The Often Unnoticed "Cinderella Gases"

By Stephen Harrison

While many think of medical gases as simply O_2 and N_2O, there are numerous other specialized and critically important gas applications in medicine ranging from anesthesia gases to incubators.

Introduction

At the mention of medical gases, the first products that usually come to mind are the oxygen used for breathing therapy and the nitrous oxide (laughing gas) used for conscious sedation. Granted, these gases are vital and are used extensively in the healthcare arena. However there is an essential group of "Cinderella" specialty medical

Figure 1. Anesthesiologists depend on the integrity of these highly sophisticated anesthetic delivery devices and to be sure of this, these devices require testing and calibration with accurate calibration gas mixtures

gases that are less recognized, but no less critical. Like Cinderella of the children's story, this group of gases is small and largely unnoticed. They are supplied less frequently and in smaller quantities, but are just as vital to patient welfare.

The account of these specialty gases reveals that they are actually used every single day at hospitals and medical laboratories, and by clinicians in other associated organizations servicing the medical/healthcare industry. The Cinderella specialty medical gases reviewed here are those that have a diversity of interesting and critical applications that harness their unique properties and are quality-critical.

> *A rigidly controlled stream of gases must flow through an incubator's chamber.*

Test Gas Mixtures

These gases are not used in a directly therapeutic way as with, for example, inhaled medical oxygen, but rather to determine the status of patient health. The criteria used in their manufacture also differ from that of therapeutically used medical gases. The same extremely rigorous quality standards apply, but once produced, the content of specialty gases have to be accurately measured to ensure that all components are present and remain at precisely the right levels.

Within this group are the gases used to test or calibrate some of the principal instruments used in hospitals today. The efficient calibration of medical equipment, used either directly or indirectly in the treatment of patients, is imperative. The technology required to produce these specialized and often mixed calibration gases, whether 100 or 1,000 parts per million, is highly sophisticated. Maintaining the mixtures at the required levels is just as important. For example, nitrous oxide is a reactive gas with the potential to decay rapidly.

Among the most common tests carried out on patients are the pulmonary or lung function tests, a group of tests that harness sophisticated diagnostic instrumentation and mixes of the Cinderella medical gases containing low levels of carbon monoxide. These measure how well the lungs take in air and how well they transport gases such as oxygen from the atmosphere into the body's circulation. The amount of carbon monoxide in the

Figure 2. Gases have to be accurately measured to ensure that all components are present and remain at precisely the right levels.

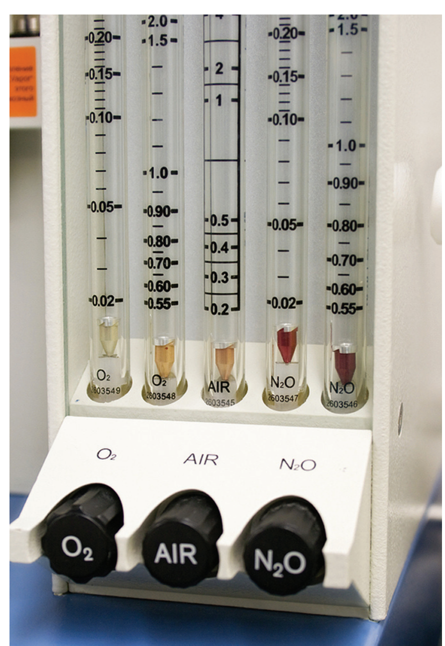

Figure 3. The efficient calibration of medical equipment in the treatment of patients is imperative.

exhaled air is measured and indicates the lung functionality. Since patients' health and condition often depend on the accuracy of these readings, highly specialized gas mixes are used to calibrate this equipment on a regular basis. The lung diffusion gases are often dispensed on prescription whether used for inhalation or for calibration of the analytical instrument, since the same gas cylinder is used for both purposes.

Blood gas analyzers are in a similar category. Blood transports oxygen around the body to the vital organs and collects carbon dioxide as a by-product. Blood gas analysis, also called arterial blood gas analysis, is a test that measures the amounts of oxygen and carbon dioxide in the blood, as well as the acidity (pH) of the blood. The equipment used to conduct this test requires frequent calibration in order to continue to give accurate and reliable readings. Again, the calibration gases required for this purpose are in the Cinderella group of specialty medical gases.

Although not specifically a medical application, blood alcohol testing using breathalyzer equipment is utilized by police forces all over the world to combat drunk driving, a growing concern in many countries among authorities and citizens alike. These tests are commonly conducted in the gaseous phase

The rare gas Xenon, is an excellent anesthetic medium

by testing the level of alcohol in the driver's breath, but the test is also carried out using blood samples. Either way, the instrument used must be perfectly calibrated and tested regularly to ensure an accurate reading.

This is critical if the result is required as evidence in a prosecution , so critical that national accreditation bodies like the United Kingdom Accreditation Service (UKAS) have established ethanol-in-air calibration standards for evidential breath testing. Calibration gases that have been accredited against these standards allow local traffic authorities to apply the breathalyzer test with the confidence that the reading will be accurate and will hold up in a court of law.

Incubators

Specialty gases and mixtures are also essential for the proper functioning of incubators. These important medical chambers create controlled environmental conditions with elements such as temperature, humidity and oxygen concentration, for the care of vulnerable infants. Incubators are also used to maintain the integrity of body parts and tissue destined for transplants and for growing certain cultures to create an aerobic or anaerobic cell growth environment. This is particularly important when identifying the presence of Methicillin-resistant Staphylococcus aureus (MRSA), the bacterium responsible for several difficult-to-treat infections in humans.

It is very important to have a controlled atmosphere that supports the intended process. When growing aerobe organisms, the ambient atmosphere is based on oxygen or air, and when anaerobe organisms are cultivated the atmospheres are based on nitrogen or carbon dioxide. Both types usually have a carbon source for maximizing the growth. A different type of growth control occurs when sterilizing mixtures are used for the opposite purpose — to get rid of all organisms. Each specific environment lends itself to the preferential preparation of cells that identify certain types of bacteria.

In vitro fertilization eggs and embryos are also stored in IVF incubators. These incubators must have very clean and constant environments. A steady and rigidly controlled stream of gases flows through an incubator's chamber continuously, so the gas mixture must be repeatable in order not to compromise the incubator's function. Certificates that guarantee the composition of these mixes and are able to prove the accuracy of a given mixing tolerance are often demanded by medical customers. The IVF mixtures are typically either 5% carbon dioxide in air, or 5% carbon dioxide, 5% oxygen in nitrogen.

In a different although health related application, incubators are used to grow many of the plants that are precursors to pharmaceutical ingredients. In the biopharmaceutical arena plants and trees are harnessed to grow and synthesize the chemicals used in pharmaceutical preparations. Here temperature, humidity and gas mixtures are also outcome-critical.

Anesthetics

Anesthetic delivery devices also rely heavily on the Cinderella specialty medical gases. During operations carried out under gaseous anesthesia it is critical to achieve and sustain the right gas mixture to be breathed by the patient. Although pure oxygen is generally used, this is often coupled with nitrous oxide for its pain relieving properties, which lowers the amount of actual anesthetic used. In addition to nitrous oxide, among the most widely used gases in general anesthesia are desflurane, sevoflurane and isoflurane.

Anesthesiologists depend on the integrity of these highly sophisticated anesthetic delivery devices and to be sure of this, these devices require testing and calibration with accurate calibration gas mixtures. Such specialty gas mixtures are supplied in small cylinders, much like aerosol cans.

Another example, the rare gas Xenon, is an excellent anesthetic medium, because it induces quick and stable anesthesia and favors neuroprotection.

Pure Gases

Pure gases, as opposed to gas mixtures, also play a significant role in the health care industry. Within the arena of medical gases and their applications, the diagnostic work conducted using these gases for preventive and diagnostic medicine is an important category.

On-site clinical laboratories or standalone contract laboratories contracted to conduct analysis for the hospital are required to carry out sophisticated tests on patient blood and urine samples. These tests often use plate microbiology requiring anaerobic or aerobic gas mixtures for cultivation. High-tech instrumentation such as liquid chromatography-mass spectrometry (LC-MS) and high-performance liquid chromatography (HPLC) are often used for diagnostic testing.

LC-MS is a powerful analytical technique used in industries requiring very low detection limits of sometimes unknown samples. The efficient physical separation of chemical substances dissolved in a mobile phase, performed by liquid chromatography, is combined with the mass spectrometer's ability to sort and identify the components (gaseous ions) in electric and magnetic fields according to their mass-to-charge ratios. The samples analyzed by LC-MS are often complex mixtures.

LC-MS requires high purity nitrogen to remove the solvent from the sample before introducing it in the mass spectrometer. Pure helium could also be necessary for degassing when using liquid chromatography

HPLC is a form of column chromatography that pumps a sample mixture or analyte in a solvent (known as the mobile phase) at high pressure through a column with chromatographic packing material (stationary phase). HPLC has the ability to separate and identify compounds that are present in any sample that can be dissolved in a liquid in trace concentrations as low as parts per trillion. This equipment also needs high purity gases such as nitrogen or helium to operate accurately.

Sample Storage

In the liquid phase, nitrogen is used by the healthcare sector, since it can be cooled to extremely low temperatures, as low as -196°C. Tissue samples, human eggs and semen can be stored for long periods of time using nitrogen, which makes it possible to freeze samples rapidly, avoiding the potential damage associated with slower freezing processes in which water crystals freeze in a different way and cause tissue damage.

Increasingly, biopsy duplicate samples are preserved using cryogenic nitrogen, enabling retesting to verify original biopsy results. The rise in demand for such storage stems from medical litigation. Both patient and patient's family, and doctor or medical facility request maintaining the integrity of biopsy samples to be used as evidence in the possibility of medical litigation.

Linde's BOC Cryobank in the UK is a "cryopreservation" facility dedicated to cryogenic bio-storage of irreplaceable samples. The concept of storing back-up or additional samples at an off-site location is intended as an additional security feature, should an unforeseen incident affect the primary facility. Linde Gas Cryoservices in the Netherlands also specializes in the field of low temperature technology, offering extensive services in temperature controlled freezing, cryogenic storage and logistics management of biomedical and pharmaceutical material.

Liquid nitrogen can be a hazardous substance to handle, and the safety issues associated with working with liquid nitrogen include the risk of asphyxiation when used or stored in poorly ventilated areas. There is also the risk of cryogenic burns and frostbite when unprotected flesh is exposed to it, and hypothermia can even develop with the low air temperatures arising from the proximity to liquefied gas.

Even though Linde has supplied its liquid nitrogen customers with training in safe practices, protective clothing and gas detection equipment to identify breathable or unsafe atmospheres, the establishment of proprietary cryobanks is a sign of a definitive shift in the medical industry. It appears to be part of a global outsourcing trend that is seeing business opting to focus on their core competencies and outsourcing other requirements to appropriate service providers. In the case of cryogenic nitrogen, safety and the proper handling of a hazardous substance dictates using the facilities of a gas company whose personnel have received correct training on the appropriate equipment to manage this technological process. G&I

__Stephen Harrison__ is a British Chartered Engineer (MIChemE) with a career in industrial gases spanning 20 years, 10 of which have been focused in the area of specialty gases. He has worked in an international capacity for both Linde Gases and previously BOC and now leads Linde's global Specialty Gases & Specialty Equipment business from Munich, Germany. Stephen has a Masters degree in Chemical Engineering from Imperial College, London in the UK.