CARBON MONOXIDE ASPHYXIA:
A REVIEW OF THE CEREBRAL CHANGES IN TEN CASES.

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Carbon monoxide asphyxia continues to be a most popular method of self destruction, and owing to the colourless and odourless properties of the gas there is always the constant liability of accidental inhalation.

Before discussing the way in which carbon monoxide inhalation causes asphyxia it is necessary to remind oneself of certain physiological and biochemical factors concerned with respiration. Man at rest breathes about 20 times per minute, taking in about 500 c.cs of air with each breath. This air mixes with the air which is already in the lungs - about 2,000 c.cs, under normal conditions of respiration at rest. The air in the lungs, the alveolar air, contains approximately 80% nitrogen, 14% oxygen and 5.5% carbon dioxide. Nitrogen is merely a diluent and plays no part in the process of respiration.

At atmospheric pressure, the partial pressure of oxygen in the alveolar air is approximately 100 m.m. Hg. whereas the tension of oxygen in the venous blood coming to the lungs is approximately 35 m.m. Hg. Oxygen diffuses rapidly from the alveolar air into the blood. Thus the arterial blood leaving the lungs contains about 19 c.cs of oxygen per 100 c.cs. at a tension of approximately 100 m.m. Hg. - equilibrium having been attained with the oxygen in the alveolar air. Oxygen is carried in the arterial blood till the capillaries are reached and then it diffuses out into the tissues where the oxygen tension is low. This/
This diffusion is incomplete owing to the rate of the blood flow; so the venous blood returning to the lungs contains about 12 c.cs of oxygen per 100 c.cs under a tension of approximately 38 m.m. Hg.

The carriage and liberation of carbon dioxide occurs in a similar way. The partial pressure of carbon dioxide in the alveolar air is approximately 40 m.m. Hg. and the tension of carbon dioxide in the venous blood returning to the lungs is about 46 m.m. Hg. This pressure difference of 6 m.m. Hg. is sufficient for the diffusion of carbon dioxide into the alveoli. Arterial blood leaves the lung containing approximately 46 c.cs of carbon dioxide per 100 c.cs. under a tension of about 40 m.m. Hg. The carbon dioxide in the tissues is constantly being produced and is under a tension of about 60 m.m. Hg. Thus the carbon dioxide in the tissues passes into the blood where the tension is low, and is carried back to the lungs in the venous blood which contains about 52 c.cs of carbon dioxide per 100 c.cs.

Oxygen is carried in the blood almost entirely by the haemoglobin contained in the red cells. The remainder, a minute amount, is carried in the plasma in simple solution. At 0°C. and at 1 atmosphere pressure, 100 c.cs of haemoglobin-free arterial blood plasma contain only about 0.24 c.cs of oxygen which is in simple solution. Whole blood under the same circumstances contains about 20 c.cs of oxygen. The difference shows the great affinity of haemoglobin for oxygen. This chemical combination is quickly affected/
Figure 1.

Oxygen dissociation curve of haemoglobin. One can easily see from the curve that man has a wide margin of safety in the provision for oxygen supply. (From Barcroft, 1914, p. 226.)
affected by the variations in the pressure of oxygen to which it is exposed. Other factors affecting the combination are the carbon dioxide tension, the temperature, and the strength of the haemoglobin solution. As may be seen in Fig. 2 the higher the carbon dioxide pressure, the greater is the dissociation of oxygen from the haemoglobin.

Although the affinity of haemoglobin for oxygen is great, its affinity for carbon monoxide is about 210 times greater; and the degree of saturation of the haemoglobin with carbon monoxide is directly proportional to the quantity of the gas in the air breathed. This greater affinity for carbon monoxide accounts for the fact that very small amounts of the gas in the air breathed can bring about toxic symptoms. As little as 0.2% of the gas in the air breathed will bring about a fatal issue in about 4 hours. Owing to its stability this chemical combination of haemoglobin with carbon monoxide dissociates slowly; but, just as the release of oxygen is promoted by an increasing tension of carbon dioxide, so carbon monoxide is freed from haemoglobin more readily when the tension of carbon dioxide rises. (Fig. 3.) Carbon dioxide not only increases the dissociation of carboxyhaemoglobin, but it also increases the rate/

* Sendroy, Lin, and Van Slyke, 1929.
Figure 2.

A series of curves representing the ability of haemoglobin to hold oxygen under different oxygen pressures when carbon dioxide under different tensions is also present. (From Bohr, Hasselbalch, and Krogh, 1904, p.409.)
Figure 3.

A series of curves representing the ability of solutions of haemoglobin to hold carbon monoxide under different pressures of the gas and under different tensions of carbon dioxide. (From Douglas, Haldane, and Haldane, 1912, p. 287.)
rate of breathing. These two actions are the basis of modern treatment of carbon monoxide asphyxia: inhalation of 7% carbon dioxide and oxygen being advocated.

The susceptibility to asphyxia by carbon monoxide is affected by the following conditions:

(1) Individual variability can occur, as with all poisons, for no apparent reason.

(2) Age and Size. Children are more susceptible than adults. This is probably due to the increased volume of air breathed relative to the total volume of blood in the body.

(3) Sex. Various opinions have been expressed in this respect and no definite conclusion has been reached so far. However, there is every reason to assume from actual cases and animal experimentation that the pregnant female is more susceptible than the non-pregnant.

(4) Degree of activity. Asphyxia occurs much more readily during great bodily activity. This may be attributed to two factors:

   (a) increased respiratory activity.

   (b) increased need for oxygen.

(5) High temperature and humidity. Greater susceptibility in this case may be attributed to the incidental increase in the respiratory rate.

(6) Low barometric pressure. As the blood becomes saturated with carbon monoxide it loses its power to give off such oxygen as it carries, and if the oxygen pressure of the air breathed is
is low, asphyxia will occur more readily.

(7) Bodily state.

(a) Anaemia. Obviously, if the oxygen carrying power of the blood is already diminished, carbon monoxide will more readily produce toxic effects. The question has been raised whether carbon monoxide may bring about anaemia of any kind. There is nothing to support this view but if anaemia occurs after carbon monoxide poisoning, it may possibly be attributed to other gases present.

(b) Heart disease. The subject with heart disease is most susceptible because carbon monoxide can produce cardiac irregularity and dilatation in the healthy subject. If anoxaemia is already present, the effect of carbon monoxide is even more drastic.

(c) Pulmonary disease. Conditions in which the ventilation of the lungs is interfered with will increase susceptibility to asphyxia.

(d) Alcohol and narcotics. Chronic alcoholics and those recovering from an alcoholic bout suffer very severe ill effects. The narcotic drugs such as the barbiturates and opium depress respiratory activity and add to the difficulty of resuscitation.

SOURCES/
SOURCES OF CARBON MONOXIDE.

Carbon monoxide is produced in varying amount whenever carbon is burnt in a limited supply of oxygen. The commoner domestic and industrial sources are generally well known, but at this time there are the added possibilities of accidental inhalation due to war activities. For instance, the gases liberated from high explosives may contain enough carbon monoxide to produce toxic effects; especially in confined and ill-ventilated "pill-boxes" and gun emplacements. The exhaust fumes from petrol engines contain varying quantities of the gas, and the ever increasing mechanization of the modern army increases the likelihood of poisoning by this source. Thus, leaking exhaust pipes in closed-in vehicles such as tanks, armoured cars, motor boats and aeroplanes may give rise to poisoning. The influence of low barometric pressure on the susceptibility to poisoning (page 8) offers a hazard to high altitude flying but this has largely been overcome by the incorporation of an added oxygen supply.

CLINICAL EFFECTS.

The effects of carbon monoxide inhalation clinically depend upon the degree of saturation of the haemoglobin - which in turn depends upon the amount of the gas in the air breathed - and the duration of exposure, not to mention the factors influencing the individual's susceptibility. The following table* gives an/

* Sayers and Yant, 1927.
an indication of the symptoms one may expect with increasing
degrees of saturation:

**Blood sat. %.**

0-10  None.
10-20  Tightness across forehead; possibly slight headache.
20-30  Headache, throbbing in temples.
30-40  Severe headache, weakness, dizziness, dimness of vision, nausea and vomiting, collapse.
40-50  Same as previous item with more possibility of collapse and syncope; increased respiration and pulse.
50-60  Syncope, increased respiration and pulse, coma with intermittent convulsions, Cheyne-Stokes respiration.
60-70  Coma with intermittent convulsions, depressed heart action and respiration; possibly death.
70-80  Weak pulse and slowed respiration; respiratory failure and death.

If recovery after acute poisoning takes place, it is usually complete; but there may be sequelae. The commoner after effects are headaches, muscular pains, long periods of unconsciousness, loss of strength, mental derangement and temporary blindness. In nearly all cases these clear up in a day or two but may persist for several months. It must be remembered that after asphyxia, apparent/
The upper curve is the theoretical curve of carbon monoxide and haemoglobin in the presence of air; the lower shows the approximate percentage of saturation that a man will develop in one hour, if he is sitting still in an atmosphere containing the amount of carbon monoxide shown in the scale below the abscissa. This curve and scale are drawn for a normal volume of breathing. (From Henderson and Haggard.)
apparent complete recovery may take place but days or weeks later after-effects may appear and precipitate a fatal issue.

There is little doubt that chronic poisoning by carbon monoxide does occur and causes disturbances in circulation and the nervous system, but the clinical manifestations reported in the literature are too vague and indefinite for quotation. It has been shown that a healthy subject can become acclimatized to small amounts of carbon monoxide over a prolonged period. The experiment reported by Killick in 1936 is interesting in this connection, Fig. 5.

**TREATMENT.**

Treatment of acute asphyxia is directed towards the following points:—

(1) Prevent further exposure, so remove the patient to an atmosphere free from the gas.

(2) Restore the oxygen carrying power of the blood as rapidly as possible by removing the carbon monoxide in combination with haemoglobin. This can best be accomplished by:—
   (a) artificial respiration if necessary (preferably carried out by the Schäfer method).
   (b) inhalation of oxygen mixed with 7% carbon dioxide.

Fig. 6.
Figure 5.

Saturation of the blood during exposure to 0.023 per cent carbon monoxide.

Curve A:— before acclimatization (Feb. 14, 1934)

Curve B:— after acclimatization (Oct. 9, 1934)

(From Killick, 1936, p. 45.)
Figure 6.

This graph shows the influence that different gases - when inhaled - have on the rate of elimination of carbon monoxide from the blood.

Curve A: normal air.
Curve B: pure oxygen.
Curve C: oxygen and carbon dioxide mixed.

(From Sayers and Yant.)
(3) Consider the heart as beginning to dilate so favour restoration of its normal tone and function by keeping the patient at rest, lying down and warm. Later he is treated as a convalescent and allowed time to rest and recuperate.

(4) Restore body temperature to normal as soon as possible with warm blankets and hot bottles etc.

(5) Prevent, as far as possible, the accumulation of fluid in the bronchi and lungs by position.

The treatment of chronic poisoning is directed towards removing the source of the gas and this comes largely into the scope of the Public Health Services.

**PATHOLOGY.**

Precise data in respect of the concentration of the gas in the air breathed and the duration of exposure is usually not known in fatal cases of poisoning, and these two factors influence the findings at post-mortem. However, the signs one might expect are as follows:

**GENERAL APPEARANCE:** The retention of the brilliant red colour of the blood gives a lifelike appearance. The skin occasionally shows blebs or herpes. When the body is opened the bright red colour of the blood and of the muscles is conspicuous.

**BLOOD:** Carbon monoxide may be detected in the blood long after death.
death, but it must be borne in mind that the blood of city dwellers may contain small amounts of carbon monoxide and death cannot be ascribed to this cause.

**BLOOD VESSELS:** The smaller vessels become fragile and haemorrhages, varying widely in size, commonly occur. These may be found in the peritoneum, under the mucous membranes of respiratory and alimentary tracts, over the surfaces of the heart, lungs, pleura and pericardium, and most important are the fine haemorrhages found in the brain and meninges. Thrombosis of these smaller vessels may have occurred as a result of injury to the vessel wall rather than any effect on blood coagulability.

**HEART:** Cardiac dilatation is a common finding. Opinions differ widely in respect of myocardial changes and no help, so far, has been obtained from experimental animals.

**KIDNEYS:** Cloudy swelling and desquamation of tubular cells with red blood cells in Bowman's capsule and tubules are the common findings. These changes are transitory; there being no pathological evidence of chronic kidney disease following either acute or chronic carbon monoxide asphyxia.

**STOMACH and INTESTINES:** Small haemorrhages from the smaller vessels may be found.

**LUNGS:** Carbon monoxide is not irritating and the pulmonary oedema, not infrequently found, is probably due to some degree of cardiac failure.

**NERVES:**
NERVES: Neuritis of moderate grade may be found in any nerve in the body. There may be seen varying degrees of hyperaemia and oedema of the perineurium; and in older cases, fragmentation of myelin with atrophy of the axis cylinders and different degrees of fibrous change.

BRAIN: The effects on the brain can well be seen from the findings of Hill and Semerak, 1918, viz:-

- Number of cases examined: 32
- Hyperaemia of brain and meninges: 29
- Oedema of brain: 21
- Petechial haemorrhages in leptomeninges and white matter: 15
- Arteriosclerosis and vascular degeneration in advance of the age of the patient: 19
- Necrosis of lenticular nucleus evident as gross softening: 14
- Lenticular degeneration found microscopically: 32

Hill and Semerak do not imply that carbon monoxide poisoning causes arteriosclerosis but they believe that the other changes in the brain occur more readily in the presence of antecedent vascular disease.
Probably the most interesting signs of carbon monoxide poisoning met with at post-mortem are to be found in the brain and the following ten case reports illustrate the more common lesions met with. In all of these cases, the source of carbon monoxide was household gas which contains about 4 - 8% of carbon monoxide. Unfortunately, the concentration of the gas and the duration of exposure were not known.
CASE: 1. Female, aged 74. Admitted to hospital 18-1-40 in coma and died after 12 hours without regaining consciousness. On section the brain showed early bilateral softening of the medial part of the globus pallidus and of the putamen on the left side. These soft areas were slightly brownish-red in colour with well defined edges. Microscopically: In the globus pallidus on both sides there were well defined patches of partial demyelination. About two-thirds of the myelin sheaths appeared to have vanished and the remaining one-third showed beading and irregularities. Microglial stains showed signs of reactive microglia but there was no free fat present. No astrocytic response was evident. Pallidal siderosis was present. The vessels showed no abnormality of the larger perforating arteries. The arterioles showed oedema fluid round them; the capillaries were congested and there were small capillary haemorrhages present. There was a great loss of ganglion cells. In the putamen there were two large arteriosclerotic scars and an area of necrosis replaced by compound granular cells and mononuclears. Capillary multiplication was evident with a largely cellular astrocytic reaction. Many of the cells were of the gemástete type. There was a little gliosis. Elsewhere in the putamen there was evidence of arterio-sclerosis; several vessels showing intimal thickening and perivascular gliosis. Cortical sections showed no abnormalities.

CASE: 2. Male, aged 50. Admitted to hospital 3-3-41 in coma and
died on 5-3-41 without regaining consciousness. Two slices of brain were examined. Section revealed a pale, sharply demarcated area, 4 m.m. in diameter, in each globus pallidus. Microscopically: The pale areas were regions of early ischaemic necrosis. Microglia were beginning to react, but no fat filled phagocytes were present. There was a very small amount of haemorrhage. Pallidal siderosis was present in a minor degree. A section from the parietal white matter showed no evidence of diapedetic haemorrhages.

CASE: 3. Male, aged 41. Admitted to hospital on 6-7-40 in coma and died 10-7-40 without regaining consciousness. Previous History: Patient was admitted to hospital on 17-10-39 and diagnosed as an early case of disseminated sclerosis and was discharged. The brain showed slight frontal atrophy, slight temporal herniation and cerebellar coning. The pia arachnoid was diffusely pale and thickened over the frontal and parietal convexities and showed marked venous engorgement. There were focal areas of sub arachnoid petechial haemorrhages. On section the brain was markedly congested, especially in the deeper grey matter. The globus pallidus, on both sides, was pale anteriorly with many congested vessels. There was a small area of petechial haemorrhage in the left thalamus. In the deeper grey matter there were small areas of petechial haemorrhages in many places; this was most marked over the parietal convexities and in the temporal regions. In places the grey matter had separated entirely from the underlying white, the line of separation being sharp. There were many small scattered plaques of disseminated
CASE: 3. Section showing marked congestion especially in the deeper grey matter, and separation of the grey matter from the underlying white matter. The medial part of the globus pallidus on each side shows an area of early ischaemic infarction. Note the widespread disseminated sclerotic plaques.
sclerosis throughout the grey and white matter of cortex, central white matter, basal ganglia and brain stem. **Microscopically:** In the anterior pallidus there were vascular dilatation and diapedetic haemorrhages (venules and capillaries). The parenchyma showed early ischaemic degeneration with very little compound granular cell formation. Pallidal siderosis was not present. The disseminated sclerotic lesions in the brain showed complete demyelination, with relatively little destruction. The degenerated myelin was present in compound granular cells. Fat was present in large amount. The astrocytic reaction was in the form of a well marked cellular gliosis. The disseminated plaques showed perivascular cuffing—lymphocytic and histiocytic—around the distended capillaries and venules. The temporal region, where the cortex had separated, showed acute recent necrosis. There were marked capillary diapedetic haemorrhages and also areas of peri-venular necrosis without diapedesis. These areas appeared to be the result of venous stagnation and not early disseminated plaques. Everywhere the veins were dilated but no antemortem thrombosis was evident.

**CASE: 4.** Male, aged 38. Admitted to hospital in coma 11-12-40 and died on 15-12-40 without regaining consciousness. The brain showed frontal gyral atrophy; there was no gyral flattening but there was slight temporal herniation and cerebellar coneing. The pia arachnoid was healthy except over the left frontal convexity where there was diffuse pale reddish thickening. The basal vessels showed patchy atheroma; the circle of Willis was symmetrical.
The surface of the brain was generally congested, being cherry red in colour. On section the white matter was particularly congested. The anterior pallidum showed, bilaterally, oval dark mottled areas. Microscopically: Sections were taken from basal ganglia, frontal, parietal and occipital cortex, from cornu ammonis and midbrain, and stained by Pickworth's method to show the vascular pattern. Certain sections were then stained for fat and microglia. The anterior globus pallidus showed early bilateral ischaemic infarction. There was no haemorrhage. Microglia in Sharlach R haematin sections showed slight activity and fat was present in an occasional compound granular cell. There was no evidence of arterio-sclerotic lesions in the putamen. In the white matter of frontal, parietal and occipital regions, in the internal and external capsules, and in the basis pedunculi there were multiple pericapillary ring haemorrhages. These haemorrhages occurred around capillaries which showed no abnormalities such as variations in calibre. Reaction on the part of the brain to these haemorrhages consisted of infiltration of the haemorrhages by active microglia, occasionally reaching the stage of a fat containing compound granular cell.

CASE: 5. Male, aged 61. Admitted to hospital in coma 24-9-40 and died 29-9-40. The brain was received cut. Further sectioning revealed slight discolouration of both anterior pallida, more marked on the right side. Microscopically: The anterior portion of the globus pallidus on each side was infarcted. There was no actual break up of the brain substance in the infarcted area, but there was a homogenization and a loss of staining reaction. At the edge of the infarct there were numerous fat-filled compound
granular cells (Sharlach R). The capillaries crossing the infarct and the arterioles in the surrounding globus pallidus showed non-specific pallidal siderosis. Routine sections of other regions of the brain showed only congestion.

CASE: 6. Male, aged 69. Admitted to hospital 10-2-40 and died 17-2-40. The brain showed no abnormality externally. On section there was a rounded yellowish discoloration in the anterior globus pallidus on each side. Microscopically: There was a well demarcated area of ischaemic necrosis in the globus pallidus. In this necrotic area there were many fat-filled compound granular cells. Nerve cells, axis cylinders, and myelin sheaths were absent, but at the periphery the axis cylinder and myelin sheaths showed beading and irregularities of thickness and direction. At the periphery of the necrotic area the capillaries showed an increase of reticulin in their walls. There was no glial response. Nearby vessels showed pallidal siderosis. There was no evidence of vascular lesions elsewhere in the brain.

CASE: 7. Female, aged 51. Admitted to hospital 18-6-38 in coma and died 25-6-38 without fully regaining consciousness. Previous history: The patient had bouts of drinking for many years, and she was in such a bout when she was found unconscious and admitted to hospital. The brain showed slight gyral shrinkage of both frontal and both temporal lobes. The pia-arachnoid showed a slight diffuse opacity with a peculiar granular appearance over the first temporal sulcus. The basal arteries were healthy. On section the brain showed very marked congestion throughout; both in grey and white matter. The anterior part of the globus pallidus on
each side presented a focus about 7 - 8 m.m. in diameter of yellowish-grey discolouration and slight friability suggesting recent necrosis. No other focal lesions were found.

**Microscopically:** The foci in the globus pallidus showed complete necrosis of all cells except those of the vessel walls and an occasional fat scavenger cell. Within the necrotic area the supra-capillary vessels were dilated and filled with red blood corpuscles; the capillaries showed marked endothelial hyperplasia, rendering them ischaemic. Pickworth preparations showed this congestion of the larger vessels and patch capillary anaemia, contrasting with the uniform filling of the vascular bed in the surrounding tissue. Within the foci there were numerous small diapedetic perivascular haemorrhages of the "net" type. The marginal zone of the foci showed loosening of the ground substance, proliferation of small glial nuclei and formation of a good many fat scavenger cells, and marked vascular endothelial hyperplasia. Sections of cortex, cornu Ammonis, hypothalamus, mid-brain and medulla showed moderate general congestion but were otherwise normal.

**CASE: 6.** Male, aged 66. Admitted to hospital 30-10-33 in coma. He regained consciousness 4 hours after admission; developed bronchopneumonia on 8-11-33 and died 12-11-33. The brain showed no gyral atrophy; the meninges were a little thickened over the vertex. The basal arteries showed a marked degree of arterio-sclerosis. On section the vessels were congested but there were no haemorrhages. Anteriorly, at the junction of the putamen and globus pallidus, there was a small yellowish area about 4 m.m. by 2 m.m. on the left
There was no such lesion on the right side. At the left termination of the corpus callosum there was a small gelatinous cystic area. **Microscopically:** The vessels showed arteriolar and arteriolo-sclerosis with hyalinization of their thickened walls. Gold stains showed a considerable amount of glial reaction in the frontal cortex. There was an area of softening in the left globus pallidus with numerous fat-filled compound granular corpuscles. Surrounding this area was an early glial reaction. There was another small area of softening in the corpus callosum, interrupting the frontal association fibres. This was surrounded by a dense glial reaction and was evidently of some standing. The vessels in the vicinity showed a few lymphocytes in the perivascular space.

**CASE:** 9. Male, aged 39. Attempted suicide by gas in 1937. Following this his movements were obscure until 18-7-40 when he was admitted to hospital in coma and died 1½ hours after admission without regaining consciousness. The brain was received cut. It was congested. There was a moderately large triangular cystic infarct in the medial portion of the anterior globus pallidus. There were multiple diffuse petechial haemorrhages throughout the white matter. **Microscopically:** The pallidal infarct showed evidence of a little old haemorrhage. The wall was composed of a dense glial scar in which were trapped many fat-filled phagocytes. Vessels crossing the infarct and around it showed well marked siderosis. In the white matter of temporal, parietal, occipital and frontal lobes, and in the internal
CASE: 9. Section showing multiple petechial haemorrhages throughout the white matter, and a moderately large triangular cystic infarct in the medial part of each globus pallidus.
capsule the capillaries were dilated and diapedetic haemorrhages were present. In mid-brain, pons and upper medulla, none were seen. Around these haemorrhages there was a very slight microglial reaction.

CASE: 10. Male, young adult. He was found in coma but recovered consciousness and was in fair health for 4 to 5 weeks. He then began to have fits (described by his medical attendants as epileptiform convulsions). These increased in frequency and severity until he died three months after the gassing, immediately following several convulsions. The section of the brain received for examination showed marked congestion throughout the white matter with petechial haemorrhages scattered throughout. There was a well demarcated darker area in the medial part of the globus pallidus. Microscopically: The only section available was taken from this necrotic focus in the globus pallidus. Within the necrotic area the nerve cells with their axis cylinders and myelin sheaths had disappeared. Glial activity was marked and there were numerous compound granular cells. In and around the necrotic area the capillaries showed endothelial hyperplasia and there were small haemorrhages present. Pallidal siderosis was present.
CASE: 10. Section showing vascular congestion most marked in the white matter; and a well demarcated area of ischaemic necrosis in the globus pallidus.
CASE: 10. Section of the necrotic area in the globus pallidus showing the destruction of tissue and marked vascular dilatation.
CASE: 10. Section of the margin of the necrotic area in the globus pallidus showing the destruction of nerve tissue and the marked glial activity.
SUMMARY.

Although the concentration of the gas in the air breathed and the duration of exposure undoubtedly varied in each case, the effects on the brain were fundamentally similar. The most typical lesion was seen in the globus pallidus and took the form of a focus of ischaemic necrosis. In all but one case this was bilateral. The changes in and around this focus varied slightly, as may be expected, with the duration of the individual's survival following inhalation of the gas.

Another common finding was vascular congestion of either grey or white matter or both, but no one area was affected more than another. It may be noted that cases 4, 9, and 10, showed petechial haemorrhages of the "net" type throughout the white matter; while in case 3 the cortical grey matter in the temporal region had become completely separated as a result of early necrosis brought about by venous stagnation. Although this case showed early signs of disseminated sclerosis this sub-cortical necrosis was almost certainly due to the carbon monoxide poisoning.

The microscopic appearance of the cystic necrotic area seen in the globus pallidus in case 9 is consistent with the history of gassing three years previously. This case does well to illustrate the possibility of survival even after considerable damage to the globus pallidus. Another possible sequel to acute carbon monoxide asphyxia is illustrated in case 10 where the individual survived for three months in spite of extensive bilateral pallidal necrosis and widespread petechial haemorrhages into the white matter.
The microscopic appearances of the pallidal necrosis may be tabulated as follows:

<table>
<thead>
<tr>
<th>Case</th>
<th>Time between gassing and death</th>
<th>Nerve cells</th>
<th>Axis cylinders</th>
<th>Myelin sheaths</th>
<th>Gliosis</th>
<th>Microglia</th>
<th>Capillaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12 hours + degen.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>congr. and haem.</td>
</tr>
<tr>
<td>2</td>
<td>2 days degen.</td>
<td></td>
<td></td>
<td></td>
<td>microglia slightly active</td>
<td>haem.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4 days degen.</td>
<td></td>
<td></td>
<td></td>
<td>few c.g.cs.</td>
<td>congr. and haem.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4 days degen.</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>congr.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5 days degen.</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>congr.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>7 days absent</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>7 days absent</td>
<td></td>
<td></td>
<td></td>
<td>few c.g.cs.</td>
<td>congr. haem. and endoth. hyperpl.</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>13 days degen.</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3 years 1 1/2 hrs + absent</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3 months absent</td>
<td></td>
<td></td>
<td></td>
<td>numerous c.g.cs.</td>
<td>congr. haem. and endoth. hyperpl.</td>
<td></td>
</tr>
</tbody>
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From this table, it may be seen that the cellular changes in the globus pallidus can help in estimating the time between gassing and death. Particularly during the first few days, the degeneration of the ganglion cells and microglial activity give definite help. Later, the nerve cells with their axis cylinders and myelin sheaths disappear and the cellular architecture
becomes looser with compound granular cells becoming more abundant. Later still (several months) it appears that the necrotic area tends to become cystic and is walled off by a dense gliosis with compound granular cells caught in the glial network.

The other cerebral changes observed may be tabulated as follows:

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</thead>
<tbody>
<tr>
<td>1.</td>
<td>12 hours*</td>
<td>Bilateral glob. pl. (early). Put.(old)</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>2.</td>
<td>2 days.</td>
<td>Bilateral glob. pl.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>4 days.</td>
<td>Bilateral Cong. in glob. pl. cortex and left Subcort. (parietal thalamus and temp)</td>
<td>Cong.</td>
<td>-</td>
<td>Dissemin. sclerosis.</td>
<td>-</td>
</tr>
<tr>
<td>4.</td>
<td>4 days.</td>
<td>Bilateral glob. pl.</td>
<td>-</td>
<td>-</td>
<td>Capill. haems.</td>
<td>-</td>
</tr>
<tr>
<td>5.</td>
<td>5 days.</td>
<td>&quot; Cong.</td>
<td>Cong.</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6.</td>
<td>7 days.</td>
<td>&quot;</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7.</td>
<td>7 days.</td>
<td>&quot; Cong.</td>
<td>Cong.</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8.</td>
<td>13 days.</td>
<td>Left glob. pl.</td>
<td>Cong.</td>
<td>Cystic area in corpus callos. (old).</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>9.</td>
<td>3 years. 1½ hrs. +</td>
<td>Bilateral glob. pl.</td>
<td>Cong.</td>
<td>Cong. Capill. haems.</td>
<td>-</td>
<td>-</td>
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<tr>
<td>10.</td>
<td>3 months.</td>
<td>&quot;</td>
<td>&quot;</td>
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</table>
DISCUSSION.

The pathogenesis of the brain lesions met with in carbon monoxide poisoning has given rise to various theories. A study of the foregoing case reports suggests that several factors are involved.

The most dominant factor appears to be anoxaemia, brought about by the diminished quantity of available oxygen in the circulating blood. This oxygen lack produces degenerative changes, not only in the nerve cells with their axis cylinders and myelin sheaths, but also in the walls of the blood vessels. Evidence of this was observed in the capillaries as widespread congestion, haemorrhage, and endothelial hyperplasia with consequent venous stasis. Thus, anoxic and stagnant anoxaemia both play a part in the necrotic process.

Why the anterior globus pallidus should be so characteristically picked out is difficult to understand, and the foregoing cases offer nothing to clarify this problem. The more tenable theories may be mentioned briefly in the following categories:

1) A special physico-chemical affinity of certain parts of the brain (pallidum) for the gas. (Vogt quoted by Hsu and Ch'eng, 1938)

2) Anatomical peculiarities and special arrangement of the blood supply to the basal ganglia. (Kolisko and Poelchen quoted by Hsu and Ch'eng 1938).

CONCLUSIONS.

1) After acute carbon monoxide asphyxia the patient may:

(a) recover apparently completely although pallidal necrosis
has occurred, or
(b) survive for several months although pallidal necrosis and
petechial haemorrhages into the white matter have occurred.

(2) The most typical cerebral lesions to be met with in acute
carbon monoxide asphyxia are:
(a) bilateral ischaemic necrosis of the anterior globus
pallidus, and
(b) generalized congestion of vessels and, less frequently,
petechial haemorrhages throughout the white matter.

(3) In estimating the time between gassing and death, the cellular
changes in the globus pallidus are of great help.

I wish to express my thanks to Professor Sydney Smith,
under whose direction this review was written, for his inspiration
and guidance; and to Doctor Blackwood for his painstaking help.

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