On Pyrexia
And its Treatment

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On Pyrexia and its Treatment.

In the following paper the term Pyrexia is used in its widest sense, including all those conditions in which there is an elevated temperature of the body.
In bringing together under review the different forms of Pyrexia, an attempt is made to maintain the proposition
"That while for most cases in which there
"is elevated temperature of the body, there
"is increased oxidation of the tissues; yet for
"a considerable number of cases there is no
"evidence of increased oxidation; and for
"some others a process of oxidation would
"only partly explain the elevated temperature.

In regard to treatment the writer has nothing new to bring forward; but one or two cases are given in which some of the new antipyretic remedies were tried.

From the time of Boerhaave in the beginning of the eighteenth century, to that of Wunderlich in the middle of the nineteenth, more than a century had elapsed.

During that time the thermometre was gradually becoming more and more recognised as a powerful aid in the practice of medicine; yet it was not till after the year 1857 that Wunderlich was able to state this fundamental law. "That certain diseases in "their progress obeyed fixed laws or rules "and that these laws could be determined "and displayed by the use of the thermometre". Wunderlich, by his works gave a new impulse to the study of febrile diseases and whereas the older physicians regulated their diagnosis and treatment by careful examination of the pulse, at present the temperature of the body is taken into consideration as much as the state of the pulse, indeed perhaps out of due proportion.—

To understand aright the meaning of an elevated temperature of the body in disease it is necessary to know, as far as the present state of Physiology will let us know what is the source of the normal heat of the body. First then, as regards. The source of the Heat of the body in health.

It seems almost quite natural that the older physicians should ascribe the heat of the body to changes going on <u>in the blood</u> or as Lavoisier did <u>in the lungs</u>.

(1780) Lavoisier supposed the heat to be produced by the chemical combination of Oxygen with hydrogen and carbon in respiration. The animal, he says has three regulators: Respiration which consumes carbon and hydrogen and produces heat; transpiration which cools the body as required; and digestion, which restores to the blood what it has lost.

1842 Liebig sixty years later considered the source of heat to be the combination of the chemical constituents of the food with the oxygen carried by the blood streams, the process being one of combustion.

About the same time Mayer seems to have the honour of first showing that the heat of the body originated in reality in the stored up energy of the food, that again being traced back to the origin of all force, namely the heat of the sun.

He ascribed the animal heat to a chemical process, an oxidation, and states that "not a hundredth part of the combustion "processes goes on anywhere else but in the "bloodvessels themselves."

Wunderlich seems to have taken Mayer's statement as representing the state of the question in his day, for he adds to the above, —"and physiology has already begun to justify the statement". Indeed in the same page we find Wunderlich stating "that the blood is in every case the agent of heat production." Even as late as 1873 Murchison ascribed the heat of the body to an oxidation of carbonaceous and nitrogenous substances furnished to the blood by the tissues and by the food. The oxidation of carbon being effected by the corpuscles of the blood, and that of the nitrogenous substances by the glands, and by the cells of the blood. Recent physiologists have pointed out, however, that the blood itself cannot be regarded as the seat, to any considerable extent of the production of heat, as the oxidations taking place in it are comparatively slight. "The muscles are "par excellence" the thermogenetic tissues," says Foster. Others would place the liver as being a most active agent if not the chief. Claud Bernard found that in a dog during digestion the blood of the hepatic vein was nearly 2°C above that of the portal vein, while as compared with the blood of the right heart it was more than 2°C warmer. Besides that, the liver is now looked upon as the chief source

B.M. Journal 377 1886/1 of urea, which is the principle form in which nitrogen leaves the body.

To these we must add the other glands of the body and also the nervous tissues as being also producers of heat, in fact we may say that wherever metabolic changes are going on in the body we may look for an evolution of heat. The muscular tissues are the tissues in which these changes go on most rapidly, next come the glands and of these the liver occupies the first place both from its important functions and from its size. Possibly during digestion we should reverse the above order and put Liver first. Following these come the nervous tissues, the brain being the seat of very active changes.

Besides the changes going on slowly in a muscle during rest, there is a rapid explosive change that takes place during a contraction and this is accompanied by an evolution of heat. The human muscle when it remains contracted for five minutes causes a rise of Temperature of 1°C in its neighbourhood.

Landois and Sterling

It is from the combustion of organic compounds used as food and containing Carbon, Hydrogen, and Nitrogen that heat is produced. This is the principle source though we might include also the combustion of such Chemical substances as sulphur and phosphorus; but the heat produced from these must be small. In other words the potential energy of the food is by a process of oxidation changed into heat; but besides heat there are also mechanical and electrical energy evolved

from food.
The elements of the food are not oxidised in a simple form, nor even can we say that the food is oxidised directly.
The lifeless food (containing Proteids, Hydrocarbons water &c) is built up into living tissue, and in doing this so much Potential energy is rendered latent, to be again liberated in whatever form may be required at any particular time.

Landois But besides the process of combustion or oxidation, there are other chemical processes by which the amount of available potential energy is diminished and heat or some other form of energy is evolved.
A good example of this is seen outside of the body in the alcoholic fermentation of grape sugar where the atoms assume a more stable position, with a greater satisfaction of their affinities, and chemical energy passes into thermal energy — heat being evolved.

To understand the origin of this potential energy aright, we must go back in the scale of life to the vegetable world and there we find a similar process going on though simpler in its details.

The food of a plant consists of simple nitrogenous substances such as Ammonia NH_3 and nitrates of the Soil KNO_3, water H_2O and Carbonic acid CO_2 derived from the air. By the aid of sunlight vegetable protoplasm is able to decompose carbonic acid of the air and build up such compounds as cellulose, Starch, sugar, and some others. These compounds as compared with the simpler forms from which they are formed are less stable; the affinities of their atoms are not so completely saturated. They contain a relatively smaller amount of oxygen.

In tabular form they appear thus,

NH_3 Ammonia			Starch $C_{12} H_{10} O_{10}$
H_2O water		changed into	Cellulose $C_{12} H_{10} O_{10}$
CO_2 Carbonic acid			Hydrocarbons, oils $C_{11} H_{10} O_1$
KNO_3 Nitrates			and vegetable proteids —

These then form the food of animals and in such substances as these, animals find the energy necessary to carry on the functions of life.

In recent works on physiology the animal body is too much represented as simply a calorimetric engine; a machine calculated to produce so much mechanical work and evolve so much heat from a given quantity of combustible material.

The production of Mechanical work however cannot take place unless the tissues are in a fit condition to produce it, and this implies the growth of muscular tissue, the storing up in some form or another of so much energy. The same might be said

of the production of heat.
The fact seems to be that constantly as energy is evolved with destruction of tissue, at an equal rate is energy stored up by the formation of new tissue.
We have no reason to suppose that any of the food taken is oxidised in a crude form to produce heat; On the other hand we have reason to beleive that all the food which has become absorbed into the blood, becomes tissue of one kind or another before it becomes waste product, and it only becomes waste product by a metabolism of the tissue.
Hence we have a storing up of energy on the one hand and an evolution of energy on the other; both processes balancing one another, and it is only when both processes thus balance that health is maintained.
Now the process begun in plant life of forming more complex compounds from the

more simple ones found in the earth, air, and water is carried on in the animal body.

So it comes that in the animal body we have chemical compounds of even greater complexity than is found in the tissues of plants. "These compound chemical "constituents of the animal body are "characterised by the complicated relative "position of their atoms, by a comparatively "imperfect saturation of the affinities of "their atoms, by the relative small amount "of oxygen they contain, by their great "tendency to decomposition, and by the "facility with which they undergo it."

Landois & Stirling Introduction

As examples we may take

Lecithin $C_{44} H_{90} N P O_9$

or. Kreatin $C_4 H_9 N_3 O_2$

Lecithin is perhaps one of the best examples of the truth expressed in the above sentence. Now Lecithin is a most unstable compound found in almost all the tissues and fluids of the body. It is most easily decomposed into Stearic and Glycerinphosphoric acids and neurin, The latter (Neurin $C_5H_{15}NO_2$ is equally a most unstable body.

The above truths may be stated in the following form, —

Landois & Stirling.

1st. The relation of chemical affinity to heat,
"Whenever in chemical processes, strong
"chemical affinities are satisfied, heat is evolved;
"Chemical affinity is changed into heat.
Infact heat is formed or evolved when chemically different atoms, form a compound body; as for instance when carbon and oxygen form Carbonic acid.

2nd The converse of the above,
"In those chemical processes where strong
"affinities are dissolved, and chemically
"united atoms thereby pulled asunder,
There must be a diminution of Temperature

"and heat becomes latent.

The formation of the complex chemical substances found in the animal tissues comes under the second of the above laws, and the same may be said of the tissues of plants. Hence we may say that in the formation of the animal tissues heat is rendered latent. In other words the building up of the tissues of plants and also of animals is a process of de-oxidation and in that process energy becomes latent. — And on the other hand the evolution of energy especially that form of it we call heat is a process of oxidation. But besides oxidation or combustion we must include those chemical processes whereby those complex chemical substances break up and form more stable compounds in the body, and these not necessarily processes of combustion.

To these Landois adds certain physical processes as a source of heat; but the heat arising in this way cannot be very great.

In connection with the question of the sources of heat of the body the following law is of very great importance.

"One form of Energy can be transformed into another, so that kinetic energy may be transformed into Potential energy and vice versa, but there is never any part of energy lost, nor does new energy ever arise spontaneously". Hence any increase in the temperature of the body above normal, must be at the expense of the energy stored up in the body. unless we may add to this that perhaps the energy so evolved _was about to be stored_ up in the body - And further it must arise from some increase in the processes that are the normal sources of heat; or in some modification of these processes.

But we must here take into consideration the fact of loss of heat from the body, for any change in the temperature of the body may be accounted for by a diminished loss as well as by increased production.

The regulation of the loss of heat as well as the regulation of the production of heat seems to be under the controll of the Central nervous System.

Warm blooded animals, or rather we should say homoiothermal animals are capable of maintaining a certain standard temperature, whether exposed to great heat or to great cold. This law has its limits however. This is seen in man, for a normal temperature of 98.4° F seems to be the rule, whether he is exposed to the cold of the north or the heat of the tropics.

Experiments on rabbits show that this regulating power is under the influence of the nervous system.

1st If a rabbit be exposed to cold an increase in the tissue metabolism takes place and so more heat is evolved and the normal temperature maintained. That tissue metabolism is increased is known by an increase in the CO_2 expired and Oxygen consumed

2nd Interference with the nervous system either by section of the medulla oblongata or by curare poisoning prevents this increase of tissue change and the temperature of the animal falls to that of the surrounding temperature.

3rd Heat acts on an uninjured rabbit in a way the converse of No1: namely it lessens tissue change and so less heat is produced; or an increase in the heat loss takes place and the normal temperature is maintained

4th If the spinal cord is cut then Heat

raises the temperature of the animal -
Hence we may say that the Central nervous system regulates the production of heat, by increase or diminution of heat production.

There is also a regulation by increase or diminution of heat loss.

When a person is exposed to cold, a contraction of the cutaneous vessels takes place, there is thus less blood exposed to the surrounding cold atmosphere and less heat is lost by radiation and conduction.

And when a person is exposed to heat above that of the body in health 98.4° F. a relaxation of the cutaneous vessels takes place, the skin becomes congested, sweat breaks out evaporation takes place and heat is lost; the body being maintained at the normal point with very little rise.
By this means persons can work in a very warm atmosphere. Foster gives an

instance where the almost incredible temperature of 260° F was borne with impunity. The writer has stood in the "stoke hole" of an ocean steamer where the firemen were working in a temperature of 140° F. These firemen drank large quantities of water and perspired freely.

The effect of evaporation was brought to the writers notice in another way during the same voyage. The Anglo Indian passengers, when ice was no longer available wrapped a wet towel round their Claret bottle, hung it in the sun and thus made it more palatable by cooling it.

Again a hot atmosphere increases the number of respirations and the expired air being loaded with moisture more heat is lost. The loss in this way overbalancing that gained by the increased respirations. Landois.

The normal temperature is then the balance between two factors, namely

Heat production and Heat-loss. Anything that interferes with either of these two processes, and causes a deviation from the normal temperature, interferes with health.

An elevated Temperature may be caused by

1st Increased Heat production,

2nd Diminished Heat loss.

In almost all cases of Pyrexia these two processes are combined.

In the lately published nomenclature of diseases we find a group "dependent on morbid poisons". They are specific febrile diseases, and in them the nature of the febrile process is probably better understood than in most other diseases in which a rise of temperature occurs. Yet the process is far from being well understood indeed as long as physiologists are in the dark as to the part played by the nitrogen compounds in the normal metabolism of the tissues, Pathologists will also be in the dark as to these compounds in disease.

These febrile diseases have one thing in common that is they arise from a morbid poison, which we now know to consist of micro-organisms. In many cases these micro-organisms have been detected in the blood or tissues during the process of the disease of which they are the cause, and further they are classified according to their kind.

Where the special organism has not yet been discovered analogy leads us to suppose that they exist.

The morbid poison consists in these cases of parasitic micro-organisms which enter the body and gain admission to the blood it may be by the alimentary canal, or by the lungs, or by a distinct local lesion as in erysipelas. Possibly there are some cases where the organisms never get further than a certain local surface where they cause changes in the way of new membranes as in Diphtheria. But whether the phenomena that follow are the result directly of these organisms floating in the blood and among the tissues, or the result of some product formed in the blood, or tissues by these organisms, has not yet been decided. Certain processes that go on outside the body in which microorganisms take a prominent part, show that we must always distinguish between the effect produced by these organisms themselves and the effect produced by some product of decomposition caused by these organisms. The Yeast plant produces alcohol, but the effect of the yeastplant in the body is very different from the effect produced by alcohol.

Certain products of decomposition have

have been seperated and are found to be
of a highly Poisonous nature.
Some of these substances known as "Ptomaines"
have properties like atropin, or curare.
Analogy might lead us to look for some such
products in the human body connected with
the presence of micro organisms and causing
all the disturbance that follows; but while
we can as yet be certain of the presence of
microorganisms we are by no means certain
of the presence of any such decomposition
products as those mentioned. Besides the
micro organisms are acting upon living tissues
While these alkaloidal substances, the Ptomaines,
are produced from decaying animal or vegetable
matter.
The probabilities are that in fevers the micro organisms
that cause the phenomena act on the tissues of
the body and destroy the tissues in some
way not easily explained— At least the
investigations pursued by Mr. Sutton and

given in his lectures (B M Journal Feby 20 - 1886) would seem to point in that way.
Mr Sutton points out that the process of Inflammation (Specific) is comparable to a contest between the cells of the animal and the "materies morbi."
First he showed that in inflammation the cells in the blood had a capacity for moving about — Wandering —. And secondly that they had the power of taking into their interior, and digesting certain substances with which they come in contact.
In Botryllus, an ascidian, Spirochaetae were found, these spirochaetae having a close resemblance to those found in relapsing fever.
These microorganisms were pursued, ingested, and absorbed by the mesodermic cells, some of which cells perished in the attempt, many being found dead with the bacterial filaments projecting from them.
The same process was seen in vertebrates in

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bacterial affections such as anthrax; the bacteria being taken up by the leucocytes of the blood; one or more of these leucocytes might coalesce and form a giant cell with one or more of the bacteria in its centre. Such a thing is seen in tuberculosis, perlsucht and other diseases.

It requires no great stretch of the imagination to suppose that the process seen here locally may be carried on generally in certain fevers, the existence of which is known to be connected with the presence of large numbers of microorganisms in the blood and tissues.

We may then state that;

1st The fever poison enters the system.

2nd The fever poison first acts upon the tissues.

One of the first things noticed after the introduction of the poison is an increased discharge of urea. Naunyn observed this prefebrile increase of urea in the septic fever of dogs, and Ringer has shown this to be the case in intermittent fever. Caley mentions that other observers have noted the same for relapsing fever and he considers it probable that the same rule holds good for enteric. These facts seem to point to this, namely that the increased tissue change, as judged by increased elimination of urea, is not the result of high temperature, but being antecedent in point of time, may justly be regarded as the cause of the high temperature rather than the result of it.
In Cullen's definition of fever we find the "pulsus frequens" put before the "calor praeter naturam". This was according to the ideas held in Cullen's time in regard to the blood

or heart being the seat of the fever.
In our own time we find Dr. Murchison putting "a paralysis of the vagus and sympathetic systems" as following the introduction of the fever poison into the body and thus he says "the heat regulating function is disturbed."
Again Virchow defines fever "as consisting essentially in elevation of temperature, which must arise in an increased tissue change, and have its <u>immediate cause</u> in <u>alterations</u> of the <u>nervous system</u>."
There is as much evidence however if not more to show that the high temperature is the cause of the altered nervous condition (paralytic or otherwise), and of the frequent pulse, than that the altered nervous condition is the cause of the high temperature.
Claude Bernard was probably responsible for the theory that fever consisted of a paralysis

of the sympathetic or other nerve centres. It was shown by him that on dividing the sympathetic nerve in the neck of a rabbit, that the temperature rose on that side, and further that the rise of temperature at first local became general.

It has now been shown that in Claude Bernard's experiment, though the primary effect is a local rise of temperature the effect on the whole body is quite the reverse, for the superficial bloodvessels being dilated there is increased loss of heat by radiation and conduction.

And further that even though there is at first a local rise, there is later on a fall of temperature arising from congestion or slowing of the blood current.

So that the ear of the rabbit with the sympathetic divided becomes after several weeks cooler than the sound ear.

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Stirling

For a like reason dilation of the surface vessels by inhalation of Amyl nitrite will cause a fall of temperature. The same may be said of paralysis of the vasomotor nerves of a considerable area of the skin by section of the cord high up in the neck; the temperature of the body falls from increased heat-loss, through radiation and conduction. On the other hand stimulation of the vasomotor nerves of a large area may cause a diminished heat loss, from the constricted vessels giving off less heat, and here we may have one cause of increased temperature in fever; for during rigor this is the very condition of the body. Indeed when we consider the very complex function of the sympathetic system of nerves it is hard to believe that in fever they are paralysed. For instance anything like paralysis of a large vasomotor area such as that supplied by the splanchnic would lead to dilatation of the bloodvessels of the abdomen, and the result would be diminished blood pressure and slowing of the hearts action —, the contractions of the heart being both slow and small.

Again as regards paralysis of the vagus, increased frequency of the hearts action may be brought about by interference with (paralysis or otherwise) the inhibitory action of the vagus; but the hearts action may be increased in frequency by stimulation of the "accelerator nerves". Now the action

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of these accelerator nerves is influenced by heat. At low temperatures their influence is slight, at high temperatures their action is more powerful and sooner developed.

Wunderlich —

Besides that, it is asserted by Schiff that feeble stimulation of the vagus accelerates the hearts action.

In the Practitioner of October 1884, Brunton has shown that in the Cat and probably in man a rise of temperature, causes a quickening of the heart action, which is at first due to stimulation of the cardiac ganglia.

Brunton — When the temperature rises to a certain point it weakens the action of the peripheral ends of the vagus, and also weakens the vagus centre in the medulla; the effect on the centre being more than that on the periphery. Although the centre in the medulla is weakened it is not completely abolished or at least not completely paralysed. From Brunton's experiments it appears that when an animal (the cat) is heated artificially to 40°C (104°F) the inhibitory function of the vagus is completely abolished. So much so that if at this point both vagi be cut there is no alteration on the pulse rate. In these experiments however Heat is the cause of the increased pulse rate. There seems to be evidence that the action of the fever poison is first on the tissues and by acting on them certain phenomena follow;

namely, increased temperature, increased pulse rate, and alterations in the sympathetic system of nerves.
There is further proof of this in Dr. Murri's experiments quoted by Dr. B. Sanderson.
"After cutting the cervical cord of dogs "he obtained a rise of temperature (Pyrexia) by injecting septic poison under the skin. The section of the cord first produced a cooling of the body, hence that was not the cause of the pyrexia.
To say however that pyrexia is essentially a process of increased tissue change will not account altogether for certain nervous phenomena that are observed at the onset or during that condition.
In pyrexia there is a new arrangement of the balance between heat production and heat loss. There is still a kind of equilibrium kept up but at a point higher than that of health. The temperature is

raised, and it is maintained at or near a definite point during the process of fever, with it maybe as in Enteric increased daily fluctuations. But before this new condition of affairs is attained there is a period during which the vasomotor system of nerves may be said to be in a state of instability, if not of excitement.

This is the period of rigors, in ague it is well marked and is called the Cold Stage. It may be assuming too much to say that the increased heat of the body, is enough to cause the rigor, and that the rigor is simply an expression of the fact that the vaso-motor system is not yet suited to the new state of affairs. But certainly a rise of temperature is sometimes observed before even the rigor takes place, and besides sudden changes of temperature whether to a higher or a lower, excites the vasomoter system in such a similar way.

In the vasomotor system there are contractor aswell as dilator fibres or elements, and while at first on being excited the contractor elements are the more powerful and a rigor is the result, later the dilator elements come into play and there is flushing of the superficial vessels with congestions and sweating.

The writer has noticed that in mild Enteric such as is commonly seen in this part of Forfarshire (Endemic and Sporadic) during the first week or so of the patients illness when the patient is as a rule still going about, shivering or a feeling of coldness is one of the leading symptoms. As soon as the patient is ordered to bed this feeling gives place to one of warmth and comparative comfort: As if the motion and exposure to the surrounding temperature prevented the vessels of the skin from assuming that new condition of greater relaxation that

allowed them to give off more heat; while rest and the heat of the bed assisted the bringing about of that condition.
And here it must be admitted that the state of rigor is in itself one factor in the increased production of heat of the body. So that though it may be caused by increased heat of the body it also reacts on this and helps to maintain it.
That during the stage of rigor the temperature of the body is raised, has long been known; but it is not to be supposed then that the feeling of cold is only subjective: for Fagge has pointed out that in a case of ague while the temperature of the body was rising from 98° to 104°7 (axilla) the temperature taken between the toes was actually falling from 98° to 86° or even to 77°. This showed that the surface vessels at the extremities were contracted and did not

allow sufficient blood to circulate so as to keep up the normal temperature. That there is really an increased oxidation of the tissues of the body, is known by the

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increased excretion of Carbonic Acid, as much as 70 - 80 percent, while the excretion of urea is increased by a third to two thirds. The uric acid is also increased, the excretion of potash may be increased sevenfold, and the urine pigment derived from the haemoglobin may be increased twenty times. The effects of an artificial increase of the temperature of the body is worthy of notice. If a high temperature is maintained for any length of time, at 42.5°C (about 108.6°F) death is almost certain to take place. Coagulation

Weikart.

of the blood is likely to take place at 42.6°C. If the heat of the body is raised 6°C (10.4°F in man as in sunstroke, death takes place. At this temperature molecular decomposition

of the tissues takes place; but if a lower temperature is maintained for a longer time fatty degeneration occurs.
The increased oxidation of tissue that exists in fever is something more than an increase of the normal oxidation that leads to heat production. It may be said that there is such a thing as purely physiological increase of heat production.
In cold climates a greater amount of fatty food is consumed to produce more heat, and there is no evidence to show that this is accompanied by an increase of nitrogenous compounds eliminated; indeed it could hardly be so considering the chemical nature of the food consumed. Again, and of more import, that increase of temperature that accompanies muscular exercise, does not cause increased excretion of urea. The heat produced in both of these cases must be at the expense of hydrocarbon

compounds. But in pyrexia the nitrogen compounds of the body are really consumed and this is known by the increase of urea, and uric acid, also by the wasting of the muscular and glandular organs.

In the muscles it leads to degenerations mostly vitreous or waxy, in the glands it leads to granular or albuminous infiltration of the cells.

These degenerations are of great and serious importance and hence the necessity of treatment directed so as to prevent them.

The fact that the increased urea is associated with an increase of potash salts points to the albumen of the muscles and of the red blood corpuscles as being its source.

We may therefore say that pyrexia is essentially a process of increased oxidation of the tissues, with very great interference with the processes of nutrition and with the nervous system

It is held by some (Traube, Goodridge) that part or whole of the process of fever consists of a diminished loss of heat. But though this must be taken into account there is evidence that the main process is one of increased oxidation.

Besides Ringer has shown that even profuse sweating, increasing the heat loss, in the cold stage of fever (ague) had little effect on the high internal temperature.

Liebermeister and Immerman have also proved by calculations that the diminished heat loss during the cold stage would not account for the rise of temperature, and that therefore there must be even then an increased production.

Wunderlich.

To sum up the above we may say then that

1st The poison enters the system:

This causes an increased metabolism of the tissues leading to

2nd Increased heat production -

The increased heat leads to alterations in the pulse rate, respiration rate, and also to interference with the Vasomotor system This latter leading to

3rd An insufficient heat discharge, though it may be really an increased heat loss.

4th There also occurs various forms of tissue degeneration; chiefly leading to fatty degeneration of the heart + muscles and glandular organs.

It may be said that the process of fever here described as applicable to Zymotic diseases, is also applicable to those forms of fever that are purely symptomatic - such as in Pneumonia, Pleurisy and other forms arising from Catarrhal diseases.

But there are other cases in which even with elevated temperature there is held to be no increased oxidation of the tissues.

In one or two diseases the chief feature of which is an altered condition of the blood, there is observed an elevated temperature.

This has been noticed in Idiopathic Anaemia, Chlorosis, and Leuchaemia, and we might also include the condition that occurs after severe haemorrhage, and the last stages of Chronic starvation.

In all these diseases the oxygen carrying powers of the blood are greatly impaired.

Coupland In Idiopathic Anaemia the haemoglobin

Bramwell may be reduced to one-fifth of its normal quantity. The red bloodcorpuscles are diminished as to number, they are also altered in size and shape. There seems to be evidence of disintegration of the red corpuscles, or if not so, then of incomplete formation of them, in particular their oxygen carrying power is greatly diminished.

Coupland- And yet we have in these diseases a pyrexia.

This febrile state is very irregular in its course, and may exist without any apparent great alteration in the patients' condition.

There may be sudden rises of the temperature even as high as 106° F, without any very well known cause.

The condition of the urine here is interesting. It is usually free from albumen, of low specific gravity and deficient in urea and uric acid.

Eight cases of Chlorosis were reported by M. Mollier in which the temperature was noted as oscillating between 101.8° to 102.8° F. And in these the amount of urea eliminated was normal, there was no increase.

Now whatever explanation may hold good for that pyrexia that occurs in Zymotic diseases, will not hold good in these cases. For 1st, As the oxygen carrying power of the blood is greatly impaired, there can be no increased oxidation of the tissues.

and 2nd there is no increase of the nitrogenous products of the urine, to show any increased oxidation of the tissues.

A case of this kind has been very fully
1884/1 260 described in the B. M. Journal.

A woman aged 32 very emaciated and having all the usual symptoms of idiopathic anaemia, was under the care of Dr W. Moore. For over a period of four months a state of pyrexia was maintained, the course of the temperature being very irregular, with evening exacerbations; on one occasion rising from 103° to 106° within three hours. The patient recovered under arsenic, but two years later came under the notice of the same writer. She was under observation for over a period of two months during which time the percentage of urea was noted as well as the morning and evening temperatures. The urine was of low specific

gravity and the percentage of urea was also low. The urea however increased somewhat towards the end of her illness, when the appetite had improved.
There was no chest complication, such as occurs in such cases, and throughout, the breathing was quiet and tranquil.
There was "pyrexia" throughout, but the temperature could be reduced by quinine a fact worth noting in passing.
Taking this fully described case as a type of the class under consideration, we must look for some other explanation than that of an increased oxidation of the tissues to explain the high temperature. Though there was one thing in particular that would lead one to think that such might be the case, namely, the emaciation was considerable; there was therefore wasting if not increased oxidation of the tissues.
To account for this anomalous form of Pyrexia

many different opinions are held.
Possibly the products of oxidation if there were any were given off by some other channel. In the above mentioned case it could hardly have been by the lungs for the breathing was tranquil and normal throughout.
Nor by the skin for there was scarcely any perceptible perspiration, and as for the bowels the writer says that on some days there was no motion, and seldom more than one. And further the writer quotes Dr Parkes, as saying that though in Typhoid, the diarrhoea favors the escape of Chlorides it is not to any considerable extent the channel for the escape of nitrogen compounds.

Dr. Moore

One is left to explain the pyrexia and wasting by some other process than that of oxidation.

Now in Landois we find as has already been noted that the normal production of heat is 1st "by processes of oxidation;

2nd "by those chemical processes in our "body by which the amount of the available "potential energy which is present is "diminished, in consequence of a greater "satisfaction of atomic affinities.

In all cases where the atoms assume more stable positions with their affinities satisfied, chemical energy passes into kinetic thermal energy.

It has already been shown that the building up of the animal body is a process of the formation of compounds of a most complex character which are also most unstable. Now these highly complex "bodies require a continual restorative "activity on the part of the blood for their "maintenance; and should this restorative "influence fail, or prove inadequate, owing "to some defect in the composition of the "nutrient fluid, the complex substance "of which the cells consist will spontaneously "decay and break up into a number of more "stable products." (Immerman) B.M.Journal 1884/I

The same idea is found expressed in Wunderlich, when speaking about those different processes by which heat may be evolved in diseased forms; he includes— "The development of new combinations of the "constituents of the body, associated with "increased generation of heat, but not "of necessity associated with or dependent "on increased oxidation"

An Hypothesis which after all is but a modification of the above is given by Dr. Anstie. He accounts for the excess of heat, independently of any oxidation of tissue by saying that "the energy "that becomes latent in tissue building is set free in the form of heat."

This however is no new idea, but is simply an application of one of the laws of the conservation of Energy, which states that; Energy is never lost but may be transformed; and again, Energy never arises spontaneously. It happens that in many of these cases very little food is taken, and especially is this the case in Chronic Starvation and even there we may find this form of pyrexia, so it would probably be better to put the statement in this form.

Energy that has become latent in the process of tissue building is set free in the form of heat; or in this form.

Energy that should become latent is arrested somewhere and dissipated in the form of heat.

Where a certain quantity of food is taken the latter of these propositions would apply, but where almost no food is taken the former would be more applicable.

BM Journal
1886
1
N. Paton

Now as the liver seems to be engaged in the production of urea, or of some intermediate products that ultimately become urea, and as the liver is one of the principle sources of heat, it is quite possible that the liver has more to do with the production of heat in these cases than has been supposed.

And it so happens too, that the liver has other means of getting rid of the products of its metabolism than by means of the hepatic vein and ultimately by the kidneys, as seems to be the case with leucin and tyrosin and other nitrogenous bodies.

It is quite conceivable that in some of these cases, the liver so acts on the contents of the portal system, rich in potential energy (food), that more heat is evolved than in health, and as a consequence less energy sent on for purposes of tissue building, and yet the products of such abnormal changes not got rid of by way of the hepatic vein and ultimately by the kidneys, but rather by the bile ducts and ultimately by the bowels. So that in cases like these untill the whole of the excreta be examined, in conjunction with a stated amount of food given we cannot say definitely that there is really less excretion of nitrogenous matter.

Be that as it may, the subject has again been brought forward by Dr. W. M. Ord in an address to the London Med. Society 1885.

Br. Journal 1885 / 2

To illustrate his meaning Dr Ord draws a comparison between the normal temperature of the human body and the normal (212° F) temperature of boiling water.

As long as water is boiling and steam is given off, the excess of heat is rendered latent in the form of steam, the water remaining constant at 212° F. If the water is prevented from boiling by increasing the atmospheric pressure or by pouring oil on the surface, then the water becomes hotter and heat is evolved by radiation and conduction.

Again if all the water passes off in the form of steam the vessel becomes hotter, and heat is evolved.

Applying this to the human body, Dr Ord finds two processes going on at the same time, namely the building up of tissue on the one hand and the disintegration of tissue on the other (by oxidation or otherwise). As long as these processes go on normally the temperature remains at or near an even point of 98.4°F, being balanced in fact by the two processes. But if the building up of tissue is interfered with then energy previously required for that purpose is evolved in the form of heat. Indeed a post mortem high temperature may be a good example of this.

To show that heat is rendered latent in growing tissue, Dr Ord chose for experiment growing fruits, and for this purpose as being more easily managed he chose growing cucumbers.

He found that. 1st the growing part of a cucumber or a young growing cucumber was 1° - 2° F. below the surrounding temperature.

2nd That the ripe cucumber or the ripe part of a growing cucumber was about 2° F above the surrounding temperature.

3rd The growing cooler part represented the formation of cellulose, starch, &c and here heat was rendered latent; while in the warmer ripe part, sugar and fruit acids were being formed and here heat was evolved.

Dr Ord complains that he could get no information regarding these points in any botanical text books, but a reference to Henfrey (1870) would have shown him that 1st The specific heat of all plants is lower than the surrounding atmosphere.

(Dutrochet's experiments, thermo electric)

2nd The specific heat is only discovered in the soft and green parts and not in the woody structures.

3rd The germination and ripening of seeds is a process of oxidation, Carbonic acid being formed and heat evolved. These observations of Henfrey's show that in growing plants energy (heat &c) is rendered latent; and it has been shown already that in animals the building up of tissues is a process of storing up various forms of energy.

Whenever the temperature of the body is above normal, it must be from some alteration in the processes of nutrition and oxidation, whereby an unusual amount of energy is given off in the form of heat.

For Energy never arises spontaneously; but one form of energy may be changed into another.

It may be asked whether after all this would account for the excessive heat of such forms of fever as that of Idiopathic anaemia, in which there is no evidence of any form of excessive wasting of the tissues <u>in the excreta</u>, urea, Carbonic acid or even any other nitrogenous end product.

If we took Immermann's explanation; That the complex substance of which the cells consist may spontaneously decay and break down into a number of more stable products, under the influence of a depraved condition of the blood, as occurs in anaemia, or leukaemia &c.

It may be pertinently asked what becomes of the more stable products.?

Dr. Ord seeks to get over that difficulty by saying — Not that the more highly organised principles of which the body consists break down. But that these highly organised principles cease to be formed, and points to the fact that the potash salts and the phosphates are in most fevers eliminated in excess while in health they are used up in the composition of these highly organised principles.

There is some evidence to support either of these theories in the condition of the blood in such diseases as Idiopathic Anaemia. In these there is great alteration in the form and size of the blood corpuscles and especially a predominance of small forms, and what appears to be broken fragments of corpuscular matter.
Either there is a spontaneous decay or there is an imperfect formation of these bodies. Besides these changes in the blood there is found in the different forms of anaemia

various stages of degeneration of the muscular tissue.

A prolonged depraved condition of the blood leads to fatty degeneration of the heart, and of the voluntary muscles as well. It even goes further and in many cases the glandular organs are affected in a similar way. Even in cases of cancer where in the late stages the blood is so much altered there is found fatty degeneration of the viscera.

If these changes go on while the oxygen carrying power of the blood is greatly diminished, it can hardly be from any process of oxidation; but rather from some process of decay, or it may be from a cessation of those processes of nutrition that are required to maintain the tissues in their normal state.

We must not here lose sight of one explanation that has been given of this from of elevated Temperature. It is this—

D. B. Sanderson That though in such cases there be no increased oxidation of tissue there is greatly diminished heat loss and hence the rise in the bodily temperature.

But the above explanations of Immerman and Ord seem to the writer to be nearer the truth, especially when we take into consideration the condition of the tissues as they are found after death.

It must be admitted however that there is still one thing requiring explanation, namely that quinine in large doses lowers the temperature. Now quinine lowers the

Brunton temperature by diminishing the oxidation of the tissues —. Hence one might say quinine lowers the temperature here too by diminishing a process of oxidation. It may be however that in this case quinine acts more upon the vaso motor centre and diminishes Temperature by increasing heat loss by radiation and conduction.

An idea somewhat similar to that of Immermann's must have been present in the mind of Foster when he wrote the following. "There is no à priori reason positively contradicting the hypothesis that the metabolism of even muscular tissue might be influenced by nervous or by other agency in such a way that a large decomposition of the muscular substance, productive of much heat might take place without any contraction caused. If it were possible to permit ourselves to suppose that the contractile material whose metabolism when resulting in a contraction gives rise to so much heat, could undergo the same amount of metabolism in so far a different fashion that all the energy thereby set free, took on the form of heat, variations in the temperature of the body, at present difficult to understand would become readily intelligible."

Now the change that goes on in a muscle, that gives rise to the production of mechanical work is an explosive decomposition, during which the muscular tissue goes through a certain chemical process whereby Carbonic acid and Sarcolactic acid are set free and eliminated. The nitrogen whether free or in the form of some compound is not eliminated; but seems to be retained and at once made use of again. So that mechanical work and a certain amount of heat evolved during mechanical work are associated with increased exhalation of carbonic acid but not with increased elimination of urea.

Such an explanation as that of Foster's would apply to a certain extent to such a fever as occurs in anaemia —

This leads us naturally to that form of elevated temperature that is seen in Tetanus.

The chief symptom in Tetanus is strong spasmodic contractions of the muscles.
In a certain proportion of cases there is a rise of temperature. Wunderlich mentions a case where the temperature rose to 112.5° F, and after death the temperature may go on rising. Wunderlich ascribes the high temperature to paralysis of those nervous centres that govern the production of heat.
Tetanus is however a physiological phenomenon as well as a pathological one, and in its physiological aspects has been well studied.
A stimulus, (electric or other) applied to a muscle produces a contraction, and if

the stimulus be repeated often enough, a number of contractions can be produced, following so rapidly on one another as to appear like one continued contraction. This condition is known in physiology as tetanic contraction, and such a condition in disease constitutes the chief symptom of Tetanus.

Now a simple contraction of a muscle is accompanied by,

1st The production of an acid (Sarcolactic),
2nd The evolution of Carbonic Acid,
3rd The evolution of Heat,
4th There is no production of urea or other crystalline nitrogenous bodies; though some observers have thought that the kreatin is increased during contraction, this is not proved. (Foster).

The amount of heat evolved by a contracting muscle has a relation to the tension of the muscle. The greatest amount of heat

is evolved when the muscle is prevented from contracting and this is just what takes place in tetanus (general), for all the muscles opposing one another, each prevents the other from contracting, or rather the contraction is wasted on the muscle itself. Hence the greater proportion of heat evolved, following here, the law of the conservation of energy.
Landois quoting Richet points out that in dogs kept in a state of tetanus by electrical stimulation, the temperature rises to 44° – 46° C (111° – 113° F.) and they die from hyperpyrexia.
Further Landois while writing on this subject, mentions that during tetanus there is great formation of acid and alcoholic extractives, but no nitrogenous products.
It is not going too far to suppose that in the disease, tetanus, the same

processes go on indefinitely. But whether or not the high temperature in tetanus (pathological) is accompanied by increased elimination of urea seems not to have been observed.

In a large number of cases reported in the B. Medical Journal 1879-1886 the temperature is only noted in a very few, and no mention is made of urea or even of the appearance of the urine. Most naturally the whole attention has been given to the spasmodic contraction of the muscles.

Goodridge writing on the febrile symptoms of tetanus in Pract. 1884 states that the temperature seems to be in direct proportion to the muscular spasms; but does not here mention anything about elimination of waste products.

We may say however that in all probability the high temperature in tetanus has a different source from that seen in zymotic diseases.

In sunstroke or heat stroke we have another form of pyrexia that differs in its etiology and pathology from that seen in zymotic diseases.
Among the conditions that lead to this form of pyrexia we find prominent, fatigue, a high atmospheric temperature and generally also the air is moist and humid.
Among the first things noticed is a hot dry skin, and a change in the condition of the urine, which now becomes copious instead of scanty as it generally is in a warm atmosphere.
The arrest of perspiration is probably enough to account for what follows; but it may be

that the "turbid swellings" (congestion?) that have been described in the kidneys and other organs are the primary lesions; for if such a condition of the kidneys leads to more copious urine and that again to a scanty or arrested perspiration, there is here enough cause for increased heat of the body.

The writer had occasion to attend two cases of sunstroke both occurring during the passage through the Red Sea.

The dryness and heat of the skin were prominent symptoms in both cases, indeed it was all the more marked because every one near was perspiring freely. The suppression in these cases is equal to shutting a safety valve for the escape of heat; and this is in the first place the cause of the high temperature of the body.

But doubtless very soon there may be

increased tissue change; so that in treatment we may have two factors to deal with, though the suppressed perspiration may be the most important.

In looking over the Reports of cases of sunstroke in the journals one scarcely finds any mention made of the urine and so it is hardly possible to say how far there may be increased heat from increased tissue change and how far it may be from diminished heat loss.

In regard to this point Sir Joseph Fayrer states B. Med. Journal 18 vol 2. 224

"In cases of Thermic fever, heat being the essential cause, the object is to reduce the temperature of the body as quickly as possible, and before tissue changes have resulted from the action of the heat. As the hyperpyrexia is due not only to the direct action of the heat on the nerve centres and tissues, but to fever set up by the disordered vasomotor arrangements, remedies such as may influence this disturbed condition have been suggested. The results have appeared in some cases to justify the theory, and the hypodermic injection of morphia and quinine have both been considered to produce good results by their influence on the vasomotor nerves, and their powers in retarding tissue change."

Landois-
& Stirling

Again experiments show that when mammals are placed in a warm bath which is 2° to 3° C higher than their own temperature, the tissue metabolism is increased, as known by the excretion of Carbonic acid and the increased consumption of Oxygen, and also by the increased excretion of urea. This applies to man as well as other warm blooded animals. Now a hot moist atmosphere is a condition somewhat similar to a warm bath, hence changes similar to those mentioned by Landois may occur in Sunstroke.

It was said above that Murri's experiment seemed to prove that a morbid poison introduced into the blood acted first on the tissues and not on the nervous centres. It does not follow from that however that the nerve centres have nothing to do with the production of heat or even with the production of high temperatures. Certain forms of traumatic fever and also of what is called neurotic fever seemed to be produced by an action on the nervous centres.
When we consider how much the action of the heart and other organs are affected

through mental emotion, fear and anxiety. And further when we remember that stimulation of a peripheral nerve (sciatic) may act reflexly upon the centre for the vaso-motor nerves of the liver and cause Diabetes, it may be admitted that the thermogenetic centres may be so acted on also.

B.M. Journal 1885

It has been pointed out in the Brown Lectures, that in a considerable proportion of cases of traumatic pyrexia the probability is that the elevated temperature is caused by stimulation of the afferent nerves.

Limiting the name traumatic pyrexia to those cases of simple injury where there was "absolutely no septic or other possible source of fever", and taking simple fracture as a good example of such, the lecturer found that he could form three distinct classes or groups. In one there was considerable swelling at

the seat of fracture, and the swelling whatever it consisted of, was looked upon as part of an inflammatory process and was enough to cause a rise of temperature.
In the other two groups there was no swelling at the seat of fracture.
In one of these groups there was a rapid rise of temperature of about 2° F. in about an hour and lasting nearly a week.
In the other similar group the rise was not so rapid, nor so high, nor did the fever last so long. The difference between these two groups seemed to be caused by difference in age. In these two groups we have the presence of a simple fracture with no swelling, but considerable fever, and in some of these the fever came <u>on immediately</u>.
After discussing the several probable <u>causes</u> namely, Fat Embolism,
Absorption of extravasated blood,

or moderate stimulation of an afferent nerve,

the lecturer (V. Horsley) comes to the conclusion that the last of these is the likely cause of fever. — Thus leaning towards a neurotic theory of traumatic fever, at least in some of its forms. He also points out that we have in such cases a condition of things such as occurs in Whitlow or in the case of a child during teething, and that a few drops of pus pent up or increased tension within a circumscribed part may be enough to cause a rise in temperature of a few degrees.
And further that whenever the tension is relieved the temperature falls.
As against all this it might be mentioned that many experiments have been tried to prove that peripheral irritation will raise the temperature of

the body and that it is generally held that such a process does not raise the temperature but rather lowers it.
And again that crucial experiments will require to be made on animals to show whether or not there is any extravasation in a simple fracture even when there is <u>no swelling</u> at the seat of fracture.

It is held by many that there is such a thing as <u>Hysterical pyrexia</u>. Cases are noted in which with many other hysterical symptoms, there is considerable rise of temperature following no law, coming and going without any known cause, connected with ovarian pain and tenderness, and only yielding to one explanation namely "Hysteria". These cases might be called simply "Neurotic pyrexia".

One of the most interesting studies in all medicine is that of the varieties in the course of temperature in different diseases. A series of typical charts such as that given in Wunderlichs' book presents a wide field for speculation.
Why, for instance should the temperature, in such a disease as relapsing fever rise for a few days, then fall for a few days and then rise again a second or even a third time.? Is it that the high temperature to which the body attains is sufficient to kill the spirochaetae, leaving only a few germs or remnants, enough to cause a second or third rise of temperature after an interval of a few days when fresh crops are developed.? Such an hypothesis has been given by Heydenreich of St Petersburg, who found that while these germs remain alive outside the body at 60° F., they die when the

temperature rises to fever heights.
Or is it that some products of decomposition are formed in the body in quantity enough to kill the germs? That such products of putrefaction of proteids (indol, skatol, phenol &c) have a detrimental effect on the life of many micro-organisms, has been shown by Wernich and others. D. B. Sanderson has shown in Practitioner 1885 that putrefaction may be looked upon as a chemical process during which phenol, skatol and Indol are produced. And these substances are just the very things mostly used for killing germs; at least phenol is used so.

In regard to ague too, we are at a loss to know why in it, the fever should be absent in some cases for a day or even two. Possibly the explanation given of relapsing fever may apply to some extent here too.

Great as the value of thermometric observations are they are incomplete in themselves, for a certain degree of heat in one case may be of more grave import than the same degree of heat in another. The state of the skin must always be taken into account. A temperature of 103°7 with profuse sweating indicates, if it continues for any time, a much greater production of heat than 103° would indicate in another case with a dry skin.

It has been pointed out that observations on the rapidity with which the mercury rises may be taken as indicating the rapidity with which the heat is being given off by radiation and conduction.

Perhaps this would explain the burning hot feeling of some diseases such as Pneumonia or Scarlet fever.

The writer has noticed cases of enteric, where by the hand a temperature very little above normal was supposed to be, whereas the thermometer pointed to 102° or 103°. While in some cases such as Pneumonia the skin feels to the hand as hot as the thermometer points to. Perhaps the explanation is that the surface ~~is~~ in Pneumonia kept as hot as the interior of the body. That this is so has been asserted by Schülein who by taking temperatures in the axilla and between the toes at the same time, found that in some diseases, Enteric Phthisis &c there was a considerable difference; while in Pneumonia Scarlet fever and others ~~they~~ rise in the axilla was accompanied by the same movement of the thermometer between the toes.

It must be admitted that in all diseases in which an elevated temperature exists that fact is in itself one condition that must always be kept in view and treated accordingly. For pyrexia "per se" seems to be so intimately connected with certain forms of degeneration that are found after death as to lead one to conclude that the high temperature must be the cause of them.

Each form of pyrexia may have its own special symptoms or its own special lesion that may require treatment, but there are certain pathological phenomena that are common to many if not all febrile diseases.

These pathological changes are of the nature of degenerations.

In the glandular organs and also in the muscular fibres of the heart and voluntary muscles is found a granular or albuminous infiltration of the cells. The protoplasm of the cells and fibres has a ground-glass appearance from this granular change;

the neuclei are obscured, enlarged, and irregular. In advanced cases this is associated with fatty degeneration.

Virchow considered these changes as inflammatory parenchymatous exudation, but they are now considered as essentially degenerative and a stage towards fatty degeneration.

Changes somewhat similar are found in the nerve cells of the central nervous system. In the striped muscles and more especially in those of the abdominal walls, and some others is found another form of degeneration, the waxy or vitreous.

Now in many forms of pyrexia a fatal termination is looked upon as depending on certain of these changes, more especially such as occurs in the heart or central nervous system.

While some doubt is thrown upon

the proximate cause of these degenerations from the fact that they may arise in diseases other than pyrexia (burns for instance or Enteric with low temperature) yet it cannot be doubted but that the high temperature is one factor in their causation. Caley states that the vitreous degeneration of the striped muscles is due entirely to the high temperature. And again granular degenerations are found in animals killed by heat even after exposure for only a few hours.

But apart from degenerations it is not doubted that the high temperature is in itself a cause of death by paralysing the Central nervous system.

The great value of Antipyretic treatment in febrile diseases cannot be doubted.

Antipyretics have been classified by Dr L. Brunton into those that

1 Increase loss of heat
  a. by abstracting it, as by cold baths
  b. by increasing loss due to evaporation
     as by sudorifics &c
  c by dilating cutaneous vessels
     as by alcohol.

2. Those that lessen production of heat
  a. by acting on tissue change,
     as quinine does & others,
  b. by acting on the circulation
     generally, as by Aconite &c
     or locally as by leeches, dry cupping &c.

The most valuable antipyretic is the application of cold in one or other form. Although it is not of universal application yet in the greatest number of cases it can be applied, always remembering certain restrictions that have been laid down in regard to the state of the heart and the presence of exhaustion.

The writer has had almost no experience of the use of cold in pyrexia, beyond the application of it to the more exposed parts of the body by way of sponging.

One very instructive case occured to the writer while assistant with Dr Thyne in London.

A child aged 18 months had laryngismus stridulus that in a few hours passed into general convulsions. Several of the usual remedies were tried and at last chloroform was administered but with little effect, for as soon as inhalation was stopped, the convulsions reappeared. As matters were becoming alarming permission was obtained to call in further advice and as Dr Thyne was from home, Dr Stephen McKenzie was brought. Among the first things he asked for was

the temperature, and as this had not been taken, the thermometer was at once used, when to the writers astonishment the mercury rose to 106.6° F.
It had never occurred to him to make use of the thermometer in such a case. Cold baths were ordered and the child was put in, the water being at 90° and then gradually cooled down, till the temperature of the child became normal. The convulsions then abated, but consciousness was never regained. The bath was repeated several times during the course of the day, but with the same effect; the child died the same evening.

The application of cold is valuable because it abstracts heat from the body, but it does more than that, it lessens tissue change, and this statement is made in spite of the fact that in health the exposure to cold increases the production of heat. Schroeder of Dorpat has shown that in fever the application of cold produces a diminution of the excretion of urea and Carbonic acid, without any aggravation of the general symptoms. Besides that, Cayley and others ascribe to the cold bath a good effect produced on the nervous system in that it regains its heat regulating power, and for this purpose recommends, in cases where certain nervous symptoms predominate, as stupor, delirium or nervous depression, a cold bath of short duration or a prolonged bath of a higher temperature.

B.M. Journal

And this again agrees with what one has written on thermic fever, where for certain forms of it a warm bath is of more value than a cold one, for the same reason, namely that it tends better to restore the heat regulating function of the nervous system.

Quinine lessens tissue change by its influence over the oxidising power of protoplasm. Protoplasm has the power of taking up Oxygen and absorbing it, and then of giving it up to other substances that are incapable of taking it for themselves. Quinine limits this power of protoplasm, and its power as an antipyretic lies in this fact. In this way the increased oxidation of the tissues in pyrexia is diminished and the nitrogen and sulphates in the urine lessened.
That its action is on the tissues and not on the nervous system is shown by the experiment of administering it to a dog after section of the spinal cord and wrapping it up in wool, even then it diminishes the temperature.

Large doses paralyse the vasomotor centre and cause dilatation of the vessels, and thus the blood pressure is diminished, while at the same time the hearts action is weakened. This must assist its antipyretic action, and probably accounts for the red rash sometimes seen during its administration.

In the following case the temperature fell 5° F under the use of quinine.

Mr P. was exposed to the contagion of Erysipelas on Oct 31st and Nov 1st and 6th 1885.

On Nov 7th he had a rigor and felt ill. The temperature that evening was 103.2°. He had all the symptoms of commencing erysipelas of the face. To get the following

R Tinct Ferri perchlor ℨiv Glycerini ℥i
Aq ad ℥vj ℥ß every 4 hours.
Quin. Sulph grs 6 Talis iv one every six hours.

For the first four days the temperature

DISEASE.

Erysipelas of face

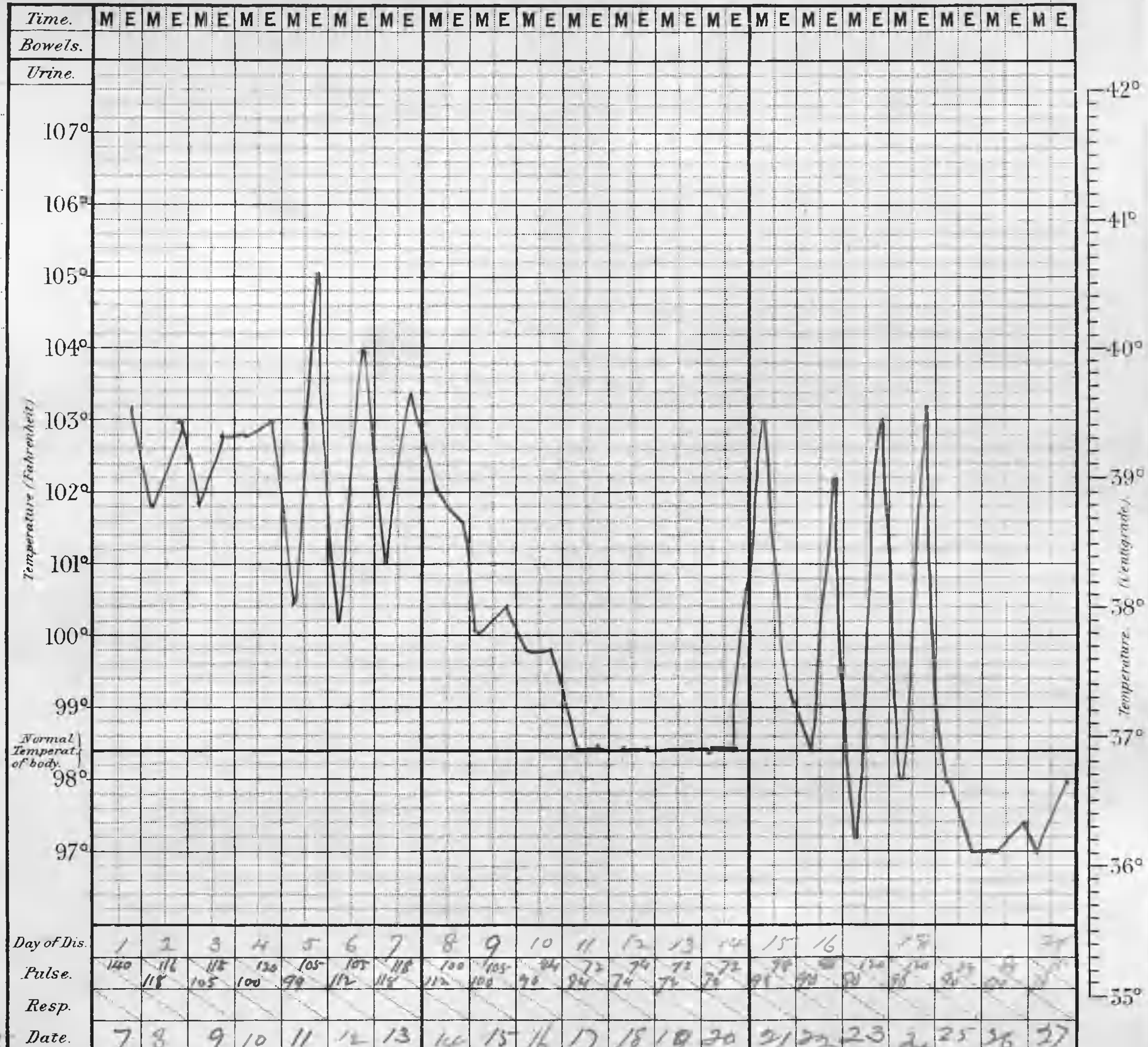
Notes of Case.

Name Mr Phillips

Age

Diet

Case Book Nº



Date of admission. November 7th 188

Result Recovered

Entered at Stationers Hall. Printed and Published by Wodderspoon & Cº, 7 Serle Street, Lincolns Inn. Gould's Clinical Chart

remained above 102°, then there was some improvement and it fell to 100.4° on the 11th. That same evening he was worse, Temperature 105°7. pulse 112 R 46. with delirium. Ten grains of quinine was administered at 10.45 pm. The temperature fell 2° in about three hours, when another dose of ten grains was given. The temperature continued to fall and at 2 pm on the 12th the temperature was at 100.2.
The result was, a very soothing effect, delirium gave place to calmness and quiet. A red rash came out after the second dose. The next evening the temperature rose and he was again delirious. Quinine brought it down again, and on the 13th a gradual fall began with improvement in all the general symptoms. After remaining about normal for four or five days the temperature again rose and he had a relapse with ultimate recovery.

Salicylic acid and Salicylate of Soda are also valuable antipyretic remedies. They are classed by Brunton among those that reduce temperature by acting on tissue change, as quinine does. But whereas quinine diminishes the quantity of urea excreted it seems that Salicylate of Soda increases it (N Paton B M Journal 1886) At the same time it diminishes the uric acid excreted and this is a reason for its use in gout and perhaps accounts for the good results derived from its use in rheumatism.

Several new valuable Antipyretic remedies have lately been made Synthetically. Starting from Chinoline $C_9 H_9 N$, which is formed by the union of Benzine with Pyridine, a number of compounds have been formed of which Kairine, Antipyrin, and Thallin are the most important

Kairin in febrile conditions reduces the temperature in doses that have no other marked effects. At the same time the urea excreted is diminished, and so too is the Carbonic acid exhaled.
Experiments on animals show that it acts by diminishing the power of the blood to absorb oxygen. It produces methaemoglobin, a product of the deoxidation of Oxyhaemoglobin, and produces a change in the shape of the blood corpuscles.
In large doses it brings on a state of collapse, which however may be recovered from. It produces violent perspiration and the temperature may rebound with fits of shivering.
At present more has been written about antipyrin than of the others, and it seems to be the favorite.

Antipyrin in toxic doses produces in animals a fall of temperature of 6.2°C.

(11·16°7) the respirations being quickened then retarded, and the hearts beats being decreased in number and arrested in diastole.

A rigid state of the muscles is produced which arises from its action on the central nervous system, as has been proved by experiment. It has not the same effect as Kairin on the haemoglobin or on the blood corpuscles, but it diminishes the excretion of urea. It produces a dilatation of the cutaneous vessels before the fall of the temperature takes place, but at the same time observers have noted a Haemostatic effect. Against its use is recorded some bad effects namely a roseolous rash, vomiting after large doses and profuse sweating. At the same time it is not so apt to produce nervous troubles, headache, tinnitus &c as some other Antipyretic remedies.

It is said to be more useful in Phthisis and Typhoid, but less useful in rheumatism.

Others again state that a patient with Phthisis having a rise of temperature every evening is better with the high temperature than with the increased perspiration caused by Antipyrin, and this was exactly the condition of affairs in one case, a note of which is appended.

This is a fragment of the history of a case of Tubercular Phthisis in an advanced stage. Joanna Young aet 17 years Factory worker. Her present condition is this; She is confined to bed, great prostration, no appetite, face pale, cheeks flushed. respiration hurried, and coughs frequently. On percussion, dulness is found over left side of chest especially upper part. On Auscultation, Creaking, whistling, and cooing rales heard all over the chest on both sides, loudest over left apex. At back and especially at bases

the rales are very moist and liquid.
She has been getting the Hypophosphites lately, with quinine grs 4 in the evening; but there has been no improvement in her condition.

March 11th: She has had a very restless night. Cough very troublesome, perspired a good deal and then shivered so as to require hot bottles.
To get Oxide of Zinc and Extract of Bellad- in a pill at night.

12th: She has had a very restless night, but did not perspire quite so much. Cough still very troublesome.
To get

℞ Sol. Morph. ʒii
Acid. Hydrocyan dil min 30
Tinct Digitalis ʒi
Sph. Chloroform ʒi
Glycerini ʒiv Aq ad ʒii [illegible]

A tea spoonful 4 times a day.

Today the temperature is higher than usual.

March 1886 13th. She has had a much better night, slept well, less cough, no sweating no shivering, no need for hot bottles, Appetite not improved.

Temperature 101° noon. 102.2° 8.30 pm

14th Has had another very good night slept well, less cough, and no sweating. "She didn't feel feverish".

To get Antipyrin grs 20 this afternoon.

15th Yesterday evening her temperature was
100.1°. lower than it had been for a month, that is for an evening temperature, but the sweating was very disagreeable. She had had not so good a night as the two previous. This morning T. 98.6 – p 120 –

15th evening Temperature 104°7.

This is doubtless connected with the fact that news of the loss of the SS Oregon was brought to her today, her brother was on board that vessel.

DISEASE.

Tubercular Phthisis

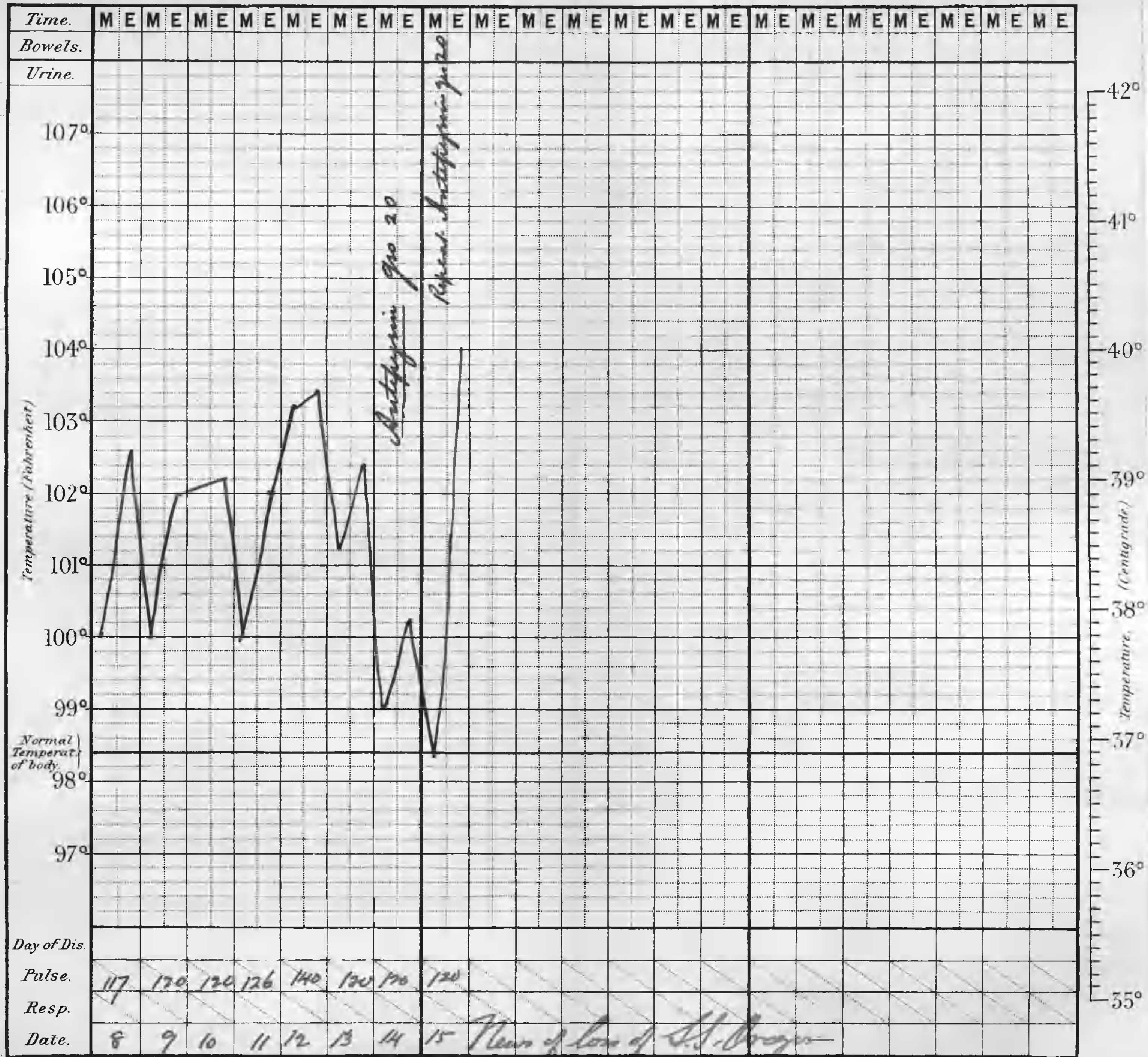
Notes of Case.

Name Joanna Young

Age 17

Diet

Case Book No.



Date of admission.

Result Still going on

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co, 7 Serle Street, Lincolns Inn.* *Gould's Clinical Chart*

In the following case Antipyrine was used with good effect and no bad results.
Mrs D. Ogilvie was confined on Feby 24th 1886
It was her fourth child, and there was nothing unusual about the labour.
On the morning of the fourth day after confinement she complained of being hot and thirsty, with pain in the back but more especially in the front part of the belly.
She was lying on her back with her knees drawn up, looking flushed and feverish, tongue brown and dry, pulse small & weak 108 per minute. Temperature 103° F.
To get Quinine grs 3 with Tinct Opii min XV every three hours, and a vaginal lotion of Solution of perchloride of Mercury 1–1000
The same evening the temperature was 102° F.
March 1st No improvement in symptoms except that there is rather less pain.
to continue the mixture. Temp 102.8° evening.

March 2nd The Temperature has fallen to 100° morning; by this time she has taken 24 grains of quinine. During the next four days of her illness there was very little improvement. The fever continued, the appetite was entirely gone. pain was less, still not absent by any means. An examination was made per vaginam when a soft doughy swelling was felt behind the cervix uteri - Probably an accumulation of pus behind the uterus, yet there had been no shivering. It was not faeces as the bowels had just moved before examination. It had more the feeling of something lying in Douglas' pouch, and not fluctuating but doughy.

On the 8th day of her illness the temperature was 102° (evening). To get Antipyrin grs 30 - After the Antipyrin the temperature fell to normal, but rose the same evening. The next day the same dose brought it down again and it did not again rise. In this case the use of Antipyrin did not give rise to any disagreeable symptoms; the patient perspired freely, but did not feel uncomfortable. The medicine was easily taken in solution and the taste not complained of. Thirty grains seemed to have the power of reducing the temperature nearly three degrees, and probably if one could have remained at the bedside to watch progress, more frequent doses might have been administered.

The writer was induced to make a trial of Thallin from reading a very favorable report of it in the London Medical Record 1885. In the following cases, it cannot be said that much is shown in regard to the action of the drug. The cases were not

DISEASE.

Puerperal Metritis

Notes of Case.

Name Mrs D. Ogilvie

Age 30

Diet

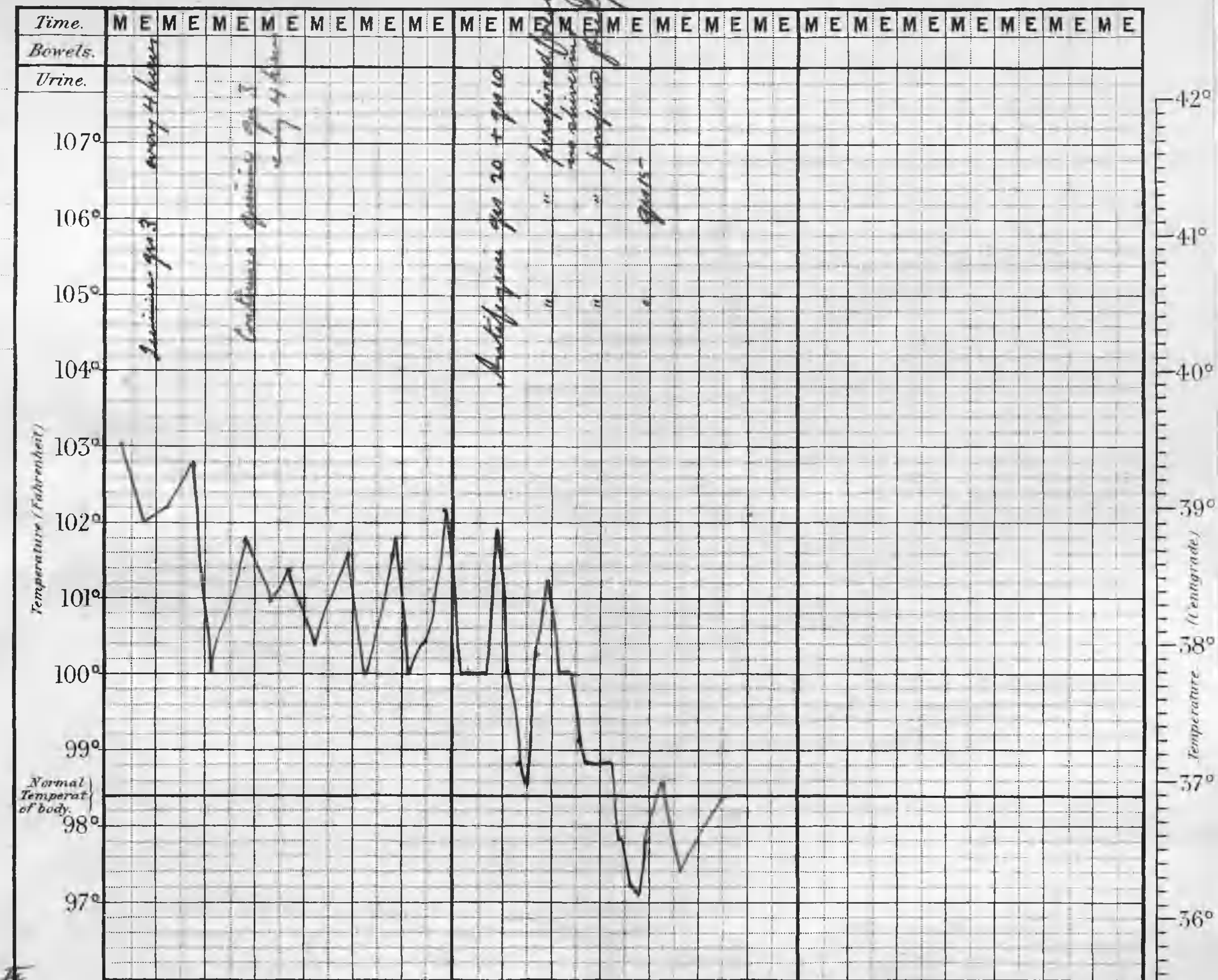
Case Book No.

Quinine —

Opium —

Antipyrin —

Confined on Feby 24th



Day of Dis.	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Pulse.	108	100 88	88	80	80	84	88 74	84 72	78 84	80 72	70 68			
Resp.	30													
Date.	28	1	2	3	4	5	6	7	8th	9	10	11th	12	13

Date of admission. Feby 28th 1886

Result Recovery

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co, 7, Serle Street, Lincolns Inn.* *Gould's Clinical Chart*

so situated as to allow of frequent observations being made, and at first the dose used was smaller than that recommended. Further trials will be necessary before the exact value of these drugs can be stated, but so far the writer would be inclined to use Thallin again should suitable cases present themselves.

In the abovementioned Journal Thallin is said to cause marked diminution of urea excreted, as much as five grammes in twenty four hours, after a dose of 0.5 gramme, larger doses causing a still larger diminution. And again two grammes caused a diminution of 0.12 to 0.4 gramme of Carbonic Acid in an hour for every kilogramme of body weight. It causes dilatation of the cutaneous vessels with profuse sweating, and in one of the writer's cases a red rash was observed.

Mrs Hastings aet 40, housekeeper, was found to have enteric fever. After three days of treatment with an acid mixture so as to note the evening rise, without any interference, four grains of Thallin were given every four hours. The result was that for four days the evening temperature from being near or above 103°, did not rise much above 100°. The Thallin was then stopped and the temperature again rose to about 102°. Thallin was again used and in a day or two the temperature became normal. In this case there was only very slight perspiration and no shivering. There was however a slight feeling of coldness, but this was not complained of.

In the second case given in which Thallin was used, the drug certainly caused some very remarkable falls in the temperature

DISEASE.

Enteric

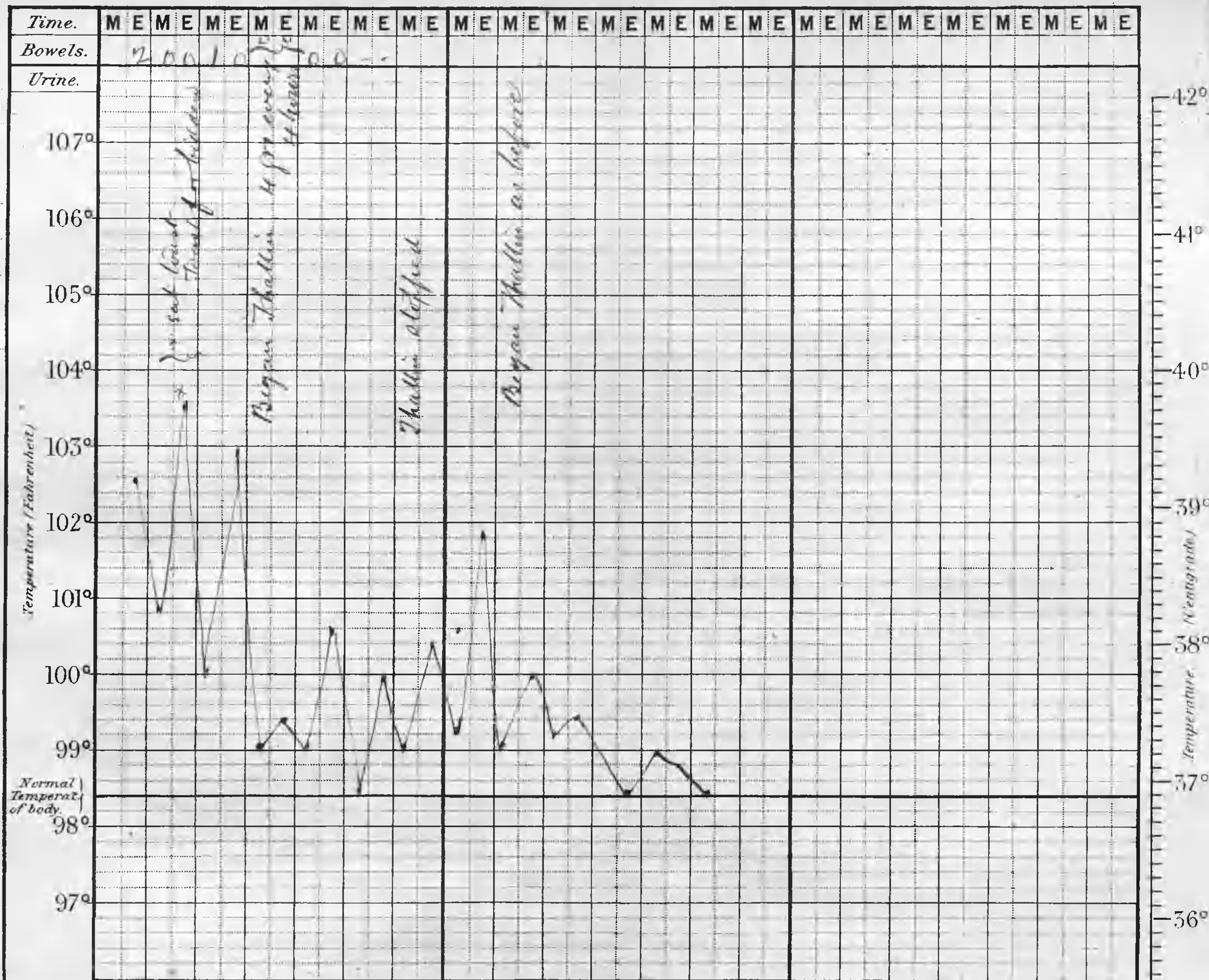
Notes of Case.

Name Mrs Hastings

Age 40

Diet Milk Beef T.

Case Book No.



Day of Dis.	11?	12	13	14	15	16	17	18	19	20	21?	
Pulse.	120	86 96	100	96	76	80	84	84	84	88		
Resp.	25											
Date.	3rd	4	5	6	7	8	9	10	11	12	13	14

Date of admission. Feby 3rd 188[illegible]

Result Recovery

DISEASE.

Pneumonia

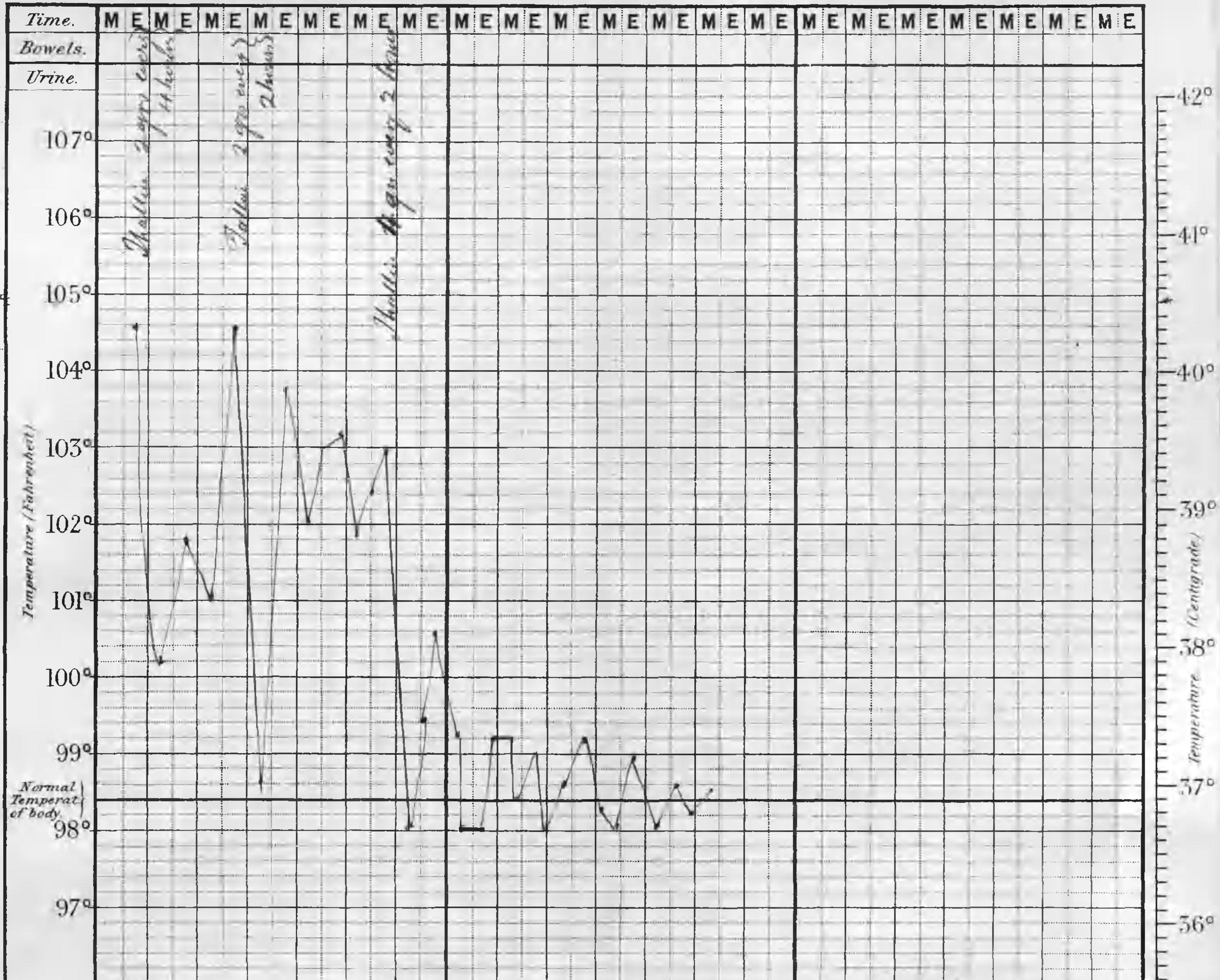
Notes of Case.

Name Jn Robertson

Age 59

Diet Soup. Arrowroot &c

Case Book No.



Day of Dis.	2	3	4	5	6	7	8	9	10	11	12	13	14
Pulse.	100	108 / 115	132 / 120	88 / 102	100 / 108	100	108	100	100	98	80	80	76
Resp.	28	24 / 26	33 / 38	20 / 35	[illegible] / 24	30	30	28	28	34	22		
Date.	10		12		14		16		18		20		22

Date of admission Jany 10th 188[illegible]

Result Recovery

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co., 7 Serle Street, Lincolns Inn.* *Gould's Clinical Chart*

J. Robertson 57 Tailor. was seen on the 10th Jan'y 1886. He had got chilled the previous day and was suffering from cough, high fever and delirium.
It proved to be a case of Pneumonia of the right side. In this case the sputum remained white & frothy till the fifth day when it became first rusty and then rather bright red.
As is seen by the chart, Thallin in two grain doses every four hours caused the temperature to oscillate very much.
It rose generally with violent shivering and most profuse sweating so much as to lead the writer to desist from its use.
On the eighth day however it was begun again in even larger doses and then it seemed to bring on crisis sooner than was expected, It was some time before the other symptoms improved.
Indeed the writer is inclined to think that

but for the Thallin the temperature would have remained at a high point far beyond the eighth day.

In this case the patient seemed to acquire a tolerance for the drug, for although the dose was increased after the third day it had less effect than during the first two. And it must be admitted that the marked effect on the eighth day may have been part of a natural crisis.

In the following case Thallin was put to a use that so far as the writer knows has not yet been done with any other Antipyretic remedy.

The high temperature of Tetanus has already been commented on by the writer in this paper.

The following case came under the writers' notice at a later date than that on

which the above was written
Jessie Walker, schoolgirl Aet 11 years,
has had a sore heel for about three
weeks, which was supposed to be better.
On Monday the eighth, March 1886 she was
at school, and on returning was chased
by some boys and had to run. She came
home very much excited and nervous
complaining of rough treatment.
On the following day she complained
of pains shooting up her limbs and
through her back and had to go to bed.
On Wednesday the 10th she was very
delirious and evidently much worse.
On the 11th She was a little more
sensible and even tried to eat. She was
seen by the writer at 5 pm.
She was found lying in bed, the head
thrown back, face flushed, Eyes staring,
teeth clenched, "risus sardonicus" very
distinctly marked. She couldn't be got to

speak, nor open her teeth, in fact she seemed to be quite insensible.
She had passed urine in bed. She was lying on her side, the legs were stretched back, the arms and hands in a state of spasm; this became much worse every two or three minutes, when she moaned piteously.
Temperature 105° F. pulse 140 weak and twitching. The foot was examined and was found to have a small sore over the tendo Achilles, with a dry scab over it; pressure brought out a small drop of pus; an incision was made over it, but no pus came, it bled a little and poultices were ordered.
Was not able to see her again till 12 pm.
At 12 pm. T 106. P 144 Resp 35 -
She lies moaning, but almost asleep, uncovering her or touching her makes her worse and raises the spasms. There are

noticed now twitchings of the facial muscles. An enema is given containing Chloral hydrate 30 grains Whiskey ℥ss ~~and some milk~~ -
On putting a few drops of milk into the mouth very little attempt is made to
March 12th swallow -

Am. 12.15 Appears to have fallen asleep.

Am. 1.30 T. 105.4° has slept well, moaning occasionally. Spasms much weaker, but still present even in sleep.

2 Am. Beef Tea with Thallin grs 4 Whiskey ℥ss. and Chloral grs 15 per rectum. Bronchial breathing at bases behind.

a.m. 2.50. T 101.8° perspiring especially on the face, which is very red, redness spreading over the chest, still sleeping but very restless, and spasms always present, Skin was very hot and dry up till this time.

DISEASE.

Tetanus

Notes of Case.

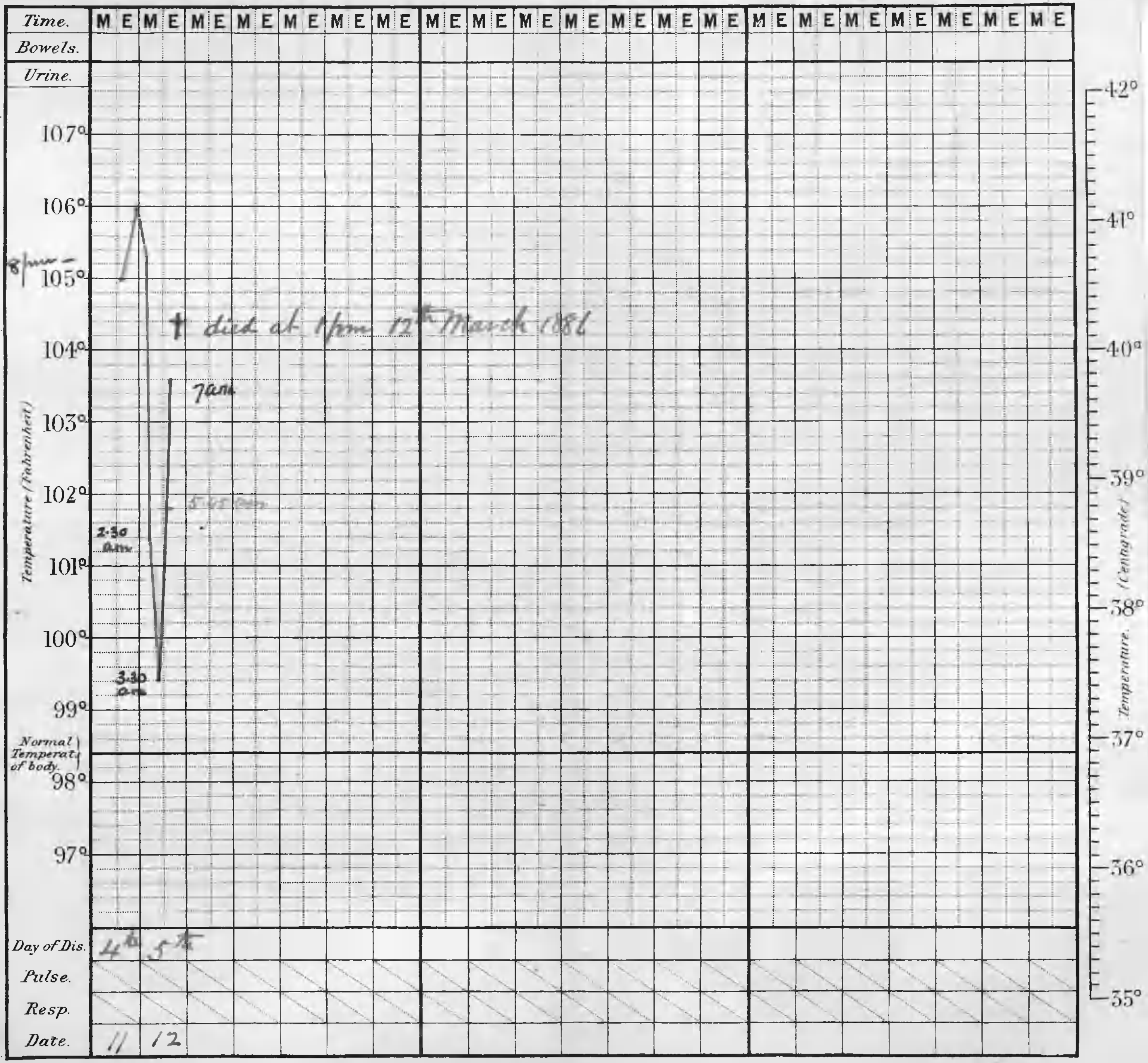
Name Jessie Walker

Age 11 years

Diet Enemata

Case Book No.

Fall of Temperature from Thallin grs 4 per rectum



Date of admission.
March 11th

Result Death

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co., 7, Serle Street, Lincolns Inn.* *Gould's Clinical Chart*

3.30 am T 99.7° lying quiet with occasional moan. P 148. R 36.
Erysipelatous blush half way up the calf. Blebs round the sore, still poulticing. Twitching of face much less.
4 am Being again very restless got Beef Tea, Whiskey, and Chloral per rectum. Breathing still rapid, but even. no catching, as previously.
5.45. P 132 R 32 T 101.8°.
Dark spots on right leg in front, much quieter. Spasms still in arms and hands.
7 am P 140 R 44 T 103.6°
Hands still Contracted, but not so much
Sleeping soundly or rather comatose, mouth partly open, and tongue very dry. Getting dusky about the face and lips, evidently sinking. She died at 1. pm.

In any case where there is pain or muscular spasm with a high temperature, quinine and Opium may be given, and the combination of these two drugs is looked upon as quite correct.

Therefore the writer argued in this case Chloral and Thallin might be used together. The intention was at first to use the Thallin hypodermically, but it was given per rectum, using a larger dose than would have been used by the mouth.

From the first the prognosis in this case was bad. The rapidity of the onset, the severity of the symptoms, and the appearance of the patient all pointed to a speedy termination. Still the writer thought it right to try the means that he knew were calculated to give some relief.

P. Scott M.B.C.M.
Carnoustie
16th March 1886.