October 31st. He got up for the first time after tea.
November 8th. He was quite convalescent.
November 10th. He was sent to a convalescent home.

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THE PATHOLOGY OF GAS POISONING, ILLUSTRATED BY FIVE RECENT CASES.

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THE following cases of poisoning by lighting gas occurred in Belfast in October, 1898, and January, 1899. I was asked by the coroner to examine the bodies, and in each case an exact determination was made of the percentage to which the hæmoglobin of the blood was saturated with carbonic oxide, the details of which are here recorded. As far as I am aware, no similar determinations have hitherto been made in cases of gas poisoning.

The lighting gas supplied in Belfast is a mixture of coal gas with about 40 per cent. of carburetted water gas. This mixture contains about 16 per cent. of carbonic oxide, whereas the coal gas contains only about 6 per cent. Water gas is now being extensively used in this country, and the serious extent to which its admixture with coal gas increases the risks to the public has just been reported on by a Home Office Departmental Committee.

On October 4th, 1898, S. H., a young woman, went to bed at 8.30 P.M., and was found dead at 6 next morning. The room occupied was of about 330 cubic feet capacity. It had no chimney. The ventilation by door and window was relatively small, as they were close fitting. The gas was found turned half on when the deceased was discovered.

Post-mortem Appearances.—A large amount of froth was observed about the mouth and nose. The lips were pink in tint. There was a distinct pink colour in the skin of the dependent parts. The left hand was extended. The right hand was flexed. *Post-mortem rigidity* was well marked.

Internal Appearances.—No pleuritic or pericardial fluid. Right heart collapsed; left heart moderately rigid. The cavities of the heart were nearly empty of blood. A few drops of blood were allowed to fall into a vessel of water, and at once showed the characteristic pink tint of carboxy-hæmoglobin. The lungs were slightly congested, but there was no oedema. The larynx and trachea were congested, and had a very pink appearance on the mucous surface. Some frothy mucus was in the bronchi. Emphysema very slight. The stomach contained half-digested food. The intestines had a diffused scarlet tint. The kidneys and liver were congested, but otherwise normal. The meninges of the brain were markedly congested. There was complete absence of any lesion to which death could be ascribed except the saturation of the blood with carbonic oxide.

Samples of the blood were taken in sealed tubes, and examined by the carmine method as soon as I had reached the laboratory. It was found to be 83 per cent. saturated with carbonic oxide. The conclusion was therefore perfectly clear that the patient had died from poisoning with carbonic oxide.

On January 4th, 1899, two fatal cases of gas poisoning occurred. A maidservant and two children had gone to bed in an attic room about 11 o'clock at night, and were discovered next morning shortly before 10 o'clock. The cubic capacity of the room was about 1,000 feet. There was a window, but no fireplace in the room. The floor and walls were imperfect in construction, and ventilation was probably fairly good. One child was discovered alive, and Dr. McHarry, by artificial respiration and other means,

succeeded in restoring it. The other child and the maidservant were dead.

Post-mortem Examination of M.A. (Maidservant).—The lips and conjunctivæ were pale. There was froth at the mouth and nose. There was a bluish-pink lividity on the dependent surfaces. *Post-mortem rigidity* was well marked. The body was scarcely cold twenty-four hours after its discovery. The muscles were red on incision. About 8 ounces of pink serous fluid was found in the left pleural cavity, and about 6 ounces in the right. About 2 ounces of a similar fluid was found in the pericardial sac. The lungs were pink in colour, and in both there was subpleural emphysema. There was a large amount of frothy mucus in the bronchi. The larynx and trachea were injected and pink in colour. There was no oedema or congestion of the lungs. The stomach and intestines were pale pink in colour. The stomach contained fluid food and its internal surface was pale. The œsophagus and spleen were blue. The liver and kidneys were redder than normal on their cut surface. The meninges of the brain were congested and bluish-red in colour, but otherwise normal. The brain substance was normal.

Samples of the blood were taken from the right auricle, and on examination by the carmine method were found to be 76.6 per cent. saturated with carbonic oxide.

Post-mortem Examination of M. C., aged 4 Years.—The appearances were similar to those of the case just described. There were some punctiform hemorrhages on the surfaces of both lungs, but no subpleural emphysema. There was, however, some vesicular emphysema in both lungs; otherwise the two cases were practically identical in their appearances.

The blood was examined by the carmine method, and was found in this case to be 69.5 per cent. saturated with carbonic oxide. The conclusion was, therefore, that in these two cases also death was due to carbon monoxide poisoning.

A point of interest in connection with these cases was that a young man who slept in an apartment, separated by a lath and plaster wall alone from that in which the escape of gas had occurred, also suffered from the effects of the gas. He was able to move about when he was discovered, and walked without assistance into the ambulance, which conveyed him to the Royal Hospital. Twenty-four hours later he had not completely recovered, and had no recollection of the occurrence, or of being brought to the hospital. It is probable, however, that the exertion he was allowed to make had a considerable effect in aggravating his condition.

On January 10th two cases of gas poisoning occurred. One of these was a woman aged 72, who had retired to bed about 11 P.M., and was found head at 8.45 next morning. The other was a young child sleeping in the same room, who was breathing when discovered, and was still alive when Dr. Tomb arrived. I am indebted to him for the following notes of the clinical condition of the case, and of the treatment he administered: "The child when I arrived was lying motionless and unconscious. The breathing was laboured, and there was froth exuding from the mouth. It had a cyanotic appearance, and the pulse was quick and thready. It was to all appearance in a dying condition. I wrapped the child in blankets, allowed free access of air to the room, and applied artificial respiration by Sylvester's method. I found a difficulty in this because when the arms were extended the muscles were thrown into a rigid condition from spasm. I administered coffee *per rectum*, and injected ether hypodermically, as the heart seemed to be in a weak, paralysed condition. The child remained motionless, but could be made to cry out when flapped with a wet towel. About three hours after I first saw it there occurred a fit of vomiting, when it died. There had been no sign of improvement during this time." I was requested by the coroner to obtain for analysis samples of blood from the bodies. There was no further *post-mortem* examination.

The blood when examined showed in the case of the woman the distinct pink colour of carboxy-hæmoglobin. It was found by the carmine method to be 57 per cent. saturated. The blood of the child, on the other hand, showed merely a recognisable trace of the pink colour and was not more than 5 per cent. saturated. As she had been exposed to at least as poisonous an atmosphere as the woman, there is no doubt her blood must have had at one time approximately the same saturation. The carbonic oxide had, however, disappeared from the blood presumably from the artificial respiration applied by Dr. Tomb.

The saturation in the cases was therefore as follows:

- No. 1.—83 per cent.
- No. 2.—76.6 per cent.
- No. 3.—69.5 per cent.
- No. 4.—57 per cent.
- No. 5.—5 per cent.

This series of cases affords an opportunity for raising some important questions in regard to the pathology and treatment of poisoning by coal gas. As is generally believed, and as was proved experimentally in an investigation which I recently carried out at the request of the Water Gas Committee, the poisonous effect of gas is due to the carbonic oxide and not to the other ingredients present, although there is no doubt that other poisonous bodies are present. The chief of these is probably benzene vapour; the quantity of this, however, which would be present in the atmosphere from accidental leakage would be harmless. Carbonic oxide

is poisonous because of its affinity for hæmoglobin, taking the place which oxygen occupies in the normal process of aëration of the blood. This affinity of carbonic oxide for hæmoglobin is almost exactly 300 times as great as that of oxygen. A sample of blood in a flask exposed to air containing 0.07 per cent. carbonic oxide, and shaken well up so as to absorb the gases until the hæmoglobin is completely saturated, will, when examined, be found 50 per cent. saturated with oxygen and 50 per cent. saturated with carbonic oxide. Similarly, if we breathe air containing 0.06 to 0.07 per cent. carbonic oxide, the hæmoglobin becomes equally saturated with oxygen and carbonic oxide. Speaking generally, the larger the percentage of carbonic oxide present in the air the higher the resulting saturation with this gas. The limit for the circulating blood is reached when its hæmoglobin is so highly saturated with carbonic oxide as to be unable to carry sufficient oxygen to support life. The first case in the series had reached the highest limit which has been observed (83 per cent.). The patient in this case had survived until only 17 per cent. of the total oxygen-carrying power of the hæmoglobin was left unoccupied by the carbonic oxide. The other percentage in the cases is distinctly lower. The same variation in saturation, however, is observed in the blood of coal miners who have died from the carbonic oxide resulting from an explosion in the pit.²

Since the most important point in such cases is the saturation of the hæmoglobin by the carbonic oxide, it may be well to refer to the method by which it is estimated. The carmine method was first described by Haldane.³ The colour of a dilute solution of blood in the normal condition is yellow, but if carbonic oxide be combined with the hæmoglobin it is pink. The intensity of the pink colour in a given sample depends on the relative proportions of carboxyhæmoglobin and oxyhæmoglobin present. It is possible by adding a dilute solution of carmine to normal blood to give it the pink colour of the blood containing carbonic oxide, and if the carmine solution be added from a burette we can measure the amount needed to give a pink of the same intensity as that due to any given saturation with carbonic oxide.

As regards the pathology of the condition, two facts of importance must be kept in view. The first is the effect of the saturation of the hæmoglobin with carbonic oxide is equivalent to that of depriving a person of oxygen by decreasing the amount in the air breathed. The patient poisoned by gas actually suffers from a form of suffocation. When a person exposed to carbonic oxide is found while still breathing and placed in normal air the carbonic oxide is gradually eliminated from the blood so that after some hours it has completely disappeared. The eliminating force is the affinity of the oxygen for the hæmoglobin. This gradually displaces the carbonic oxide, and the higher the percentage of oxygen the quicker the elimination. The case of the child No. 5 is of importance because it is the first on record in which it was proved that in three hours practically the whole of the carbonic oxide had been eliminated from the blood. In any case, when urgent symptoms of suffocation are present, pure oxygen should be administered, or if this cannot be procured, artificial respiration should be performed. It is desirable that the patient should remain as short a time as possible under the influence of the carbonic oxide, and for this reason oxygen should be administered even when the sole advantage would be a hastening of the recovery.

To the second fact—the after-effect on the patient of being nearly suffocated—I wish to call special attention, since it forms the real problem with which a physician has to deal. The more important elements of the after-effect are as follows:

1. A most important effect which the deprivation of oxygen has on animals is a fall in the body temperature. This is especially true of very small animals, such as mice; it is probably also true of man. The patient, if cold, should be warmed as rapidly as possible by the ordinary means, applied externally and internally. It has been noted by Haldane that after an explosion in a coal mine the men are often observed to become unconscious or even to die suddenly when they reach the outside air. The comparative coldness of the fresh air is in all probability an important factor in producing this sudden effect. Again cases are recorded in which the temperature has risen before death, suggesting that the nerve tissues concerned in regulating the body heat have been

seriously damaged by the deprivation of oxygen. In this condition of the nervous system the effect of cold air may be greatly exaggerated.

2. When the blood is over 30 per cent. saturated with carbonic oxide even slight muscular exercise such as walking produces violent headache, and if the saturation be a little higher the exercise unless extremely moderate causes the person to become giddy and unable to proceed. In the record of the cases Nos. 2 and 3 I mentioned that a young man in the next room had suffered from the effects of the gas, but that at first he was able to walk about and yet did not recover for over twenty-four hours. The probability is that he aggravated his condition by the exertions he made. When the blood is highly saturated with carbonic oxide treatment should include complete rest. Any exertion causes a drain on the available oxygen, and when this is much reduced the smallest additional drain is probably very serious. A most valuable account of the effects of exertion on those poisoned by carbonic oxide will be found in the Blue Book on the Snaefell Mining Disaster. An abstract of this report was given in the BRITISH MEDICAL JOURNAL of July 2nd, 1898.

3. An increased excitability of the nervous system is seen in the convulsions or tetanic spasms which occur. Effects of this nature have been obtained by the partial suffocation of animals, and it is not infrequently the case that patients die from damage to the nervous system hours, or it may be days, after they have been removed from the gas. On this question interesting notes will be found in Dr. Shaw Lyttle's Appendix to Haldane's Report on Colliery Explosions, 1896.

4. The heart is frequently affected. Dr. Tomb remarks that the great source of difficulty in the case he treated (No. 5) was the condition of the heart.

5. More remote effects still have to be noted. Dr. J. R. Davison, of Belfast, described a case of gas poisoning in which the patient died after four days from pneumonia. This patient never completely recovered consciousness. Part of the general damage which the suffocation had caused was a lowering of the normal resistance to the pneumococcus.⁴

The fact on which all the symptoms depend is the deprivation of oxygen. The mechanism of the circulation and various nerve centres are affected because they continue in activity, during the period of suffocation, at approximately the normal rate, while the available oxygen has been reduced to a minimum. This doubtless causes in the living tissues profound pathological changes. The nature of these changes is unknown apart from their functional manifestations.

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¹ Report of the Committee, 1899, Appendix 7. ² Vide Haldane's Report on the Causes of Death in Colliery Explosions, 1896. ³ *Journal of Physiology*, vol. xviii, p. 430. ⁴ Report of Carlisle meeting of British Medical Association, 1896.

THE NEUTRALISING POWER OF CALMETTE'S ANTIVENOMOUS SERUM: ITS VALUE IN THE TREATMENT OF SNAKEBITE.

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It will perhaps be well to state at the outset that it is not our intention in this paper to enter into the controversy as to the nature of the antagonism between snake venom and antivenomous serum, but to confine ourselves to detailing the experiments which we have performed under Professor Wright's direction with a view to determining what is the amount of venom which a given quantity of serum is capable of neutralising. We propose further to consider the question of the application of our results to the practical therapeutics of snakebite. The method¹ which M. Calmette recommends for estimating the antitoxic power of his serum is briefly stated as follows: The dose of venom which will kill a rabbit of 2 kilos. weight in from 15 to 20 minutes, when injected into the marginal vein of the ear, is determined; then the minimum amount of serum which will prevent death when