Current Paediatrics (2004) **14**, 1–7

ELSEVIER

Current PAEDIATRICS

www.elsevierhealth.com/journals/cuoe

Neonatal intensive care monitoring

Sarah Nicklin[a,*], Yapa A. Wickramasinghe[a], S. Andrew Spencer[a,b]

[a]*North Staffordshire University Hospital, City General Site, Newcastle Road, Stoke-on-Trent ST4 6QG, UK*
[b]*School of Medicine, Keele University, Thornburrow Drive, Hartshill, Stoke-on-Trent ST4 7QB UK*

KEYWORDS
Neonatal monitoring;
Pulse oximetry;
Transcutaneous monitoring;
Neonatal intensive care;
Near infrared spectroscopy;
Clark electrode

Summary The monitoring of physiological parameters is an integral part of neonatal intensive care. This article describes the rationale for the development of neonatal blood gas monitoring, leading on to a review of current practice in the UK. Possible means of improving current techniques are described, including biocompatible catheters and sensors, signal-processing, intelligent monitoring and telemetry. Techniques such as near infrared spectroscopy and cerebral impedance tomography, which have the potential to provide real-time monitoring of the cerebral circulation, are discussed. The importance of risk management in the introduction of new technology is highlighted, and future research directions are outlined.

Practice points

- Avoid arterial stabs
- Use continuous carbon dioxide monitoring during first 48 hours
- Monitor carbon dioxide trends using transcutaneous carbon dioxide monitoring
- Ensure the early placement of umbilical artery catheters
- Adopt pulse oximetry with proven artefact and false alarm rejection capability

Research directions

- Improvements in transcutaneous technology, which might include smaller and lighter probes to facilitate attachment and reduced heating with improved sensor detection, hopefully resulting in less skin trauma
- An improved biocompatibility of catheters and sensors, reducing the number of catheter insertions required
- The development of microsensor arrays to facilitate the continuous monitoring of a larger range of parameters, including glucose, with placement in peripheral arteries or subcutaneous tissue
- The application of fuzzy logic and neural networks to develop intelligent monitoring systems that will alert clinicians to significant trends while avoiding multiple false alarms
- The continued development of techniques such as near-infrared spectroscopy and cerebral impedance tomography that have the potential to provide real-time monitoring of the cerebral circulation
- Randomized controlled trials of new monitoring methods, with long-term neurodisability as main outcome measure.

*Corresponding author. Current address: Wordsley Hospital, Stourbridge, West Midlands, DY8 5QX, UK. Tel.: +44-1384-456-111.

E-mail addresses: senicklin@doctors.org.uk (S. Nicklin), yapa.wickramasinghe@nstaffsh.wmids.nhs.uk (Y.A. Wickramasinghe), andy.spencer@uhns.nhs.uk (S. Andrew Spencer).

0957-5839/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.cupe.2003.09.006

Introduction

The term 'monitoring' can be applied to any measurement that is made repeatedly in order to maintain physiological parameters within predetermined limits. During neonatal critical care, monitoring may be continuous, as for heart and respiratory rate, or intermittent, as in blood gas, glucose and electrolyte estimation. Monitoring is a key component of modern neonatal intensive care, in which virtually all babies undergo some form of physiological monitoring. The sickest and most vulnerable will require the continuous monitoring of 5–10 parameters. These babies can be extremely challenging, and the information provided by the monitoring equipment is an essential adjunct to the clinical skills of the staff in making decisions on the baby's management and acts as an alert to any change in condition.

Despite advances in monitoring, the incidence of neurodevelopmental problems remains high, particularly in infants of less than 26 weeks' gestation.[1] There is evidence that neurological damage may occur antenatally as a result of chorioamnionitis, but there is still a concern that failure to maintain homeostasis contributes to the development of cerebral hypoxic/ischaemic lesions.[2]

Experience with retinopathy of prematurity[3] demonstrates that oxygen monitoring is a requirement. There is some evidence that continuous monitoring improves outcome,[4] but the scope of the research is narrow and the evidence inconclusive. This is unfortunate as preterm babies readily deteriorate when undergoing painful procedures[5] so the potential benefits of invasive methods must be balanced against the negative effects. Consequently, the best method of monitoring babies is still open to debate, a fact that is reflected by the large variation in current practice.

Historical perspective

Since the experiences in the 1950s of uncontrolled oxygen use leading to a high incidence of retinopathy of prematurity,[3] the importance of monitoring oxygen therapy has been recognized. Early methods for measuring blood gases were crude, and only intermittent measurements were possible. Although the concept of continuous oxygen monitoring was proposed as early as 1953, it became possible only when a polarographic partial pressure of oxygen (pO_2) electrode was developed by Clark in 1956,[6] followed by the introduction of a sensor with a membrane. This allowed the non-invasive measurement of oxygen dissolved in a fluid. In 1957, an attempt was made to measure the pO_2 of newborn infants by placing their feet in warm water and measuring the pO_2 of the water after allowing for equilibrium.[7] These initial methods were not, however, suitable for routine clinical use as a result of poor arterialization. The heated transcutaneous oxygen (TcO_2) sensor, based on the Clark electrode, was not developed until 1972.[7] Because of the pressure gradient from the artery to the skin surface, this methodology was never intended to provide a precise measurement of arterial pO_2 (PaO_2), but it is able to determine trends in oxygenation subject to stable skin perfusion.

The evaluation of a commercially available indwelling arterial Clark oxygen sensor was reported in 1976.[8] The sensor, mounted on a PVC umbilical catheter (Neocath Biomedical Sensors, High Wycombe, UK), has remained virtually unchanged over the years. This device provides continuous measurements based on precise calibration against blood gases.

A catheter-mounted fibreoptic device has also been used to measure arterial saturation (SaO_2) by reflection. In one commercially available instrument (Shaw Catheter Oximeter OS/1270A), light at three wavelengths was sequentially transmitted at a rate of 244 Hz through a single optical fibre to illuminate the blood. A portion of the reflected light was collected by the optical fibre and processed to calculate the SaO_2. This was an invasive method so attempts were made to determine SaO_2 non-invasively. Shaw developed the eight-wavelength ear oximeter in 1964, and a commercial device marketed by Hewlett-Packard (HP Model 47201A), became available in 1970. This device used the overall absorbance by the ear pinna to calculate the arterial oxygen saturation (SaO_2). Reliable measurements of SaO_2 were not, however, possible until 1974, when the first pulse oximeter became available. This optical instrument extracted the pulsatile waveform of blood flow (photoplethysmograph) and related the amplitude to the oxygenation of the blood. It took a while for this technology to be adopted in neonatalogy because it is poor at detecting hyperoxia,[9] a major cause of concern because of the association with ROP.

The continuous measurement of carbon dioxide has been even more difficult. A transcutaneous carbon dioxide ($TcCO_2$) sensor, similar in design to the TcO_2 sensor, was based on a design proposed by Stow-Severinghaus in 1957 but did not become a clinical tool until the late 1970s. The optimal measurement of $TcCO_2$ requires a lower skin temperature than is required with the TcO_2 so separate probes were initially required. Further

advances lead to the development of the combined probe. A favourable evaluation in neonates was published in 1980.[10] As with all transcutaneous technology, calibration, probe attachment and burns to the skin remain a problem. An umbilical artery catheter with three fibreoptic sensors for the continuous determination of Pao_2, arterial Pco_2 ($Paco_2$) and pH has recently been introduced (Neotrend MPIAS, Diametrics Medical Ltd, St Paul, USA). Evaluation against arterial blood gas estimations is promising.[11]

Current monitoring practice

A recent survey of infants of birthweight less than 1.5 kg has provided detailed information on the monitoring of blood gas parameters and blood pressure in the UK.[12] During the first 3 days of life, about three-quarters of these babies had arterial access, normally used for intermittent blood gas estimations and continuous blood pressure monitoring. Intra-arterial sensors were used in about a quarter of cases. Unfortunately, arterial access could not be maintained and fell to less than 50% by days 4–6, mainly due to failure of the umblical artery catheters.

Considering the group as a whole, Sao_2 monitoring was almost universally applied, whereas only about 8% experienced transcutaneous monitoring, normally using a combined $Tco_2/Tcco_2$ sensor. Surprisingly, the use of transcutaneous monitoring was not increased in babies with failed arterial access. Many neonates were monitored with pulse oximetry and capillary gases for a substantial proportion of their critical care. Nearly a third of all infants were subjected to at least one arterial stab during their stay in the neonatal unit. Frequent intermittent arterial blood gas estimation via an indwelling arterial catheter is considered to be the gold standard against which other monitoring techniques should be judged.[13] The survey highlights the practical difficulty of implementing this throughout critical care. Capillary gases are now commonly used as a substitute and provide a good estimation of pH and $Paco_2$ but not Pao_2.[14] Arterial stabs may be used, but as the trauma from this type of sampling invariably leads to obvious desaturation, it probably adds very little.

Transcutaneous monitoring has obvious benefits in terms of the early detection of adverse trends and the ability to provide information about carbon dioxide levels prior to arterial catheterization. This raises the question of why this technology is so underutilized, particularly as it proved popular with consultants in a previous opinion-based survey.[15] The practical difficulties of attaching the probe, inevitable trauma to friable skin, the need to perform frequent recalibration and the difficulty in interpreting trends when the actual values are often far removed from the blood gas results are probably responsible for this.

Continuous measurements of either Pao_2 (Neocath) or combined $Pao_2/Paco_2$/pH (Neotrend) in any baby with successful umbilical artery catheterization should be of benefit if close monitoring improves outcome. Problems with biocompatibility leading to catheter blockage and sensor failure have 'however' been well described for the former.[16] The latter is not currently in widespread clinical use.[12]

A number of approaches to improving neonatal outcomes are possible. First, there are actual and potential improvements in current technology that could be applied. Second, it might be possible to make better use of the monitoring information currently available. Third, research is ongoing into techniques that might more accurately reflect the situation in the brain rather than simply relying on blood pressure and blood gas estimations.

Potential improvements to current monitoring systems

Biocompatibility

One of the main reasons for suboptimal monitoring is the failure to establish or maintain intra-arterial access via either umbilical or peripheral arterial catheterization.[12] One reason for catheter failure is the deposition of plasma proteins on its surface, which leads to platelet activation, adhesion and thrombus formation. This may lead to blockage and, when intra-arterial sensors are involved, to malfunction and sensor failure.[16] The risk of colonization and infection is also increased.[17]

The material from which the catheter is constructed is important. Although manufacturers claim that new-generation polymers such as Neoflon and Vialon are better than Teflon and PVC, catheter blockage or infection still frequently occurs.[18] One solution is to coat catheters and sensors with a biocompatible surface. A family of polymers based on 2-methylacryloyloxyethyl phophorylcholine, which mimic natural cell membrane structures, have been developed as dip-coating material. There is good evidence that they significantly reduce fibrin deposition.[19]

Nevertheless, there are still problems in relation to this method of application. First, the dip

technique is not applicable to the lumen of the catheter. Second, greater adhesion is required in binding the new polymer to the underlying material in order to prevent the surface from stripping during insertion. Further development is required, but the potential for improving monitoring is enormous if the life of arterial catheters and sensors can be extended.

Signal-processing

As it is simple to attach a pulse oximeter probe and obtain a reading, it is easy to become blind to inaccuracies in Sa_{O_2} measurement that commonly arise because of motion artefact[20] or poor perfusion. The Masimo signal extraction technology system (Masimo Corporation, Irvine, USA)[21] was developed to address these issues. Elementary pulse oximetry is based on the ratio of the instantaneous photoplethysmography pulse height at two wavelengths, one in the visible and the other in the infrared range. Analogue and digital filters with fixed characteristics are used to reduce artefacts. Although most instruments could display the 'beat-to-beat' value of Sa_{O_2}, these include artefact-generated values so manufacturers use averaging methods to smooth out these variations. Since movement artefacts are not 'fixed', filters that can change their characteristics according to the properties of the artefacts improve the accuracy of the calculated Sa_{O_2}. The Masimo system utilizes this 'adaptive filtering' technique. Benefits include accuracy during motion and reliability during low perfusion, leading to an improved detection of both bradycardia and hypoxaemia, and a reduction in the number of false alarms.[22]

Intelligent monitoring

One of the problems with current monitoring systems is that they produce frequent false alarms[23] but fail to alert clinicians to significant adverse trends that might predict worsening disease or complications. Presenting staff with continuously updated trend data is helpful in the early identification of significant physiological change and has been shown to improve the standard of care.[24] Improvements in sensors, leads, signal extraction and artefact detection can improve the reliability of monitored data, leading to a great reduction in the number of alarms caused by artefact.[25]

Even if artefact could be excluded, monitoring information is still displayed in a raw form, with very little intelligent data integration or processing.[26] Methods of integrating and assimilating data, recognizing patterns and trends and relating data to the clinical situation are required so that it is possible to distinguish between transient self-correcting events and those requiring intervention. It is possible to develop such systems through the utilization of fuzzy logic and the use of neural networks to predict events.

Fuzzy logic deals with the problem of uncertainty. Alarm settings are currently based on the principle of defining acceptable limits. A value is either normal or abnormal, and an abnormal value triggers an alarm. Fuzzy logic chips are able to deal with degrees of abnormality. When combined with neural networks, which are able to undertake complex modelling and learning, it is possible to create systems that can assimilate data from numerous sources over time and use this information to determine whether an alarm should be triggered. This has similarities with human decision-making but has the advantage that the intelligent monitoring equipment is constantly attending to the patient, whereas human assessment can only be undertaken intermittently.

Telemetry

Monitoring systems require numerous attachments to wall-mounted or cotside equipment. This results in infants getting tangled in the leads. It is difficult and time-consuming to remove the baby from the incubator for cuddles or weighing. There is also a risk when babies need to be transported because equipment must be disconnected. Telemetry provides the means whereby signals can be transmitted from a small mobile box adjacent to the patient to larger and more remote display equipment. The potential has been available for many years: indeed, it has been possible to transmit an ECG signal since 1949.[27] Important parameters that warrant continuous transmission from the sick infant by telemetry are heart rate, respiratory rate, blood pressure, Sa_{O_2} and temperature. Several manufacturers of multichannel monitoring equipment are able to provide this facility. Transcutaneous monitoring requires more development because of the requirement to heat the probe but would be a valuable addition.

Developmental techniques

Improvements in monitoring are required to protect the brain from cerebral hypoxic ischaemic injury. New techniques aim to monitor the brain

directly or provide more sensitive information about the need for circulatory support that can be provided by conventional means. Unfortunately, none of the techniques described below is ready for routine clinical use.

Cerebral impedance tomography

This technique has been proposed as a method of real-time detection of regional changes in cerebral blood volume and intraventricular haemorrhage.[28] The technique makes use of the fact that biological tissue can conduct electricity. The difference in the resistance (impedance) of different body tissues allows the mapping of a slice of cerebral tissue by positioning an array of 16 electrodes around the head. An alternating current is introduced, and the resulting voltage is measured to determine the respective impedance component. A sectional image is reconstructed from the multitude of impedance information obtained. Although images of the human brain have been produced, which show changes as a result of external stimuli,[29] there are still many problems to be overcome, including electrode placement and low resolution.

Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) was developed principally to enable the non-invasive monitoring of tissue oxygenation and haemodynamics. Jobsis introduced the initial in vivo use of NIRS in humans in 1977, and the technique was first applied to neonates in 1985.[30]

Biological tissue is relatively transparent to light in the near-infrared spectrum, and the absorption of light at certain wavelengths is different for oxygenated and deoxygenated haemoglobin. By applying algorithms, changes in both haemoglobin saturation and concentration can be monitored. The technique has been extensively applied to the neonatal brain to monitor changes in cerebral oxygenation and central blood volume. In babies undergoing critical care, a change in arterial saturation can be used as a tracer to calculate absolute values for cerebral blood flow and volume. Intermittent partial jugular venous occlusion allows the determination of cerebral venous saturation. This measurement, combined with Sa_{O_2}, allows the calculation of fractional oxygen extraction,[31] which might prove useful in determining whether the brain is adequately oxygenated.

The perinatal applications of NIRS have recently been reviewed in detail.[32] NIRS has not progressed to the cotside because of problems with quantification. The standard technique (continuous-wave NIRS) provides only trend data with no fixed point to define normality. Although the technique is useful in research, it is not possible to base management decisions on this type of data. Quantification through intervention is possible, as described above, but it is difficult to achieve consistent results outside a highly controlled environment. New prototype machines such as those involving phase- and time-resolved NIRS have the potential to measure cerebral saturation directly, but these techniques are still only research tools.

Peripheral oxygen consumption

NIRS can be used to measure peripheral oxygen consumption (V_{O_2}) using either venous[31] or arterial[33] occlusion applied by a standard neonatal blood pressure cuff. This may provide valuable information regarding the circulatory status of neonates as, early in circulatory compromise, compensatory mechanisms maintain oxygen delivery to vital organs by redistributing blood away from the peripheries, leading to a fall in peripheral V_{O_2}. The assessment of peripheral V_{O_2} may thus provide an early indication of circulatory compromise. Evaluation has shown that the technique is sensitive to changes in skin temperature,[34] global metabolic rate[35] and blood pressure.[31] A great deal more work is required to determine whether this technique has clinical application in determining the need for circulatory support.

Risk management

In an article that seeks to invoke improvements in monitoring techniques, it is important to deal with the significant issues involved in introducing new technologies to the neonatal environment. Many advances in monitoring technology have arisen when clinicians have worked with bio-engineers to develop new equipment or make modifications that have subsequently been commercialized. Many hospitals have the capacity for in-house developments, which may form part of their research and development programme.

The responsibility for ensuring that equipment meets essential requirements for safety and performance normally rests with the manufacturer, who is required to sign a declaration of conformity. A CE (Conformity European) mark is awarded and displayed on the equipment, which allows free marketing in the European Economic Area. Any

local modification to the equipment will invalidate the CE mark so that such equipment must be indemnified by the hospital concerned. Before new in-house or modified technology can be used clinically or for research, the hospital consequently has to ensure that:

- the risks of using the equipment lie within acceptable limits;
- all potential risks have been minimized;
- the benefits of using the device outweigh the risks.

A risk assessment tool to assist in this process has been described[36] in an attempt to support ongoing developments in this important area.

Conclusions

A review of the current status of neonatal monitoring has raised a number of important issues. These include variations in practice, invasiveness of monitoring, increasing the scope of continuous monitoring, improving the interpretation of existing monitoring information and the need to prove long-term benefits from existing and new technology.

References

1. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure Study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics* 2000;**106**:659–71.
2. Wiswell TE, Graziani LJ, Kornhauser MS, et al. Effects of hypocarbia on the development of cystic periventricular leukomalacia in premature infants treated with high-frequency jet ventilation. *Pediatrics* 1996;**98**:918–24.
3. Kinsey VE, Hemphill FM. Etiology of retrolental fibroplasia and preliminary report of cooperative study of retrolental fibroplasia. *Trans Am Acad Opthal Otolaryng* 1955;**59**:15–24.
4. Bancalari E, Flynn J, Goldberg RN, et al. Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. *Pediatrics* 1987;**79**:663–9.
5. Gonsalves S, Mercer J. Physiological correlates of painful stimulation in preterm infants. *Clin J Pain* 1993;**9**:88–93.
6. Clark LC. Monitor and control of blood and tissue oxygen tension. *Trans Am Acad Opthal Otolaryng* 1956;**2**:41–8.
7. Eberhard P, Mindt W. Skin sensors for continuous oxygen monitoring of newborns. *Biotelemetry* 1977;**4**:48–76.
8. Conway M, Durbin GM, Ingram D, et al. Continuous monitoring of arterial oxygen tension using a catheter tip polargraphic electrode in infants. *Pediatrics* 1976;**57**: 244–50.
9. Paky F, Koeck CM. Pulse oximetry in ventilated preterm newborns: reliability of detection of hyperoxaemia and hypoxaemia, and feasibility of alarm settings. *Acta Paediatr* 1995;**84**:613–6.
10. Whitehead MD, Halsall D, Pollitzer MJ, Delpy DT, Parker D, Reynolds EO. Transcutaneous estimation of arterial Po2 and Pco2 in newborn infants with a single electrochemical sensor. *Lancet* 1980;**8178**:111–4.
11. Morgan C, Newell SJ, Ducker DA, et al. Continuous neonatal blood gas monitoring using a multiparameter intra-arterial sensor. *Arch Dis Child* 1999;**80**:F93–8.
12. Ganesan V, Malbon S, Jones PW, Spencer SA. Blood gas monitoring in very low birth weight infants receiving respiratory support: a survey of current practice in the uk and ireland. *J Clin Excell* 2003;**4**:403–10.
13. Joint Working Group of the British Association of Perinatal Medicine. Development of audit measures, guidelines for good practice in the management of neonatal respiratory distress syndrome. Arch Dis Child 1992;**67**:1221–7.
14. McLain BI, Evans J, Dear PR. Comparison of capillary and arterial blood gas measurements in neonates. *Arch Dis Child* 1988;**63**:743–7.
15. Spencer SA, Dimmock PW, Brookfield DSK. Survey into current neonatal practice in relation to preterm monitoring. *J Clin Excell* 2000;**2**:15–27.
16. Spencer SA, Rolfe P, Murphy A, Wright T, McKenna S. In vivo assessment of catheter-tip Po2 sensor: sampling lumen fabrication. *Med Biol Eng Comput* 1995;**33**:157–62.
17. Mermel LE. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2002;**132**:391–402.
18. Maki D, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters. *Ann Intern Med* 1991;**114**:845–54.
19. Yang Y, Zhang SF, Kingston MA, Jones G, Wright G, Spencer SA. Glucose sensor with improved haemocompatibility. *Biosens Bioelectron* 2000;**15**:221–7.
20. Wickramasinghe YABD, Spencer SA. Photoplethysmography: a futuristic view for neonatal care. *Acta Paediatr* 2000;**89**:769–70.
21. Goldman JM, Petterson MT, Kopotic RJ, Barker SJ. Masimo signal extraction pulse oximetry. *J Clin Monit Comput* 2000;**16**:475–83.
22. Bohnhorst B, Peter C, Poets CF. Pulse oximeters' reliability in detecting hypoxemia and bradycardia: comparison between a conventional and two new generation oximeters. *Crit Care Med* 2000;**28**:1565–70.
23. Tsien CL, Fackler JC. Poor prognosis for existing monitors in the intensive care unit. *Crit Care Med* 1997;**25**:614–9.
24. Cunningham S, Deere S, Symon A, Elton RA, McIntosh N. A randomized, controlled trial of computerized physiologic trend monitoring in an intensive care unit. *Crit Care Med* 1988;**26**:2053–60.
25. Belal SY, Taktak AF, Nevill AJ, Spencer SA, Roden D, Bevan S. Automatic detection of distorted plethysmogram pulses in neonates and paediatric patients using an adaptive-network-based fuzzy inference system. *Artif Intell Med* 2002;**24**:149–65.
26. Kohli-Seth R, Oropello JM. The future of bedside monitoring. *Crit Care Clin* 2000;**16**:557–78.
27. Holter NJ, Gengerelli JA. Remote recording of physiological data by radio. *Rocky Mt Med J* 1949;**46**:747.
28. Weindling AM, Rolfe P, Tarassenko L, Costeloe K. Cerebral haemodynamics in newborn babies studied by electrical impedance. Preliminary results. *Acta Paediatr Scand Suppl* 1983;**311**:14–9.
29. Tidswell T, Gibson A, Bayford RH, Holder DS. Three-dimensional electrical impedance tomography of human brain activity. *Neurol Image* 2001;**13**:283–94.
30. Brazy JE, Lewis DV, Mitnick MH, Jobsis van der Vilet FF. Non-invasive monitoring of cerebral oxygenation in preterm

infants: preliminary observations. *Pediatrics* 1985;**75**: 217–25.
31. Wardle SP, Yoxall CW, Weindling AM. Peripheral oxygenation in hypotensive preterm babies. *Pediatr Res* 1999;**45**:343–9.
32. Nicklin SE, Hassan IA, Wickramasinghe YA, Spencer SA. The light still shines, but not that brightly? The current status of perinatal near infrared spectroscopy. *Arch Dis Child* 2003;**88**:F263–8.
33. Hassan IA, Spencer SA, Wickramasinghe YA, Palmer KS. Measurement of peripheral oxygen utilization in neonates using near infrared spectroscopy: comparison between arterial and venous occlusion methods. *Early Hum Dev* 2000;**57**:211–24.
34. Hassan IA, Wickramasinghe YA, Spencer SA. Effect of limb cooling on peripheral and global oxygen consumption in neonates. *Arch Dis Child* 2003;**88**:F139–42.
35. Hassan IA, Wickramasinghe YA, Spencer SA. Effect of a change in global metabolic rate on peripheral oxygen consumption in neonates. *Arch Dis Child* 2003;**88**:F143–6.
36. Nicklin SE, Wickramasinghe YABD, Nevill A, Ellis SJ, Spencer SA. An essential health check for all medical devices. *Clin Med* 2003;**3**:543–5.