"The physics of chloroform inhalation"

Thesis for M. D.

by

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Contents

Appendix with calculations referred to elsewhere.

Atmospheres

By an atmosphere is meant the percentage of chloroform vapor in a given quantity of air. This percentage may be stated by weight or by vol, though the difference between these two is frequently mistaken or ignored in text books.

The following points must be borne in mind:

(1) When chloroform evaporates the volume of its vapor must be added to the volume of the air.

(2) This volume increases with the temperature; hence other things being equal, increase of temp. means dilution

(3) On evaporation the vapor exercises a certain pressure or tension on the surrounding air. This tension rises with rise of temp.; hence other things being equal, increase of tension means concentration.

(4) If the measure of the combined volumes of air and vapor is to remain unchanged some of the air must be displaced to make room for the vapor.

(5) The neglect or improper estimation of these data has uniformly led to wrong conclusions regarding the strength of atmosphere.

The amount of chloroform vapor required to saturate one litre of air at different temperatures & pressures is easily calculated. (See Appendix p 1–2)

Then to saturate one litre of air at 60°F and under a pressure of 760mm

(1) Weight required = 1·1707 grammes. (see Appendix p 2)

To saturate one litre of air at 61°F and under a pressure of 760mm

(2) Weight required = 1·1973 grammes. (Appendix p 2)

A weight of 1·1707 grammes of chloroform in one litre of air = 23·1 per cent of vol (Appendix p. 4)

A weight of 1·1973 grammes of chloroform in one litre of air = 23·6 per cent of vol (App p. 5)

<u>Hence for Temperatures near 60°F a difference of 1°F = 1/2 per cent</u> [illegible]

The percentage by weight is obtained by dividing percentage by vol by 4·14 (or 4·2 Dumas)

Atmospheres

Compare the saturating weights for a tropical climate where the average temperature is 80·6°F and pressure = 710 m m.

The weight required to saturate one litre of air at a temp. of 80·6°F & pressure 710 m m :—

(3) Weight = 1·75 grammes. (Ap. p. 5)

The weight required to saturate one litre of air at a temp of 81·5°F; pressure 710 m m :—

(4) Weight = 1·78 grammes. (Ap. p. 5)

A weight of 1·75 grammes of chloroform vapor in one litre of air = 38·4 per cent of vol (Ap. p. 6).

A weight of 1·78 grammes of chloroform vapor in one litre of air = 39·0 per cent of vol (Ap. p. 6)

Hence for temperatures near 80°F a difference of 1°F = 1 per cent of vol

Atmospheres

Summary of preceding

Air saturated at 60°F and 760 m m = 23·1 per cent of vol.
Air saturated at 61°F and 760 m m = 23·6 per cent of vol.

Air saturated at 80·6 F and 710 m m = 38·4 per cent of vol.
Air saturated at 81·5°F and 710 m m = 39·0 per cent of vol.

Thus a table might be constructed giving the percentage of chloroform of volume in one litre of air at any given temperature. The most important point to notice however is that for temp. near
60°F a difference of 1°F means a difference of 1/2 per cent.
near 80°F a difference of 1°F means a difference of 1 per cent.

Further note at 60°F percentage of oxygen = 16·15
nitrogen = 60·75
$CHCl_3$ = 23·10

at 80·6 F percentage of oxygen = 12·94
nitrogen = 48·66
$CHCl_3$ = 38·40

Atmospheres

When the proportions are compared a most striking result is obtained :—

At 80·6°F compared with 60°F the chloroform vapor <u>increases</u> 60%
" " " " " oxygen <u>decreases</u> 80%.

These ratios will be kept up with weaker atmospheres (Ap. p. 15.)

The bearing of these facts upon the supposed greater safety of chloroform in the tropics will be hereafter referred to.

Clover's inhaler gives 3·548% of vol of chloroform vapor. (Ap. 13-14 14-15

Junker's inhaler gives 4·892% of vol of chloroform vapor (Ap. 14-15

Sir Joseph Lister's experiments recorded in Holmes' Surgery Vol <u>III</u> Ed <u>III</u> p. 620-621 gives on his own showing a percentage of 1·17 but really taking into account the expansion of the chloroform to vapor it should be 1·24% (A. p. 12.)

Clover's and Junker's inhalers are regarded as giving off

Atmosphere

moderately strong atmospheres and it seems doubtful if an atmosphere 4.20% would produce anaesthesia in such a short time, if at all. The doubtful data in his calculation are the loss of evaporation at the upper surface &c ... Hence his calculation founded upon an ingenious guess cannot be relied on at all.

Any attempts at accurate determination of percentages must depend on exact analysis of the mixture inhaled or must take into account the expansion of the chloroform into vapor.

In considering this subject various modes of analysis presented themselves, the principle of which was to aspirate a certain volume of the air and vapor into a closed vessel where the analysis of the constituents might be determined.

(1) The mixture of air & chloroform vapor might be analysed by absorbing the chloroform vapor in an alcoholic solution of caustic potash :—

$CHCl_3 + 4KHO = \underline{KHCO_2} + 3KCl + 2H_2O$

Then estimate the formate of potassium as CO_2

Estimation of atmospheres

(2) Dissolve the $CHCl_3$ in the mixture by shaking it up with water saturated with air & noting the absorption; which would give the volume of $CHCl_3$ present.

(3) Decomposing the vapor of $CHCl_3$ by passing it over heated zinc in a combustion tube and estimate the chlorine.

(4) Absorbing the oxygen of the mixture ~~by~~ by means of a solution of pyrogallic acid in caustic potash.

As none of these methods proved satisfactory, thrown on my own resources entirely, it occurred to me that the oxygen might be absorbed by burning phosphorus in the mixture; if the $CHCl_3$ were not decomposed. This plan succeeded beyond expectation; and if the phosphorus be burnt over mercury in a closed tube the most accurate results may be obtained.

The method adopted was as follows. Over a tube 18¼ inches long and about 1 inch in diameter was fixed a piece of iron gauze covered over with several folds of cloth on which the chloroform was poured

Estimation of atmospheres

The height of the gauge was varied & the air was drawn thro' the tube by means of an air pump at a constant rate till the mixture in the tube was of uniform strength with ~~that~~ entering at the mouth.

Closing both ends of the tube ~~without~~ allowing the mixture to escape the lower end was introduced over a cup containing the burning phosphorus. By dexterous management the loss of vapor in the tube was infinitesimal. The phosphorus was burnt over water; not mercury which would give more accurate results. The cloth was kept saturated with chloroform all the time

The data are: —

(1) Note the absorption of the volume of the mixture in the tube, allowing for changes of pressure.

(2) The absorption denotes the amount of oxygen absorbed

(3) The amount of air = vol of oxygen × 100/21

(4) The amount of chloroform vapor = total vol - air

Two series of experiments were performed. (See pp. 7. 8. 9.)

Estimation of atmospheres

The following are the results

First series temp = 83°F pressure = 29 inches

(1) Distance between cloth and tube = 1/2 inch percentage of $CHCl_3$ = 23·53
(2) = 1 inch " " = 18·29
(3) = 1½ inch .. .. = 14·10
(4) = 2 inches .. .. = 10·96

This shows that the strength varies exactly with the distance
23·53 : 18·29 : 14·10 : 10·96 :: 1·28 : x = 1

Second series temp. not noted exactly but lower than 83°F p = 29 inches

(1) Distance between cloth and tube = 1/2 inch percentage of $CHCl_3$ = 18·82
= 3/4 inch " " = 16·20
= 1 inch " " = 12·62
= 1½ inch .. " = 8·34.

This also shows that strength varies with distance
18·82 : 12·62 : 8·34 :: 1·49 : x = 1

Local effects on the lungs

As regards strength of atmosphere, temperature and tension cause the strength to vary in opposite directions. Also as regards distance and temperature, increase of temperature is equivalent to diminution of the distance

Local effects of chloroform on the pulmonary surfaces.

(1) The importance of the observation that chloroform causes contraction of the fine arterioles and capillaries of the lungs is very great. Dr Newman estimates that the average contraction for arterioles is 1/6: for capillaries 1/9. This however more directly concerns the action of the heart of which more hereafter.

(2) The above observations were made on frogs, otherwise another phenomenon of scarcely less importance might have been noticed. "The initial effect of contact... is contraction of irritable protoplasm": (International Encyclopaedia of Surgery p 411 Vol I.) The muscular fibres of the blood vessels are not the only irritable protoplasmic material of the lungs. There is

Influence on respiration

the muscle of the bronchi also the nerves & ganglia (p 161 and 164 Landois Physiology) Unfortunately the frog has no bronchi but it is almost certain that in animals where bronchi exist, these will contract. The dyspnoea of early anaesthesia may be regarded as in part an expression of this. As the function of the ganglia is not clearly understood no inference can be drawn from the action of the anaesthetic on them.

Influence on the respiratory process.

(1) We have seen that the minute blood vessels are contracted. They offer a smaller surface to the gases in the lungs, hence absorption of gases will be diminished. Likewise elimination of CO_2 will be prevented.
(2) The contraction of the small bronchi will aggravate the existing condition — further hindering gaseous interchanges, as in asthma &c
(3) The effect of chloroform on the blood itself is to lessen the absorption of oxygen & to hinder the elimination of carbonic acid. (Harley) The absorption of oxygen helps the elimination of CO_2 Landois Physiology p 44 also 192

Influence on respiration

(4) In the mixture part of the oxygen is displaced by the chloroform. The partial pressure of oxygen is diminished in proportion to the diminution of the volume. Hence its absorption is delayed while the proportion is diminished (Landois Physiology p 192)

Thus there is a notable diminution of the oxygen absorbed & the CO_2 eliminated from the above sources. The element of asphyxia enters not by mechanical hindrance of the exit of carbonic acid but through hindrance to diffusion but because CO_2 appears to be both chemically & physically more closely bound while chemically & physically oxygen absorption is fettered. This is burning the candle at both ends & asphyxia must play an important part in the process of anaesthesia.

In passing let us note that the greater safety of chloroform in tropical countries may be explained here. The following facts seem to throw some light on the subject.

(1) In childhood & pregnancy chloroform is given with greater security than usual. Dr Wm Hunter in drawing attention to this in a recent number of the Glasgow Medical Journal supposes an extra store

of oxygen in these cases. The fact however is that while more oxygen is [illegible] for anabolic purposes it is more quickly used up and an excess of carbonic acids exists in these cases in the blood. See Landois: Physiology p 188–189.

In the tropics

(3) In warm-blooded animals the respiratory activity and the CO_2 given off diminish while the pulse remains nearly constant (Landois; Physiology p. 189). The degree of diminution is reckoned by Rattray as 18·43% less. Parkes' Hygiene p 387. The respirations are lessened in number; the air being hotter contains less oxygen for the same volume, compared with a temperate climate. Instead of 240 c inches being inspired per minute only 195·7 are inhaled

240 : 196 :: 100 : x = 81·66%

i.e. diminution is 100 − 81·66 = 18·43%.

The diminution is twofold (1) in the amount of air inhaled (2) in the oxygen of the amount inhaled. Hence excess of CO_2 in the system and a diminished quantity of oxygen.

The further bearing of this in lessened likelihood of primary syncope will be again referred to.

See Dr Newman Glasgow Med. Journal No 1 Jan 1891. p 7-8.

Effect on the Heart

To sum up: the effects of chloroform on the internal respirations are:-
(1) deprivation of oxygen from mechanical & chemical causes
(2) increase of CO_2 from mechanical & chemical causes
(3) circulation of a poison through the tissues.
(4) the deprivation of oxygen is of less consequence than accumulation of CO_2

Effect upon the heart. A Right ventricle B Left ventricle

(a) Mechanical (a) If it be true that arterioles contract by 1/6 and
A (1) capillaries by 1/9 then average contraction is $\frac{1}{2}$ of $(\frac{1}{6} + \frac{1}{9}) = .14$.
The calibre of the pulmonary capillaries is in some cases sufficient only for the passage of one row of red corpuscles.
Any contraction in such cases means occlusion. But suppose no occlusion to occur this contraction in the capillaries leads to a diminution of their discharge proportioned to the fourth power of their diameters. see appendix p.
To keep up the velocity the power of the heart must be at least doubled & up. 16
(2) Further there is not only contraction of the vessels of the lungs but increased adhesion of the blood corpuscles to the walls of the vessels. The increased resistance to the flow of the blood from this cause is as yet an unknown quantity but must be reckoned as of high import

Effects on the heart

(3) The doubled velocity means quadrupled friction because the fluid friction varies with the square of the velocity. See A. p.

The extra strain thrown on the heart from these causes can scarcely be reckoned as less than four times the normal strain

N.B. The blood pressure in the pulmonary circulation is a most important factor in this respect yet no observations have been made upon the point.

B (1) The left ventricle must also experience some strain from the increased adhesion of the blood & the walls of the vessels.

(2) The partial asphyxia due to the causes mentioned (p) causes constriction of blood arteries vessels temporarily thro the system, rise of blood pressure and increased work.

The strain on the left ventricle is probably much less than that on the right as the right ventricle has to overcome the congestion in the lungs which is very great.
Hence in valvular diseases of the left heart little additional strain may arise & while the tension in

N.B. The curves of the Glasgow Com. are much more expressive of a heart labouring to overcome obstruction than of a heart weakened by chloroform;– the slow rise, the rounded apex &c ...

Primary Syncope

the right heart is enormous & travels partly thro' the venous system & the left heart, its general freedom of disease wards off any serious consequences. General atheroma and fatty degeneration are formidable conditions in this respect.

Primary syncope.

The main theories regarding its causation may be briefly summarised :—
(1) By the action of $CHCl_3$ on the heart causing dilatation of all its cavities
(2) By reflex inhibition of cardiac ganglia thro' the vagus
(3) By reflex action dependent on shock or other powerful reflex causes
(4) By reflex action of the vagus caused by accumulation of CO_2 in the system
(5) By rapid withdrawal of chloroform vapor.

At first sight these ~~causes~~ theories seem hopelessly at variance yet a deeper insight into physiological processes may unify the whole

The main facts associated with primary syncope are :—
(1) It may occur at any stage of administration
(2) It may occur almost at the outset of administration before much vapor is absorbed
(3) A strong atmosphere freely administered (Snow)

Primary syncope

(5) Discontinuous and insufficient administration

In criticising the theories advanced as above that which associates vagus action with inhibition of the cardiac ganglia seems insufficient

(1) Because too little is known of these ganglia in the human subject to dogmatise upon their function. McKendrick believes they are not so much originators of cardiac action as regulators of it.

2) McWilliam believes that the vagus may act directly on the cardiac muscle (Landois: Physiology 669)

(3) The vagus being one of the nerves of vegetative life is among the least susceptible to volitional stimuli or the action of higher centres.

Again the 5th theory scarcely deserves attention in the form in which it is stated the sudden withdrawal has been at least once known to cause syncope (See Dr W. Huntly's case Ed. Med Jour)

The unification of these theories would seem to lie somewhere in the following line — viewing the heart as a blood vessel & the blood vessels as in some sort, hearts.

Primary Synopsis

(1) Both are hollow muscles lined with endothelium - the blood vessels with 2 sets of muscular fibres which are designed to empty them of their contents, - the heart with a complicated system of muscular fibres adapted to the same end.

(2) Both are supplied with ganglia under the control of centres in the medulla oblongata -

(3) Both are under the control of two sets of nerve fibres (a) inhibitory or anabolic (b) motor or katabolic.

(a) The inhibitory of the heart is the vagus whose stimulation causes slowing of the heart and diminishes also the amount of its work (Coats) This diminution of work points to relaxation of its fibres

The inhibitory of the vessels are the depressors whose stimulation causes dilation or relaxation of their muscular fibres

(b) The motor of the heart is the sympathetic, the motor of the vessels are the pressor nerves found in various regions

(4) The heart is endowed with a highly developed rhythmic system. The blood vessels have also a rhythmic function. See the rabbits ear, the bats wing, the frogs foot. (Landois 675)

Primary Syncope

(5) The cardiac & vasomotor centres while not having a common centre, have apparently a preestablished harmony.

Thus both centres may be directly stimulated by the same causes:—
(1) sudden anaemia of the medulla oblongata
(2) sudden venous hyperaemia
(3) increased venosity of the blood
((4) rise of blood pressure in the cerebral arteries?)
Landois: Physiology p 667.

Again both centres may be indirectly stimulated thro' pressor or depressor i.e. thro' their respective motor or inhibitory centres

Thus if the vasomotor centre is destroyed or paralysed the heart may beat with a changed rhythm yet be pale bloodless collapsed. Again if the vasomotor system be paralysed over a large area the heart action is weak & small, if a large area of the vasomotor system be stimulated so is the heart.
See Landois: Physiology p. 673.

Do these facts throw any light on primary syncope?

Primary Syncope

(1) We have seen that the cardiac and vasomotor centres are co-ordinate

(2) With these two centres the respiratory centre is also co-ordinate "The cardiac centre may be stimulated by the same causes stimuli ~~that~~ act upon the respiratory centre" Landois Physiology p 667.

(3) We have seen that in the primary stage of chloroform inhalation the vapor has an irritant action producing (a) contraction of the bronchi (b) contraction of the capillaries &c (c) congesting and enormously straining the right ventricle and likewise the left, tho' to a less degree. "Over-strain may paralyse the heart" (Coats)

"Imagine the heart to be pumping blood thro the vessels. If from some cause the smaller vessels become constricted so as to offer greater resistance to the passage of blood the arterial pressure in the large vessels is increased; and the heart has more work to do to overcome the resistance. When the resistance reaches a certain extent the heart will be in danger of exhaustion in endeavouring to overcome it. But of the depressor the danger is removed, as an influence may pass along the fibres of the depressor to the vasomotor centre the effect of which is to inhibit the activity of the centre and allow the small vessels to dilate. Thus to a certain

·✕: So Gaskell: and M'Kendrick: Physiology p 292.

Primary Syncope

extent there appears to be in the heart itself an arrangement which governs its own work" (McKendrick Physiology p 293-294)

This idea may be expanded. The depressor fibres of the vessels carry an impulse to their ganglia from the vasomotor centre and the depressor nerve of the heart (the vagus) likewise carries an impulse to its ganglia from the cardio inhibitory centre. The effect in both cases is inhibition - dilatation - anabolism.

Recalling the fact ~~that~~ in extreme contraction of the capillaries of the lungs there is extreme strain on the right heart & to some extent on the left likewise, the inhibitory action of the heart comes into play and while the heart is not paralysed by its over-distension but struggles to overcome it, it passes ~~thro~~ the stage of "delirium cordis" to extreme inhibition on which will ensue extreme dilatation & ~~tho~~ the dilatation is not in itself fatal the heart from the extreme inhibition stops in diastole

~~Primary Syncope is therefore (1) dilatation of all the chambers of the heart (2)~~

Primary Syncope

Primary syncope may therefore appear as follows :—

(1) dilatation of the cardiac chambers due to the chloroform

(2) inhibition of the cardiac ganglia thus disordered & extreme pressure intra cardiac

(3) reflex action thr the vagus caused of CO_2 accumulating and affecting the respiratory centre which is coordinate with the cardiac & vasomotor centres

(4) withdrawal of chloroform when the vagus may rapidly recover and have the action of the heart over to its motor nerve almost entirely.

N.B. In every case the dilatation of the chambers ensuing on vagus stimulation will explain the primary syncope, if the theory be accepted ~~that~~ the cardiac & vasomotor centres are analogous & almost simultaneous in function, their efferent fibres on being stimulated causing dilatation; and lowering of blood pressure.

Primary syncope is associated with operations in certain regions — Operations on the great toe

— Operations about the jaws – removal of teeth &c.

— Operations about the mamma

·X· the laryngeals, the splanchnics, the lingual & hypoglossal of the tongue.

Dangerous regions

These phenomena are more easily understood when it is borne in mind that the most powerful vasomotors are those ~~that~~ act on blood vessels of peripheral parts as the toes the fingers the ears &c... Landois: Physiology p 673.

(1) Depressor fibres are specially associated with the vagus the great auricular, the tibial, and many sensory nerves. Landois: Physiology p 675.

(2) Pressor fibres are specially associated with the trigeminus, the
* cervical sympathetic *, the laryngeals and many sensory nerves. (McKendrick)

(3) The sensory nerves of the skin over the thorax are known to be ~~coord~~ coordinated with vasomotor ~~centres~~ fibres going to the lungs Brunton's Therapeutics p 342.

In the causation of primary syncope the absence of the respiratory movements is supposed by Dr Newman to be an important factor. He however over-estimates the value of the respiratory movement, since it does not probably amount to more than 1/120 of its whole work per

Inhibition a safeguard

minute Appendix p. 19.

Inhibition is a safeguard not a danger according to the Hyderabad Commission
(1) This they found on experimental grounds as it delayed the conveyance of poisoned blood to the nerve centres.
(2) If it be true according to McKendrick that inhibition of the vagus means anabolism, and if this be further intended to apply to the action of the vasomotor centres in causing dilatation simultaneously with inhibition of the heart then truly inhibition of the heart & cardiac & vascular ganglia with its fall of blood pressure must be a safeguard. The mechanical effect in removing obstruction to the blood current is also self evident in the inhibition of both.

Inhibition therefore both cardiac and vascular is a safeguard (1) Mechanically by removing obstruction
(2) Mechanically by restraining the flow of blood
(3) Physiologically by attempting to restore the poisoned tissues.

Prof. Foster when shewn by Dr Lawrie the tracings of the Hyderabad

Artificial respiration

Commission after noting the fall of blood pressure said "Against this we must remember that when a poison is introduced into the system everything that happens afterwards is of ~~the~~ necessity in the nature of a safeguard."

In cardiac syncope artificial respiration is effective

(1) by direct pressure on the heart (see McWilliams experiments) which relieves the right and empties the left ventricle

(2) by direct pressure on the pulmonary vessels also relieving them by emptying the left ventricle.

Absorption of $CHCl_3$ into the blood.

The accepted theory postulates

(1) At first there is rapid absorption
(2) Later on if the inhalation is continued a balance is struck between absorption and elimination
(3) after removal of the chloroform elimination is very rapid & the whole of the chloroform ~~may~~ be absorbed may escape in 20 seconds.

Rate of absorption

This theory has the merit of simplicity but certain facts are against it

(1) Recovery is more speedy when little has been inhaled
(2) After long continued inhalation there may be lasting depression
(3) No decisive figures, indeed no figures at all have ever been offered as far as known to me.

Further there are certain positive facts on the other side

(1) Oxygen is absorbed till the haemoglobin is saturated. Elimination never occurs unless mechanical or chemical means are specially employed
(2) How can elimination and absorption proceed pari passu as the theory requires The same vapor would be re-absorbed and re-eliminated constantly - a game at hide and seek ? All that would be required to keep up anaesthesia would be mechanical hindrance to the escape of the chloroform vapor.

(3) Chloroform is a vapor not a gas. Its elimination does not follow the law of gases. When absorbed it is dissolved in the blood and its elimination

Storage in the system

of the lungs must be a very slow process. See p. p..

(4) The rate of absorption of chloroform vapor of the blood is as high as 3 parts to 100. This is the mean of many experiments upon fresh blood.

(5) Hence there must be storage of the vapor in the system. This conclusion is confirmed of observing the fatty degenerations produced in animals of long inhalations. (The name of the observer I have forgotten. It was in one of the German medical journals where extensive experiments on all kinds of animals were recorded).

What is the rate of storage? A 4% atmosphere is moderately strong and is very effective in producing safe anaesthesia.

N. B. An atmosphere of 4% at a temp of 60°F diffuses into the ~~lungs~~ blood at end of the first minute 7½ minims and thereafter with the same atmosphere about 11 minims per minute. But as the atmosphere is lessened after anaesthesia the rate of absorption is much lessened.

In Dr Newman's account of experiments on frogs related in Glasgow Med. Journal.
150 cc of chloroform vapor were used.

Now a fair sized frog is far from weighing 1 lb = 444 grammes.

But suppose we had one whose weight = 500 grammes.

150 cc of vapor of chloroform = ·76 grm

Prop. of $CHCl_3$ absorbed to total weight of the animal = ·76 : 500
= 1 : 658

Prop of $CHCl_3$ absorbed to total weight of the blood = ·76 : 1/13 of 500
= ·76 : 38
= 1 : 50.

Average man = 2240 ounces
Wt of blood = 1/13 of 2240 ounces = 172 ounces
If man could absorb as much as the frog it would be 1/50 of 172 ounces
= 3·44 ounces

N.B. The frog in the above recovered !!

Storage in the system

According to Sir S. M'Leod with proper arrangements anaesthesia may be brought about in 1-2 minutes i.e. if in one minute with a 4% atmosphere there will be about 10 minims in the blood; if in 2 minutes the amount will not exceed 20 minims see Appendix p. 20

If blood absorbs 3/100 [by] volume then as the volume of blood in an adult = 4½ litres the amount absorbed will be 3/100 of 4½ litres = 135 cubic centimetres = 135 × 17 minims = 2295 = more than four and a half ounces! Before this death would occur!

Elimination would not commence [by] the lungs till the quantity was absorbed

Hence artificial respiration can do but little towards elimination of $CHCl_3$ except from the air passages & air cells. It cannot eliminate it from the blood when once absorbed.

Seat of storage.

In its action upon nutrition chloroform resembles phosphorus & arsenic i.e. they limit absorption of oxygen & elimination of carbonic acid and bring about fatty degenerations. The seat of the storage is probably

Effect on cardiac muscle?

the lungs and the kidneys. Elimination may occur to some slight extent by the skin and the lungs but excretion will probably be shewn in excess of chlorides in the urine & increase of carbonic acid from decomposition of potassium formate in the blood.

Does chloroform directly affect the cardiac muscle?

(1) According to Sir George McLeod we have seen that anaesthesia may occur in one minute i.e. with about 7½ minims of chloroform in the circulation. The B. P. gives 10 minims of chloroform as a safe dose. Of this amount we may be sure that 7½ minims are taken into the circulation without the slightest ill effect being noticed!

(2) There is no evidence whatever to shew that the heart muscle is peculiarly sensitive to chloroform vapor.

(3) We must suppose ~~that~~ after the local irritant action of chloroform and its immediate consequences it acts thro' the great nervous centres.

Conclusion

Conclusion

(1) Chloroform with proper precautions about inhalation is exceedingly safe

(2) As the respiratory centre is the first of the three coordinate centres to be affected, it gives the earliest note of warning.

(3) Watching of the pulse post-dates the action of the vapor on the heart and on the lungs.

(4) In stagnation of the circulation as in primary syncope injections into the veins can be of little service; so also can electric stimulation, because the heart stimulated to the utmost has passed into extreme inhibition.

(5) Artificial respiration if prompt and effective, perhaps opening of the jugular vein in primary syncope might be useful.

over

Climatal differences

Chloroform is supposed to be much safer in the tropics. It is by no means the case that deaths are unknown as a few are on record.
(1) In seeking to explain this we recall the fact that in the tropics there is excess of CO_2 in the blood. — the action of which is to hasten the anaesthesia as already noted (2) Tho.
(2) the atmospheres are relatively much more potent almost by 60 % (see appendix p. 5) yet as the total volume inspired is 20 % less than in the temperate zones. the stronger atmosphere with the excess of CO_2 hastens the anaesthesia further so that less will be absorbed probably in bringing about anaesthesia primarily which will then be followed by a milder atmosphere
(3) The excessive CO_2 in the blood renders the respiratory and correlated centres less sensitive to vapor of $CHCl_3$ hence a violent reaction at first is improbable & hence primary syncope is also less likely to occur. I have never seen it myself here.

Appendix

Molecular weight of $CHCl_3$ = 119.5

Density of $CHCl_3$ (H = 1) = 59.75

Wt of one litre of $CHCl_3$ at $0^\circ C$ & 760 mm = 5.3536 grm.

Density of $CHCl_3$ (air = 1) = 4.2. (Watts's Roscoe's Organic Chemistry)

Dalton's laws (See Ganot's Physics).

(1) The pressure and the quantity of vapor which saturates a given volume are the same for the same temp. whether that space contains a gas or is a vacuum.

(2) The pressure of the mixture of a gas and a vapor is equal to the sum of the pressures which each would possess if it alone occupied the same space

Hence to find the weight of $CHCl_3$ which would saturate one litre of air at $15.55^\circ C$ (= 60 F) in the same it is required to

Tension = 16·62 c.c See Regnault $t = 60^\circ F = 15 \cdot 55^\circ C$

Tension = 18·04 c.c See Regnault $t = 61^\circ F = 16 \cdot 11^\circ C$

Appendix

find the wt of $CHCl_3$ vapor which alone would occupy one litre at 15·55°C and under its own partial pressure for this temp – 166·2 m m. (See Regnault's Comptes Rendus for tension of $CHCl_3$ &c)

60°F $W = (\rho V p\ 273) \div 760 \times (273 + t)$ See Ganot's Physics

$= (5{\cdot}3536 \times 16{\cdot}62 \times 273) \div (760 \times 288{\cdot}55) = 1{\cdot}1707$ grm.

If temp $= 16{\cdot}11°C\ (=61F)$ partial pressure $= 18{\cdot}0\,c$

61°F $W = (5{\cdot}3536 \times 18{\cdot}04 \times 273) \div (760 \times 289{\cdot}11) = 1{\cdot}193$ grm

Wt of one litre of $CHCl_3$ at 0°C & 760 m m = ~~1·223~~ 5·3536 grm.

Wt of one litre of air at 0°C & 760 m m = 1·293 grm.

Wt of one litre of $CHCl_3$ at 15·55° & 760 m m = 5·064 grm.

Wt of one litre of air at 15·55° & 760 m m = 1·223 grm

Appendix

To find the percentage of $CHCl_3$ of vol in saturated air.

By Dalton law given a mixture of a gas and a vapor

Let P = total pressure of the mixture p, p', the partial pressure of the constituents

Let V = total volume of the mixture v, v', the partial volumes of the constituents

Then $$PV = pv + p'v'$$

As the chloroform evaporates in the open air it does not cause any local increase of pressure. If PV is to remain unchanged pv and $p'v'$ must each be less than PV.

Let $p'v'$ be the product of the partial pressure & partial vol of $CHCl_3$

$p'v'$ is already known:—

It requires 1.1707 grms of $CHCl_3$ vapor to saturate one litre of air = 1000 cc (datum)

Also one litre = 1000 cc of $CHCl_3$ vapor at 15.55°C & 760 = 5.064 grm

Appendix

Therefore a weight of 1·1707 grm gives the following volume :—

$5{\cdot}064 : 1{\cdot}1707 :: 1000 : x = 231{\cdot}2$ cc.

i.e. the vol of $CHCl_3$ vapor in the mixture of one litre = 231·2 cc.

$$PV = pv + p'v'$$

i.e. $760 \times 1000 = 760\,v + 760 \times 231$

whence $v = 769$ cc.

∴ If 769 cc of air at 15·55°C and 760 m m pressure is added to
231 cc of $CHCl_3$ vapor at 15·55°C & 760 m m pressure the
total = 1000 cc of a mixture of air & $CHCl_3$ vapor at 15·55°C & 760 m m

Thus the air displaced = 1000 − 769 cc = 231 cc.

Hence percentage of vol in the mixture is :— air = 76·9
$CHCl_3$ = 23·1
100.

Barometric height at Hyderabad for Oct Nov Dec averages 710 m m

See Meteorological Tables for India 1890

Appendix

Similarly for 61°F when saturating wt of $CHCl_3$ = 1·1973 grammes.

the percentage of vol in the mixture is :— air = 76·4 %
$CHCl_3$ = 23·6 %

80·6°F Tension of $CHCl_3$ vapor = 255 m m t = 80·6 F = 27° Cent.

Saturating wt for one litre = (5·3536 X 255 X 273) ÷ (300 X 710)

= 1·75 grammes.

81·5°F Tension of $CHCl_3$ vapor = 260 m m t = 81·5° F = 27·5° C

Saturating wt for one litre = (5·3536 X 260 X 273) ÷ (300·5 X 710)

= 1·78 grammes.

The percentage of $CHCl_3$ vapor of vol is as follows :—

Appendix

Wt of one litre of $CHCl_3$ vapour at 27°C & 710 mm = 4.551 gm.

Find the vol of 1.75 gm of $CHCl_3$ at 27° & 710 mm

$$4.551 : 1.750 :: 1000 : 384.5\ c.c.$$

Air displaced = $CHCl_3$ vapour present = 384.5 cc

∴ percentage in the mixture at 80.6°F & 710 mm :—

air = 615.5 cc
$CHCl_3$ = 384.5 cc

i.e. percentage by vol of air = 61.55
of $CHCl_3$ = 38.45
100.

Similarly for 81.5°F percentage by vol of air = ~~39.00~~ 61.00
$CHCl_3$ = 39.00

Appendix

Experiments on the strengths of atmospheres

(1) Distance	= 1/2 mile	absorption	= 2·92 mile
(2) "	= 1 mile	"	= 3·12 mile
(3) "	= 1 1/2 mile	"	= 3·28 mile
(4) "	= 2 miles	"	= 3·40 mile

A glass tube was used whose length was 18 1/4 inches. To simplify the calculation multiply the length of the tube & each of the preceding absorption figures by 5·5. Then tube is nearly = 100 inches

The above figures then become:—

(1) absorption = 2·92 × 5·5 = 16·06 inches
(2) " = 3·12 × 5·5 = 17·16 "
(3) " = 3·28 × 5·5 = 18·04 "
(4) " = 3·40 × 5·5 = 18·70 "

The absorption denotes amount of oxygen present. Hence the air present = vol of oxygen × 100/21 because oxygen forms 21% of vol of the air

Appendix

Hence air present in (1) $= 16{\cdot}06 \times {}^{100}/_{21} = 76{\cdot}47$ inches

(2) $= 17{\cdot}16 \times {}^{100}/_{21} = 81{\cdot}71$ inches

(3) $= 18{\cdot}04 \times {}^{100}/_{21} = 85{\cdot}90$ inches

(4) $= 18{\cdot}70 \times {}^{100}/_{21} = 89{\cdot}04$ inches

Hence $CHCl_3$ vapor present in (1) $100 - 76{\cdot}47 = 23{\cdot}53$ inches

(2) $100 - 81{\cdot}71 = 18{\cdot}29$ inches

(3) $100 - 85{\cdot}90 = 14{\cdot}10$ inches

(4) $100 - 89{\cdot}04 = 10{\cdot}96$ inches

Note $\;{}^{23\cdot53}/_{18\cdot29} \;:\; {}^{18\cdot29}/_{14\cdot10} \;:\; {}^{14\cdot10}/_{10\cdot96} = \dfrac{1{\cdot}28}{1}$

i.e. the strengths of the atmosphere is proportional to the distance between the source of the vapor & the tube.

During the above experiments the temp was 83°F & pressure 734 mm (29 inches)

In another set of experiments when the temp was not noted but which was certainly below 83°F. the following results were obtained :—

(1) Distance = 1/2 mile Absorption = 3.1 mile
(2) = 3/4 mile = 3.2 "
(3) = 1 mile = 3.37 "
(4) = 1 1/2 mile = 3.50 "

(1) $3.1 \times 5.5 = 17.05$ absorbed
(2) $3.2 \times 5.5 = 17.60$ "
(3) $3.37 \times 5.5 = 18.53$ "
(4) $3.50 \times 5.5 = 19.25$ "

The same tube = 18.25 inches was used
$18.25 \times 5.5 = 100$ nearly.

Atmosphere of air (1) $= 17.05 \times 100/21 = 81.18$
(2) $= 17.60 \times 100/21 = 83.80$
(3) $= 18.53 \times 100/21 = 87.38$
(4) $= 19.25 \times 100/21 = 91.66$

Atmosphere of $CHCl_3$ (1) $100 - 81.18 = 18.82$
(2) $100 - 83.80 = 16.20$
(3) $100 - 87.38 = 12.62$
(4) $100 - 91.66 = 8.34$

Note $18.82/12.62 : 12.62/8.34 : 1.49/1$

Appendix

Lister's data in Holmes Surgery Vol II Ed III p 620.

Total evap = 138 - 25 = 113 gr in 4 minutes
= 113/4 = 28·25 grains for 1 minute

Consumption = 2/3 of 4/11 of 28·25 grains per minute

= 6·9 grains per minute

Air inhaled = 450 c inches = 31 X 4·5 grains = 139·5 grains

∴ 139·5 : 6·9 :: 100 : x = 4·9% of wt

N.B. In above 6·9 grains go to 450 c inches air (Lister)
~~or 1 gramme to 15·373 litres of air~~
or 1 gramme to 15·8 litre of air

Now 1·1707 grm of $CHCl_3$ saturating one litre of air gives 23·1% $CHCl_3$
∴ 15·8 X 1·1707 grm of $CHCl_3$ saturating 15·8 litres of air gives 23% "
∴ 18·497 grm of $CHCl_3$ " 15·8 " " " "

According to Listers data $^{6.9}/_{15.4}$ grammes go to 450 c inches
= 7.377 litres
or 1 gm of $CHCl_3$ to 15.80 litres

If 18.497 grm $CHCl_3$ when saturated gave 23% what is the percentage when when the same vol of the mixture – 15.8 litres contains only 1 gm.

$$18.497 : 1 :: 23.0 : x = 1.24 \text{ of vol.}$$

Lister neglecting the expansion of $CHCl_3$ gives the percentage of vol as 1.17?

Appendix

Clovers inhaler is said to furnish 4%

1000 c inches air are mixed with 32·5 minims

(See Bruntons Pharmacology p. 804)

1 cc of vol = 17 minims

1·9 cc of vol = <u>32·5</u> minims

1·9 cc of vol of $CHCl_3$ × density of $CHCl_3$ gives wt.

Density = 1·497. (Brunton's Therapeutics)

1·9 × 1·497 = 2·844 grammes = 32·5 minims

The calculation is made for a temperate climate where $t = 60°F$ $= 15·55°C$ & $p = 760$

To find the vol of vapor from 32·5 minims = 2·844 grms.

273 : (273 + 15·55) :: 1000 : x = 561·5 cc

5·3536 2·844

i.e the vol of $CHCl_3$ vapor at 15·55°C & 760 = 561·5 cc

Total air vol = 1000 c inches = 16386 cc

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∴ air in mixture = 16386 − 561·5 = 15824·5 cc

Hence percentage is :—

15824·5 : 561·5 :: 100 : x = 3·548.

i.e. percentage of $CHCl_3$ in the mixture at 15·55 C & 760 mm
= 3·548 and not 4 as Clover supposed.

Junker inhaler is supposed to give one minim of $CHCl_3$ to 6000 minims of air.

One minim of vol = 1/17 cc ∴ 6000 minims = 353 cc

Thus one minim of $CHCl_3$ goes to 353 cc of air
one minim of $CHCl_3$ liquid furnishes 17·27 cc of vapor

∴ percentage is got :—

353 : 17·27 :: 100 : x = 4·89.

Appendix

Summary Clover inhaler gives 3·548 $CHCl_3$ per cent.

Junker inhaler gives 4·892 $CHCl_3$ per cent.

At 80·6° F compared with 60° F the oxygen is decreased in percentage.

% at 60·F % at 80·6 F
16·15 : 12·94 :: 100 : x = 80% for oxygen

At 80·6° F compared with 60° F the chloroform vapour increases

% at 80·6 F % at 60 F
38·4 : 23·1 :: 100 : x = 60% for $CHCl_3$

Appendix

Increase of the work of the heart from diminution of pulmonary capillaries: –

Discharge varies as the fourth power of diameter of capillary tubes
~~Friction increases~~ as fourth power of ~~dia~~meter of capillary tubes

Let Q = Quantity discharged of tube of diameter $2R$
Q' = Quantity discharged of tube of diameter $2R'$

Then in capillary tubes

$$Q : Q' :: R^4 : R'^4$$

$2R$ initial calibre $2R'$ = final calibre If $2R = 1 \therefore 2R' = 1 - \cdot 14 = \cdot 86$
where $\cdot 14 = \frac{1}{2}$ of $(\frac{1}{6} + \frac{1}{9})$

Therefore $Q : Q' :: 1^4 : \cdot 86^4$
i.e. $Q : Q' :: 1 : \cdot 547 \quad \therefore Q' = Q \times \cdot 547$
i.e. the quantity discharged is diminished by more than half.

To prevent accumulation in the lungs the velocity must be increased

$$Q : Q' :: V' : V$$

or $Q : Q \times \cdot 547 :: V' : V$

$$\therefore QV = Q \cdot 547 \times V' \quad \therefore V = V' \times \cdot 547$$

Appendix

{ i.e. the velocity must be doubled at least
{ i.e. the power must be doubled at least likewise

In the above friction is left out but it is enormously increased from two causes (1) the doubled velocity of the blood stream
(2) the increased adhesion of the blood corpuscles.

The fluid friction from the velocity of the blood stream may vary with the square of the velocity and with a doubled velocity will therefore rise to the fourth power. The adhesion of the blood corpuscles to the wall judging from the time it takes to disappear can scarcely be less.

N.B. Strain on the right ventricle (1) from contraction of pulmonary vessels
(2) from fluid friction due to increase
(3) from adhesion to wall of vessels of velocity

Effects of respiration on work of the heart :-

In calm expiration pressure = 760 + 2 - 6 = 756 m m
In calm inspiration pressure = 760 - 3 - 9 = 748 m m.

(1) In inspiration the left ventricle is relieved thro aspiration of the right auricle of 756 - 748 = 8 m m

(2) In inspiration the left ventricle is hindered thro dilatation of the aorta of 756 - 754 = 2 m m (?)

(3) In inspiration the right ventricle is relieved thro aspiration of the left heart of 756 - 748 = 8 m m.

Total relief to the left ventricle = 8 - 2 + 8 = 14 m.m.

In expiration right ventricle is relieved of 756 - 748 = 8 m m
" " left ventricle is helped of 756 - 748 = 8 m m

Total relief for expiration = 8 - 8 = 0.

Appendix

Total work of 14 m m Hg = $14 \times 12{\cdot}32 = 172{\cdot}48$ m m of blood

Work per minute in kilog. metre = $\cdot 17248 \times 15 \times \cdot 188 = \cdot 4886356$

$$+ \; {}^{v^2}\!/_{2g} = \underline{035814}$$

$$\cdot 522170.$$

Total work of heart per minute = 60 kilogram.. metres per min

∴ Ratio of work done of respi to work done of the heart $= \cdot 5/60$
$= 1/120.$

Thus the effect of respiration is really infinitesimal

Appendix

Rate of absorption into the blood of the lungs of a 4% atmosphere with a temp of 60°F.

Respirations per minute = $\cdot 5 \times 15 = 7 \cdot 5$ litres

Of this however only part is absorbed namely $\cdot 33 \times 15 = 4 \cdot 95$ litres per min the rest being returned ~~without~~ absorption. (M'Kendrick)

An atmosphere of 4% contains $\cdot 2036$ grm to 1 litre
$= 2 \cdot 255$ minimum

Hence chloroform which enters the blood per minute
$= 2 \cdot 255 \times 4 \cdot 95$ minimum
$= 11 \cdot 275$ minimum

This amount of chloroform and air enters only after 5 respirations = 1/3 minute
At the end of 20 seconds diffusion begins
In the remaining 40 seconds amount diffused of $CHCl_3$ = 2/3 of $11 \cdot 275$
$= 7 \cdot 5$ minimum

N.B. At end of the first minute of anaesthesia has occurred only about 7 1/2 minimum are present.

Appendix

If 2 minutes are required then amnt in blood $= 7.5 + 11.275$
$= 18.77$ minimum

To obtain the coefficient of absorption of blood 100 cc of pigs blood was used as fresh as possible and defibrinated. This was placed in a glass cylinder and the mouth closed by an india-rubber stopper which had 2 holes one for connecting the cylinder with the flask containing $CHCl_3$ the other with an open manometer. The $CHCl_3$ was sometimes admitted as a liquid sometimes drawn in as a vapor then the blood shaken at frequent intervals & kept at 98.6°F. The moment the manometer shewed an increase of pressure was taken to denote that absorption was complete.

The laws relating to the vapor from mixed liquids are:—
(1) If the liquids do not at all dissolve each other the pressure is the sum of the pressures of the mixed liquids
(2) If the liquids slightly dissolve one another the pressure

Appendix.

is slightly less than that of the most volatile

(3) If the liquids dissolve one another in all proportions the pressure is intermediate between that of the separate liquids.

This solution distinctly retards escape of the dissolved vapor & may even prevent it for a lengthened period of time.