 colonies per cubic centimeter of blood.

If we are to influence our mortality by treatment, this toxic or positive blood culture group must be affected. It is our opinion at the present time that supportive, or if we may say physiologic, methods are quite unable to accomplish this result. One wonders whether a similar series of positive blood culture cases, treated adequately in an oxygen tent, would show mortality figures any lower than those given in our tables for dextrose therapy. Osler's⁵ statement made in 1888 is still true: "there is no acute disease with so few cases in which the issue of life and death lies in the administration of drugs." It appears to us at the present time, more forcefully than ever, that the only hope in treating this disease in its toxic forms, is by directly counteracting the pneumococcal infection, or, in other words, specific therapy.

Chad *Glaser*

Conclusion. After a fair trial in the use of dextrose in the treatment of pneumonia, we have observed that it has not reduced the mortality and have, therefore, concluded that it has no essential place in the treatment of this infection.

BIBLIOGRAPHY.

1. MacLachlan, W. W. G., Kastlin, G. J., and Lynch, Ralph: *Am. J. Med. Sci.*, 1930, **179**, 93.
2. Avery, O. T., Chickering, H. T., Cole, Rufus, and Dochez, A. R.: *Acute Lobar Pneumonia*, Monograph of the Rockefeller Institute for Medical Research, 1917, No. 7, 37.
3. Koch, K. R.: (Personal communication, article in press).
4. Topley, W. W. C., and Wilson, G. S.: *Principles of Bacteriology and Immunology*, 1929, **2**, 1097.
5. Osler, William: *Univ. of Pa. Med. Mag.*, 1888-1889, **1**, 77.

A CLINICAL STUDY OF ARTIFICIAL HYPERTHERMIA INDUCED BY HIGH FREQUENCY CURRENTS.

BY FRANCIS W. BISHOP,
ASSOCIATE IN MEDICINE (RADIOLOGY),

CHARLES B. HORTON, M.D.,
INSTRUCTOR IN MEDICINE (PSYCHIATRY),

AND

STAFFORD L. WARREN, M.D.,
ASSOCIATE PROFESSOR OF MEDICINE (RADIOLOGY),

WITH THE TECHNICAL ASSISTANCE OF MISS EMMY LEHMAN, R.N.,
ROCHESTER, N. Y.

(From the Divisions of Radiology and Psychiatry of the Department of Medicine of the University of Rochester, School of Medicine and Dentistry, and the Strong Memorial Hospital.)

THERE are several methods of producing fever artificially in the human body. Some of these act indirectly while others act directly. The passage of high frequency currents through the body is a direct and rather quantitative procedure which can be controlled more carefully than any other method. The elevation of the temperature can be determined and accurately maintained by a simple and safe method which will be described. The use of this method in uncomplicated cases or cases not already impaired to the point of their being a poor surgical risk is practically devoid of danger. Other workers (King and Cocke³, Neymann,⁴ Hinsie and Carpenter²) have attempted to parallel, by this electrical method, the fever alternations of malaria therapy already used with considerable success in the treatment of paresis. We have felt that it was the

Amer. J. of Med. Sciences 184 : 515-533 (1932)

sum total of the fever bouts, rather than the short fever with intervals between, which was responsible for the clinical improvement of the paretics. This idea has its corollary in the occasional report of the subsidence of a chronic disease following an acute infection, usually respiratory, with a high temperature over a considerable period of time. Certain German workers in analyzing the results after malaria have added up the number of hours of fever above various temperature levels and have pointed out that the higher the temperature the shorter the period of fever necessary to bring about clinical improvement. Even at a temperature of 41°C . this total added up to quite a long time, somewhere around 48 hours, and at 40°C . 72 hours.

After careful survey of the clinical records of patients having high fevers, and after 2 years' preliminary work on dogs,¹ we set the limit of the therapeutic fever at 42°C . for the patient. Cases have been observed in which patients have survived higher temperatures than this, *i. e.*, insolation and sepsis. We know from our experience with 100 treatments that 42°C . is a dangerous temperature level, for more than a very short period. We can maintain temperatures slightly below this however (41.5° to 41.7°C .) for a period of at least 5 hours without difficulty or damage to the patient, and this has become our standard procedure. There are several reasons which dictate the choice of the 5-hour fever period in the treatment of disease by this method. It is the longest period well tolerated by the patient. It fits in well with the 8-hour working day for the personnel. It corresponds to preliminary studies of the thermal death time of certain cultures, especially gonococci, in water-bath experiments to be reported later, and most important of all it is long enough to be followed by clinical improvement.

At first we had great difficulty in obtaining enough power to raise the patient's temperature rapidly enough to make it possible to treat him in 1 day. The matter of heat insulation and the proper handling of the patient at all times during the procedure was another serious problem. After a great many changes the following method has now become practically standardized for the use of the "300-meter wave length" currents in this clinic.

Method. In order to eliminate the use of blankets, which are cumbersome and give the patient a sense of restraint, a cellotex chamber was built, which covers the patient and prevents loss of heat (Figs. 1 and 2). The upper portion is shaped like half an octagon. The lower half consists of a box containing a mattress, into which the upper half fits snugly, to prevent the leakage of heat. At one end a semicircle is cut to allow the patient's head to remain outside of this chamber (Fig. 2). There are 5 carbon filament lamps in the foot end of the box and 3 in the head end. These are controlled from the outside and maintain the air temperature within the box at a level sufficiently high to compensate for loss of heat by the patient through radiation, etc. (usually around 45°C .). Drapes surround the patient's neck to prevent leakage of air in this direction.

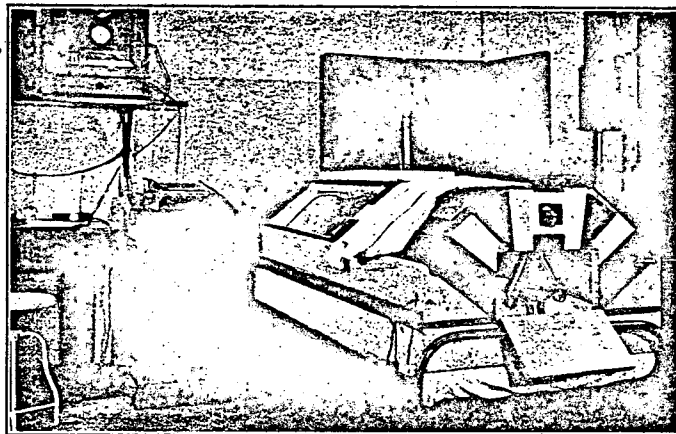


FIG. 1.—This shows the general arrangement of the cabinet and treatment machine and the various openings in the upper portion of the chamber which surrounds the body of the patient. The block-tin electrodes and the many-tailed surgical binder are visible on the top of the cabinet.

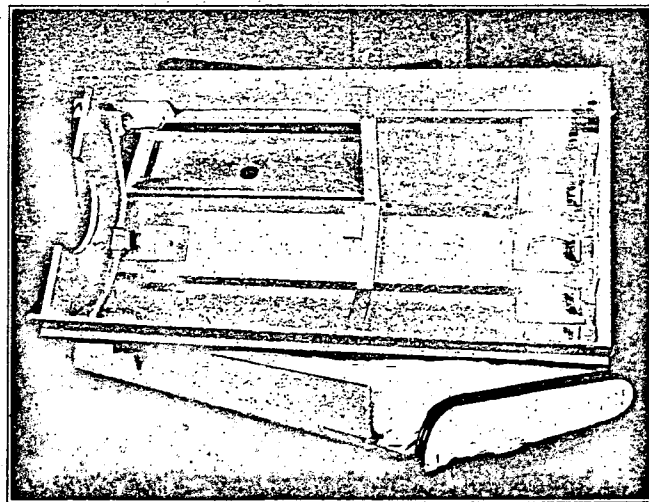


FIG. 2.—Detail of the interior of the half octagon cellotex cabinet showing the arrangement of the lights and the hole for the patient's neck.

Various apertures for the recording rectal resistance thermometer and electrocardiograph leads, etc., are present.

The patient is placed on the mattress and block tin electrodes, 28 by 46 to 60 cm., are bound on the anterior and posterior surfaces of the trunk by means of a many-tailed surgical binder. The patient is then covered by a sheet. The electrodes are connected to the high frequency machine. The lights within the cabinet are turned on and the rectal thermometer inserted. The pulse and respiration, as well as the temperature, are recorded every 10 minutes.

The high frequency apparatus is a slightly modified "diathermy" machine able to pass 5000 to 6000 milliamperes through the patient's trunk between the block tin electrodes.

Clinical Progress. After the current has been turned on it is raised as rapidly as the patient permits to between 5000 and 6000 milliamperes. No lubricant appears necessary, since the patient begins to perspire almost immediately. During the first 10 to 30 minutes no change may occur except for the rapid outpouring of perspiration. Then there is a flushing of the skin which may progress to the point where the patient becomes a deep red color (not cyanosis). Perspiration fairly runs off the skin. Immediately after this the temperature begins to rise and continues to rise at an even rate until the current is turned off. If the elevation of temperature has been rapid the rectal temperature may continue upward about a half a degree after the current is turned off, but if the rise has been fairly slow this continued rise will be reduced or may not occur. This is apparently due to the redistribution of the heat which has been absorbed by the trunk in the neighborhood of the electrodes. During the elevation of the temperature the rectal temperature is at first higher than the mouth temperature. When the body temperature reaches about 38° to 39° C. the mouth temperature usually becomes higher than the rectal temperature and remains so or equals it until the current is turned off. This, we believe, is due to the heating up of the lung substance faster than the blood can remove the stored heat, so that the expired air is hotter than the blood in the rectal vessels. As soon as the current is turned off the mouth temperature equals or becomes slightly less than the rectal temperature (Fig. 3).

When the required temperature level has been reached and the current turned off, the electrodes are removed from the trunk and the patient remains in the box covered only by a sheet. The air surrounding the patient is kept at an adequate level, and in so doing the patient's body temperature is maintained at the predetermined height. If, for any reason, the body temperature rises the surrounding air is cooled off. If it drops the air temperature may be raised as high as it can be tolerated (perhaps 50° C.) and slowly the body temperature is built up to the desired level.

Many patients become slightly delirious even though mentally normal beforehand. They are hypersusceptible to slight noises

and are apt to become excited and pugnacious. They sometimes lose all mental restraints and barriers, and their speech reverts to their fundamental type. With this excitement the pulse and respiration mount rapidly. If they are not quieted heat is produced by physical exertion in sufficient quantity to raise the body temperature still further (Fig. 4). Immediate measures must be taken to quiet the patient for the temperature is already near the upper safe limit. Often calmness and reassurance on the part of the

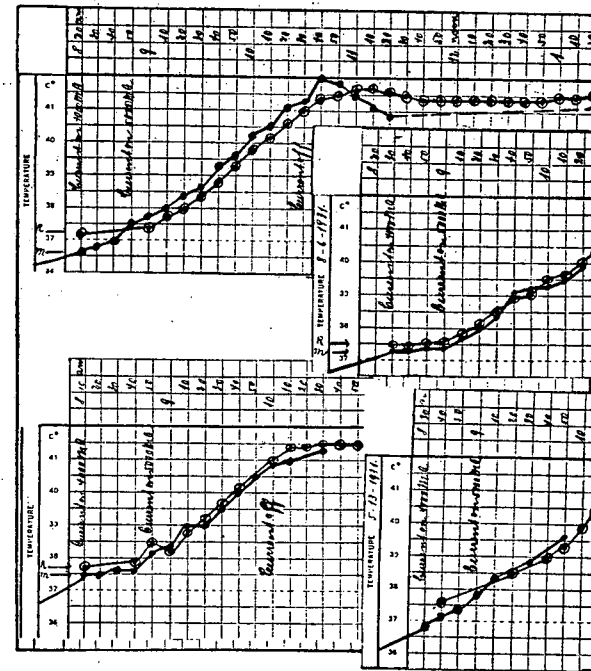


FIG. 3.—This chart shows the vagaries of the mouth (dots) and rectal (circles) temperatures during the establishment of the fever.

attending doctor and nurse, stroking of the patient's head, requesting him to be quiet while the blood pressure is taken and similar maneuvers are sufficient to quiet the patient. Many sedatives have been tried, but none well suited for general use has been found. All have some more or less serious disadvantage, of which is the period of excitement produced by the drug before the narcotic stage is reached. Nearly all are depressants of the respiration or blood pressure or both. This is in keeping with

clinical experience with patients in delirium during high fever. Chloral hydrate in doses up to the narcosis point has been very

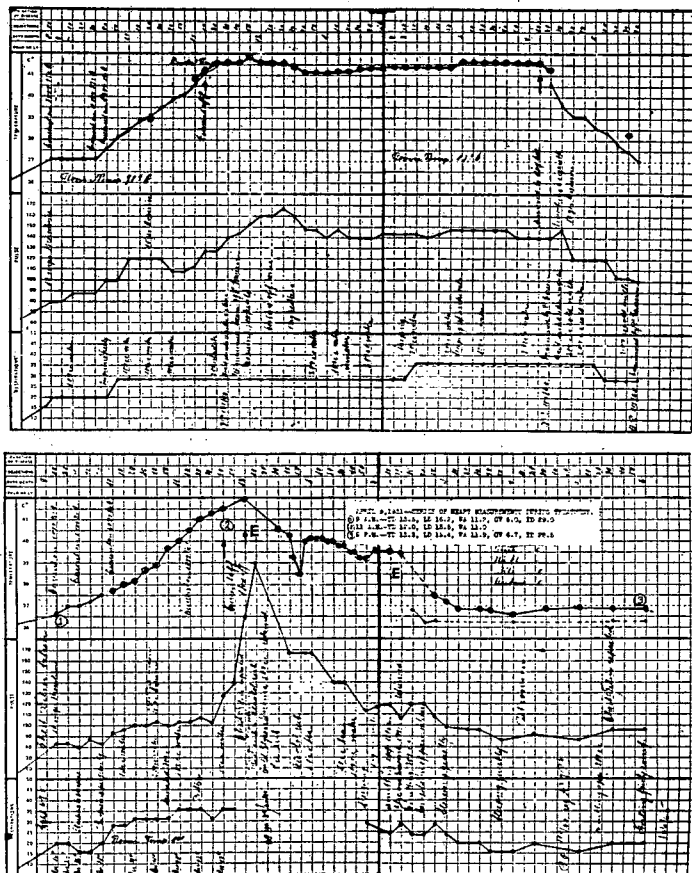


FIG. 4.—This patient had one treatment with the usual sequence of events (upper chart). A month later, during his second treatment, the patient became excited before enough sedative could be given and started doing his "setting up exercises." The exertion caused his temperature to rise to 41.9° C. and the pulse to 250 per minute and the respiration to a very high irregular rate. Ice rubs and air cooling and cold enemata (E) brought the temperature, pulse, and respiration down to their normal level.

effective, though at times even this amount is not ample. An occasional patient requires no sedative.

The pulse and respiration usually rise in keeping with the temperature (Fig. 3, *f*). The pulse usually reaches a level between 130 and 150, where it may be maintained for the duration of the treatment. Periods of excitement are always indicated on the chart by a rise in the pulse rate. In nervous patients the entrance of the doctor or visitor can almost be registered by changes in the pulse of from 10 to 20 beats. During excitement the respiration may vary greatly as will be evident in some of the charts shown (Figs. 4 and 5). During the treatment the patient is allowed to drink as much warm fluid as he requests and is also given food if he wishes it.

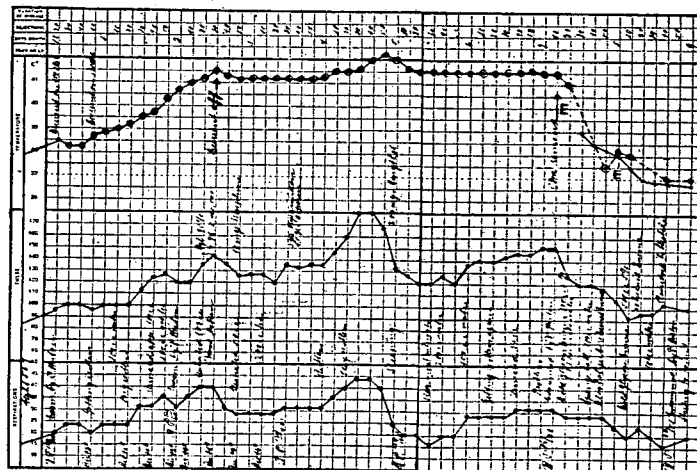


FIG. 5.—This chart shows the simultaneous variation in temperature, pulse and respiration as a result of restlessness. The effect of sedatives, cooling measures, and the subsequent continuation of the treatment as the patient quieted down are well illustrated.

When it is desired to terminate the fever the box is removed from over the patient and the body exposed to room air. It is possible to allow currents of very cool air to blow across the patient without causing a subsequent ill-effect. A drop in temperature of about 4° C. of the skin surface is apt to cause local shivering and contraction of the hair follicle muscles. If this occurs the patient is uncomfortable, and it is better to cover the body with a sheet. If nothing further is done the body temperature will gradually return to normal in about 3 hours. This may be expedited somewhat by alcohol and ice rubs, but these are not very efficient since the skin capillaries contract at the touch of the cold, and heat is

retained rather than radiated. It was found that a cold retention enema would greatly hasten the cooling process (Fig. 6). After

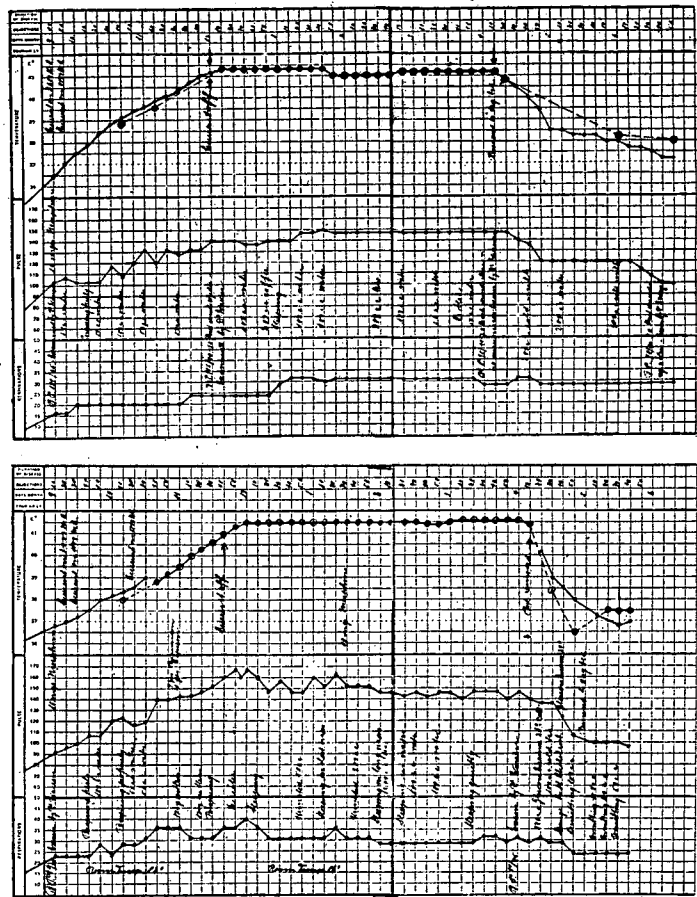


FIG. 6.—Temperature, pulse and respiration curves in a 50-year-old patient with chronic arthritis. Circles represent the rectal, and dots the mouth temperature. The lower chart illustrates a second treatment one month later and shows the effect of a cooling enema as compared to the upper curve where none was given. At this stage of development of the technique, treatments were restricted to 4 hours in cases of arthritis. Pulse and respiration curves show the normal variations.

removing the box 500 cc. of 0.6 per cent saline containing 25 gm. of glucose are instilled per rectum. The temperature of this fluid

may be as low as 10° to 15° C. without causing shock. Abdominal cramps are practically always present, but they are not severe. After 20 minutes or more another 500 cc. are given per rectum. By this procedure the temperature returns to normal within 1½ hours after the removal of the box.

The patient should never leave the treatment room until the temperature has returned to normal. It is necessary to record the temperature only at hourly intervals thereafter for 4 hours. We have found in a few cases sent back with temperatures higher than normal that the temperature rose subsequently, but removing the covers was sufficient to bring it down again. In no patient who was returned with a normal temperature has there been a rise at a later period. We have not found the mouth temperature to go below 36.5° C.

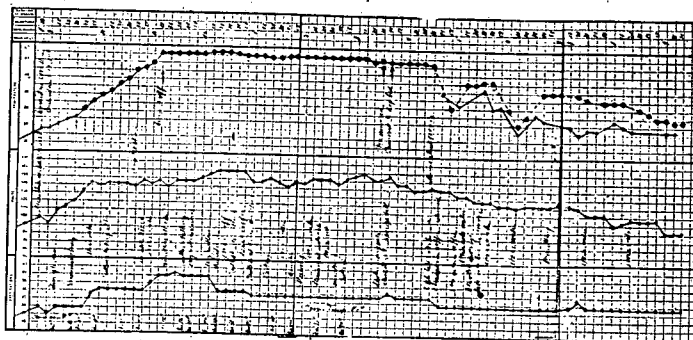


FIG. 7.—This was an obese 57-year-old arthritic patient who responded in the usual way to the fever treatment except for the delay in the fall of the temperature upon exposure to room air. Two cold enemas lowered the level of the temperature, but two hours longer than usual were required to bring the temperature back to its normal level. Further enemas were contraindicated because of vomiting and dropping blood pressure. Note the influence of the cold enema on the mouth temperature.

Immediately after removing the patient from the box the pulse and respiration begin to return to their normal, though occasionally both may remain slightly above their original levels for some time. The patients are given cold fluid to drink after removal from the box, though this is restricted to about 1000 cc., especially if a large amount was taken in during the treatment period. Too large an intake is apt to result in vomiting when the patient moves about or when he is shifted back to his own bed. Cold ginger ale, probably because of its sugar and alkaline content, is very well tolerated during this last period. Too much fluid intake may produce acute syncope in the period just after the enema is given, and in 1 patient who developed this symptom it was possible to demonstrate that the fluid content of the blood was greatly increased.

It occasionally happens in obese people that the temperature does not come down as rapidly as it should (Fig. 7), possibly due to insulation by the layers of fat. Colder enemas should thus be given to obese people than thin ones and a longer period expected for the return of the temperature to normal.

The color of the patient is a good index of his condition. This, together with the blood pressure and the temperature record, are three most valuable aids in indicating the patient's condition. Cyanosis of the lips, a beginning pallor especially of the face about the mouth, even if not accompanied by other changes, is a warning sign of failing peripheral circulation. It is usually followed very soon by a drop in systolic and diastolic pressure. The respiration may or may not change. If the respiration decreases in rate at such a time the temperature may rise, probably because of the reduced loss of heat by means of the expired air. A change in color (pallor) is usually accompanied by a stage of excitement, although sometimes the stage of excitement occurs first. With the onset of these symptoms, the patient should be watched very carefully, and if they continue the box is removed and the temperature returned to normal as soon as possible. The most efficient agent for this purpose is the cold enema.

The blood pressure (Fig. 8) usually rises with the elevation in temperature, although occasionally it remains at its original level throughout the treatment. If it has risen during the elevation of the fever it usually begins to fall when the patient reaches the maximum of his flush and perspiration (39° to 40° C.). It then continues to fall throughout the rest of the treatment period, and in the average patient reaches a rather constant level in the last hour of 80 mm. of mercury systolic, 60 diastolic. Occasionally in patients who already have a systolic pressure of around 100 there may be a steady fall from the beginning of the treatment. It usually reaches in such a case the low level of 70 systolic, 60 diastolic. The lowest pressure which we have seen was reached in a patient who had been chronically invalidated by arthritis for a long time. She reached the astoundingly low level of 40 systolic and 30 diastolic, which she maintained for a considerable period (3 hours) without any other evidence of difficulty, and with a gradual return to a 90 systolic and 70 diastolic the next day.

In general, electrocardiograms show the decrease in voltage of the action currents of the heart consistent with a low blood pressure. While there are other changes apparent in the electrocardiograms, their exact relation is not clear.

The general reaction of the patient throughout the treatment can be improved by close attention to a great many small details. The room should be darkened. All noise should be eliminated as much as possible. A registering or indicating thermometer makes it unnecessary to disturb the patient to take the 10-minute rectal

temperatures, thus allowing him to sleep as much as possible. An atmosphere of calmness must be created by the personnel. Sedatives should be given to make the patient doze but not enough to

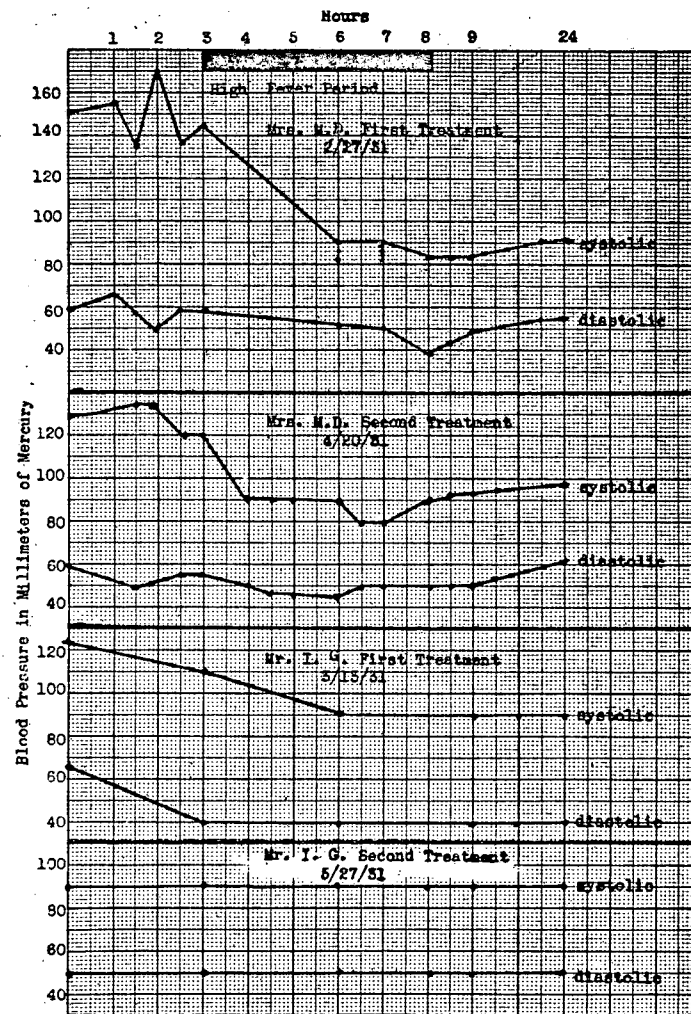


FIG. 8.—These 4 typical curves of the variations in the blood pressure cover the usual ranges. The pressure is generally lower and shows less fluctuation during the second treatment.

make it difficult to ask him questions about his sensations and to get him to drink the amount of fluid necessary to maintain the proper water balance. Two to 4 kilos of weight may be lost during the treatment from waterloss.

At the end of the treatment the patient should be lifted to his bed and not allowed to move suddenly lest vomiting occur, which may continue if once started for some hours. We have thought that paraldehyd and morphin, as well as the barbital derivatives, intensified the vomiting after treatment and even caused it to continue for 2 or 3 days. This happened too consistently to be purely

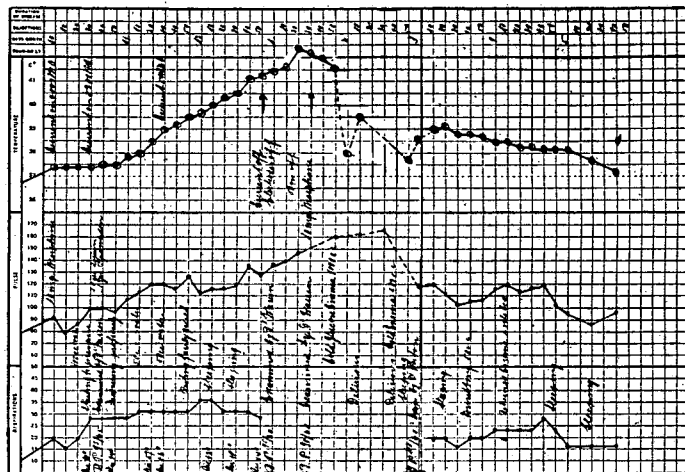


FIG. 9.—This parietic patient suddenly stopped breathing during treatment while sleeping. Artificial respiration was necessary six times during the next hour. The temperature rose to 42.4° C. The pulse and blood pressure changed very little during this period. This patient swallowed his tongue whenever his head rolled face upward. This was finally discovered and the tongue held out with a hemostat and caused no further trouble. The temperature was reduced efficiently by cooling and instilling two cold enemias. This patient is on parole (3 treatments).

circumstantial. With badly degenerated parietics who are apt to become deeply asleep or unconscious during the treatment, care should be taken that the tongue does not fall back and block the respiration (Fig. 9).

The most uncomfortable portion of the fever period for the patient occurs while the patient's temperature is at from 39° to 40° C., at which time the sedatives are usually administered. The patient is restless and feels very hot and oppressed. A slight delirium is often noted. It is a great relief to the patient when the temperature rises above 40° C., as these sensations then disappear to a great extent.

The patient relaxes and usually sleeps in short naps without further sedatives. The patient, of course, feels quite hot throughout the treatment. He is apt to feel very tired near the end of the 5-hour elevation in temperature, and unless he has been told exactly about the duration of the treatment beforehand he is apt to get somewhat restless. This can often be prevented by placing a clock where he can see it during the last hour of the treatment. It is not wise to push the sedative too much at this time, since the patients are apt to sleep soundly as soon as the temperature drops, and it would be impossible to force fluids after the treatment is over. The latter is an essential portion of the recovery period because the patient is apt to feel weak the next day if his fluid intake has not been sufficient.

The ambulatory patient in good general condition is allowed to go home by noon the day following treatment unless he comes from a considerable distance, in which case he is kept over another day. Except for nausea which could be attributed directly to the narcosis and occasionally weakness lasting for a few days, there have been no deleterious after effects. This, of course, does not include the occasional burn under the electrode. These have responded well to tannic acid dressing and usually heal in about 10 days without difficulty. They are rarely more than simple blisters. One in our series was followed by a keloid which had to be treated with radium.

Results. One hundred treatments have been given to 57 patients, from February, 1930, to August 1, 1931. The artificial hyperthermia procedure has been greatly modified and refined within this period. The method now used will give good results in careful hands with properly selected patients. We feel that the conditions under which we had to work and the type of patient whom we treated at first were not of the best. There have been 2 fatalities.

TABLE 1.—TYPES OF CASES TREATED BETWEEN FEBRUARY, 1930, AND AUGUST, 1931.

	Cases.	Treatments.
Syphilis, C. N. S. (paresis)	18	33
Arthritis, chronic (infectious and noninfectious)	15	26
Arthritis, G. C.	9	16
Vaginitis, G. C.	2	4
Meningitis, G. C.	1	3
Multiple sclerosis	3	4
Encephalitis, chronic	1	3
acute	1	1
Hypernephroma	1	3
Miscellaneous	6	7
Total	57	100

Oldest patient, aged 65 years; youngest patient, aged 3 weeks.

Case Abstracts. CASE 1.—The first fatality occurred with the second patient treated: a colored girl, aged 25 years, who had just recovered from alcoholic hallucinations. She had central nervous system syphilis and her mental status was poor. Her prescribed antisyphilitic treatment was not

consistently pursued because of her drunkenness. She rarely took treatment at the proper interval. After recovering from the delusional state she seemed to be in good general condition on physical examination. In view of this fact and the difficulty in giving her the regular form of treatment, artificial fever therapy was suggested and attempted. At that time blankets were used to prevent the patient from losing heat. These caused a sense of restraint and the patient was apprehensive about this. After a good deal of trouble with the treatment machine the temperature was finally elevated at the end of six hours to 41.5° C. by mouth thermometer and 42° C. by rectal thermocouple. This was maintained for about 1 hour, when the patient became delirious and struggled violently to get out of bed. She became short of breath. The covers were removed. She vomited a large amount of fluid, and the pulse and respiration stopped. The patient could not be resuscitated. The pulse rate at its highest was 170 per minute and the respiration 45. At autopsy there were small hemorrhages in the epicardium such as are seen after sudden death, a somewhat enlarged thymus, and no obvious cause to account for the sudden exitus. The final diagnosis was chronic alcoholism, central nervous system syphilis, hypertrophy of the thymus. After much discussion it was concluded that chronic alcoholism was the major factor in the demise of this patient.

CASE 2.—The second fatality occurred almost exactly 1 year later. This patient was a white woman, aged 26 years, with a diagnosis of chronic encephalitis lethargica, with symptoms of 8 years' duration. She had been steadily going down hill in spite of various therapeutic measures. Among other symptoms, the patient was subject to attacks of noisiness, screaming and crying, with seizures of twitching of the extremities, vertical nystagmus and incontinence, lasting 24 to 48 hours. These attacks were repeated at intervals of from 2 to 3 days, and had increased in severity and number during the last 6 months of her life. The patient was given an artificial fever treatment on February 27 and another on April 20, 1931, with marked improvement in the symptoms. A third treatment was started on May 20. The temperature rose in the same manner as it had on the previous occasions, and the current was shut off at the end of 2 hours, when the temperature had reached 41° C. The temperature then rose to 41.5° C. in the usual manner. Suddenly the patient began to have one of her usual attacks except that it was of marked severity. The blood pressure began to drop, and within about 1 hour had fallen from 100 systolic and 60 diastolic until it could no longer be measured. The radial pulse was not palpable. The heart rate continued unchanged. The sounds were of good quality. The color, of course, changed to a pallor. The respiration became slower and slower and finally irregular. The head was lowered and various medications tried without effect. The temperature began to rise steadily as the respiratory rate decreased, and when the respiration had almost completely ceased the temperature reached 43° C. The patient was put in an ice pack and given an ice cold enema which was not retained. Various mixtures of oxygen and carbon dioxide were successful in stimulating the respiration for about 1½ hours after this. There was very little cyanosis as long as the respiration and heart rate were maintained. When the respiration began to fail, in spite of the oxygen and carbon dioxide mixture, the patient was put in a Drinker respirator. The heart was failing, and it stopped entirely by the time that the neck piece of the respirator was adjusted. The temperature had fallen to 40° C. before the heart stopped.

Autopsy showed no variation from the normal in any of the organs except for the few epicardial hemorrhages such as are commonly seen in acute exitus. The heart was otherwise in good condition; the muscle well developed. It was not dilated. The brain showed no gross or microscopic lesions on careful search. The results of studies with special stains are not

yet available for report. Chemical analyses made on the heart's blood 1 hour after exitus showed: Nonprotein nitrogen, 43 mg. per 100 cc.; chlorid, 460 mg.; sugar, 95 mg. per 100 cc.; hematocrit, red blood cell content, 51 per cent. In other words, there is no evidence from the data at hand to explain the cause of death.

This case illustrates the rise in temperature coincident with the drop in the respiration rate. The failure of the circulation to maintain the blood pressure was probably due to the peripheral dilatation which did not respond to the usual stimuli. The ice packs failed to be of use either in bringing down the temperature or in raising the blood pressure by contracting the peripheral vessels of the skin. A continuous cold enema seems to have been the most effective agent in bringing the temperature down from the high point to 40°. The period above 41.5° was approximately 15 minutes in duration, which of itself should not have been the cause of death. The fall in pressure and the failure of the respiration were apparently the main contributing factors.

It is felt that the first fatality could have been avoided if the treatment had been conducted with the present technique. The possibility of damage to the respiratory mechanism in patients having central nervous system lesions increases the risk of treatment in such cases. All those concerned realized before treatment that the patient with the chronic encephalitis was a very bad risk. The treatment of similar cases should be undertaken with caution.

In summarizing our experience with 100 treatments of 57 patients having various diseases, we feel that the contraindications for treatment are somewhat similar to those which would hold for an abdominal surgical operation. Chronic alcoholism and obesity, arteriosclerosis with its possibility of a ruptured vessel in case the pressure should rise too high during the first stages of the fever, central nervous system lesions involving the respiratory mechanism, cardiac damage with lowered cardiac reserve are all specific contraindications. The blood pressure readings still remain the simplest index of the efficiency of the vascular system during treatment.

Preliminary Clinical Results. The first patients treated were chosen from a group of badly disoriented and degenerated paretics. Some of these were in very bad physical condition. Two who were especially disintegrated, and who had been in bad physical condition for many months, were given artificial fever and tryparsamid, but they continued to go down hill and died several months after the fever treatment. The rest have shown great clinical (Fig. 10) and psychic improvement and gains in weight of from 20 to 30 pounds. All have been paroled, and of the 14 only 1 has relapsed, but this patient has had only 1 treatment of a 5-hour fever. The remainder have had from 2 to 4 treatments at intervals of from 10 days to several months apart. The chemical changes have been consistent and resemble the changes after malarial therapy. The

gold sol. curves, the protein and the number of cells in the spinal fluid returned to the normal. The Wassermann reactions in the spinal fluid and blood have changed somewhat but have not yet become negative. The shortest period between treatment and parole was 5 months, the longest 9 months.

<i>Elizabeth Kiehl</i> 2/6/30	<i>Elizabeth Kiehl</i> 5/20/30
<i>Kiehl</i> Before Treatment	<i>Elizabeth Kiehl</i> 10/26/30
<i>Elizabeth Kiehl</i> 2/7/30	<i>Elizabeth Kiehl</i> 12/17/30

FIG. 10.—This group of signatures illustrates the subsidence of the ataxia in a paretic patient after four artificial fever treatments. The patient is on parole.

The next series treated was an arthritic group. In this group those who responded most were patients suffering with arthritis of gonorrheal origin. The acute lesions subsided rapidly, lost their redness and tenderness, and there was gradual recovery from the stiffness. The chronic lesions became painless and there was gradual relief from the stiffness, with increased mobility. Two treatments were given from 10 days to a month apart. The effectiveness of the 5-hour fever period in gonorrheal infection is supported by water-bath experiments on the thermal death time of gonorrheal cultures, the results of which will be reported elsewhere. A series of patients with chronic infectious arthritis with soft tissue proliferation and bone atrophy or with joint destruction was treated next. Immediate relief from pain occurred and in some patients joint pain has not returned within a period of 8 months. There has been increased mobility (Figs. 11 and 12) and a reduction in the size of the soft tissue swelling. As the patients have used their joints more, some of them have been troubled with muscle pains. The usual rehabilitative measures are, of course, necessary after the fever treatment. It is too early to speak of the permanent results in arthritis at this time. This will be reported elsewhere at a later date.

Gonorrheal vaginitis and cervicitis in adults has been cleared up in from 1 to 2 treatments with no evidence of infection by

culture or smear after the next menstrual period following treatment. These cases had all been resistant to the usual forms of therapy.

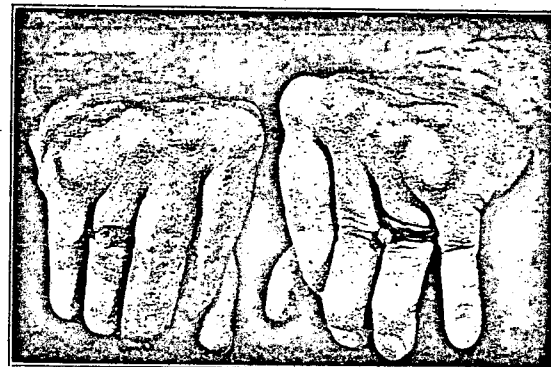


FIG. 11.—The appearance of the hands of a 50-year-old patient with advanced arthritis. This shows the maximum extension before treatment.

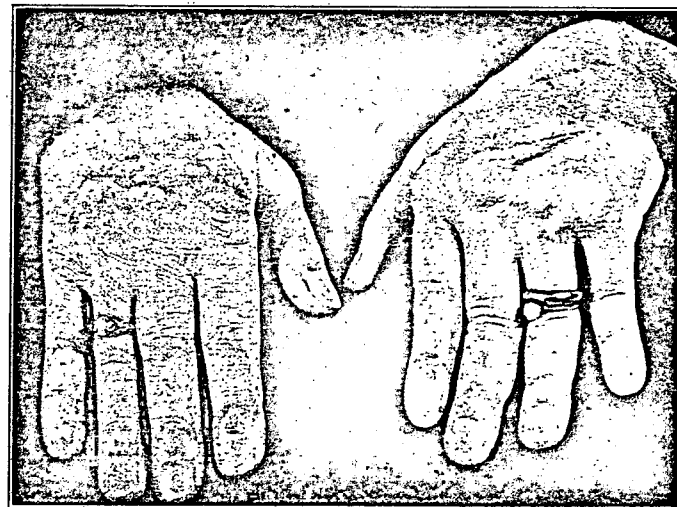


FIG. 12.—The hands of the same patient 1 month after fever treatment showing the increased mobility of the joints. This has been retained for 7 months.

Other disease entities have also been treated, but the number has been too few and the time too short to draw any conclusions from these cases. We wish to emphasize that the above statements are tentative and are based upon periods of observation of relatively short duration, the longest that the patients have been under observation being only 1½ years. It can be stated definitely that immediate clinical improvement in the paretic group, certain types of the arthritic group and the group having gonorrhoeal infections is very encouraging. How lasting these results will be can only be determined by observations over a longer period of time.

Summary. Artificial hyperthermia can be carefully and accurately controlled by a rather standardized procedure well within the scope of the average hospital. The whole body temperature is elevated by the passage of high frequency currents through the trunk by means of large block-tin electrodes. The temperature is maintained at any desired level below 42° C. for 5 hours without danger to a patient in ordinary physical condition. This is accomplished by keeping the patient surrounded by air at a temperature sufficiently high to compensate for losses by radiation, etc. The temperature can be lowered at will by cooling the patient's environment, by cold drinks and, most important, by a cold enema. The condition of the patient is determined by temperature, pulse and respiration readings taken every 10 minutes, by blood pressure determinations at frequent intervals, and by noting the color of the skin. The fluid balance should be maintained. Excitement is avoided by proper sedatives and calmness on the part of the personnel.

One hundred treatments have been given to 57 patients in 19 months, with a mortality of 2 per cent, based on 100 treatments; if based on the number of patients then the mortality is 3.5 per cent.

A careful selection of patients should be made until sufficient experience with the method of treatment by artificial hyperthermia has been acquired to evaluate the possibility of damage to patients in poor condition.

NOTE.—We wish to express our great appreciation for the cooperation of the various members of the clinical services who have referred these cases to us for treatment. Especial thanks are due to Dr. William S. McCann, Chief of the Medical Service; Dr. J. R. Murlin, Director of the Department of Vital Economics; Dr. Eric Clarke, in charge of the Division of Psychiatry; Dr. F. D. Streeter, Clinical Director of the New York State Hospital; Dr. R. Plato Schwartz, in charge of Orthopedics, and Dr. Charles Carpenter for their suggestions and criticisms of the method of treatment; Dr. G. H. Whipple and Dr. W. B. Hawkins for their very careful postmortem study of the 2 fatal cases; Dr. W. R. Whitney, Director of Research of the General Electric Company for a great deal of technical advice and interest in the methods used; Mr. A. Page, of the General Electric Company, and Mr. H. E. Gordon, of the Rochester Telephone Corporation, for many helpful suggestions; Mr. Charles Renaud, of the General Electric X-Ray Corporation, for the loan of certain equipment. This work has been supported by a special grant from the Rockefeller Foundation.

BIBLIOGRAPHY.

1. Nasset, E. S., Bishop, F. W., and Warren, S. L.: Physiological Effects of High Frequency Currents: I. Respiratory Metabolism and Certain Changes in the Blood of Anesthetized Dogs. *Am. J. Physiol.*, 1931, **96**, 439.
2. Carpenter, C. M., and Hinsie, L.: Radiothermic Treatment of General Paralysis, *Psychiat. Quart.*, 1931, **5**, 215.
3. King, J. C., and Cocke, E. W.: Therapeutic Fever Produced by Diathermy: Application in Treatment of Paresis, *South. Med. J.*, 1930, **23**, 222.
4. Neymann, C. A., and Osborne, S. L.: Treatment of Dementia Paralytica, with Hyperpyrexia Produced by Diathermy, *J. Am. Med. Assn.*, 1931, **96**, 7.

BACILLUS PROTEUS SEPTICEMIA WITH RECOVERY.

BY H. V. PARYZEK,

AND

E. E. ECKER,

CLEVELAND.

(From the Institute of Pathology and Maternity Hospital, Western Reserve University.)

ALTHOUGH *Bacillus proteus* is often associated with a multitude of inflammatory conditions in man, its occurrence in septicemias and bacteremias is extremely rare. As early as 1902 Berthelmann and Mau¹ reported its presence in the blood stream of a case of urethral fever and pyelonephritis. Since this publication, case reports have appeared from the hands of Jochmann,² Lenhartz,³ Goebel,⁴ Maymone,⁵ Reye,⁶ Warren and Lamb,⁷ and Irimonoiu and Popa.⁸ In the case of Warren and Lamb, the antemortem blood culture showed an unidentified Gram negative bacillus while the postmortem cultures yielded an organism of the *B. proteus* group. Irimonoiu and Popa's organism was also obtained at autopsy. Most authors agree that the organism is rarely recovered during life. In view of the rarity of the infection, we desire to present an unusual case of *B. proteus* septicemia with recovery.

Case Report. Patient R. D. F., aged 24 years, primipara, was referred to us through the courtesy of Dr. J. T. Smith, Jr., July 15, 1931. She was admitted to Maternity Hospital July 9, 1931, for the purpose of inducing labor, since the child was too large for the contracted pelvis. A Voorhees' bag was inserted July 10, 1931, at 11.45 p.m. and was expelled 8 hours later. Labor began about 3 hours after induction, and was completed by podalic version after manual dilatation July 11, 1931, at 11.45 p.m.

The pregnancy was uneventful and at no time were there any symptoms suggestive of genitourinary disease. A short time prior to delivery the patient began having an irregular temperature ranging from 38° to 39° C. (see temperature chart). This continued until the fourth postpartum day, when she had three very severe chills, which were followed by a temperature of 40° C. An irregular, septic type of temperature, accompanied by