Poisoning

by

Nitro-Benzole.

R. Prosser White.
A Clinical Study of the Poisonous Effects of Nitrobenzole.

By

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Genital Symptoms
Symptoms which show slight attacks of poisoning by Nitro-perchlorate, or their compounds, are very frequent amongst the men who are employed in their manufacture. The attack was in general with the close of the poison absorbed. The mental symptoms noticed are as follows. There is sleepiness, headache, with throbbing of the temples, a forehead, great lassitude, depression are complained of. The urine becomes darker in colour. The hands are moist; sometimes quite wet. This is probably to be accounted for by the fact, that Bengole is intimately mixed with a deliquescent part of Ammonia in the manufacture, with which lamp connected. These slighter symptoms are for all practical purposes removed, if the men are absent from work for a few days. After such rest they immediately feel in excellent health and spirits. Upon more careful examination
of the cases it is found that they suffer from a very severe form of anaemia. The muddy hue of health gives place to a uniform colouration of the skin. The chest becomes pale, and the general surface of the skin body changes to a dull yellow cast, which does not disappear upon pressure. It has the appearance of jaundice, but is not so white. The exposed surface of the body, where the skin is thin becomes darker. This dusty colour is of a blue or black cast, gradually deepening with the amount of poison absorbed, but decreases as it begins eliminated. These changes are most marked in the face, especially the eyelids, the tongue, and mucous membranes generally. The skin appears as if suffering from the effects of ether inhalation. There is invariably a general loss of weight, and the muscles are flabby. A week. The diarrhoea, and tendency to
Sleep is very great in severe cases. The men say it is almost impossible to keep their eyes open during the night. They sleep soundly, unless prevented by the incessant headache, which is a constant symptom. In the morning they awake unrefreshed and heavy. The headache is very intense, and chiefly situated in the frontal and temporal regions. The men say it feels like a quick succession of tapping going on inside the brain. It is increased by stooping, or when the head is laid upon the pillow in bed. Giddiness though sometimes present is not a prominent symptom in the early stage. Slight apathy, irritability of temper are generally experienced. Slight noises, little annoyances are resented. The appetite is at first good, but soon becomes capricious, late or fails altogether. Meats, strong food are disdained, fruits, milk, puddings, other light articles of diet being
preferred. Breakfast is a meal usually partaken of, a cup of tea or coffee with an egg, but in it is all the desire. During an hour's interval in the middle of the day, the hunger is roused, much as it is left indolent and tasty. Supper is always the best meal, after a couple of hours absence from work, perhaps a walk in the air, a very heavy supper is consumed: as the men say, they then make up for the deficiency of the rest of the day. The sense of taste is undiminished. Nausea is occasionally observed following sickness, the vomited matter consisting of a greenish coloured slime, is independent of the presence of food in the stomach. The tongue is fairly clean, though very dark in colour, later develops a yellowish white fur. The temperature of the body is slightly raised, but very rarely more than one degree. The heart's action is somewhat
excited but the number of beats is not greatly increased. Occasionally palpitation is complained of, a tight feeling around the chest. Pains are most variable in distribution, character, intensity. Usually they are dull, heavy, felt most in the muscles, back when getting out of bed, or a tired stiff sensation upon movement of the joints. The breathing is always quick, short especially with the slightest exertion. Fatigue is rapidly produced. At that quick, [a] prolonged work is impossible. The extremities are soon chilled when exposed to cold air, or water. A soft systolic murmur is sometimes heard over the pulmonic area, a continuous humming in the jugular veins of the neck. Exceptional symptoms are crosses in the head, or dark spots floating before the eyes.
Where larger doses of the poison have been absorbed, unconsciousness may become absolute; the eyes roll slowly from side to side, the pupils are widely dilated; the conjunctiva is insensitive to touch. Both the deep and superficial reflex arcs are in abeyance. The inspirations are increased to twice double their normal number, they become irregular and they are in character. The skin is cold, of a bluish cast. The limbs are quite flexed, or one or more joints may remain stiff, usually when this is the case, three of the upper limbs. Eventually this stiffness entirely disappears. The hands, feet, and face become remarkably cold and dry. Sometimes there is edema of the neck with a fullness of the glands, and lip, or drops of the lower extremities caused by a spasm of the vasomotor nerves.
I have myself paralyzed take place after eight, twelve, and sixteen hours of unconsciousness.
The effects of the poison are shown in a marked manner upon the muscular system. The men have not the appearance of being employed in manual labour. When stripped, the muscles are seen to be flaccid, and the skin loose. The body lacks fulness, form, and precision. Fatigue quickly follows any muscular exertion. The grasp becomes feeble, the legs are weak. Pain and stiffness in the knees are common after a walk from work. I have known instances of men who are usually good walkers, but when suffering from the poison, take three hours to walk as many miles. They are often mistaken for being drunk, for they do not know where their legs are. Frequently they fall, and are unable to rise themselves up without great difficulty. If asked to close their eyes, they walk backwards. Their movements are so uncertain. Other
symptoms of Ataxia. I have been unable to observe. The objective symptoms are remarkable; such as, excessive wasting of the muscles, especially those of the extremities as has been particularly pointed out by Dr. Mos. (Medical Chronicle, May 1889). "Those of the hands" are seen to be very much atrophied. The spaces between the meta-carpal bones are more distinctly marked than in normal. The ground between them is not noticeable. The muscles of the Thenar and Hypothenar eminences are soft, distinctly wasted, especially the abductor indicis muscle. Patients cannot without considerable trouble and difficulty cause the tip of the thumb and little finger to meet. Sometimes this is more observable in one hand than in the other. The Phalangial joints must be bent otherwise there is inability to flex the thumb strongly into the palm, at the same time the joint
"of adduction is feeble in the thumb". All the finer and more delicate movements of the hand are greatly restricted in severe cases. Small objects such as pins cannot be readily felt & held.

The act of walking loses much of its elasticity, 9 spring, 9 the balance of the body is with difficulty maintained. The big toe in the advancing foot does not manifestly drop, & is only slightly flexed into the pole. There is usually no ankle drop 9 the power of raising the toes from the ground whilst the foot is flat upon it, is not lost.

The symptoms of weakness, & are usually observed in the muscles of the foot, are usually not so well marked as those seen in the hand.
Neurotic Symptoms
Pains, shooting, stabbing, or darting in character, are of very frequent occurrence. They are felt in any part of the body. A common position is under the feet, or in the arm-pit (neck, or jaw). The legs are rarely affected. When the pains are localised in the stomach, the bowels, they are of a gripping nature. Sometimes pricking, or burning sensations are described which are felt in the chest, forehead, and eyes, or restricted to the soles of the feet. These sensations are not accompanied by tenderness to the touch. More or less irritation of the peripheral nerves is always present. It shows itself by tingling, itching of the skin,
of the fingers, palms, & back of the hand, sometimes extending to the wrist. In a certain proportion of cases, the tingleings are felt in the feet as well as the hands. They may be restricted to the feet, I only noticed when the men have their close on, to cross their legs. Whilst sitting, or at rest in bed, the pains are very acute. They are always confined to the edges of the feet, never being felt in the soles, I disappear upon standing or walking. Occasionally the severity of these symptoms is more perceptible in the extremity, or extremities of one side of the body. When this is the case the left side is more generally affected.

Hypesthesia is a most characteristic symptom in all these cases of poisoning. As far as I know the varying degree of tenderness to pressure...
Both of the skin and deeper structures has not been indented upon as much as it ought. In all my cases it was present; but in each it varied in its intensity, and in the part of the body it affected. In some situations it is much more common as the following examples indicate. In one case it was curiously restricted to the toes, both the upper and under surfaces, the latter to a less extent even under to pressure. In the right foot it was more decided than in the left. In another instance rubbing, or lightly striking the ulnar surface of the skin of the forearm causes tingling to be felt all over the cutaneous distribution of the ulna nerve. Striking the outside, or dorsum of the foot causes electric pains to run all over the leg. Pressure or tapping beneath the internal malleolus on inside of the calves of the leg had no effect.
Another example which I witnessed or
accompanied. The hyperesthesia was restricted
as follows. The upper, outer, 9 inner
surfaces of the dorsum of the foot were
exceeding tender to light pressure.
A slight touch induces the feeling
of needles, 9 pains all over the ankle,
causing the finger very gently over these
sensitive areas, sent shooting pains
up about four inches of the leg.
The sole of the foot was not affected
by a light touch, but a sharp blow,
tap, or jar, or a false step in walking
caused painful sensations as high as
the knees. These symptoms were
more acute in the left than the right
leg. Sometimes only a small portion
of the skin becomes hypersensitive;
for instance, a small portion of the
outer surface of the dorsum of the foot.
It may be limited in distribution to the area of a nerve such as the Ulner. Again in another case, where there was partial right Hemianesthesia, a small patch of skin three inches below the inferior angle of the Scapula on the same side, was exceedingly sensitive to the prick of a pin. I have observed the nerve trunks of the legs to be sensitive to pressure, while superficial, and if pain to be caused all over the distribution of the Occipital Nerve, by pressure on the Trunk. The muscles are often very tender, especially those of the upper arm. Sometimes squeezing the Bicep muscle will cause very severe pain to shoot through the shoulder, back of the neck, making the patient cry. In the majority of cases tenderness upon firm pressure is not found in the
muscles of the forearm, thighs, or calves or those of the trunk. It may be localised in only one line of the body, as for instance, the middle third of the Rectus Femoris of the left thigh. In these cases it is often difficult to differentiate superficial from deep tenderness.

Sensation is often impaired to a slight extent in the extremities. In my experience, it is a less marked symptom than Hyperesthesia. Patients almost invariably complain that the skin of the hands, soles of the feet is less sensitive than is usual in the healthy state. The fingers are numb, clumsy, the hand feels as if it were swollen. The impression of cold, or snow is conveyed to the feet when standing or walking. Sometimes the impaired sense of touch instead of differing
upon the two sides of the body, varies in
the upper, lower half. If 9 cold test
tubes when applied separately are with
difficulty distinguished the one from the
other. I applied two test tubes containing
hot water varying in temperature from
right to ten degrees. In one case, the
arms, trunk, readily appreciated the
difference, but from the hips downward.
the patient was utterly unable to say
which of the two tubes was the hotter.
It applied together "about three inches apart"
the sometimes experienced both as cold.
Generally speaking, the skin of the body
is more sensitive than that of the limbs,
but in all parts great variations occur.
Upon using a Faradic current of a given
strength which was with difficulty borne
by the thighs, arms, in trunk, there was
no perceptible impression produced in
The calves or legs. In the panic situation, the compasses must be separated three inches to be known as Cape Two Joints.

The transmission of touch.

Pain is made clearer than normal, the sensations or at any rate, are not as readily suspended as in health.

The extremities become very quickly chilled. On the slightest exposure to a low temperature the fingers look pale, bloodless, feel as if they were dead. The feet are always cold. This causes them to freeze even in water while washing. In a case of great emaciation.

Weakness due to prolonged absorption of the poison. I noticed a coarse tremor of the limbs which are increased by movement. It was most observable in the arms, when the hands were holding a small object. The reflexes in this case.
are very distinct.

Tactual, taste are as far as I

know unaffected.

There is very great loss of energy:

turbidity, paresis, depression are invariable
concomitants. The sexual appetite is
notoriously weakened, or lost, & erections of
the penis rare.

The reflexes are very variable,
sometimes they are exaggerated. This
happen in is not usual. Usually speaking
they are enfeebled. When they are
affected they are not equally as throughout
the body. I have seen the penis jerk
increased, & the superficial reflexes lost.
But in other cases the pryatic contraction
of the anus were absent, yet the superficial
reflexes remained normal. Dr. Reynolds
mentions a case, where the patient was
comatose, the three jock persistent. The cremasteric and plantar reflexes are those most commonly absent.

The muscles react readily to a moderate faradic current, but different groups of muscles vary in their sensitiveness to the faradic strength of current. All the muscles mentioned below reacted to the weakest current of a faradic battery the rod being pulled out one inch.

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Right Leg</th>
<th>All</th>
<th>Left Leg</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibialis Ant.</td>
<td>20</td>
<td>30</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Ext. Long. Dig.</td>
<td>25</td>
<td>30</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Froncei</td>
<td>15</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Nucleus Lemosis</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>25</td>
</tr>
</tbody>
</table>
The eye symptoms are as a rule negative. There is sometimes puffiness of the conjunctiva, sometimes lachrymation. The pupils are occasionally uneven, but readily accommodated themselves to light, and distance. In all my cases the fundus was practically normal. There was no restriction either of the field of vision, or of colour. This is in keeping with German opinion. Sometimes patients complain of partial blindness: when the eye is fixed for any length of time in one position. I may mention the case of a man, who felt totally blind when he was combing his hair. The mirror in which he looks is placed above the level of his eyes. If the mirror is raised for a short space of time to the glass, a film comes over them, and he cannot see. Upon lowering the eyes the sight at once
returns. In my experience such symptoms are most exceptional. Dr. Reid of Bochum (Edinburgh Medical Journal 89) says, only in one case out of twenty-five which he examined, did the poison affect the condition of the eye. In this vision was reduced too. There was great concentric restriction of the field of vision, but no corresponding restriction for colour, the boundaries of which came close up to those of white. Ophthalmoscopically there was marked hyperemia of the retina, and distinctly discolorable exudation surrounding the principal descending veins. Vision remained much the same for four weeks, and then slowly became normal.
Urine
The appearance of the urine is characteristic, one of the earliest symptoms. It becomes darkened in colour, and as a maroon cast. It may best be compared to deep, tawny, just wine colour. There is irritation, frequency in making water. I have never been able to find blood corpuscles, nor the reaction to the Guaiacum test. In rare cases, the odour of "bitter almonds" has been obtained after warming the urine.

For convenience of reference, the results from thirteen different cases are given below in a tabulated form.

Where marked *true* the substances have not been tried for.
<table>
<thead>
<tr>
<th>Date</th>
<th>SPG</th>
<th>Reaction</th>
<th>UPQ</th>
<th>Presence</th>
<th>Absence</th>
<th>Present</th>
<th>Bill Remains Listed</th>
<th>Sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aug 15</td>
<td>x</td>
<td>Acid</td>
<td>x</td>
<td>None</td>
<td>None</td>
<td>Present</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Aug 22</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Sept 6</td>
<td>x</td>
<td>do 4.7pp</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Jan 22</td>
<td>x</td>
<td>do 3.4</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>Present</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Jan 21</td>
<td>x</td>
<td>Acid</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Jan 24</td>
<td>x</td>
<td>Acid</td>
<td>x</td>
<td>do 4.6</td>
<td>do</td>
<td>do</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Jan 6</td>
<td>x</td>
<td>do 2.5</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>Present</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>1029</td>
<td>1029</td>
<td>do 2.6</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>Present</td>
<td>do</td>
<td>x</td>
</tr>
<tr>
<td>14</td>
<td>1022</td>
<td>do 2.8</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>Present</td>
<td>do</td>
<td>x</td>
</tr>
<tr>
<td>1020</td>
<td>1020</td>
<td>do 3.3</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>21</td>
<td>1030</td>
<td>do 3.3</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>25</td>
<td>1015</td>
<td>do 3.0</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>do</td>
<td>do</td>
<td>x</td>
</tr>
<tr>
<td>Jul 5</td>
<td>x</td>
<td>do</td>
<td>x</td>
<td>do</td>
<td>do</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
From the foregoing table, it will be seen that the urine was acid, in most cases, rather strongly so. Aniline was found in all the cases that were tested for it, but only in very small quantity. An interesting point is in what time does nitro benzoic become changed into aniline in the urine, after being taken up by the body. In one fatal case I detected it in less than twenty hours after the man had been exposed to the poison.

The urea varies from 2.5 to 4.9 percent. In those of high percentage upon the addition of nitric acid, urea nitrate crystals form an almost solid mass. It is most difficult to isolate the coloring matter in a separate state, the actual quantity is probably very small.
The wide difference in the proportions of Urea, may occasionally be caused by individual peculiarities. More common it is brought about by the large ingestion of Nitrogenous food, which increases the actual amount. So great are the feelings of lassitude, malaise felt by the men, that they partake freely of eggs, beef tea, milk, and meat, in order to strengthen themselves. This explanation however is only partially satisfactory. In bad cases the appetite is lost, and there is great dislike of this class of aliment. The increase in the quantity of Urea is probably due to the metabolism of the tissues of the body, which is readily observed by the decreased weight, a symptom so well marked. The presence of Calcium oxalate, also of sugar, are
of accidental occurrence. Triphosphates were found in one sample of Urine, which had been standing nearly a week. Aniline was found in all the Urines which were examined for it; a deep colored product, of the reduction, Dinitro-Benzole is due the deep Port wine tint.

Aniline is probably formed from the reduction of the Nitrobenzole with which the Dinitro-Benzole of Commerce is usually contaminated. \( \text{NO}_2 \) of the Nitrobenzole being replaced by \( \text{NH}_2 \) thus:

\[
\text{C}_6\text{H}_5(\text{NO}_2) + 6\text{H} = \text{C}_6\text{H}_5(\text{NH}_2) + 6\text{H}_2\text{O}
\]

In the same way Dinitrobenzene may be reduced to several compounds depending upon how far the reduction is carried, as for example:
Dinitrobenzene & Nitrilene

\[ \text{C}_6\text{H}_4 (\text{NO}_2) + 6\text{H} = \text{C}_6\text{H}_4 (\text{NO}_2) + 2\text{H}_2\text{O} \]

By carrying on the reduction further, Phenazine diamine is produced.

Nitrilene & Phenazine diamine

\[ \text{C}_6\text{H}_4 (\text{NO}_2) + 6\text{H} = \text{C}_6\text{H}_4 (\text{NH}_2) + 2\text{H}_2\text{O} \]

What is the exact chemical change which take place in the body. It is very difficult to say. A very similar color to that seen in the urine may be produced by reducing Bi-NitroBengale.

The nascent hydrogen evolved from zinc & sulphuric acid or zinc acting upon isomorphous diamine with dilute sulphuric acid. A purple tinge is also obtained, by heating nitrobenzole with acetic acid, iron filings, and adding to the product, an alkaline hypochlorite.
That such reducing action does take place in the body, has been shown by Ebulech, as mentioned by Landri Brunton in his Common Lectures (British Medical Journal, Jan 29, 1889). He says, the power of the living cell to effect chemical changes in the substances it absorbs is almost incredible, for Alizarine blue one of the substances Ebulech has employed, which can only be reduced by the most powerful reagents, outside the body, is completely reduced within the living body. In the liver, cortical substance of the kidney; after death by the heart, liver, muscular substances,

In all the cases examined there was evidence of the presence
of bile in the urine. The bile pigments
are found not only immediately the
poison is absorbed, but for many days
after. Pathological urobilin gives a
sherry red tint to the urine. The
presence only to a small extent accounts
for the peculiar dark colored water the
men make. The source of the
 bile pigments is the hemoglobin of
the blood, the daily excretion of these
pigments, points to the existence of
some cause at-work in the blood,
leading to a daily destruction of
hemoglobin. The large deposit
of urates, the high specific gravity
of the traces of bilirubin pigments
found in the urine is strong corroborative
evidence, that there is a certain
daily destruction of blood corpuscles.
On the method employed for the detection of aniline in urine from 50 to 150 Cub cent. are first acidulated with sulphuric acid, and cautiously evaporated to one fourth its bulk, then mixed with alcohol & filtered. To the filtrate basic lead acetate is added, as long as a precipitate is formed, again filter, then throw down the excess of lead, by sodium sulphate, again filter, concentrate the liquor near to dryness, when cold add sodium carbonate in excess, agitate with ether, which dissolves the liberated aniline. The ethereal portion, is agitated with a little very dilute sulphuric acid which dissolves the aniline. Separate from the ether, & if necessary, concentrate with a very gentle heat. To this
solution, placed in a watch glass upon white paper, add Sodium Carbonate in excess, then a drop of Carabolic acid. Very carefully add Sodium Hypochlorite. In a few minutes the beautiful characteristic blue color of Sodium Pyridine Phenate is developed if Aniline is present.
The Blood
The heart action is quickened in recent cases, probably from diminished activity in the inhibitory fibres of the Vagus. It is readily excited by exertion or strain, but soon becomes slower under the influence of rest.

The pulse is small, thread-like, feeble, and shows a very low condition of arterial tension. The capillaries are flexed dilated, and cause the line of descent in the accompanying phymographic tracings to be very rapid. In all severe cases the pulse is full, diastolic, and displays all of the most marked features in these cases, the loss of Vaso Motor Tone.
The blood invariably becomes darkened Rehablo Medical Chronicle Aug 1 1885, calls it a chocolate Brown colour. In one case of bleeding I saw from the mucous membrane, it was black.

The number of blood corpuscles is very much decreased. This depends upon the time they have been subjected to the action of the poison. I counted in one case 2,670,000. Thomas says there may be less than half the normal number. The amount of haemoglobin I mention in the case I mention above was 35%.
"Regent's Medical Chronicle May 1889

Pay that the blood give a spectrum
very similar, if not identical, with
acid haematin, namely a great
absorption band in the red, two between
Dr E somewhat like those of boy
Hemoglobin & the fourth, more to the
right." Their lines have been previously
described by Siebeck & Starkow. Met-
Hemoglobin produces an almost similar
spectrum. It is a curious fact that
these appearances have not been found
in blood which has been mixed with
nitrobenzole outside the body. In
such experiments Ewell did not
detect either spectroscopic or microscopic
changes in the blood. Newin says,
"This is due to fault manipulation,
"as he obtains the same peculiar
spectrum from blood mixed with free
Pilbylengole, allowing it to stand for two or three hours or even a shorter time, is heated to 40 or 50° C. In this state, an identical spectrum is obtained with Di nitro benzole or styptic oil or commercial petroleum ether. File this poison as a bitter with Di nitro benzole, but was unable to obtain this special spectrum. Two bands on the violet side of the B line were not reduced to one, on the addition of Ammonium Sulphide as quickly as in the blood of a healthy man, obtained for comparison.
The clue + channels which absorbed
A very interesting point is the manner in which the poison gains access to the body.

Firstly, it may be taken into the stomach. Secondly, it may be inhaled in the form of a vapour. Thirdly, it can be absorbed by the skin. When introduced into the stomach, 15 drops are reported to have caused death. Lethal in filia says that the fatal dose varies from 2 minims to 2 drams. It is sparingly soluble in water, which may account for its reputed peculiarity that its action may be suspended for hours. It has little local irritant action upon the skin, or the mucous membrane of the stomach and bowels.

Taylor says the inhalation of the vapour is much more painful as a poison than taking the liquid into the
ploment. This is decided by my opinion, but it must be remembered, it is impossible to gauge the amount inhaled. Sine, says, that if it is injected into the body, its action is almost as rapid as Hydrocyanic acid poisoning. He also states that it has no cumulative action. It is believed that Nitro Benzole is absorbable by the skin. This fact I have tried to elucidate, but the process of manufacture I am acquainted with, gives no many channels for it to scan access to the system, prevents me giving an absolute opinion from my own experience. In the manufacture of Roburite, the Benzole compound is volatilized by heat, it is diffused into the atmosphere in small particles, thus gaining admission to the respiratory tract, it comes into direct contact with the skin of the head.
9 hands, & 3 the latter were introduced into the mouth. That the poison is capable of being absorbed by the skin is shown by the following practical experiment, which was carried out in Germany.

A communication to one of the managers of the works. A number of men were provided with close-fitting respirators, covering the nose & mouth. The respirator had a tube leading to the open air, through which they were allowed to breathe. But even with this precaution, the number of sick cases was not materially decreased.
Physiological Chemistry.
Of great interest is the question, what causes the familiar coloration of the blood in these cases of poisoning. That there is an interference with the absorption of oxygen by the Hemoglobin is admitted by all writers upon the subject. This interference will naturally cause the blood to become darker and produce the symptoms of partial asphyxia, due to the retention of carbonic acid in the blood. Against this view the following points are of weight. In carbonic acid poisoning there is an intense feeling of agitation; the respiration are marked quicker; the inspiratory and expiratory efforts are powerful; the arterial tension is increased. All these symptoms are absent in nitrobenzole poisoning, as far as I have observed.
Since the red blood corpuscles have primarily a respiratory function, it follows that their destruction will be attended by breathlessness after exertion, which is invariably a symptom of nitric oxide poisoning.

It may be contended, we need not presume any direct of the poison upon the tissues or respiratory centre, to account for this usual symptom: the dyspnoea being the result of anemia, caused by the destruction of the red blood corpuscles. In this respect, these cases seem closely allied to toxicous anaemia. In both, the poison is hemolytic in character. A large decrease in the red blood corpuscles takes
Place, whilst the percentage of Hemoglobin remains relatively high.

Hunter, British Medical Journal, August 1889 says,

When the red corpuscles are killed by a poison, as for instance Nitroprussic acid, the leukocytes seize upon the corpuscles, and remove them from the circulation in the course of a few hours.

The source of the bile pigments in the urine is the Hemoglobin of the blood. The daily excretion of these pigments points to the existence of some cause at work in the blood, leading to a certain destruction of Hemoglobin.
and presumably as the red corpuscles. One of the special functions of the liver, is to remove pigment (matter from the system according to Hunter, when the distinction of blood corpuscles is active, the Hemoglobin instead of remaining in the red corpuscles, escapes from them into the plasma, i.e. great part excreted by the liver as bile pigments.

With reference to the exchange of gases of the blood, the experiments of Flouquet are of great interest. He penis the blood in poisoning by nitrobenzole, loses its power of carrying, imparting color to the tissue, it becomes less energetic in removing carbonic acid.
The normal amount of oxygen gas, which the blood of a human will give up, is found to be 17 per cent, but in the case of a dog, which had been poisoned with Nitrobenzole, was only 1 per cent. During the expirations from which the dog suffered, the carbon dioxide was greater than the normal amount. The arterial blood, which should have given up 30 per cent of Carbonic Acid, only gave up 9 per cent. Medical Chronicle May 89.

A condition similar to this case, is also found in poisoning by Aniline, some of its products, such as Antifelin, Antisprin, Pyridin, probably Methacetin, Phenacetin. It is asserted that Nitrobenzole is changed by Oxidation and Reduction in the body into Aniline and Nitrobenzole.
into one or more of the Phenyl 
Diamine perox. From I have 
believe that Aniline may undergo 
an oxidation at the surface of the 
body. Sibree however strongly dissent 
from these opinions, & states that 
Nitrobenzol in the body is neither 
converted into Aniline nor 
Hydrocyanic acid. It is accepted 
Lethaby's view, that Benzole only 
acts as a poison after it has changed 
by a process of reduction into Aniline, 
& may find that it combines not 
only with the Hemooglobin of the 
blood corpuscles, but also with the 
serum. The similarity of 
the symptoms produced by 
Nitrobenzol, Dinitrobenzol, Aniline, 
& its derivatives seems to point to 
the fact, that all these cases of
Poisoning have a common basis, whatever it may be.

Lethez says, In rapid cases of fatal poisoning of Dinitrobenzole it can be detected in the body readily, but in slow cases the material may be so entirely changed, or eliminated, as to escape observation. A question still undecided is the exact chemical changes which Dinitrobenzole undergoes during the process of reduction in the body.

It would also seem possible that these substances may form nitric acid in the blood. A dog has given 3-tablespoon 15 grams of Dinitrobenzene. At autopsy, the whole mucous membranes of the intestinal
Tract covered with a yellow layer, which chemical analysis proved to be Picric acid. It may be that the yellow colour of the skin and conjunctiva, which is noticeable in men suffering from nitrobenzole poisoning, may be caused by Picric acid staining.
The reports of experiments upon animals with these substances are most contradictory.

"Selyez found that death took place in rapid cases of poisoning, in from twenty-five minutes to two hours. In slower cases symptoms did not come on nineteen to twenty-four hours had elapsed from the time of taking the poison. In these cases death was delayed four or nine days. "Tonic palsy," in frogs, paralysis only has been seen, but in warm-blooded animals, twitchings in the limbs, and epileptiform convulsions have been observed. Each once saw tonic spasm of the flexors of the upper extremities. Spasms of the muscles must
I think the case in the human subject, & convulsions, though they have been reported to me, I have never witnessed. I have only observed tremors in one case, probably due to a weakened condition of the muscles, or sustained contraction not being possible. It may have been caused by some deficiency in the efferent, or efferent fibres of the reflex arc. The stimulation of holding a small object between the fingers not being enough to produce a continuous tonic contraction.

In some experiments I have performed upon frogs, & exposing them to the effect of Dinitrobenzol, for a time, varying from half an hour to three hours, a marked
Pericardial symptoms were observed. The heart action after an initial rise became very slow. The respiration, which were at first quickened, became flickering, spasmodic, or absent. There was much muscular spasm, followed by an amount of paralysis, far too great to be put down to exhaustion. The animals so affected could be crushed. At other times, the least noise, or even a breath of air brought on spasms almost like those of strychnine poisoning, but not nearly so marked. In some cases the fore legs were paralyzed, whilst the hind ones suffered from extreme spasms.
The pathology of these cases of poisoning is as controversial a theme as in (The chemistry. This poison acts on local action upon the mucous membranes when taken internally. Their effects upon the system prove them to be allied to that mass interesting, a recently described group of nervous diseases, to which the prominent attention of the profession has recently been brought, by the writings of Buzzard, Ross, Frischfeld, Virée, and Vaillard. This group is known by the name of "peripheral or "multiple neuritis." This "neuritis" is found in cases of poisoning by Alcohol, Arsenic, Lead, and Bisulphide of
Carbon. It accounts for many of the symptoms seen in Syphilis, Syphilitis, Rickets, Leprosy, Diabetes, some of the fevers, and perhaps Rheumatism and Gout. It consists of a "Parenchymatous inflammation of the peripheral nerves, or an interstitial degeneration of the nerve sheaths." Chronic Nitrobenzole poisoning chiefly affects or at least is most perceptible in the terminal nerves of the hand or feet, & is a distinct implication of the sensory, motor, & viscous motor nerves. The reason why particular poisons single out special portions of the nervous system, in preference to others, is at present entirely unknown. But the fact remains patent...
As evidence by Lauder Brunton:

"In treating Antiphlogistic in poisonous doses, it produces all the symptoms of spastic Paralysis, and it is quite possible it may affect the lateral columns of the cord. The continued use of Ergot produces sclerosis of the posterior lateral columns. The Haloid derivatives of the Benzile group when administered, act upon the brain, a final chord, and produce symptoms of disseminated sclerosis. He, and each have also found that they cause an affection like ataxia, \( \text{Ataxia} \), the symptoms of which may be

Peripheral Deformity, in contradistinction to a Central lesion, in cases of poisoning by Nitro and 2 Nitro Benzole."
are in my opinion still unmarked. The neuritis may lead to irritation or degenerative changes in the nerve, and may affect not only those of the extremities, but also those of the trunk, or viscera. The want of uniformity in the distribution of the symptoms; as for example; "the area of one nerve, or only a portion of one nerve is mainly affected," this again may be symmetrical, or unilateral; "the association of paralysis, or paresis with hypesthesia, occasionally anaesthesia." "The wasting of individual muscles, a group of muscles." "Sometimes symptoms of ataxia, or pseudo ataxia." "The absence of either bladder or rectal troubles, or the
An implication of the celiac sympathetic region, as we may add the uncertain condition of the superficial, & deep reflexes. These several points bear much doubt. That the central nervous system is alone responsible for all the symptoms described. It must also be remembered as possible, that nitroglycerin may be a muscle poison acting directly upon them, without the intervention of the nerves. Brunton supports this view. Figure pays an injection into a bloodless, & innervated muscle causes contraction in a few seconds, & produces them in the heart after a previous diastolic standstill. It may affect the spinal cord secondarily by
*As will be seen from my foracious arguments, I do not accept this view (letter)*
The passage of the process of the
inflammation from the periphery, 
this process lasts for proof. There is a wealth of competent opinion 
supporting the view that the 
Spinal cord is directly implicated.
When nitric oxide is absorbed by the 
lood, it produces an area of the 
Medulla Oblongata, its 
subsidiary centre in the spinal 
trunk & causes the congestion 
which is usually present before & 
after death. x
nethers
Pharmaceutical Journal 1863
"Caco, it is evident, is powerful 
"Narcotic." It does affect the 
brain, in strong cases by the 
mental lethargy, apathy, & 
drowsiness, which are so well 
marked in chronic cases, & the
deep coma which occurs in severe poisoning. Reynolds says, "death is due to coma in most cases, occasionally it may be caused by convulsions." I am only aware of one death I have seen. Ibrahim was brought about by failure of the heart action. The man never developed convulsions, he had recovered consciousness after a long period of deep coma, but died pining from the exertion of being lifted out of his bed. Dr. Reidon thinks the immediate cause of death is massmotor Paralysis of the Heart.
Vestigial Appearances
Its cavities were full of blood clots excessively soft in consistency. The blood throughout the body was exceptionally fluid. The liver was very pale. The fluid matter of the vertex of the brain was dry and opaque. The veins of the back matter in the varietal region were tense, distended, full of black blood, especially those of the right side. The veins were not distended in the parietal, temporal, frontal regions, nor at the base of the brain. The blood was characteristically fluid, it immediately returned into the veins when the pressure of the finger was removed from them. The brain was a dull grayish than usual. The other organs seemed normal. Lethargy was found post mortem a bluish color of the skin.
congested brain, with the ventricles full of bloody serum. He says, the blood is everywhere black, and thick. He describes the lungs as being dark colored, and the liver of a purplish tint. He says, there may be the smell of nitro benzole in the stomach, brain, and lungs, if the death is rapid, but in other cases this is absent, and analysis cannot detect it. Sometimes aniline may be found in the brain. This description is entirely at variance with the appearances observed in my case.
Diagnosis
The prognosis, in cases of poisoning by nitro-di-nitro bengole is influenced by the actual amount absorbed, the time during which they have been exposed to it, and the physique health of the workers.

The headache, general malaise caused by small doses are usually recovered from in the course of a few days. I find that a weeks absence causes them to again. Their energy and appetite; the urine becomes porous in colour, but aniline has been found after a longer period. The anaemia is a very persistent trouble. If the percentage of blood corpuscles becomes greatly decreased, it takes months to restore it. The peculiar dusky tint of the skin can be detected by those who are conversant with.
The symptom, four or five months after. It is possible that a certain amount of pigment may be deposited in the skin, internal organs which is only removed after some years. In more acute cases when the focus cerebral function are implicated some hours elapse before consciousness is restored. Personalized brain known recover take place from insensibility which have lasted in periods ranging between eight to twelve hours. In my experience of one fatal case, consciousness returned after about thirteen hours of insensibility, but the man died suddenly half an hour afterward. Some months elapse before muscular power is thoroughly restored, but the symptoms of the disease
gradually disappear. It is an interesting question whether the profound anaemia does not leave its mark permanently upon the constitution. I am disposed to think that in the generality of cases it is absolutely recoverable. The men often affirm that after a time they become accustomed to the effects of the poison. By experience I can vouch for this: out of eight men, two or three who go to the work for the first time, come for treatment in about a fortnight since, but I do not see them again for months after. I attribute this to their want of care that knowledge (in the manipulation of the poison) to other the symptom an
New, it strange to them, but eventually they come to regard them as a necessity of their work, known from their own experience, that in a few days leave from work, they will feel away. It is to be suspected that any natural weakness, work or aggravated by working such poisons. As a matter of routine, they are always examined before they are allowed to work, or any case of chest, either of heart or lungs are rigid excluded. Preexisting anemia must necessarily be made worse. A case of "albminuria" which had been unwittingly admitted, worked for many months, although he
occasionally had pleurisy attacks, I did not observe any aggravation of kidney mischief. The only case of death was a man who suffered from a weak, dilated heart.
Precaution
Big men who are physically strong should be employed in factories where they are exposed to nitric or dinitrotoluenes, or are required to handle these substances. Obese men with a speedy flow of demasculine blood, full its effects, are poorer able to recover from the anemia which their adoption produces.

The diet should be liberal, easily assimilated, and largely nitrogenous. A nitrogenous chyle is to be recommended: (1) to build up the tissues which are so greatly wasted; (2) it has a tendency to cause the blood to become more acid, and thus less easily acted upon by reducing agents. It is customary I believe in all border
When these materials are manufactured to provide milk, for the use of the employees, it probably because it is a food easily digested it may also have some slight action in controlling the poison. Alcohol, in any form should be partaken of sparingly, as it is a powerful solvent of the poison. The material should be touched as little as possible with the naked skin. The hands, face, or other exposed parts should be washed after work, especially if this precaution necessary before eating. This requires a plentiful supply of water, soap, and toilet articles. Special clothing should be provided, and washed at frequent intervals.
When it becomes permeated with the substance. Respiration, &
gloves should be worn when possible.
Whenever practicable machinery should be used to mix the materials,
also to file, empty, & clean out the pans.
& especially should flues be provided,
if necessary with artificial currents,
to carry off the heated vapour.
Ventilation should be thorough & free. The air in the work rooms
ought to be dry, as moisture in the
atmosphere causes a great increase of sickness. A low temperature
is generally followed by a proportionate
decrease in the sick rate. In the
winter, the number of invalids is
very small, in the hot summer
months it is greatly increased but
even then the proportion varies.
Men should not be allowed to work more than six or eight hours consecutively, if exposed to the influence of the poison, or even that length of time should not be persisted in daily unless unavoidable. Those who are constantly employed ought to refrain from excessive muscular strain which this poison unfit for.
treatment
There seems to be no certain antidote for these poisons. If taken into the stomach they often remain concealed for some time, and therefore may be removed by an emetic, or washed out of the stomach promptly with very probability of recovery. The stomach being emptied, it is advisable to give a purgative, as which, the saline cathartics are to be preferred. Pills, fats, and alcohol are contraindicated as remedies. When these poisons have been introduced into the system either by respiration or absorption, the symptoms as they occur must be combated. The faradic battery should be used to stimulate, to cure the patient, with pinaspermia to the chest, a friction of the limbs, a stimulant in the form of ammonia.
may be given. Wells administered
Camphor, 9 injected ether with
good effect. Transfusion may be
performed, artificial respiration
should not be neglected.
Use in Chemistry
Nitrobenzole C6H5NO was first made from benzene in 1834 by Nitric acid, and was also obtained by John Leach, in 1842. He exhibited it as a dinitrobenzole, at the meeting of the British Association held that year in Manchester. It is a light yellow, strong refractive liquid having a boiling point of 188°C. Its smell is pungent, being similar to that of bitter almonds; it possesses a sweet and burning taste. It boils at 150°C at a low temperature and solidifies in large crystals, melting at 30°C. It is freely soluble in water, but readily dissolves in alcohol, ether, benzene, and concentrated nitric acid.

Nitrobenzole was first introduced into commerce by Collas, under the name of "Essence of Turban," or artificial oil of bitter almonds. G. Mansfield in 1874 patented a process for its preparation.
from coal tar. It is now prepared on a very large scale. Its chief uses are, the manufacture of the explosive "Nitroite," the painting of rocks, & flavouring of confectionery. It is exclusively in the manufacture of pure aniline blue, black, and magenta dyes.

Dinitrobenezole, $C_{6}H_{4}(NO_{2})_{2}$, has a boiling point of 135°C. It melts at a temperature of 90°C. Its principal uses are in the manufacture of the explosives Nitroite, Bellite, Securite, & of some dyes.

Chloro nitrobenzole, $C_{6}H_{4}ClNO_{2}$, boils at a temperature of 236°C. It melts at 45°C. It is not used commercially, except in the manufacture of...
Voburite.
This explosive is composed chiefly of Chloro nitrobenezole, 9 in small proportions of Dinitrobenzole, with a very small quantity of Nitrobenzole. This latter being only amounting to 1 in 10 parts of Dinitro benzole. Chloro nitrobenezole is probably not acutely poisonous: 9 ce it only boils at 236° cent. and melts at 45°, little of its vapour is disseminated into the air, during the process of the manufacture of Voburite. The pamp may be made of Dinitrobenzole, which is rarely raised X to its melting point at 90° cent. We are therefore forced to
The conclusion is, that it has little, if anything to do with the poisonous symptoms described in the preceding pages. If this reasoning is correct, we must infer that the clinical picture I have discussed arises from the absorption of nitrobenzole, which has escapes the process of chlorination. In a liquid at ordinary temperatures, it gives off its vapour readily when warmed.
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White Traditones J Sullivan 1859
Reynold Mid Chronic 4th X Aug. 1859
Knight Case of Sauberkeit Toisoning
Laran Jul 13, 1859 Case of Pobreute Toisoning
Abstract of results of experiment on two pine-cone scars weighing together 124.5 grammes. Duration of Experiment 121 minutes (4:12 - 6:13 Pm). Ventilation current 360 litres per hour. During interruptions only three intermittent determinations were made.

A. Heat Production Losses

At 4:14.3

\[
\begin{align*}
\text{Temp. of air chamber} &= 22.2^\circ C \\
\text{loss through copper vessel per minute} &= 0.06380 \text{ cal} \\
\text{by air current} &= 0.00186 \\
\text{Calculated loss by evaporation} &= 0.01717 \\
\text{Together} &= 0.08283 \\
\end{align*}
\]

At 4:55.5

\[
\begin{align*}
\text{Temp. of air chamber} &= 22.5^\circ C \\
\text{loss through copper vessel} &= 0.06510 \text{ cal} \\
\text{by air current} &= 0.00186 \\
\text{Calculated loss by evaporation} &= 0.01717 \\
\text{Together} &= 0.08413 \\
\end{align*}
\]

At 5:15.5

\[
\begin{align*}
\text{Temp. of air chamber} &= 23.4^\circ C \\
\text{loss through copper vessel} &= 0.05922 \text{ cal} \\
\text{by air current} &= 0.00221 \\
\text{Calculated loss by evaporation} &= 0.01717 \\
\text{Together} &= 0.07860 \\
\end{align*}
\]

Average loss per minute = 0.08185 cal.

B. Respiratory Exchange

\[
\begin{align*}
\text{H}_2\text{O} \text{ given off} \quad 4:12 - 6:13 & \quad 3.510 \\
\text{Oxygen taken in} & \quad 3.180 \\
\text{CO}_2 \text{ taken in} & \quad 4.315 - 7.825 \\
\text{Oxygen of CO}_2 \text{ given off} & \quad 3.180 \\
\text{Oxygen absorbed} & \quad 3.190 \\
\end{align*}
\]

\[\text{Oxygen absorbed} = \frac{3.180}{3.190} = \frac{1}{1.02}\]

Loss of heat per hour

\[
\begin{align*}
\text{H}_2\text{O} \text{ given off} &= 4.911 \text{ calories} \\
\text{CO}_2 \text{ taken in} &= 1.740 \text{ grammes} \\
\text{Oxygen taken in} &= 2.140 \text{ grammes} \\
\text{Oxygen absorbed} &= 1.58 \text{ grammes} \\
\text{Total} &= 3.929 \text{ calories} \\
\end{align*}
\]
Abstract of results of a twenty-four hours' experiment of the respiratory exchange of four snails.†

The determinations were made every two hours, the results being obtained in the manner described on pp. 67-71 above. The manner of calculating results is shown in greater detail in the table on p. 71. The animals weighed together about 1100 grammes. Before being put in the apparatus, they had had no food since the previous day. The $H_2O + CO_2$ in the air of the room were estimated with every two hours with the small apparatus. The temperature of the room varied from 14.4° to 14.7°. Between each two periods there was an interval of about four minutes - the time required for weighting, replacing the animals. This interval is allowed for in calculating the results.

First Period, 5:30-7:30 P.M.

$H_2O$ given off by animals

† For assistance in this general other experiments I am indebted to Mr. Pembrey
In the above experiment the alternating rise and fall in the respiration seemed to be due to the air sent into the chamber being alternately more or less dry. This arose from a difference in the arrangement of the two measuring flasks. During the whole experiment the test flask of the one set of absorbing flasks did not vary at all in weight, while that of the other set only gained 0.07 gram.

The most interesting point in the experiment is the large increase in oxygen absorption during absorption of the meal. The O2 elimination is only slightly increased by the meal, yet this increase might be due to the increased muscular activity during the eating of the meal.