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Thesis,

for the degree of
Doctor of Medicine
on

"Paraldehyde
as a Pulmonary Sedative"
A Clinical Study
with Cases.

by

John William MacKenzie.
MB, ChB Edin. 1898.
"On the use of Paraldehyde as a Pulmonary Sedative"

When House Physician in Cardiff Infirmary in 1899, I was struck with articles in the "Lancet" of February 11th 1899, by Dr. MacGregor of the London Hospital for Consumption, and in that of March 18th 1899, by Dr. MacKie, Elgin regarding the value of Paraldehyde in such chest troubles as Asthma and Bronchitis, principally the former.

Of till that time, as far as I was able to determine, very little reference had been made on this subject in medical literature. Indeed Dr. MacKie seems to have been the first, as far as I can make out, to draw attention to the subject in the "British Medical Journal", 1893, page 65, in which he stated that he had used the drug with great success in cases of asthma.
there being moran inducing sleep.

On referring to text books of medicine
and Therapeutics of quite recent date,
such as

"Clifford Allbutt's System of Medicine

"Fagg & Pye Smith's Medicine" 1902.

"Twentieth Century Practice of Medicine

"Others Practice of Medicine" 4th edition

"White's materia medica" 1898.

"Mitchell Binnie Materia Medica and
Therapeutics" 1899.

"Hale White's Materia Medica and Therapeutics" 1902.

"Burney Veo's Manual of Medical
Treatment" 1902.

I found absolutely no reference to
any action in bull diseases. All the
writers stated that the drug was a mere
hypnotic and used exclusively as such in
medicine.

The only text book in which I have
found any reference to its further
action is Hale White's "System of
Therapeutics" 1902. In which its use in asthma is indicated briefly
In the medical journals, one finds
Much earlier reference to its use in these pulmonary affections.

Apart from Dr. MacKie's original paper (ante), and additional remarks on its value in the "Lancet" March 18th 1899, we find it recorded by Dr. Hearder in the "British Medical Journal" 1896, P. 725, and later by Dr. MacGregor, who writes in the "Lancet" February 11th 1899, and in the "New York Lancet" April 1899, regarding the value of the drug.

The "Practitioner," September 1901, gives an extract taken from MacKie's and MacGregor's papers written in 1899 on this subject.

Dr. Adam in "Glasgow Hospital Reports" 1901, page 178, in a paper on the nature and treatment of Asthma, says that Para-phenyl-hyde is often successful internally.

Dr. Byron Bannwell in his "Clinical Studies," January 1st, 1903, page 112, speaks highly of this drug, saying that in many cases it not only relieves, but prevents the attacks if given early.

Therefore seeing that the literature on the subject is comparatively scanty
I feel myself justified in adding my experiences to the testimony of the above mentioned practitioners, as the drug in its capacity as a sedative and an expectorant in Bronchitis and Asthma deserves wider fame.

To obtain a better knowledge of Paraaldehyde and its action, let us study its chemistry and Pharmacology for a little.

It was originally discovered by the German Chemist Kadenbusch. I

In order to understand its preparation, let us turn first all to the preparation of its antecedent, Acetic Aldehyde or simply, Aldehyde.²

This Aldehyde is formed by taking three parts of Potassium Bi-chromate & dissolving it in twelve parts of water. Put the solution into a retort. Then add three parts of Alcohol and four parts of Sulphuric acid in mixture through a funnel. The Aldehyde passes out through an inverted condenser containing water at 30°C and is condensed in a tube surrounded...
with ice and salt. Instead of condensing, the aldehyde is allowed to pass as an escaping gas through dry ether. Then ammonia vapor is passed into the ether and a compound of aldehyde and ammonia called aldehyde-ammonia \( \text{C}_2 \text{H}_4 \text{O} \cdot \text{NH}_3 \) separates out in cubical crystals. This mixture is dissolved in three parts of water and distilled with a mixture of three parts of sulphuric acid and five parts of water. The vapor is passed through a tube of calcium chloride warmed to 25°C. and is then condensed in a receiver at 0°C. for thus getting aldehyde formed.

Paraaldehyde is derived from this aldehyde by

1. Adding a drop of concentrated sulphuric or nitric acid to it, an almost explosive action taking place, the aldehyde being polymerized into paraaldehyde.

2. More usually by adding sulphuric acid to the aldehyde, and in a few days it changes into paraaldehyde. The latter is a clear colourless liquid.
with a characteristic ethereal odour.
It congeals below 50°F. and boils at 124°F.
It has a specific gravity of 0.998 at 75°F.
Its vapour density corresponds to the formula \( C_6H_2O_3 \), and has the following structure:

\[
\begin{align*}
&\text{CH}_3 \cdot \text{CH} \cdot \text{-O-CH} \cdot \text{CH}_3 \\
&\quad \downarrow \\
&\text{CH} \cdot \\
&\text{CH}_3.
\end{align*}
\]

It has a burning taste at first and then a cooling one.

Penkaz and Kipping hold that it has none of the ordinary properties of an aldehyde and that it does not probably contain the aldehyde or \( \text{CH}_2O \) group.

Its solubility is 1:100 by weight in water, at 60°F. and is less soluble in hot water.
It mixes easily with spirit or methanol.
It gives a faintly acid reaction and should be kept in corked, well-stoppered bottles in a cool place. It is very
readily transformed into aldehydes by distilling it with sulphuric acid.
Pharmacology.

As I have already mentioned, the literature on this drug is somewhat scanty and on looking through such books as Cushing's "Textbook of Pharmacology" 1902, Halé White, Whitla's "Thomson's materia medica," very little is to be found regarding its action.

However, I find that fairly complete accounts of its more important actions are given in valuable papers by Gordon of Aberdeen University, 1889, and by Richard Friedländer, 1893. There is also a short account of the drug in Halé White's System of Therapeutics, 1902.

The first person to experiment on the action of the drug was Cornelius of Palermo, who worked in Strasbourg University Laboratory under Schmerling in 1881. He experimented both on animals for himself and found it was a hypnotic of no mean power. The results published by him were the means by which the drug was first brought before the medical profession.

Externally, it produces a slightly
cooling sensation owing to its quickly evaporating.

Internally it has a disagreeable and burning taste, which often persists until the following morning. The burning is experienced not only on the mucous membrane of the tongue but also on that of the fauces, causing dryness and intense thirst. Its colour is peculiar and characteristic of itself. Many people cannot tolerate it on that account especially in private practice. In some cases it disorders the stomach. Rank & Berger reported cases in which it were caused retching and vomiting. However, Congruent Van Hoorden & Morseell hardly ever saw any manifestations of such a kind. Gordon and Strachan show that there was no loss of appetite and no increase in thirst and that it did not disorder digestion.

Friedlander says that the drug ought not to be given in inflammatory conditions of the stomach and oesophagus unless freely diluted owing to its irritating effects on the mucous membranes.
16. Demonstrate that it is not the quantity of the drug swallowed which upsets the stomach, for he found in some cases that with small doses, caches of the stomach and vomiting were set up. Gordon found that the drug accelerated digestion of fibrin, that the more paradolhydr added, the quicker was digestion and the less fibrin added, the less quickly did the process take place.

17. Cramer however found the reverse happened for with a concentrated solution of paradolhydr 1:50, a definite delay in the action of artificial gastric juice on fibrin took place and on the pancreatin, in very dilute solution. Gordon found that it was gently laxative in a few cases (in man). Bokai & Baresi found that it caused excessive intestinal peristalsis in animals due to paralysis of the inhibitory centre for the intestines. Therefore, Hoyt warns us against its use in gastric and intestinal disorder.

18. In moderate doses, from one to two drachms
it does not depress the heart but it diminishes the frequency of the pulse. Friedlander on reviewing the literature on this point says that a definite, though trifling action is exerted in man, mostly of the nature of a slight slowing, very occasionally getting slight distortion and irregularity of the pulse. 

Vivant finds that in animals, small doses accelerate the pulse and 

Dunquand found that large doses retarded it. Gordon finds that the blood pressure is only slightly reduced by small doses, larger ones doing it more so the larger the dose but only after distinct slowing of the respiration. 

Bozai & Banesi found that the drug occasionally produced vasodepression of the peripheral vascular system, central in origin, mostly in cases where the drug had been given in large doses and for a prolonged period.

The nervous system.

It is powerfully hypnotic in small doses usually in doses of overdosage
but sometimes from 30-40 minutes are
sufficient but always in cases without
pain. It quickly in acting as such,
usually in 10-15 minutes. It produces
quiet restful sleep without dreams
and the patient is roused without any
confusion being manifested. Once
they are aroused, they do not tend to
drop off to sleep again.
There is no marked period of excite-
ment before it acts as such. Although
some have reported that in cases where
it fails to act it produces some mental
excitement and restlessness.
It is not hypnotic in persons who are
not suffering from insomnia except
in large doses. As such it acts
principally on the cerebrum and also
slightly on the medulla. In toxic
doses it paralyses the anterior cornu
of the spinal cord and therefore abolishes
reflex action. It also acts by
diminishing peripheral sensation
the nerve endings, having their
sensibility dulled and thus it acts
as a sedative and slight Analgesic.

24
25
26
It speedily diminishes and in large doses destroys the excitability of motor nerves and equal doses of the drug diminish the excitability of motor nerves sooner than that of muscle. It does not cause any headache. 27

It is not a very poisonous drug. One person having taken a dose of three and a half ounces by mistake and recovered consciousness in thirty-four hours after treatment. 28

Muscular System.

Gordon found that small doses first excited, then diminished, the excitability of muscle; that large doses speedily destroyed temporarily the excitability; that there was a tendency to complete recovery in muscle after a sworn to a small dose, but seldom after a large one, and that curarized muscle showed an increased excitability over non-curarized when treated with equal doses of Paraldehyde and equally stimulated.

Thus, by its power of diminishing the excitability of motor nerves and
of muscle fibres, especially non-striped and of diminishing the sensations of peripheral nerve endings, it becomes quite an efficient antispasmodic.

**Urina System**

Carnelloci, Morselli and Syon find that Paraldehyde acts as a diuretic. Lich holds that it is not. Gordon however has investigated the point and finds that

1. It causes an increased secretion of urea.
2. It does not affect the chlorides.
3. In some of his cases it increased the secretion of the fluid of the urine, but that in the majority of his cases the fluid was diminished. He found that the drug was not excreted unchanged in the urine, the odour being perceived in about four hours, especially if it were given in large doses.

He does not irritate the kidneys, for in cases mentioned by Krafft-Ebing's last row in which albuminuria was found after the drug had been given, if there were casts indicating chronic.
Inflammatory changes were found in the skin.

Gordon found that in some cases there was a tendency to purifying, after the exhibition of the drug, which was controlled by atrovent.

Occasionally erythematous rashes are seen in persons who have been taking the drug for some time.

Langreuter finds that it sometimes produces peripheral conjunctivitis.

Temperature

The effects of this are tripling, mostly causing a fall of from $2-3$ to a degree. Benzen noted a fall of $1.05^\circ$ in one case, according to Truquand, an overdose of the drug causes the body temperature to fall while the elimination of CO$_2$ is lessened, and the colour of the blood is changed, due, as he thinks, to methaemoglobin. Hennegue 32 homens says that the change in colour is due to reduced haemoglobin.
Respiratory System
The well-marked odour of the drug is quite perceptible in the breath of the patient a varying time after taking it. Gordon says that it takes about eight hours to do so; but from what I have observed myself, after making patients wash out their mouths on swallowing a dose (in Cardiff Infirmary), I think the odour can be perceived in from one half to one hour afterwards.
Respiration is slowed and becomes steady after and tranquil, after full doses of the drug are given, it appearing to act on the depression centre in the medulla.
Wood found that toxic doses in frogs, produced death by paralysis of the respiratory centre, and that in rabbits 35-40 minutes induced profound sleep with diminishing respiration and finally death from asphyxia. This action is probably associated with the reduction of the Haemoglobin and to the lessened absorption of CO₂.
In respect to the above action, Friedländer says that Paraaldelyde should be avoided as a hypnotic in patients suffering from dyspnea as it reduces respiratory frequency and may induce asphyxia, growing as an instance a paper by Rollinson in the "Practitioner" 1888, P.341, where such an accident occurred.

He also states that the drug is contra-indicated in all diseases of the respiratory tract, especially in Phthisis with involvement of the Lungs, owing to the irritation produced by the drug on the mucous membrane causing fits of coughing.

This was the opinion of Van Noorden of Lanzow.

We find that we get the same results from the drug when administered per rectum as by the mouth. It does not seem to produce any marked craving for its continued use as morphine, Chloral Cocaine, or other drugs do. Only a few more cases have been recorded. Bokai says it is the physiological antidote to strychnia.
Such being a resume of the more important Pharmacological actions of the drug, culled from various journals, the finds that those which prove most beneficial in helping us in our enquiries are the actions on the Respiratory and Circulatory and to a considerable extent on the Nervous systems.

These are principally, "the slight slowing of respiration;" "the slowing of the pulse rate without any great diminution of the heart's action;" and the relief of spasm of the muscles by its action on the individual fibres and by diminishing the excitability of both them and of the nerves supplying them and by its diminishing the sensibility of the termination of sensory nerves in mucous membranes, especially as will be later shown in the lungs. It thus is of benefit in relieving dyspnoea, irritating coughs and by its antispasmodic action is a sedative in Asthma."
In reporting the following few cases out of a considerable number in which I have prescribed Paraldehyde, for I have used the drug extensively in the last two and a half years, while in practice here (Wishaw), they are typical illustrations of the beneficial action of the drug in these diseases.

I find that they divide themselves into three main groups.

A. Those of Chronic Bronchitis with acute or subacute exacerbation.
   This group subdivides itself into
   
   A. Cases of Primary Chronic Bronchitis without or with cardiac complication secondary to it.
      These are six in number. Four males and two females. All advanced in life.

   B. Cases of Chronic Bronchitis secondary to cardiac disease and more of the nature of secondary congestion in the lungs due to backward pressure, but with all the symptoms...
of bronchitis.
Three are three in number, all males.

The second group consists of those suffering from bronchial or asthmatic asthma, that is asthma in which there is a complicating element of bronchitis.

The patients are four in number and all were subject to the condition for a long time, except Case three, whose second attack it was, but who had had repeated attacks of bronchitis previously, and indeed all of them were subject to the latter.

Three were females, the fourth a male & son of Case three.

Cases of reflex coughs, due to irritation of some branch of the vagus, e.g. as in the case at example, due to irritation of the trachea and large bronchi by enlarged bronchial glands.
Group I,

Case 1.

J.K., male, age 71.

Subject to Chronic Bronchitis for many years. He is very susceptible to catching cold, often resulting in acute and subacute exacerbations of the disease. He had as well some Aortic valvular disease, there being a loud rough aortic systole & a diastolic murmur, with well marked hyperastheny of his left ventricle. No evidence of enlargement of his right ventricle. He did not suffer from dyspnoea, had no oedema, nor enlargement of liver or albuminuria. The aortic lesion was fully compensated.

He was seen in October 1899.

Had taken a chill, which had brought on an increase of cough. Temp. 101.5. Pulse 100, Resp. 30.

Complains of pain under sternum aggravated with coughing, with some rawness & oppression in chest. He had numerous ronchi all over, with
A few medium expectorations. Effusion was
slowly brought up with difficulty. No
cough in chest. Tongue casted hard
sight anorexia.
Ordered linseed poultices to his chest and
3½ Carlsbad salts. Statum Sumendum.
and to take the following mixture
R1
Paraldehyde \frac{m}{x} \times 4
$\xi_{2} \times \frac{m}{x} v$
\text{ago ad 3 p.}

\underline{5 o 8}
Take talcum every 4 hours.
Three doses of this gave him marked
relief. He said that he felt the pain under
sternum very much easier and that
the cough was very much diminished
in frequency and severity.
In twenty four hours the spit began to
come up more easily but was not in-
creased in quantity. It was looser
but not watery. His chest contained
fewer nonchlo. Expectorations were
in stigmas. He looked very much
easier. In two days, his temperature
was normal the man out of bed for
two hours at the end of five day.
His cough was now much better and his general condition much improved. He objected strongly to the first two or three doses, owing to the taste, he saying that it made him sick. However, owing to the great relief he speedily got from taking the drug, he persevered in taking it, with the result that it undoubtedly cut short his attacks of bronchitis, as he usually had to remain in bed for about ten days with an attack of similar severity.

Since that time he has passed through several similar-like attacks whenever he felt one coming on, the cough increasing in severity, he at once resumes taking the medicine and gets speedy relief. He declares that no medicine had helped his condition so much as the preparations he had used.

This patient was one of the earliest I tried the drug on and its great benefit in this case led me to go on with it in others.
Case II.

J. M. 60 yrs. Baker. Used to work as a miner for many years. Subject to recurrent attacks of bronchitis for last 15-20 years.

I saw him on October 15, 1900. Had been ill for four days previously, with exacerbation of his cough due to his settings wetting.

He was thin, weak man, hollow, in bed.

T = 100 F. P = 92. R = 32.

Cough incessantly, terribly hurting his forehead (frontal sinuses), and sides of chest along attachment of the diaphragm.

Expectoration bloody every cough.

Chest hand-shaped, hyperresonant.

Breathing, harsh, wheezing with humerus medium rales at high butched bronchi.

Tongue coated, appetite nil.

Ordered him Tincture of Potash 31d. am.

Heft day 7.16

Elevated himself as feeling greatly relieved, said his breathing was much easier and freer. His Temp = 99 F.

P = 90. R = 28.

Cough is much less hacking, not
hurting his head and sides to such an extent. He said that his expectoration was coming up more easily, he not having to "hack" and strain himself so much to get rid of it. He said that after three doses of the mixture, he felt his chest easier and less troublesome during the night, allowing him to get about five hours sleep, off and on during the night, which he had not had for the last four nights owing to the hacking cough, distressing and hurting him so much.

Consultation showed that the rales were more copious, but that the roentgen was less pronounced in number and size.

Hashing for several hours today.
Cough much better, just a few occasional
paroxysms. Expectoration less. Very
few rales, & ronchi in chest now mostly
at bases of lungs. Says that he feels
very much better and that he seldom
recovers so quickly from such like
attacks.

Since then he has hashed through
three similar attacks, in February,
May & in October 1902. He was given
the Parallelol at intervals in each,
indeed he begged for it, as it had done
him so much good previously.
Each time I got the same satisfactory
result from its use, by its so speedily
relieving the tightness of breathing
& causing the Cough to be diminished
in severity, and allowing the tough
phlegm to be expelled with ease.
A. C. 64 yrs. male.

Has been the subject of Chronic Bronchitis for many years, affecting him so much as to incapacitate him for work, owing to incipient secondary cardiac changes.

He is broken down, capable of doing very little work. Dyspnoeic, face slightly cyanosed, fingers clubbed, occasional oedema of ankles.

Suffers from constant short cough often paroxysmal, accompanied with frothy spit. He gets attacks of subacute Bronchitis two or three times yearly.

Was seen by me in November 1900 for the 1st time. He was suffering from constant paroxysmal cough with some dyspnoea. Temp. 100.2. Pulse 88. R. = 30.

Nemasegnum Paraldehyde NXX

Hourly, a few doses of which had a very soothing effect, by diminishing the severity of his paroxysms of coughing and they becoming less, the expectoration being easily brought up, no tightness...
of chest, his breathing a good deal easier.
Two days being quite sufficient to
accomplish this.
He undoubtedly was greatly benefited
by the use of the drug, the severity of the
attack being greatly modified.
Since then he has passed through
several such attacks, for which
he was not attended; but he
sent up to the surgery to have his
"old bottle" prescribed again for them
as he had such faith in it.
He says that at the beginning of an
attack, if the headache is very tough
and scanty, a few doses are quite
sufficient to allow it to come up
easily.
Has suffered from Chronic Bronchitis for many years, with occasional acute exacerbations. Stout florid old lady, always has got slight short cough, has occasionally some shortness of breath on exertion and some occasional oedema of the ankles especially by the evening.

Seen April 1st, 1902.

Says that she got a fresh dose of cold yesterday. Cough had been very troublesome during the night, keeping her from sleeping, owing to the constant hacking cough which hurts her chest. Very little expectoration and very cough.


Chest: Hyperresonant on percussion. Resonating cardiac dulness due to emphysema of lungs.

Breathing, very harsh venereal all over chest, almost masked with medium fluid sonorous bronchi. Not many râles heard. 7 medium type.
Cough constant short, shuffling and very often hoarse. Pain, burning in chest.

Heart 80, seems somewhat dilated on right side. Cardiac sounds muffled & weak. Initially masked by emphysema. No murmur heard. Slight oedema legs.


By 10 a.m. Digitalis y:x
Sph. Ammon Acrobat y:x
Paraldehyde y:xx
Sph. Armat y:xv
agg ad 3:1

4 hourly.

and ordered poultices to her chest.

2nd

Feels much better. Passed away good night. Slept for two and three hours at intervals. Cough not nearly so troublesome, not hurting her chest to such an extent. Her breathing was easier, not being nearly so tight. No requiring to make so much effort. Her skin was somewhat cooler.
And coming up with much less effort and more energy.

Consentulation showed that the bronchi were not so numerous as formerly but the rales were increased.

Seeing that she was better, hot camphorated oil was ordered to be rubbed on the chest & frontabing stirred.

3rd


4th

Passed a very good night, slept well. Cough troubling her very little indeed during the night and only occasionally in the morning. No more aspiratory wheezing to be heard. Chest now much cleaner. Feeling stronger in herself. She says that this medicine which the
has been taking has helped her Bronchitis more than any she previously had had. It seemed to relieve the tightness & difficulty of breathing. And as well it seemed to sort the cough and allow the expectoration to come up.

She was convalescent very speedily & in four days' time was able to attend to her little shop.

She said that previously such an attack usually kept her at home for from 10-14 days & that she felt weak & useless for a few days after that but that after this one she was able to go about much stronger. She thinks that this was due to the tightness in the chest and the hard cough being so speedily eased.

Since then she has had several such like attacks, nearly all of the same severity & duration for which she takes Paraldehyde alone without any Digitalis, getting the latter only if her heart seems weak & I have great satisfaction in seeing the condition so greatly helped by the drug.
FEBRUARY 56th, OCTOBER 1902.

Patient is a small emaciated woman, slightly built. Always had been healthy until last several years, since when she has had several attacks of bronchitis. At the end of October 1902, she caught cold which occasioned some cough. She continued at her household work however. On 2nd November she took to bed owing to sudden severe acute pain in the left side over her heart. "Catching her breath". When seen on that day, she was found to have some dry pleuritic friction over 3rd, 4th, and 5th ribs in left anterior axillary line. Temp. = 100° F. P = 104. R = 30. She was coughing considerably, the cough being short and dry. Very little expectoration coming up. The chest on auscultation also showed numerous medium vibrations with fine rales. On auscultation allowed chest, back and front. The breathing was harsh. Vesicular sounds were heard on one side. The side of the chest was given an mustard.
8th. R/ Ammon Carb 9 gr

Vin Theca 1/4
Bip Ammon Aetat 3 gr
8 gr Toluene 3 gr
2 oz Camphora ad 3 gr

4 hourly.

As her expectoration was so tough, she was frightening to give her any Osmin to relieve the pain in the chest in case it rendered the phlegm tougher and thereby increase the cough.

The pain in the homemaker was greatly relieved by poultices.

When seen next day the phlegm was much thinner, the homemaker a good dealer in the cough homemaker was very hacking still and expectoration no loosen. Her temp. = 99°F.

Poultices were continued.

5th. Pain in chest gone now. Can take a deep breath without causing any degree of pain.

Her cough homemaker was as severe as ever as her expectoration was very tough and she required to cough to strain.
to much in order to get it up. She had slept very little during the night on this account. I therefore added twenty minims of Paraaldehyde to each dose of the mixture, and administered the mixture she was taking every four hours.

When seen next day, she said she felt even so much better. She had slept well and had coughed very little indeed, and that after four doses she noticed that the phlegm got distinctly loose, and easier to bring up.

The ronchus in her chest was fremer, and the sputum coarser, and after a fit of coughing her chest got much cleaner than it had been before she was put on the Paraaldehyde.

She did not care at first for the drug owing to its taste, but after getting so much relief from the first few doses she persevered with it. She speedily convalesced, after this, the cough disappearing in about a week’s time.

I was very pleased with the result of the drug in this case, owing to the speedy relief which the patient derived after so few doses.
T/L. act 52. miner.

For past several years, he has been subject to attacks of bronchitis, contracted while at his work. For the last two years he has been getting short of breath and suffers more or less constantly with a slight cough. He is very liable to acute exacerbations of the condition, the least cold bringing them on.

1st Seen November 10th 1902.

Had been ill for the last three days, having caught a chill which brought on an increase of the cough.


Heart slightly irregular. No bruit heard. Slight dilatation of right ventricle.
Ordered Poultries to Chest overnight twenty minutes of Paraldehyde in syrup of orange every four hours.

11th. Patientathemeshimselfasbeing greatly better. He slept for several hours, as owing to the great relief from having to cough so often he was able to enjoy it. He did not cough half so much as on the previous night. He does not feel his chest nearly so tight.

Temp. = 100° still, P = 90, but breathing 26 per min., but still slightly rhot.

Patient is able today to take a longer breath. Respiration not nearly so wheezy. He said that he felt relief after taking the second dose of the drug. He also finds that the phlegm is coming up more easily than not to strain his chest in getting rid of it.

12th. He is much improved today. Breathing considerably easier, Cough much less, much easier on him, not hurting his chest now. Expectoration much looser & quite yellow, not watery. He had slept for a considerable part of the night.
and was able to do with two fellows only.

14 in. breath improved. Tray, normal.

R = 22 easy. Very little wheezing in chest. Pulse 80 per min. Cough very

much less frequent, not at all painful

and only coming occasionally in

haemoptysis. Chest very much cleared

very few sputum and rotenone.

Appetite improved and looking a great
deal better.

16 in. has been up for a few hours

today. Feels almost well. Still

confusing a little homuncle.

In a few days he was quite well.

Patient strongly expressed his opinion

that the drug had helped him very

much and rapidly, much better than

any he had had before as being subject

for several years to these attacks, he

had found nothing which had so

speedily given him relief as the

paracelschele. He said he found it

deceived the number of coughs and

it allowed the phlegm to come up

easily and it dispelled the tightness

in the chest.
The notes of this case are very interesting as the patient was the first I used the drug on, when House Physician in Cardiff Infirmary and as such I was able to take full and careful notes of the case and also notes of the patient's condition in a relapse which he took some months later when he was readmitted to the Infirmary.

J.B. aged 60 yrs. house liar.

Admitted March 12th 1899 to Cardiff Infirmary.

Complains of "Shortness of Breath, swelling of feet and Cough".

Has been troubled with cough and shortness of breath for past several years. For the last two years his feet have been swelling especially by evening when they get stiff and painful. Has been much worse for the last six months.

Tendays ago he "caught cold". Cough increased in severity, his shortness of breath got worse and also his oedema. Has not slept for several nights past and is quite delirious.
Present Condition.

Broken down man (very debilitated), orthopneic. Respiration = 36 per min. & very labored. Also was working. Cyanosed. Pulse = 104 per min., small and irregular, unequal & low tension. Temp. = 107.4. Coughing considerably causing much pain in chest under sternum. Pupils equal. Tongue coated, bull manure odors of both feet and legs.

Respiratory System

Muscles of extra respiration constantly used.

Vocal fremitus present.

Frenums of trachea & bronchi distinctly felt. Vocal fremitus weak.

Consonants somewhat hyporesonant especially along margins of lung, especially at sides which mingle with his neck when he coughs. No dulness anywhere except slight flattening. No note at both bases posteriorly.

Auscultation reveals harsh vesicular breathing all over chest with very prolonged expiration, wheezing in character. The type often marked by the numerous loud rales and bronchi both in inspiration & expiration especially at both bases behind.
* Eruption: Ovarian cysts present.
* Vocal Resonance: Not increased.
* Congestion is constant, wheezing in character.

** Circulatory System **

Infection of Heart: shows no bulging or thrill. Aortic heat imperceptible, felt with difficulty in 5th interspace, one inch outside left Mammary Line.

Pulitation felt in Epigastrium. Has slight occasional pain over the pericardium.

Heart: difficult to hear, owing to emphysema.

Upright:
- L.H. B. = 3rd rib in left parasternal line.
- L.F. B. = 1 1/2 inches outside left Mam. C.
- R.H. B. = 1 inch to right side of sternum.

Sounds: muffled and indistinct.

Faint aortal systolic murmur detected.

Other heart sounds feeble except the pulmonary which was accentuated.

** Alimentary System **

Tongue: covered, white, but free from hoarseness or vomiting.

Liver: enlarged to 3 inches below C.M.

Spleen: slightly enlarged.


** Nervous System **: Very sleepy.
He was put into a bromelitic tent and made to inhale To. Bengoin boomerang from kettle. He was given Pulm. Colchicinum 81/1

- R. Paraldehyde
- Th. Digitalis
- Th. Ipecacuanha
- Ammon. Compositum
- Syr. Toluca: ad 3/1

and put on light diet. 4 hours.

When seen at night, after he had two doses of the medicine. He said that he felt his chest not nearly so tight. T = 100.8, P = 100, R = 34.

The odour of the Paraldehyde was well marked, coming from his breath.

13th. Says he feels much easier this morning. Passed a better night, had slept for about 3/4. He ate twice on several occasions during night. Feels his chest less tight and cough less troublesome. T = 100, P = 100, R = 32.

At night. His wheezing was less marked and breathing more freely. Continued effort of cough in sp. Chest = less bronchi but rales still continuous. T = 100.4, P = 102, R = 34.

14th. Slept better during night, had about 4 1/2 hours altogether. Consequently feels easier. Cough not so troublesome.
Pleurisy: Respiration much less marked.
Pain under sternum much better. Less rales
+ bronchi in chest. T = 99.6. P = 100. Systolic +
+ steadi = R = 30. Less cyanosis feet &
+ wrists cyanosed. Passing more urine. 
+ Less albumin = 10%. In the evening, he
was still easier. T = 100.4. P = 100. R = 30.
The bronchial asthma was less marked, the
+ expiratory wheeze being almost gone. He
had been coughing up more phlegm
15% passed much better. Might sleep
+ about 5 hours. Breathing easier and not
+ nearly so laboured & 18 per min.
+ Pulse getting much fuller & steadier = 96.
+ per min. The Digitalis evidently taking
effect. He can take longer inspirations,
+ how as the wheezing is practically
+ away from his chest. His cough is
+ much easier, not nearly so frequent.
+ The sputum is quite without effort.
+ Condition improving. Sputum not so
+ large. Temp = 99.6.
16th. Still improving. Cough much better
+ not nearly so frequent. Slept well during
+ night. Chest much cleaner, not
+ nearly so many rales. Very few ronchi.
Tongue much cleaner & more milky for post.

17th
not troubling him very much, just occasional phlegm. Chest much clearer.
Heart sounds much more audible now.

Initial systole more pronounced & more
blowing in character. Sleeping better
had some chicken for dinner today.

18th. T went taken away. Inhalations dis-
continued. Feels none the worse for this

taking the Paraldehyde mixture steady.
Pulse 84. Full steady, Cough much
improved not bothering him very
much. Expectoration diminishing in
quantity. No edema of feet now.

Urine contains only a trace of albumin.

Improving rapidly. Sleeping well.
Still coughing a good deal but not dis-
troubling him to any extent. P=80. Full &
steady. Heart not so dilated. A few about
half an inch outside the right sternal line.

Liver still the same in size.
Chest has now a few scattered crepitations & an occasional ronhamus throughout the lungs, mostly at bases. Elevation less.

41st Day. Doing well. Cough much better.
On full hospital diet now.

Shortness of breath gone. Put on Bell’s Amy. 3 i.t.d.


Patient was readmitted on May 31st, for a recurrence of the trouble. He had rested well for about 2 weeks but got a wetting of the lungs which brought on the cough again, making him short of breath & his ankles started swelling.

Other news, 32 had been embossed. Complaining considerably and in paroxysms. Eclacetion copious and feverty. His general condition was much the same as on the former occasion and need not be repeated.

He was given

\[ \text{To Digitelis X} \]

\[ \text{To Inure Vom X} \]

\[ \text{Sn Ammon Czncr X} \]

\[ \text{Sy Amcunt ad 3 fs.} \]

\[ \text{4 hour.} \]

No Paraldehyde was given him in order that some idea of its utility might be come to.

4th. Patient scarcely slept at all owing to his constant hard cough. T=107. P=104

irregular & weak. R=32. Shocked. Cough is causing some pain in chest along the attachment of the diaphragm. Due to his food, only taking some milk.

Begged that he might have the same medicine as he had had when he was in hospital previously as he declared he had been much the better of it as it had helped his cough.

At night \[ \text{X} \] Paraldehyde were added to each dose of above mixture to test the result.
5th. T = 99.4. This morning. Passed a much better night. Had slept about 4 hours at intervals. Did not cough so much. Feels his chest not so stuffy. Resp. = 30 per min. P = 100. Chest very wheezy with numerous rales & bronchi heard on auscultation.

In the evening he was still easier and he seems to have decidedly improved since he had the Paraldehyde.


Condition. Heart sounds clearer and stronger, not as weak & murmur as on admission. Still numerous rales & bronchi in chest. & ronchiation frequent.

The progress of the patient from this date was well marked & quite similar to when he was in previously. He was discharged on 29th June, his cough not troubling him to a great extent and his heart much the better of the rest period.

In discussing this case which was small probability one of mitral disease
With the Bronchitis superadded and accompanied with a good deal of pulmonary congestion, there was no doubt but that the Digitalis Stigemin played an important part in the speedy recovery by the stimulating and tonic action on the heart muscle but without standing this, as was seen on the patient's readmission, the Paraldehyde must be credited with a good share in the cure as it diminished notably the coughing and thereby eased the strain in his chest. It soothed him & helped him to sleep. Yet it was not given in hypnotic doses. The expectoration came away easily, but of course the Ammonia had some helping hand in this respect it does.

My Chief, Dr. Fred Evans was greatly pleased with the result of this treatment. He had never used the drug in such cases before & was quite satisfied that it had a most beneficial effect on him by soothing the cough & allaying the general restlessness of the patient & at the same time without taking up the expectoration which thing would occur if one had used Opium, HCN or Chloral.
H. L. aged 60 yrs. male.

Subject to shortness of breath for some years past. Also takes occasional attacks of bronchitis. Within the past 2-3 years these latter attacks have become more frequent, the least exposure to cold bringing them on, causing him to take to bed owing to his chest becoming tight & to the increased violence of his cough. Seen by me on December 10th 1900.

He had caught cold at his work two days previously, which brought on his cough again made him short of breath.

He complained of pain in his left axillary region aggravated by his cough. Felt his chest tight & breathing short & difficult. Has slight rauiness in throat & chest.

Tongue coated & dry. Appetite diminished.

T = 100°1 F. P = 90 irregular & intermittent.

Respiration = 30 per min. Slight orthopnea.

Breathing somewhat wheezy in character. Respiration scanty & tough.

Cough frequent & haemoptysis pain in his sternum & in left hypochondrium in mid axillary line.

Chest on percussion shows slight hyper-
Auscultation reveals loud harsh vesicular breathing with prolonged wheezing & ronchi, all over chest. Breathing almost masked especially posteriorly at bases with fine and medium rales, mostly on inspiration, and a few medium bronchial friction.

Heart. Apex 1 cm outside left mammary line in 5th intercostae. The heart is diffuse and feeble. All the borders enlarged, both ventricles being dilated. Cardiac sounds feeble, low pitched mitral systolic murmur being heard. No allurnin murmur. Cannot sleep owing to cough. Evidently a case of dilatation of heart with commencing subacute bronchitis.

Ordered: houttes to sheet and a mixture

- Paraldehyde <sup>myxx</sup>
- <sup>1/2</sup> Digitalis <sup>myxx</sup>
- <sup>1/2</sup> in. bromide <sup>my</sup>
- 0.9 Camphorae ad 3 fl
- 4 hours

11 **"** Patient had a good night. Had slept about 5 hours altogether. Did not cough much. He said that even after the
1st dose, he felt his chest not so tight and his cough easier, it continued to hacking. $T = 100^\circ F. \quad P = 90. \quad$ Headier $\&$ fuller. $R = 30.$

Still quieter $\&$ shallow but easier in his voice. He uses his extra respiratory muscles largely the cardiac dilatation entirely accounted for this.

There is less wheezing to be heard in his chest. Still numerous rales present. Efflorescence coming away more freely and with less effort, not increased in amount however.

He says that he feels considerably relieved it is certain that the medicine has helped him considerably as on previous occasions he had to be put into a hospital in order to attain such a degree of respiratory freedom.

12th. Passed a still better night. Slept through longer. Had comparatively little cough during night. Efflorescence coming up more easily. Says it is better.

$T = 99^\circ. \quad P = 84. \quad$ Full $\&$ strong. $R = 28. \quad$ Easy.

No wheezing. Chest cleaner, fewer rales.

Heart sounds stronger.

Appetite improving.

16th. Improving considerably. Little cough now. Opine a good R = 24 per min. No tightness in chest. No wheezing. Few rales through now at upper bases of lungs. Heart stronger. Pulse fuller at 76 per min. Not showing any irregularity. There is less evidence of dilatation now, the heart borders being less. Patient expressed himself as being very much better. Menu normal.

18th. Upright, feeling much better. Throat well. Coughs only occasionally, very little expectoration. Was fairly at work again.

Since that time he had two slight bronchitic attacks in February and May 1901, for which he was not attended but used the Paraldehyde mixture, which he said helped him considerably.

In September 1902, he showed evidence...
of heart failure, slight general dyspnoea with a little albuminuria. Very little cough however: with digitalis & strychnia he gradually recovered to such an extent that in about 5 weeks he was able to resume work. He however was left with a troublesome cough evidently due to pulmonary congestion which was greatly benefited by a mixture of digitalis, paraldehyde and strychnine.

In March 13th, 1903, he got wet while brought on an acute pleurisy of right side. He got very dyspnoea, oedema of body quickly appeared due to dilatation of right ventricle. Principally, his cough, which was very distressing, was greatly relieved with paraldehyde but in spite of general cardiac remedies he died suddenly of heart failure on 27th March.

This case is of value as it shows the beneficial sedative effect of paraldehyde in a person suffering from pulmonary congestion and subacute bronchitis by its speeding the thing & diminishing the cough and allowing expectoration to become easy.
Wm. Ht. 55 yrs. miner.

1st seen in July 1907 for shortness of breath. Coming on within the last year. Examination showed "well marked dilatation of his left ventricle with a mitral systolic murmur."

In the following week he went to Prestwick for a holiday. When there, one evening when out in a boat, he caught a chill and developed a severe constant hacking cough with very little coughing. Got short of breath. Came home to within last day & took to bed. Seen next day.

He had edema of face & legs generally slight jaundice. Orthopnoea 36 per min. Constant hard hacking cough with heavy sputum, hurting his chest & forcing thembing buns from sleeping. Pulse = 108 irregular, intermittent & deep medium fulness.

Examination of heart showed dilatation of right & left ventricles with loud blowing mitral systolic murmur. Chest was bulging slightly emphysematous being hyperresonant along the borders of
of his lungs. There were numerous small
nodes in both lungs, especially at the base,
posteriorly. He was evidently suffering
from acute cardiac failure with accompanying con-
gestion of the lungs. Temp. 99.

He was put on Saline Purges and a
mixture of Paraldehyde rubbing, the Digitalis
rubbing, Styrchium and hydrargyrum rubric.

The beneficial result from this
mixture was very striking, the trouble-
some cough which had constantly
distressed him was much eased after
three doses and he was able to get some
sleep. The tightness in his chest and
dyspnoea were considerably relieved.
It was 17 weeks before he was able to
resume work, during which time he
took the above mixture steadily, but
when his heart had regained tone,
and his pulse settled to normal which
took about 12 weeks, the Digitalis and
Styrchium were omitted, the
Paraldehyde alone being given to him
as throughout the illness the cough
showed a tendency to recede if he om-

muttered to take the mixture. He recovered completely through a trifling dyspepsia at the end of the day.

On 29th January 1903 he developed a moderate attack of influenza but got up too soon and took a relapse which set up acute bronchial catarrh with considerable amount of hard hacking cough with scanty sticky phlegm. For this he was given an expectorant mixture 8

\[ \text{Vom Distilled Water} \]
\[ \text{Ammon Brom} \]
\[ \text{Hy Ammon Acetat 3} \]
\[ \text{Tobutami 1} \]
\[ \text{aqua ad 3 to 4 hours} \]

which he took for three days with a little relief, the cough being a handkerchief and hurting his chest. So the above mixture was stopped and he was given Paraldrops in twenty minutes doses every 6 hours. Three or four doses of this gave him the greatest relief, his cough becoming much less frequent, much softer and not hurting his chest. He was able to sleep and spit came up quite easily. He was soon convalescent.
Dear Sir,

I have D. act. 50. mulitphn.

Patient has been subject of chronic bronchitis for several years past, associated with asthma. She usually has three or four attacks, such a kind yearly, the asthma coming on first, clearing her with bronchitis which usually lingered for from 10-14 days. She has tried all sorts of asthma remedies.

Medically she is in great need of an internal & inhalant with less or more relief, only cutting short the paroxysms to any great extent.

She is a thin, pale, woman, always with a slight cough which always gets worse after an asthma attack.

Cheeks emphysematous and a few crepitations to be heard on auscultation, even when quite well. Heart slightly galloped, no murmur.

The first attack was in October 1900. She was suffering from a moderate asthma which became attacks of bronchial asthma complicated with bronchial catarrh.

She was on the nurse's nightly care, Q. 36 hemin, calomel, very asthmatic.
in Character. Numerous rales and bronchi in inspiration & especially in expiration.

Pulse 96, uniform, full time & regular.
Temp. = 99°F. She had a slight paroxysmal cough, hoarseness.

She was put on a mixture of:

- Para-alkaloid 3 lbs
- Anjum 3 lbs
- Aq ad 3 lbs

4 hours if necessary.

The effect of this was very remarkable. When seen next day she said that the
first dose had a wonderful effect in
stopping the paroxysm, the breathing becoming
easier, the tightness in chest disappearing
and also the wheezing, in half an hour
after the 1st dose. She however con-
tinued taking more and found that
the hoarseness began to come up more easily after the 3rd dose and the cough
did not hurt her chest. She expressed
herself as having much better as indeed
she was. Her relatives said that they
noticed a great difference very soon after
the first dose. She was convalescent in
two days but for her residual bronchitic
cough. She said that she had been
treated during her many previous attacks with many asthmatic remedies but now has been given her so much relief as the Paraldehyde.

Another point noticed about this case was that the drug cut short the bronchitic attacks, the latter resolving very speedily, whereas before it used to last 30 or 40 days for 10 days.

She has had several such attacks since then but has used the Paraldehyde for them but recently one finds that it does not have the same effect in half drachm doses, it requiring to be increased to 1-1/2 2's before the same relief is felt.

Some nasal polyps have recently made their appearance and are to be removed and their disappearance will probably help her condition very materially. However I find that she has had only one attack in the last six months (March 1903) it is possible that the Paraldehyde may have helped to ward them off. I was quite satisfied with the results given by the use of the drug in this case.
Mrs L. 40 yrs. pulv.

Subject to asthmatic attacks for years, at first coming on every 2-3 months. Latterly they have been getting more frequent and for the last two years they have been fortnightly. They are always worse in winter. Each is followed by much cough and expectoration. The attack usually lasts for from 3-4 days then gradually subsiding leaving her very weak. Her strength has been failing considerably recently as owing to her fortnightly attacks (which do not correspond to menstruation or midway between the periods) she scarcely recovers from one before the next one comes on.

Seem 30th March 1901, at 9 PM. Suffering from typical asthmatic seizure which had come on during the day. Got much worse as the evening came on. In bed after midaight, gasping for breath. Complaining considerably with great effort. Expectoration very scanty, though thought up with great difficulty. In account of this fever.

From a hypodermic of morphia of Atropine 1/6 and ordered her Paraldehyde s/4x every four hours in a mixture.
She was in great distress and sweating copiously.

31st: When seen she expressed herself as feeling a little better, the morphia and atropine had helped the spasm a little. She has taken for an hour or so but after that the spasm got as bad as ever she was not able to sleep at all. She only has had one dose of the paraldehyde then felt much easier since then the chest does not feel so tight and her wheezing and dyspnoe also much less. R = 30 now. She is coughing considerably, ordered to take the paraldehyde every two hours until she feels easier.

Apr. 1st:

Much better today. Says that after she took the third dose she felt they much relieved the spasm leaving her chest only a little wheezing remaining. Her cough got better and less distressing to her and she was able to breathe up the phlegm easier. She can lie down.
bed now. Had slept about four hours during night. Feels very weak as all the food she has been able to take since attacks came on is some milk and bread.
Temp. normal. P = 80.

9th Passed a very good night. Slept for 6 hours. Dry sputum. P = 24/60 mm.
Cough much easier, not frequent now.
To hand Peraddehyde this morning now.

no more Asthma. Bronchial Catarrh improving.

6th Cough very much better, troublesome mostly at night. Expectoration lighter.
Talking more food.

11th Complain today of tightness common in chest again and some difficulty in breathing just as she usually feels before an attack comes on, it being now about a fortnight since she had the last one. She was put on Peraddehyde.

12th Every four hours.

Feels quite well, tightness in chest quite passed away. No discomfort felt.
Cough much improved.
18th. Still well. Attack evident about 17th. no further attack. Keeping much better. is stronger in herself as she has had no attacks for about three weeks. She has still a slight cough.

Put then in Fellows' syrup, 3½ teaspoon.

8th. She had Paraldehyde.

9th. no further attack. Feels much stronger now. Ordered to take Paraldehyde every three or four hours if subject her chest getting the least tight.

Since this time she has kept well, only having a few slight attacks for which she had not been attended; but for which she took with much relief, the Paraldehyde.
Mrs. F. 58 yrs. widow.
Suffers from dilated heart, bronchitis 
and asthma.

Has been troubled with shortness of breath 
for several years past. 2 years ago had an 
attack of asthma which lasted for a week. 
This left her with a cough which has per-
sisted more or less since then.

Seen by me on July 25th, 1901.

Complains of "shortness of breath, tight-
ness across chest, and hacking cough, since 
the last week."

Four weeks ago had an attack of eczema 
on left forearm. Cured with tannic acid.

A week ago, during the early morning, 
felt her breathing very tight, waking her up 
from her sleep, evidently having 
developed an asthmatic attack.

Since then she has been wheezy and short 
of breath. Has not been able to sleep at night 
during to the oppression and stifling in 
her chest and difficulty of breathing, 
the asthma evidently getting worse 
that time. 

Temp. normal. P = 96. Weak 
time regular. R = 36 wheezing and...
Asthmatic in character, expiration prolonged, wheezing, with numerous medium and fine sibilations especially at inspiration. Coughing considerably with difficulty. Effusion in scanty amounts.

Heart: a soft beat diffuse, normal one inch outside left nipple-line in 5th interspace. Sounds normal, no murmur.

No oedema of feet. No albuminuria.

Temperature: 99.6°F.

Paraldehyde 20 cc.
Camphor 10 cc.

To be repeated 3 times.

4 hourly.

When seen next day, she was found sitting by the fire-side. Her asthma was gone. She said that after two doses of the medicine, it had practically disappeared.

She was still dyspnoeic. R = 30 per min. Pulse quick and weak = 96 per min. She was ordered back to bed and digitalis 1/4.

4 hours later, she was generally much improved, her heart returning to the slowing down to 72 per min. Her dyspnoea left her considerably.
Comfortably in bed, her cough was almost gone and spit quite easily brought up. There was no return of asthma.

Three months later, she passed through a similar but slighter attack for which she was not attended, but sent for a similar prescription to what she had had before as she had derived so much benefit from the first drug. It helped her equally well as on the previous occasion.

IV.

J. F. age 28. Son of above.
Subject: Since boyhood, bronchitis and asthma.
Attended on February 28, 1903, for an attack of bronchitis associated with asthma. He had much difficulty in obtaining sleep at night owing to the tightness of breathing & cough.
He was given half a dram of Paraldehyde in tea or four times daily which helped him most beneficially, even after the first dose he felt considerable ease, the tightness in his chest going...

away. He was out to work in three days, quite recovered, except for the cough. He was quite pleased with the relief given him so speedily as he always counted on being at any rate a week's work after taking such an attack, he being confined to the house usually for about that time.

Since this time, whenever he feels his chest getting the least tight, which happens whenever the weather feels damp and foggy, he always starts taking his Paraldehyde and he finds that this is sufficient to dispel the asthmatic seizure, and at the same time it helps the accompanying bronchitis cough and allows the expectoration to come up easily.
M.R.C. art. to nr. Schlegel.

Pale, thin, delicate, growing weaker.
Has had a loud hacking cough, deep pitched for the last year. She is not troubled much with it during the day but when she lies down at night she starts coughing and often keeps her parents awake owing to its severity.
Takes her food well. Always hungry.


Chest well formed symmetrical.
Movement of both sides equal & good.
Vocal Emotions is equal all over.
Breathing resilescent all over, somewhat pant at apices anterally.
A few occasional scattered excitations heard at end of inspiration in both lungs.
Resonance good all over except over top of sternum down to level of 2nd rib and extending about one inch on each side then is slight dulness.
Vocal Resonance equal & good all over.
Cough only occasional during day is short sharp, deep pitched almost croaky in character.
no expectoration. No difficulty in breathing.

Respiratory: Chest. Heart normal.

A well-marked nasourous hump head, at the root of her neck when she stretches her

head back. Nothing in Larynx. No

enlarged glands in the neck. Alimentary system normal.

She never had whooping cough.

The condition was first fully associated

with enlarged bronchial glands in

which part of anterior mediastinum.

She was put on a mixture of

Alcohol 3

Et malti. Liquida ad 3 f. 4 hourly.

The drug being ordered in malt to
disguise its taste: and to take OC. morhum

3 f. I.d. I.c.

She was not seen again until the

14th. When her mother said that she

was much better, that she had

scarcely coughed at all. During the

night after she had commenced taking

the Paraldehyde, the mother not leaving
to get up, to give her glycerine and

hot drinks, such as domestic.
remedies. and that each succeeding night
was better than the previous one. She
scarcey coughed at all during the
day.

18th. Cough almost gone now, she
scarcey coughs at all during the
night. Chest practically quite clean
of catarrh. Still some dulness
over the right stigmata. Ordered her to
paint this part of chest with Tincture
of iodine. The child looks better.

In a few days she was quite well
the cough having quite disappeared

The parents were highly delighted
as nine months previously she had
been attended medically for the cough
for about three months, without
much benefit.
In reviewing all these cases, provides that the predominating features in them all are a troublesome irritating cough and usually a tightness or irritation in the chest associated with dyspnoea or phlegm of the bronchial muscles and with more or less difficulty in expectoration. The drug given in the manner described afterwards indicate relief of all these conditions and does so speedily. How is this action to be explained?

Let us in the first place consider the nature of the drug! What is its chemical position? It is a liquid of low specific gravity and therefore of quick diffusibility being intermediate between alcohols and ethers and allied to them in composition. When Paraaldehyde reaches the lung, it is excreted from the pulmonary tissue and its odour is distinctly appreciated in the breath, and as it so exactly resembles that of the pure drug we must conclude that the Paraaldehyde is passed through the lung tissue unchanged. How does this
come about? We know that the epidermis of the alveoli of the lung is exceedingly thin, being of flat squames immediately implanted on the capillaries of the pulmonary system. The drug being of low specific gravity diffuses itself out from the blood in these capillaries into the alveoli and from there passes into the bronchioles and larger air passages. It may also pass out through the columnar epithelium of the bronchioles and bronchi. One of the chief results of this action on the lung tissue is that the peripheral terminations of the sensory nerves in the lung have their sensibility diminished (Gordon anaesthesia). The drug thus acts directly as a Sedative on the pulmonary apparatus. It further acts by reducing the number of respirations owing to its depressing action on the respiratory centre in the medulla oblongata. It also dilates the bronchial muscles so that the majority of the cases complained of their coughs hurting their chests, especially those suffering from an
acute or subacute exacerbation of chronic bronchitis (Group I A.), but after two or three doses of Paraldehyde do they ceased to complain of this, finding that their cough was distinctly easier, that they did not require to strain themselves to much and consequently their diaphragmatic strain was very much reduced and that they felt easier and more settled in themselves.

Furthermore, one found that evacuation was greatly facilitated, it becoming loosened speedily so that it was brought up with little difficulty and one found that this happened after taking three or four doses of the drug. How does this come about?

We know that both in bronchitis and in asthma there is a swelling of the mucous membrane, in the former of an inflammatory nature, in the latter more of a temporary congestion accompanied with narrowing of the bronchial muscles. In addition for get increased secretion of mucus from the bronchial mucous membranes
in Bronchitis being the natural sequela of the inflammation; in Asthma it being associated with the Phasmodia condition (Other 4th Edition Asthma).

Moreover, in the first stages of these conditions, this mucous secretion is very tough, the bronchitic patient coughing considerably and hurting his large bronchial tubes, owing to the irritation caused by the hyperaemia, or the evaporation of tough mucus which is fortissimo with great difficulty after much effort.

In the Asthmatic, on the other hand, the mucus is practically never set up in the first or acute stage, the Phlegm being so tough and the patient so dyspnoeic owing to the asthma constant that coughing is rendered very difficult.

If you administer in the first stage of these affections, the Paraldehyde in hot excessive doses, say twenty to thirty minutes every three or four hours, what do you find as a result?
In Bronchitis, even after the first dose, the patient says that the irritating feeling in his chest is somewhat relieved, that the tightness is less that the cough is not so irritating. After two or three more doses, by the end of twelve hours or so the expectoration begins to come up more freely, the patient has not so much difficulty in breathing and the cough is less troublesome and there is much less rawness under the sternum. In twenty-four to thirty-six hours, the difference for the better in the patient's condition is decided marked; the expectoration coming up quite easily, the tightness and feeling of oppression in chest for the most part disappear and the cough much less severe.

Regarding expectoration in fluid that not withstanding its coming up so easily, with less effort on the part of the patient, there is no evident increase of its watery constituents, it being quite yellow and thick.
and as some of the patients addressed it "quite rotten cooking". This, one notices about the third day after commencing the use of the drug whereas with ordinary festivities such as "yacca" and the allarres one would not expect the same change for 48 hours later: and we also find that the spuutum is not nearly so sticky and glutinous but more purulent yet not increased in quantity to any extent, as in cases treated otherwise and there is a correspondingly definite improvement in the condition of the patient. It thus seems to have some definite hormone in aiding the resolution of an attack of bronchitis.

In Asthma you find that a dose of half a drachm to start with and followed by twenty minims every three or four hours, or oftener if necessary, tends to bring about great relief from the spasm, the very first dose even often being effective in easing
the condition. Bramwell and Adams (antea) both state that they give doses of one dramum to start with.

I find that in my cases it was quite unnecessary. Small doses, I have already stated, give quite definite satisfaction in the relief of the symptom when repeated often and when this is relieved, these small doses tend to promote ex- reation, the viscid tenacious mucin being brought up, as coughing is facilitated.

I think that the drug, when inhaled through the pulmonary mucous membrane, must stimulate the mucous cells to secrete a less tenacious mucin, presumably owing to the irritating effect of the drug on mucous membranes as described by Friedländer (antea), as the excretion is not increased in quantity, yet it is much thinner and less sticky, therefore it is quite in reason to suppose that the above action does take place.
The same reasoning applies both to Asthma and Bronchitis. In all my cases of the former suffered from Bronchitis as a consequent and whenever the bronchial spasm was relieved, the repeated small doses tended to soften the phlegm, ease the cough & thereby quicken the course of the Bronchitis.

I never required to push the drug to obtain its hypnotic effect; but as all the patients were undoubtedly soothed their restlessness allayed after two or three doses, they were thus indirectly permitted to get some hours of sleep. This was considerably more due to the action of the drug in relieving the chest symptoms than to the action on the brain through these must have been some sedative action on the Cerebrum itself as exemplified by the case of a woman aged 40 years the subject of a dry post-influenza bronchitis with hacking irritable cough and hay fever; after getting one dose of twenty minutes, she
slept in her chair from 11.30 A.M. until 2 P.M. to the detriment of the Sunday dinner. This case shows that the hypnotic dose in some people may be very small and yet quite effective and also proves that the small dose constantly repeated and keeping the drug circulating in the blood must have a continuously sedative effect on the brain cells and thereby helping to calm and soothe the patient.

In contrasting its action with that of other well-known drugs used in the treatment of asthma and bronchitis, I find that in cases with hacking cough and tough sputum, aspiration and with tightness and irritation in the chest, where one would be tempted to give quinine in some form or other, to relieve the hacking cough, or chloral or hydrocyanic acid or some such like sedative but whose use would be disastrous by clogging up the bronchi with the already tough mucus, by giving Paraldehyde the latter difficulty is quite overcome, forget the sedative action of the drug...
Speedily asserting itself by diminishing the severity of the cough by allaying the irritation of the bronchial sensory nerve endings: and in a few hours the expectorant action becomes asserted by causing the phlegm to become softer and less glutinous; and in the Asthmatic the spasm of the bronchial muscles is relieved, allowing the respiratory difficulty to disappear.

One might be inclined to argue this! Why not give Alkaline or other such expectorant in such cases for example Soda of Potash which is known to be of the greatest benefit in the treatment of bronchial affections?

In contrasting the two types of drugs we find that the Soda of Potash tends to increase considerably the watery constituents of the phlegm, that it loosen the latter in this way and thereby facilitates expectoration.

On the other hand, Paraldehyde does not appear to increase the watery element of it but rather to act on the mucin itself, softening it and
rendering it less glutinous and protecting it. 

By either the Paraldehyde vapour or alcohol the air passages become less glutinous and protecting it. 

Besides rendering the mucus more fluid, or by its stimulating the mucus cells in the epithelium to secrete a more fluid mucus. 

The total quantity of the phlegm is increased with the iodide, but not with Paraldehyde, and it seems to become 

insoluble much sooner when this latter drug is given. 

The iodide does not tend to soothe the cough directly, but patient coughing as much as ever, if not more so, in order 
to get rid of the increased quantity of secretion forced into the bronchi. 

cough diminishes eventually as the quantity of phlegm settles. 

The iodide is not a direct sedative. 

Whereas Paraldehyde by its soothing action both centrally on the brain and locally, on the sensory terminations 
of the bronchial nerves, tends to allay cough from the start and yet it does not
increase difficulty of expectoration but rather facilitate it considerably owing to its solvent action on the mucus. The Paraldehyde is an acid solution and as such when it reaches the pulmonary tissue, one would expect that instead of facilitating expectoration, the reverse would take place as happens when acids are administered. We must attribute this result to the stimulating of the mucus cells in the epithelium by the drug. In addition, the slightly depressing action of Paraldehyde on the respiratory center in the medulla must be also taken into consideration, though I must submit that the doses I employed were on the small side to produce any such marked effect. As far as I could gather from the review of the literature already mentioned regarding the Pharmacology, all the doses there referred to were hypertonic ones and therefore large (from one to two drachms at one time).
Indeed they might be harmful by causing a pro-
genous sleep, and thereby allowing the chest to get full
of phlegm and eventually cause some much ill results.

These large doses for my purpose were quite superfluous,
and I find that from twenty to thirty minims
are sufficient at a time for this
purpose.

In Asthma, Potassium iodide acts
by its depressing the general circulation
and causing the blood vessels to become
relaxed thereby the bronchial muscles
become relaxed indirectly thus
relieving spasm of them. It has
no sedative effect on the nerve ter-
minations in the lungs.

Paraldehyde by reason of its lower
specific gravity is able to reach the
lowermost tract quickly, quicker
than the iodide, does not depress the
general circulation to any appreci-
able extent but directly relieves
the spasm of the bronchial muscles
by relaxing them and thus alleviating
the symptoms.

As all the cases of Asthma treated
were of the Bronchial type, that is the
patient being more or less subject to
bronchitis in addition to the Asthma
and had been treated during the spasmodic attacks with hypodermic injections of morphine, with Belladonna, Pholicium, and strammony, one of them Case 2, group 2, with the much vaunted "Tudor's" cure, in addition without any benefit; although the spasm was alleviated by these drugs, they were then used for a similar purpose, yet the resultant bronchitis was aggravated owing to the mucous secretion from the bronchi being dried up and reatmosphered thereby rendered difficult.

By the use of paraaldehyde in such cases much difficulty was experienced, e.g., Case 1, group 11, the very first dose relieving the spasm and dyspnoea, and the succeeding doses speedily resolving the bronchitic catarrh which followed. This case was very typical of the benefit bestowed upon the rest of that group.

Owing to its rather unpleasant and peculiarly distinctive taste, some people object to taking it as
they say it sickens them. The majority of my patients took it fairly well though they complained about the taste. None of them were sickened by it, but as it was given in small doses the tendency for it doing so was not great. Moreover they felt so much benefit from the use of the drug that they persevered in taking it.

My usual formula in cases of Bronchitis with an irritating hacking cough with scanty expectoration is

\[
7 \text{ Paraalcohol } \\
8 \text{ hr. amount } 3 \text{ fl. oz.} \\
\text{q.d. } 3 \text{ fl. oz.}
\]

\[\textbf{S Coy. To be given every four hours well diluted in water.}\]

I find that four or five such doses gain considerable relief.

Owing to its ready miscibility with other liquids it can be readily be prescribed in a mixture along with other drugs, such as \textit{Digitalis or Stramonium or Strophanthus} and on this account it can be administered in such combination where you
With special attention directed to the cardiac condition and combining with the cardiac tonics, the sedative action of the Paraldehyde, as for example in Case 7. B. Group 1, in which the patient was greatly benefited by the addition of the latter to the cardiac tonics; Dr. Evans the Physician in Charge of the patient declaring that it very materially hastened the progress of the case and the patient asked that the same medicine he given him as he had had, when in Hospital, two or three months previously.

In the case of enlarged Bronchial glands with irritative cough, Group 3, I thought that in order not to disgust the little patient by its taste by mixing the drug in liquid Extract of Malt, the taste would be disguised if he would not object to it.

This plan worked well.

\[ \text{By Paraldehyde } \frac{mX}{10} \]
\[ \text{Et. Malti Fluid. ad } \frac{3}{4} \]

Sig: every four hours if necessary.
In December 1902 and January-February 1903, I have prescribed the drug extensively in cases of Bronchial catarrh following influenza. In this condition you get an exceedingly tough mucoust and gurgles giving rise to a constant hacking cough with little spit.

I find that the drug given alone is of the greatest benefit in such cases, except where there is much depression as in old persons. In the latter cases I combine it with Digitalis or Strophanthus and Stepharia. In all these cases, I never saw any ill results from the use of the drug.

Rollaston mentions the case of a woman suffering from Encephalitis and Bronchitis with a dilated heart in whom doses of one drachm of Paraldehyde produced alarming dyspnoea and collapse, due to depression of the Respiratory Centre when given as a hypnotic at bed time. I never experienced any such alarming occurrence with
any of my patients, and I think that
if smaller doses of the drug were given
day twenty minims. Combined with
full doses of strychnia, caffeine or
digitalis every two three or four hours
one would ultimately have got
a small amount of hypnosis with
a minimum of respiratory depression
as an example of such benefit I may
again quote Group 1 B, Case 1, who
though exanied and anaemic and
orthopneic, travelled wonderfully
and did not show any sign of
respiratory collapse. On the other
hand he was wonderfully benefited
by the small doses.
Some of the patients especially those
suffering from Bronchial Asthma
notably Cases two and three, Group Two,
seemed to attain a certain degree of
tolerance for the drug after it was
used for some little time, in order
that its specific effects might be
produced and requiring that the
cloage be increased from twenty
to thirty minims every three or
four hours. The increased dosage
did not render any of the sick at all, nor did it upset their stomachs. Several practitioners record that the drug has often to be increased in dose especially when used as a hypnotic.

Moreover, I find that none of the primarily bronchitic patients required to have any increase of the original dose ordered, viz. twenty minims every four hours, this amount being quite sufficient to soothe cough and promote expectoration, and I find that the patients can take the drug for quite a long time without it seeming to lose any of its effects.

I do not know of any other sedative and expectorant which has got the same ideal action in these two diseases Bronchitis and Bronchial Asthma for having tried many other drugs in such cases, I find that phenylephrine is the one which I can safely rely on as being of the greatest use and comfort to the patient and relieves the pain in the chest, for the coughing and
facilitate restoration and it does not to any practical purpose depress the heart.

In chronic bronchitis unfortunately it is only a palliative; the nature of this disease being such as forbids us in this climate to hope for a cure.

Many cases of asthma may have the same remark said about them, especially in those cases where nasal treatment does no good; a change of climate, due to secondary changes, taking place in the heart, recrudescence.

In bronchial catarrh it is undoubtedly by curative. In the other above-mentioned cases, its use aids us very considerably in adding to the patient's comfort and well being and thereby prolonging their days, which is the aim and ideal of every physician.
References

4. Vide page II.
8. Friedländer (antea) who quotes the following references in his paper.
13. Morselli
   "Ann. Fr., 1883, XXV, 3.

14. Gordon, vide no. 5.


16. De Novo
   "Bulletin general de Thérapeutie."
   1885. Bulletin 30e, P. 52.

17. Gordon, ante a.

18. Cramer, "Therapeutische Monatshefte"
    1888, S. 357.

19. Ronai & Barezi
   "Pharmaceut Post" April 1886.

20. Hoyt
   "New York Rez" 1890, Nov 8, P. 425.

    Strachan, ante a.
    Gordon, ante a.


23. Urquhart
    "Compte Rendus de la Société de Biologie"
    1884, S. 142.

24. British Medical Journal, Report on
    Hypoties, 1890, Vol II, P. 737.
26  Hodgson
    "British Medical Journal" 1885 Vol II P. 99.
27  Mackenzie
    "British Medical Journal" 1891 Vol II P. 125-4
28  Kraft-Ebing
    "Therapeutische Monatshefte" 1886 S. 8-44.
29  Lastrowitz
    "Deutsche Medizinische Wochenschrift" 1889. S. 33.
30  Borkai Barlag Antea
31  von Reben
32  Hennique
    "Comptes Rendus de la Société de Biologie" 1884. S. 146.
34  Burney Yeo
35  Rolleston
    "Practitioner" 1889. Page 833.