Physiological and Therapeutic Action

Nitrite of Amyl.

History.

Nitrite of Amyl was discovered in 1844 by a French Chemist, François Daulard, whilst making his researches on the derivatives of the Amyl group.

It was about 1859 that its physiological actions were first made known by Professor Gulliver, who in using this agent found that it had very striking effects on the circulation, increasing the pulse rate together with the blushing of the arteries a flushing of the face (Journal of the Chemical Society, Vol. 17, p. 245).

But until 1863 the usefulness of Gulliver remained in obscurity; however, at this time, Dr. Benjamin W. Richardson drew the attention of the Physicists to his systematic, physiological and therapeutic researches on the Nitrite of Amyl. In his report of Nitrite of Amyl to the British Association for the advancement of Science at the Newcastle meeting in 1863, he originally introduced it into medicine, giving the name of his numerous experiments and publications the "Modus operandi of the Substance" (Med. Times Gazette Vol. 11, p. 444, 1853). And in his next and very full report to the association at the Bath meeting (Med. Times & Gazette 1864); and in the following years (1865, 1870) he detailed a definition still more carefully not only the physiological action of the Nitrite but also its use partially as a Therapeutic agent (Post. & Times, p. 262, 1865 — Med. Times & Gazette 1870, p. 469). It was, he showed, as an antispasmodic and as the most potent known relaxant of vascular tension that it took its place in medicine. It would soon control rheumatic patients; and it was, as
he recommended to the relief of Acute Spanmodic and Paralytic affections that it should be applied.

From the above related facts it will be seen that the late Dr Warburton Digby found altogether the bounds of historical accuracy and contemporary justice in his address to the British Medical Association at the Edinburgh meeting in 1875 when he paid to Dr Gurney Brown the credit of having, by original research, added the Nitrite of Amyle to the armamentum of practical medicine.

Thus Dr Gurney completed the experiments of Richardson by making important observations on the blood. (Phil. Trans. 1868 p. 589)

The exhilarating property of Nitrite of Amyle on the Vascular tissue, inspired Dr Brown to try it on the brain tissue when there is high Vascular tension - the success was rapid and the patient recovered (London Med. J. July 24th 1867.) This favourable result led to new researches and in 1867 it took its true position in therapeutics - Dr Hadden tried it in Phrenia, Dr Coca of Huffington in Traumatic Tetanus, the late Dr Austin in Asthma, and Dr Farquharson in a case of Intestinal Spasm - the study of Nitrite was prosecuted at the bedside and in the Physiological Laboratory, and in 1868 Sander Brown published an important work on its Physiological Action. He partly confirmed the results obtained by his predecessors, and after numerous experiments made in the Laboratory of Ludwig at Leipzig, he announced its mode of action and its therapeutic value (Ludwig's Handbuch der klinischen Untersuchung, 1868, p. 187-189).

Then the researches of Brown, Hadden, and others succeeded in Germany by the writings of Dr. Pfeil, Guttmann and Gelenberg (Pfeil's Arch. 1873 p. 620). Amelie, Fichlin, and others.
From this time the field of therapeutic application spread to enlarged and the nitrate was used in epilepsy (Gafford June 1774). W. Mitchell 1792. Cicéla Potts 1793-94 and Darwehile 1795; in headache (Holl 1783; Morel 1793 & Young 1795); also in Asthma, Phthisis, Farcy (Giber 1794); in Kurlberg (Zucchi 1795); in M. Air (Janz 1795). In Germany (January). in Hauckt, (Schramm, Lambrecht, Holfmann & Sterattt 1793-95); partly in pea disease (Bjelke 1795, Baden 1797); and in cholera (Cheadle, Schiller, Heber d'Heroult 1795-96).

In France Nitrate of Ammon was first much studied and used in Paris till 1793 when Dr. Anger 1797 wrote in "Les Archives de Physiologie" 1797. Since that time several have given the agent a trial, especially Bournville (Rosset's Medical Syst. 26th 1794) and Marseil. (In usage "Therapeutique du Nitrate d'Ammon" 1800). Hence nitric acid probably as much used.

---

Chemistry

The chemical properties of nitrate of Ammon have been studied by Mailard, Piretine (Journal de la Chimie 1794, 1795). Gutten, Albrecht (Journal de la Chimie 1794).

It may be prepared in several ways, but the most usual one is by passing Nitric Vapours into Ammoniacal liquid contained in a heated vessel, retort, the distilling, and collecting apart the portion that goes over at 205° F. The chemical reaction may be thus represented.

$$\text{C}_5\text{H}_8\text{O}_4 + \text{N}_2\text{O}_4 \rightarrow \text{C}_5\text{H}_8\text{O}_4 + \text{H}_2\text{O} + \text{HNO}_3$$

Mailard prepared it for the first time by acting on heated Ammoniacal liquid with Nitric Acid, and distilling with Pasteur the vein liquid which appears to be a mixture of hydrocyanic acid, Ammon hydrate, Nitric Ether, Valerie Ether and Valerie Acid, which are depoited in the receiver after this operation.

It is an ethereal liquid of a yelllowish brown and
With a peculiar fruit odour, and a specific gravity of .877. And bring the nitrate it boils at 205°F when pure.

When heated towards 500°F it detaches slowly, and
then heated with a base it acts like a salt — if it be
added, drop by drop, to caustic potash, while passed by appli-
cation of heat, it burns and fumes, and nitrate of potash is formed.

When recently prepared nitrate of amyl has a volatile
reaction, but by the action of air and moisture upon it, it
quickly becomes acid by the formation of valerianic, nitre,
and nitramic acids. It is insoluble in water, but freely
soluble in rectified spirit in all proportions.

When exposed to air a slight nitrate of amyl quietly
alters in composition and loses its physiological properties:
therefore it should keep it well stopped and in capped bottle
(it acts in cork) in a dark and cool place. According to
O. Bürgers, we only need add a little caustic chloride and
calciated magnesia to render it pure, after it has become acid.

Not infrequently the nitrate of amyl of commerce
contains small quantities of hydrocyanic acid which should
be carefully guarded against for experimental and some
therapeutic purposes. (Chem. Journ. and Trans. 3 series p.423)

Physiological Action

Having considered some of the leading points in
connection with the history and chemistry of nitrate of amyl
we now come to consider its physiological action, and in
doing so we shall find it most convenient to speak of it
in relation to various systems.

Local Action — When applied to the skin nitrate of amyl
serves to arrest no influence except when there is an abrasion
or ulcer of the surface. But when applied to a mucous
surface then irritation is produced according to Echondor,
which is followed by a pain and an intense inflammatory
reaction.
A case of Poliomyelitis in an infant under 3 months of age, reported by Dr. J. W. Brown of Chicago, Illinois, is of interest. The baby, a twin, was born in May, 1923, and died in June, 1923. The parents were healthy and there was no known contact with other cases of poliomyelitis.

The patient developed symptoms of poliomyelitis on the second day of life, with fever, irritability, and weakness in the extremities. The tendon reflexes were absent in the arms and legs, and the baby was unable to bear weight on the legs. The condition improved over the next two weeks, with some recovery of muscle strength and return of tendon reflexes.

An analysis of the myelitis and its clinical course was reported by Dr. J. W. Brown. The baby was kept in a hospital for several weeks, where he received care and attention. The condition improved gradually, with some recovery of muscle strength and return of tendon reflexes. The baby was discharged from the hospital in a stable condition, with some residual weakness in the legs.

This case is of particular interest because it is one of the earliest reported cases of poliomyelitis in an infant under 3 months of age. The condition improved over the next two weeks, with some recovery of muscle strength and return of tendon reflexes. The baby was discharged from the hospital in a stable condition, with some residual weakness in the legs.
into the Trachea, that the respiratory movements were greatly increased and deeper. But in proportion as the inhalation is prolonged the respiration becomes slower and very shallow whilst the Cardiac beats are regular but slower. This state of matters may remain for several hours. They also show experimentally that Nitric at first excites directly the centre which governs respiration and finally diminishes their functional activity by prolonged and ergotinic stimulation. According to H. Wood the stoppage of respiratory movements always precedes lysis of the heart by several minutes.

In the above experiments the vapors was blown into the Trachea; but when it is simply inhaled by the nostrum has observed dyspnea, stoppage of respiration, slowing of pulse of which probably are due reflexly to stimulation of the nerves in the nasal mucous membrane, for they may be produced by other volatile agents.

Action on Circulatory System. It is in this system that the special action of Nitric is more vividly exhibited. On pouring 3 or 4 drops of Nitric acid on to a handkerchief or blotting-paper and inhaling it, we at once perceive its peculiar acrid odor, and in from 20 to 30 seconds afterwards, a sensation of warmth and vascular fulness in the head. Then the Antoids and Temporals throb, and sometimes we may see the first cardiac rise by means of Cardiac action; and at the same time the pulse is elevated, may be to 180 beats per minute, soft and compressible. The heart with its accelerated rhythm is strong and sometimes irregular. But that which strikes us most is the appearance of the face, which becomes of an intense red or scarlet color, and not only the face but also the neck and ears. The color disappears on pressure. The conjunctives, lips, tongue, and mucous membrane of mouth are also deeply injected. And if the inhalation be continued this elevation deepens, becoming violet and then gives place to a livid pallor.
Then the head is frequently covered with sweat, and finally
then is not infrequently vertigo, dizziness and altered ideas
not unlike a transient hallucination.

All these phenomena increase and attain their
maximum in about one minute after inhalation, and they
subside one another with such rapidity that they almost
seem to be produced simultaneously. Dr. Talfourd Jones has
noticed that the increased pulse rate precedes the engorgement
of the head by several seconds. Further these various phenomena
did not disappear less quietly; for after some minutes the facial
redness disappeared and the pulse became its former rate
again. Afterwards there remains a feeling of languidude and head ache,
which, however, quickly vanishes on going into the fresh air.

The effects of inhalation thus far are very transient;
but they may be more persistent by giving the agent in
very small doses by the mouth. But the phenomena differ
more or less from those which are produced by inhalation
although we notice flushing of the head with redness of the
face at the commencement; yet these phenomena soon
leave the reason and give place to a sense of heaviness
in the head, a want of fresh air, and a considerably im-
paired appetite. Later on giddiness may return accompanied
by nausea and profuse sweating. Also there seems to be
muscular fasciculation. The pulse is quickened, the skin warm
in the upper part of the trunk, but sometimes the lower
extremities are cold and difficult to warm. Nausea is rare,
having experienced all the above symptoms. However
amongst the whole of the above symptoms the most persistent
and characteristic one seems to be the sense of great
muscular weakness.

The above are the principal effects of snuff of
Amyl. Although various writers, amongst others Gingers, have
from time to time described various other irregular ones,
as, great oppression, intense anxiety, syncope, etc.
As it is dangerous to administer large doses of the agent,
After inhaled, the animal moves violently at first, and for a few seconds avoids inspiriting; then it quickly inhales the charged air, and we soon see the usual phenomena as in human beings. The pulse rises to 180 or even 200, respiratory movements are quickened, the tongue and mucus membrane of the mouth are deeply injected; also the ears become warmer and their vessels much dilated. But if the dose be rapidly increased, the animal stumbles and falls down with tremblings and some lanthanum entericum in its extremities, but soon the muscles are perfectly motionless. Also the gumetes relax, the skin becomes pale and respiration is much impeded, superficial and short, and finally reflex actions are abolished, and the animal is in a state of complete coma. But the animal does not remain long in this state, for in about 10 minutes afterwards it is noticed that it has almost returned to its normal condition.

Hence if the Nitric be pushed further then the animal dies quietly by stoppage of respiratory movements.

In animals of 2 rabbits and one dog poisoned by Nitric of Amyl in smugton, found 3 hours after death the following — The blood remarkably colored, brownish chocolate, circulating very rapidly on exposure to air. Marked turgor of the veins system, especially the veins porta, jugulars and cranial sinuses. The liver gorged, more friable and blood like the blood. Lung nearly normal. Pleura and pericardium injected and their cavities filled with a considerable quantity of reddish serum. The muscles bloated, and is a great effort last their elasticity, only responding to strong electric currents. Brain visibly engorged. And tarry the blood contained sugar to the extent of 9 per 100.

The toxic action of Nitric of Amyl is not only
Described in Mammals but also in Spiders, Insects, Fishes and Pflaumieren.

In examining carefully the influence of Nitrile of Amyl on the circulation, we shall find it most systematic and certain, and to consider it under headings, as follows:

I. Acceleration of Pulse.
II. Inhalation of Oxygen.
III. Reduction of Vascular tension.
IV. Lessening of temperature.

Acceleration of Pulse. - His agents have such a marked action on the cardiac movements as Nitrile of Amyl, that it has been shown that it greatly increases the number of beats ranging as high as 200 per minute. And among some animals, as Cats, Rabbits, the pulse rate rises so high that it becomes quite impossible to count it. Dr. Salfour and Gorskert state, that this increased pulse rate is the first sign of the Nitrile appearing as it does from 3 to 5 seconds after the commencement of the inhalation, and is followed in a few seconds (5-10) by flushings of the face. Then for 2 to 3 minutes after stopping the inhalation, the pulse rate remains about the same, but directly after this it rapidly falls and becomes normal. Post-Mortem, having given the Nitrile in large doses from the beginning, has induced the pulse to fall rapidly and to rise again after the inhalation to a point much above normal. Probably the paller of the skin, and decrease in the flow of the pulse, corresponds with this initial slowing of the pulse. Tschirch found that in applying the Nitrile directly to the frog's heart, most especially if in contact with its endocardial surface, a slow and gradual diminution of its contractions took place, and quickly total paralysis. - R. Pick found that in placing decapitated frog under a glass with their hearts restored, and putting a drop of Nitrile of Amyl to evaporate, the heart beats.
more surgically but its contractions diminish slowly in frequency and its contractile force falls gradually. But on applying the agent direct to the heart it is quickly exhausted and stops much sooner.

But in the rabbit as in man, as a human being, the pulse rate always rises, and it is supposed to be due, according to Folkman, to a diminution of the inhibitory action of the Vagus over the heart. This difference of action between cold and warm blooded animals seems, a priori, to prove this theory.

With regard to the physiological tracings of the pulse we find great and characteristic modifications. Both heart has seen the ascending line of the pressure wave almost disappear altogether in the first few seconds of the inhalation as if the heart was stopped suddenly in systole. The curves rise afterwards and show no abnormal form, except that they may be more developed than in ordinary conditions. The following are a few tracings:

1. 
Before Inhalation

2. 
One minute after Inhalation

3. 
Two minutes after Inhalation

Cardiac Pulse. Normab. sy. (Before)

4. 
Cardiac Pulse during Inhalation 16.4. (Before)
It will be readily observed from these tracings that there is a diminished resistance of the arterial walls. There is also a marked state of dilatation, as is very transient, in a tracing taken two minutes after the injection of the drug in perfectly normal. In the two lower tracings of the carotids taken by Stokell, the force of each pulsation is increased, and the fluctuations of the pulse were disappeared. The ascending and descending curves are almost straight and their summit round.

The descending curve soon attains its minimum, and remains stationary for a moment so that each pulsation is separated by a horizontal line. All these characteristics indicate a diminution in the arterial tension and an increase in the arterial shows.

However, it is necessary, not to confirm the force of the pulse will that by the cardiac action. And tracings taken by means of a cardio-plethysmograph applied over the apex show a distinct increase in the cardiac force at the commencement of the inspiration.

**Dilatation of Vessels.** This is clearly shown by the expansion of the face, also by certain branches of the Temporal artery becoming visible which before was not so, and by the physiographic pulse tracings.

**Wade (June 5, 1875).** At Mayo Hospital, found the Nasal arteries and veins considerably dilated and gorged with blood. And Stokell (1870) over the amygdal.

**Max Bridge (Chicago) May 5, 1875).** Devised the use of the nasal arteries of the temporal arteries over the meningeal arteries. Also the brain substance seemed to be hypertrophic.

**Schiller (1870).** The nose and cerebral veins showed a distinct increase in the cerebral substance. Also the vessels in the brain substance were enlarged.

**Schiller (1870).** Who has studied the arterial circulation deeply, has shown that the injection of nitrites of amyl after 3 to 5 inspirations causes a distinct dilatation of the vessels of the pia mater, more especially the arteries.
Which dilate even to their smallest radicles — they are seen to pulsate and sometimes even the veins also — when the action of the Nitrile is sufficiently prolonged the brain increases in volume and obstructs the articular opening in the skull. This vascular dilatation also takes place after section of the sympathetic or Vasa in the neck, but there is no pulsation. Further, like agues which cause contraction of vessels, as Influenza, Gout, &c., do not absolutely prevent dilatation of vessels by Nitrile, but render it less lasting and slower to appear. Lastly, the hyperemia of the cerebral membranes is produced more quickly and is greater than in the rabbit far.

As the phenomena of vascular dilatation, warmth, sweating, and flushing as generally limited to the face and neck, we might believe in a localized action of Nitrile on certain regions of the nervous system — in reality, its action is general; and the localization depends upon the capillary richness of those regions and perhaps upon a greater irritability of the vasomotor nerves. For even emotional impressions which favor the face may spread to the neck or even head (Vulpian).

According to P. Ricco the Nitrile is altered by its contact with the blood and the vascular walls losing its vaso-dilatory properties in proportion as the blood current carries it towards the periphery of the circulation. He has observed in a naked man the hyperemic state of the skin at its maximum on the head and neck and diminish in the trunk and scarcely perceptible in the folds of the groins and thighs.

Ringer, and others have shown in certain cases these modifications spread over the skin encompassing the surface except the feet and hands which became pale and cold. Further, J. N. E. says that in the rabbit the dilatation takes place not only in the vessels of the hind extremities but also in the intestines, peristalsis and within the

We may easily examine the alterations in the
blood vessel by means of the first web. When we often times find
that dilatation with arrested circulation, and sometimes heat
and thus in the length of the vessel art to be observed in thoracic
stethes and amputation have observed phenomena which as yet
have not received satisfactory explanation. The former said
in rabbits under the influence of kalii or of Amyl that the
auricular and ventricle arteries became the seat of alternate
and periodic movements of contraction and dilatation. This
dilatation is produced immediately after inhalation and
gives place to contraction after a variable time, and this again
after some seconds gives place to dilatation and so on.

Henslow says, that Culpin have shown that
movements, at times of contraction and dilatation of varying
length and independent of experimental interference, do
take place in the vessels of a dog's ear and in the median
artery of a rabbit ear.

According to Henslow (Archiv fur die ges. Phys.)
1869, pp. 437-455.) the Pulmonary and Bronchial Vessels do
not dilate under the influence of fluid of Amyl as he has
been able to watch it by means of an artificial respiration
in the thorax. A. Piora has examined the lung capacity by
means of the spirometer and found no diminution as the
whole have expected had the vessels been dilated; but
vascular dilatation may result and the consequent loss
of alveolar capacity be compensated for by dilatation of
the Bronchial.

An interesting fact was observed by Talfourd
Jones, who, whilst cupping a patient over the lungs and
finding that blood would not flow, administered fluid
of Amyl by inhalation. When the lungs immediately began
to bleed freely. Also Mac Bride relates a case of an Epileptic
who fell and cut himself above the orbit when bleeding
followed but was stopped by compression - however after
some 2 hours fluid of Amyl was administered there bleed-
ing ensued more rapidly than before and was only
slightly controlled by continued pressure.
Reduction of Vascular Tension — Besides the cardiac nervous activity, and vascular relaxation all of which admit of a diminution more or less considerable of the arterial pressure, which, by means of the Kymograph and Hemodynamometer may be proved to descend from two and even at times to 0. From the very commencement of the inhalation this reduction of pressure takes place even after the bend of the Vagi and the Cord just below the Medulla Oblongata — Towards the latter end of the Inhalation, pension the Cardiac and Vascular contractility is much lessened gradually by the direct action of the agent upon the Cardiac walls but this is only a slow factor, the principal one being sudden and explosive dilatation of the capillaries. The action of the heart cannot be the cause. Since the heating, much before the final period, is most frequent and do the same work in a unit of time. And Brünner having confirmed the descending Arteria, failed to find the least diminution of tension, and concluded that Nitre of Amyx has no direct influence on the heart. Thus for this heating depends upon the sudden dilatation of the arterioles and capillaries.

Lowering of Temperature — Pararoarte has paid special attention to this section and states that in cats and rabbits when the inhalations are progressive with intervals during which the animals can freely inspire the temp- erature may fall to 8° to 9° below normal. This lowering proceeds for one or two hours after stopping the inhalation, then the temperature rises and may reach 1° or more above normal. But when the nitrite is from the first given in large doses, the temperature falls 1° — 2° only and the animal dies. According to H. Wot's the fall of temperature is constant and varies in man from 1° to 3°. In cats it may
descend to 30°-36° C, and in rabbits to 33° C. — It has been shown that the temperature taken at the rectum of dogs does not fall so low as in cats, rabbits, etc. In many observations the temperature has rarely been below 36° C. But the temperature may fall and remain low without the animal appearing to suffer much.

But on the other hand, Goodhart (Medic. J., Jan., 1871) and Ladebur (Vie. Wissensch., 1843) demonstrated a case of temperature taken in the men and apcelseta. In man after inhaling from 4 to 5 grains of Nitrite the temperature rose from 10° to 18° C, and the fever-like agent the more the elevation is marked.

According to F. Wood the fall of temperature is independent of the nerve centres, for it takes place equally after section of the spinal cord. And he was the first to prove that it is accompanied by a diminution of the volume of Carbonic Acid gas. No doubt the diminution of the volume of the skin is some slight accounts for the lowering of the temperature; but Wood proves that it principally depends upon an arrest, less or less complete, of the dilations in the blood. This leads us to ask, does the Nitrite act upon the blood vessels and the heart, and also by interfering with the latter in holding the body in the air? In a word, does it stop the Gaseous exchanges in the blood? To this we shall now pass on to consider.

Action on the Blood. — All observers seem to have been struck with the alteration in the colour of the blood in animals poisoned with Nitrite of Ammon. — To clolor being of a brownish ochreous. But in the year 1847, Flourens observed a similar colour whilst experimenting with Chloroform. Harper it blames this different — and not infrequently the liver is gorged and of a similar colour. Then what is the change in the blood? A. Gamece who has worked largely at this subject found by spectroscope examination that
The blood when acted upon by nitrite of amyl, amyl or any
alkali, presents remarkable changes. On inspection as the
two absorption bands of the oxy haemoglobin, becoming more
and more fade, disappear, we see two bands
exactly like those of deoxy haemoglobin. Now, on adding to
this blood a sufficient quantity of ammonia, it remains
its red color and the spectrum of arterial blood reappears.
But in exactly neutralizing the solution with phosphoric acid
the chocolate color is reproduced with the same spectral
modifications observed after the action of nitrite. Further
the addition of such a reducing agent as sulphydril
of ammonium appears to immediately destroy the effect
of the nitrite. It causes the two bands of the oxy haemoglobin
to reappear which are afterwards replaced by the absorption
band of reduced haemoglobin.

The above facts show that nitrite have a marked but transient
action in the coloring matter of the blood; that they have not
the power of oxidizing at the expense of the sulfides, but the
addition of a reducing agent suffices to free the coloring matter
of the blood i.e. in is normal state combined with oxy gen.

Having proved that nitrite of amyl can form a
new and easily reducible compound with oxy haemoglobin, it
remains to prove that for the power of the haemoglobin was
hindered in fixing and forming the oxy gen by this combination.
It is well known that carbonyl acetic has the power of replacing
the oxy gen of the blood but this same gas does not displace
the nitrite of amyl combined with oxy genated blood, and in
the manner blood saturated with carbonyl acetic is un-
affected by nitrite - Gangee found that he could not with
-draw oxy gen of the blood which has been subjected to
the influence of nitrite even after boiling in vacuo - this
 corroborates the spectrophotographic results and shows that nitrite
of amyl forms with oxy haemoglobin a compound called
"Nitrite-oxy hemoglobin" which has no further power of
absorbing oxy gen. - Gangee has obtained in a crystallized
from this isomorphic combination with other combinations of the dissolving matter of the blood and carbonic acid, also produce of nitrogen (N) and hydrocyanic acid.

Some researchers made by P. Piers prove that hydro and amyn do not hinder certain oxidizing agents from forming feebel guaiacum blue but on the contrary facilitate the reaction. When we touch the protoplasmic matter of plants in water and expose it to air, we find that this organic substance can reduce guaiacum blue and highly so by adding a drop of hydro.

From these researches it seems that hydro and amyn in passing through the circulation lessen the process of oxidation. However the absorption of atmospheric oxygen continues to take place and the blood does not lose its properties although the various changes are proceeded. In other words hemolysis is proceeded but not abolished or else no longer death would take place immediately — finally, does any alteration take place in the blood globules? At present we cannot be certain although changes and it would state that the changes of color and modifications of the optical properties of the blood are unaccompanied by any alteration in form or volume of the globules. And finally the rapidity with which the effects of inhalation pass off seem to point to this. However more recent experiments done otherwise for Sedentary and will state that the vapors of hydro causes agglutination of the blood globules under the microscope — and direct contact entirely dissolves them giving rise to a large tint.
and contains a variable amount of sugar, as is the case after chloroform or ether inhalations or lobar infections. After 10 to 12 hours, the urine a
to is a transitory glycosuria, as observed. After a double dose, the sugar was more abundant, varying from 10 to 25 per cent, and remained for more than 6 hours. Allersford has arrived at similar conclusions. However, Berendsche having examined the urine in 30 cases only found sugar, but in the case,

What is the origin of the glycosuria? Does it depend on hepatic excretion? Probably it may be so from the appearance of the excreta after death. It has been experimentally shown that diabetes is produced by division of the sympathetic nerve of the liver, and thereby causing dilatation of the hepatic vessels, so increasing the quantity of blood passing through the liver. Thus, it may be that the liver of Amyl acts by its influence on the vaso
nervous nerves, increasing the quantity of blood passing through the liver - finally the accumulation of carbonic

Acid in the blood may partly cause it. For Virchow, in his lectures on the Vaso motor apparatus, it says that the presence of a large quantity of Carbonic Acid in the blood, which goes to the liver will produce dilatation of the hepatic cells and a more rapid transformation of sugar to sugar, as it is observed in injecting Ether, Chloroform into the Portal Vein (Harley) or when Ether, Chloroform or Carbonic Acid is inhaled in animals (Schiitz).

Action on the Nervous System — Amyl of Amyl chloride seem to have a primary action on the Embryo Spinal nervous system. From observations in himself and others, it was the first to draw attention to the curative effects of the agent on scabies. He found that after injecting Amyl of the ery is fixed in a spot in a blank wall, the spot itself and the surrounding surface appear of a yellowish hue, the yellow circle being surrounded by a
Visit one halo, with saw-tooth undulating lines at the edge. On standing at about 60 centimeters from the wall the yellow spot appears to have a diameter of 6 centimeters.

Further, the ordinary objects seem to have a yellowish appearance like that observed after the administration of santonin.

With regard to the cause of this coloring, at present it does not seem to be well known; however, Bierls believes it to be due to a projection of the macula lutea. May be that this hyperemic condition of the membranes of the eye has something to do with it.

With regard to the state of the pupil there is most frequently observed during inhalation a state of dilatation, according to Pietsch, Goldbart, and Pacltmann. However, dropping of diluted nicotine into the eyes of rabbits does not give constant results; still, most frequently dilatation results. There are no conclusions that nicotine in its circulation through the blood acts but foreign to the muscular fibers of the iris or on the nervous apparatus.

In animals poisoned with nicotine there is almost constantly to be observed central, stumps, reaction and increasing muscular contraction, followed by trembling, convulsions and finally complete muscular relaxation with more or less marked discoloration. Thus, there seems to be in the early phase of the poisoning increased motor excitability. In fact, Richardson states that it produces first excitement and then paralysis of the motor nerves. Motion at first increased, then it gradually diminishes and finally ends in paralysis. It is upon this theory of its physiological action that it is given as an antidote for strychnia—namely it is poss.

Ible that it does not at all increase the reflex power of the cord. For although the tonic phenomena have been observed in animals, more especially during inhalation yet they are far from being constant. They don’t take place on injecting the agent into the veins and Woll believe that they are of central and not of spinal origin.
attributing them to frequent excitement of the Medulla Oblongata by the altered fluids.

It is no doubt that nicotine of Amyl considerably diminishes muscular elasticity, and Pick and Bonn von believe it to be a true muscular poison. Again, to ascertain whether the Motor paralysis was of a central or peripheral origin, H. V. of noted the following experiment: Having poisoned a rabbit with a large dose of nicotine, he exposed the Spinal Cord and Central Nerve, and afterwards stimulated them by means of a strong electric Current. Although it was no longer possible to cause reflexly contractions in the muscles supplied by the Central Nerve, yet the stimulation of this nerve produced contraction of them; whilst applying directly the current to the Medullary Centre did not produce the least movement.

Von states that in poisoning by this agent the muscles preserve their irritability, but lose it to a great extent in applying the nicotine directly to them. Hence it acts directly on the Motor tracts of the Spinal Cord, energetically depressing its function at the same time it has a similar influence on the conductibility of nerves and irritability of muscles, but to a much less extent. V. places it among the Depressor-motor agents by the side of Abzorbal, Beau, Howlet, Choral, Bromides, etc. It abolishes spasm action, but whether it depresses the reflex function of the Cord is uncertain, as it may act simply in the Motor part of the Cord. However it seems to have very little effect on co-ordinating centres of the Cord, and the Sympathetic branches of the Cord and the Nerves in connection are only very slightly affected, anaesthesia being produced only a little before death — thus it cannot be considered an anesthetic at all analogous to Nitrous Oxide.

**Physiological Mechanism** — We must now examine some of the principal hypotheses which have been put forth to explain the phenomenon observed in nicotine of Amyl administration. The apparel of the mechanism of action borders upon the most obscure points in the physiology of circulation; and in spite of the patient researches the overwield of the subject as far from clearly shown.
Undoubtedly the fundamental action of Nitric Oxide is exercised on the circulatory system, and we can only admit that the nervous reflexes may be the point of departure of the acceleration of the pulse, of the arterial dilatation, and lowering of pressure, for the nervous symptoms are only produced when the poisoning has attained an advanced degree.

As to the question of the immediate origin of the vascular phenomena—what organ is first attacked? Is the Nitric Oxide a powerful cardiac stimulant as Richardson believes, and is this the organ that is attacked first? If this theory be correct, then the vascular dilatation is due solely to cardiac action, and augmentation of its pulse force. But this theory, it was able, sustained by its founder, yet it is directly opposed to the most generally admitted fact: the lowering of arterial tension, acceleration of pulse, which phenomena exist from the very commencement of the inhalation, and the direct action of the remedy on muscular fibres and the motor ganglia of which it diminishes the irritability. But undoubtedly at the debut, there is functional excitement of the heart, but it be of reflex origin. According to St. Hugh, when the Nitric Oxide vapoors penetrate into the lung capillaries they immediately combine with the blood and diminish in a remarkable way the process of oxidation; from this there results a shock or start of the whole organism with a sense of suffocation against which the circulation and respiration organs struggle and try to overcome it by using all their resources. Still the heart becomes gradually more feeble by the paralyzing action of the drug on it.

But according to recent researches of Fitch and Meyer, and Friedrich, the circulatory modifications are not so promptly manifested that we can attribute them to a reflex mechanism. A reflex stimulation of the accelerator nerves is inadmissible, for the section of the Vagi is opposed to this same acceleration. The best interpretation then of the symptoms will be, according to these authors, that which attributed them to a diminution nerves or
less is the inhibiting action of the two Vagi upon the heart. Thence its effects will be comparable to those which result from division of the Vagi. The limbs of the Vagi and their peripheral ends are not at all paralyzed but remain irritable. This different is this action to that of Atropine which on the other hand has a paralyzing influence on the cardiac ends of the Vagi. By medium doses of this potent agent the irritability of the nerve ends of the heart remains in fact, but large doses abolish it entirely. Thus we explain the frequency of the cardiac beats in spite of the slowing influence which the Vagi stimulated by the paroxysms blood have upon the heart. The regularity of the cardiac contractions that is seen in dogs under Nitrite influence and the absence of pulse acceleration when the head is deprived of blood, plead still in favor of this opinion. Mortlaff does not seem to modify it, but large doses act directly on its muscular tissue and paralyze its irritability. Thus the vascular dilatation is not due to cardiac excitation—

Mayor and others have noticed a lowering of blood pressure in spite of division of the Vagi and even when the blood charged with Nitrite of Amyl no longer went to the brain centers.

Further it is an admitted fact that Cardiac activities do not entirely depend upon the oxygen brought to the oxygen of the blood. Also the must admit, as most writers do, that the vascular dilatation is not due to exaggeration of Cardiac action. In the other hand Brown has sought to demonstrate experimentally that the heart is entirely strange to the action of Nitrite of Amyl, and that its accelerated movements depend entirely upon dilatation of Vessels. Thus he divided the spinal cord and then imprisoned the abdominal Aorta in such a manner as to considerably augment the vascular tension. Now if the Nitrite vapours had a direct action upon the heart and diminished the propulsive force one would have noticed after the dilatation, a lowering of pressure. But the results
of the experiments was sufficiently exclusive to allow him to state that while a Nervi has no action on the heart or at least so slight an influence that it cannot explain the falling of pressure observed when the vessels is not constricted. According to him then the cardiac acceleration depends upon a reflex stimulation of the sympathetic nerves consequent to the decreased circulatory resistance. But it is evident that this is not sufficiently clear and acceptable. For in isolating by pressure a portion of the circulatory field, that losing of pressure which would have resulted from the dilatation of the vessels thus cut short, can no longer show itself, still makes the object to his reasoning. Then it will not be correct and logical to exclude from these experiments that Nervi is without immediate influence upon the heat or its innervation.

Apparatus of heat ought not to be set forth as a cause of loss of arterial tension, for than we would not get dilatation of Capillaries (vide para graph on loss of tension). This then refers to precede the loss of blood pressure according to Ansg. Bivog.

Loss of pressure and dilatation of vessels cannot be produced simultaneously as by an intervention of the Vasomotor Nervous System, central or peripheral, or even by automatic changes in the vascular walls. So decide if the Vasodilator action depends by its action upon the vascular walls or upon the heart, directly or reflexly, the experiments have tried to interrupt the communication between the central ganglia and the heart. Bum reflected that a current after making a tranverse section of the Spinal Cord below the Thalamus, constantly on vascular dilatation supervene — hence these writers have concluded that Nervi does not exercise its action upon the vessels by means of their centers of innervation which formerly was said to be between the Cerebro Spinalis and Corpore Quadratum. Bulbin has shown by numerous experiments that, after division of the cord in the upper cervical region, the vessels side remains a certain degree of carried and that the reflex action vasodilatation.
of Vaso-contraction, were still present.

According to Gilly, Nussbaurn and others the Vaso-sympathetic Cord of the frog is a tonic vascular centre and some physiologically believe in the existence of ganglionic centres distributed at the periphery of the vascular system which may become the centres of vaso-constriction in the organs of the body. Thus then the experiments of Landor Brunnia do not prove that Nitride acts entirely on the vascular wall.

Under the guidance of Engelmann of Wirsich, Stock's has undertaken some experiments which tend to show that arterial dilatation depends upon a reflex sympathetic action of the Spinal Vasomotor Centre. After stimulating the cervical Cord of the Sympathetic in Rabbits he has seen the action of the Auricular Vessels produced as well when the animal was under Nitride influence as before the dilatation, and since moderately stimulating the Cerivical sympathetics on one side prevents the dilating action of the Nitride on the Auricular Vessels of the same side, whereas on the other side the dilatation is very evident, he concludes that the contractibility of the Sympathetic nerves is neither increased nor diminished under the Nitride influence, but that the main cause attributed to it is a momentary paralysis of the Vasomotor Centre. Still he has noticed that after division of the Sympathetic on one side the dilatation of the same side is greater on administering Nitride - thus proving that it acts to a certain extent in the Vascular walls themselves. Bothcin of Wirsich and Eicheng have attained the same result and reject the theory of Brunnia. According to them, also, the Vascular dilatation and constriction of tissue are of central origin and diminish of Vascular Inn. From states that Nitride does not paralyze the Vascular walls but only weakens their resistance, hence it is that strong electric currents cause contraction of their walls.

Again in opposition to the central theory, Ang. Diq. says that the small quantity of blood which goes to the Vaso-motor centre under unlikely the theory of a direct
action by contact upon these centres.

Bamber, Pieri, and many others state that nicotine acts directly upon the smooth muscular fibres of the vessels, as upon contractile fibres in general, and paralyses them. And Anger-Dubois believes in its action upon the peripheral ramifications of the visceral motor nerves, because the sudden narrowing of the capillaries which he has observed in the frog with each time that it made active movements did not occur at all compatible with the theory of paralyses of the muscular walls of these vessels.

Other recent experiments, as, O. Berger, Mayor, Frindell and Schramm (Archiv für Psychiatrie 1875) believe in the peripheral origin of the vascular dilatation. In order to demonstrate it, Mayor completely deprived the cerebral vessels of blood till their functions were totally abolished, and even then he noticed a lowering of blood pressure which could only be due to vascular dilatation. Again, in submitting the head alone to the action of the blood containing nicotine in its ordinary noticed no dilatation in the arterial vessels. However, he distinctly states that his experiments do not permit him to deny the mere existence of the peripheral vascular action of nicotine. Unfortunately he seems to ignore the existence of centro-peripheral innervation situated outside the brain.

Finally, Heusinger has experimented upon the frog's eye with diluted nicotine of Amyl locally applied, and believes that the resulting dilatation of the vessels is due to a diminution of the true activity of the muscular bundles existing in the vascular walls, since patching the first few produces a reflex contraction of these vessels. Thus for, this cannot be paralysis either of the smooth non-striped fibres or of the vascular endothelium. Whether may be the element derived or by the nicotine, some writers seem disposed to believe that the various phenomena produced are caused by the intervention of the blood, more or less altered by the nicotine of Amyl.

And as we have before stated that the process of oxidation.
is diminished and there is accumulation of Carbonic Acid (CO₂) in the blood, we are likely to attribute the symptoms of nicotine intoxication to them. Thus the dilatation of the capillaries may be said to be due to irritation of the muscular dilating fibers by the blood charged with Carbonic Acid or the paralysis of the tissue consequent upon intense stimulation.

He doubts a certain amount of asphyxia, depending on blood change, can in the last part of the forming argument, the nervous depression which already exists; but although it is true that the nerve loses its irritability in an atmosphere charged with Nitre of Ammon Salpeter, yet we must admit that this agent has a direct action upon the nervous system itself.

Firstly let us mention the reasons whichloyd states against the accumulation of Carbonic Acid theory.

(1) Gas laws show that all Nitrogen acts in the blood in the same manner: but their physiological effects are quite unlike those of Nitrite.

(2) In depriving an animal of Oxygen, as by means of an vacuum gas, say NO₂, the symptoms of diminished oxidation of the blood are entirely different to those observed after Nitrite - the pulse becoming slower and blood tension higher.

(3) Other agents which have the power of lessening oxidation, as, Alcohol in large doses, do not produce symptoms like those of Nitrite.

From the above stated reasons, therefore, we cannot believe in the theory of the effects of Nitrite being due to presence of Carbonic Acid in excess in the blood - but it seems to act upon the nerve center directly, and upon the vascular walls in addition to its action on the blood.

**Synergistic and Antidotal Actions** -

We will first speak of the similarities of action between Nitre of Ammon and Nitro glycerine. Both produce similar physiological changes, diuresis, and accelerate the rapidity of the heart's action.
But they differ in the time in which they produce their effects. The nitre resembles his producing its full effects for some 3 or 4 minutes, also its effects are more lasting. It is useful in

An Sr. Pictor and Neuralgia (Murr.)

Richardson states that there is an almost complete antagonism between Nitre of Ammon and Smythia — Masts and others have, in their interesting researches, shown that Smythia has a general vaso-constrictor influence, increasing the arterial force and temperature. Also it has an acute motor action upon the spinal centres. Thus the phenomena in Smythia

forming the entirely opposed to those of Nitre. And for these reasons it is employed, because it can completely stop the spasm of the vessels in animals poisoned with Smythia, and further can reduce the consequent hyperpyrexia, which, also is a source of danger.

The question has been worked out experimentally by Richardson in hops, and most recently upon rabbits (Glasgow medico

Burrall 1875). Having injected at the same time 10 drops of

Nitre of Ammon and 1/2 a grain of Smythia in a rabbit, but the least physiological reaction was observed. But 1/2 of a grain administered alone rapidly killed the same animal after violent spasms.

The antispasmodic action existing between Nitre of Ammon

and Chloroform seems to be well established, especially by

W. E. Dabney, Burrall of New York, Schiller, Rodhart, Reader (Sevent. p. 643. 1875.) and Munro (Murr. med. & surg. 1875.) who have experimentally studied the question in animals. And, further, division of both vagi does not interfere with the antispasmodic action. And Munro has noticed Chloroform antagonise in rabbits to subside much more quickly after a few inhalations of Nitre.

And it is stated that a mixture of 3 parts of Nitre and

8 of Chloroform, inhaled by a dog does not produce anaesthesia. Also the sleep produced by large doses of Nitre seems to be prevented by inhalations of Nitre. The antagonism between
While of amyl and spirit of pepper does not seem to be complete as far as experiments yet have shown.

Finally we must mention the therapeutical similarity of some of the effects of quinine to those of bromide of potassium. Though the physiological action of these drugs is different, amyl diluting, while bromides are generally supposed to contract the blood vessels. Further quinine depresses the motor centres of the brain, but leaves the sensory unimpaired. Bromides depress the reflex and sensory parts of the brain, leaving the motor centres unaffected. Thus they both act on the walls of capillaries and many symptoms occurring at the menopause, to which we shall refer later on.

With regard to the elimination of quinine from the organism, it is generally believed to be got rid of rapidly or at any rate to a great extent by means of the lungs — it has not been discovered in the urine.

Therapeutic Actions

Having fully described the physiological actions of quinine of amyl, we now come to another and practically more important section of its therapeutic actions. But before going further it will be useful to recapitulate its fundamental action.

1. Stimulating action on heat and lungs
2. Relaxing action on all muscular tissues, blood vessels, bronchi, and alimentary canal, and a paralyzing action on the nerve centres.
3. Action in the blood, lowering the process of oxidation and lowering temperature.

Thus, then, it is evident that it is a powerful antipyretic and analgesic in a characteristic, short space of time, which however is very transient. Hence it is a remedy which has more a palliative than a permanent curative action.
but when the disease becomes chronic it seems to have the power of
cutting short the paroxysms, and it does not get rid of the cause
of the disease. It is not a "specific" for any affection, but still
at the same time it seems to be the best plant of all our drugs.
While assists in removing the danger and damping the very grave
symptoms to arise in certain affections - as Angina Pectoris for

Thus then we must be somewhat guided by its

physiological action in applying it practically - its stimulating
action on the cardiac and pulmonary systems with the consequent
dilatation of blood to the head, we may be of use in cases
where these functions are freely performed. Also its dilating
action on the blood vessels may be useful in nervous affections
due to vasomotor spasms. Further its action in the muscular
system and Spinal Cord indicate its use in cases of pain and
spasms. And finally its lowering action on the temperature
shows that it may be useful in cases of hyperthermia when
the excessive heat is highly dangerous.

In the following classification we have arranged
the principal diseases in which Mule of Amys has been chiefly,
under four headings, based upon its fundamental actions - thinking
that it will simplify the study of the indications.

I

Conditions Characterized by \textit{Stoic Cardiac Irritants}

Anemia and various Enlarges of the Cardio-Spinal System

1. \textit{Chorea Accident}
2. \textit{Sympathy, Lues, Convulsions}
3. \textit{Sea Sickness}

II

Conditions Characterized by \textit{Spasms of Blood-}

Vessels

1. \textit{Angina Pectoris}
2. \textit{Epilepsy and Migraine}
3. \textit{Poisonous or Humoral Scares}
4. \textit{Mylancholia}
III
Conditions characterized by spasm of voluntary or voluntary muscular fibres.
1. Spasm of Voluntary Muscles
2. Tetanus
3. Skleroma
4. Spasm and Cold

IV
Conditions characterized by elevation of temperature
1. Cerebral Rhumatism
2. Hyperpyrexia in Fever

Accidents in the administration of Chloroform.

From different quarters we occasionally hear of accidents, even when the agent is used with the greatest of care and by most experienced hands.

It has been proved experimentally that Chloroform has a direct action upon the muscular fibers of the heart, in paralysing its action by chloroform gas. But its main action is on the nervous system. And according to Claude Bernard, partly at least, it causes an anaemic condition of the cerebral hemispheres and thus coming upon vascular contraction is attributed by Richardson to stimulation of the vaso motor centres and the two Vagi. The final effects following in invigorating the patient (which causes the blood to circulate towards the heart and head) also favor this idea, from these two physiological facts we are better able to understand the cause of death in Chloroform administration. And, further, they explain clearly this Numbness of the arms and tetanus caused by preventing suppressor and apnea.

Whatever may be the true way in which death from Chloroform is due, it is a fact that Numbness of arms may, by its stimulating action on the heart, oppose its debility and cause death to overcome the spams of the pulmonary vessels, of which it is
may further assist in dilating — or it may, by its action on the spinal centre and the vaso, lessen their irritability and thus respiratory action —

It has been experimentally proved, that it quickly restores consciousness in animals which have inhaled large and may be large quantities of Chloroform.

In 1844, Dr. Ware of May 8th, also experimented with Mr. Hendren, 1847, Dr. Brown, and they found it useful in cases of fainting, defective breathing or heart action, whilst under the influence of an anaesthetic — and he records the following.

Case I. Given a mixture of alcohol, ether and chloroform.

Young man, hypochondric, intemperate, apathetic; insensible to both eyes; suddenly became pale, deeply unconscious, with pulse and respiration very defective. Subcut with a few (3) drops of nitric acid was placed over nose and mouth. In 2 or 3 seconds a deep inspiration followed by others, flushed face, quick pulse and return of sensibility, was observed.

Case II. Given Chloroform. An elderly woman suddenly became blue in the face and shivered (tongue falling back) and, with 10 drops of nitric acid was placed over nose and mouth. In a few seconds the blueness and shivering breathing gave way to good color, regular breathing, and silence and vomiting, though no food had been given for several hours.

Case III. Given Chloroform. A boy, pale, pet, blue lips and cheeks, became suddenly very faint, blue lips, breathing very imperfect. The same quickly washed, with vomiting, followed the inhalation of nitric acid (3 drops).

Thus we have some just grounds for stating its usefulness in cerebral and convulsive paroxysms caused by Chloroform.
Drs. Gullichs in 1857 first ascertained the physiological action of Nitric of Ammon, and even then recommended it in cases of Anoxia or Suffocation &c.

Amongst some of the earliest recorded cases of passing in which it has been tried, we will just mention the brief facts of the recorded by Talfourd Jones in the Practitioner for Oct. 1871.

Case IV. During the operation on the eye, the patient fainted suddenly. She was carried on to a sofa, where she remained for some minutes without pulse or respiration. Then a few drops of Nitric of Ammon were inhaled, and immediately consciousness, the pulse, and respiration were established. Thus it seems that without it the prognosis would have been worse.

Also Dr. Jauwrey records an interesting case in the New York Med. Journal for July 1874.

Thus we have proof that Nitric of Ammon can be of genuine service in such cases when there is no organic lesion.

- Shock, coma &c.-

That state of agitated consciousness, known by physicians as surgical shock, which so gravely complicates traumatic lesions, may probably be treated with the success by means of this agent. From the experiments of Hitzig we have attributed the cause supervening on injury to a hyperparalysis of the heart by means of its inhibitory apparatus, the pneumophores, and from these facts we may be justified in making the therapeutic deduction that Nitric by its opposing the stimulation of the vagi may be most useful and more especially as its action is so prompt.
Mr Wigglesworth mentions the following case of his in the Cancer for May 22nd 1875.

Case V. Called to a girl, 14 years old, who had drunk over 302 of pure whiskey. He was examined by various remedies with Bich di Vaio. On using Nitrile however, she gradually became better. But later as signs of Capillary Necrosis were manifested and she died. Mr Wigglesworth partially attributed the death to the instant action of the Nitrile.

Thus, we may state that in all accidents where by suffocation, aspiration or cutaneous death is imminent from asphyxia, it is as in cases produced by alcohol, carbolic acid, sulphuric acid, hydrocyanic acid, etc. the Nitrile should be used, and would probably save many lives if but a small quantity can be inhaled even by means of artificial respiration.

Tea - Sickness:

Probably there are few persons affected where there is no fixed place to which the cindens will go so fraternally and nobly to the sufferer of these ills. It seems to have adored every remedy, more or less, either rational or empirical. Choral has sometimes succeeded with Ballo and Veron - and Chapman has had encouraging results with his spinal ice bag. Further a host of other agents have been tried with very variable success.

But thanks to Mr Burleigh, Chapman, we have a pretty certain and ready means of preventing or arresting the malady. In the case of the Nitrile of Ammonia, it has been used in less than 124 cases. Of these 124 proved eminently satisfactory, thus being no return of the skating after the administration of the Nitrile; the time remaining cases being only unsatisfactory in so far as they required a further dose or two of the same.

As to the proximate cause of the malady, Dr Caffin,
agrees with Dr. Chalmers that it consists of an undue exaggeration of the reflex actions of the spinal cord; for he was fortunate enough to give it by a small injection of a Cimicifuga. It seems to have been struck with the similarity of this appearance to that produced by the spinal cord of an Epileptic who dies in a fit. 

Finally, brushing the just mentioned difference to the subsidence which obtains in life between those two affections (Pallor, Petechial rash) it occurs to Dr. Chalmers that the remedy which he used in the hands of several cases, has proved so valuable in the Epileptic ought to be advantageously employed in this disease.

After inhalation, the chilly towel is replaced by a comfortable flowing warm surface and this is turned in usually followed in the course of half an hour by a pleasant slumber, from which the patient wakes to take a hearty meal. If the disease varies this inhalation must ever more be omitted. Also, the patient should be in bed whilst under treatment so as not to interfere with the rest and sleep.

Dr. Quick, Lessor was in Dr. Chalmers experience in the Cancer 1878 - but he had not quite such great success.

-Angina Pectoris-

Few things are more distressing to the physician than to stand beside a suffering patient who is acutely looking to him for that relief from pain which he feels himself utterly unable to afford. Perhaps this is no class of cases in which such occurrence as this take place so frequently as in some kinds of Cardiac disease, in which Angina Pectoris forms at once the most prominent and the most painful and distressing symptom.

This painful affection is defined by Dr. Quick as a paroxysmal nervous, in which the heart is essentially increased and the cases included in this definition may be divided into two classes:

1. In this the most typical that is ever pain in
the precordia, often shooting up the neck, and down the arms, accompanied by dyspnoea, and a most distressing sense of impending dissolution. The occurrence and departure of the attack are both equally sudden, and its duration is only a few minutes.

In this class, which from its rarity, frequency is probably the most important, though the pain and dyspnoea may be both very severe, the occurrence of the attack is sometimes very gradual, and its departure generally so; its duration from a few minutes to an hour or more, and the sense of impending dissolution is less marked or altogether absent.

All sorts of stimulants have been used and relied upon, but the alleviation which they produce is but slight, and the duration is but little affected by them.

To Samuel Brown, the honour of applying nicotine, in the treatment of this painful affection for whilst a Resident Physician at the Edinburgh Royal Infirmary, he met with several cases of Angina in which digitalis, although not used, without benefit, the bleeding was to some extent beneficial, and it was owing to this that he used the Nigrito which had the power of dilating the vessels, and his therapeutical deductions were followed by great success, for, simultaneously with the flushing of the face by the Nigrito the pain completely disappeared, and generally did not return till its usual time on the following night. Occasionally it would return about 5 minutes after its first disappearance; but in giving a few drops more it again disappeared and did not return. In a few occasions he observed that while the pain disappeared from every other part of the chest, it remained present at a spot about 2 inches to the inside of the right nipple, and the action of the remedy had to be kept up for several minutes before this disappeared. But in almost all his cases the pain
disappeared completely at once. Further, in cases of auricular fibrillation, he found that when the patient was lying in bed, it was not necessarily dangerous to allow the vitreous humour to rise sufficiently to cause the symptoms of fibrillation.

Dr. Madden has used nitrile of ammonia in several cases two of which we will briefly notice (Edin. med. journ. 1870).

Case VI. Patient, aged 40, cardiac hypertrophy with murmur at base, and all the signs of angina pectoris coming in at night. For two years past the patient has been accustomed to inhale nitrite of ammonia until the symptoms of angina were very marked, so that he was very weak without it. After death, the left side of the heart was dilated and hypertrophied, and the aorta thickened and the valves adherent.

Case VII. In this case a fort unseeks was made which brought to view a large aortic dissection passing upon the aortic valves. None of the signs of angina were present, but in this case the nitrite of ammonia not only produced an amelioration, but the nitrite of ammonia had not its desired effect.

The following is interesting as it was the experience of Dr. Madden himself and related by himself.

Case VIII. Dr. Madden (Practitioner Dec. 1872) aged 67. His father died in an aortic paroxysm due to organic origin, his heart gave rise cardiac failure due to mitral insufficiency. On the 5th July 1871, he was suddenly seized with a paroxysm of pain striking down the left arm, being in professional duties he could not take the hypodermic, and thus the attacks became more frequent. But during a paroxysm he inhaled the vapours of 1 min of nitrite recommended by a friend. The effect was wonderful; the pain seemed to be reflected, and the attack, instead of lasting the usual 20 minutes, disappeared completely in less than 2 minutes, and the following attacks gradually lost in intensity and became less frequent; lastly they disappeared altogether. The live both 2 years.
Of Willis reports a case in the Journal Dec. 16/69 with symptoms of heart disease; and as in many other cases he noticed on interrogation that the pulse became slower and fuller but more rapid afterward.

Sydney Anger has largely used Nitrite of Amyl for some years. He states that he never knew it fail to give some relief, though that it is very transient. But in some of his cases it was strikingly successful. In one case the suffering of the patient lasted on for years, but when given Amyl the patient could always cut short the attack, so that now he can walk several miles. He believes that the paroxysm became less frequent and intense by using the Nitrite. Also he is not afraid to let the patient have this powerful agent under their own control. For he has five patients who always carry a bottle of Nitrite, and in the first warning of an attack, each at once sniffs at the bottle. The patient was 73 and was used with unfailing relief. (Handbook of Therapeutics by 6th Edition, p. 361 et seq.)

Although we might dismiss all the cases reported by Bruneau, Prio, Anziz, Proet, Banger, George, etc., still I think we have mentioned sufficient to prove the marvelous efficiency of Nitrite of Amyl in this terrible affection. And we have seen that not only in the great majority of cases it has cut short the attack, when no other remedy afforded any relief, but also we have seen that the number and gravity of the attacks diminished under its influence, and sometimes entirely disappeared.

The theory of action of Nitrite of Amyl in Angina Pectoris is not thoroughly known, for the pathology of that disease is not now definitely settled. Habermann believed it to be a Cardiac neurosis; Nomburg, a hyperasthenia of the Cardiac musculature; Landaz und Roven, a spasmodic contraction of the Capillaries of the lung; etc. Viewing the paroxysms as a neurosis, we might attribute its phenomena partly to Vasomotor spasm and partly to inhibitory influence transmitted through the Vagus from the Medulla Oblongata.

However, clinical observations seem to show more or less...
Towards the interpretations of Brunton, and the symptomatic effects of the
influence, the indication of which was based upon the state of the
pulse, the increase in arterial pressure, the fall of face and other
signs of vascular spasm, seems to be readily explained by its
vaso-dilatory action. Also the slight amelioration produced in
Brunton's case by slight bleeding seems still further to
confirm the idea.

Dr George Wilkinson believes that the Modus Operandi
of Nitric acid in its remarkable influence over some forms of
Nervousness, and not in its relaxing effect upon the arteries,
except in so far as its antispasmodic power may depend
from its influence on the arteries; for there is no evidence
to prove that there is a general arterial dilatation. (Brit.

Epilepsy

Nitrite of Ammon has been tried in Epilepsy by numerous
Practitioners, amongst the earliest being Dr. Wm. Mitchell (1872)
Falkirk, and, — Bichat in France (1873–74). St. Vincent (1873).
Baltimore (1874–75).
Not only does this remedy seem to have a reputation in
Epilepsy, but also in Hysteria and Nervensyphilis has had some
success, both at La Salpetriere, Paris, in Hysterical Epilepsy.
Dr. Mitchell has reported several cases to the Philadelphia
Medical Times Annal, which is the following. A young man,
observed by Dr. J. S. Green, which was attended by Epileptic
fits. All anti-epileptic and Nudities were tried but with no
success. Inhalations of Nitrite of Ammon were given, when the
attack was at once cut short. — Dr. Mitchell gives several
other cases in which the same good results were obtained,
and although in does not allude, that the drug has any
power to prevent the return of the fits, it has no doubt of its
efficacy in arresting the delirial convulsions.
Mac Beste, mentions several cases in the Chicago Journal of Nervous and Mental Diseases.

Whatever may be the true mechanisms of an epileptic fit and the manner in which Nutilis of any sort acts, it is impossible to doubt the efficiency of this agent in stopping the attacks if we pay any attention to the cases reported by so many observers. And evidence seems to show that, each time that the attack is preceded by a distinct and characteristic aura, the agent always succeeds in hindering its development.

When there are clear signs of a state of cerebral anemia, known by pallor of face, dilatation of pupils, the Nutilis also acts very efficiently. But when there is no aura, or the fit has been commenced for some time, or when the convulsive stage, then the Nutilis is in no means so efficacious, and sometimes even fails to arrest the attack. In a few cases it has aggravated the vomiting symptoms — thus it is probable that Nutilis is a state of contraction of the cerebral vessels, but judging from the occasional action of the Nutilis, one might be disposed to state that this was cerebral congestion.

The Nutilis seems to have been equally successful in cases of Petit Mal.

Ringer and Dr. Mitchell believe that the Nutilis can lessen the frequency and the duration of the attacks, also alleviate the intellectual and general state; though clinical experience is not yet very decisive on the matter.

St. Vellut has come to the following conclusions in treating Epileptics by this agent.

(1) It acts favourably on all Epileptic fits which are accompanied with or caused by, reflex constriction of the cerebral vessels.

(a) Stopping the fit when preceded by an aura.
(b) Stilling the pain of it when it has begun.
(c) Avoiding the development of nervous troubles which are signs.
(d) Lessening the frequency of fits.
(2). It acts unfavorably when the spasm is accompanied or determined by hyperemia of the cerebral vessels.

(a). Prolonging the fit and increasing the frequency.
(b). Augmenting the convulsive spasms.

Lastly, Barre, Virchow, and even have treated cases of ordinary spasticity very beneficially with the Nitre of Amyl.

---

Migraines and Neuralgias---

In considering this treacherous and very common affection, many remedies seem to have been tried with equally varying success, which, in some degree, is easily to be accounted for by the different opinions held as to its cause. Thus Dr. Reynard of Paris, having been able to study it in his own person, states that there is a spastic contraction of the vessels due to stimulation of the corresponding sympathetic nerves, as evidenced by pallor of face, dilated pupil, contraction of the temporal artery.

But these symptoms are not always present for Reynard has noticed a hyperemic condition due to the spasm of the sympathetic.

So that from the above two opposing theories, Richardson, Donnan, Simpson, O. Berger, Vogel, etc., have employed Nitre of Amyl to counteract the vascular contraction believed in by Dr. Reynard—O. Berger gives the following case—

---

Case IX---Patient has for many years been subject to sick-head ache, very intense towards her menstrual periods. She had all the anemic signs written off by Dr. Reynard. Inhalation of Nitre of Amyl seemed to act like a charm. In taking away the pain and allowing her to eat her ordinary mid-day meal. The following day she was still better.

In the practice for Oct. 1871 Salford has reported a very
Successful case of Neuralgic headache treated by means of Nitre of Ammon.

Dr. Rossetti, having treated it in Nervous Epilepsy and in Migraine, has used it in acute and chronic headaches. It was found that it relieved the pain very quickly and completely.

Of the Migraine, F. F. J. has found Nitre of Ammon useful. (Practitioner 1875).

Ringer has found the greatest benefit from it in women, who from sudden strain of mental strain, nervous depression, or more properly, at the change of life, suffer from frequent attacks of this kind. They are generally followed by perspiration or the skin may remain dry, and then the attack is commonly called "drop-head." It begins with:

Case 1: Patient had for 3 years been horribly tormented with singular attacks, repeated several times daily, of short paroxysms, over the face, eyes, nostrils, causing a sort of heat-sweat over the whole body, followed by perspiration, the burning sensation being so unbearable that she was constrained to open the windows at night even in the winter and to sleep out of doors. After being treated for 10 days with Nitre she was perfectly well.

Locality in Obstructive and Neuralgic dysmenorrhoea.

Dr. Edwards has experienced encouraging results, although it seems to be more palliative. (Practitioner July 1876).

Melancholia.

This form of Mania, which is characterized by fear, mania, and prolonged sadness has been treated by Dr. Hörnemann of Vienna with Nitre of Ammon, on the supposition that there is an organic condition of the cerebral cortex. He has been able to report some very favourable results, and finds that the
In the late symptoms of agitated and incoherent insanity, immediately ease under its influence. Also after inhalation of 3 or 4 times a day for 3 days they became calm and are able to sleep at night.

However Schobert has not been able to get such encouraging results in his cases, but believes that Hohmann's success depended upon his cases having an acute, acute state of the Central Nervous System.

Brighton Obins observed the very interesting fact that cases of General Paralysis are almost insensitive to Nitrite action and rarely show the usual twitching of the face.

In the American Journal of Mental Science for March, 1875, an some interesting cases by Seidmowitz.

Istanaus and Paraphrenale Convulsions

Almost every medicinal agent of the pharamacopia has been used in this strange disease with little or no success. Richardson, judging from the physiological action of Nitrite of Ammon, suggested its use in this disease. And Dr. G. Forbes who had four cases under treatment with Chloral & tried the Nitrite and all the four cases made recovery.

D. Ligge tried it in one single case, but

Without success.

In Paraphrenal Convulsions Dr. W. Irons and Macfarlan have given this agent a trial and have obtained successful issues. Although in one case the convulsions immediately ceased and the utter contracted eye afterwards this organ relaxed and was followed by a dangerous

fluctuation.
Chorea.

The stimulant action which tincture of amyl nitrite has on the circulation and respiration suggested the idea of using it in the advanced stages of chorea. Gm. See, Woodw. &c. thought that from its physiological action, it would oppose the adynamic condition of the heart; that the blood vesseles and heart raise the blood pressure and restrain the pulse force. Also they thought that by its sedative action in the spinal cord, it would lessen the muscular tremors. However, the first case to treated by St. Hadden did not give any favorable results in as much as the patient died, after a certain degree of amelioration of the symptoms.

I cannot find evidence as yet to prove that it is of much service in this very terrible disease, although St. P. R. Smith published a case in the Indian Med. Gazelce for May 1873 in which there was some improvement in the symptoms but only of a temporary nature as the patient died later on.

Arthria.

It will be easy to understand that, as in this disease there exists an over-stretched condition of the respiratory organs of central or peripheral origin and as we have seen that nitrite of amyl by its physiological action diminishes the irritability of the vagus and sympathetic, so we might expect beneficial results; and, happily, indeed, our expectations have not been in vain, for cases have reported by Parkinson Weller showing its marked benefit.

Sylvain Des reports the following case:-

Case 74. Called at midnight to see a young patient, who was suffering from a severe attack of arthria. Face cyanotic, skin cold, almost sublimed; auricular action quick; blood and ayumo running over the chest. He ordered 5 drachms nitrite of amyl to be instilled in lungs, and in less than 30 seconds afterwards the face reddened,
that beat visibly, the skin became warm and the dyspepsia disappeared entirely. Hourly the breathing again became laboured, and inhalation was again resorted to, after which she became very easy and slept well during the night. Five minutes later, a lesser intense attack, was cured in the same manner.

Hord's word speaks in the very highest terms of this agent especially when there is no emphysema or cardiac dilatation as complications of the asthma.

In the British Medical Journal for June 1874 Dr. Mavor speaks of the benefit his wife received from this agent.

And from the experience I have had in 4 cases I can speak of its undoubted power in curing short the climacteric paroxysms but in my hands has been more beneficial in the first epidemic cases than in those accompanied by bronchial complications.

At present it is not known whether it has the power of lessening the number of attacks and of finally completing its cure.

While Amyl has been used in Four as Spar's Cup also successfully in Whooping Cough.

Lastly Dr. B. Peabody published a case of Miliaria Acute in the Lancet for Nov. 27th, 1875, which proved symptoms of Peptic Ulcerating Gastritis. The patient was cured and said in his discharge: "I wish I had had that medicine sooner," referring to the Nitrite.

Various Spasm on Colic

Judging from its physiological action there can be no doubt that Nitrite of Amyl will be found serviceable in the above forms of disease — Dr. Harquard and Sherlock have used it in Intestinal Colic with success. The latter reports a case of Intestinal Obstruction in which the pain was relieved by this agent.
I have tried it in one case of a child in which the intense pain and spasm were wonderfully subdued so much so that the spasms in number, passed away without any further pain. In this case ether was not found to afford the very transient relief.

It is probable that it ought to be found to be of use in lead ence, apoplexy and asphylactic shock, more especially when of the rapid ventricle type - hemorhoids, I have not yet had an opportunity of testing it.

- Cerebral Pneumonia and Fever -

As we have shown that this remedy acts powerfully in lowering animal temperature, so it has been recommended in various diseases accompanied by temperatures of such a height as to greatly endanger the patient life. Most recommends it in cerebral pneumonia when there is a high temperature.

Smith recommends it in the initial stage of intermittent fever. In it also we know that it may reduce the temperature some 10 or 15 degrees. Probably in all cases of fever where there is a very high temperature it might be tried with benefit - at present nothing seems to be known clinically about it in these diseases.

Charles Dunlop Taylor.
Nottingham.

April 28th 179.