THE THERAPEUTIC ADMINISTRATION OF OXYGEN.

By J. S. HALDANE, M.D., F.R.S.,
OXFORD.

It is well known that the administration of oxygen often produces at least temporary benefit in cases of serious interference with the respiratory or circulatory functions; but sufficient attention has not hitherto been paid either to what precise benefit may be expected from the administration of oxygen, or to how it can best be administered. In the present paper I propose to discuss both these questions in the light of existing physiological knowledge, and to describe an apparatus designed for the clinical administration of oxygen.

Our knowledge of the physiology of respiration has advanced very rapidly within the last few years, and certain points which have been elucidated in this advance must first be referred to. Under normal conditions the breathing is so regulated as to keep the mean percentage of CO_2 in the air of the lung alveoli practically constant at a level which varies slightly for different individuals, but is about 5.6 per cent. The marvellous accuracy of this regulation was a revelation to physiology. A rise of about 0.2 per cent. in the mean alveolar CO_2 percentage doubles the amount of air taken into the lungs, while a fall of 0.2 per cent. produces apnoea. The rise in CO_2 acts through the blood on the respiratory centre in virtue of the very minute decrease in alkalinity which it causes; and the regulation of the blood alkalinity by the respiratory centre, kidneys, liver, and probably other organs, is so exact that no existing chemical or physical method of measuring variations in "reaction" (hydrogen ion concentration) can detect the more minute changes to which these organs are constantly reacting. For the present purpose it is, however, sufficient to remark that changes in the amount of air breathed are, under ordinary conditions, almost entirely dependent on the amount, not of oxygen, but of CO_2 in the blood leaving the lungs, and consequently passing to the respiratory centre. By reducing the CO_2 in the arterial blood apnoea can easily be produced in a person blue in the face from want of oxygen; and an animal from the blood of which sufficient CO_2 has been removed by forcible artificial respiration is not only apnoeic for a time, but will die from want of oxygen without drawing a single breath.

Want of oxygen does help to excite the breathing, but only in a very limited sense. If air containing a sufficiently low percentage of oxygen to cause slight cyanosis is suddenly breathed, there is an immediate great increase in the breathing; but this soon moderates, while the cyanosis increases and consciousness begins to fail. What happens is that the want of oxygen lowers at once the alveolar percentage of CO_2 which is required to excite the respiratory centre. In consequence of the presence in the blood, etc., of a considerable store of preformed CO_2 the breathing is greatly increased at once, and remains increased till the preformed CO_2 is reduced so as to correspond to the new level. The breathing then quiets down, and in consequence the alveolar oxygen percentage falls still lower, so that cyanosis and the other direct symptoms of oxygen want increase. If the lowering of the oxygen percentage in the air is gradual, or if oxygen want is gradually produced by gradual CO poisoning, or by a gradual ascent in a balloon or aeroplane, there is no evident hyperpnoea. The formidable symptoms (paralysis of movement and loss of consciousness) come on without warning from increase in the breathing. It is a mistake constantly made, but which ought now never to be made, to regard the breathing as a sufficient index of the existence or non-existence of oxygen want. If the breathing is greatly and persistently increased, some other cause is present than oxygen want.

The physiological effects, immediate and remote, of oxygen want must now be considered. When suddenly produced, oxygen want acts almost instantly in increasing the sensitiveness of the respiratory centre to CO_2, and so producing an urgent desire to breathe. The rapidity of this action, as compared with the normal and much slower reaction to accumulation of CO_2, is the explanation of periodic or Cheyne-Stokes breathing. To produce this sudden reaction (which is less readily produced in some persons than in others) the percentage, or rather the partial pressure, of oxygen in the alveolar air or blood supplying the respiratory centre must, however, fall below normal limits. At high altitudes, or in air with a greatly reduced oxygen percentage, the necessary reduction in the alveolar oxygen pressure occurs quite easily, and periodic breathing is a normal occurrence, which is stopped at once by increasing the oxygen percentage in the air breathed, just as Cheyne-Stokes breathing in a patient is stopped by administering oxygen. Periodic breathing, which is a sign of impending oxygen want, is simply the "hunting" of a too quickly acting respiratory governor, which is constantly overshooting the mark.

As already remarked, the initial hyperpnoea produced by rapid onset of oxygen want is soon relieved by the consequent washing out of CO_2 from the blood, provided that this washing out is free to occur. If not, the hyperpnoea will continue, even in spite of relief of the far more dangerous symptoms of oxygen want. Great hyperpnoea accompanied by oxygen want is characterized by marked rise in pulse-rate, palpitation, great rise in arterial blood pressure, and, what is still more remarkable, a simultaneous great rise in venous blood pressure. The latter phenomenon is indicated by distension of the lips, face, tongue, etc., with blue venous blood, distension of superficial veins in the neck and chest, and the other signs of "acute" cyanosis. The high venous blood pressure is very apt to lead to over-distension of the right side of the heart and consequent paralysis of the heart and death. For this reason, free venesection may be of the greatest service in conditions of acute cyanosis. The great and immediate benefit arising from free venesection in acute asphyxial conditions arising from irritant gas poisoning was, so far as I am aware, first pointed out by Drs. Irvine and Macaulay of Johannesburg, and was also independently observed by Dr. Hale White in a case brought to Guy's Hospital. In consequence of their experience, the utility of this mode of treatment in cases of acute cyanosis from chlorine poisoning was pointed out in France, and its success was recorded recently by Captain S. Hebblethwaite, R.A.M.C.[1]

If the washing out of CO_2 in the lungs is not interfered with, "acute" cyanosis and hyperpnoea do not occur at all, or are only temporary. The other effects of oxygen want then become more and more prominent. The lips become of a leaden or grey, rather than blue, colour, since they are not distended with blood. Sensibility, mental control, and memory begin to fail rapidly. At a further stage of oxygen want the legs are usually first paralysed, then the arms, and later the head and neck. The senses also go one by one, hearing being the last. If, as often occurs in CO poisoning, loss of consciousness from oxygen want has continued for some hours, ultimate recovery of the central nervous system is very doubtful, and the heart and other organs, such as the kidneys, may also suffer badly, great cardiac dilatation and valvular incompetence, lasting for weeks, being not infrequently observed. The mistake is often made of not grasping the serious, widespread, and lasting effects caused by want of oxygen. Even when the want of oxygen is completely removed these effects remain. This is very strikingly seen in CO poisoning. When an unconscious man is removed from the poisonous air the CO is very rapidly washed out of his blood; but he may still be unconscious, and in a dying condition, with his blood perfectly free of CO, and the cause of the oxygen want thus completely removed. The damage done by oxygen want depends partly on the degree of oxygen want but still more markedly on the duration of the exposure, and it is this latter factor which I wish specially to emphasize, as its importance is seldom realized.

If the degree of oxygen want is slight and only temporary the immediate symptoms are trifling, and may hardly be noticed except on muscular exertion, but if the exposure is continued for some time formidable effects are produced. These are severe headache, nausea, and extreme depression. They are seen typically in mountain sickness, and in the effects of a pretty long exposure to a comparatively low percentage of CO, and they are doubtless mixed up in the clinical picture of many cases of respiratory and circulatory affections. In cases of CO poisoning it is usually after the exposure that the symptoms develop, and in mountain sickness several hours'

exposure are usually needed. Those who have experienced the extreme depression of mountain sickness or CO poisoning will readily realize that such a condition may make all the difference between life and death to a patient battling with illness.

From the foregoing remarks it seems clear that a physician ought to make every effort to avert the effects of want of oxygen or cut them short. It may be argued that such measures as the administration of oxygen are at the best only palliative and are of no real use, since they do not remove the cause of the pathological condition. As a physiologist, I cannot for a moment agree with this reasoning. The living body is no machine, but an organism constantly tending to maintain or revert to the normal, and the respite afforded by such measures as the temporary administration of oxygen is not wasted, but utilized for recuperation.

Let us now consider in more detail how oxygen want is produced, what seems to be possible in directly combating it by oxygen administration, and what risks have to be avoided. We may begin with a simple and easily intelligible case—that of poisoning by CO, or by a nitrite, chlorate, or other poison which causes death by disabling the oxygen-carrying power of the blood. In such a case acute want of oxygen is produced by the poison disabling the haemoglobin, so that it is unable for the time to carry sufficient oxygen to support life. Normal human arterial blood carries about 18.1 c.cm. of available oxygen per 100 c.cm. of blood. Of this, about 17.75 c.cm. are combined with the haemoglobin and 0.35 c.cm. are in simple solution. In passing round the circulation during rest this blood loses only about 4.5 c.cm. of oxygen. In poisoning by CO and similar respiratory poisons, death occurs when about 80 per cent. of the haemoglobin is disabled. If the patient is still alive there will, therefore, still be 20 per cent. of his haemoglobin available. But by administering pure oxygen we can at once increase the amount of oxygen in simple solution to about 2.5 c.cm. This promptly averts any further danger from want of oxygen, and in CO poisoning the oxygen rapidly drives out CO from the haemoglobin, so that after fifteen or twenty minutes of continuous administration the oxygen may be discontinued. In poisoning by nitrites, etc., there is also a fairly rapid return of the blood towards the normal, consequent on the gradual elimination or destruction of the poison. Experiments on animals have shown quite clearly that oxygen actually does avert death in the cases just considered.

In acute inflammatory conditions of the lungs there is sometimes also want of oxygen, as shown by cyanosis; and where the inflammatory condition is accompanied by the presence of "oedematous" exudation throughout the lungs the cyanosis is often very great. This condition is seen typically in the acute stages of poisoning by nitrous fumes or chlorine. What is its probable cause? When a portion of the lungs, including even the greater part of both lungs, is entirely blocked by consolidation, as in croupous pneumonia, there is commonly no cyanosis. This indicates that very little blood is passing through the consolidated parts. What passes through the healthy portion is amply sufficient for respiratory requirements during rest. It must be borne in mind that the normal lungs and circulatory organs are adapted for meeting about ten times the respiratory requirements during rest, since the respiratory exchange is often about ten times as great during work as during rest. Hence during rest in bed a very small proportion of normal lung will suffice for meeting respiratory and circulatory requirements, provided there is but little circulation through parts which are useless. But when cyanosis due to a lung affection exists, in spite of the fact that air is entering the whole or a great part of the lungs freely, we seem driven to the conclusion that the entry of oxygen into the blood through the alveolar walls is impeded by exudation and increase in thickness of the alveolar walls.

It is very important to realize that this may occur without any serious impediment to the passage of CO_2 outwards. CO_2 is about twenty-five times as soluble in water as oxygen, and hence it passes through the alveolar walls far more easily, with a given difference of partial pressure, than does oxygen. Moreover, a comparatively slight increase in the breathing will enormously increase the small difference in diffusion pressure on which the passage of CO_2 outwards depends; but the same increase in breathing produces only a slight proportional increase in the diffusion pressure which drives oxygen inwards. Hence we may have cyanosis, and consequently very formidable effects from oxygen want, without marked hyperpnoea. The grey look of the patient's face will be a good index of this. There will probably be no increase of venous blood pressure with its accompanying full blue cyanosis.

If great hyperpnoea accompanies the cyanosis there must be some other complicating condition. This accompaniment is seen typically in the acute stage of poisoning by chlorine or nitrous fumes; and the results of *post-mortem* examination, together with clinical observation during the recovery stage, seem to reveal the cause. In the acute stage the alveolar walls become extensively torn in efforts to breathe despite the blocking of many of the bronchi by exudation or constriction. In consequence of this there is widespread emphysema, which is very evident on *post-mortem* examination. The areas round the emphysematous cavities are partially collapsed and very imperfectly ventilated, so that the CO_2 percentage rises in them to an abnormal extent. The emphysematous cavities are excessively ventilated, but this ventilation is of little use since the proportion of sound alveolar wall to air is far too small. In consequence of this the CO_2 content of the arterial blood is raised, and hyperpnoea, along with increased arterial and venous blood pressure, results. As the oedema clears up the cyanosis disappears, but the hyperpnoea remains for some days, since it takes a considerable time for the emphysema to heal up.*

When there is cyanosis (whether of the deep purple or grey type) due to hindered passage of oxygen through the alveolar walls, this can be combated by raising the percentage of oxygen in the alveolar air and so increasing the diffusion pressure. The normal alveolar oxygen percentage is about 14, or 7 per cent. less than in the external air. By raising the percentage of oxygen in the inspired air to 35 we raise the alveolar oxygen percentage to 28, and thus much more than double the effective diffusion pressure, since the oxygen pressure in the venous blood passing to the lungs will probably be at least 4 per cent. It will probably, therefore, require only a moderate increase in the oxygen percentage of the inspired air to remove the cyanosis. Even in ordinary cases of croupous pneumonia the alveolar oxygen pressure may be a matter of decisive importance. This is clearly shown by the fact that these pneumonias do very badly at high altitudes. At Cripple Creek (altitude about 10,000 ft.) in the Rocky Mountains I found that this was so well recognized that all cases of pneumonia were put in the train and sent down to the prairie level.

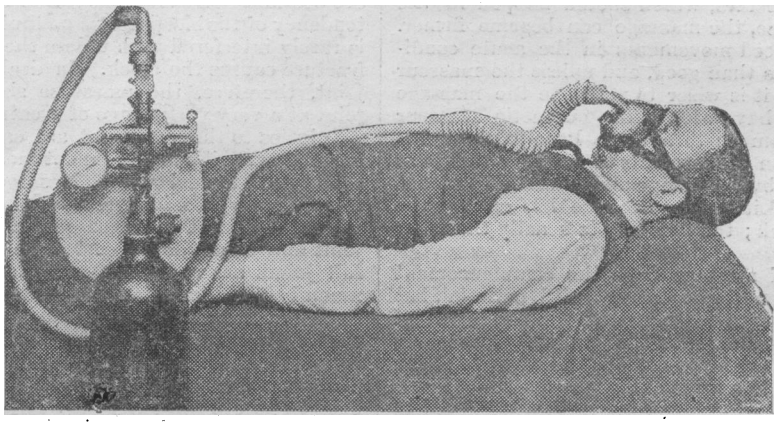
Where, in lung affections, an addition of oxygen to the inspired air is needed in order to combat want of oxygen, it is evidently desirable to continue the administration over long periods. It was shown by Paul Bert that oxygen at a pressure of about three atmospheres is capable of producing convulsions and rapid death; but Lorrain Smith found that, apart altogether from this action on the nervous system, pure oxygen at high pressures produces pneumonia pretty rapidly, and even at ordinary atmospheric pressure acts slowly on the lungs, ultimately producing fatal pneumonia after several days in animals. This effect was even occasionally produced in about four days by a mixture containing only 80 per cent. of oxygen. It is evidently desirable, therefore, to keep the oxygen percentage as low as possible during long administrations, and to know roughly what percentage is being breathed.

In cases where the source of danger is failure of the circulation, the inhalation of oxygen may also be of use, and I have seen the cyanosis in a case of valvular disease clear up at once on the administration of oxygen. The effect was so striking that it could hardly be attributed to the increased amount of oxygen going into simple physical solution in the arterial blood. It seemed more probable that owing to back pressure in the lungs and consequent exudation, etc., there was hindrance to the diffusion of

* It may perhaps be pointed out here that hyperpnoea means increase in the volume of air breath d per minute. The frequency of breathing is no reliable index of hyperpnoea. If in a normal person the frequency of breathing is voluntarily varied from three a minute to sixty a minute, the depth of each breath being left to itself, there will be not the slightest increase in the lung ventilation (as measured by the composition of the alveolar air) when the breathing is at sixty a minute. There are various causes of increased or diminished frequency of breathing, the vagus nerves being specially concerned with the regulation of frequency.

oxygen inwards, and that with the increased oxygen percentage this was overcome. Nothing but practical trial, for which I have at present but few opportunities, will show to what extent, and under what conditions, the administration of oxygen is of use in various pulmonary and cardiac affections. Cyanosis may always be taken as an indication that oxygen inhalation should be considered.

The immediate effect of suddenly giving an abundance of oxygen to a cyanosed person may sometimes be unpleasant, as I well know from experiments on myself and others. The heart may become tumultuous in its action, and the breathing irregular for the time, or the patient may wake up to the realization of pain or discomfort. His respiratory centre may also wake up to reaction against accumulated CO_2. It is well, therefore, not to add oxygen too rapidly to the inspired air in cases of cyanosis.



Existing methods of giving oxygen are nearly always very crude and wasteful of oxygen, and it is not possible to graduate efficiently the percentage of oxygen administered. The simple apparatus now to be described is designed to remedy these defects and render practically possible the prolonged administration of air enriched with as little oxygen as will suffice for the purpose aimed at.

An ordinary 20-foot oxygen cylinder is fitted with a pressure gauge and adjustable governor of the type employed in mine-rescue apparatus. By means of the governor the delivery of oxygen can be varied at will from nothing to 10 litres a minute. The oxygen is delivered into a small bag of thin vulcanized rubber of about 2 litres capacity. From this bag there passes to a facepiece on the patient a flexible tube of about five-eighths of an inch in diameter. At its origin from the bag this tube is provided with a non-return mica valve. The last part of this tube is of light and perfectly flexible corrugated rubber tubing of the kind introduced by Mr. Fleuss for mine-rescue apparatus. The facepiece is of the ordinary type, fitting over the mouth and nose, but so designed as to leave a minimum of dead space when applied to the face. It can be secured in position by an elastic strap. Besides an inlet for oxygen, the facepiece has inlet and outlet valves for air, so that if no oxygen is turned on the patient can breathe air quite comfortably and freely. Some air will also leak in and out round the facepiece which need not be at all tightly applied.

When oxygen is turned on it accumulates in the small bag during expiration, since the very slight expiratory pressure in the facepiece closes the non-return valve, and this prevents the issue of oxygen from the bag, and, of course, at the same time prevents expired air from entering the bag. During inspiration the bag is emptied, the oxygen passing into the facepiece and thence into the patient's lungs. If only a little oxygen is turned on the patient will be breathing mostly air, but by turning on more oxygen the proportion of oxygen can be increased till nothing but pure oxygen is being inspired, and the bag does not completely collapse till the very end of inspiration. Thus no oxygen is wasted, and enormous economy of oxygen results, so that prolonged administration of oxygen becomes practicable.

Where prolonged administration of oxygen seems desirable, the minimum quantity of oxygen which will remove the cyanosis should be carefully ascertained by observation of the patient, and the governor adjusted to give this minimum quantity, which is likely to be anything from 1 to 3 litres per minute. The quantity needed will of course depend on the weight and age of the patient; and if hyperpnoea due to CO_2 is present, a larger quantity will be needed to reach a given percentage. A man at rest usually breathes about 7 litres of air a minute.

The probable risks of prolonged administration of pure oxygen must be borne in mind, and if necessary balanced against the risks of allowing the oxygen want to continue. No fixed rule can be given. The proper course to pursue must be determined by the physician after careful observation of the patient, and in the light of experience and knowledge. Many points with regard to the utility of oxygen administration are still obscure, owing to the haphazard methods hitherto used in administering the oxygen.

The apparatus is shown in the accompanying figure, and is made by Messrs. Siebe, Gorman, and Co., Westminster Bridge Road, London, S.E. A simple resistance meter can also be supplied for rapidly checking the indications of the governor on the cylinder.

REFERENCE.
1 BRITISH MEDICAL JOURNAL, July 22nd, 1916.

MINOR INJURIES TO JOINTS.

BY
FRANK ROMER, LIEUT.-COLONEL R.A.M.C.(TEMP.).

AT the Croydon War Hospital, where we receive every class of crippled limb, I frequently come across cases of ordinary sprains and dislocations where recovery has been delayed from want of suitable treatment in the initial stages. The conditions of active service render men particularly liable to such injuries, but when the medical officers have many serious cases requiring urgent surgical attention, those who are incapacitated by minor injuries are often unable to receive the attention they would otherwise get. It is in no carping spirit of criticism, therefore, that I refer to this point, but with the view of drawing attention to the importance of immediate treatment when dealing with men sustaining these injuries in England, since by so doing they can be returned to duty more quickly than by waiting for treatment at a later date. Delay not only renders recovery more difficult, but prolonged acquaintance with hospital life is apt to sap the *moral* of the men.

A sprain has been described as an incomplete dislocation, and is said to occur where a joint has been wrenched by a force sufficient to overstretch or rupture the controlling ligaments and tendons. It may vary from a condition where the joint is completely incapacitated to a mere deviation from the normal, where pain is only elicited by some particular movement.

Hitherto textbooks have made scant reference to the treatment of these common injuries, yet the disability caused by them often persists long after all active trouble has subsided. Treatment should be directed not only to the relief of the immediate pain but to the prevention of those common sequelae—weakness and stiffness of the joint.

If we examine the history of a sprain—and most of us have at some time or other experienced it—there is the curious sickening and painful sensation of its reception, followed by a sense of numbness, which is quickly followed by swelling of the joint and increase of pain. This pain is due to pressure of the extravasated blood and lymph on the sensory nerves, and the more quickly this effusion is absorbed the sooner may recovery be looked for.

For many years absolute physiological rest, combined