

THE INORGANIC GASES IN ANESTHESIOLOGY *†

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THE anesthesiologist uses the inorganic compressed gases in his every day anesthetic practice, oxygen therapy, and other therapeutic procedures. Few things used by him are taken for granted as much as these auxiliary agents. Familiarity with the practical aspects of the chemistry and physics of these gases is not only desired but essential since they are intimately concerned with the physiology and pharmacology of anesthesia and inhalation therapy. The inorganic gases of chief concern to the anesthetist are oxygen, nitrogen, carbon dioxide and helium. Certain data, particularly physical data-applicable to all inorganic gases, have been summarized to include those pertinent facts of practical significance to the anesthesiologist. Since oxygen is the most important gas used, it will be discussed first, and this discussion will include the majority of these generalizations. Although nitrous oxide is an inorganic substance, it is omitted from this discussion as it is best included in a summary of anesthetic drugs.

Oxygen.—This element was first discovered by Priestley in 1774 and identified by Lavoisier in 1777. Oxygen (1, 2) for medical purposes originally was prepared by interacting sodium peroxide with water in a special device known as the "Oxone" generator (3). This method of preparing oxygen even on a small scale was cumbersome as well as expensive. The modern commercial method of preparation is to distill liquid air fractionally. Nitrogen, which boils at a higher temperature (B.P. -195 C.), passes off first, leaving liquid oxygen as a residue.

Liquid air is usually prepared by one of two methods. The Linde process allows compressed air to reexpand around a series of tubes through which fresh successive portions of compressed air are entering. The reexpanding gases absorb heat and reduce the temperature of these successive portions to the critical temperature. The critical temperature may be defined as that temperature above which a gas

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cannot be liquefied regardless of the magnitude of the pressure. Therefore, a pressure must be maintained above a certain value known as the critical pressure, which may be defined as the pressure below which a gas will not liquefy, regardless of the extent of cooling. The Claude process allows a greater degree of cooling by using the reexpanding gas to work a piston to compress the incoming air. The compression of air or oxygen must be accomplished without the use of oily lubricants for the pump cylinders, since under pressure in the presence of oxygen these materials form explosive mixtures.

A less popular method of preparation of oxygen is to decompose acidulated water by electrolysis. Oxygen collects at the anode; hydrogen at the cathode. The method is usually employed when hydrogen is desired primarily; the oxygen is merely a by-product. An older process, the Le Brinn process, which has been supplanted by these aforementioned methods, takes advantage of the fact that barium oxide (BaO) heated in air at red heat (500 C.) is converted to the peroxide (BaO_2). The peroxide at white heat (800 C.) is decomposed once more to the oxide with the reliberation of oxygen which is collected and stored. The process can be almost perpetual.

There is no difference between oxygen for "medicinal" use and that for "commercial" purposes. It all conforms to the specifications of U.S.P. XI which insists upon a purity of 99 per cent (4). The method of manufacture may vary, but the purity and cleanliness of the product must be assured in all circumstances.

It is perhaps needless to mention that oxygen is an odorless, colorless, and tasteless gas. The atomic weight is 16.00; the molecular weight is 32, since, as with most inorganic gases, the molecule is diatomic. Equal volumes of different gases at identical temperatures and pressures contain the same number of molecules (Avogadro's law). Thirty-two grams of oxygen occupy the same space as 2.008 grams of hydrogen (5). At 0 C. and 76 cm. pressure this volume, often referred to as the gram molecular volume, equals 22.4 liters. In clinical discussions the weights of gases are expressed by specific gravity, which is the weight of a liter of gas compared to the weight of a liter of air under the same conditions of temperature and pressure. Oxygen is heavier than air since its specific gravity is 1.429.

Under the influence of a silent electric discharge pure oxygen is partially (2 per cent) converted to ozone (O_3) which has a triatomic molecule and powerful oxidizing properties.

Since oxygen requires a low temperature (-119 C.) and a high pressure (50 atmospheres) for liquefaction it can only be dispensed as a compressed gas at ordinary temperatures. Solid oxygen melts at -219 C. (6). Liquid oxygen is used for medical purposes to supply the gas. Open thermos bottles, from which the daily loss averages 5 per cent of the total, are used for storage and shipping.

Cylinders for dispensing oxygen, as well as other compressed gases, are constructed of steel of a minimum thickness at any point of $\frac{3}{8}$ of an inch (7). Larger cylinders, in which excessive weight becomes a factor, consist of an alloy of chrome molybdenum whose density is approximately 80 per cent that of steel. Cylinders for interstate shipment are under the surveillance of the Interstate Commerce Commission. This organization has instituted rigid regulations regarding their construction and testing (8).

Cylinders to be charged with oxygen or other gases at a service pressure exceeding 450 pounds per square inch (ordinarily including all cylinders for anesthetic purposes) must resist an internal hydrostatic pressure of five-thirds of their service pressure. An "E" cylinder for oxygen (capacity—130 gallons—530 liters) whose service pressure must not exceed 2015 pounds per square inch must withstand an internal pressure of 3400 pounds per square inch. In addition they must have elasticity, but in no case may the expansion due to this elasticity exceed 10 per cent of the total expansion. The maximum pressure at which a cylinder may be used when in service must be clearly engraved upon its shoulder (fig. 1). Cylinders must never be refilled to a greater pressure than that which was originally intended.

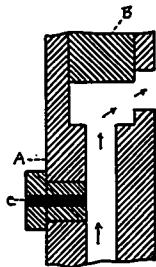


FIG. 1. Arrangement of the safety device which allows evacuation of cylinders at high temperature. The hollow bolt (C) is filled with a low melting point metal and placed in the body (A) of the valve below the valve seat (B).

At five year intervals cylinders must be subjected to tests similar to those performed at the time of manufacture and the date of such test engraved upon its shoulder. The required hydrostatic pressure is applied for a minimum of thirty seconds during which an automatic recorder prepares a graphic chart of the sustained pressure.

Cylinders must be equipped with a safety device approved by the Interstate Commerce Commission which will permit evacuation in the event of exposure to fires or other high temperatures. This device usually consists of a bolt with a core filled with a low melting point metal. This bolt is inserted in the valve stem proximal to the valve seat (fig. 2).

The core (Wood's metal) melts should the cylinder be exposed to temperatures over 200 F. and allows the cylinder to exhaust itself of its contained gases, which would otherwise expand and explode.

The weakest part of a cylinder is its valve which is easily damaged by dropping or rough handling. Protective caps, if available, should always cover the valve when cylinders are not in use to prevent damage to its delicate mechanism. The valve should always be opened slowly with a minimum force and with the aperture through which the gas

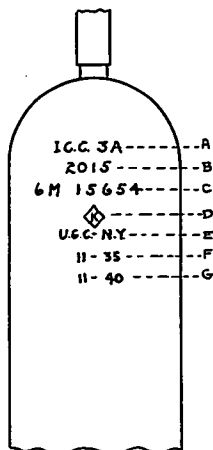


FIG. 2. The engraving markings on the shoulder of cylinders for storing compressed gases.

- A. Interstate Commerce Commission type 3A for filling at pressures over 450 lbs. per square inch.
- B. The maximum pressure to which the cylinder may be filled.
- C. The manufacturer's number of the cylinder.
- D. The initials of the laboratory which tested the cylinder.
- E. The initials and address of the manufacturer.
- F. The date of the original test.
- G. The date of the five year "follow check up" test.

escapes always pointed away from the user. Gases should never be allowed to mix within a cylinder. Any device or valve which permits the backflow of one gas into a cylinder containing another gas should never be used.

Oxygen and other gas cylinders are best stored in well ventilated, dry rooms away from oils and greases, fumes and extremes of temperature. Cylinders should be securely fastened in an upright position to prevent injury to the valve. They are best transported on trucks especially built for the purpose.

The moment of greatest hazard in the compressed gas industry is compression of any gas. Considerable heat may be liberated by the during the filling of cylinders. Heat is always liberated during the recompression of the molecules within the cylinder during the filling process. These sudden energy changes cause more accidents at this time than at any other in the manufacturing process. Those physicians who refill small portable cylinders from large reservoirs (transfilling) in many respects reduplicate the filling process which takes place at the manufacturer's plant. Unknowingly they may be exposing themselves to a hazard. In the interest of safety the practice should be condemned. One must also remember never to use oil or grease on any valve gage or meter for compressed gases.

A vacuum is applied to all cylinders returned to the manufacturer for refilling to evacuate them completely. Valves on all cylinders, whether completely exhausted of their contents or not, should be completely closed when returned to the manufacturer to prevent contamination by noxious agents. Each cylinder is thoroughly cleaned at the time of each quinquennial testing by first washing thoroughly with water, then spraying with a solution of potassium hydroxide, then rinsing with water, and then blowing in steam, following which the cylinder is thoroughly dried. The valve, after being tested for leakage, is then reinserted, and the cylinder is refilled to its proper pressure. The exterior is then painted and labeled according to the recommendations recently suggested by the United States Department of Commerce (9) (table 1). The various sizes and capacities of cylinders for anesthetic and other compressed gases are shown in table 2.

TABLE 1

THE COLOR MARKING OF ANESTHETIC GAS CYLINDERS RECOMMENDED OF THE NATIONAL BUREAU OF STANDARDS, DEPARTMENT OF COMMERCE

Oxygen	green
Carbon dioxide.....	gray
Nitrous oxide.....	light blue
Cyclopropane.....	orange
Helium.....	brown
Ethylene.....	red
Carbon dioxide oxygen.....	gray and green
Helium and oxygen.....	brown and green

Oxygen is carried in blood in two ways—in simple solution in the plasma and by chemical combination with hemoglobin. Four and ninth-tenths cc. of oxygen dissolve in 100 cc. of distilled water at 0 C. and 76 cm. pressure. The solubility of gases decreases with rises in temperature. At body temperature (37.5 C.), therefore, less (2.7 cc.) will dissolve per 100 cc. of water at 76 cm. pressure. The amount of a gas absorbed by a liquid which does not combine chemically with the gas is directly proportional to the partial pressure of the gas if the temperature remains constant (Henry's law) (10). In a mixture of gases

TABLE 2
DIMENSIONS AND CAPACITIES OF CYLINDERS

Approximate Dimensions (with Valve)	Approx. Net Weight	Gas	Approx. Pressure	Weight of Gas	Volume		Valve Type
					Cu. Ft.	Gal.	
3½"×16" "B"	8½ lbs.	CO ₂	800 lbs.	1 lb. 9 oz.	13.6	100	Anesthetic
		O ₂	1800 lbs.	7½ oz.	5.35	40	"
		N ₂ O	800 lbs.	1 lb. 9 oz.	13.6	100	"
4½"×20" "D"	14½ lbs.	CO ₂	800 lbs.	3 lbs. 14½ oz.	34.0	250	"
		CO ₂ -O ₂	1500 lbs.	Variable	10.7	80	"
		O ₂	1800 lbs.	15 oz.	10.7	80	"
		N ₂ O	800 lbs.	3 lbs. 14½ oz.	34.0	250	"
4½"×29" "E"	20½ lbs.	CO ₂	800 lbs.	6½ lbs.	57.0	420	"
		CO ₂ -O ₂	1500 lbs.	Variable	17.4	130	"
		C ₂ H ₄	1250 lbs.	3½ lbs.	44.5	330	"
		O ₂	1800 lbs.	1 lb. 8 oz.	17.4	130	"
		N ₂ O	800 lbs.	6½ lbs.	57.0	420	"
5½"×55" "F"	70 lbs.	CO ₂	800 lbs.	20 lbs.	174.0	1280	½ inch
8½"×55" "G"	110 lbs.	CO ₂ -O ₂	1500 lbs.	Variable	153.7	1150	"
		N ₂ O	800 lbs.	50 lbs.	436.0	3200	"
		O ₂	1800 lbs.	13 lbs.	153.7	1150	"
9"×55" "H"	130 lbs.	CO ₂ -O ₂	1700 lbs.	Variable	220.0	1650	.903 inch
		O ₂	2000 lbs.	17½ lbs.	220.0	1650	"
8"×34" "Low Pressure"	40 lbs.	CO ₂ -O ₂	240 lbs.	Variable	13.6	100	Special
		CO ₂ -O ₂	300 lbs.	Variable	17.0	125	"
		O ₂	240 lbs.	19 oz.	13.6	100	"

Dimensions, capacities and pressures of currently used anesthetic gas cylinders are shown.

each gas exerts an individual pressure independent of the other gases. This pressure, known as the partial pressure or tension, is the same as if the gas were occupying the space alone. The total pressure of the mixture is equal to the sum of the partial pressures of each gas (Dalton's law). A gas dissolved in a liquid establishes an equilibrium with the free gas over the surface of the liquid. The pressure or tension of the gas in the liquid is the same as that over the surface of the liquid. The inhalation of 100 per cent oxygen raises the tension in the alveoli to almost 76 cm. and quadruples the amount of oxygen dissolved in blood plasma, but raises that combined within the blood cells only slightly since hemoglobin of arterial blood usually is about 95 per cent saturated (11). This increase of the portion in simple solution which amounts to about 10-15 per cent of the total (19.2 to 22.2 vols. per cent) becomes of practical significance in medicine since the increased partial pressure of oxygen is transmitted to tissues with a subsequent reduction in the partial pressure and displacement of nitrogen from them. This displacement of nitrogen assumes importance in various clinical conditions such as intestinal obstruction, anaerobic infections and in preventing

aero-embolism (12). Rapid or sudden lowering of atmospheric pressure as may occur in deep sea diving or high altitude flying favors a release of dissolved gases due to the decrease in pressure in blood and tissues. When air is inhaled under these conditions, the bulk of this dissolved gas which is released is nitrogen. Since nitrogen cannot be utilized by tissues, it forms bubbles in blood and tissues, giving rise to serious symptoms. Substitution of pure oxygen for air relieves this objection, since the cells can utilize the oxygen. Patients who have intestinal obstruction or have undergone encephalography have mostly nitrogen in the hollow viscera. A high oxygen pressure developed in plasma and tissues establishes a gradient which will favor the diffusion of this nitrogen from the viscus in which the pressure is high to the plasma where it is low (13).

The quantitative estimation of the oxygen content of gas and blood samples is becoming a widespread practice of considerable value in inhalation therapy and anesthesia. Better understanding of fundamentals of gas analysis should be encouraged. Although the chemical methods of gas analysis are numerous, often complex, and in many cases devised for individual gases, the more important types of apparatus used may be resolved into three general types based upon certain fundamental general principles.

The first and most common type is that in which the temperature and pressure are kept constant and changes in volume are measured. A measured sample of gas at a known temperature is drawn into a calibrated burette by means of some displacing fluid, such as mercury or some salt solution in which gases have a low solubility, and then forced into an absorption pipette containing reagent which absorbs it. The nonreactive, or unabsorbed gas which remains, is redrawn into the burette and the decrease in volume is observed. This remaining gas may be passed into another pipette containing a different absorbent and a second gas be quantitatively measured. Several or all gases in a sample may be determined if a series of pipettes with the proper absorbents is used. In this type of analysis the pressure is of necessity barometric and the temperature that of the room. The Orsatt (14) and its various modifications, the Haldane, and the Van Slyke apparatus employ this principle (15) (fig. 3).

The second type of apparatus is that in which changes in pressure resulting from chemical absorption are measured at a constant volume and temperature. A calibrated burette into which specimens may be introduced and measured, a manometer and a leveling bulb filled with mercury to draw and expel reagents into the burette are interconnected. The gas to be determined is absorbed with the proper reagent, and the fall in pressure is measured after the remaining unabsorbed gas is readjusted to the original volume. Computations of the volume of absorbed gas follow according to Boyle's law (16) which states that the volume of a gas varies inversely as the pressure if the temperature

remains constant. This type of apparatus is adaptable to liquids from which gases may be liberated chemically or extracted under reduced pressure. Corrections for solubility of gases in liquids and vapor pressure must be made in computations for this type of apparatus. The Van Slyke-Neill apparatus, based upon this principle, is used to measure

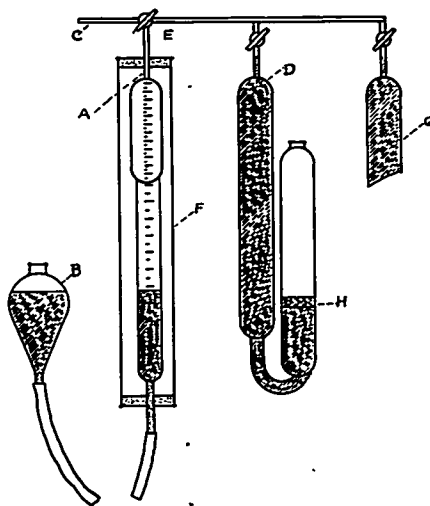


FIG. 3. Schematic diagram of a gas analysis (Orsat type) apparatus which measures changes in volume at a fixed temperature and pressure. (A) The measuring burette connected to the leveling bulb (B) containing displacing fluid, usually mercury, to aspirate the sample from inlet (C) into the burette and force it in and out of the absorption chambers (D) through the three-way stopcock. (E) The pressure is adjusted at atmospheric by adjusting the leveling bulb with the level of fluid in the burette. The glass jacket (F) tends to maintain a constant temperature. Several chambers (G) may be used each containing a different absorbent for separate gases. Mineral oil (H) may be used to protect the reagents from air (or rubber bags connected to rubber tubing may be used to seal the opening). The displaced liquid from the absorption pipette passes in and out of the lower chamber through the U tube.

oxygen content and other gases in blood and body fluids (fig. 4). The ordinary, older form of the Van Slyke apparatus may also be used for fluids but it employs the principle of analysis of change in volume (17).

The third but less common method of analysis is that in which a measured volume of gas at a known temperature and pressure is converted into a nonvolatile chemical substance which is quantitatively isolated and determined by gravimetric, volumetric, or colorimetric methods. For example, cyclopropane may be oxidized by hot iodine

pentoxide to form carbon dioxide and free iodine. The iodine which is liberated quantitatively is collected and titrated with standard sodium thiosulphate solution from which the amount of cyclopropane is calcu-

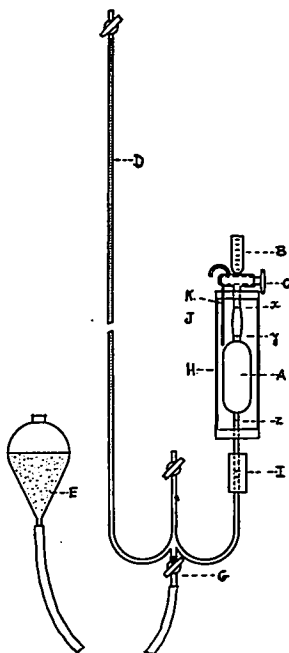


FIG. 4. The manometric type of apparatus (Van Slyke and Neill) used principally for measuring gases in liquids is shown. The 50 cc. burette (*A*) with a measuring cup (*B*) and double stopcock (*C*) for drawing in and ejecting samples and reagents is connected to a closed manometer (*D*) and a mercury leveling bulb (*E*) which can be closed off by the stopcock (*G*). The water jacket (*H*) maintains a constant temperature measured by the thermometer (*K*). A vacuum can be created to extract liquids in the bulb of the burette by lowering the leveling bulb below the level of the apparatus so the mercury falls to the 50 cc. mark *z*. The extracted gases are compressed both before and after absorption to a constant volume (2 cc. or 0.5 cc.) by adjusting the meniscus of the liquids in the chamber to mark *x* or *y*. Differences in pressure before and after absorption are used to compute the volume. The flexible joint (*I*) allows a to and fro motion for agitation of the reagents by a mechanical shaker. The entire apparatus is usually mounted on a base board.

lated (18). The volume of a gas at a constant pressure is proportional to the absolute temperature (-273 C.) (Charles' law). This must be born in mind in computations, but is seldom used as the basis for any type of analytical apparatus.

Some methods of gas analysis may be highly complex, particularly those used in research and industrial practices. Many devices for special purposes are based solely upon physical principles such as changes in thermal or electrical conductivity, changes in velocity of sound, etc., rather than chemical methods. These are too complex for discussion here.

In referring to gases the volume is expressed in two ways. One may use the Bunsen absorption coefficient, often expressed by the Greek letter alpha, which is the volume of a gas absorbed by 1 cc. of a liquid at 0 C. and 76 cm. pressure (19). The other, usually used in biological studies, is the Ostwald coefficient which is expressed by the Greek letter lambda, and refers to the volume of a gas absorbed by 1 cc. of a liquid at the temperature and pressure of the experiment. Gas content of specimens in biological studies is expressed in volumes per cent which means the number of cubic centimeters of gas in 100 cc. of the liquid (or gas in gas mixtures) at the conditions of the experiment.

Oxygen in gas samples is best analyzed for clinical purposes by the change of volume method. The most common analyzer employed is of the Orsatt type, in which mercury or water displaces the gas from a 10 cc. burette to the pipette containing the absorbent. Simpler forms used for clinical purposes may employ a syringe-like 10 cc. burette with a ground glass piston to replace the displacement fluid. This modification for convenience and simplicity is at the sacrifice of the finer grades of accuracy. The room air surrounding the burette maintains the temperature constant. The Orsatt-Henderson type has a glass jacket enclosing the burette which better insures maintenance of an even temperature during the analysis. The accuracy of this type of apparatus varies with the construction and the type of burette. The ordinary type for clinical use may have an accuracy to 1 per cent but this is sufficient for ordinary clinical purposes. The Haldane apparatus likewise consists of a burette (10 cc.) and absorption pipettes. The burette is more accurately calibrated and surrounded by constantly agitated water to maintain a constant temperature. Accurate determinations (error .1 per cent or less) of small samples of respiratory gases are possible with this analyzer.

The oxygen content of whole blood may be determined volumetrically with Van Slyke's apparatus or manometrically by the method of Van Slyke and Neill (17). The blood, usually a 1 cc. sample, is agitated in a vacuum in the extraction chamber common to these devices with a mixture of saponin, which causes lysis of the red cells, and potassium ferri-cyanide, which converts the oxyhemoglobin to methemoglobin. This conversion of oxyhemoglobin to methemoglobin liberates gaseous oxygen from it. The volume of the extracted gas is measured directly at atmospheric pressure on the volumetric type of apparatus and then converted to standard conditions. On the manometric type the liberated gases are compressed to 2 cc. and the pressure noted. An oxygen ab-

sorbent is drawn into the chamber in either type and the residual gas is measured. The difference in volumes is used to compute the result in the volumetric type (Van Slyke), the differences in pressure in the Van Slyke and Neill (manometric) type. Tables with factors to facilitate computation have been prepared for both types of apparatus.

Three types of solutions may be used to absorb oxygen. The first of these takes advantage of the fact that pyrogallic acid, a tri-hydroxy benzene, is converted quickly by oxygen to various nonvolatile quinones (17) (Winkler's reagent). The acid (50 Gm.) is dissolved in potassium hydroxide (1000 cc. of a 22 per cent sol.). This absorbs best after standing over night. Absorption may be slow and may require up to twenty minutes for completion, but it may be accelerated by increasing the surface over which liquid spreads by placing hollow glass tubes in the absorption chamber. The dark brown staining properties of the oxidized product is an objectional feature of this solution. The second type of absorbent takes advantage of the ease with which metallic copper is oxidized to copper oxide (CuO) or cuprous ions are oxidized to cupric (Cu^{++}) ions (18). Cupric oxide, hydroxide and other cupric salts dissolve in ammonium hydroxide to form deep blue solutions containing the tetramine cupric ion ($\text{Cu}(\text{NH}_3)_4^{++}$). A colorless solution of an ammonium salt and ammonium hydroxide in contact with metallic copper in air or oxygen is rapidly converted to a deep blue one. Ammonium chloride saturated in half-saturated ammonium hydroxide (Badger's solution) in contact with a metallic copper screen placed in the absorption pipette is the most frequently employed reagent for oxygen analysis in routine determinations for tents and other clinical appliances. This copper-ammonia solution works well, is rapid, is simple to prepare, safe to handle, inexpensive, stable, and causes little damage from careless use. The third type of oxygen absorbent utilizes the power of oxygen to convert soluble sulphites to sulphates. Sodium hydro sulphite ($\text{Na}_2\text{S}_2\text{O}_4$), a white granular powder (10 Gm.), and sodium anthra quinone Beta sulphonate (1 Gm.), which catalyzes the oxidation, are dissolved in 1.0 normal sodium hydroxide (50 cc.). A mahogany brown solution forms which rapidly absorbs oxygen to form sodium bisulphite and sodium sulphate. The brown color is converted to a pale yellow when the solution is exhausted. This solution is stable for short periods of time (less than twenty-four hours) and must be preserved anaerobically under oil or over mercury. This solution has been found best for use in the Van Slyke and the Van Slyke and Neill types of apparatus (17). All the aforementioned oxygen absorbing solutions are alkaline and will combine with carbon dioxide and other acidic gases if these are present. They must be removed first, otherwise serious errors may be introduced into the oxygen determinations.

NITROGEN

Nitrogen (1, 2) was first prepared by Rutherford in 1772. This obstinately inert gas, which undergoes chemical combination only under

unusual circumstances, is a valuable diluent for inhalation mixtures as well as a quenching agent for inflammable mixtures. The nitrogen molecule like that of oxygen also is diatomic (N_2). The gas, because of its inertness, is tasteless, colorless and odorless. The element is abundant since it comprises 78.1 per cent by volume of the atmosphere or 77.5 per cent by weight. The atomic weight is 14.006; the molecular weight is therefore 28.012. The gas is lighter than air, having a specific gravity of .9674 air (air=1). The nitrogen which evaporates from liquid air (19) during the manufacture of oxygen is the commercial source for the preparation of the gas. In the laboratory small quantities may be prepared by heating ammonium nitrite in air. Under high pressure, in the presence of an electric spark, the gas combines with hydrogen to form ammonia or with oxygen to form various oxides. The simplest of its five oxides, the monoxide or N_2O , which is used as an anesthetic agent, is the least toxic. The higher oxides are anhydrides of acids such as nitrous or nitric. They are toxic since when inhaled they combine with water to form these acids which are irritants. Nitrogen combines directly with certain metals to form nitrides.

Nitrogen compresses to a liquid at -146 C. under 35 atmospheres' pressure. Like oxygen, therefore, it must be dispensed as a compressed gas, since it does not liquefy at room temperature under any circumstances. There is no suitable absorbent available for it in gas analysis because it is so chemically inert. The nitrogen contained in air, blood, or other samples known to have no other inert substances is determined quantitatively by measuring the remaining fraction after all other gases have been absorbed by their respective reagents.

Nitrogen is transported in blood only by simple solution. The dissolved nitrogen in tissues plays a role in several physiopathological processes. The water solubility of nitrogen is 2.35 cc. per 100 cc. at standard conditions. Nitrogen is less soluble than oxygen. The solubility at 37 C. and 76 cm. pressure is still less, amounting to 1.28 cc. The solubility of nitrogen in lipoids is greater than in water (olive oil/water ratio is 3.24). These inert simple gases, like the inert lipid soluble anesthetic drugs, exert narcotic effects in accordance with Overton-Meyer's rule. In divers, working under several atmospheres of pressure, the increase in dissolved nitrogen due to the greater pressure raises the concentration in nerve cells sufficiently to produce a narcotic effect which results in dulling of the sensorium and other symptoms of nervous system depression (20). This may be avoided by substituting other gases (helium) for nitrogen.

Inhalation of a nitrogen-free mixture favors diffusion of nitrogen from blood into the lung and that from tissues into blood. Inasmuch as the nitrogen passes into the bag with successive rebreathing, changing the mixture frequently reduces the nitrogen in blood and tissues to almost zero. The blood during anesthesia is usually depleted to the zero level within thirty minutes. When mild narcotic agents such as

nitrous oxide are used, attempts are made to displace this tissue nitrogen by "washing" out the lungs at frequent intervals with pure nitrous oxide. This procedure is known as "secondary" saturation (21). Complete desaturation of tissues may, however, require hours. Nitrogen requires sixteen hours to diffuse from an isolated lung lobule with its communicating bronchus occluded in completing the process (22). Gases which combine chemically with water or constituents of blood are highly soluble and diffuse rapidly in such an arrangement. Under similar conditions, diffusion of oxygen occurs within fifteen minutes. Inert gases are supplied as a prophylactic measure at the termination of anesthesia when rapidly diffusing gases have been used for prevention of massive collapse (23).

HELIUM

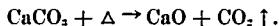
Helium (1, 2) first discovered by Ramsay in 1905, is a member of a group of gaseous elements known as the "rare elements." These gases are unique in that they are chemically inert and combine with no other known element except under extremely unusual circumstances. Other members of the group are argon, krypton, xenon, radon, and neon (24). All are found in air; none is essential to life. (25).

The helium molecule, unlike the other inorganic gases, is monoatomic and has an atomic and molecular weight, 4.002. It is twice as heavy as hydrogen and the second lightest element known. The chief source of this element is from natural wells of Texas and Kansas in which it occurs to the extent of 2 per cent. Air is a poor source for it, since only 5 volumes per million are contained in it. Helium is the least soluble gas known and the most difficult to liquefy. It is, therefore, easily isolated from the organic gases which liquefy first. The remaining gas is washed by passing through potassium hydroxide solution. Liquefaction of helium is easily accomplished at a slight pressure (2.26 atmospheres), but requires an unusually low temperature (-268 C.). The element also has been solidified (-272.2 C.). This low melting point is of interest since it is the lowest temperature which has ever been attained and approaches absolute zero (-273 C.) at which point all molecular motion is believed to cease. The specific gravity (air = 1) is .1785. The lightness, chemical inertness, low water and fat solubility make this gas ideal as a diluent in anesthesiology and in inhalation therapy. In clinical conditions such as asthma, chronic obstructions and other cardiorespiratory diseases it is invaluable because of its lightness and rapid diffusibility (26). The rate of diffusion of one gas into another varies inversely as the square root of the molecular weights of these gases (Graham's law) (19). Nitrogen which is 7 times heavier than helium will therefore diffuse $\frac{1}{\sqrt{7}}$ times as fast. Helium not only diffuses in and out the narrowed passages with greater ease than nitrogen, but be-

cause of its lightness, also decreases the effort required to move it. The quenching power of inert gases depends upon their molecular heat capacity and thermal conductivity. Helium has a lower molecular heat capacity than nitrogen, but almost 6 times the thermal conductivity. Helium mixtures are more difficult to ignite by electrical sparks than mixtures with other inert gases. The inertness and the high thermal conductivity render the gas a valuable quenching agent for inflammable mixtures in anesthesia (27). Absorption from the isolated lung lobule requires some time because of its slow diffusion through epithelium (twenty six hours—nitrogen=16). The gas may be used to replace the quickly absorbable gases in the lung after termination of anesthesia to prevent atelectasis. Helium has a low lipid solubility (1.48 cc. per 100 cc. at 37 C.) as well as a low water solubility (.87 cc./100 cc. at 37 C.) and, therefore, a low oil/water ratio (1.87 at 37 C.) (28). In deep sea diving helium is, therefore, substituted for nitrogen since less dissolves in blood and lipid tissues under the increased atmospheric pressure than nitrogen. Less inert gas passes into the brain cells and the narcotic effect is thereby diminished (29). The depression of the nervous system has been found to be far less with helium than with other inert gases. Desaturation from tissues once saturated is slow, requiring five and one-half hours; when under similar conditions nitrogen requires ten and one-half hours. The quantitative estimation of helium is not a simple matter because it is inert and cannot be absorbed by chemical agents. However, at low temperatures activated charcoal absorbs most gases but not helium. The gases are cooled, treated with activated charcoal and helium is assumed to be and is measured as a residual gas. Boothby (30) and his co-workers have recently devised a method for the determination of helium in gas mixtures by measuring the velocity of sound. The reader is referred to their paper for details. Helium is usually supplied mixed with 20 per cent oxygen although mixtures containing 25 per cent or 15 per cent are available.

CARBON DIOXIDE

Carbon dioxide (CO₂) is obtained for commercial purposes as a by-product of kilns and smelters where alkaline earth oxides are prepared by heating their respective carbonates (2, 4). A typical reaction would be the decomposition of limestone:



The alkali metal carbonates, such as those of potassium and sodium, do not readily decompose to the oxide and carbon dioxide. In localities where there are no kilns, coke is burned and the carbon dioxide passed into sodium hydroxide to form the carbonate from which the gas is later liberated and tanked. Carbon dioxide, from fermentation of grains for

the manufacture of alcohol, is likewise collected in large plants where enough is produced to make this procedure profitable (24).

Carbon dioxide is a stable gas requiring very high temperatures for decomposition (9000 C.). The odor is pungent. In high concentrations it is irritating to the mucous membranes. Carbon dioxide readily combines with water to form carbonic acid. This accounts for its high water solubility. One hundred five cc. dissolve in 100 cc. at 20 C. The carbonic acid is a "weak acid"—only .1 per cent of it is ionized at 20 C. The molecular weight is 44; specific gravity is 1.54 (air = 1) (1, 2). The gas is easily compressed at 50 atmospheres' pressure at 20 C. to a colorless liquid. In view of the relatively high critical temperature the commercial product exists at room temperature as a liquid in the storage tanks. Solid carbon dioxide melts at 56.6 C. The solid passes to the gaseous state without melting. Carbon dioxide is absorbed by alkalis with formation of carbonates and water. Carbonates react with excess carbon dioxide to form bi- or acid carbonates. Carbon dioxide acts as a quenching agent for flames in as low concentration as 5 per cent. Some workers feel that its absence in air-conditioned atmospheres prevents the dissipation of static charges since the formation of carbonic acid with moisture favors ionization and the conduction of electricity. Its concentration in atmospheric air varies from .02-.04 per cent depending upon the locality.

Carbon dioxide is determined volumetrically by absorption with 30 per cent potassium hydroxide or sodium hydroxide in the Orsatt or Haldane apparatus. In blood it can be measured by liberating the combined gas with lactic acid and extraction in either the Van Slyke-Neill apparatus and subsequently absorbing this with normal potassium hydroxide. The total carbon dioxide is a measure of the free carbon dioxide, that combined in the form of bicarbonates, and that combined with hemoglobin in the form of carbamino compound. The total, expressed in volumes per cent, amounts to approximately 50 in arterial blood and 54 in venous blood.

Frequently plasma equilibrated with air containing CO_2 at a tension equivalent to that found in the alveoli is analyzed in a similar manner. The result also expressed in volumes per cent is referred to as combining power. The normal combining power of human plasma is 50 volumes per cent. The difference between combining power and total carbon dioxide content is that combining power measures the ability of the plasma bases to combine with carbon dioxide at alveolar tension (47 mm. Hg) to form the blood carbonic acid derivatives while total carbon dioxide is a measure of the carbon dioxide actually present in whole blood at any one given moment (17).

Carbon dioxide-oxygen mixtures are prepared by flowing the carbon dioxide into the cylinder first to prevent layering of gases, and then filling with oxygen. Mixtures are required to be accurate to 1 per cent by the U.S. Pharmacopeia.

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