The oxygen trail: measurement

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Tissue hypoxia may be defined as abnormal oxygen utilization such that cells are experiencing anaerobic metabolism. Tissue hypoxia can be defined biochemically by low levels of ATP, high levels of NADH, or decreased oxidised cytochrome aa₃. It is possible to measure these biochemical markers in the laboratory setting with, for example, nuclear magnetic resonance spectroscopy. However, this is not as yet a clinical option. There is no 'gold standard' for the diagnosis of clinical hypoxia. We can detect the gross consequences of tissue hypoxia, such as organ dysfunction and metabolic markers of anaerobic metabolism (e.g. lactic acidosis). We have also become familiar with the measurement of both global and regional oxygen dispatch and consumption. However, organ dysfunction and metabolic acidosis consistent with established tissue hypoxia commonly exists in the presence of normal and even supra normal global measures of oxygen dispatch and consumption. Therefore, we should ideally make measurements at the end of the oxygen trail, i.e. cellular oxygen delivery and effective utilization.

Clinical assessment

We readily recognise the clinical manifestations of cellular hypoxia (e.g. reduced mental acuity, myocardial ischaemia, oliguria). Clinical indicators are neither sensitive nor specific. They also have little to offer in terms of monitoring as they do not warn us of potentially harmful tissue hypoxia, but rather support the diagnosis. On the other hand, all the physiological and biochemical variables that we may use to try and assess tissue oxygenation should be interpreted in the light of clinical findings. For example, it is extremely unlikely that an overtly healthy and alert patient who has a blood lactate level measured outside the normal range is experiencing clinically significant tissue hypoxia.

Metabolic markers

pH

One of the commonest abnormalities present in patients who have established tissue hypoxia is a metabolic acidosis¹. Tissue hypoxia is
associated with anaerobic metabolism and thus the production of lactic acid\textsuperscript{2,3}. The presence of a metabolic acidosis has repeatedly been demonstrated to be predictive of a poor outcome in critically ill patients\textsuperscript{4}. The calculation of base excess helps with the bedside interpretation of data from blood gas analysis. The presence of a metabolic acidosis determined by arterial blood gas analysis is a systemic, and thus rather crude measure of tissue anaerobiosis. It may represent a global disturbance, for example secondary to hypovolaemic shock, or a highly localised problem \textit{e.g.} a segment of dead bowel. In animal models, the time course for the development of a detectable metabolic acidosis is relatively slow, as in the early stages buffering systems will tend to mask any signal. It must also be remembered that not all metabolic acidosis is secondary to tissue anaerobiosis\textsuperscript{4}. For example, diabetic ketoacidosis and renal tubular dysfunction may result in metabolic acidosis that is independent of cellular oxygenation. It is also important to appreciate the contribution of strong anions to the development of a metabolic acidosis as most of the resuscitation fluids in clinical usage are hyperchloraemic and thus have the potential to contribute to acidosis\textsuperscript{5}.

\textbf{Lactate}

Plasma lactate is relatively easy to measure and is useful in the differential diagnosis of acidaemia\textsuperscript{6}. Plasma lactate has also been shown to be a good prognostic indicator in critically ill patients\textsuperscript{7}. An elevated blood lactate in the absence of an acidaemia does not constitute a lactic acidosis and is not indicative of tissue anaerobiosis. Furthermore, a lactic acidosis can exist in the presence of tissue normoxia secondary to drugs or toxins such as the biguanide hypoglycaemic agents\textsuperscript{8}. Critically ill patients with combined renal and hepatic failure may have a lactic acidosis following the transfusion of large volumes of intravenous fluids containing bicarbonate as lactate (\textit{e.g.} lactated Ringers or lactated dialysate used for haemodialysis). As a monitor of tissue hypoxia, the measurement of plasma lactate has similar problems to those described above with blood pH, \textit{i.e.} a relatively crude whole body measure. Local tissue lactate sampling may overcome this problem (see below).

\textbf{Arteriovenous CO\textsubscript{2} difference}

CO\textsubscript{2} is produced in the tissues during both aerobic and anaerobic metabolism. During aerobic metabolism, the rate of CO\textsubscript{2} production is determined by the basal metabolic rate and the respiratory quotient. During anaerobic metabolism, CO\textsubscript{2} is produced from the bicarbonate
buffering of metabolic acid. Thus the measurement of venous PCO$_2$ provides an index of tissue oxygenation\textsuperscript{2}. Venous PCO$_2$ is dependent on the absolute arterial PCO$_2$ and so most readily interpreted as the arterial-venous CO$_2$ difference. Measures of right atrial and pulmonary artery delta PCO$_2$ have been shown to have limited predictive ability in critically ill patients\textsuperscript{5}. Venous PCO$_2$ is not very different from arterial PCO$_2$ and thus the measurement of delta PCO$_2$ is prone to errors. Furthermore, as flow decreases to a tissue that remains normoxic, oxygen extraction increases and venous CO$_2$ rises as a result of stagnation. For a diagnosis of tissue hypoxia, venous CO$_2$ must rise dramatically in excess of the fall in venous oxygen saturation\textsuperscript{10}. Arterial-venous PCO$_2$ difference is not recommended for routine clinical use but may help in the differential diagnosis of a persistent metabolic acidosis.

**Global oxygen dispatch**

Global oxygen dispatch or delivery (DO$_2$) is defined as the quantity (in ml) of oxygen available to the body per min and is the product of the oxygen content of arterial blood (CaO$_2$) and the flow of blood leaving the left side of the heart (cardiac output, CO)\textsuperscript{11}.

\[
DO_2 = CO \times CaO_2 \quad \text{Eq. 1}
\]

With normal, healthy values of CO at 5 l/min (5000 ml/min) and CaO$_2$ of 20 ml/dl (0.2 ml/ml), DO$_2$ is 1000 ml/min.

CaO$_2$ is the sum of the oxygen carried in arterial blood bound to haemoglobin and the small amount of oxygen dissolved in the plasma. The oxygen bound to haemoglobin is the product of the haemoglobin saturation (SaO$_2$), the hemoglobin concentration ([Hb]) and a constant (the oxygen-combining capacity of haemoglobin now taken as 1.31)\textsuperscript{12}.

At a normal arterial PaO$_2$ of 13 kPa, the dissolved oxygen is approximately 0.3 ml/dl.

\[
CaO_2 = (SaO_2 \times [Hb] \times 1.31) \quad \text{Eq. 2}
\]

At different arterial PaO$_2$, the dissolved oxygen is given by $0.023 \times$ PaO$_2$. The complete equation then becomes:

\[
CaO_2 = (SaO_2 \times [Hb] \times 1.31) + (0.023 \times PaO_2) \quad \text{Eq. 3}
\]

Using normal values for an adult male:

\[
19 \text{ ml/dl} = (0.97 \times 14.7 \times 1.31) + (0.023 \times 13) \quad \text{Eq. 4}
\]

The dissolved oxygen makes only a small difference to the result and so, in practical terms, the global oxygen dispatch is the product of cardiac
output, haemoglobin concentration and haemoglobin saturation. While a small change in only one variable will have a modest effect on the total delivery, a change in two or more will have an amplified effect.

About 300 ml/min of global oxygen delivery is required to sustain life at rest. A fall in cardiac output to 3 l/min combined with a reduced haemoglobin of 8 g/dl reduces global oxygen delivery to below this. Similarly, relatively minor falls in saturation, cardiac output and haemoglobin concentration are commonly seen in many patients following surgery, trauma, etc.; these will combine to result in a significantly reduced global oxygen delivery. The complexities of the distribution of an apparently normal or an elevated global oxygen delivery are the subject of the rest of this chapter. Global reductions are, however, still common and left untreated may be the trigger for the complex immuno-inflammatory processes we see all too often in the critically sick patient.

The variables included in the calculation of global oxygen delivery are all measured and monitored with varying frequency and using a variety of techniques in intensive care patients.

**Cardiac output**

**Thermodilution**

The cardiac output measurement required is the volume of blood passing forward through the aortic valve per unit time. This is usually measured indirectly using the dilution of a known volume of an indicator in the blood flowing through the heart. The cumbersome dye dilution methods have been replaced by the use of cold dextrose. In adults, 5–10 ml of cold dextrose are injected quickly into the right atrium via the most proximal lumen of a modified pulmonary artery catheter. The temperature fall in the pulmonary artery is measured by a small rapidly responding thermistor on the tip of the catheter. A small microprocessor measures the area under the thermodilution curve and calculates the cardiac output. Modern systems have disposable insulated syringes, cooling coils and injectate temperature probes with the microprocessor commonly incorporated into a modular physiological monitor. The results are intermittent and despite the ease of making measurements care must be exercised if reliable results are to be achieved.

Several attempts have been made to construct semi-continuous dilution systems. One commercially available thermodilution system uses a small heating coil on the intraventricular portion of the pulmonary artery catheter. Small pulses of current are applied to this coil in a complex pseudo-random sequence and the resulting changes in temperature are
looked for in the pulmonary artery. The temperature changes are much smaller than those seen in conventional thermodilution measurements and the signal to noise ratio is often poor. When compared to intermittent injectate thermodilution, the continuous measurements are usually only slightly biased but tend to be imprecise especially in patients with rapidly changing cardiac outputs.

**Thoracic bioimpedance**

Applying a constant high frequency current, typically 70–100 kHz at 2.4–4.0 mA, through two circumferential electrodes around a cylindrical part of the body allows changes in impedance of that part to be measured. A change in blood volume in that part will alter the impedance and changes can be measured continuously. Applying the electrodes to the thorax allows measurements of the changes resulting from the different blood volumes during systole and diastole to be made and stroke volume can be calculated. The method has the attraction of being totally non-invasive and continuous but has never yet achieved the repeatable levels of accuracy and precision required for clinical measurements in sick patients.

**Ultrasonic Doppler velocimetry**

The ascending aorta may be insonated by a beam of ultrasound either through the supra-sternal notch or through the trachea. The descending aorta can be insonated via the oesophagus. Measuring the Doppler frequency shift of the return signal allows the velocity of the blood in the aorta to be calculated. If the angle of incidence of the beam is known and the cross sectional area at the point of insonation is either estimated or measured, then approximate figures for aortic blood flow can be produced. Transoesophageal Doppler probes are available commercially either as disposable devices or with a protective sheath. Considerable estimation is used in the calculation of cardiac output with these devices and, in most studies, they have again suffered a lack of precision especially at the extremes of measurement. The velocity time signal may, however, contain useful information about myocardial contractility and the adequacy of volume replacement therapy.

**Haemoglobin concentration**

Full blood counts are routinely undertaken on most ICU patients on a daily basis. In addition, many of the more modern blood gas analysers incorporate some form of haemoglobin or haematocrit measurement.
allowing more frequent estimations to be made in sick patients. Analysers that use only single wavelength haemoglobin photometry or conductivity estimations of haematocrit are relatively inaccurate and care should be used in basing treatment on the results obtained. Multi-wavelength CO-oximeters are used in many ICUs and should give accurate measurements of haemoglobin concentration. Continuous transcutaneous haemoglobin measurements are theoretically possible but are made impossible by the variations in pathlength produced by the transillumination of body parts.

**Blood gas analysis**

The standard blood gas analyser has pH, PCO$_2$ and PO$_2$ electrodes in a temperature-controlled chamber. Automated sample transport, and calibration are also incorporated$^{16}$. The current flowing through a suitably polarised oxygen electrode is proportional to the number of free oxygen molecules present in the sample and thus in whole blood measures the oxygen dissolved in the plasma fraction of the sample. As indicated above, the dissolved oxygen is only a very small part of the total oxygen content and it is the oxygen bound to haemoglobin that we need to measure.

**Haemoglobin saturation**

The relationship between PaO$_2$ and arterial haemoglobin saturation (SaO$_2$) is described by the oxyhaemoglobin dissociation curve. This relationship is sigmoid in shape and is affected by several factors including temperature, pH and PaCO$_2$. Many standard blood gas analysers make an estimate of haemoglobin saturation from the measured pH, PCO$_2$ and PO$_2$ using well-established algorithms for the calculation of saturation in adult blood. The multi-wavelength CO-oximeter uses 8 or 12 different wavelengths of visible and near infra red light to make a much more accurate estimation of different haemoglobin moieties. The value of SaO$_2$ should be calculated from:

$$SaO_2 = \frac{[HbO_2]}{[HHB] + [MetHb] + [COHb] + [HbO_2]} \times 100 \quad \text{Eq. 5}$$

This calculation takes into account the effect that marked increases in abnormal haemoglobins have on the oxygen content of arterial blood. As the blood passes through the systemic circulation it looses approximately 25% of its oxygen and returns to the right side of the
heart with a saturation of around 72% in health (97–25%). Different regions of the body extract slightly different amounts of oxygen and true mixed venous saturation (SVO$_2$) should be measured after blood has mixed in the chambers of the right side of the heart. Blood is sampled from the pulmonary artery using a pulmonary artery flotation catheter, or measurements can be made continuously using a specialised fibre optic pulmonary artery catheter. SVO$_2$ is affected by changes in oxygen delivery and oxygen uptake and changes when an imbalance occurs. SVO$_2$ is a complex, composite measurement of cardiac output, haemoglobin concentration, arterial saturation and oxygen uptake. All of these variables change in critically ill patients and make the interpretation of changes in SVO$_2$ complicated.

Arterial haemoglobin saturation may also be estimated continuously using transcutaneous pulse oximetry. Here light of two different wavelengths (one red, one infrared) is shone through a digit or the ear lobe. The different wavelengths of light are shone alternately at several hundred times a second, usually with a dark phase in-between. The near-infrared light is close to the isobestic point of haemoglobin where oxy- and reduced haemoglobin absorb to a similar extent. The visible light is in the red spectrum and is absorbed to a very different extent by the two haemoglobin species. The arterial blood produces the pulsatile component of the transmitted light at a signal strength of approximately 2% of the total absorbed. The ratio of the red to infrared absorption is affected by haemoglobin saturation and, using an in-built calibration table, measurements of arterial saturation are displayed. The ratio nature of the measurements reduces the effects of path length variations. Pulse oximetry is used widely in intensive care medicine and has been a major advance in continuous monitoring. The pulsatile component of the signal falls with poor peripheral perfusion and the precision of the estimate of arterial saturation deteriorates under these circumstances.

**Global oxygen consumption**

In health, only about 250 ml of the ~1000 ml of oxygen delivered to respiring tissues is used, this reduces the saturation of haemoglobin from 97% in the arteries to around 72% in the mixed venous blood returning to the heart. When breathing air, the body stores of oxygen only amount to around 1000 ml and so oxygen uptake measured at the mouth closely matches the body’s total utilisation.

Oxygen consumption falls with sedation and anaesthesia and rises with an increase in body temperature and markedly during shivering.
Measurement of global oxygen consumption

Traditionally, physiologists have measured global oxygen consumption using water sealed bell spirometers filled with oxygen enriched air. The subject breathes to and fro from the spirometer through a CO$_2$ absorber, the slope of the reduction in volume of the spirometer against time is the oxygen consumption in ml/min. This is cumbersome in clinical practice and is now seldom used.

If the inspired and expired minute volumes can be measured with high accuracy and the difference in inspired and expired oxygen concentrations can also be measured with very sensitive and accurate analysers, then global oxygen consumption can be measured on a continuous basis. Equipment to do this is commercially available but the measurements are still prone to errors, small leaks in the breathing system, including the endotracheal tube, and drift in the oxygen analysers all contribute to imprecise readings.

The more commonly used approach in the clinical setting is to multiply the cardiac output by the arterial-to-mixed venous oxygen content difference, the so-called reversed Fick method. This measures the oxygen consumption by the respiring tissues between the aorta and the pulmonary artery but does not include the oxygen consumed by the lung. In health, this is small and the error can be ignored; however, several authors have described increases of up to 50 ml/min in patients with pneumonia, undergoing cardiac surgery, etc. The potential of using this difference in the measured oxygen uptake as an early marker of lung disease is still under investigation.

Relationship between oxygen consumption and delivery

The relationship between oxygen consumption and delivery is complex and in health is non-linear. Above a given level of delivery (critical delivery ~ 550 ml/min) the oxygen consumption is independent of delivery (supply independent oxygenation)$^{19}$. Changes in oxygen delivery above this point result in changes in oxygen extraction from the arterial blood and SVO$_2$ changes while the consumption remains fixed. Below the critical delivery point there is a linear relationship between oxygen supply and consumption (supply dependent oxygenation). Falls in oxygen delivery below this point are accompanied by a rise in markers of anaerobic metabolism, such as lactate, and are strongly predictive of poor outcome in ICU patients$^{20}$.

The situation in septic ICU patients is even more complex and it is a common finding that oxygen consumption continues to increase as delivery is increased in the range of 400–900 ml/min/m$^2$. Indeed some
groups have been unable to demonstrate that supply independent oxygenation ever occurs in these patients. These results have encouraged the use of inotropes to achieve supra-normal levels of global oxygen dispatch in these patients. There are, however, several problems in this interpretation. Firstly, as discussed above, measuring the oxygen consumption by the use of the reverse Fick technique ignores pulmonary oxygen consumption. Secondly, the calculation of delivery and consumption both use the term cardiac output and small errors in the measurement of cardiac output will produce a mathematical coupling between delivery and consumption. Finally, inotropes increase myocardial oxygen consumption and, thus, would be expected themselves to produce an increase in total oxygen consumption.

Regional blood flow

Any shock state can result in the redistribution of regional blood flow and thus the measurement of regional blood flow may help in the detection of tissue hypoxia. Methods based on the Fick principal have been used to measure blood flow and metabolism in brain, kidneys, splanchic bed and other organs. For example, a continuous mixed venous catheter can be positioned in the jugular venous bulb or hepatic artery under fluoroscopic guidance and thus allows the measurement of regional venous effluent oxygen saturation and sampling of blood for pH, CO₂ and lactate determinations. These still provide relatively crude measures of cellular oxygenation, are cumbersome to use clinically and carry with them the risk of venous thrombosis.

Hepatic blood flow can be estimated by the rate of decrease in plasma indocyanine green (ICG) concentration after an i.v. bolus. Assuming that ICG is cleared completely by the liver, hepatic flow is equal to the systemic clearance of the dye. In man, ICG is not in fact eliminated completely by the liver and variations in ICG extraction mean that this technique is not viable for clinical determination of hepatic blood flow.

Doppler flowmetry can be used to detect blood flow in accessible tissue beds; for example, a Doppler probe can be intra-operatively replaced either on the external wall of the gut or around a blood vessel. Both these methods require a surgical approach, which makes them unsuitable in normal clinical practice. Transcutaneous determination of large vessel flow to major organs is also possible (e.g. brain, liver, kidneys) but only allow determination of gross flow abnormalities. Doppler probes can be advanced through the biopsy channel of an endoscope and placed under direct vision on the intestinal wall; they can thus be used for measuring gastric mucosal flow. They are prone to
artifacts as the flow measurements are influenced by breathing movements, peristalsis of the gut and the quality of contact between the probe and the intestinal wall. Colour or radiolabelled microspheres can be used to determine perfused capillary density but require tissue biopsy and the technique is prone to systematic errors\textsuperscript{26}. All these methods have research utility but poor clinical viability.

**Tissue oxygen delivery**

**Oxygen electrodes**

Polarographic oxygen electrodes can be inserted into tissue beds and provide a measure of regional PO\(_2\). This is an invasive technique that produces tissue damage and thus raises some questions about the value and meaning of subsequent measurements\textsuperscript{27}. For accessible capillary beds, vacuum fixed oxygen electrodes may be a better alternative, but there are still concerns regarding flow modifications secondary to the fixing process\textsuperscript{28}. Such techniques have been used for research purposes but, once again, have questionable clinical viability.

**Gastrointestinal tonometry PO\(_2\)**

It has been demonstrated that gut mucosal PO\(_2\) can be determined by the measurement of the PO\(_2\) of fluid aspirated from the gut lumen using a routine blood gas analyser\textsuperscript{29}. It is prone to many systematic errors, most important of which is the swallowing of air which will give a markedly elevated value. It has been described experimentally but not utilised clinically.

**Reflectance spectrophotometry**

Using the same principles as pulse oximetry, it is possible to monitor the oxidation reduction state of haemoglobin, myoglobin or cytochrome aa\(_3\). At least for research purposes, infrared and near infrared spectrophotometry have been used successfully to measure oxygen delivery to both the gut and the brain\textsuperscript{30-32}. The measurement of cytochrome aa\(_3\) provides the potential for getting a true measure of tissue hypoxia. However, the techniques available for clinical practice still provide a fairly gross and crude signal and there are issues surrounding depth of penetration and the impact of skin perfusion.

The main worry with the regional measures of both blood flow and
oxygen delivery is that oxygen delivery is no guarantee of adequate oxygen utilization. Measures of regional blood flow and tissue oxygen delivery may readily detect stagnant, anaemic or hypoxic hypoxia. However, inadequate oxygen utilization resulting in reduced production of ATP can occur in the presence of a normal cellular $\text{PO}_2$ (cytotoxic hypoxia). It is increasingly recognised in animal models of sepsis that cytotoxic hypoxia is commonly associated with organ dysfunction.

**Tissue oxygen utilization**

*Luminescent oxygen probes*

The intramitochondrial redox state can be assessed by the measurement of the absorption spectrum of the fluorescence of NADH. This technique is still under development, but laboratory *in vivo* experiments are encouraging. At least hypothetically, it should be possible to measure the phosphorescence of mitochondrial enzymes and thus determine the difference between normal and abnormal cellular function. However, even if such probes were available, the question would still be where should one place them.

*Nuclear magnetic resonance spectroscopy and positron emission tomography*

These are both highly successful and established research tools. Both methods have sufficient resolution to allow characterization of regional metabolism. Logistic problems limit the use of these techniques in the clinical environment.

*Tissue pH and lactate*

Microdialysis catheters can successfully be placed in different tissue beds, e.g. heart, liver, brain, and used to determine tissue levels of pH, lactate and other metabolic markers of tissue hypoxia. As yet, these remain research tools and, yet again, have the problem of where would you put them.

**Gastrointestinal tonometry**

In pursuit of a clinical monitor of tissue hypoxia, there has been much attention focused on the gastrointestinal (GI) tract in recent years. Its inner-most mucosal layer has a counter-current system of arterioles and
venules that improves absorptive function but makes it susceptible to reduced oxygen delivery states. Splanchnic vasoconstriction is an early response to a reduction in global oxygen delivery as blood is diverted to organs such as heart and brain. Whether due to a reduction in cardiac output and/or hypovolaemia, the reduction in splanchnic blood volume is disproportionately greater than that seen in other beds. There is also considerable evidence to suggest that splanchnic ischaemia may be a significant factor in the pathogenesis of the multiple organ dysfunction syndrome.

Gastrointestinal tonometry relies on the measurement of the partial pressure of carbon dioxide ($PCO_2$) in the lumen of the gastrointestinal tract. As discussed above, $CO_2$ is produced in the tissues during both aerobic and anaerobic metabolism. Gastrointestinal luminal $PCO_2$ ($PgCO_2$) may rise as a result of normal oxidative phosphorylation and impaired removal of $CO_2$. Consider, for example, where the flow is reduced to the gut mucosa but delivered oxygen exceeds a fixed requirement. Venous oxygen saturation will fall (i.e. oxygen extraction ratio increases) and venous and tissue $CO_2$ will rise proportionally (the ratio dependent on the respiratory quotient). Only when oxygen supply falls below demand will anaerobic metabolism result in release of metabolic acid (such as lactate) and the liberation of $CO_2$ from bicarbonate. This sudden rise in tissue $CO_2$ will be disproportionate to the reduction in venous oxygen saturation. The degree to which mucosal $PCO_2$ can be accounted for by aerobic or anaerobic metabolism has been determined by Schlichtig et al in a canine model of cardiac tamponade. They conclude from their measurements that gastrointestinal tonometry can be a valid measure of tissue hypoxia but calculated that the maximum human aerobic generation of $CO_2$ can exceed 70 mmHg (at an RQ of 1.0 and plasma pH of 7.26). Therefore, a high $PgCO_2$ in relation to arterial blood should be regarded as an index of the balance between gastrointestinal perfusion and metabolism and not an absolute indicator of tissue hypoxia.

Gastrointestinal tonometry can be performed clinically using the Trip® NGS (gastric tonometer and sump) catheter (Datex-Ohmeda, Tonometrics Division, Instrumentarium Corp., Helsinki, Finland) used commonly in gastric saline and automated air tonometry. The catheter consists of a gas impermeable tube connecting distally with a gas permeable silicone balloon placed in the stomach. Carbon dioxide freely equilibrates between regional blood vessels, the gut wall, gastric luminal and balloon contents. Catheters may also be placed in the colon and have been refined in size and shape over recent years. They are available in a range of sizes for adult, paediatric and neonatal usage.

Gastric luminal $CO_2$ using saline tonometry can be measured by the installation of 2.5 ml of 0.9% saline into the balloon of a Trip® catheter.
placed in the stomach. The PCO\textsubscript{2} of the saline in the tonometer balloon following equilibration with that of the mucosa is determined using a standard blood gas analyser. This technique has not proven to be popular in clinical usage\textsuperscript{37}. A laborious, meticulous technique in the handling and measurement of saline samples from the tonometer is needed to produce worthwhile and reproducible results\textsuperscript{38}. Strict anaerobic conditions are required within the catheter involving a time consuming priming procedure. Long equilibration times (30–60 min) are required between samples, so results never truly reflect the patients' current condition. Furthermore, blood gas analysers exhibit errors in bias and precision because they are calibrated for the determination of PCO\textsubscript{2} in blood. For most commonly used machines, errors are small but certain analysers have been shown to exhibit large and significant errors\textsuperscript{39,40}. Thus saline tonometry is not clinically viable and has been superseded by automated air tonometry using the Tonocap® monitor (Datex-Engstrom)\textsuperscript{41}.

The Tonocap® is an automated, semi-continuous combined air tonometer and capnograph and it overcomes many of the methodological problems presented by the saline technique. It demonstrates greater accuracy and precision with faster equilibration times and is a closed circuit thereby limiting atmospheric contamination. The Tonocap® monitor is attached to a standard Trip® catheter. The tonometer catheter balloon is automatically filled with 5 ml of room air, which is kept in the balloon for a preselected equilibration period to allow CO\textsubscript{2} diffusion from the gastric lumen. The cycle time automatically sets to 10 min intervals. The sample then empties back into an infrared measuring chamber for analysis. The air is recycled to the catheter balloon to avoid CO\textsubscript{2} depletion in the catheter system, thereby decreasing subsequent equilibration times. Using a catheter attached to the patients endotracheal tube the Tonocap® samples and analyses airway gases end-tidal carbon dioxide (EtCO\textsubscript{2}) and respiratory rate which are continuously displayed.

PgCO\textsubscript{2} is influenced by systemic arterial PCO\textsubscript{2} values (PaCO\textsubscript{2}) which in the critically ill population can vary rapidly. This can be corrected for by calculating the gastric-arterial CO\textsubscript{2} gap (PgCO\textsubscript{2}–PaCO\textsubscript{2}). Furthermore, The Tonocap® is able to measure end-tidal CO\textsubscript{2} (EtCO\textsubscript{2}). By assuming that patients without significant ventilation/perfusion mismatch have a constant PaCO\textsubscript{2}–EtCO\textsubscript{2} difference, this can be taken to represent PaCO\textsubscript{2} which removes the need for blood gas analysis in the calculation of CO\textsubscript{2} gap\textsuperscript{41}.

It is important when using a monitor that its strengths and weaknesses are known along with possible reasons why it may or may not be working properly. There are several sources of error inherent to the technique of GI tonometry and some specific to the Tonocap® which result from the fact that measurement of PgCO\textsubscript{2} is now in the gaseous phase. These include: (i) incorrect positioning; (ii) luminal generation of CO\textsubscript{2} not related to
tissue perfusion which can be caused by the reaction of gastric acid and bicarbonate; (iii) enteral feeding; (iv) suctioning of gut luminal contents; and (v) variations in core temperature effecting $CO_2$ solubility$^{41}$.

Alternative methods for the measurement of gut luminal PCO$$_2$$ have been described. For example, success with balloonless air tonometry has been reported in an animal model$^{42}$. This involves lavaging the lumen of the gut with 20–200 ml of air and then measuring the PCO$$_2$$ of the aspirated gas sample using a routine blood gas analyser. This technique has the advantage of avoiding the expense of using a special catheter or monitor. However, there is no published human data using this technique. A new method for truly continuous measurement of gastric luminal PCO$$_2$$ has been described using a fibre optic sensor but, as yet, this technique is not clinically available$^{43}$.

Conclusion

Tissue hypoxia can be defined and recorded biochemically but there is no ‘gold standard’ for the clinical diagnosis of hypoxia. We commonly detect the gross consequences of tissue hypoxia, such as organ dysfunction, and have become familiar with the measurement of both global oxygen dispatch and consumption. However, organ dysfunction secondary to established tissue hypoxia can exist in the presence of normal and even super normal global measures of oxygen dispatch and consumption. There are a number of clinically viable monitors of regional oxygen uptake but none are established in routine use. Gastrointestinal tonometry is the most widely used monitor of the balance between cellular perfusion and metabolism but its clinical utility remains controversial. A reliable clinical monitor of cellular oxygen utilization is still a ‘pipe dream’.

References

Oxygen trail: measurement

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