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Oliver Field.
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Antipyrine was first introduced to the
profession as an antipyretic some years
ago, and has obtained a very wide popularity
for that purpose. It has been found
useful in reducing the temperature and
fever, from whatever cause, in specific
fevers, such as typhoid, scarlet fever or
erysipelas, or in fever following surgical
operations and injuries. Whilst it is
useful in all these, yet I have found it
fail in cases of hyperpyrexia, in which
I have tried it, so that I have come
to the conclusion that it is of no value
in cases where the temperature rises
much higher than 105°Fahrenheit.

Since its introduction, many
other applications have been found for
it, depending chiefly on its anaodyne
action, and it is principally these
action, with which I here concern
myself.

The use of antipyrine as an anaodyne was
suggested first by Professor Chromyakoff
In the following year Dr. Hantschel reported it to be useful in other kinds of cephalalgia.

Mr. Germani of Paris made extensive trials of it, and by communication to the Académie de Médecine, thought it promising. Before the notice of the medical profession

since then it has been used for nearly every kind of pain, with professional advice; and also without it; so, indeed, it has become such a popular remedy that it is in danger of being taken out of the hands of the medical profession altogether. This is a regrettable fact, as though usually a harmless drug, yet sometime symptoms of poisoning have been produced by it, which ought to prevent its indiscriminate use, without competent advice.

Antipyrine occurs as an amorphous powder or as finely white crystalline scales; it melts at 283° Fahrenheit; it has a bitter taste, it is readily soluble in water. This solubility in water gives it a great advantage over antipyrin in regards convenience in dispensing. For, though the latter has very similar actions, it is very little soluble in
water. The watery solution gives a deep red colour with ferric chloride of iron. It also forms with spirit of ether a greenish substance which crystallizes in bright green needles and which is reputed by many to be highly poisonous. Dr. Ludwig Brener of New York, however, who has investigated its behaviour, says it is not poisonous (British Medical Journal Dec. 15, 1878). M. Edler of St. National Druggist, who has given it to animals, has taken it himself, complaining. It is safer however to consider the two drugs incompatible to avoid prescribing them together.

The drug may be administered by the mouth, or rectum, or hypodermically, when a 50 per cent solution in distilled water is usually made use of. If a dose of 10 grains is injected in this way, there is at first a sensation of burning pain experienced at the seat of injection, which however soon passes away. Then follows a diminution of tactile sensation over the whole limb, while for a small or varying area round the point of injection, there is complete anaesthesia. Many pains yield more quickly, or completely to the drug. Administered in this way, than by the mouth, or this is particularly the case with sciatica.
The physiological actions, as discovered by clinical observation, do not agree entirely with what has been found by experimentation on animals, but some facts have been clearly proved. It is of the greatest importance that the exact physiological actions should be made out, in order that its therapeutic application may be more clearly defined than at present, for, as it is, there is hardly any kind of illness in which antifebrin is not warranted of someone as an infallible cure.

As to its action on the circulation. In no man, either in the fibrile condition or in health, it is found almost invariably to make the pulse less frequent, and at the same time, to increase its arterial tension. This slowing of the pulse is frequently very marked in fibrile conditions, usually precedes the fall of temperature.

I have several times noticed the marked slowing of the pulse in patients who have been taking the drug for cephalalgia, for instance, even 1.50 per minute, as reported by Dr. Jameson in the Lancet. May 26, 1880, it was sufficient to excite the alarm of an intelligent patient. This, however, is not quite invariable in man, and experiments of Sawadowski carefully conducted show that it is not so with dogs.

This & the following experiment of Sawadowski
are published in "Centablatt für die Medizin Wissenschaft." Nos. 8, 9, and 10. 1883.

He came to the conclusion, that a close of from 0.018 grammes to 0.3 grammes per kilogramme of body weight in dogs caused acceleration of the pulse, whilst the blood pressure showed a slight initial fall followed quickly by a rise to 20 per cent above the normal. This he considers to be due to direct action on the excited motor ganglia of the heart, and on the cardiac centre in the medulla, because the found that it occurred even when the vagi nerves were divided, or the spinal cord. The rise of pressure is due to increased cardiac activity, and to increased resistance in the arteries, as the latter showed dilatation, due to the direct action of the antifugue. This he conclusively proved by passing blood containing the drug solution through living vessels, with the invariable result that they dilated. These results he contradicted the view that a rise of the pulse whether the used dogs in a normal condition or those that were febrile. This action in dilating the arteries affords a probable explanation of the good effect produced by antifugue in some cases of angina pectoris. It is generally believed that the pain is due to the unavailing efforts of the heart to overcome increased arterial
resistance. Büstowé (Medecine p. 535) says, "There is reason, however, to believe, that "from the paler appearance of the surface, which "alters the onset of the attack, to form "pysemographie observation, that an essen-
tial feature of the disease is peculiar "escheeme contraction of the systemic arteries," "which both prevent the free passage of blood "to the capillaries, and, diminishing it up a "it were, in the heart, excites that organ "to unwonted, but more or less quitted "efforts." The relaxation of the muscular "wall of the arteries would relieve this "embarrassment of the heart, and the strenue-
lation of the latter would force the blood on more completely.

It must be remembered that the doses "used by Swedowwsc are in the whole in "excess of those used medicinally. A very big "medicinal dose would on exceed 0.03 "grammes per kilogramme of the body weight. "He also found that a solution of 0.5 per cent of "blood, mixed with 5 per cent of antitoxic, "remained unchanged for 12 hours. In blood, "however, he found that a 2 per cent solution "destroyed the red blood corpuscles in 2 or 3 "hours, while a 3 to 5 per cent solution "turned the blood into a jelly condition in 1½ to "2 hours. There was no change, however, in the
oxygenation function of the blood, for a solution of haemoglobin, when it had been exposed to
the action of antitsyrup, can be reduced or
peroxidised by the usual methods, showing
that the haemoglobin is practically unchangeable.
Sawadowski confirmed previous observations
to the effect that antitsyrup is an antiseptic,
proving that a 2 per cent solution
inhibits putrefaction, but does not prevent
it completely; it requires a 3 or 5 per cent
solution to do that. In therapeutic doses
no effect was found in the secretion of gastric
juice or on the digestive processes in the stomach,
but a 2 per cent solution inhibited gastric
digestion.

According to Dr. Antonio Grasselli, (Giornale
Internazionale delle Scuole Mediche 1880,
pp. 358) who made numerous
experiments, antitsyrup is most readily
absorbed from the stomach, but is also absorbed
from the rectum, one dram dose being
easily given in that way. It is not at all absorbed
from the skin, it is eliminated almost entirely
by the kidneys, a very little being found in
the feces or none whatever in the urine,
sweat, mucus, expectoration, pleural effusion,
or fluids of hydrated cysts.

Antitsyrup undoubtedly diminishes the
endogenous secretion as estimated by the amount
of urea. This has been proved by Tammachs (Archiv. f. exp Pathol. und Pharmakol.) by putting himself and other healthy individuals on a uniform constant diet to estimate the amount of urea excreted. Then he administered antisyphus for some days, continued the experiment for some days, after leaving off the drug. He found the excretion of nitrogen during the second period, while taking antisyphus, fell as much as 10 percent. During the third period the excretion rose to the former normal level no higher, thus proving that there was no mere retention of waste products, but an actual lowering of the metabolism. One series of experiments extended over five days and another over fourteen, and the results corresponded.

Purine experiments have been carried out in febrile conditions, notably by Reiss in case of typhoid fever, and the result all agrees with Albert Robin from experiments at the Laboratory of the Hôpital des Enfants Ménages in Paris, published in the Bulletin de l'Académie de Médecine Vol xlvii p. 701 et seq. Just the reduction of the total amount of nitrogen excreted at 14½ percent. He concludes as well that the proportion of nitrogen completely oxidized in the form of urea to the amount in less oxidized substance, such as urea acid, & creatin,
which is normally as 80 to 20, is lessened to the proportion 72 to 28, or in other words that the percentage of completely oxidised nitrogen to the total nitrogen excreted falls from 80 to 72 percent under the influence of antipyrine. The percentage of phosphorus contained in the most completely oxidised form as phosphoric acid, falls more than 60 percent, so the same is true of the sulphur excretion. So that these elements are excreted in less quantity or in less oxidised forms. Assuming that the less oxidised forms are more harmful than the more oxidised, it would be injurious, on theoretical grounds, to give the drug in disease, where it is important that the excreta, particularly the kidney, should act freely, as for instance in typhoid, or where there is any difficulty in elimination, as for instance in kidney disease. The total quantity of the urine is also diminished.

Sawadowski, however, could find no alteration in the amount of urea excreted, whether in healthy, or in febrile, dogs. Very interesting experiments are related in "Compt. Rendu" N° C vi p. 1023 and N° C vii p. 416. By Lépicié's Forlet hearing on the influence of antipyrine on the amount of frequency the body. They found that where
guinea pigs were given doses of antipyrine of 0.1 gramme per kilogramme of body weight. The liver contained one-fifth more glycogen per kilogramme than was the case in a similar series of animals, who were in exactly the same condition as to food but without the antipyrine so that the amount of sugar in the first series of animals was proportionately less. Similar results were obtained with antipyrine, quinina, or salicylate of soda. Hence they conclude that these drugs hinder the change of glycogen into sugar in the liver, a fact was confirmed by further experiments. Two portions of fresh liver were placed, one in water alone, the other in water containing antipyrine, and allowed to remain for four hours. The result was that there was less sugar made glycogen in the portion soaked in the antipyrine solution than in the other. By a similar mode of experimentation they found that a dose of 0.3 gramme per kilogramme of body weight of antipyrine, given to guinea pigs, increased the amount of glycogen in the muscles, so that, comparing a series of animals, treated with antipyrine with a similar series pretreated, it was found that the proportion of glycogen in the muscles of the former to that in the latter was as
0.3 is to 0.235 percent. These doses are of course very large, much larger than medicinal ones.

These investigations have a direct bearing on the usefulness of the drug in diabetes mellitus, as found from clinical observation.

On the nervous system it acts as a general sedative, but it is not yet satisfactorily determined on what particular parts of the nervous system it acts or how all the many different effects produced can be explained. Germain de Lévy regards it as acting on the peripheral nerve terminations, as well as on the nerve centre; Quinacreg regards it as a general true-resinie poison, which, therefore, tends to lessen the vital processes in all the tissues.

See (see Bulletin de l'Académie de Médecine, p. 23, 1881) injected large doses of anticholinic into animal showed that chronic spasms of the muscles were produced, followed by a condition of tonic spasm, if the doses were sufficiently large, or ultimately by paralysis. If however the sciatic or cranial nerves of a limb were divided, convulsions did not occur in that limb, showing that the centre, probably in the cord, are stimulated to cause the muscular contraction. He found that injection of smaller doses into a limb caused diminution of sensibility in it, or sometimes of the opposite
one, a shown by diminished response to ordinary stimuli. If then he stimulated 
the sciatic nerve of the injected limb, the 
resulting movement of the opposite one were 
slow or limited. From these experiments, he 
concludes that antipyrine produces a paraly 
of the sensory nerves in an injected limb, or 
insures the conduction of reflex nervous 
impulses through the spinal cord. Strophanine 
on the other hand increases these reflex 
action apparently by increasing the con 
ductivity of the nervous tracts, at all evul 
exaggerated reflex movements are produced by 
very slight stimuli; under the influence of strophanine. 

Chengzik in a communication to the Societe 
de Biologie on July 16th, 1889, drew attention 
to the antagonistic action of these two drugs, mi 
this respect. He described that, if antipyrine 
is first injected into a pea, the subsequent 
jection of strophanine did not produce its char 
acteristic effects. If, however, a sufficient 
clone of antipyrine were injected, to produce 
clonic seizures, then the convolution of 
strophanine were not prevented from appearing, 
but were not so severe or violent, as when 
antipyrine had not been first given. Also if 
antipyrine were injected after the administration 
of strophanine had caused its characteristic 
convulsion effects, it checked the convulsion.
s soon sometimes caused the clonic spasms, peculiar to it, to replace the clonic convulsion.

Dr. Macalister in his Croonian Lectures in 1886 went very fully into the action of antipyrine & attempted to give an explanation to include all the different special actions of the drug. He suggests that, instead of being considered a nervous depressant, it should be considered as a stimulant of the inhibitory nerve tracts & centres in the spinal cord & brain. The first effect of stimulation of the inhibitory apparatus in connection with the muscles would be to diminish reflex movements. If the stimulation were excessive it would lead to exhaustion of the nervous mechanism, so allowing the excitatory nerve more & more uncontrolled action causing clonic & tonic contractions.

This would lead to the exhaustion of the motor nerves concerned, & consequent paralysis of the muscles. This is obviously what he found in his experiments.

On this hypothesis the action on the circulatory system is a stimulation of the cardiac-inhibitory & vaso-inhibitory nerves. Certain arterial dilatation is generally produced or slowing of the heart action, but also a rise of blood pressure. This cannot be explained by
stimulation of the vagi nerves, for, in proportion as the heart beats are less frequent, they must become more powerful, in order that the blood pressure may be kept up. Sawadowski (quoted) considers that there is a direct action on the walls of the heart's or those in the muscular wall of the arteries. It will be remembered that Sawadowski found acceleration of the pulse rate using very small doses of strychnine comparable to the results of Sici's experiment, in which he produced excessive muscular action with large doses. Possibly, had Sawadowski used medicinal doses, he, too, would have found the heart made to beat more slowly.

Clearly, however, the raised blood pressure with medicinal doses proves that the total effect is to cause more expenditure of force on the part of the heart, since the arterial resistance is certainly not increased, but rather diminished.

Maclustee considers migraine to be due to irregular contraction of the cranial arteries, or the relief experienced from the drug to be due to the drug being due to the dilatation caused by it. Other kinds of headache however and allied especially to migraine are an equally relieved.

Assuming that there is an inhibitory mechanism to control metabolism, its stimulation would cause diminution of
That metabolism.

As to its action as an anaodyne, Dr. Macalister considers that pain is produced by excessive stimulation of the tactile centre in the hippocampal convolution, as localised by Ferrier, so that the action of that centre is held in check by higher centres. He instances the fact that intense concentration of the attention prevents us from feeling pain, so that serious wounds are often unfelt on the battlefield. The stimulation of the centre would therefore prevent us experiencing a sensation of pain. It would however be equally the effect all over the body, it would also diminish tactile sensation uniformly. The injection into a limb should, therefore, not produce any more effect on that limb than on the opposite, or any other part of the body if it acted through the circulation on a common centre. It is however found to have a greater effect by soothing pain in the limb, or part, in which it is injected, than on other parts of the body, so there is unrevealed the local anaesthetic effect at the point of injection.

We are therefore driven to the conclusion that there is an influence exerted on the sensory nerves at or near their peripheral terminations so that, that must be the
explanation of the anaodyne action, to some extent.

It is interesting to note that clinically antiphurin is sometimes found to act as a distinct stimulant. Thus a case of nervous insomnia cured with antiphurin by Mr. Block, is mentioned in the British Medical Journal in January 1st, 1888. The insomnia occurred after lunch every day, had been troublesome for years, in a man of neurotic constitution. Mr. Block considered its action similar to that of black coffee, only stronger and more effectual.

Hence, whether antiphurin acts as a nerve depressant, or as a stimulant of certain portions of the nervous system, cannot be said to be as yet entirely proved, but Macleod's theory as an attempt to give a scientific explanation of the mode of action of this group of remedies (for antiphurin and the other so-called nervous antiphurinics acts in the same way) is very valuable.

Phosphoric was the first efficacious agent in which antiphurin was given, and having been used for three years by multitudes of people for this distressing complaint, it still holds its place as the most efficacious remedy. It is best given as a preventative of the attack, when the aura, that generally precedes it, are present, or a dose of 15 grains will nearly always ward off the attack. As if it has already
developed), antipyrine promptly cut it short. Professor Seé (Bulletin de l'Académie de Médecine) had only one failure in five cases of the first series he mentioned in his paper.

Dr. J.S. Robertson, in a paper read before the Neurological Society of New York (Medical Record May 7th, 1884) stated that he had used antipyrine in no less than 80 cases of migraine, and that he had failed to give some relief in only 8. In 54 of his cases the favourable action of the drug was noticed in from thirty minutes to one hour. In 16 other cases recourse had to be had to chloral, bromides or other drugs, but it was not found necessary to give such large doses as usual. He gave 20 grain doses in a little linctus water, or repeated in 2 hours if necessary. There have been very many reports in the medical press referring to its action since the date of the above.

As regards the dose, 1 grain is very often sufficient, but as 10 grains are not any more harmful than 1 grain, I usually give the larger dose as there are some cases that will not yield with less. I always repeat it if necessary in an hour.

I have only had one case in which it has failed to benefit, and that was the case of a young woman subject to migraine, who
was in an extremely feeble state of health from overwork, and rapidly got better with the aid of potassium greenide. I have recently, within the last month, had five well-marked cases, in all of which very great relief has been obtained. In three of these, the attacks have not only been relieved, where they occurred, but they have very greatly diminished in frequency, and when the attack has come on, or before the drug is taken, the pain is found less severe, there is less pictures, so the general malaise slighter than was formerly the case.

This may be looked upon as no great achievement, on the part of anyone, but it makes a vast difference to men of regular occupation, who had previously been compelled, every now and then, to miss a day or two from their work, on account of this trouble; and, considering the great amount of migraine amongst those who do much intellectual work, the use of the drug must be held to be of considerable benefit to mankind.

The following is an illustration of the influence of the drug in these cases.

Mr. P., a single lady, aged 30 years, has been a sufferer from migraine for the last five years, previous to that she was not troubled by it. She has been subject to attacks of dizziness for
The last 2 years, but this did not begin for 3 years after she was troubled by the cephalalgia. She has also been subject to great dysmenorrhea without any distinctly pathological condition in the pelvic organs. The attacks of migraine occur generally once a week, but the worst ones are always coincident with the commencement of the menstrual flow. The attacks are generally succeeded on the previous evening by some delirium, if arising from malaise, or in the morning the awakener with the headache very return, accompanied by painful throbbing, starting from the left temporal-frontal region, confined to the left half of the head. There is tenderness behind the above the left orbit. These symptoms, set more power usually last six hours accompanied by vomiting. Under treatment by dieting, regulated exercise, with the usual gastric sedatives, & 2 grani dose of iodide of potassium, the digestive symptoms greatly improved, but the headaches did not yield to Bromide, Belladonna, Arsenic, or any of the remedies ordinarily used. Then I gave antipyrine bi 2 grani dose, three times a day for a fortnight, during which there was no headache, & the patient felt intellectually more active & stronger. I recommended her to take a 1 grani dose whenever she felt the attack.
coming on, & if that did not ward off the attacks to repeat the dose twice of necessity at intervals of a month. This is invariably successful, & the case now prevents the train of symptoms from coming on. There has been much less pain also at the menstrual periods, & she can go about at those times, instead of lying up as she was formerly obliged to do. After several months' experience she is as pleased as before with the result, & finds that she has to have recourse to the medicine much less frequently, seldom more than twice a month sometimes only once in three months.

As to the relief given from the dysmenorrhea, I have often noticed improvement in each case. Lastly, I have had 2 cases of severe pains, in which only temporary relief was obtained, but also quite permanent. In one case this, & in the other three, months followed with but little pain, though the drug was not administered after the first menstrual period in which I had given it. My pains close every three hours during the first day of the period, 2 then three times a day for a week. These results are in conformity with the statement of Dr. Groppi in his communications to the Société de Physiologie on July 16th.
Nov. 19th, 1887. The success in the latter communication the case of a woman aged 35, who was suffering from a large myoma of the posterior uterine wall, with great haemorrhage, which occurred between the menstrual periods. The haemorrhage was arrested, but the pain was so great that he was obliged to stop it. He administered large doses of morphia which relieved the pain, but caused the uterus to relax so that the haemorrhage reappeared, so that he again used ergot with the same results. The attack of pain lasting 2 or 3 hours, Dr. Chevigne then gave an enema containing 30 grains of antipyrinum in 20 minutes. The pain disappeared. He then proceeded as the man; gave an injection of antipyrinum and in half an hour the dose of ergot. No pain was experienced but active uterine contraction was set up, and the haemorrhage was arrested. Dr. Chevigne concludes that antipyrinum relieves the pain caused by uterine contraction produced by ergot, without diminishing the contraction, and he believes it acts upon the spinal cord.

Several cases have been reported of relief of the pains of labour by this method.

In the Comptes-rendus of la Societe de Biologie for Dec 30th, 1887, Dr. E. Lapert relates
The case of a young lady, who had already
been twice pregnant, was taken
with the pains of labour after 5 months
pregnancy. The pains were very severe and
treatment was obtained from enema of causticum,
which were given at intervals of 4 hours.
On the third day, the pains being almost
continuous and unbearable, an enema con-
taining 50 grains of antispasmodics was given,
which relieved the pains, and a second dose,
in an hour, time, caused them to diminish
in a remarkable way. The uterine contraction
continued every 8 to 10 minutes, with little
pain, and in 3 hours the foetus
was borne, followed by the placenta. The
patient had no afterpains, and the convalescence
was normal. Dr. Lago conducted that
Department of the contractions were not
diminished, but that, on the other hand, the
exhaustion caused by excessive pain being
relieved, the contractions were more effective.
Dr. W. Helshin in "Wisdomsce Lekarstvi" 20 1888 p. 288, states that he has
previously cured 6 cases of labour at full term, and
in one case of another abortion at the 4th month.
He came to the conclusion, that the drug, in many
respects, is much superior to all other means, which
have been hitherto recommended, for the relief of
the pains of labour. He usually gave 1 gramme
quantity, when necessary repeated the dose every 2 hours. The result was invariably excellent. A few minutes after dose the pain ceased almost entirely, while the force of the uterine contraction did not decrease in the least. The patient felt only the pain accompanying the passage of the foetal head through the perineal canal, which was less pain was, beyond all comparison, less than in preceding labours. Several other cases, similarly successful, have been reported in the medical press. In instance in the "Lancet" June 30th, 1888. It is mentioned that Steinthal had one case, in Vienna.

More recently however doubts have been expressed as to whether the uterine contractions have not been made weaker by the exhibition of antipyrine. To test this Dr. Ermano Pianzani made the following experiments related in the "Gazzetta degli Ospedali" Feb 10th, 1887. In 5 cases he simply kept his hand on the uterus before and after the administration of the drug. In eight other cases (in which he made in all 23 experiments) he passed an indiarubber ball, first disinfected, then filled with a warm solution of corrosive sublimate, into the uterus and connected it with a manometer, which was judged accurately the pressure exerted by the uterine contraction on the fluid within the
ball. Irritation was reduced to a minimum by warming the fluid put in the ball to the temperature of the body, so a considerable interval was allowed to elapse after the introduction, before the observation was taken. In the first set of experiments, 3 grammes doses were given by the mouth; in the second the doses were from 1 to 3 grammes. Dr. Angani came to the conclusion that the pains were relieved, simply by lessening the force of the uterine contractions. He found that the effect of the drug was produced in 1 to 2 hours after administration by the mouth, and in 2 hours after hypodermic injection. He also noticed that infants suckled by women, who had had antipyretic given them in labour, were apt to suffer from diarrhoea. He therefore concludes that it is not advisable to give antipyretic in labour. These doses it will be noticed are larger than those recommended above. Germani has found in his experiments with animals that he could cause paralysie of muscle by giving a big enough dose, but only those after convulsions. The method of measuring pressure with an indiarubber bag, must have been exceedingly difficult to carry out, and liable to error. Perhaps more reliable results would be obtained, by comparing the length of labour in a large series of cases.
At first and whether antiperspirin prolongs it at all. As far as the cases that have been reported, no delay has been noticed.

I have only given it in one case of labour, that of a healthy woman aged 26 confined with her second child. When I first saw her, the os was dilated to the size of a two shilling piece, and was the usual cutting pain. In order to try the effect, I administered 10 grains dissolved in 20 minims of distilled water hypodermically.

In half an hour she was greatly relieved, so much so as to feel but little pain. The uterine contractions went on, and there seemed no descent in the traction of the bag of membranes, which bulged as usual during the pains, and the os dilated quite normally, as quickly as I expected. The child was born in 2½ hours from the time I first saw her, and the effect of the antiperspirin extended over the 2nd and 3rd stages of labour. The pains felt was comparatively slight. I was much pleased with what seemed a very favourable result, with no unpleasant symptoms. There were very slight after pains. The child, though nursed, did not suffer from diarrhoea. I think the drug will prove of great use in cases of women, being of the case is typical of its action, nearly as efficient, very much more convenient.
Their cholera-like especially in private practice.

It is not only in headaches of the nature of migraine, but in those of all description that relief is obtained by antipyrine. These depending on cerebral tumours even, are, in many cases, no exception. Some of these headaches, depending on grave organic lesion of the brain, entirely revert relief to the drug. I have come across a case of cerebellar tumour, in which it was of no use at all.

I have heard of several others.

Besides these headaches, antipyrine is recommended for many nervous pains. Dr. Halstead (London, April 20, 1886) found it useful in cases of ciliary neuritis,

headache accompanying various eye diseases.

He reported 22 cases of age varying from 17 years to 75 years. All of whom, excepting 3, were free from any disease but that of the eyes. He found it particularly valuable in headache following on operation. In cataract, even in cases complicated with iritis. In most of the cases pain was relieved in an hour. Some relief was given in 4 cases of cephalic pain accompanying different forms of keratitis. In a case of double optic neuritis, in 2 of atrophy of the optic nerve, and in one of scleritis, less satisfactory results were obtained. Dr. Grand Clement of Lyons.
confirmed these statements, at the meeting of the Académie de Médecine, May 8th, 1886. He used hypodermic injection in the temporal region of 25 centimetre centigramme with half a centigramme of cocaine. He was successful in relieving orbital and periorbital pain, to some extent ocular efflusions. Many cases of keratitis, uveitis, glaucoma, iridochoroiditis, of standing hermiania, monocular hemianopia, several cases of tic in the orbicularis palpebrarum, of anterior poliocrisis, and heterochoroiditis, and of floating bodies in the vitreous humour, were amongst those benefited. He never had any abscesses at the point of injection.

Prof. Dufreze in the "Lyon Médical," Aug. 16, 1886, stated that a patient suffering from the lightning pains of locomotor ataxia, who had been too long accustomed to morphine, who dreaded the After effects of sodium salicylate, great relief was obtained from antipyrine in a daily quantity of 15 gr. in two doses. He found that there was some accompanying insomniæ, which the patient actually overcame with chloral, and some temporary increase of nicoordination, which ceased at once when the drug was left off.

Dr. Giornini, in "published a series of cases in the Bulletin de l'Académie de Médecine," Aug., 1887, in which he states that he found very marked
relief in 4 cases out of 5, in which he tried it, and these were no disagreeable effect. He has more recently (Bulletin, Vol x vii p. 340 et seq.) reported other cases quite like satisfactory result of treatment of州。(British Medical Journal Jan 11, 1887) in that he found it give relief in 3 cases of locomotor ataxia. A man aged 48 was kept free from the severe pain in the legs for a week by two 10 grain doses. On the return of the pain then, it was banished by a further dose, & the patient stated that he had and felt as well for a year.

Other observers have corroborated this, for example Dujardin-Beaumetz, Mendel, and Martius.

The following case is illustrative of its effect on these pains. J. S. aged 48, has been gradually losing the coördinating powers of his limbs for 2 years. During the last 6 months, he has been suffering greatly from shooting pains in his legs occurring often every few days, sometimes many times a day. He has also had frequent gastric crises of the usual extremely painful kind, and shooting pain up the left side of the head. He is hardly ever free from pain of some kind at any time. He had been treated with morphia, but headaches and general discomfort had so distressed him, that he did not feel much pleased with the relief.
From pain that he obtained. I gave him 10 grains of antipyrine 3 times a day, and after the first two doses he felt free from pain, and the following day he told me that he had a pain of well being & comfort, that he had been a stranger to for months. There was no improvement, but no aggravation of the incoordination, so that the drug acted purely as an anodyne & not as at all as a curative agent, except that when he left off taking it regularly, which he did in 3 days, the pains did not return so frequently. The gastric crises were as effectively relieved as the headache pains.

I instructed him to take a dose when the pain came on, & he has been sometimes able to go 3 or 4 days without having recourse to it. Whenever he has done so relief has invariably followed in half an hour.

In some cases that have been reported tolerance of the drug has occurred so that the dose has had to be increased, and even then has lost its effect. This has not been so in this patient case, though he has been taking it from time to time for 14 months. I have not found tolerance produced in other cases, such as migraine, in which I have prescribed it for long periods.

In another case of nervous pain antipyrine has not been of the least use. J. B., aged 48, an engineer, has been suffering for 7 years
From nervous symptoms, dating from a fall on the back of his head. He has been gradually losing the power of coördination of his legs, with mental confusion and loss of control of the emotions. He has had 3 attacks of convulsions affecting the left arm, leg, and left side of his face, with a short period of unconsciousness, succeeded by saving chloroform lasting for from some hours to 2 days. The convulsions were followed by paralysis of the affected parts which was gradually recovered from in the course of a few months. In December 1887 he presented symptoms like those of Lanchester Ataxia, viz: absence of plantar reflexes, and atactic gait, but with no eye symptoms, except contraction of the field of vision affecting chiefly the left eye, no ocular change visible with the ophthalmoscope. Since then the reflexes have partially returned, and in Nov. 1888 he had a fourth attack, similar to the others, but has not recovered from the paralysis, and the mental symptoms have become more marked. He has throughout complained of great pain in the left temporal region and around the left eye; also vertigo, pain in both legs. Hypertonia and the pain has caused mannacul excitement, could not be stopped. I have tried antipyrin on several occasions for
several days at a time, in 20 grain doses every four hours, but have not proceeded in relieving the pain at all by it. An ointment of cocaine, 10 grains in 1 oz. caused some temporary relief, but its influence seemed to be lost in a few weeks. The was shift without sleep altogether, in day or in a fit by his suffering and the drug that I have found to be a good one, is hydrochloride of hyoscine. About 1/100 grain injected hypodermically, has always cured the pain to put the patient off into a quiet sleep, & the pain has not returned on awaking, for 6 to 48 hours. This case however is probably more allied to general paralysis of the insane than to locomotor ataxia.

The case of J. R. illustrates the action of antipsue in neuralgia as effecting a cure not merely relieving. She is a domestic servant aged 20 well nourished healthy looking, with no physical signs of disease. She complained of pain in the region of the stomach, passing through the chest to the blade of the left scapula, the pain was occurring especially after food but at irregular intervals, often before meals. It is often so severe as to prevent her from eating. For several weeks I tried arsenic,
genuinely, and so often remedied but without any success. The appetite was good, but the pain came on in the same way, often several times a day, and lasting generally for about half an hour. I then tried antipyrine in ro grani doses and after three doses the pain disappeared and has never returned since.

I have treated many cases of neuralgia, chiefly facial, by it and have never failed to give relief. Generally I have found that administering this drug by the mouth has stopped the pain in half an hour; in three cases I injected the grani hypoiodometrically, but did not find any advantages over administration by the mouth. I have found it useful in giving temporary relief in cases of neuralgia depending on carious teeth, when the swelling has been too great to allow of immediate extraction of the tooth, or where for other reasons, that necessary procedure could not be adopted. In panes the discomfort, much, too, when carious teeth have gone on to join an abscess.

Another case still more clearly shows what a very useful drug it is, in the treatment of neuralgia E. H. a married lady aged 28 with 2 children, has been subject to attacks of severe pain affecting the hypogastric region, and shooting through the body to the back. She
The pains, from time to time, since she was a girl, have been much worse since her marriage. During the first year of married life, lately, she has had them more often and more severely. They do not occur especially at the menstrual period, but at regular intervals and are associated with ovarian tenderness on deep palpation. The bowels are regular. Her function is normal. The pain persists after an enema, but is persistent. She has had a variety of treatment, without success, and as her health has been otherwise good, she felt obliged to discontinue it. She tried antipyrin, 10 grains of which have always given relief, but without success. This case is an example of the pain in which antipyrin seems particularly useful, for she was not sufficiently ill to render the use of morphine, with its attendant discomforts and dangers, advisable, and with antipyrin, as good a result was obtained, without any concomitant ill effects.

Dr. Jamieson in "Lancet," May 26, 1880, relates a case of neuralgia due to a stone in the kidney, originally, kept up by ill health. The pain was in the left lumbar region and shooting round to the left groin. He was completely relieved in 30 days by the continuous administration of the drug, 3 times a day.
I think there is no doubt that antipyrine is a certain and quick remedy for all cases of neuralgia; to be accompanied, of course, by removing the cause, if possible.

In consequence of its influence on these nervous complaints, it has been tried in epilepsy. The general opinion is that it is of much value. Dr. Hyrett Brooks in a paper read before the Oxford Branch of the British Medical Association on April 24th, 1888, says: "I have not tried it in many cases of epilepsy, but I was not favourably impressed with the results when I did try it." F. Tracy in a thesis published in the beginning of 1888 concluded that it had an action similar to that of the alkaline bromides, and influence some cases of epileptic convulsions. He found that very large doses were necessary; however, as much as 3 to 4 grammes per os, and in a large number of cases general malaise resulted, necessitating a discontinuance of the drug.

Mr. Lemoine of Nancy at a meeting of the Société de Biologie at Paris January 1880 stated that in many cases antipyrine was inactive, but in some cases, such as where the convulsions were associated with menstruation, and also in migraine following epilepsy, it gave great relief. It was then found better than Bromide of Potash and the dose
was 30 grani. given for a long time.
Mr. Roberton in the Practitioner Vol. 40 p 266
gives particulars of 20 cases of epilepsy treated
by it. In 14 cases fits were prevented and
made less frequent, in all those benefited
the aura were well marked. He gave the
drug during the aura in a 10 grani dose.
I have not myself had any experience of it.
But on the whole opinion does not seem to
be much in favour of it.
In some on the other hand it is reported to
be of value.
Legros (quoted in Lancet for
Jan 7th 1880) gave it in six cases in doses of
15 grani. three times a day. He concludes that
it is a very useful remedy, rapid in certain vi
action.
Dr. Grün of Putney report a
case (Lancet Jan 21 1880) of a child 5 years
old, who could not stand or feed himself.
He gave 30 grani. doses and in 3 days she
could stand, walk, & feed herself.
Dr. Tyrell Brookes (id.) says that, in the
cases in which he had used it, the movements
diminished rapidly. In one child to whom
he gave the drug, it had to be discontinued,
owing to the cardiac depression which
accompanied its use.
Mr. Roberton in the Practitioner p 1880.
vol 40 p 269 gives particulars of 10 cases treated
in that way. In 6 cases no benefit resulted. In
In the chorea case cured, but in two of these cases a rash was produced, and in one case delirium followed by diarrhea.

In other paresmoebic nerve affections, such as hay fever or whooping cough, the drug is recommended by Adolph Bloch. Formerly Physician to the London Hospital, used it with excellent results in hay fever. (Sturton's British Medical Journal, Jan. 7th, 1888.) The patient was a man aged 33, who complained of cold in the head, from which he had suffered for 2 years. The affection manifested itself in the morning on rising, and in the afternoon, when the window was opened. The painful attacks of sneezing, with a copious discharge of watery mucus, and the patient was also aware itching & pricking in the eye, which caused irriation. A pain in the head over the frontal processes. The symptoms completely disappeared during the interval between the attacks. Various methods of treatment, including full doses of bromide of potassium, belladonna, and the local application of cocaine, were adopted without success. But Mr. Block gave 30 grains of quinine at the time, morning and evening, when the attacks came on. After the first dose the affection ceased and during 8 days, only 2 slight attacks occurred. The treatment was discontinued for 6 days during which there was no attack; it was then resumed. During 20 days, only 2 slight
attacks occurred, and the antipyrin was decreased to 15 grains before breakfast daily, and was continued from Sept. 20th to Oct. 3rd, and on Nov. 8th the patient stated that the hay fever had disappeared since the early part of October, though he had ceased to take antipyrin.

I have found the drug useful in a similar case that of a young man aged 24, a clerk. His duty compelled him to sit at a narrow table and write from the dictation of a superior, who sat at the opposite side of the table, whose breath he thus inhaled. The table was subject to hay fever in the summer time, and my patient, though he had never had it before, became affected in the summer of 1861. He had injected of the conjunctivae, purulent lachrymation, frequent sneezing, and copious watery discharge from the nose. Painting the interior of the nose with a 10% solution of cocaine, and the internal administration of salicylic acid and bromide of potassium, caused improvement, but the condition returned in a few days. I then gave him 15 grains of antipyrin three times a day, and on the same evening he felt much better and had no more trouble. The antipyrin was continued for 4 days, and then left off without any return of the symptoms.

Sonnensieger (Centralbl. f. inn. Med. 1887, p. 628) has tried antipyrin in 70 cases of whooping cough.
and has obtained satisfactory results: he lost only 1 case. The doses he made use of were
1 grain for infants, 4/12 grains for well grown children, and 15 grains for adults. He considers
that it must be administered systematically and
continued during the whole course of the cough.
Other practitioners agree with Sommerberge, but
as whooping cough is one of the diseases for
which new specifics are so constantly being
advanced, which have their day and are forgotten,
careful proof or prolonged trial, will be needed
before a specific curative action can be admitted.
In 3 cases I have given antipyrin. The
patients being children aged 3 yr. respectively,
and these certainly seemed to be a striking
abatement of the violence of the explosive cough,
but in spite of continuing the drug, the cough
persisted for over 3 weeks in one case and over
a fortnight in the other, of the same characteristic
kind. It was, however, certainly less severe than
the time of giving the drug. I do not think,
however, that in these 2 cases the effect was
any better than can be obtained from the
use of carbolic acid & belladonna.
In the New York Medical Record for Nov. 28 1887
Dr. F. W. Bixley dwells on the value of antipyrin
in insomnia and states that it will produce
sleep, after the failure of the usual remedies. He
relates the case of a woman aged 36 of very
delicate constitution, who was much reduced and rendered very nervous, irritable by a trying labour. Six days after delivery symptoms of metritis set in, and during the next day she had not slept more than 2 hours. Her mind was wandering and she was restless, sometimes laughing, sometimes crying. Chloral, Bromides, or Morphia were tried in vain. Then 6 grains of antipyrine with 2 of antifebrin, were administered with the result that she fell asleep in an hour, and slept for 6 hours. The antipyrine was repeated on the following nights, with the same result, each time producing refreshing sleep.

Reports as to the action of antipyrine in acute Rheumatism are very contradictory. Some regard it as having specific antirheumatic properties, others regard it as useless.

Prof. M.N. Khromykhoff and Dr. Voff, report in "Vrach." Jan. 1886, that it is useful in acute or chronic rheumatism. They state that the redness and swelling are reduced, and the pain relieved quickly, and that in 2 cases it was successful when salicylate of soda failed. They regard it, too, as useful in muscular rheumatism, and rheumatic pains of the head and limbs, in neuralgia of rheumatic origin.

Dr. Clements, in an article in the Lyon Medical News, 29th, 1886, wrote enthusiastically of its value.
in acute rheumatism. He finds its effect rapid and certain, and it causes no vertigo or dizziness, so commonly caused by the palicylate. He also states that in every case, when it has failed in his hands, palpicylate have failed too, and on the other hand it succeeded in those cases, in which palpicylate failed. He gives details of 8 cases, in which rheumatism was complicated by grave cardiac valvular lesions and pericarditis, and in all of these the heart improved too. He does not rely on small doses only, one drachm to one and a half drachms a day.

Dr. Traubell in a paper read before the "Verein für Innere Medizin" at Berlin October 15, 1886, stated that he had prescribed it in 34 cases of acute rheumatism, and regarded it as a specific. Rapid recovery ensued in 9 out of 13 mild cases, and in four of 21 severe cases. He gave it in large amounts of 15 grammes daily during the first 3 days, and of 3 grammes daily during the next 6, and considered it superior to the palpicylate, in being pleasant to take, free from the physiological effects of the latter, he only once found vomiting twice the citrufuric rash. The depression was always accompanied by profuse sweating, but he could not speak as to protection from endocarditis. He records, however, that in 2 cases no good results were obtained, and in 13 cases there was a relapse. He summed up by
The effect that antiphosphine is a specific anti-
Pneumonic agent, that it triphysically effects, make it important to prescribe at first
in every case of acute articular rheumatism, but
that it is no substitute for the calomelate, some
case reacting to the one drug and some to the
other. Dr. Paul Guttman (cit) states
that in 18 cases of acute rheumatism treated with
antiphosphine, the average duration was 23 days, and
in 6 treated with calomelate 33.2 days.
Dr. German. In mi. mi. communication to the
Academia de Medicin. Sep. 6, 1887. Menion,
15 cases of subacute rheumatism, which had
resisted the usual curative or alcaliate of soda,
in which the swelling appeared in the joints, dis-
appeared in a few days or did not return, the
administration of antiphosphine being continued in
small doses for a week. The same results were
obtained in acute attacks of joint, whether
unparalleled or not to the chronic affection, ni
jaunchie deposits or tophi, and localized in the
wrist, or joints, of the lower extremity, when
the drug was given in doses of from 4 to 6
grammes in the 24 hours, the face or swelling
disappeared in from 2 to 4 days, without
any undesirable effects being produced
in the heart or kidneys.
Dr. Raymond Johnson in Lancet Aug. 28, 1886
reports 4 cases of acute rheumatism, in which
antipyrin was given and these favourable opinions were corroborated. They were men,
aged 17, 19, 22, and 32 years respectively, & suffering from their first and 2
from their 2nd attacks. They were left without medicaments for 12 to 24 hours, to avoid errors due to
such in their comfortable menstruation expected.
In 2 of the cases, antipyrin continued for
from 24 hours to 3 days, from reduced the
temperature, but had not any effect on the
pain and swelling of the joints. In the fourth
case, as which palpitation of pulse had not
influenced the symptoms, though continued for
a fortnight, antipyrin was given in 80
granules dose, in 3 successive hours, and on the
following day in 10 grain doses, every 2 hours.
The joints were also blisters. The swelling of
joints were relieved & the drug being continued
as above doses, the recovery was complete.
It would appear, from these and other reports,
that in acute rheumatism, antipyrin will
relieve in those cases, which are occasionally
not written, & which the paliegiates fail, but
that antipyrin will not cure all cases, or
that it is probable that these cases will
require the paliegiates. There are however
but few cases that do not quickly yield
to the paliegiates.
I tried antipyrin in the following case of
acute rheumatism. A. I., aged 27 years, was suffering from his first attack of acute rheumatism, with swelling of both ankles and left wrist joint. Temperature 102°F. on the morning, when first seen. Ordered 10 grains of antipyrine every 3 hours. In the evening the temperature was 98°F. and in the following morning 98.2°F. But the joint pain was not relieved and the right knee joint was affected as well. In the evening the temperature was 98.0°F., but the joint pain was not better or still other pain becoming affected.

Ten grains of salicylate of soda every 3 hours were given. In the following morning the temperature was normal, and all the joint swelling, the joint pain nearly gone. Recovery was rapid, there were no cardiac complications and no relapse.

In another case very similar were the results, I had to have recourse to salicylate of soda in 3 days as there was no decided improvement. This was the case of a man aged 28, also suffering from his first attack. There was the same rapid fall of temperature to below normal, which in itself gave the patient some relief, but there was very little influence exerted on the joints, at which remained painful. The salicylate caused him to recover rapidly.
Antipyrin did not prove any more serviceable in a case of acute gout, in
which I have tried it. I. J. aged 40,
was suffering from an attack of acute gout,
afflicting the ball of the right great toe, the
swelling spreading over the dorsum of the
foot & right ankle joint. He had not had
any previous attacks. It had been a total
absence for 2 years & temperatures before that.
There was a gouty family history, & the
patient had been doing an excessive amount
of walking, with exposure to the inclemency
of the weather. On the first evening of the
attack, which came on suddenly just
as he was going to bed, with the usual
acute pain, and a temperature of 103 ° F.
I prescribed antipyrin 1/4 grain, every 3 hours, with opium, foot baths,
and foot movements. The pain was not in any way
relieved until next morning, when the
foot became more comfortable, but remained
red, swollen, & tender. In the evening the
fever returned to the same extent. Then I
continued the antipyrin, as continued regularly. The
temperature on that day might have
been normal. The patient was passed as again
again. So on the next day gave full dose
of colchicum, with bicarbonate of soda
instead of antipyrin. So the next night was
some comfortable, with less pain. The swelling gradually subsided, the pain diminished, and the foot was normal, except for some slight stiffness, in four days. This has been my only experience of antipyrin in acute gout.

Dr. Oscar Jordan also mentions a case in the "Lancet," Dec. 19 1879, in which the drug did no good.

In a case of subacute gout, that of J. R., aged 40 years, a brewer's drayman, who, in spite of frequent warmings, consumes several joints of ale a day, & who has a strong gouty family history, I found antipyrin of much service. He has had attacks of gout, inflammation, affecting the ball of the great toe of both feet generally, and sometimes also other joints, such as the knee joints, usually one about every 9 months for the last 3 years. This has not generally been much fever, but much joint redness & swelling. On all these occasions he has gradually recovered, with rest and the administration of calomel and ather, in about a week. In the last occasion, the attack being similar in every respect to the preceding ones, the only drug exhibited was antipyrin in 1/5 grani doses every 3 hours, and he recovered and returned to work in 4 days. This was the
second attack, that he had experienced. This seems to show that in some cases, at least, antipyrin has antipyretic properties, but in what cases it is not yet evident.

In chronic rheumatic affection, antipyrin is extremely useful, not only in relieving the pain but also in curing the affection.

The following are notes of 3 cases of chronic rheumatic arthritis, example of many others which have come under my notice.

Mrs. W., aged 45, who has had a large family, has been suffering from chimaerotic disturbance for 2 years, during which time she has had successive irregular menstrual flow, altogether losing much blood. In the last 2 years too she has noticed the finger joints of both hands and the knee joints pellagrous, and there has been much stiffness of pain. In October 1884 and in March 1885, she had severe attacks of pain in the knee joints, without much fever, but with very great prostration and exhaustion, so much so that on both occasions, there was imminent danger to life. Salicylates, iodides, alkalis, and many other remedies were tried in both attacks, but did not influence the pain, and it was only after many days and by the use of large doses of morphine subcutaneously, which added to the patient's pain, that the pain was got under.
Both illnesses were very similar in character, and terminated in the same way, leaving her in an extremely weak condition. Towards the end of 1888 she was again attacked with acute pain in the right knee joint and in the right hip, with the same great depression, so that it looked as if she were going to have another serious attack. Then came the a soft systolic murmur that never had existed before. She was then treated with antipyrine in doses of 1/8 grain every four hours, no other drug. After 3 doses she experienced some relief. In a day the joint were less painful and she began to recover her strength. The progress was rapid, and in 3 days she was quite free from the acute pain, there being only stiffness and some dull pain remaining. She was able to get up and go about a little. I continued the drug regularly; 3 times a day for a month, and found that the nodular thickening of the joint lessened appreciably, and the joint moved more freely, so that she was better than she had been for 15 months. Coincidently with beginning to take antipyrine, of which she had experienced an occasional dose for the pain, the metrorrhagia began greatly to diminish, so that it was not troublesome any more.
Mr. A., aged 47, has been passing through the characteristic period of his illness, suffering from severe pain in the joints and difficulty of movement. There has been a change in the nature of chronic rheumatoid arthritis coming on gradually, swelling of the joints, particularly of the fingers and wrists, and stiffness of the joints and other parts. These changes have come on slowly, the patient has lost much blood, being an example of the apparent cause of chronic rheumatoid arthritis, which is so frequently noticeable. In this patient there has been an additional source of loss of blood, from a tumour growing from the upper part of the rectum, etc., with profuse bleeding from the bowel. She has suffered from much pain in the limbs and joints, and has from time to time, when the pain has been severe, had to lie up. In her case antipyrine given by the mouth has been attempted with very poor results. The pain has been very much lessened, and, indeed, caused entirely to disappear, after a few grains close, for 6 or 6 hours. There has, too, been a great lessening of the melorrhagia of the nose. She has been taking antipyrine regularly, but no marked difference in the joint swellings.
has been noticed.

Mr. A. J. is another woman who, I think, has much reason to be grateful for the drug. She is aged 50-60 and has similar symptoms to those of the 2 preceding cases. She too has great menstrual loss coming on at least every fortnight sometimes more frequently, so being very severe. The rheumatic pains, which are continually present, are always worse after the uterine haemorrhage has come on. The reduced to quite a helpless condition for 3 or 4 days, losing the power of doing anything with her hands or arms. There is no uterine disease other than slight enlargement and flatulence.

In her case too, antipyrine has relieved the pains and checked the haemorrhage. On the last occasion when the haemorrhage has come on, 15 grains of antipyrine every 6 hours have slipped it in 2 days, so banished the intense agony in the arms that she had previously. It has not been continued after this has been accomplished, as being a working woman, the expense of the drug is a serious obstacle. But she can now do more than she has been able to do for many months, though no cure has been effected and the trouble seems from time to time. Previously absolute rest in bed, ergot, iron, salvarsan, & homeopathic nostrums have just checked the bleeding for 4 or 5 days and of course have not influenced
Mr. Jameson. — The "Lance" May 26, 1887, relates a somewhat similar case, that of a woman at the period of commencing menopause, with profuse menstruation, acute backache, frontal neuralgia. He found antipyrine 5 grani doses every half hour relieved the pain and stopped the haemorrhage.

From these cases, I think, that antipyrine has a decided influence on uterine haemorrhage at all events at the climacteric period. This is not easy of explanation. From experiment referred to above, it would appear that the drug does not increase uterine action, even if it does not diminish it. It has, however, by different observers been found to have haemostatic properties. Thus, in the "Meditsinskoë Obozrenie" No. 5, 1887, p. 520 80 Mr. Byvalshenok states that it is an excellent remedy for pulmonary haemorrhage of every kind. He supports the statement by relating 10 cases of haemoptysis in patients suffering from pneumonia, bronchietasis, cardiac disease, or injury of the chest. He gives 30 grani every 2 or 3 hours, and in 8 of the cases were more than 2 doses required, completely to arrest the haemoptysis, even when the daily loss amounted to 2 fluid pounds. In some of the patients, ordinary haemostatics such as ergot, ergotin, digitale, antipyrine had been previously
tried without effect.

A. Lecher, (quoted by George Brookes in his paper read at Dr. Hill, April 27, 1888) has also used it as a haemostatic in haemoptysis. He used a solution of 15 grains in 1 oz. and made patients breathe through it for 4 or 5 respirations, repeating the use of it every half hour. In all the 6 cases tried, the haemorrhage was diminished.

In the "Concours Medical" July 14, 1888, Dr. Marie relates the case of a boy aged 14, who suffered from chronic bleeding after extraction of a molar tooth. The cavity had been flushed with podochrome firm, without effect, and so much blood was lost that syncope was caused. On recovery, the haemorrhage broke out again, and podochrome firm was again tried, but to no purpose. Dr. Marie then plugged the cavity with 2 or 3 pledgets of charcoal packed in antipyrin solution, and the bleeding at once ceased and did not recur.

In the "Gazetta degli Ospitalli" Sep. 30th, 1885, Casali states that he employed it successfully in a case of eruitania in 6 percent solution, and he found that after operation haemorrhage was arrested in 3 minutes by a 6 percent solution. He considers it preferable to podochrome firm, whenever that is indicated, because it leaves the mouth clean, without an eschar, and it has advantage over ergotin in being non-poisonous.
in large doses he considers that it is a powerful haemostatic and rapid in action.

Menogyn and Buchard have stated too that the drug has haemostatic properties.

Glinsky (Transactions of the Kharkow Medical Society, part I, 1887, p. 25) does not confirm these observations, however, and concludes that it has no great local haemostatic action and

Illingworth (British Medical Journal, Jan. 7, 1888) states that the effect of acetylsalicylic acid is to make the clothing less friable, which is not consistent with its having local haemostatic properties. However, I certainly think that in many cases of uterine haemorrhage it gives quicker relief. In one case of excessive uterine haemorrhage I failed to check, either by the mouth or hypodermically.

It has been recommended as a dressing for wounds. I have found it very useful as an ointment, mixed with vaselin (10 grains to 183)
in irrigable places of the lips, particularly parotid ones. It quickly relieves the pain and permits to lessen the congestion, and altogether promotes healing, so that I regard it as a most useful application in these cases.

Other pains, such as lumbago, muscular rheumatism, yield rapidly to acetylsalicylic. Lumbago I have found to be much satisfactorily treated by injection with the substance of the
munch of the case: I usually inject gracin
and have used it to give relief in from
half an hour to 2 hours. It is often necessary
in acute cases to repeat the dose or two hours when the
effect has worn off, and 2 doses generally cure
When it is most convenient to inject I give
antipyrin by the mouth, which answers well.
I have not failed in any case and quite
rarely have had 6 cases. Before using
antipyrin hemalago was always a troublesome
thing to cure and to grin, but antipyrin
days, had to be expected usually, whereas,
ow, I can cure in 2 days, so that there are
undoubtedly many many advantages in the
use of antipyrin in these cases.
Sciatica again usually yields rapidly.
See reports 3 cases. (Bulletin de l'Académie
de Médicine 4, 6th 1839) ni which relief
resulted. I have found it act well
in the only case of sciatica ni , which I
have tried it. The patient was a lady aged
36 years, and the sciatica was in the right
leg. There was no especial cause for it, and
it was not apparently rheumatic, and it
was not accompanied by any rheumatic
symptoms. She had been suffering from acute
jaw for a week and it had n't yielded to
guinée, arsenic, iron, or other unusual
remedies. It was only subdued by hypodermic.
injection of morphia and returned when the effects of the morphia passed off. Antipyrin 16 grains was then injected into the thigh posteriorly and a half an hour the patient was relieved. This was accomplished by 15 grains by the mouth repeated every 4 hours and continued for 5 days. The patient became free from pain and experiencing no discomfort. Then the medicine was left off, when there was a slight return of pain. It was renewed in 10 grain doses, then twice a day, diminished to twice a day in 2 days, then stopped. There was then no recurrence of pain.

A case of a similar cure by Dr. Gabriel Covarrubias of Lima, is reported in the "Revista Medica de Chilie" (quoted in "British Medical Journal" March 16, 1888). The patient had been confined to bed for 2 months, he could not move his left leg, he suffered excruciating pain so that she had not been able to sleep for some nights. Injection of morphia in the affected parts, acetylene applications, general antirheumatic treatment, salicylate of soda, iodide of potassium, sulfite of gummoine, mixture of salicyclic and bismuth, or salvarsan, etc., were all tried without the least effect. Some treatment with iodide of iron, coal oil, ointment, etc., proved equally futile.

Antipyrin was then given in doses of 50 centigrammes with an equal quantity of gummoine 3 times a day. The day after the treatment was commenced
The patient refused to get up. The pain had ceased, and he could move his affected limb quite freely. Ten days afterwards he left the hospital quite cured, and having gained considerably in weight.

The report of Dr. O'Reilly (British Medical Journal, March 30th, 1892) states, two cases successfully treated with antipyrin, in 10 grains dose, every 3 hours, both cases being severe, and having yielded to numerous remedies. In one case the pain was relieved in a few hours, in the other a day.

In hyperpyrexia, antipyrin proved to be a most useful curative agent, so many have found it to be good in these cases. The following case surprised me with the value of the drug.

J. S., a man aged 36, of uniform constitution, subject to chronic rheumatism, was attacked by herpes zoster along the course of the 7th and 8th intercostal nerves, on the left side. The rash was preceded by accompanied by severe pain, so severe that the patient could not bear the weight of the bedclothes on his side, and sleep was made impossible. Morphine had to be used to give him some sleep, after several nights without it. The condition was such as to render the patient very uncomfortable, but it was under the circumstances unavoidable. After the vesicles had appeared for nearly a fortnight,
and then being many scabs, superficial pustules, and showing signs of healing, and the pain continuing very severe, without any intermission, except when under the influence of morphine, I tried antipyrine in 15-grain doses, 3 times a day. The pain entirely disappeared after 2 doses. In 2 days there was a remarkable influence produced on the rash. The peels began to fall off, and the pores to heal up, so that in 5 days from the commencement of this treatment, he was quite well again, except for remaining weakness. This case leads one to suppose that antipyrine has an influence on the trophic nerves of the skin, and stimulate them. Another case has made this view more probable. A girl aged 21 years, healthy, nothing to note anemic, complained of frequent attacks of a skin rash during the last 3 years. The came of a rheumatic family, her father and several of his relatives having had rheumatic fever. She has hardly ever had acute rheumatism, but has often had wandering pains in the limbs. Her appetite is good and, besides the rash, the only complaint she makes is that she easily tires. Two years ago the rash first appeared as spots of various sizes all over the body, especially in the legs. They would last 4 or 6 days, gradually getting less bright, and then fade away, becoming
...konan before disappearing. Then into few days, some fluid would appear. They always occurred more abundantly at the menstrual period. The menstrual flow was not excessive, has been no hemorrhage from the kidneys, but she says she has been suffered from epistaxis, usually three or 8 times between the periods, so sufficiently severe to give her much trouble. She has had a great deal of treatment without much success. When I first saw her there were numerous hemorrhagic spots, some punctuals, some half an inch in diameter. They were scattered here and there over the hands, thighs, but were most numerous on the dorsum of the foot, and anterior surface of both ankles, and on the backs of the thighs. There was some oedema of the feet, but no marked oedema of the other parts. The patient complained of some pain especially in the feet & ankles. There was no heart affection & the appetite & digestion were good. There were no hemorrhage from the mucous membrane. The effect of 10 grains doses of antipyrine 3 times a day was immediate; to relieve the pain, the spots faded away as usual, leaving coppery brown. No fresh ones, stake, appeared. She continued the treatment for a month with expressed herself as much stronger. I saw her 6 weeks afterwards, and she had had no return
of the purpura. Whether the fact that the patient was phaeopathic, determined the benefit she derived from the drug, or why, is open to question. The fact that many cases of antipyrin rash have been reported, shows that there is a specific relation to the cutaneous eruption, and it is therefore very probable, that a curative action may be exerted by the drug in small doses on many other lesions.

The power of antipyrin in checking metabolism has been made use of in the treatment of diabetes. The quantity of sugar as well as the quantity of urine is diminished by it. In the British Medical Journal Oct. 29, 1887, it is mentioned that Mr. Gurney tried antipyrin in daily doses of 45 grains in a case of diabetes of 7 years standing. The patient was a gentleman aged 60 years, with 2.8 per cent sugar in his urine. In 3 days the urine gave but an indistinct Trommsdorff reaction. Not a trace of sugar remained after this patient had taken 27 grains of the drug. Dr. Buchard (British Medical Journal June 2nd, 1888) gave 3 grains a day to a woman suffering from marasmus, who passed from 24 to 28 litres of urine in the 24 hours. This quantity was reduced to 5 litres by the drug.

Mr. Neipart - Beaumetz used it in 2 cases of
Polyuria. The amount of urine being diminished in this case. Germanicus he has recommended it for, a chocolate.

I have found it useful in a case of slight polyuria with excess of water-societies. The patient was a middle-aged lady aged 42 years. The symptoms were frequent micturition and thirst. She passed about 2000 fluid ounces with a diet restricted in fluids. No albumen and no sugar were found, but an excess of urea accounting in the day to an average of 520 grains. She was subject to headache of a periodic or migraneous character, for which she took antipyrin. Found when she took the drug, which relieved the headache, that she was less troubled by frequent micturition and on examining the urine again, the average daily amount was 20 oz., and the daily excretion of urea 155 grains. The diet had not been altered in any way.

Antipyrin has been regarded as a specific in polyuria. It is mentioned in the British Medical Journal in Dec 17, 1887. M dash Dr Eugene Dupuy employed it in 11 cases with invariably success. Many other reports of success in this direction have been given, and I have not seen any case mentioned, in which it has failed.

In the vomiting of pregnancy, too, it is
recommended. I have tried it in a number of cases, and recently have invariably found it to be very efficacious, as superior to any of the ordinary stomachic remedies I have not found it to fail once.

D. O. F. Jennings in the Lancet Dec 17, 1887 reports the case of a woman in the 6th month of pregnancy, who had suffered from vomiting for 10 weeks. The usual remedies were tried unsuccessfully. The antipyrine was given twice in the morning, but she vomited it at once. It was then given 15 grain doses at night, with the result that there was no vomiting but nausea, to relieve which a further dose was given, which was at once brought up. Then 20 grains were given one night and the dose before getting up in the morning, so this was quite successful. In every case I have found difficulty in retaining the dose.

Dr. Thor of Bucharest (British Med. Journal Feb 18, 1888) has recommended it for emotional emission in doses of 7 to 15 grains before going to bed. He thinks that it is as good as the bromide, and is preferable in not causing acne, when continued for a long time.

In some cases of angina pectoris, as stated by Gernandt, the quick relief is obtained.

W. E. a physician, male aged 30 years, of forty...
constipation was attacked suddenly in the night with acute pain in the chest, shooting down the left arm. There was dyspnoea, coldness, swelling of the face, accompanied by Jermey's purgation. Pulse small & irregular and 110 per minute. The cardiac murmur to be heard; arteries rigid & atheromatous. Inhalation of amyl nitrite & strychnismia internally did not relieve, so the patient's condition got worse. The breathing was very embarrassed, and the patient in a most destitute condition. I then injected 10 grains of antipyrine into the arm and in half an hour he was much better; pulse fell to 90 per minute & regular, & pain nearly gone. I continued the drug to 3 grains, close by the mouth, and after the first the patient soon fell asleep. The pain did not return again, and he has remained well since, now 6 months, taking, of course, particular care of himself.

Dr. Ferranti in Complete Prescriptions No. IV has 103 recommends its hypodermic administration in all cases of pain when morphia is indicated. In Neuralgia, Lumbago, Gallstones, Renal Calculi, Dyspnoea of asthma, and pain of malignant disease. He thinks it active powerful in morphine & being free from causing delirium, vomiting or any unfavorable symptoms, and that it
can advantageously be given in renal disease and other cases where morphia is not admissible. Mr. Bachurkow (Brit. Med. Jour. Jan. 2nd, 1889) thinks that its use is contraindicated in these very cases, owing to its diminishing the urinary flow. He thinks that in typhoid, therefore, it should be avoided. Dr. Truchet-Baudot (Med. of France (this) still more strongly that it is dangerous in kidney disease, and should be no more given than opium or salicylate of soda, in these conditions, or in arterio-sclerosis, even where the kidney are not affected. It is not likely to be any means substitute morphia, for it is much less powerful than for both.

In Brit. Med. Jour. P. 38. Vol I, 1888, it is stated that Truchet has calculated that the effect of 5 grains hypodermically is equal to 1/30 grain of morphia in local action.

Some cases of pain depending on instance in cancerous disease do not yield to it. I gave very full doses in a case of cancer of the abdomen, where there was great pain, as a substitute for morphia, but found no relief. I have come across many cases of pain from malignant disease when it has failed, so that I have given up trying it at all in these severer pains. It seems especially remarkable in pain of a nervous origin, especially
where there are no appreciable organic changes. Unpleasant symptoms have from time to time been reported from the use of this drug. Considering, however, the very extensive use that is made of it for so many different kinds of illnesses, the number of these cases is very small. They are usually explained as being due to personal idiosyncrasy, and it has been suggested, though probably wrongly, that they are also caused by impure samples being used.

Dr. Germaine Klei has written so much about antipyretic fago in Bulletin de l'Académie de Médecine Vol XIX p. 704 "once in 12 to 16 cases antipyretic produces - but only when it is continued for more than 12 to 15 days and in large doses, and especially in women - an eruption like urticaria or a rash on the hands and feet, which lasts 2 to 3 days and disappears without leaving any traces - it is a medicinal exanthem like that of quinine". In other eruptions however the results are represented as more serious, and the following are cases of this kind that have been recorded.

Several cases of death from collapse have been reported, where antipyretic has been used as an antipyretic in fever, for instance in a case of typhoid by Streiss u. Leuweh, Oct. 2nd, 1885 in The Practitioner Vol 36, p 261.
Dr. Jane Bloomfield records two cases of
aphthosis, in which an erythematous rash
appeared and spread all over the body, in one case
with vesicles, after the continued administration
of antipyrin for 13 to 14 days respectively. The rash
gradually disappeared when the drug was stopped.

two cases in which the rash very much resembled
that of measles, except in not appearing first on
the face and then mostly on the extremities,
and being accompanied by no general symptoms.
It subsided quickly when the drug was left off.

mention a similar rash appearing first on the
elbows and knees, spreading over the limbs & trunk,
which disappeared by degrees where the drug
was given in smaller doses.

More alarming symptoms are described by
Dr. Bernouilli in "Correspondenz-Blatt für
Schweizer Arzte" June 15, 1887 in the case
of a strong, well nourished woman aged 32,
suffering from chronic rheumatic arthritis. On
3 occasions, administration of 16 grains of
antipyrine (though she had previously taken
large doses without any ill effect) was followed
in 3 or 4 minutes by severe pain in the chest
and abdomen, mental anxiety, cold perspiration,
followed by rapid rise of temperature reaching
39.5°C and 40.2°C. The pulse was 120 and
full. There was swelling with edema of the face and an erythematosus rash all over the body. These symptoms gradually disappeared in a few days after discontinuing the remedy. Similar cases have been reported by Dr. S. Zacho, in "Centralblatt für Klin. Med." Vol. 4, p. 82, and P. Frasenfeld in "Deutsche Medical Wochenenserien," No. 49, 1886.

Dr. Whitehouse, "New York Med. Record" mentions that certain jaundice fever, with loss of consciousness and watery-look rash followed 1/2 grain given to a child, in 2 minutes. Dr. Baber (ibid) after a 1/2 grain done from an erythematous and watery rash with much itching, which symptoms were relieved by emetic and purgatives.

Dr. Oscar Jennings, "Lancet," Feb. 23, 1888 describes the case of a lady aged 6g, who experienced nausea, giddiness, sleeplessness, with a sensation of icy coldness, but no fever, and accompanied by an erythematous rash spreading all over the body of face with decula so that the eyes could not be opened, after a daily dose of 37 grains in 8 days. The symptoms passed off in a few days.

Dr. Brit. Med. Jour. Feb. 4, 1878. D. Alan Sturgis reports a case where, after administration of only 5 grains of auriculine, in 16 minutes, pricking, injection of eyes, profuse lacrimation, and secretion
of mucus from the nose, and expectoration. Bronchial discharge, with hard and laboured breathing and a feeling of suffocation, came on. Followed in half an hour by an urticarial rash on the sides of the thighs and on the abdomen, with much itching. There was also a disagreeable taste
and smell and pricking in the ears. The symptoms
began gradually to disappear in 3/4 hours.
Dr. McDonald. (Brit. Med. Journ: Feb 7th, 1832)
report a case of typhoid in which an urticarial rash appeared all over the body, excepting on
the face, after taking antipyrine in 12 days.
There were no other symptoms and it faded away
on discontinuing the drug.
Dr. Longland Taylor. (Brit. Med. Journ: March 31st, 1832)
reports a case where typhus produced exactly
similar effects as in Dr. Sturge's case, & he further
mentions that he found antipyrine cure the
meningitis equally well, without causing any
unpleasant symptoms.
Dr. W. K. Buell. (Brit. Med. Journ: May 26th, 1833)
maintains that itching and burning sensation
were produced all over the body, but on reaching
the hands after 3 weeks close.
A meeting of the Société Médicale de Genève
noticed a Brit. Med. Journ: Oct 6th, 1833 a case in
which alarming symptoms, such as cyanosis and
collapse occurred. A general consensus of opinion
was shown in favour of great caution in the use of
The drug

A paper was read at the meeting of the South End Health District Medical Society Oct 11, 1880 by Dr. C. C. Claremont on Antipyrine Rash, in which he described 2 cases that he had seen. He states that the rash was generally of a papulo-erythematous type, and began on the exterior surface of the elbow of knees. In one case it had been described as commencing on the face, and in another as extending to the mucous membrane, and in another vesicles had been present. Its most constant character were its bilateral symmetry and its duration of about 5 days, irrespective of the continuance or withdrawal of the drug. In several cases alopecia has been given as an antidote, and it is maintained that it causes the symptoms to decline more quickly. In normal course, however, appears to be for them to pass off in a few hours, without the administration of any antidote. I have not met with any case of rash, though I have prescribed it extensively, and it appears to be of extremely rare occurrence. We are not warranted therefore in considering this as an unimportant drawback to the administration of antipyrine; certainly rashes are not so commonly caused by it as by bromide, iodide. In instance, there is no doubt that antipyrine has not yet been put into its proper position as a
curative agent, and the tendency is, at present, to prescribe it as a universal panacea for all ills. There is still much work to be done, in the way of accumulating careful clinical observations, and the recording of results, before its position will be decided, and because many of the troubles, in which it has been found useful, are not of a grave kind, we should not therefore hesitate to spend time and trouble over these enquiries, remembering that these slighter ailments cause more discomfort to a greater number of people than do many of the more serious ones.

No doubt, in a little time, the evidence will be sifted, and we shall be able to say, in what cases, and to what extent, antipyrine will prove useful, and I think, we shall then come to the conclusion that it may be added to the Pharmacopoea as a valuable acquisition.

I certify that this thesis has been written

*Compacted by myself*  
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