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The Kettering hyperthermia; a form of fever therapy

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THE KETTERING HYPERTHERM
A FORM OF FEVER THERAPY

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GRADUATING THESIS

CONTENTS

1. Introduction - - - - - Page 1
2. History - - - - - Page 5
3. Physiology - - - - - Page 9
4. Mechanics - - - - - Page 24
5. Clinical Resume - - - - - Page 29
6. Case Report - - - - - Page 35
7. Summary - - - - - Page 41
8. Conclusion - - - - - Page 42
9. Bibliography - - - - - Page 43

THE KETTERING HYPERTHERM
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INTRODUCTION

When an inexperienced individual such as myself attempts to write on a relatively new phase of fever therapy and in view of the fact that the field has been opened only since 1929 and that for six short years an amazing amount of results have accumulated from diligent research on the part of the initiate investigators and confirmed partly by the follow-ups, I leave myself open to criticism, in that what little I may have to offer in the way of evidence shall represent only one small unit of this particular type of therapy.

Due to the almost unlimited material as far as Fever Therapy per se extends and has accumulated in the past decades, I shall limit my paper mainly to the specific type of Fever Therapy known as the Kettering Hypertherm developed first by Dr. Charles F. Kettering, Director of the Research Laboratories of the General Motors Corporation and Mr. Edwin C. Sittler of the Research Laboratories of the Frigidaire Division of the General Motors Corporation in 1929. The Clinical aspect being taken by Dr. Walter M. Simpson, M.D. F.A.C.P. of Miami Valley Hospital, Dayton, Ohio. Dr. Simpson modifying the original Kettering Hypertherm to strictly an air conditioned cabinet in 1933. This cabinet is now known as the Kettering Hypertherm. Dr. Simpson is in complete charge of this particular type of hyperpyrexia being aided by Mr. Sittler, B.S. (Eng.) and Fred K. Kislig M.D. F.A.C.S. (1)

Dr. Whitney had observed in 1928 that his workers, exposed to high frequency currents produced by short-wave radio transmitters developed fever- the word "Radiotherm" resulting from a change in the radio transmitting apparatus so as to alter the energy concentration between condenser plates. (2) Dr. Kettering tuned over the original Inducotherm Radiotherm to Dr. Simpson in 1930 and

Simpson and Sittler have improved the cabinet on a straight air conditioning basis, eliminating the short wave transmitter entirely. Thus, this type of "Fever Cabinet" has a different source of energy that either Diathermy and Radio-thermy.

There are some forty of these specially built Hypertherms in existence today, being assigned to only sixteen Class A teaching institutions by the General Motors Corporation as experiments. Description of the cabinet will follow.

Thru the diligent efforts of Dr. A.E.Bennett, Assistant Professor of Neuro-Psychiatry, the University of Nebraska College of Medicine was assigned one of these cabinets in November 1934. Later another was added, making two. Due to the fact that the College of Medicine has no active Neuro-Psychiatry unit at this time, Dr. Bennett succeeded in having the "fever machine" installed at the Lutheran Hospital in Omaha under the auspices of the University faculty for experimental study, focusing mainly on the treatment of Neuro-Syphilis, Multiple Sclerosis, certain types of Arthritis, Neisserian infections in both male and female. Later the trend was lengthened out to include all other cases of any Etiology that would be fair risks.

Certain risks are obvious in this type of therapy, therefore arbitrary age limit of between six and sixty was arrived at. Also, the presence of Tuberculosis, Chronic Pulmonary Cardiac and Renal conditions were to be regarded as contra-indications to this type of therapy. Dr. B. R. Austin, resident physician at Lutheran Hospital is in active charge of the units, working under Dr. A.E.Bennett, Dr. L.E.Hanisch (Medical Director) and the Fever Therapy Committee of the College of Medicine University of Nebraska which include, Dr. A.S.Rubnitz, Pathology; Dr. Lynn Hall, Therapeutics; Dr. Morgulis, BioChemistry; Dr. O.J.Cameron, Dermatology; Dr. Chas.Moon, Obstetrics and Gynecology; Dr. H.Johnson, Orthopedics; Dr. E.J.Kirk, Medicine; Dr.C.W.Poynter Jr., Dean; Dr. J.H.Judd, Ophthalmology; Dr.C.A.Owens, Urology; Dr. E.E.Simmons, Medicine; Miss Sophia Peiper, R.N. Supt. Lutheran Hospital. The purpose of

this body is to investigate, formulate or censor any phase of this particular type of fever therapy that comes under their domain. This group of workers, all excellent investigators, will act as a governing body in the determination of merits of the Kettering hypertherm and thru their chairman, Dr. A.E.Bennett, will submit any and all evidence pro and con as concerns all the various cases treated here in Omaha at the National Fever Therapy Committee that meets in Dayton, Ohio on May 1, 1935. At that time concensus of opinion will be pooled in order to determine the advance or otherwise of this particular type of therapy thru out the Country.

At the present writing the only other "Fever Cabinet" west of the Mississippi, other than the two in Omaha, is at the University of Colorado in Denver under the direction of Dr.Ebaugh, Psychiatrist, University of Colorado. The others are chiefly in the East.

Due to the obvious risks of the "Fever Cabinet", a corps of trained nurses is necessary to make up a smoothly running personnell under direction of the Resident Physican (B.R.A.). Their duties consist of watching every movement of the patient, listening patiently to his demands and to be on the lookout for any mechanical or physiological upsets. It is probable that these personnel units thruout the Country, together with the one in Omaha, thru such efforts has never had a fatality. The most serious dysfunction that has occured was thru brain Edema that occured in one patient, but the quick and intelligent action by the Omaha personnel in giving hypertonic glucose brought the patient back to safety in a very short period of time.

To date, after five months of work, there have been seventy two cases run in Omaha, some of which have been disappointing, others not so, some with good results and others have had excellent reaction, which all in all does mean something. It is far too early to shout loudly about the effaciousness of "Fever Therapy", but not to be enthusiastic about it would be like shutting the door against Spring's first breath. "Fever Therapy" is here to stay. If, when the pro and cons are lined up in May 1935 at Dayton, Ohio, the par-

tial benefits will not outweigh the deficits, then we should start back to the pre-Listerian era and say that there are no bacteria.

Certain groups of individuals will approach this project with the same hater that a cross-eyed duck has for a rotten carrot, but eventually the tide of progress will push them on or they will drown in the overflow.

The purpose of this paper then, is to present all the data concerning the present status of the Kettering Hypertherm, and to give the results as far as this paper permits, the lineup at Omaha.

A superficial survey of the various types of fever therapy will be alluded to from time to time in order to bring in parallelisms in the selection of cases, mode of treatment and end results arrived at.

HISTORY OF ELECTROPYREXIA

In the fall of 1929 Kettering, deKruif and Simpson, while engaging in a friendly chat, deKruif remarked that heretofore the Engineers and the Doctors had never done anything together to amount to "a hill of beans" and it was time "to get together". Kettering has just recently and prior to this incident been talking to Whitney, who had observed the production of fever in his workers, who were or had been exposed to the high frequency field produced by short-wave radio transmitters. Kettering replied to deKruif and cited Whitney's observation. deKruif in his unimitiable way soon was presupposing the possibilities of this observation in the treatment of late Neurosyphilis (3). A short while afterwards deKruif's book "Men Against Death" appeared and in Chapter 9 pp 267-279 can be found these thoughts set down in his own style.

Dr. Whitney was soon persuaded to venture a preliminary fund for the building of one of these radiotherm cabinets and so the Kettering Hypertherm was born. This was the first radiotherm constructed. (4)

Diathermy proceeded this as a form of Electropyrexia by two years, being first introduced by Neymann and Osborne in the treatment of disease. Before this, to reminisce a bit in the conception of fever therapy, we find that the Early Egyptians constructed elaborate bathing palaces for the production of fever. Undoubtedly the secondary manifestations of lues must have been lessened by these procedures. As the centuries rolled by these baths were copied in whole by the Greeks and Romans, not only for bodily hygiene and amusement, but also for therapeutic benefits. Later in Medieval Japan and Java, intensely hot baths were and still are used for their curative properties. (6)

Marco Polo, in returning from the Orient, re-introduced this method in Europe, spreading the "fad" as far North as Sweden. Finally numerous semi-civilized and barbarous tribes used steam and hot water baths to such an ex-

tent that they were incorporated in their religious rituals for frightening and banishing the demons of disease.

The American Indian put his diseased brother in a smoke and steam filled tepee to rid him of the ravages of Smallpox etc. The so called Turkish bath used for rheumatism and other aches and pains, is amongst the most popular methods in use today.

In 1883 Phillips (7) clearly demonstrated and reported the fact that fever could be induced in man, by means of hot baths. This form of therapy was re-discovered and applied to animal experimentation by Weichbrodt and Jahnel (8) in 1919 again described and advocated for the treatment of human syphilis by Schamberg (9) in 1927, studied by Walinski (10) in 1928, reapplied by Rosanoff (11) and finally clarified by Mehrtens and Pouppert (12) in 1929. Thus quoting Neymann et al, it took forty-six years to arrive at a practical goal.

Kahler and Knollmeyer (13) were the first to use external electric heat (Electric Light Cabinet). They made no attempt to maintain the fever for any great length of time. The majority of their cases being confined to the arthrites and myositites etc.

Penetrating heat in the form of high frequency current was first employed clinically by Neymann and Osborn (14) in 1929, using the diathermy apparatus. King and Cocke (15) soon followed using Diathermy in the treatment of paresis and then finally Whitney, Kettering, Simpson et al using radiotherapy and later air-conditioned (radiant energy) cabinets in the treatment of neuro-syphilis.

It is gathered by this writer that since the classical research work of Wagner-Jauregg in 1917 (16) on treatment of late syphilis by the injection of benign tertian plasmodium Malaria, followed three years later by the relapsing fever of Plant (1920), the rat bite fever of Solomon (1926) and the non specific protein fever of Kundle (1927) that better and safer methods of inducing fever in parietic patients have been sought after, since the above have certain disadvantages which will be alluded to later. Malaria treatment of dementia paralytica was introduced in this country at Saint Elizabeths Hospi-

tal in Washington D.C. in December 1922. Having discovered Diathermy and Radiothermy, the treatment channels were naturally broadened out to include other disease entities.

In 1930 Whitney and Kettering turned over the original Kettering Hypertherm (Radiotherm) to Simpson who discarded the short radio waves in 1933 and perfected the idea of air-conditioned cabinets thru experimentation with the small hot air blowers employed in radiotherm apparatus for the evaporation of moisture from the patients and for maintenance of the temperature. Simpson's final checkup in the summer of 1933 found that patients temperatures can be raised and maintained consistently by air conditioning alone without resorting to radio waves.(18) Simpson was aided technically by Sittler who at present is the field man for Kettering and Simpson. He also alludes very suggestively that Diathermy and Radiothermy have their disadvantages. Simpson's final report will undoubtedly cause much consternation among therapists when it appears probably sometime after May 1935.

Besides the above methods used in production of fever, may be mentioned hot baths, hot packs, electric blankets, hydrotherapeutics, spray cabinets and so called sun baths.

Simpson declares that the ideal method for the artificial induction of fever is one which is subject to complete control of the physician and which can be employed with safety and comfort to the patient. He further states that "despite the brilliant results which have been obtained with therapeutic fever following inoculations with malaria, rat bite fever, and relapsing fever, the fact remains that the engrafted infection is capable of producing great damage, even death and may be difficult to control, and is in constant in its fever producing properties and rarely possible to achieve adequately effective febrile reactions with foreign protein substances and hot baths (17).

Perhaps a more simpler way may someday be found to produce fever artificially, however I doubt much, whether or not a safer way, other than the

Kettering Hypertherm will ever be. Ten years of carefully controlled research will suffice to establish the final check up on the efficiency of the Kettering hypertherm.

PHYSIOLOGY

For centuries physicians viewed with alarm a temperature that would exceed 104 F. in the face of an infectious process and would take immediate steps to bring down the fever by either antipyretic drugs or by application of moist or liquid substances as a topical means of bringing down a temperature. It was popular opinion to do this and undoubtedly nature was thwarted in several ways. In the first place, the first line of defense is taken away when temperature is made to drop, that is, B.M.R. is decreased and leucocytes lose or choose to lose their increased phagocytic actions. Secondly, the heat center is thrown out of control by exogenous means and although not always present, a clinical reaction can often be seen, such as in the former treatment of Typhoid fever, when twenty-five years ago it was common teaching to sprinkle water over the hot bodies of patients (19) the temperature would shortly come down and the patient would soon become delirious, show increased psychomotor activity and often attempt to exterminate himself.

The physiology of the high fever in Typhoid was not understood then, nor is it understood today. However, the explanation, that if Typhoid fever were left alone, that no disturbance of the already disturbed but partly controlled heat center would ensue. We say that bacterial toxins cause fever. We do not know whether or not they do directly or indirectly. We surmise, since the advent of foreign protein injections, that fever can be produced with introduction of a bacterial toxin into the body and that it is logical to suppose that the body responds either to, or to spite the foreign invader. Regardless of how the body responds, fever is produced and manifests its properties in such a way that health eventually reoccurs.

With the advent of fevers produced by external means an entirely new line of thought was opened up. Wagner-Jauregg may be considered the push that set the ball rolling in the endless search for better and safer methods in the

treatment of disease. Preventive medicine was born, a new era of medicine was opened, but the physiology of fever is still unexplained. There is a difference between a fever of central origin (bacterial ?) and external origin (artificial means). The result of such fevers is still a controversy. Perhaps the most minute essential differences between these fevers, physiologically speaking will never be solved. Much of this work, to me, will be deduction. Therefore it cannot be scientifically proven. Clinically it may be proven, in that the patient gets a remission of symptoms and the physician gets the gratitude of the patient. It will be the Bio-physiologist and the Clinical Pathologist that will give us, if ever, the physiological differences of the action of body cells, etc., of fever produced of central origin and one by external means.

With respect to the regulation of the body temperature fundamental differences exist among animals. In the so-called cold-blooded or poikilothermic the temperature of the body depends upon the temperature of its surroundings. In the so-called warm-blooded or homothermic animals, on the other hand, the body temperature is maintained at a fairly constant level and the activities of the animal are more or less independent of its surroundings. The human species fall in the later class and has as its mean, a temperature, orally at 98.6F and rectally at 99.6F.

The temperature of the body is determined by the relation which exists between the amount of heat produced and the amount of heat eliminated. The heat produced, in a normally acclimated individual, depends upon the basal body metabolism and upon excesses above this resulting from muscular activity, the ingestion of food and certain unknown factors, which in themselves are perhaps negligible.

Heat is lost mainly thru conduction, radiation and thru evaporation of water from the skin and respiratory tract (20). Under the normal conditions prevailing in a temperate climate from two to three times as much heat is lost by conduction and radiation as by evaporation, and during rest the losses

by evaporation are about equally divided between the skin and the lungs. It becomes evident that the skin is the main organ thru which heat is lost from the human body.

In the mechanics of heat regulation, the body temperature may be seen to drop after one takes a cold bath, the compensatory mechanisms involved are (a) constriction of skin vessels by virtue of which less blood is brought to the surface of cooling, (b) contraction of pilomotor producing the characteristic "goose flesh" and (c) the increase in tonus of muscles or induction of shivering.

Conversely, when the body is exposed to a medium which is higher in temperature than the body, reactions are seen which consist of (a) dilation of peripheral blood vessels (b) sweating by sweat glands are promoted (c) respiration increases in rate and amplitude, thus throwing some of the excessive heat out of the body by means of the respiratory tree.

The question is raised, "How or why does the body do this?"

The great integrater, the central nervous system, is undoubtedly the controlling mechanism. These centers seem to be guided in this regulation by two factors. (a) The temperature of the blood coming to them and (b) Reflexes from the skin.

When the temperature of the nervous centers be raised either by warming the carotid blood going to the brain or by the direct application of heat thru small tubes introduced into the region of the Corpora striata, the various physiological changes that characterize the regulation against overheating takes place. (21)

Apparently in man also the temperature of the blood is an important factor in setting in operation the mechanism for increasing its heat losses. Thus, when a person is immersed in a hot bath, compensatory sweating does not occur until the body temperature has been raised from 0 to 1.4F. This illustrates the reflexes (b) of the skin, in that compensatory sweating (motor action) did not or could occur until the skin reflex (sensory) had

been stimulated to evoke a response. The stimulation of the skin by an increased flow of blood, to that area, also enhances this response. During muscular exercise, on the other hand, it is not improbable that the chief stimulus to the heat regulatory centers may arise from the elevated temperature of the blood, for the skin is often cool from perspiration. In the type of heat production used in the Kettering hypertherm we probably have a combination of (a) and (b).

Barbour (22) and others (23) observed that the distribution of water is altered. Cold increases the concentration of blood and increased the store of water in the liver, but decreases the amount in the skin; heat causes a dilation of the blood, an increased volume with decreased water content of liver and internal viscera, but increase in the water content of the skin vessels. In this way water elimination is not only governed by secreting activity of sweat glands but also by the insensible perspiration.

According to Howell (24), the concensus of most physiologists, as far as the mechanism of temperature is concerned, is that Heat production (chemical regulation) and Heat loss (physical regulation) are the essential factors to consider which are tabulated as follows:

Heat loss

(Physical regulation)

1. Sweat centers and sweat nerves.
2. Vasomotor center and Vasomotor nerves.
3. Respiratory center.
4. The water content of the blood.

Heat production

(Chemical regulation)

1. The motor nerve centers and motor fibers to the muscles.
2. Stimulating action of food on metabolism.
3. Hormonal action?

These two "regulators" working in sympathy with one another thru controll of the "heat center" make for normal temperature.

Hyperthermia may be defined as an elevation of body temperature with its attending changes in function. Fever is a more complex phenomen in

which the effects of hyperthermia are usually complicated by other chemicals or toxins which have been alluded to in the past pages. Fever as produced by this type of hyperthermia is a dis-balance between the amount of heat production and the amount of heat dissipation, in that, the normal mechanism for dissipation has been interfered with. Conversely, it is also true that heat production has been artificially produced and increased.

The individual that is placed in a bath with a temperature of 39.C first comes in equilibrium with the surrounding water. This is accomplished, probably thru Ruffini end bulbs, which stimulate, by reflex action (by way of the heat center) to dilate the peripheral vessels. Secondly, the peripheral blood is warmed. This increases cellular metabolism, and later B.M.R. (20-30%).

Similar effects occur in a hot humid atmosphere, for in this way, evaporation sweat and loss of heat by vaporization of water in expired air cannot occur (25). This is a reason why extremely high temperatures are better borne when the air is dry and in motion and apt to be less distressing.

Heat stroke represents a form of physical hyperthermia which occurs as a result of a hot humid atmosphere alone, or combined either with prolonged muscular exertion or a weakened body, which interferes with heat regulation.

Neurogenic hyperthermia has been alluded to before, by Barbour et al. Consensus of opinion has it, that fevers cannot be produced by Central action (bacterial et al) when the brain stem has been sectioned above the mid brain.

Aldrich in 1928 (26), surveying the ventilation problem in the school houses of New York City, wanted to know what the total amount of heat loss by radiation and the relation to the total loss under various conditions of humidity and air motion would change this total heat loss by radiation.

His observation will serve as a basis for the explanation of the physiology of the Kettering hyperthermia.

It must be borne in mind that the normal individual loses body heat by three main methods -viz, evaporation, convection and radiation, and a negli-

gible amount by feces, urine and expired air.

The heat required to evaporate the moisture both in the lungs and from the body surface is a real loss, heat loss by evaporation does not enter into the problem of ventilation, because it has disappeared in the form of "latent heat of vaporization". The convected heat, which under normal conditions of rooms, is transferred by conduction to the air which surrounds the body, the air, thus heated, expands, rises and may be readily removed and replaced by cooler and less saturated air. In these two ways, two of the three forms of body heat loss are accomplished. Of the third form, namely radiation, very little experimental work had been done until Aldrich wrote his classic. He reasoned, that if the humidity was kept high around, and that the circulating air was around and with the pupil average clothed, that ventilation would be adequate so as to give a comfortable environment.

In 1920, the Smithsonian Astrophysical Observatory designed a new instrument that would measure the amount of radiation of body heat and called it the "Melikeron". Thru exhaustive studies and under perfectly controlled conditions, they found that the human body radiates twice as much heat at a room temperature of 15.C than when the temperature is at 26.C. They also found that the B.M.C. remained practically unchanged thru-out this range of temperature. The average loss of heat per square centimeter of body surface as measured by the "Melikeron" at 15.C was .1109 large calories and at 26.C was .0673 large calories. Thus as the outside temperature raises, less body radiation occurs or vice versa.

The loss of heat of the average man, quoting Rubner, in still air, is roughly as follows; warming of inspired air, 35; warming of food, 42; evaporation of water, 558; convection loss, 823; radiation, 1181; total loss 2700 Kg.calories.

Now, when air motion of the room is increased, the percentage radiation loss is decreased and convectional is slightly increased.

Air motion	% Radiation loss
0	0
75 sq.ft.per.min.	41
130 sq.ft.per.min.	35
190 sq.ft.per.min.	25

Secondly total body radiation decreases with increasing air motion.

Air motion	Total Radiation loss (mean for 10 subjects)
0-50 sq. ft.per.min.	30.7 large calories per sq. meter per hr.
50-100 sq.ft.per.min.	29.3 large calories per sq. meter per hr.
100-150 sq.ft.per min.	25.7 large calories per sq. meter per hr.
180-250 sq.ft.per min.	23.2 large calories per sq. meter per hr.

Thirdly increase in room temperature produces a progressive lowering of radiation loss. The ratio $\frac{\text{Radiation loss}}{\text{B.M.R.}}$ decreases with increase of room temperature.

Room temperature	$\frac{\text{Radiation loss}}{\text{B.M.R.}}$
21.3 C	.80 (Mean of 10 subjects)
24.1 C	.75 (Mean of 10 subjects)
22.1 C	.84 (Mean of 10 subjects)
24.5 C	.74 (Mean of 10 subjects)
25.6 C	.66 (Mean of 10 subjects)

Fourthly, normal fluctuations in humidity indoors, produce negligible effect on radiation loss. Human bodies are about 300 degrees absolute, and radiate between the wave lengths 4 μ and 50 μ with a maximum at 10 μ . Absorption is so strong for so much of this range and so nearly negligible near the maximum 10 μ , that its possible effect is nearly fully produced even by the humidity of an ordinary room.

Aldrich, further found that in measuring radiation loss from different parts of the body that the area between the legs and in the axillae did not radiate to a full hemisphere of wall, thus producing less calories percent per square centimeters, this all in all could account for an eight percent error which on a mean basis would mean nothing to the total.

In the average summer heat of 90 degrees F it has been found by American Society of Heating and Ventilating Engineers Guide, (27) that with an air turbulence of 15 to 25 ft per minute and with relative humidity from 59 to 52, relative comfort can be obtained.

Simpson and Sittler, found after several months of study on varying air velocities and humidities that the temperature could be elevated and kept elevated as long as the air velocity and humidity were decreased, when and after the maximum temperature was reached.

At present they can raise a temperature to 105-106 F with impunity by having an air velocity of 450 cubic feet per minute, an external temperature of 145-150 F and with a relative humidity from 35-45 percent.

We have seen in review, Aldrich's findings on the preceding pages, viz, (a) with increase of air motion radiation loss is decreased (and according to Rubner-radiation loss is approximately one-half total loss of normal body heat) (b) Total body radiation decreased with increasing air motion; (c) Increase in room temperature (Cabinet temperature) produces a progressive lowering of radiation loss, (d) normal fluctuations in indoors humidity produce negligible effects on radiation loss; and we have learned thru the A.S.H.V.E. (27) that a relative humidity of 80% with a temperature of 64.F makes for normal heat loss, so it takes nothing but mere mathematics to arrive at the means of producing a fever by the Kettering hypertherm. Three elements, Humidity, Air Velocity, and External temperature are juggled around so as to produce a deficiency in the means of eliminating heat. Since the source of heat is kept constant by this method, the simple drop in relative humidity from the norm of 80% to around 35-45%; the increase of temperature from 64.F to around 145-150F; and an increase of air velocity from 15-25 to 450 cubic feet per minute.

We have reviewed heat production and heat elimination and have concluded that the cause of hyperthermia was a deficit heat dissipation. Upon viewing an individual in the Kettering hypertherm, we see an individual bathed in sweat. This one observation shows that the physical regulators for the control of fever are hard pressed to maintain an equilibrium. One asks the question, "Why if this is so, if sweating occurred immediately after being put into the fever cabinet could temperature be obtained?" Sweating does not occur, usu-

ally within 15-20 minutes after the onset of treatment.(28) This short interval is probably occupied, in readjusting the heat center and completing the reflex are back to the sweat glands. Remember all the time, the temperature of the cabinet is going up steadily and when sweating first occurs, the cabinet temperature is between 110-120 F. As the cabinet temperature increases, relative humidity or the percent of air saturation starts to drop and the ability to dissipate sweat by evaporation and by radiation becomes less and less.

It is obvious now, what is happening. With an increasing cabinet temperature and an impaired heat dissipating apparatus, the patients temperature continues to rise. It will continue to rise until a fatality occurs. This however is prevented by adequate controlling of the wet bulb or raising the relative humidity. When this occurs, more of the condensed moisture is taken from the body, the air becomes more saturated. Secondly, the control driving the heating element is stopped thus maintaining the cabinet at a constant of around 145-150 F. This in brief, then is the mechanism of production of this particular type of fever.

In my own personal contact as a control patient, in this cabinet, my first impression or reaction, as every part of my body except my head, became cognizant of this heated air, was one of dread, a feeling of being burned alive. The hum of the motor driving the circulating air around me, causing me to think that my time was up. As soon as perspiration started, I felt doubly worse. I began to get abdominal cramps (psychic?). I wanted to get out of this coop despite the earnest and diplomatic coaxing of the nurse-technician, Miss A. Margaret. The occasion was the presentation of the cabinet to the fever committee of the University of Nebraska and Lutheran Hospital staff and so I decided to stick it out a while longer-because the members would be there in a few minutes. Then I began to notice that the arteries of my head were starting to pulsate rather vigorously. I started to shout for water, I wanted the side doors opened up, to let in some cooler air etc., next I began to have

ringing sensations in my ears, and I could feel the external carotid vessels pounding in my throat. The staff finally came in, after having been very slow in getting there, (At least it seemed so to me) and after having the mechanics of the cabinet explained to them by Doctors Bennett and Austin, they opened up the side doors to investigate the interior and also the condition of my skin. The cool air felt wonderful. The staff then wanted to see a patient removed, and much to my delight, the nurse removed me from the "hot box." I was sweating very freely, and could still feel strong arterial pulsation in my throat and head. I shall never forget the complete relaxation that came after having gotten free of that "whirling air." My temperature, rectally, in the hour I was in, never exceeded 101.F. I shall never go in the cabinet again without the benefit of at least 9 grains of Sodium Amytal or at least 1/4 grain of Morphia.

This personal observation, is one that exists in every patient more or less. It seems that the robust athletic built and the extravertine types do not tolerate the first two hours of the fever very well, even with medication. On the other hand, there are individuals who are sick enough, who will tolerate anything. Patients have informed me that after the first hour or so (when the temperature is around 102.F or higher) that they feel fine, in fact, we had one case, who will later be discussed, who begged to go in the cabinet every day because of his being miserable all the time he was outside.

In a superficial survey of the physiological phenomena observed in response to induced fever (Diathermy, Radiotherapy or Air Conditioned Cabinets), little or no difference is to be observed. It makes little or no difference what the source of the heat is, the physiological results are the same. (29)

Phosphorus Equilibrium -Bischoff, Maxwell and Hill (3) , found that no phosphorus is eliminated in the perspiration during hyperthermia induced by radio waves, that the decrease in rate of urinary phosphorus excretion is accounted for by the decrease in phosphorus elimination with increase of meta-

bolism and the conversion of inorganic to organic phosphorus in the blood with an alkaline shift of blood pH. The decreased rate of urinary nitrogen excretion is accounted for by the increased nitrogen elimination through the perspiration.

Acid-base Equilibrium, Bischoff, Long and Hill (31) again found that there is no difference in physiological response to induced fevers. They report a loss of CO₂ with a rise in blood PH from 7.47 to 7.70, also there is a shift of bases to the blood proteins and increased oxygenation of hemoglobin of venous blood. No condition was obtained that the body was attempting to compensate for the condition of alkalosis thru the urinary or perspiratory excretions.

A marked hypernea is sometimes noted in patients being treated in the Kettering cabinet, whether this is due chiefly to psychic response or to lowered CO₂ tension. According to Bazett (32), this hypernea may lead to circulatory failure because of a primary acidotic condition of the blood. It seems to me, that the increased respiratory rate, that is noted, is compensating more than enough to offset this initial acidosis. Blood studies by Krusen (33) shows an increase of leucocytes, a slight decrease in erythrocytes and a slight decrease of hemoglobin in 24 treatments at a temperature of 105-106.F for five hours.

In blood chemistry, he found increase in Chlorides, Sugar and Urea Nitrogen and a marked decrease in CO₂. His table appears below,

Examination	<u>Blood Counts</u>			
	Finger		Venous	
	Before	After	Before	After
W.B.C	6,818	13,225	6,825	13,025
R.B.C	3,860,000	3,780,000	3,750,000	3,710,000
Hemo.	12.0 gms	11.8gms	12.5gms	11.9gms
Polys	64	80	63	82
Lympho.	24	11	24	10
Monos.	4	3	3	2
Eosino	5	2	6	2
Baso	1	0	1	0

Blood Chemistry

Examination	Before	After
Chlorides	463 mg per 100 cc	470 mg per 100 cc
Sugar	86 mg per 100 cc	103 mg per 100 cc
Urea Nitrogen	12.3 mg per 100 cc	17.2 mg per 100 cc
CO ₂	50 volume percent	42 volume percent

In an analysis of his results we see, in the blood counts, capillary versus venous, a striking similarity, This probably explains that the heating changes are not due to merely a surface hyperemia alone, but probably to a gradual penetration of the heat, thru a deficient dissipating mechanism.

The disproportion between increase in leucocytes and the drop in red cells would also indicate that leucocytosis cannot be explained on a concentration basis.

As far as the blood chemistry is concerned, the increase of chlorides is probably on the basis of having given the patient from one to five liters of 0.6 percent N.S. solution, notwithstanding, the enormous loss of chlorides thru the perspiration. The increase in blood sugar and urea nitrogen, on the other hand is probably a concentration phenomenon.

In a complete report by Hench and Slocumb of the Mayo Clinic (34) on all physiological results observed in patients being treated in the Kettering hypertherm, we observe: See table below.

Bacteriolysis

Gonococci-generally at a temperature from 106-107 for five to six hours.

Streptococci- no data available.

Blood flow

Pulse rate- increase up to 130-150 per min.

Circulatory rate- increased

Cardiac output-increased minute volume output.

Blood pressure- initial rise, subsequent fall.

Blood volume- no change to slight concentration.

Viscosity- no change (if intake is encouraged)

Nail bed capillaries- increased in number and size.

Blood - cellular elements

Erythrocyte count- no change

Sedimentation rate- ~~Conflicting~~ data. Some workers report little or no rise, others an increase.

Leucocyte count- rise to 15,000 per cubic millimeter.

Leukocytes- increased rate of p

Blood Chemistry

Non nitrogenous elements (urea, uric acid, creatinine)- slight increase
(blood concentration)

Sugar, phosphorus, plasma lipoids, serum calcium- no change or slight
increase (blood concentration)

Inorganic phosphorus- converted to organic form.

Serum protein- increase.

Acid base equilibrium- slight alkalosis.

Chlorides- may be marked drop.

Oxygen content and capacity of venous blood- increased.

CO₂ combining power- decreased.

Blood- immune bodies

Agglutinins: variable data (rise or fall)

Complement: variable data (no change to a slight reduction)

Opsonic index: no change.

Gastric Secretion- loss of Chlorides

Sweat- Loss of 18 to 26 grams of Sodium Chloride in 3 to 4 liters of sweat
in each session.

Increased lactic acid content.

Urine- Amount- generally temporary oliguria

Reaction- unchanged to slightly alkaline.

Metabolic Rate- Increased 7 percent per degree of fever.

Electrocardiogram- Contractions of lowered voltage.

Body weight- Gain: 0.5 to 6.0 pounds (79% of all cases)

Loss: 0.5 to 6.0 pounds (21% of all cases)

This report is complete in what research work has been done. Checking the observations of Bennett, Austin et al (35) of physiological responses of their patients against the computations above, we found, that in gonorrhoeal epididymitis and chronic gonorrhoeal cases and in the arthritis, the sedimentation rates were lowered proportionally with the number of treatments each patient received. Also, there is an increase of leucocytes and an initial rise in systolic blood pressure (about 30 m.m.) within the first hour and then a subsequent fall to about 20-30 mm below a norm of 70mm.

The thermal death time of *Treponema pallida*, according to Epstein and Cohen (36) after observing and substantiating Carpenter, Warren et al, classic (37), is a temperature of 40.C (104.F) for two hours in vitro. In shorter periods of time at higher temperatures this fact is also observed. Likewise, the thermal death time of *Neisseria gonorrhoeae* was worked out by Carpenter, Boak, Mucci and Warren (38) in 1933, and found that 99 percent of the gonococci were killed in two hours at a temperature of between 41.5C (106.7F) and 42.C (107.6F). The other one percent required heating from seven to twenty hours at 41.5C or from five to fifteen hours at 42.C.

It is gathered that both the Spirochete of Syphilis and Neissers Gonococcus, find a high temperature an unhealthy environment. Since, and according to Poynter (39) the normal body cell in vitro, will not perform physiological functions at a temperature of above 110.F, we have only a slight margin of safety between the thermal points of some organisms and that of the body cell. Perhaps, since the advent of fever production, individual types of cells will be studied more thoroughly by the histologists in an effort to gain more evidence as to altered cell metabolism, resistance to infection and general reconstruction of the physiology of the cell after invasion by the responsible organisms.

The literature of the physiology of Asthma and Pulmonary tuberculosis

is so limited that no evidence will be presented here.

The physiological responses to fever as produced by the Kettering hypertherm are many and varied. Much more time and evidence will have to be produced before an intelligent answer can be given as to the combined relationship between heat center and physiological response.

MECHANICS

The present Kettering hypertherm represents about four years work on the part of Kettering, Simpson, Sittler et al, in the development of a machine that would produce an adequate temperature, coupled with optimum comfort and safety to the patient and provide maximum convenience for the physician and nurse-technician.

The first attempts were with radiotherapy, in which they tried to duplicate the results obtained by other workers, who were using radiant heat cabinets, hot baths, electric blankets, heater pads and diathermy. Radiotherapy, a term being coined to describe an altered radio transmitter, whose energy was concentrated between two large condenser plates. The heating effects were produced by a vacuum tube oscillator, composed of two 500 watt radiotrons, producing a high frequency field of approximately 10,000,000 cycles per second (30 meter waves) between the condenser plates.

The radiotherm differs from the diatherm used for fever production in that it operates at a frequency approximately ten times as great; the diatherm operating at a frequency of approximately 1,000,000 cycles (300 meter waves). The spark gaps of diathermy produce damped waves while the vacuum tube oscillator of radiotherapy produce an even flow of continuous waves (40). In fever production by diathermy, alternating currents of high frequency pass between large electrodes applied directly to the skin surfaces of the anterior chest wall, abdomen and back. If the electrodes are not maintained in direct contact surface, arcing occurs, resulting in skin burns. In the fever production by radiotherapy, the patient lies on a stretcher between the condenser plates; no electrodes are applied to the skin surfaces.

Due to the large incidence of burns, Kettering, Simpson, Sittler et al, realized that a safer or more comfortable cabinet should be built. They hit upon the idea of producing an air conditioned cabinet solely without condenser plates. Before that, they had tried to maintain the patients temperature with an air conditioned apparatus after having first raised the temperature

by the radio equipment.

The three elements of an air-conditioned cabinet of this type are Humidity, Temperature and Constant air Velocity. At first, heated air at 500-1000 cubic feet per minute at 150-200 F or 66-93.C with a relative humidity, 0-10 per cent, was shot over and around the patient. In this way dissipation of sweat was attempted. The incorporation of recirculation ducts makes it possible to re-utilize any quantity of heated air. This added refinement, prevented arcing and added enormously to the safety and comfort of the patient.

In 1932-1933 these investigators again rearranged the temperature of the cabinet, the relative humidity and the velocity of air reducing their burns to almost a minimum. Using a cabinet temperature of around 145-150.F, a relative humidity of around 35-40% and an air velocity of 450 cubic feet per minute and found an ideal situation.

The Kettering hypertherm consists of a roomy box, about $7\frac{1}{2}$ feet long, $3\frac{1}{4}$ feet wide and $3\frac{1}{4}$ feet high, that is suspended by four metal feet that separate it about $2\frac{3}{4}$ feet from the ground. At one end is a bed, which may be pulled in and out. (Fig.1)



Figure 1. Shows vertical panel in place.

The patients head protrudes from one end of the box, after the vertical panel has been lowered. This seals the chamber hermetically. The patient lies on a comfortable air mattress in the bed. The walls of the cabinet are doubly insulated. In the roof of the cabinet may be seen perforations about the size of a dollar, thru which the air escapes, to the top layer, hence back to the re-circulating duct.

Along each side of the cabinet, a sliding panel is seen, (Fig.2) which can be opened up by the technician or physician when examining the patient. At the foot of the chamber, in a special compartment, is the simple machinery that heats and humidifies the air. (Fig.2.) This consists of a humidifying pan, fed with water from a glass jar outside the cabinet (marked #1 in Fig.2); air blowers used for the circulation and recirculation of air thru the cabinet (marked #4 in Figure 2); a set of heating elements (marked #3 in Figure 2). A thermostat to regulate the air temperature is also present. A humidostat to control the relative humidity and wet and dry bulb thermometers (Fig.3) complete the setup. The wet and dry bulb thermometers permit humidity readings and to indicate the temperature of the cabinet. A fan is used to blow cold air over the patients head which is usually packed with ice.

The patient is placed in the cabinet, (which has a temperature of around 120.F) stripped except for woolen booties, which add in prevention of foot burns, the vertical panel is lowered and the treatment starts. The average treatment lasts five hours at a temperature of 105.F and is called a fever unit.

Ordinarily it takes from 30 to 60 minutes to raise the rectal temperature from normal to the desired height (105-106.F or 40.5-41.1C). The mouth and rectal temperatures, pulse and respiratory rates are recorded before the treatment is begun, and every 10 to 20 minutes during the course of the treatment. Each individual must be watched closely, because of the non-uniformity in individual response.

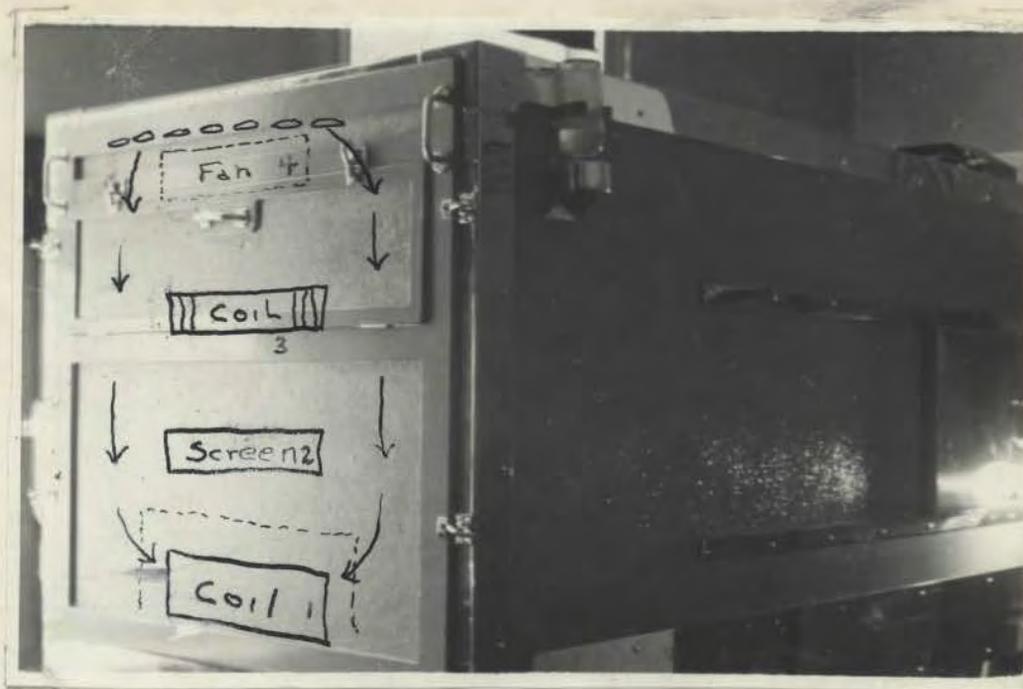


Figure 2. With super-imposed drawing showing direction of air from fan and also coming back from cabinet.

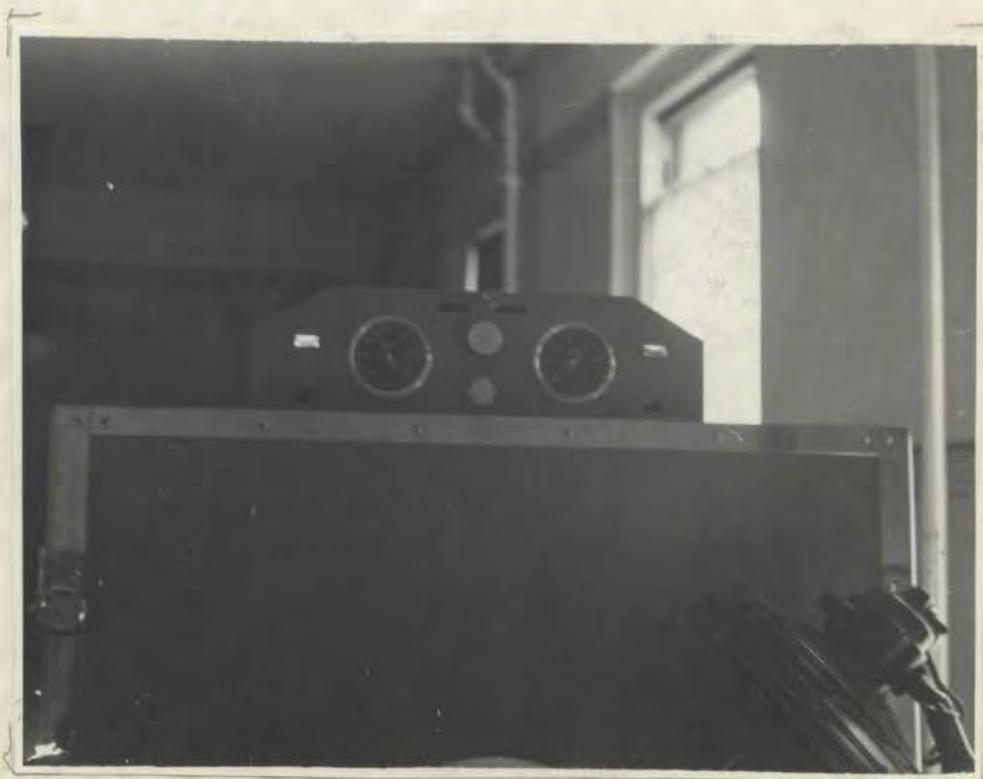


Figure 3. Showing dry and wet bulbs.

Blood pressure readings are taken before, during and after each treatment.

Premedication of Morphia, Pantopon or Chloral hydrate makes for a better and easier treatment. The patient is given from 1-5 liters of 0.6 Sodium Chloride solution to make up for chloride loss in the sweat.

The administration of 10 grains of Calcium gluconate will minimize tetany.

Occasionally intravenous glucose 50 cc of 50% will bolster a heart rate of 150. Coramine, one ampoule (1cc) is sometimes used.

Austin (41) is now using alternating normal salt solutions, in replacement of water loss. He finds less nausea and vomiting with this method.

In the treatment of first and second degree burns, tincture of Benzoin compound has been used with some success. I have advocated a 25% solution of glucose and glycerine, applied topically. The results cannot be given at this time because of the limited number of cases tried.

In the advent of the patients temperature getting out of control, he is immediately removed from the cabinet and allowed to cool off. Glucose may be given intravenously.

After a routine treatment, the patient is allowed to rest for one hour or until the temperature comes down to normal. He then may dress and go home unless he is to be hospitalized.

CLINICAL RESUME

The Kettering Hypertherm is placed in sixteen different places thruout the country. Reports from all of these centers are not available at this time. A few available reports will be cited here to demonstrate the interest in this type of treatment, and also the results if possible.

Simpson (42) in reporting the progress of artificial fever therapy at the Miami Valley Hospital, states that since 1931 to 1934 two hundred and fifty three patients were treated. Of these one hundred and seventeen were luetics, the course of treatment being completed in eighty-seven cases. Eighty-three patients were treated for some form of arthritis; twelve of these were treated for gonorrhoeal arthrites. Of nine cases of acute gonococcal arthrites the disease was abolished in eight cases after two to five treatments each of five hours duration at a temperature range of 106-106.8F. The ninth patient left the city before completing the course of treatment, making in all a 61% cure.

In three cases of chronic gonococcal arthritis, 50-75% improvement was noted after 4-19 treatments at weekly intervals.

In cases of neurosyphilis, Simpson combined specific therapy (bismarsen, iodobismitol or tryparsmide) with at least fifty hours of sustained fever at approximately 106.F. The patients having been given injections one-half hour before the fever treatment is started. After completion of artificial fever therapy, the patient was given a course of twenty specific treatments at weekly intervals.

In reporting on sixteen patients with dementia paralytica, all of which had received long continued specific therapy, including Malaria, Simpson got total remission in twelve of the cases, two were markedly improved and two with little or no improvement. The spinal fluid Wassermanns and Kahn reactions were reversed in six cases, became less positive in six cases and three remained positive. The blood Wassermann and Kahn reactions were reduced to negative in eight cases, became less positive in three cases, and remained positive

in four. All of these patients had been reexamined every six months, and in those showing reversed serological reactions, no relapse has occurred.

There were seven patients in the tabo-paretic group. Improvement in mental orientation was seen in six. Subsidence of root pain in all, two patients had reoccurrence of root pain, but it later disappeared after further fever therapy. Gait improvement was noted in four of the five patients with ataxia. It was shown that the shorter a period of time ataxia was noted, the higher the chance for complete remission. Spinal fluid Wassermanns and Kahn reactions were reversed to negative in two cases, became less negative in one case. The blood Wassermann and Kahn reaction were reversed to negative in four cases, became less positive in three, remained positive in two.

In ten cases of diffuse central nervous system, there were seven cases of congenital lues and three cases of acquired lues. Ages ranging from fourteen to thirty years, averaging twenty two years. Spinal fluid Wassermann and Kahn reactions were reversed to negative in one case, and became less positive in nine cases. The cell counts and solids were reduced to normal in all cases.

Simpson is now studying seventy five cases of early syphilis, twenty five of these patients are being treated with fever alone, twenty five of the same amount and kind of specific therapy as is used in the third group of twenty five, who are now being treated with a combination of fever therapy and specific therapy. His final report will be published in May 1935.

Warren, Boak, Carpenter (43) report in nine cases of Gonorrhoeal cases in both male and female, that seven of these cases received complete remission since the treatment.

Duncan and Mariette of Glen Lake Sanitorium, Minnesota (44), report five cases of Pulmonary tuberculosis treated by hyperpyrexia, three of which, had resolutions in 10-11 days, sixteen days in one case, and seventeen in another case.

Tenney (45) reports favorably on treatment of arthritis.

Sternberg (46) reports that patients suffering of intractible asthma, are helped considerably by hyperpyrexia.

Desjardins et al (47), at Mayo Clinic report thirty three cases of gonorrhoeal infections in both male and female, from December 1933, to Sept. 1934 in which twenty five cases out of a controll of twenty nine, received complete cure. The average number of sessions of fever being at 5.4. The largest session of fever being at 12, the lowest at 3.

Bennett and Austin et al report at Omaha, over five months time, seventy two cases that started treatment, twenty-nine of which completed the treatments and sixteen were advised to stop or stopped treatment of their own accord. Twenty-seven cases are still under treatment at the end of the first five months. Two-hundred and fifty five treatments are the total given during five months, averaging fifty plus treatments per month. The average now is ninety treatments per month.

The following diseases have been treated at Omaha:

<u>Diagnosis</u>	<u>No. Patients</u>	<u>Treatments</u>
Gonorrhoeal Infections (Male & Female)	20	59
Multiple Sclerosis	11	48
Arthritis (all types)	12	33
Neurosyphilis	9	52
Epidemic Encephalitis	5	26
Psychoses (all types)	7	14
Chronic Sinusitis	2	4
Sciatic Neuritis	1	1
Sub acute Bacterial Endocarditis	1	6
Chronic Melitensis	1	4
Bronchiectasis	1	5
Subacute Iritis	1	1
Rheumatic Fever	1	2

Complications with Fever Therapy

Symptoms	% to No. of Treatments	% to No. of Patients
Nausea and vomiting (a)	25	55
Herpes	14	36
Vertigo	11	22
Headache	9	25
Burns (a)	7	25
Cerebral Edema and Hyperpyrexia (b)	1.7	5.5
Diarrhea	1.7	5.5
Tetany	1.4	4.1
Vaso Motor Collapse	.9	2.8
Conjunctivitis	.9	2.8
Corneal Herpes	.4	1.4
Acute Exacerbation of symptoms	.4	1.4

(a)- more frequent in prolonged G.C. treatments.

(b)- more frequent in Multiple Sclerosis

Central Nervous System Infections

Diagnosis	No. of cases	Completed Treatment	Under Treatment	Results
Multiple Sclerosis	11	5	6	One case in full remission Three in partial " Two were ataxia & asthenic much improved.
Epidemic Encephalitis	5	2	3	No change
Neuro Syphilis	9	4	5	Symptomatic improvement in all cases Gastric crisis after failure with other methods.
a. Tabes dorsalis (gastric crisis & pain)	5			
b. Cerebral Syphilis				
Paresis	3			Too early to draw definite conclusions.
Vascular	1			
Toxic Infections	2	2	0	Both cases promptly relieved
Sciatic Neuritis	1	1	0	Improved, returned to work. Failed to improve from other therapy

Miscellaneous Infections

Diagnosis	No Cases	Completed Treatment	Under Treatment	Results
Arthritis	12			
Infection				
Atrophic	5	2 (1st course)	3	General improvement in pain, swelling & freer joints. It is too early to draw conclusions.
Hypertrophic	4	3	1	
Rheumatic Fever	1	1		Some relief?
G.C.Arthritis	1		1	Good results, working full time
Spondylitis	1	1		No change.
Chronic Melitensis with arthritis	1		1	Slightly relieved. Too early to draw definite conclusion.
Chronic Sinusitis	2	1	1	Too early to draw conclusion.
Bronchiectasis	1		1	" " " "
Sub-acute bacterial Endocarditis	1		1	" " " "

Gonorrhoeal Infections
Twenty patients.
Fifty nine treatments

Patients	Treatments	Male	Female	Completed Treatment	Discontinued Treatment	Average No. Treatments
20	59	15	5	16	4	4 plus

Type of Infection	No.Cases	Relieved	Unimproved	Remarks
Female -				
Acute Cervicitis & Urethritis	1		1	Discontinued treatment
Chronic Salpingitis & Cervical infections	4	3	1	" "
Male -				
Acute Anterior Urethritis	4	3	1	" "
Chronic Prostatitis	3	2	1	Recurred in six weeks
Chronic Prostatitis & Epididymitis	6	6		Six relieved from pain and swelling Three cures Two discontinued treatment One still under treatment

Gonorrhoeal Infections - male cont'd

Prostatic Abscess	1	-	1	
Paraurethral Abscess	1	1	-	Completely relieved.

Summary on Gonorrhoeal Infections

12 possible cures (3 females and 9 males) 5 failed to complete treatment, and 2 improperly treated.

Impression

1. Temperature of 106-107.F for six to seven hours every three days are necessary.
2. Results better if patient is constantly hospitalized.
3. Acute cases, fever therapy alone is sufficient.
4. Chronic cases with complications need local treatment combined with fever therapy.
5. Fever therapy is well worth while in gonorrhoeal infections.

These superficial surveys do not adequately cover the complete field of results in four years of work in this particular line of therapy. It is not within the scope of this paper. The fifth annual Fever Committee will give a complete clinical report on all literature after its meeting in Dayton, Ohio in May 1935.

AN INTERESTING CASE BEING TREATED WITH FEVER THERAPY AT OMAHA

J.F. a white male, aged 25, single, of Omaha, entered University hospital on December 12, 1934 complaining of, (1) pain in the right hip, (2) excessive fluid in both knees, of a duration of six months.

This patient had a cough for two weeks about eight months previous and had raised considerable sputum. At this time the patient began to notice a little stiffness and pain in the left shoulder and left elbow joint simultaneously. Stiffness has persisted.

A few days after noting the stiffness, he noticed tremendous swelling of both knee joints. These became very sore and painful but never "got hot or red." Both knees were surgically drained by Dr. S. with some relief. In three weeks the procedure was repeated, after which the knees "started to get well."

About Aug. 1, 1934 following an attempt at swimming, the patient noticed suddenly increasing pain and swelling of both knee joints again. Patient was forced to go to bed and in November 1934 the right knee was aspirated. Cloudy fluid being obtained, as in the previous procedures. There has been no relief since. Has not been able to work since May 1934. Has lost twenty-two pounds, appetite poor, and bowels are normal.

Ten days before entry, he noticed a transient pain in the right hip, that seems to be exacerbated only when fluid receded from the knees. The left knee began to swell very much while the right knee would recede. This procedure has been noticed in the past several times. Has never had a fever and has noticed generalized weakness and fatigability since May 1934.

Five years ago had a similar but more sever attack of generalized arthritis that lasted one year, then disappeared with no residual.

Past History- Appendectomy in 1928

Family History- Essentially Negative.

Physical Examination- Shows a well deveolped, poorly nourished white

man of stated age, lying quietly in bed, apparently in no pain, marked pallor, skin warm. Head- Essentially Negative; Eyes- Essentially negative; Ears- Essentially negative; Nose- Essentially negative; Throat- tonsils cryptic, slight hyperemia, slight exudate squeezed out of tonsils on pressure; Neck- slight bilateral cervical adenopathy; Thyroid- negative; Thorax-bell shaped type of chest, lung fields clear thruout; Heart- sounds normal in rate and rythm with an accentuation of second sound over entire precordial area; Abdomen- old appendectomy scar in R.L.Q. shot like inguinals; Extremities- Left shoulder negative, left elbow negative except for diminished extension power, some muscle atrophy. Right knee shows bilate swelling around the patella which fluctuates and is painless. Left knee, essential the same as right knee. Left ankle, essentially negative. Right ankle, shows diffuse swelling and tenderness. Left foot has only four toes, (one lost in accident) Reflexes normal.

Impression; (1) Recurrent Infectious Arthritis.
(2) Secondary Anemia.

On December 14, 1934, two days after entrance the laboratory work was done. Hb-52%; R.B.C.-3,440,000; W.B.C.-5000; Polys-Seg.65; Staff. 12; Lymph.17; Mono 5; Eoso 1; Urine, essentially negative. On January 15, 1935 the Hb.-65%; R.B.C. 4,150,000.

On December 15, 1934, the attending Senior internist, Dr. Pratt, suggested a diagnosis of Melitensio. An agglutination reaction was run and came back postive 1-50. The right knee was very painful at this time and measured fifteen and one-fourth inches. The left knee, fourteen and one fourth inches.

Follow up, agglutination reactions came back positive.

Melitensis baccine Therapy was statted on January 16, 1935; 0.25cc being given. This was repeated on January 19, 1935, and January 23, 1935.

The temperature varied from 98.6 F to 100.2F while in the hospital.

On January 28, 1935 the patient was dismissed waighing 105 pounds and not feeling any better.

He entered dispensary service, and had three .5cc vaccine shots.

During my out call service, I was instructed by Dr. Sharpe to continue the vaccine therapy, at home, because of the patients poor condition. He received six 1.0 cc shots from February 8, 1935 to February 28, 1935 given bi-weekly. He did not feel any better. The temperature ranging from 98.6 F in the morning to 101.6 at nite. There was some pain in the knees. Daily circumference measurements over three weeks time showed the right knee to be from fifteen to sixteen and three-eighths inches, left knee fourteen and one-half to fifteen and three fourths inches.

He entered the fever therapy department at the Lutheran hospital for his first fever treatment on March 8, 1935. A blood titer was taken (was found to be postive 1-500) before commencing treatment. During the treatment, which was poorly taken during the first two hours, he complained of a gnawing sensation in the esophageal region. The temperature was sent up to 104.6 and held there for four hours. After the treatment, and after careful questioning, he told us, that the gnawing sensation had been bothering him for the past two months.

The second treatment was given on February 15, 1935, both knees were aspirated (Fig.1) for culture study (returned negative). The right knee measured sixteen and one half inches in circumference, the left knee fourteen and three quarters. (Fig 2.) He took a stormy treatment and had a residual for the next week, complaining of pain in both knees and the right shoulder. The third treatment was given on March 29, 1935 after which the patient stated that he felt much better. His weight went from 101 to 108 in one week. The gnawing sensation (Esophageak ulcer,) in the epigastrium had completely disappeared. This symptom according to Bennett, is a common one in Chronic Melitensis.

The fourth treatment was given on April 5, 1935 and consisted of a temperature of 105 for five hours and the patient had a good treatment and rested well for one week.



Fig.1 Aspiration, Right Knee on Feb.15, 1935, obtained 90cc rich creamy pus.



Fig.2 Right Knee
16 $\frac{1}{2}$ inches
Left Knee
14 $\frac{3}{4}$ inches
2/15/35



Fig. 3 and 4 showing hydro arthroses Feb. 15, 1935



At the fifth treatment on April 12, 1935, both knees were again aspirated for culture (returned as a gram positive bacteria from the left knee- contamination?) and the patient again had a stormy session the next week.

The sixth treatment was given on April 19, 1935, which lasted four hours at 103.8- 104.8 with good results.

This patient has been materially aided by this type of therapy. He feels stronger, is gaining weight, has more movement in his knees than before treatment and has a better morale. His sedimentation rate has not decreased in (figures not available) speed but the knee circumferences are gradually diminishing. He is practically free of evening fever at this time.

This case is interesting from two angles, the first being, the only case yet on record to be treated with the Kettering hypertherm and secondly, the third case ever recorded in the literature having, these particular arthritic complications (Sharpe].

SUMMARY

1. A paper has been presented concerning the Kettering hypertherm.
2. History of fever therapy has been given.
3. Physiology of induced therapy has been given and a theory propounded concerning the vital factors involved.
4. Mechanism of production of fever in the Kettering hypertherm has been given.
5. Clinical resume has been given touching only superficially, the results as yet obtained, nationally and locally.
6. An interesting clinical case, being treated at Omaha has been discussed.

CONCLUSIONS

1. Fever Therapy (Kettering hypertherm) is a valuable asset to the treatment of disease.
2. This type of therapy is equal to, or superior to all other known types.
3. Certain types of diseases are best treated by this unit.
4. The Kettering hypertherm is here to stay.
5. This hypertherm has opened up a new field of clinical medicine.
6. Ten years of intensive research will be necessary to complete available reports and results.

Note: I am greatly indebted to A.E.Bennett, M.D. and B.R.Austin, M.D. for their help in the preparation of this paper, especially for their permission to publish their tabulated results in my paper.

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