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THE TONER LECTURES

INSTITUTED TO ENCOURAGE THE DISCOVERY OF NEW TRUTHS FOR THE ADVANCEMENT OF MEDICINE.

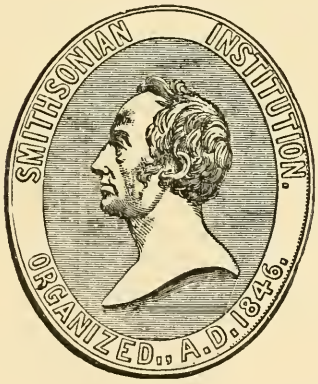
LECTURE IV.

A STUDY OF THE NATURE AND MECHANISM OF FEVER.

BY

HORATIO C. WOOD, M.D.

DELIVERED JANUARY 20, 1875.



WASHINGTON:

SMITHSONIAN INSTITUTION.

FEBRUARY, 1875.

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The FIRST LECTURE of this series was delivered March 28, 1873, by Dr. J. J. WOODWARD, "On the Structure of Cancerous Tumors and the Mode in which adjacent parts are invaded." Published by the Smithsonian Institution, November, 1873. 44 pp. 8vo.

The SECOND LECTURE was delivered by Dr. BROWN-SÉQUARD, but the manuscript has not been furnished for publication.

The THIRD LECTURE was delivered May 14, 1874, by Dr. J. M. DA COSTA, on "Strain and Over-Action of the Heart." Published by the Institution, August, 1874. 32 pp. 8vo.

JOSEPH HENRY,
Secretary Smithsonian Institution.

SMITHSONIAN INSTITUTION,
Washington, February, 1875.

LECTURE IV.

Delivered January 20, 1875.

A STUDY OF THE NATURE AND MECHANISM OF FEVER.

By Horatio C. Wood, M.D.

I have settled upon a Study of Fever as the subject of this evening's discourse, partly because my attention has long been attracted to the phenomena of fever, and partly because the subject is of such general character that every medical man must share the interest in it. In approaching a physiological or pathological process for the purpose of studying its mechanism and nature, its essence should, if possible, be first determined. Fever has been defined to be "an acute derangement of all the functions;" this it certainly is. Yet the definition gives to the mind no idea of the phenomena of fever. When these are analyzed, it will be found that the most important of them are capable of being grouped in three sets: acceleration of the heart's beat, and disturbance of the circulation; nervous disturbance; elevation of bodily temperature. The first step in my study of fever to-day shall be to demonstrate that of these groups, the first two are merely secondary to and dependent upon the third, *i. e.* that the essential part of fever is elevation of temperature.

A misunderstanding as to my meaning may possibly arise from the unfortunate double value or meaning that attaches to the word fever. It is hardly necessary to state that I am using the term in its abstract sense only. In a fever the pulse-rate and the nervous disturbance, for instance, are dependent

upon various circumstances; in fever, I expect to show that they are due simply to the elevation of temperature.

The demonstration shall consist in proving the following propositions; their truth once acknowledged, the final conclusion is inevitable.

First. External heat applied to the body of the normal animal, so as to elevate the temperature, produces derangement of the nerve functions, of circulation, etc. etc., precisely similar to those seen in natural fever; the intensity of the disturbance being directly proportionate to the rise in temperature.

Second. Heat applied locally to the brain or to the heart produces in the functions of the organ those disturbances which are familiar phenomena of fever, the intensity of the disturbance being directly proportionate to the excess of heat in the organ.

Third. The withdrawal of the excess of heat in fever is followed by a relief of the nervous and circulatory disturbances.

When a dog, cat, or rabbit is shut up in a box heated either by the sun's rays or by artificial means, the temperature of the animal rises, and at the same time the pulse-rate becomes *pari passu* more rapid, the breathing grows more and more hurried, and the restless, uneasy movements of the victim show the general distress it is suffering. As the temperature increases the nervous disturbance becomes more and more apparent; stupor, coma, partial paralysis, convulsions, and finally death by arrest of the respiration occur. These phenomena sometimes come on gradually, but sometimes are developed suddenly.

The temperature at which death occurred in my experiments, varied in the rabbit from 111 to 114½° F.; in the dog it was about 111° F. In man a similar series of phenomena are developed by exposure to excessive heat, although

owing to man's extraordinary power of cooling his body, and of protecting it against cold, he is able to bear extremes of temperature far beyond the points which would prove fatal to any given species of animal.

It must not be lost sight of, however, that man is no more able than the animal to bear an excess of interual or bodily heat. He resists the heating of his body from without, but when his body is heated his arterial and nervous system are found to be as susceptible to the influence of an excessive temperature as are the same organs of the animal. The terrible mortality of sunstroke, or, as it is called with more scientific correctness, thermic fever, is a witness to this susceptibility.

The facts and arguments which have thus been briefly sketched are certainly sufficient to prove that an exposure to external heat will suffice to develop all the phenomena of fever. If any of my audience is desirous of seeing this matter developed more in detail, he will find, what he seeks, in my little brochure on Sunstroke.

The first proposition having been disposed of, the consideration of the second is next in order.

For the purpose of determining the action of heat upon the nerve centres, some years since, in a number of experiments upon cats and rabbits, I caused a stream of hot water to flow through a pig's bladder, fitted as a sort of bonnet to the head of the victim. It is evident that with small animals we can in this way heat the brain without heating materially the remainder of the body. These experiments have been already reported in full,* and I shall therefore here only mention their results. It was found that coma, with or without convulsions, was produced. Sometimes the stupor came on gradually, hebetude slowly deepening into coma, but in other

* Thermic Fever, Philad. 1872, pp. 76 and 82.

instances the unconsciousness was developed very suddenly. In either case death was finally brought about by paralysis of respiration or apnœa. A thermometer plunged into the brain directly after death indicated a temperature of 113° in a cat, and of 111° F. in a rabbit. In a second series of experiments the skull was opened, and the thermometer placed in the brain so soon as there was decided coma. The brain temperature under these circumstances in the cat was determined to be about 108° F. As in these experiments it was found that pouring cold water upon the head at once relieved the coma, the conclusion is logically irresistible that the coma was produced by the heat. The degree of temperature at which, in the locally heated brain, consciousness was lost, and at which death occurred, was found to closely correspond with the degrees at which the same phenomena occurred when a general augmentation of the bodily heat was produced by exposure to the sun, or to artificially heated air.

It having been determined that heat applied to the brain of an animal is capable of causing cerebral symptoms similar to those seen in fever, the next point to be studied is the action of the same force upon the heart.

In an admirable paper on this subject* Dr. T. Lauder Brunton has collected the evidence, and repeated the experiments so thoroughly, that it is unnecessary here to discuss the matter at length, and I shall content myself with stating the chief facts; referring the reader to Dr. Brunton's paper for the proof. When the cut out heart of a frog is exposed to a rising temperature, the cardiac pulsations constantly become more and more rapid until a heat limit is nearly reached, at which the action of the heart ceases. The increase in the rapidity of the movements of the heart is not in direct relation to the increment of temperature; at first the increase of move-

* St. Bartholomew's Hospital Reports, vol. vii.

ment is slow, but the rapidity of the increase becomes more and more rapid as the temperature rises until the maximum rate is reached. Panum has found that the cut out heart of the rabbit responds to heat in the same way as does that of the frog, and Brunton has experimented by bringing the rabbit profoundly under the influence of the chloral, and then surrounding him with a jacket of hot water. These experiments of Brunton are of course completely parallel with those in which I exposed animals in hot air; in both instances there was a great rise in the rapidity of the cardiac action.

It is, of course, impossible to experiment directly upon man, but the brain and the heart of man must be subject to the same laws, so far as regards gross forces like heat, as the brain of other animals. It is simply inconceivable that what has been proven as true of the lower animals is not true of man. Moreover, we have very direct evidence that heat does affect the organs of man as it does those of animals.

Thus we have an elaborate study on the action of fever heat upon the pulse of man, by Dr. C. Liebermeister, who analyzed the records of 280 cases of acute disorder not directly affecting the brain or heart, accompanied by a rise of temperature, and mostly observed by himself. The following table represents the minimum, maximum, and mean:—

Temperature (Centigrade)		37°	38°	39°	40°	41°	42°
Pulse	Minimum	45	44	52	64	66	88
	Maximum	124	148	160	158	160	168
	Mean	71.6	88.1	97.2	105.3	109.6	121.7

There are so many factors entering into the causation of increased action of the circulation in febrile diseases, that it is to be expected that the minimum and maximum can scarcely obey any fixed law, but in a very large number of observations the action of the general cause of the increased pulse-rate

becomes manifest, and the table shows with what great regularity the pulse rises with the temperature.

In regard to animals, then, our second proposition has been actually determined to be true by rigid experimentation; in regard to man, it is, of course, from the nature of the case, impracticable in a Christian country to make an actual demonstration, but it is, humanly speaking, a scientific impossibility that the proposition be other than true.

The proof of the third proposition is contained in the following experiment, which I have repeated several times with similar results: A rabbit was placed in a heated atmosphere, and allowed to remain there until consciousness was entirely lost. He was then taken out and plunged into a bucket of cold water. The temperature of the body fell very rapidly to the normal point, that of the water rising two degrees, and consciousness returning so soon as the body was cooled. In a few minutes the rabbit was able to walk, and the next day had entirely recovered. A few moments' more exposure to the high temperature would have killed the animal; undoubtedly, the consciousness was suspended by the action of the heat upon the brain, and undoubtedly it was restored by a withdrawal of that heat.

I have been so fortunate as to have the opportunity of observing in man a series of phenomena perfectly parallel to that just narrated as occurring in the rabbit.

I have a number of times, in typhoid fever with high temperature, seen stupor, delirium, subsultus tendinum, etc., subside under the use of packing in sheets wrung out of ice-water, and the testimony of Jurgensen, Liebermeister, and others to the same effect is simply overwhelming. The following single instance of so-called cerebral rheumatism is so striking and so demonstrative that it would suffice of itself at once to prove and illustrate the proposition.

Some time since, upon entering my ward in the Philadelphia

Hospital, my attention was instantly attracted by the expression upon the face of a patient. He was a young, temperate Irishman, twenty years of age, and of a vigorous physique, who had passed through a severe attack of inflammatory rheumatism without cardiac complications, and was suffering from a relapse, which first appeared as a subacute inflammation of the knee. I had not seen the man the previous day, but I find in the note-book of Dr. Bruen, my interne, the following:—

"Second day of relapse. This morning an acute inflammation of the wrist-joints has set in; the fever is very high; temperature in the axilla 104° Fahr.; ordered potassii bicarb. gr. xx every two hours."

As we walked to the bed, in reply to a question, "What ails our rheumatism patient?" Dr. Bruen said, "Nothing, unless it be pericarditis. When I saw him at 10.30 A. M. there was much less inflammation of the joints than the preceding morning, and although his temperature was as it had been, 104° Fahr., and, as I thought, a pericardial friction-sound could be heard, yet the man was doing fairly; perfectly rational, with a good pulse." It was now about half-past twelve, and our patient was apparently dying. The pulse was between 160 and 170, exceedingly feeble and thready; the pupils strongly contracted, though not to pin-points; the respirations fifteen per minute, exceedingly irregular, mostly deep, jerking, and interrupted; the skin pale and dry; the consciousness completely lost, violent shaking and shouting in the ear only eliciting a few grunts; the temperature in the axilla $108\frac{4}{5}°$ Fahr.; the wrists pale, and no signs of pain elicited by violently moving them. On auscultating the heart I could find no murmur; the first sound was very feeble, somewhat prolonged, and the second sharply accentuated.

Coming to the conclusion that our patient was dying of heat, we determined to cool him at all hazards, and, as the surest and most rapid means, to employ the cold bath.

The following is the record made at the time:—

1.24 P. M. Patient put in a full bath at 60° F.

1.25½. Shows signs of consciousness; will put out the tongue when loudly asked to do so.

1.27. Seems to recognize that the bath is very cold, and struggles to get out.

1.30½. Man has a fair degree of rationality. He has been in six minutes and a half, and now ordered to be taken out at once.

One minute after the bath.—The patient was partially wiped and laid directly upon a gum blanket, and covered only with a sheet, in a room whose temperature was about 65° to 70° F. He has just received a hypodermic injection of six grains of quinine.

Three minutes.—Temperature in axilla 94° F.; in mouth, 105°⅗ F.

Eight minutes.—Temperature has been steadily falling; is now 103° F. in mouth. The man has become perfectly rational, and answers to his name.

Pain and sensibility have returned somewhat to the wrist. Ice-bladders were applied to head ten minutes after bath. The attendants state that he passed a very little urine at 11 o'clock; bladder is now entirely empty.

Twent-yfour minutes.—Temperature in mouth 104⅘°.*

2 P. M. Pulse 140, weak. One-half fluidrachm of tincture of digitalis, with two ounces of raw whiskey, were given.

2.45. Temperature in mouth 101°, in axilla 102°, in rectum 102¾°.

4.15. Digitalis and whiskey were repeated, but were immediately vomited. Pulse 140; temperature 101⅘°. No urine had yet been secreted into the bladder. He was cupped ten ounces of blood over the kidneys. Ordered an enema, also ʒij of acetate of potassium every two hours, with two ounces of infusion of digitalis applied on cloths to the abdomen. Small quantities of milk and lime-water were given at intervals.

8 P. M. The patient says he feels very much better; recollects nothing of the past, excepting that in the morning he was very dizzy, and just afterwards became unconscious. Application of digitalis renewed. Pulse 128, temperature 102½°.

12 midnight. Pulse 116, much stronger; temperature 99½°. Complains of feeling cold, but in other respects is better. Has passed about a pint of urine. Since his bath he has been lying on the gum blanket, covered only by a sheet, as at first. He is now ordered to be put into a warm bed, and covered with blankets. Ice still kept applied to head. Other treatment continued, excepting the digitalis poultice.

April 9, 9 A. M. Is much better. First sound of heart very weak;

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* Up to this point the temperatures were taken by myself or under my immediate supervision. After this by Dr. Bruen.

second sound very strongly accentuated, both pulmonary and aortic. There is no murmur.

Was ordered to take, during day, ʒss citrate of potassium, in one-half pint of water, every two hours; ten drops tincture of digitalis, and two grains quinine, every three hours; one-half pint milk every four hours. Temperature 100¼°, pulse 120.

At 12, temperature 101¾°, pulse 124.

3 P. M. Temperature 101°, pulse 120.

8 P. M. Treatment all carried out, excepting the milk, which caused great nausea and vomiting; it was therefore given one ounce at a time, and about one pint, with eight ounces of beef-tea, was retained during the day. Medicine was all retained without difficulty. He has passed urine freely during the day—about three pints in all. Temperature 102½° F., pulse 122. He complains of severe pains in wrist-joints and in the shoulders. Treatment continued during night, when awake. Five-grain Dover's powder ordered; the same dose to be repeated at 12 o'clock, if awake.

April 10, 9 A. M. The patient slept during the past night, for the first time since the 8th. Took his medicine without any nausea being experienced. Says he feels much better. Ice-cloths to head discontinued; other treatment continued. The condition of joints of wrists and shoulders is about the same as on the morning of the 8th; they are very swollen and painful. Pulse 120, temperature 101° F.

6. P. M. Condition as in morning. Has taken one quart of milk during the day. Temperature 100⅗° F., pulse 116.

April 11. Temperature 100⅕° F., pulse 92. Quiniæ sulph., fifteen grains daily, ordered. Digitalis and the potassium salt continued.

April 12. Is very much improved. Pulse 96, temperature 100°. Citrate of potassium ordered every three hours; thirty drops tincture of digitalis in twenty-four hours.

April 14. Feels very little pain in joints, has good appetite, and looks, indeed, almost well. Citrate of potassium discontinued. Iodide of potassium, ten grains, t. d.; tincture of chloride of iron, gtt. xx, t. d. Quinine continued. Temperature 99°, pulse 72. Tincture of digitalis stopped.

May 4. From the time of previous note he steadily progressed towards entire convalescence under a tonic treatment, and has been for some days going about freely. To-day he is to be discharged, perfectly well. There is no cardiac lesion whatever.

Let me call your attention, gentlemen, to the rapidity with which, under the influence of the cold bath, the symptoms abated in our patient. He was not in more than a minute and a half before he exhibited very distinct signs of returning con-

sciousness, and in three minutes had sense enough to attempt to get out of the tub. What could the bath do to affect the man so much but withdraw the heat, which, as you know, we have found to be a poison to the nervous system? That the heat was withdrawn, the thermometer proved. If the drowsiness had been due to simple congestion of the brain, very certainly would the bath, by driving the blood from the surface, have increased the trouble.

It must be borne in mind that this case is by no means unparalleled; similar instances of the good effects of the sudden withdrawal of heat in rheumatic hyperexia have been reported by both English and German observers, and recent Continental literature is full of reports of the relief of nervous symptoms in various pyrexias by the abstraction of heat.

These cases, when taken in connection with the parallel experiments upon the lower animals, establish to my mind with absolute certainty the truth of the third proposition.

We have found, then, that excessive heat is present in fever; that this excessive heat, when present, not only is able to, but is forced, so to speak, by its own attributes, to produce disturbance of the functions of innervation and circulation, and that the withdrawal of the excessive heat in fever is followed by instantaneous relief of the symptoms of disturbed innervation and circulation; surely the conclusion is logically inevitable, that excessive temperature is the cause of the other symptoms of fever—that it is the essential portion; that fever and excessive bodily temperature are synonymous.

It is evident that the increase in the amount of caloric in the body during fever can only occur through a lessened giving off of heat by the body, or by an increased production of heat in the body. Had not so great an authority as Traube (*Allgemeine Cent. Zeitung*, 1863) espoused the theory that the elevation of temperature in the febrile state is due to increased retention rather than increased production of heat, it would

seem scarcely worth while to prove that the chemical movements of the fever patient are vastly above normal. The elaborate experiments of Liebermeister (*Beobachtungen und Versuche über die Anwendung des Kalten Wassers bei Fieberhaften Krankheiten*, Leipzig, 1868), of Kernig (*Reichert's Archiv*, 1860), upon the effects of cold baths in fever and in health, have abundantly proven that fever patients yield a vastly greater amount of heat to the water in which they are immersed from hour to hour than do healthy men, and yet their temperature remains above normal. The proven excessive elimination of carbonic acid in the breath and of solid matters in the urine in fever, the well-known emaciation that fever causes, all bear similar witness to the experiments just quoted, so that it must be received as an axiom, that *the essential part of fever is increased chemical movements throughout the system.*

Having arrived at a clear idea as to what fever is, we are prepared to investigate its mechanism —to determine, if possible, in what way the rise of bodily temperature is produced.

In fever all portions of the body usually are in unison; the increased tissue-change which is at the basis of the elevation of temperature, apparently occurs everywhere throughout the system. It is plain that there are only two bonds of union between all portions of the body, two organs or tissues which fuse, as it were, all parts of the system into one; and that any physiological or pathological process which is equally shared by all must have its origin either in the blood or in the nervous system.

Is fever, then, a hæmic disorder, or is it a neurosis? Very possibly many of you, especially those whose military experience causes pyæmia to be ever present in the thoughts, will reply at once, it is hæmic. In many exanthemata there is undoubtedly, either as a cause or as a result of the disease, an altered state of the blood. In pyæmia a blood-dyscrasia is certainly a primary phenomenon; and in animals we develop

septicæmic fever by the injection of putrid matters into the blood. Let us pause a moment to understand clearly, however, what we mean by fever being hæmic or neurotic. If the poison carried by the blood into all parts of the body acts upon the various tissues everywhere in such a way as to increase in them tissue-change—or if, upon entering the blood, it excites such changes in that fluid as to cause the blood to incite the tissues everywhere to fever, then that fever may be called, with scientific strictness, *hæmic*. Suppose, however, we have a fever-centre in the nervous system, and that irritation of a peripheral nerve is capable of causing fever by affecting that centre, such fever would certainly be a *neurosis*. Granting the existence of a "fever-centre" of this kind the laws of life teach us that there must be poisons capable of acting upon it directly so as to produce fever. Such a fever would certainly be neurotic, although produced through the blood, the vital fluid acting simply as a "common carrier." With this understanding of the terms, certainly clinical proof is at present wanting that the fever of pyæmia, of the exanthemata, or of any so-called blood poisoning is strictly hæmic. It may be due to an action of the poison upon the central nervous system.

There are, however, numerous febrile reactions in regard to whose origin there can be no doubt. Take one of the most common conditions, that due to the irritation of a local inflammation. It is scarcely possible that the inflammation develops any substance which acts as a general irritant to the tissue; it is much more probable that the fever is produced through the agency of the nervous system. Irritative fever comes and goes so quickly, is accompanied by so little perceptible general derangement of the system or of the blood, that it seems as though it were as distinctly the result of irritation of peripheral nerves as is tetanus, with its intense fever.

The intense fever which is sometimes excited by the passage of a catheter, as asserted by Bilroth (*Archiv für Klin. Chi-*

rurgie, Bd. VI., p. 441), is an example of a pure neurosis. It is impossible, in some of these cases, that there can be injury to the urethra, much less any alteration of the blood. The fever is due to a mere local irritation, which effects no local nutritive change, and it must therefore be produced through the nervous system.

The following case of *urethral fever* occurred in the practice of a friend, and may here serve as an illustration :—

——, æt. 40, was treated in the Philadelphia Hospital during August, 1873, for very tight irritable stricture of the urethra. It admitted, when treatment was commenced, only a small-sized whalebone bougie. About two weeks were occupied in treatment by gradual dilatation until it was sufficiently dilated to admit a Holt's dilator, when the stricture was ruptured, after which a No. 12 Thompson's sound was introduced. There was a good deal of subsequent shock and urethral fever, which yielded to treatment. *Four* days afterward, on Sunday morning, the attending surgeon found some contraction in the calibre of the canal, and introduced with difficulty No. 12 Thompson's sound, following it by Nos. 14 and 16. Considerable difficulty was met with in their introduction; the patient suffered a good deal of pain, and bled freely from the urethra. This operation was performed about 12 o'clock; about 3 o'clock the patient had a chill, followed by high fever, thermometer registering 103°–104° F. He was treated by quinine and opium, which controlled the symptoms somewhat; the next day, however, at about 9 A. M. the temperature, in spite of treatment, rose again to 103°. There was an increase during the morning to 104° at ten o'clock. The man was rational; the pain had been relieved by opium; no immediate danger was apprehended. The resident physician (Dr. Bruen) was sent for about three o'clock in the afternoon, with news that the man was dying. He found the patient was entirely unconscious; breathing stertorous; pupils fixed, neither dilated nor con-

tracted, would not respond to light. Temperature had risen to 110½°. Other thermometers were procured, and in fifteen minutes after the temperature taken again in the axilla, mouth, and rectum. In the latter place it was 111¼°, in the axilla 111° F. The man was ordered to be laid in the bath-tub, but there was no water at hand, and when some was procured in half an hour from the time the resident first saw the patient, he was dead. His urine, when drawn by catheter, was scalding hot, but no albumen was found in it, nor any pus.

Post-mortem examination sixteen hours after death revealed only intense congestion of kidneys, and of all the genitalia and pelvic viscera. There was no apparent inflammation of any part of the genital passages. The brain was very much congested, as were also the sinuses of the dura mater, and the vessels of the brain. The brain substance appeared healthy; there was some effusion into the ventricles. There was also congestion of the lungs.

A very curious phenomenon, which is in itself sufficient to prove that fever is not due to a diseased condition of the blood, irritating, or in some way acting locally upon the tissues, is in the confinement, in some cases, of the fever to a part. This is more especially seen in malarial disorders, but is occasionally witnessed in other affections. I have never myself seen such a case, but it is said that sometimes a portion of the body not larger than the finger will pass through all the stages of an ague paroxysm, chill, fever, and sweating. In acute apoplexy I have known of an intense paroxysm of fever confined to the affected side.

It is unnecessary, I think, to dwell upon this point more in detail. The conclusions to be drawn from the clinical consideration of the subject are: in some cases fever is undoubtedly a neurosis; whilst in other cases clinical medicine is unable to decide with certainty whether the elevation of temperature is neurotic or hæmic.

Having investigated the mode of origin of fever from the clinical standpoint, as far as we are able, it is evident that we must supplement this study by an experimental investigation. As it has been shown that the elevation of temperature is at least sometimes brought about through the agency of the nervous system, the experimental inquiry will first be directed to discovering to what extent, and in what way, the nervous system does influence animal temperature.

In 1870 P. Heidenhain announced (*Pflüger's Archiv*, p. 504) that when a sensitive nerve is stimulated, a fall of temperature occurs simultaneously with the rise of the blood pressure. I shall not attempt to follow this memoir closely, but shall simply state the results of the experiments, the conclusions drawn, and the evident reasons there are for not allowing the justice of the deductions made.

The experimental facts which were reached are as follows:—

1st. Irritation of a sensitive nerve causes a rise in blood pressure but a fall in temperature.

2d. This fall occurs in the posterior part of the body even after the circulation has been cut off by forcible compression of the aorta.

3d. When, in animals which have been thrown into a high fever by the injection of putrid matters, a sensitive nerve is stimulated, a rise of blood pressure occurs as in the normal condition, but no *change of temperature.*

Dr. Heidenhain believes that when the blood pressure rises the blood current moves more rapidly, and that the fall of temperature is due to the surface blood being returned more quickly to the internal organs and thereby cooling them more rapidly than normal. It seems scarcely necessary to point out that if the blood is returned more rapidly to the interior, it of necessity remains upon the exterior for a shorter period, and is cooled less than normal. It makes no difference whether a quart of fluid cooled one-tenth of a degree, or a pint cooled two-tenths

of a degree, is returned in a given time so far as the temperature is concerned. More than this, in a very quick passage the blood probably loses less than a proportionate amount of caloric. Be these things as they may, the second and third experimental facts seem, to my mind, entirely sufficient to prove the incorrectness of the theory of Heidenhain—a theory whose utter improbability is shown by the circumstance that in some of his experiments, though the animals were wrapped in wool, yet the temperature fell steadily after galvanization of a nerve. Under such circumstances it seems incorrect to attribute the fall of temperature to increased evolution of heat from the body owing to changes in the circulation.

The work of Heidenhain has been reviewed and extended by Dr. F. Riegel (*Pflüger's Archiv*, Bd. iv. 1871).

In Dr. Riegel's experiments the fall of temperature did not always occur when the nerve was irritated, although the pressure always rose. Moreover, he noticed that the temperature usually remained at the minimum point for a long time after the withdrawal of the stimulus, although the blood pressure returned at once to the normal point.

The experiments and results of Heidenhain were, indeed, not entirely novel. The same ground appears to have been covered by Mantigazza. Where his memoir is published I am unable to say, but his results and conclusions, as quoted without reference, by Redard (*Archives Générales*, VI. Série, t. xix., p. 35), are as follows:—

1. Intense pain transmitted by spinal nerves and the skin causes a rapid fall of temperature, which in the rabbit amounts to from 0.68° C. to 2.48° C.; the mean being 1.27° C.

2. The temperature falls perceptibly during the first minute, and arrives at its maximum in ten to twelve minutes.

3. The lowered temperature may last for an hour and a half.

4. The fall is most marked when the pain does not give origin to muscular spasms.

5. The same phenomena occur in man.

6. The grave abatement of temperature produced by a pain lasting ten minutes would appear to be dependent upon an alteration of the chemical actions of the body, and not merely to an indirect influence exerted upon the vaso-motor nerves.

In order to clearly determine the truth concerning the influence of irritation upon a sensitive nerve I have myself performed the following experiments, which are, of course, repetitions of those of earlier observers. The records of these experiments are as follows:—

Experiment 1.

A young pup. Crural and axillary nerves exposed and thermometer placed in peritoneal cavity.

Minutes.	Temp.	
0	$101\frac{1}{4}^{\circ}$	Intense current to brachial; violent cries and struggles.
$1\frac{1}{2}$	$101\frac{1}{2}$	
$2\frac{1}{2}$	$100\frac{3}{4}$	Current withdrawn.
4	$100\frac{3}{4}$	
$4\frac{1}{2}$	$100\frac{5}{8}$	
$5\frac{1}{2}$	$100\frac{1}{2}$	
7	$100\frac{3}{8}$	
9	$100\frac{3}{8}$	Current reapplied.
10	$100\frac{3}{8}$	
11	$100\frac{1}{4}$	Current broken.
13	$100\frac{1}{8}$	
17	100	
19	$99\frac{7}{8}$	
21	$99\frac{3}{4}$	
22	$99\frac{5}{8}$	
24	$99\frac{1}{2}$	Current reapplied.
25	$99\frac{1}{2}$	
26	$99\frac{1}{2}$	
27	$99\frac{3}{8}$	Current broken.
29	$99\frac{1}{4}$	
67	99	
97	100	
127	100	Dog killed.

Experiment 2.

A stout tom cat. The animal was closely wrapped up in flannels, many folds around the body and legs. Thermometer in peritoneal cavity.

Minutes.	Temp.	
0	101⅝°	
5	101½	Brachial nerves cut down upon and exposed since last note.
6		Intense current applied to nerves.
7	101⅜	Violent cries and struggles.
8	101½	Current interrupted.
20	101⅝	
25	101½	
26		Current applied.
26½	101⅞	Violent struggles and cries.
27	101½	
28	101⅜	Current broken.
30	101½	
33	101½	
35	101½	Cat killed.

Experiment 3.

An adult rabbit. Under chloroform, axillary nerves exposed, and a thermometer inserted through a small opening in the linea alba into peritoneum.

Minutes.	Temp.	
0	102¾°	
2	102¾	Current applied to nerve; violent struggles and cries.
3½	102¾	Temperature of room 83°. Current broken.
4½	102⅞	
5	102⅝	
7	102⅝	
8	102⅜	
10	102⅜	
13	102¼	
15	102⅛	
18	102	
19	101⅞	Current applied; struggles and cries as before.
20	102	Current broken.
21	102	

Minutes.	Temp.
22	$101\frac{3}{4}^{\circ}$
26	$101\frac{5}{8}$
29	$101\frac{1}{2}$
32	$101\frac{3}{8}$

Experiment 4.

An adult rabbit. Prepared as in previous experiments, except crural nerve used.

Minutes.	Temp.	
0	$103\frac{1}{4}^{\circ}$	
2	$103\frac{1}{4}$	Current applied to nerve.
$2\frac{1}{2}$	$103\frac{3}{4}$	Violent struggles and cries; current broken.
4	$103\frac{1}{2}$	
10	$102\frac{3}{4}$	Rabbit quiet.
12	$102\frac{1}{2}$	
14	$102\frac{3}{4}$	
15	102	
17	$101\frac{1}{2}$	
$21\frac{1}{2}$	$101\frac{1}{4}$	Anæsthesia has been induced and the opposite crural nerve exposed, and used through rest of experiment.
22	$101\frac{1}{2}$	Current applied.
$22\frac{1}{2}$	$101\frac{1}{2}$	Current broken.
$23\frac{1}{2}$	$101\frac{5}{8}$	Rabbit squealing and struggling.
25	$101\frac{5}{8}$	Current applied, giving rise to violent struggles and cries.
26	$101\frac{3}{4}$	Current broken.
27	$101\frac{3}{4}$	
29	$101\frac{1}{2}$	
32	$101\frac{1}{8}$	
35	$100\frac{7}{8}$	
40	$100\frac{1}{4}$	
47	$99\frac{5}{8}$	
49	$99\frac{1}{2}$	Rabbit killed.

An examination of these records will show that rarely did the temperature fall whilst the current was being applied, and that in several cases there was even a perceptible rise amounting from an eighth to a half of a degree. This rise I believe to be due to the rise of blood pressure and to the violent muscular exertion which the pain caused. It certainly occurred at the

period at which the blood pressure was increased. In many experiments upon the action of irritation of a sensitive nerve upon the arterial pressure, I have found that if the rise occurs it is immediate, and that in a very brief time after the cessation of the irritation the arterial pressure becomes normal. In all of my experiments, here reported, the fall of temperature did not fairly commence until after the period of disturbances of the circulation; in most cases it was very persistent and progressively increased for many minutes. In Experiment 4 the fall amounted to three degrees and three-quarters, and did not reach its maximum until twenty-three minutes after the last irritation of the sensitive nerve. Without occupying more time with the matter, it is evidently absurd to attribute the fall of temperature to disturbances of the circulation, since, at the time of the fall of temperature, the circulation is not profoundly affected.

The conclusion, from all the data which has been brought forward, seems logically inevitable that *the fall of temperature which results from the irritation of a sensitive nerve, is independent of the circulation, and is due to a direct influence of the nervous system upon the heat-producing function of the body.*

The clinician knows full well that in certain conditions of the system a fall of temperature occurs in man apparently independent of the circulation; and in animals the same thing can be experimentally shown to follow severe injuries. According to Horwath (*Centralblatt für die Med. Wissensch.* 1870, No. 35) and other observers, binding an animal upon a table is sufficient to provoke a very decided fall of temperature. When the animal is seriously wounded this fall is more pronounced; and during the late Franco-Prussian war P. Redard (*Archives Générales*, vi. série, t. xix.) determined that serious gunshot wounds are always in man followed by a very decided abatement of the bodily heat. Out of fifty-one observations made

upon as many individuals, the maximum temperature was 37° C., the minimum 34.2° C., and the general in the neighborhood of 36° C. Perfectly parallel phenomena have been found to occur after large burns; Redard reports some such cases.

Certainly these facts are enough to prove that the nervous system has the power of directly influencing calorification, but the complete elucidation of their signification must be postponed until later in my lecture.

In 1837 Sir Benj. Brodie (*Medico-Chirurg. Trans.*, 1837) observed the case of a man in whom, after a traumatic section of the spinal cord, the temperature rose in the course of a few hours to 111° F.

Acting upon this hint, Sir B. Brodie made experiments upon animals, and found that in them, under certain circumstances, the temperature rose very greatly after section of the cord.

Studies of the effect of division of the cord upon the temperature have, since the time of Brodie, been made by very many observers, notably by Bernard (*Compt. Rend.*, 1852, 1853), Schiff (*Untersuchungen zur Physiologie des Nervensystems*, Frankford, 1855), Chossat (*Meckel's Archiv*, 1852), Tscheschichin (*Reichert's Archiv*, 1866), Naunyn and Quincke (*Ibid.* 1869), Rosenthal (*Centralblatt*, April, 1869), Binz (*Virchow's Archiv*, 1870). It is hardly necessary to trace, step by step, the various views which have been held by these authors, and I shall only speak of the results obtained by the more recent observers—results which I have myself experimentally determined to be correct.

If the cord of a rabbit or other small mammal be cut in the lower cervical region, the temperature at once falls; and if the air of the apartment be decidedly below the warmth of the body this fall is permanent, and even increases, so that at death the animal heat is several degrees below normal. If, however, the animal be thoroughly wrapped in raw cotton or in wool, and if the external temperature be not too low, the fall just spoken of

is but temporary, and is succeeded by a rise of temperature which passes far beyond the normal point, so that the animal dies in a state of intense fever. In my own experiments, the cooling of the body after death has often taken place more slowly than normal, but I have never seen that post-mortem rise of temperature which has been noted by Naunyn and Quincke, and by other observers, but which appears to be only an occasional phenomena absent in the majority of cases. According to my own experience (and the testimony of other investigators is in accord with it), if the external temperature be much below that of the body of the animal, no amount of wrappings will suffice to bring about the febrile reaction; and if an animal in which the fever has already come on be exposed to external cold, the temperature falls. The time that elapses between the division of the cord and the rise of temperature varies from a few minutes to many hours, and is dependent upon the external conditions. If the animal be in a heated room, breathing heated air, the period of fall is a very short one. In none of my own trials, however, and in none of those reported by other observers, so far as I am aware, has the fall of temperature been altogether absent. In the experiments of Naunyn and Quincke, although the animal was put at once into a warm chest where the temperature was between 80° and 90° F., yet it was always several hours before the normal temperature was reached. The question here naturally arises, is the subsequent rise of temperature really due to the division of the cord, or is it due simply to the external heat to which the animal is exposed? An experiment completely crucial as to this point was performed by Naunyn and Quincke. They first placed the uninjured animal in the warm box, and when after some hours no rise of its bodily temperature had occurred, divided the cord and replaced the animal in the warm chest, when intense fever came on in a very short time. Again these observers opened the spinal canal so as to completely expose the cord without

cutting it, and placed the animal in the warm chest for the space of ten hours; at the end of this time the bodily heat had risen six-tenths of a degree only. The following day the cord was divided and the animal replaced in the warm chest: in the first twenty minutes the bodily temperature fell nearly one degree, but in the next hour and twenty minutes, at end of which time death occurred, rose three degrees.

It seems to me indisputably established that the secondary rise of temperature, after division of the cord, as well as the primary fall, are in some way produced by the operation.

The question here logically presents itself, Is the first fall of temperature due to a lessened production of animal heat or an abnormal throwing off of the bodily heat? Tscheschichin (*loc. cit.*, pp. 154, 177) found that the temperature in the interior of the body sank more rapidly than that of the external parts after section of the cord; thus, in one experiment, the mercury in two thermometers, which had their bulbs respectively in the intestines and underneath the skin of the animal, differed before the operation in height eight-tenths degree F., whilst some time after the operation they only differed one-tenth degree F. Dr. Tscheschichin seems to believe that this experiment proves a markedly increased throwing out of heat after the operation —an induction which does not seem to me logically correct.

Granting that after division of the cord the inner parts of the body always lose their heat faster than do the outer parts, I do not see that this proves anything more than that after the operation the intercommunication between the interior and exterior portions of the body is freer than normal. In fact, however, the phenomenon is not constant, as is proved by the following experiment, in which the external thermometer fell much faster than did the internal.

Experiment 5.

A stout female cat. The bulb of one thermometer introduced through an opening in the linea alba into the peritoneal cavity, that of the other thrust under the skin to a considerable distance.

Time.	Int. Temp.	Ext. Temp.	Remarks.
10.25	102¼°	101½°	
10.30			Cord cut in the extreme upper dorsal region.
10.35	102⅛	101⅛	
10.40	102⅛	101	
10.45	101⅞	100⅞	
10.49	101⅝	100⅝	
11.	101	100	
11.13	101⅛	99	
11.15	101⅛	98	Cat just dead.

It is in truth very difficult to determine exactly to what the primary fall of temperature after section of the spinal cord is due. The fact that after the secondary fever has been developed the temperature will fall, if the animal be exposed to a cool air, certainly shows that the body throws off heat more rapidly than normal. The dilatation of the vessels in the lungs, and on the surface, and the slowly moving blood current are certainly well calculated to produce an abnormal loss of animal heat. Since, however, Naunyn and Quincke have found that the fall occurs even when an animal is operated upon in an atmosphere at 86° F., it is probable that there is immediately following division of the cord *diminished heat* production as well as *increased heat evolution*. The influence of atropia upon the temperature, the effects of nerve sections, and various facts which it is not necessary here to reiterate, seem to me to indicate that vaso-motor paralysis, *i. e.*, lessened arterial pressure and dilatation of the vessels, always tends towards the production of these phenomena. Be this as it may, facts which it would be premature to bring forward at this time,

prove that the fall does not occur when the section is above the vaso-motor centres, and consequently that it is directly connected with the vaso-motor paralysis, and the consequent derangement of the circulation.

Tscheschichin states that in a single experiment, instead of cutting the cord he divided the medulla oblongata at its junction with the pons, and that the rise of temperature was in this case immediate, not preceded by a fall. Led by this I have performed the following experiments.

Experiment 6.

A large powerful mongrel dog.

Time.	Temp.	Remarks.
12.	102¼°	
12.20		Since last note have opened skull above the foramen magnum with a trephine; in doing this I have undoubtedly wounded a sinus, as the dog has lost fully ¾ pint of blood. I have just severed medulla.
12.25	103¼	
12.30	103¾	
12.40	104	Breathing regular.
12.50	104½	
1	104¾	
1.10	105¼	
1.30	105½	Thermometer put into abdominal cavity.
2		Cardiometer inserted into femoral artery. Art. pressure 75; upon galvanization of a sensitive nerve it fell to 50. The pneumogastric nerves were now cut; pressure after this was 45–55; on galvanization of a sensitive nerve the pressure rose to 65°. The breathing is now very much affected, and paralysis both of sensation and motion is seemingly complete.

Autopsy.—Medulla oblongata divided at its junction with the pons. Cerebellum wounded.

Experiment 7.

A terrier bitch of moderate size and strength. Opened skull.

Time.	Temp.	Remarks.
11.45		
11.47	103¼°	Cut the medulla. Breathing at once ceased almost entirely, so that dog was at one time thought to be dead, and artificial respiration, by compressing the body with the hand, was resorted to.
11.53		Dog beginning to breathe voluntarily, eyes not sensitive, nor is any portion of the body.
11.54	103½	Room 70°.
11.60	103¾	
12.15	103¾	Dog shows no signs of life but the slow, regular breathing.
12.30	103¾	
12.40	104	
12.45	104¼	Breathing noisy, irregular.
12.55	104¾	General muscular rigidity, with constant convulsions. Tremor has come on; both symptoms are much aggravated by any irritation of the surfaces. Legs stiffly extended, tail forcibly drawn down between them.
1.15	106	Room 70°.
2.10	107¾	Thermometer is now in abdominal cavity (has been in the rectum). The dog has been vomiting freely of matter.
2.15		Arterial pressure 150–160; galvanization of a nerve caused it to fall to 120–125.
2.20	108⅛	Cut the par vagum. Breathing at once almost suspended.
2.22		Respiration only at very long intervals. Blood in arteries venous. On connecting a cardiometer tube with the femoral, the mercury rose to the top of the tube (205) and flowed over in abundance.
2.25		Has been no breathing for some minutes. Heart has not ceased to beat.

Autopsy.—Knife has passed through the cerebellum, scraping the posterior surface of upper portion of medulla, and cutting it very obliquely at its junction with the pons.

In looking over the records of these experiments, it will be found that they are very conclusive, in regard to the rise of temperature, which follows division of the medulla high up. One of the most powerful means of lowering the temperature

at our command is venesection, and yet, although the dog in Experiment 6 was almost bled to death, the temperature rose from the time the medulla was divided. In Experiment 7 no bleeding of any moment occurred, and the elevation of temperature was therefore more marked than in the first trial. The rise commenced immediately after the division of the medulla, and amounted to almost five degrees, and was still increasing when the animal was killed. As the temperature of the surrounding air in both cases was not over seventy, the evidence is conclusive.

These experiments show very decidedly that fever is entirely independent of the circulation. In the small animal the arterial pressure was high, but in the large dog it was reduced to the lowest point compatible with life, and yet, in both instances, the temperature rose. Again in neither case was there vaso-motor paralysis, in the first experiment. After division of the par vagum, galvanization of a sensitive nerve was followed by a slight but distinct rise of the arterial pressure. The reason of this rise being so slight was probably the very small amount of blood in the vessels, so that contraction of the latter was not followed by the usual effects.

In the smaller dog, the evidence that the vaso-motor system was intact, was unimpeachable. At first galvanization of a sensitive nerve depressed the pressure, very decidedly, on account of the influence of the pain on the par vagum.

The mere height of the arterial pressure was, however, sufficient to prove the integrity of the vaso-motor system, for if the vessels had all been dilated, the mercury in the tube of the manometer would certainly not have stood over 100. Whenever asphyxia is produced in the normal animal, an enormous rise of arterial pressure results, owing in part to the vaso-motor spasm, which is caused by the excess of carbonic acid in the blood.

In Experiment 7 this rise of pressure followed the arrest of

respiration, and as there were no disturbing struggles, the universal paralysis being complete, must have been solely due to the action of the carbonic acid upon the heart and the vaso-motor centre.

The evidence that the section was practised above the vaso-motor centres, derived from the experiments themselves, is therefore conclusive, but it is well to call attention to the fact that it is already established that the vaso-motor centres are in the medulla oblongata, a fact which strangely enough has been overlooked by most, if not all, recent English writers, finding, for instance, no expression in the very elaborate and recent work of Dr. Flint.* A review of the evidence at this place would interrupt the thread or line of the present argument, and I shall therefore defer it for a few minutes.

In the following experiment the changes in the temperature which followed separation of the medulla from the pons, are apparently different from those previously obtained, but before discussing the point, let me offer you the record of the experiment itself.

Experiment 8.

A stout young dog above medium size.

Time.	Temp.	Remarks.
10.30	$103\frac{10}{4}$	
10.50		Brain freed with slight hemorrhage.
10.55	$104\frac{1}{8}$	
11.5	$104\frac{1}{8}$	
11.20	$104\frac{3}{8}$	
11.35	$103\frac{1}{8}$	Medulla cut. Absolute paralysis of motion and of sensation at once developed.
11.37	103	
12	103	

* Since I received the proof of this lecture a number of the Boston Medical and Surgical Journal has come to hand containing an article from Prof. Bowditch on the work done abroad concerning the vaso-moter centres.

Time.	Temp.	Remarks.
12.30	103°	Arterial pressure 120; on galvanizing nerve it fell at first but soon rose to 185, no movements except in muscles supplied by nerve were elicited.
1	101¾	
1.20	101	
1.25		Dog put in a box at temperature 90°.
1.45	101⅝	Temperature of box 102°.
2.30	104¼	" " 104.
2.45	104½	" " 90.
3	105	" " 88.
3.30	106½	" " 94.
4	107	" " 84.
4.30	107	" " 82.
4.40	107	" " 76.
5.30	107	" " 72.
8	106	" " 64.
8.30	105	" " 64.
9	105	" " 64.

Next morning the dog was found dead.

Autopsy.—Medulla was nearly severed obliquely, where it merged into the pons.

In this experiment you see a fall of temperature preceded the rise, which was apparently due to the dog's being placed in a hot box. The cause of this fall I cannot completely establish; certainly, however, the fever, when developed, was independent of the external heat, for whilst the latter was steadily falling from 104° to 72°, the animal heat rose from 104° to 107°. In this experiment the arterial pressure rose from 120 to 185, when a sensitive nerve was galvanized, and the vaso-motor system was therefore intact. The fact that the medulla oblongata was not completely divided probably accounts for the want of as rapid a rise of temperature in this as in the previous experiments; if there be a "fever centre," the separation of it from the rest of the body was not complete but partial, and, therefore, it was not to be expected that the rise of animal heat would be as rapid or intense as in the previous experiments. What-

ever may have been the cause of the primary fall, the fact that the subsequent elevation of temperature was independent of the external heat shows that the primary fall was due to some temporary cause, and that the experiment really corroborated the others.

J. Bruck and A. Günter (*Pflüger's Archiv*, Bd. iii. p. 579) have also experimented upon the effect on the temperature of section of the medulla oblongata at the border of the pons. They used rabbits, and operated without opening the skull. Out of seven operations they found that once the temperature rose enormously after the section, once it rose very decidedly (1.1° C.) and in four cases fell continuously. The reason of the varying result seems to me to be found in the small size of the animal used. It must be remembered, that, if the vaso-motor centre be injured directly or indirectly in the operation, a fall of temperature must occur precisely as if the spine were cut lower down, and, as Bruck and Günter did not bring the animals into a warm place, such fall of temperature would necessarily be permanent. No effort was made by the observers to determine whether or not the vaso-motor nervous system was affected; and, as, in the rabbit (speaking from memory), the distance between the point assigned by Owsjannikow as the vaso-motor centre and the border of the pons cannot be more than a tenth of an inch, I think it is a fair inference that the vaso-motor centres were affected. No details of the experiments are given, but the reporter says, that the "bad success of the operation seemed to have its foundation in the too quick death of the animal." Taking all these circumstances into consideration, I do not think I can justly be accused of any desire for special pleading when I come to the conclusion, that, whilst the successful experiments of Bruck and Günter confirm those already detailed in this paper, the failure in other cases of the temperature to rise in no wise invalidates the conclusions to be

hereafter drawn from the experiments of Tscheschichin and myself.

Having now given you the experimental facts, it is proper to enter finally upon their discussion, and I shall take up first the subject of the position of the vaso-motor centres.

In a number of experiments,* which I have performed, galvanization of a nerve after section of a cord in the lower cervical region has failed to affect the circulation, or in other words, to influence the vaso-motor centres. To-day we have seen that after separation of the medulla from the pons nerve irritation does influence the circulation. Evidently then the vaso-motor centre is in the medulla. As already stated this conclusion is in accord with that of previous observers.

It is true that Prof. Cyon (*Mélanges Biologiques tirés du Bulletin de l'Academie Imperiale des Sciences de St. Petersbourg*, t. vii.) found that when the cerebral hemispheres are removed, leaving only the medulla oblongata and the cerebellum, irritation of a sensitive nerve is not followed by a rise of arterial pressure. The shock and the bleeding from such an operation are, however, so great that the results of the experiments are of little value; certainly the loss of blood and nervous disturbance might of themselves very conceivably utterly paralyze the vaso-motor centres, supposing them to be in the medulla oblongata. Therefore it cannot be allowed that the experiments of Prof. Cyon really contradict those about to be cited, which are in accord with those which I have myself performed.

Dr. C. Dittmar† (*Berichte über die Verhandlugen der Königl. Sachs. Gesellschaft der Wissenschaften zu Leipzig. Math.*

* See as an example Experiment XXVIII. in an "Investigation into the Action of Veratrum Viride upon the Circulation," *Phila. Medical Times*, vol. iv., also pamphlet reprint.

† Von Bezold may have ascertained the same experimental fact in his Untersuchungen über die Innervation des Herzens, Leipzig, 1863, but I have never seen his memoir.

Phys. Classe. 1870, Bd. xxii.) is the first experimenter to whose original paper I have had access, who proved that after separation of the medulla from the pons irritation of a sensitive nerve still causes a great increase of the arterial pressure. Thus in his experiment *a* (p. 33) on a rabbit, the medulla having been previously cut, the pressure rose 29 millimetres in 16 seconds, and in experiment *b*, both peduncles of the crus cerebri having been previously divided, the rise amounted to 30 millimetres.

I. Owsjannikow (*Berichte, etc.*, Bd. xxiii.) has experimented very elaborately, and has found that in cats and rabbits the vaso-motor centre is in a space whose upper boundary is one or two millimetres below the corpora quadrigemina, and whose lower boundary is four to five millimetres above the point of the calamus scriptorius, a space of about four millimetres.

Owsjannikow divided the nerve centres with very fine knives and employed the effect upon the arterial pressure of galvanizing a sensitive nerve as a test of the integrity of the vaso-motor centre. His experiments have every appearance of care and accuracy.

R. Heidenhain (*Pflüger's Archiv*, Bd. iv. p. 552, 1871) has also, in numerous experiments, determined that separation of the medulla from the pons in dogs does not prevent the rise of arterial pressure when a sensitive nerve is irritated.

The results obtained severally by Dittmar, Owsjannikow, Heidenhain, and myself are therefore in accord, and seem to prove that the chief vaso-motor centre is in the medulla oblongata, probably in the exact position indicated by Owsjannikow.

It does not follow, however, that this centre in the medulla is the sole generator of vaso-motor force. It is much more probable that it is simply of the nature of a governing or starting centre, and that the chief generators of vaso-motor force are placed in the cord. These cells, if they exist, may, under ordinary circumstances, not have the power of generating vaso-

motor impulses—but it may be their function to receive the impulse from above as their normal stimulant, which shall excite them to send an impulse, which is received, not by the vaso-motor muscle fibres, but by cells of the so-called sympathetic ganglia. The anatomy of the nervous system appears to me to point to this method of action, but a still stronger indication of it is afforded by the experiments of Schlesinger (*Wiener Med. Jahrb.* 1874), who found, in agreement with other observers, that when the cord is cut in the dog irritation of a sensitive nerve has no effect upon the arterial pressure, but who also discovered that if the animal were poisoned with strychnia, irritation of a sensitive nerve did induce rise of the arterial pressure.

If there be no fallacy underlying these experiments, it would appear a rational explanation of these results that strychnia so excites the nerve cells of the spinal cord as to cause them to respond to an impulse from below, which, under ordinary circumstances, is unable to affect them. Be these things, however, as they may, the cardinal fact seems absolutely proven by the concurrent experiments of five observers that the *chief or governing vaso-motor centre is in the medulla oblongata.*

From the facts and arguments which have been adduced, it is very certain that the rise of temperature which follows separation of the pons and the medulla is not due to any disturbances of circulation, the vaso-motor centres not being implicated by the operation. Moreover, as already stated, in my experiments the rise occurred in dogs in which the bloodvessels were almost empty, as well as when the arterial pressure was rather above normal.

Can the rise be due to changes in the respiration? Certainly not. In the first it is not conceivable that any departure from normal respiration should have the power to induce such rapid

increase of the chemical movements of the body. In the second place the temperature rose in my experiments during every imaginable condition of the respiratory movements. In one instance these were so far abolished that life had to be sustained for a time by alternately squeezing the chest and allowing it to dilate; at another time the breathing was natural; in another case it was hurried. Under all circumstances the bodily heat steadily increased.

The fever then which follows separation of the medulla from the pons is independent of the circulation and the respiration. I believe with Tscheschichin that it must be due to the removal of the influence of some repressive force, and that there must be *in the pons or above it a nerve centre whose function it is to inhibit or repress the chemical movements of the body*, i. e., *the production of animal heat.*

It certainly is an accepted deduction in physiology that section of a nerve induces abolition of function, and that the symptoms which follow such section are paralytic in their nature. Applying this obvious axiom or rule to this case, it is plain that the rise of temperature is owing to a paralysis, and that this paralysis must be of something which keeps down temperature. It would seem hardly necessary to discuss this point in detail, had it not been asserted (*Pflüger's Archiv*, Bd. iii. p. 581), that the rise of temperature which follows section of the medulla at the border of the pons is due to an irritation of the medulla. Heidenhain states that he was led to this conclusion by noting that the rabbits, upon which Bruck and Günter experimented, showed symptoms of irritation of the medulla in that their breathing was exceedingly rapid. Acting upon this, he suggested that the effect of puncture should be tried, and accordingly Bruck and Günter instituted such experiments. The temperature rose more uniformly than in the previous experiments in which section was practised. It was found that two or more punctures were more effectual than a single one,

and that the effect was still more pronounced, if two of the lance-shaped needles were plunged in at once, and allowed to remain (*in das Gehirn senkt und dieselben liegen lässt*).

In commenting on this, I want to call attention to the fact that in some of my experiments the temperature rose at a time when, so far from there being irritation of the medulla, this organ was so depressed by the shock that the animal had to be kept alive by artificial respiration. It is evident that in the experiment of Bruck and Günter, the nerve centres were actually wounded, and I see no reason for disbelieving the possibility of this wound affecting the conducting power of the nerve fibres, especially as it is plain that the deeper and larger the wound, *i. e.*, the more numerous the needles, the greater was the rise in temperature. The paralytic effect of plunging a needle into a nerve centre certainly reaches, at least for a time, beyond the obvious wound, and the effect of leaving a needle in must be to increase this paralysis by pressure. The reason the rise was obtained more frequently after the "stick" than after the section of the medulla, seems to me to depend upon the circumstance that in the former case, the vaso-motor centres were not so apt to be involved as in the latter.

It must be borne in mind that the rise in temperature which follows this section of the medulla oblongata is obviously of the same character as that which follows section of the cord lower down. Now it is simply inconceivable, that irritation of a nerve centre should give rise to the same symptom as section of the nerve, which runs from the centre. If irritation of a cerebral nerve centre be followed by a rise of temperature, section of the spinal cord ought to be followed by a fall of temperature. As the facts are, it seems to me as logical to attribute the loss of voluntary movement which follows section of the medulla oblongata to irritation, as to attribute the rise of temperature to irritation.

Whether we do or do not grant the existence of the inhibi-

tory chemical centre, the experiments which have here been detailed, undoubtedly prove that the nerve centres influence directly the chemical activities of the body. The increase of reflex activities, which follows section of the medulla, is universally believed to be due to the separation of the cord from an inhibitory motor centre, and why should it seem so strange that there should be an inhibitory heat centre? the evidence in the two cases is completely parallel.

Although I am now advancing beyond actual demonstration, it is very possible that this inhibitory heat centre does not act directly upon the tissues, but that through the whole length of the cord there are cells whose function it is to preside immediately over chemical activities, and that upon them the inhibitory centre exercises a controlling influence. Without going into any further discussion of this point, let me say that the clinical facts of the so-called infantile palsy seem to point in this direction.

The nervous physiologist very often has called to his aid pathology and the records of clinical medicine, and confirmation of asserted physiological facts and conclusions from such sources is always considered to be entitled to much weight. I have never myself had a case of severe hemorrhage into the pons, but others have, and the records are in accord with the theory of an inhibitory chemical centre. I shall not cite individual cases, but, as more authoritative, the general results put forth by Dr. Bastian in his recent lectures on the differential diagnosis of the clot in apoplexy. He says (*London Lancet*, Oct. 31, 1874), after severe hemorrhage into the pons, when the life is prolonged for a few hours, the temperature of both sides of the body steadily rises, till, at the time of death, it may have attained to 109° or 110° F., a condition of profoundest coma continuing throughout. Why should the fever of a clot in the pons be more a result of irritation than is the palsy which follows a clot in the corpus striatum?

It is a matter of the gravest scientific interest to decide exactly where this inhibitory heat centre is situated. I have not yet had time to undertake a research upon this point, but hope soon to do so. The known facts of clinical medicine seem, however, to indicate that in the optic thalami, or their neighborhood, are the ganglia which control chemical changes. Thus, lesions of the optic thalami, according to Bastian, produce a rise of temperature in the paralyzed limb which amounts to from one and a half to two degrees, and "persists for a long time, it may be for many weeks." There is, of course, no reason for believing that, in this case, the increase of temperature is due to a vaso-motor paralysis, because the vaso-motor centre is far below the part affected. More than this, those who would attribute all these changes in temperature to vaso-motor paralysis are here between Scylla and Charybdis. The limb of the unfortunate child is *permanently icy cold*, because in infantile palsy there is *vaso-motor paralysis*, and the limb of the unfortunate man is *permanently burning hot*, because in apoplexy of the optic thalamus there is *vaso-motor palsy*. I believe it to be a matter of grave doubt whether pure vaso-motor paralysis is ever followed by a permanent rise of temperature; the local fever which occurs after section of the so-called sympathetic nerves being very probably due to these nerves being composed of two sets of nerve fibres, the vaso-motor and those which proceed from the chemical centres to the periphery.

If what has already been asserted in this lecture be true, namely, that the fall of temperature which is produced by galvanization of a sensitive nerve is independent of the circulation, and that there is a controlling chemical centre, it is *à priori* exceedingly probable that the fall of temperature is induced by an excitement of this centre, consequent upon irritation of the afferent nerve, or, in other words, that the fall of animal heat

which follows galvanization of a sensory nerve is the result of a reflex excitement of the inhibitory chemical nerves.

If the experimental results be found to agree with this reasoning, the asserted correctness of the premises is greatly corroborated. The following experiments were instituted to test the matter.

Experiment 9.

A stout young dog. Medulla nearly cut through at its junction with the pons.

Time.	Temp.	Remark.
1	$101\frac{3}{4}^{\circ}$	Galvanization of a sensitive nerve with an intense current for half a minute had no perceptible effect on temperature. Dog watched many minutes.

Experiment 10.

A stout terrier. Medulla oblongata very nearly severed from pons.

Time.	Temp.	
2.10	$107\frac{3}{4}^{\circ}$	A very intense current passed for one minute through the axillary nerves had no influence on the temperature. Animal watched many minutes.

Experiment 11.

A powerful dog. Medulla oblongata separated from pons.

Time.	Temp.	Remarks.
1.30	$105\frac{1}{4}^{\circ}$	Galvanization of a large sensitive nerve with a very strong Faradaic current for one and a half minutes had no perceptible effect on the temperature. Animal watched many minutes.

The results of these experiments certainly are in accord with and corroborate the *à priori* reasons. As a contrast to them, may be profitably studied some which I have made on animals suffering with pyæmic fever. The temperature was not very high, but it was the highest that I have seen developed in a

number of experiments. The results obtained are at variance with those of some previous observers, but of this more anon.

Experiment 12.

A moderate sized male cat.

Time.	Temp.	Remarks.
10 A. M.	101½°F.	Injected one fluidrachm of pus into the flank.
4.20	106½	
4.40		Abdomen opened in linea alba and thermometer inserted; temperature remainder of experiment taken from it.
4.45	106	
4.53		In cutting down for femoral nerve an artery wounded, and about f℥ss of blood was lost.
4.55	103	
4.59	103	Current of moderate strength applied to nerve for about half a minute.
4.60	102½	
5.5	102	
5.15		Current applied for a brief space.
5.20	101	
5.24	100¾	A very strong current applied for three-quarters of a minute.
5.25	100¾	
5.26	100¼	
5.29	100½	
5.30		Very strong current applied to nerve for about a minute.
5.31	100	
5.33	100	
5.34	99¾	Cat killed.

Experiment 13.

A moderate sized male cat.

Date.	Time.	Temp.	Remarks.
12.15	10 A. M.	102°	A half fluidrachm of pus injected into cellular tissue.
12.16	10.		A fluidrachm injected.
	4.30 P. M.	105½	
12.17	11.35	105	Opened linea alba and transferred thermometer to peritoneal cavity.

Time.	Temp.	Remarks.
11.40	104¼°	
11.45	104	Strong current applied to femoral nerve.
11.47	104	Current broken.
11.50	104	
11.55	103½	
12	103	
12.5	102¾	
12.7	102½	Current reapplied.
12.8	102¾	Current broken.
12.12	102¾	
12.16	102¾	
12.20	102	
12.45		Thermometer retransferred to the rectum.
12.47	102	Cat killed.

It is proper to state at this place that both of the last two series of my experiments have yielded seemingly different results from similar experiments made by R. Heidenhain. (*Pflüger's Archiv*, Bd. iii. p. 510.) That observer states that in a number of instances he has found that irritation of a sensitive nerve, after separation of the pons from the medulla, is followed by a fall of temperature. On examining the record of the single experiment, I find, however, that the fall took place solely during the application of the galvanism to the nerve, and amounted at such times only from .05 to .1 of a degree (C.). Indeed, throughout the experiment, the temperature really rose, so that at the end it was decidedly higher during the periods of nerve excitement than it was before the nerve had been irritated at all; and at the close, when the nerve was not stimulated, the bodily heat was .2 C. higher than at first. This very slight fall of temperature, occurring during the period of stimulation, is something very different from the profound fall which occurs some time after the stimulation, and of which I have been speaking all through the evening. This slight, evanescent alteration of temperature is very probably due to alterations in the respiration or circula-

tion. I cannot allow, therefore, that the experiments of Heidenhain contradict, much less disprove, what I have previously asserted.

His experiments on animals suffering from pyæmic fever have also differed from mine, in that he did not obtain any fall of temperature. The explanation of this is probably to be found in the fact that he employed very feeble currents. It may be that it is more difficult to depress the temperature of a feverish than of a normal animal. Upon this point I shall speak more fully a little later in my lecture.

A knowledge of the existence of an inhibitory chemical centre throws a flood of light upon many hitherto inexplicable puzzles in clinical medicine.

Thus it has long been known that high bodily temperature may coexist with any condition of the circulation; and so long as it was believed that the rapidity of the production of animal heat was directly dependent upon the activity of the blood-current, the coexistence of high fever and of lessened arterial action was a very strange phenomenon.

Another class of cases completely cleared up by discovery of inhibitory chemical nerves, is the so-called cerebral rheumatism, an instance of which was detailed earlier in the evening. The fever so universally present in acute rheumatism is probably, in most cases, a merely "irritative fever," essentially different, in the method of its production, from the high temperature of "cerebral rheumatism." It is caused by the articular inflammation of the joints, precisely as it is in cases of simple, non-specific, acute inflammation of joints, and in a manner which shall be explained directly.

The *materies morbi* of rheumatism, whatever its nature may be, is seemingly whimsical in its choice of attack. One day it is the wrist, the next the ankle, the next, perhaps, the pericardium or the pleura, which receives the blow. We cannot tell why any individual part is attacked or is spared in any indi-

vidual case. Now, with seemingly as little reason, sometimes the *materies morbi* expends its force upon the inhibitory chemical centre, and overwhelms it, paralyzes it; a general and rapid rise of temperature results. The pain and sensibility in the joints disappear, not because the disease has left the articulations and attacked the brain, but because sensibility is everywhere destroyed by the heat, as is shown by the fact that in the case here reported, just so soon as the heat was abstracted and the general sensibility restored, the pain and tenderness reappeared in the joints.

The mode of origin of an ordinary case of *irritative fever* is rendered very evident by a knowledge of the inhibitory chemical centre. A boil, a pneumonic lung, or any local focus of irritation, sends an impulse up an afferent nerve to the inhibitory chemical centre. Perhaps, at first, this inhibitory centre is excited to action, and the animal heat is reduced, and a chill is caused. If the irritation be more persisting, the inhibitory centre is weakened or paralyzed, and an elevation of temperature results.

The complete analogue of this exists in the case of the ordinary motor nervous system. One irritation to a nerve results in the production of a distant spasm; another in the production of a distant paralysis; in other words, just as a peripheral irritation may produce reflex functional excitement or reflex functional depression of a motor centre, so may it cause a reflex functional excitement, or a reflex functional depression of this heat-centre; the difference being, that whilst in the former instance there is a spasm or a paralysis, in the latter there is a chill or a fever.

It is well known that the slightest splinter will sometimes cause the most intense motor disturbance; hence it is not strange that the irritation caused by the passage of a catheter should produce an intense disturbance of the inhibitory heat-centre, and consequently of the production of animal heat.

Because fever in some cases is produced by a paralysis of the inhibitory nerve-centre, it by no means follows that it is always so; indeed, it is most probable that there are other methods of its causation. The inhibitory centre must have an antagonistic force which tends towards the formation of chemical changes. Whether this activity does or does not reside solely in the tissues themselves, is not at present positively ascertained. It may be that there is a nerve-centre whose function it is to increase chemical movements. Be this as it may, reasoning from what is known of inhibitory nervous action, it would seem most probable that there is an accelerator as well as a depressor chemical nerve. If there be such, it must also play a *rôle* in the production of fever. We must be careful, however, not to theorize beyond our facts, and we have no positive knowledge of the existence of any chemical nerves except those which control the chemical movements.

Again, it is certain that there are substances which affect these chemical movements either by acting directly upon the tissues or upon the blood. Thus I have ascertained by recent experiments that the nitrite of amyl will lower the temperature, *i. e.*, lower the chemical activities of the body after the latter has been separated from the upper nerve-centre by division of the cord; and Binz and others have proven that alcohol and certain other drugs have the same power.

It has not hitherto been proven that fever ever occurs as the result of a direct action of any agency upon the tissues, but it may be accepted as a necessity, that if some materials exist which are capable of directly lessening the chemical movements of the tissues, there must be other agencies which directly stimulate these same tissue actions.

No disease is more directly traceable to entrance of a poison into the blood than is pyæmia or septicæmia, and none is more constantly attended with fever, or more easily produced in the lower animals.

I have, therefore, endeavored to determine whether, in pyæmia, the chemical nerve-centre is affected, but my experiments have not been pushed far enough to be absolutely conclusive. Since, in pyæmic fever in the rabbit, the temperature—at least in my experience—never goes above 106° F., it is evident that there cannot be a complete paralysis of the inhibitory chemical centre, for if such paralysis existed, the fever would be much more intense. The results in my experiments, already detailed, coincide with this view of the case, and thereby corroborate the truth of our deductions. They are, however, at variance with those of Heidenhain. I found that the temperature in pyæmic fever was profoundly affected by peripheral irritations, whilst he found that it was not influenced.

Without doubt, the experiments were in each case accurately performed and correctly reported; the diversity, in all probability, depends upon his having employed feeble irritations—such as he had found would influence the temperature in the normal animal, whilst I applied very intense faradaic currents directly to large nerve-trunks. It is an almost necessary inference that, in septic fever, the inhibitory or chemical centre has lost, in part, its susceptibility, but is still capable of responding to very powerful stimulation; or, in other words, that the inhibitory chemical centre is, in pyæmia, in a condition of paresis, but not of paralysis.

That the centre is not paralyzed is shown by the comparatively low temperature attained in pyæmia. After section of the medulla, the temperature in the dog rose rapidly to 108°, and was still rising when the animal was killed; whilst in the rabbit, whose natural temperature is higher than that of the dog in pyæmia, I have never seen the thermometer mark higher than 106°.

In bringing this long lecture to a close, there are many thoughts in regard to pathological and especially therapeutical

subjects which I might venture to bring before you, had I not trespassed so much on your patience: as it is, I must take leave of you with the expression of the hope that some of you, having been shown, at least, glimpses of truth new to you, will think and experiment, so as to aid in determining which, of the many things that I have said to you this evening in all honesty, are true and which are false; to the end that out of the labors of many minds the whole truth may at last be evolved.