Application for
Wilderness Medical Society
Herbert N. Hultgren Research Grant

Performance of oxygen and volatile anaesthesia delivery systems under hypobaric conditions simulating high altitudes

Altitude Anaesthesia Research Collaboration

Ross Hofmeyr, Richard E. Moon, Mike Grocott, Mike James

Contents

Application Form

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Wilderness Medical Society Research Grant

Title of Project: Performace of oxygen and volatile anaesthesia delivery systems under hypobaric conditions simulating high altitudes

Grant Category (Houston, Research-in-Training, Hultgren, Hackett-Auerbach, WMS Adventure Travel):
(Please do not choose more than one category.)

Herbert N Hultgren Research Grant

Please list up to 6 MeSH keywords for your project:

altitude, anesthesia, atmospheric pressure, analgesia

Applicant's Name: Dr Ross Hofmeyr

Medical School or Residency/Fellow Program: University of Cape Town

Address: c/o Department of Anaesthesia & Perioperative Medicine, Groote Schuur Hospital, Observatory

City: Cape Town **State:** Western Cape

Postal Code: 7925 **Country:** South Africa

Tel: +27845499259 **Fax:** n/a

E-mail: ross.hofmeyr@uct.ac.za

Section A: Project Summary

1. Introduction and background

A quarter of the world's population live at more than 500 m above sea level and nearly 10% reside higher than 1500 m.[1] Many occupy highly populated cities, such as Denver, Mexico City, La Paz, Quito, Lhasa, Nairobi, and Johannesburg. Moon and Camporesi[2] stated that approximately 140 million people worldwide live permanently at altitudes greater than 2500m. This number is likely equalled by people visiting high altitudes each year for employment, recreation or religious pilgrimages, many of whom will require medical care. Provision of anaesthesia services are therefore frequently required at altitudes above 1500m and higher, and inhalation anaesthesia at such altitudes is common. However, modern anaesthesia machines are primarily designed to function at sea level, and there is a paucity of literature on how the performance of these critical instruments behave under conditions of altered barometric pressure. Furthermore, we have previously highlighted that the entrenched use of concentration (rather than partial pressure) as a measure of volatile and gas delivery, regardless of changes in ambient pressure with increasing altitude, illustrates a gap in practitioner comprehension of device performance at altitude.[3]

Vaporisers

There is clearly a massive gap in the literature in terms of the performance of a variety of vaporisers with changes in barometric pressure. In a recent textbook, Eisenkraft commented that there are few reports available concerning the use of vaporisers under hypobaric conditions, and therefore these authors limited their discussion to theoretical considerations only.[4] In this discussion, mathematical predictions based on vaporiser splitting ratios concluded that hypobaric conditions would result in substantial increases in vapour concentration, but much smaller increases in vapour partial pressure that would probably not be of clinical significance. However, no confirmatory literature was offered to support this theoretical argument. The last study of vaporiser performance with changes in barometric pressure was conducted over 3 decades ago (1984), using the apparatus available at that time.[5] There appear to be no publications dealing with the performance of modern agent vaporisers, such as those for sevoflurane and desflurane. The desflourane vaporiser functions on a totally different principle from the standard plenum vaporisers, and, again, although the theoretical

considerations published by the manufacturer states that higher vaporiser control settings will be needed at increased altitude,[6] there appears to be no research publications confirming this theoretical analysis. As accurate knowledge of the performance of these devices is critical to the avoidance of anaesthetic awareness, there is an urgent need for a properly conducted study on the behaviour of these instruments under conditions of altered barometric pressure.

Several inhalational anaesthesia systems have been designed for use under field, military, resource-constrained, or disaster settings. Examples include the Oxford Miniature Vaporiser, Triservice vapouriser, and disposable handlheld vapourisers for analgesic administration of methoxyflourane. Despite these devices being favoured for remote site use, no literature on their performance at altitude is available. Furthermore, recent mountain rescue recommendations have suggested that methoxyflurane may be a valuable analgesic during rescue operations,[7] but there are no studies of the performance of vapour delivery systems for this agent.

Flow Meters

A variety of devices are used within anaesthesia systems to measure the flow of gases being delivered to the anaesthetic system. The most extensively studied are those dependent on the flow of gas creating a pressure drop across and orifice with an associated device for display of the consequences of that drop in terms of gas flow.[8] These devices depend on either the density or viscosity of the gas being measured, largely dependent on whether the gas flow is laminar or turbulent. In some devices, increasing flow leads to a change from laminar to turbulent flow as the flow rate increases, resulting in unpredictable errors occurring with changes in barometric pressure.[5] However, many modern devices use electronic flow meters that may use other principles including thermal capacity of the gas being measured. There are no formal studies of the performance of such devices with changes in barometric pressure, but these may have serious consequences for patient safety at altitude. Errors in these devices induced by altitude may not only effect the accuracy of gas volumes being delivered, but may also influence the performance of proportioning devices designed to ensure that hypoxic gas mixtures cannot be delivered.

Gas Analysers

Capnographs and agent monitors all respond to a physical property of each individual gas and therefore measure partial pressure, although almost all are calibrated in percentage units that will vary with changes in barometric pressure. This error may "introduce important errors that must be prevented when specialized equipment will be used and increasing altitudes".[9] This principle is well established and, while it would be useful to confirm this principle in modern anesthetic machines, it need not necessarily form part of a current hypobaric investigation.

2. Hypothesis and specific aims

We hypothesize that, as per our theoretical understanding, performance of gas delivery systems is affected at high altitudes, resulting in altered levels of volatile anaesthetic and oxyen than at sea-level, which in turn increases the risks of patient awareness, hypoxia and adverse events.

Specific aims:

We propose to perform accurate laboratory measurements in a hypobaric chamber at simulated high, very high and extreme altitudes of:

1. Modern vapouriser performance (minimum isoflourane, sevoflourane and desflourane)
2. Draw-over vapouriser and methoxyflourane inhaler performance
3. Mechanical and electronic oxygen flow-meter performance
4. Medical oxygen, capnography and agent analyser performance

If time and budget allow, to assess/corroborate earlier studies on the performance of oxygen concentrators in a hypobaric environment.

3. Study design and methods

This is a laboratory-based study assessing equipment performance. No human or animal subjects will be involved. The investigators will be required to adhere to strict accepted protocols while working in the environmental chamber at Duke University.

Vaporiser performance will be assessed at low, moderate and high flows using calibrated partial pressure gas analysis and confirmed with absolute volumetric measurement at each

designated simulated altitude (sea level, 1500 m, 3500 m and 5800 m) to ensure accuracy. Multiple repeated measures will be used to assess intra-measure reliability and precision.

Flow meter performance will be assessed at low, moderate and high flows using absolute volumetric measurement at each designated altitude (as above). Multiple repeated measures will again be used.

Gas analyser performance will be assessed using samples of exact calculated concentration and practical pressure using an absolute volumetric approach for each designated altitude (as above). These samples will be compared with calibrated and uncalibrated measurements to calculate any systematic or random error (bias and accuracy, respectively).

4. Data analysis plan

The complete data set and all derived measures will be available on request, and may be published. Individual variables will be reported as mean (standard deviation), median, range and interquartile range depending on normality of the aquired data. Absolute values and percentage differences will be reported. Bland-Altmann plots will be used to describe bias and precision for the gas analyser performance.

5. Time frame

The experimental portion of the work in the altitude chamber will be completed by the study team during the week of 4 September, 2017. Data analysis and description will be undertaken during September to December 2017, with submission of findings to WEMJ or planned for early 2018.

6. Facilities

The study will take place in the altitude chamber at the Duke Center for Hyperbaric Medicine and Environmental Physiology at the Duke University School of Medicine. Anaesthesia delivery systems will be loaned from the Department of Anaesthesia, Duke University (Dr Moon). Further equipment will be provided by Dr Hofmeyr and Profs Grocott and James.

Section B: Significance to the field of Wilderness and Environmental Medicine

As stated above, hundreds of millions of people worldwide live at altitude above 1500 m, where reduced ambient pressure leads to relative hypoxaemia and effects both delivery and affect of medical gasses and anaesthetic volatiles.[1-3] This is compounded by the large numbers traveling to high, very high and extreme altitudes for employment, recreation or religious pilgrimages, many of whom will require medical care, frequently under wilderness and/or austere conditions. However, the literature remains very sparse with regards to the performance of medical gas delivery, measurement and monitoring systems under hypobaric conditions. The only available studies are decades old, featuring equipment and methods that have become obsolete. This places patients at considerable risk. This study will contribute accurate, thorough and modern assessment in a true hypobaric laboratory environment, which will guide development of protocols and equipment to serve patients in wilderness and adverse environmental settings. It is likely to be highly referenced as the only modern, definitive work on the subject.

Section C: Detailed budget

All research tasks will be carried out by the investigators. The measurements will be carried out in the Hyperbaric and Environmental Research Unit at Duke University. Costs in USD are approximated below.

Description	**Budget**
Hypobaric chamber staffing and laboratory use. Cost estimated at USD 1200 per diem for a period of 5 days, allowing adequate time for repeated measures.	$ 6000
Disposables, sampling and consumable materials	$ 1000
Flight costs ex Cape Town to US (Economy class, 2 pax; RH, MJ)	$ 2300
Flight costs ex London to US (Economy class, 1 pax; MG)	$ 700
TOTAL EXPENSES	**$ 10 000**

Grant funds will be administered in an audited research fund. This can be under the stewardship of Dr Hofmeyr in a dedicated account under the Department of Anaesthesia & Perioperative Medicine at the University of Cape Town. However, as the majority of the investigators are based outside of the US, whereas the majority of the study costs will be at Duke University, if it should ease the administrative process for the WMS, we will request that stewardship of the funds be delegated to Prof Moon in a research fund at Duke on behalf of the study group.

Section D: Letters of support

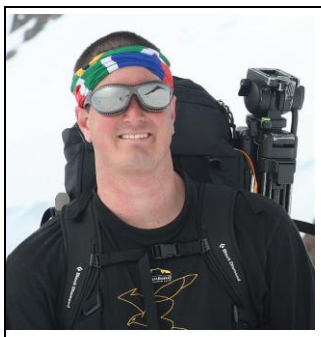
As per grant application instructions, this is not required for applications for the Herbert N. Hultgren Grant. All laboratory work will be carried out at Duke University in the unit of which Prof Moon is Medical Director, but the four member of the study group. No further outside assistance is required, although new suggestions for collaboration will be favourably met.

Section E: IRB approval

This study is a laboratory-based assessment of equipment performance with no human or animal subjects. There are no risks to participants, data subject to confidentiality, or issues of ethical concern. IRB approval is therefore not required.

Section F: Curriculum Vitae

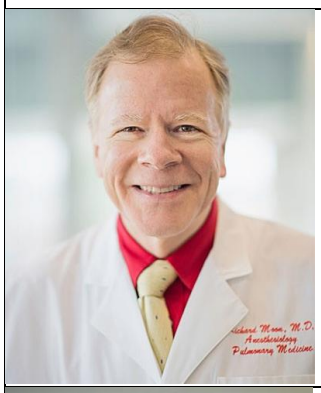
Brief biographies of the research group are provided below. A summarised vitae for the PI is included, and complete CVs for the members of the group are available on request.



Dr Ross Hofmeyr, MBChB, MMed(Anaes), FCA, FAWM

Consultant Anaesthesiologist; Airway Lead; Clinical Research Fellow in Airway and Thoracic Anaesthesia, University of Cape Town. Expedition doctor, co-founder and Medical Director, WildMedix. Academic liaison, Wilderness & Expedition Medicine Society of Southern Africa.

https://scholar.google.co.za/citations?user=wvS2pDkAAAAJ



Prof Richard Moon, MD, CM, MSc, FRCP(S), FACP, FCCP

Medical Director, Center for Hyperbaric Medicine and Environmental Physiology; Professor of Anesthesiology (General, Vascular & Transplant); Professor of Medicine (Pulmonary, Allergy & Critical Care), Duke University

https://scholars.duke.edu/person/richard.moon

Prof Mike Grocott, BSc, MBBS, MD, FRCA, FRCP, FFICM

Professor of Anaesthesia and Critical Care Medicine; Head: Integrative Physiology and Critical Illness Group; University of Southampton. Director, Caudwell Extreme Everest Hypoxia Research Consortium. Lead: Fit-4-Surgery Research Collaboration. Co-founder and former Director, Centre for Altitude, Space and Extreme Environment Medicine (CASE).

http://www.southampton.ac.uk/medicine/about/staff/mpg1c08.page

Prof Emeritus Mike James, MBChB, FRCA, FCA, PhD

Professor and former Head, Department of Anaesthesia & Perioperative Medicine, University of Cape Town. Honorary Professor, University College London. Former President, College of Anaesthetists of South Africa and South African Society of Anaesthesiologists.

https://scholar.google.co.za/citations?user=_tSzRb0AAAAJ

Abbreviated Curriculum Vitae

Dr Ross Hofmeyr

MBChB (Stell), DipPEC, DA (SA), MMed (Anaes) (UCT), FCA (SA), FAWM (WMS)

Biographical Information

Name	Michael Ross HOFMEYR
Postal Address	17 Margaret Avenue, Pinelands, Cape Town 7405, Republic of South Africa
Contact Number	+2784 549 9259
E-Mail	ross@wildmedix.com / ross.hofmeyr@uct.ac.za
Twitter	@rosshofmeyr
Google Scholar Profile	https://scholar.google.co.za/citations?user=wvS2pDkAAAAJ
Document Version	Updated 13 January 2017

Qualifications

2016	**Fellowship of the Academy of Wilderness Medicine,** Wilderness Medical Society
2015	**Master of Medicine in Anaesthesiology** with Distinction in the Dissertation, UCT
2015	**Fellowship of the College of Anaesthesiologists,** Colleges of Medicine of SA
2010	**Diploma in Anaesthesia,** College of Anaesthetists of South Africa
2009	**Diploma in Primary Emergency Care,** College of Emergency Medicine of SA
2005	**Bachelor of Medicine and Bachelor of Surgery,** Stellenbosch University, SA

Current Appointments

2015 to present	**UCT-Storz Fellow in Airway and Thoracic Anaesthesia** Department of Anaesthesia, University of Cape Town
2015 to present	**Consultant (Attending) Anaesthesiologist** Department of Anaesthesia, Groote Schuur Hospital
2005 to present	**Medical Director, WildMedix** Wilderness and Expedition Medical Support and Training

Postgraduate Experience

2011 to 2015	**Registrar (Resident), Anaesthesia & Critical Care** Groote Schuur Hospital, Cape Town
2009 to 2011	**Senior Medical Officer, Anaesthetics & Critical Care** GF Jooste Trauma & Emergency Hospital, Cape Town
2007 to 2009	**Expedition Leader & Doctor** South African National Antarctic Expedition
2007	**Community Service Medical Officer** Khayelitsha Community Health Centre, Cape Town, and Emergency Unit, GF Jooste Trauma & Emergency Hospital

Additional Professional Experience

2013 to 2016	**Senior Anaesthesia Cover,** Dept Anaesthesia, Mitchell's Plain Hospital
2010 January	**Expedition Doctor – Polar Star, Antarctica**
2009 to 2011	**Emergency Medicine –** Milnerton MediClinic Emergency Unit
2006 to present	**Aviation Medicine –** Red Cross Air Mercy Service
2000 to present	**Wilderness Search and Rescue (WSAR)** Emergency Medical Services
2004 to 2005	**Academy of Emergency Care** Cape Peninsula University of Technology

Research Interests

Masters' Dissertation	"***Blind intubation through the 3gLM supraglottic airway: A randomised comparison of two endotracheal tubes.***" Extensive literature review of existing techniques, and RCT comparing blind intubation through the novel 3gLM SGA. Degree awarded with distinction in the dissertation.
Airway Research	Founding member of the UCT Airway Research Group; core or lead researcher for four clinical trials and two laboratory-based airway device trials over the past 4 years, including first assessments of both the 3gLM supraglottic airway and Totaltrack VLM worldwide. Supervisor for the latter project, which was also awarded an MMed with distinction. Currently supervising a MMed of self-directed learning of fibreoptic dexterity, PI on an international collaborative study on introducer techniques, and am conducting further research in pursuit of a PhD in the field of ***"Context-sensitive airway management in resource-constrained settings***, with an African focus.
Perioperative Outcomes Research	Management Committee, South African Perioperative Outcomes Research Group (SAPORG). Chair and research lead, SAPORG Airway Research Group. Currently undertaking a series of national audit projects to in airway outcomes.
Extreme Cold & Thermoregulation Research	Founding member of UCT Thermoregulation Research Group, and hold a research grant in extreme physiology and adaptation, including laboratory and field research. We have one paper in press, have completed another study using the same research tools (telemetric core temperature monitoring) to determine the effects of spinal anaesthesia on core temperature of parturients undergoing caesarean section, and are currently gathering data using ultrasound at very high altitude on Kilimanjaro in two studies
Non-invasive Monitoring	Clinical trial of utility of a non-invasive haemoglobinometer in critically ill children in ICU, and am supervising an MMed study of the clinical accuracy and utility of compact, highly portable fingertip pulse oximeters.
Point-of-Care testing	Stemming from our extreme physiology work, we have undertaken a study of the effect of freezing on point-of-care blood analyser cartridges, and are now completing a multi-centre trial comparing traditional coagulation assays to POC tests for cardiac surgery.
Anaesthesia & Analgesia at Altitude	Current studies of performance of anaesthesia vapour, gas delivery and monitoring devices at moderate to high altitude for analgesia in remote, resource-constrained or rescue settings

Grants & Awards

Research Grants	**South African Society of Anaesthesiologists – Jan Pretorius Research Fund** R45000 for the extreme physiology and thermoregulation research, including the potion to be completed in Antarctica. Laboratory-based components have continued and are nearing submission for publication; field measurements commenced this February on Mt Kilimanjaro **University of Cape Town Research Committee – Short Research Visit Grant** R16000 awarded to undertake airway research with collaborators in the United Kingdom, June 2016
Awards	**2nd place, Equipment category, World Airway Management Meeting 2015** UCT/Storz **Fellowship in Airway and Thoracic Anaesthesia** (2015-2017) UCT Anaesthesia **Registrar of the Year** (2014) UCT Anaesthesia **Registrar's Registrar of the Year** (2014) SASA **Registrar's Communications Prize** (2013) UCT Anaesthesia **Registrar's Registrar of the Year** (2013) Tom Rutmann Prize for the **Best Registrar in Intensive Care** (2012)

Publications

Book Chapters

Hofmeyr R. **Preventing Airway Disasters**. *Handbook of Anaesthesia and Critical Care 2016 (Vol 4)*, MIMS, Cape Town, South Africa, 2016, pp 67-72

Hofmeyr R. **The Aging Intensivist and Younger Colleagues**. In: Crippen D (Ed), *The Intensivist's Challenge: Aging and Career Growth in a High-Stress Medical Speciality.* Springer International 2016. Chapter 11, pp 81-88.

Hofmeyr R, Dyer RA. **Maternal hypotension during neuraxial anaesthesia.** In: Husain, Fernando, Segal (Ed), *Obstetric Anaesthesiology: An Illustrated Case-Based Approach*, Cambridge University Press (in press, 2016). Chapter 31.

Hofmeyr R. **South Africa: Where Are We Going?** In: Crippen D (Ed), *ICU Resource Allocation in the New Millennium.* Springer 2013. Chapter 22.

Journal Publications

Hofmeyr R, Matjila M, Dyer RA. **Preeclampsia in 2017: Obstetric and Anaesthesia Management.** *Best Practice & Research Clinical Anaesthesiology* 2017 (online ahead of print) http://dx.doi.org/10.1016/j.bpa.2016.12.002

Hofmeyr R, Meyer W, James MF, De Decker R. **Recognising and mitigating the risk of altitude-related illness.** *South African Medical Journal* 2016;106(9):834-835. http://dx.doi.org/10.7196/SAMJ.2016.v106i9.11389

Fortgens P, Du Toit L, Hofmeyr R, Dyer R. **Performance of the i-STAT point-of-care analyser cartridges after ambient and sub-zero temperature exposure.** *Point of Care,* 2016;15(4):132-136

James MF, Hofmeyr R, Grocott M. **Losing Concentration: Time for a new MAPP?** *British Journal of Anaesthesia*, Editorial, first publication (online) 21 May 2015, DOI: 10.1093/bja/aev151

Jacobs GEA, Buss CS, Hofmeyr R. **Post-laparotomy haemoptysis due to broncho-abdominal fistula caused by retained abdominal surgical swab**. *Southern African Journal of Anaesthesia and Analgesia,* 2016;22(5)160-162.

Kluyts H, Hofmeyr R, Biccard B. **The United Kingdom National Audit Project Program – an opportunity for South Africa?** *Southern African Journal of Anaesthesia and Analgesia*, Editorial, 2016;2(22):4

Choonoo J, Hofmeyr R, Evans NR, James MF, Meyersveld N. **A New Option in Airway Management: Evaluation of the TotalTrack® Video Laryngeal Mask**, *Southern African Journal of Anaesthesia and Analgesia*, 2016;22(2):52-56, http://dx.doi.org/10.1080/22201181.2016.1159784

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Hofmeyr R, Myburgh A. **Use of transabdominal ultrasound to enhance safety during oesophageal dilation.** *British Journal of Anaesthesia*, 2013; 111 (1): 125-126. DOI: http://dx.doi.org/10.1093/bja/aet185

Hofmeyr R, Gordon PC. **Pioneers in South African Anaesthesia: Tom Voss and the "Elephant Tube".** *Southern African Journal of Anaesthesia and Analgesia*, 2013;19(5):239-241

Hofmeyr R. **State of the art: Video and optical laryngoscopy**. *African Journal of Emergency Medicine* 12/2013; 3(4):S16. DOI: 10.1016/j.afjem.2013.08.042

Hofmeyr R. **State of the art: Rescue intubation through supraglottic airways.** *African Journal of Emergency Medicine* 12/2013; 3(4):S6. DOI: http://dx.doi.org/10.1016/j.afjem.2013.08.011

Hofmeyr R. **Extreme Medicine – The Antarctic Doctor**. First published in *Association of Emergency Physicians First Line Newsletter* 2008(5), and *Junior*

	Doctor Magazine, accessible at http://www.juniordr.com/index.php/working-overseas/extreme-medicine-the-antarctic-doctor.html
Articles in Press	Du Toit L, van Dyk D, Hofmeyr R, Lombard C, Dyer R. Core temperature monitoring in obstetric spinal anaesthesia using an ingestible telemetric sensor. Accepted (*Anaesthesia & Analgesia), in press 2017*
Online Publications	I am a passionate supporter of the #FOAM (Free, Open-Access Meducation) movement, and curate a website dedicated to open-access airway teaching material, www.OpenAirway.org

Teaching & Congresses

Teaching & Simulation	**Teaching anaesthetic skills** to medical students, interns and others rotating through our department is a daily requirement. I serve as the Airway Lead for the Department of Anaesthesia, co-ordinate teaching of **airway management skills**, acquisition of suitable equipment, and manage the **Airway Skills Laboratory**. I enjoy instructing frequently on **International** and **Advanced Trauma Life Support, Advanced Cardiovascular Life Support** and **Advanced Airway Management** courses. Furthermore, I regularly give both lectures and practical skills training to the national diploma **para medic students**, as well as act as a supervisor during their clinical rotations, and lecture on the **Aviation Health Care Provider** course. I have been a key roleplayer in developing simulation training at UCT and Groote Schuur Hospital. Over the past decade I have played a pivotal and leading role in developing practical and academic education in **wilderness medicine** in South Africa, culminating in the first internationally accredited training courses on the continent.
Conference Presentations & Posters	**Invited speaker, research presentations and workshop co-ordinator or instructor at more than 20 local and international meetings** Association of Anaesthesiologists of Mauritius Annual Scientific Meeting, 2016 SMACCdub, Dublin, Ireland, 2016 7th Networking World Anaesthesia Convention, New York, 2016 International Conference on Emergency Medicine, 2016 Southern African Society of Anaesthesiologists Congress, 2016 Big 5 Anaesthesia, Skukuza, 2015 1st World Airway Management Meeting, Dublin, 2015 6th Networking World Anaesthesia Convention, Vancouver 2015 19th World Congress on Disaster and Emergency Medicine, 2015 Southern African Society of Anaesthesiologists Congress, 2015 Paediatric Anaesthetic Congress of Southern Africa, 2014 5th Networking World Anaesthesia Congress, Vienna 2014 Southern African Society of Anaesthesiologists Congress, 2014 Emergency Medicine in the Developing World, 2013 Southern African Society of Anaesthesiologists Congress, 2013 Aviation Medicine Congress, Cape Town, 2012 Southern African Society of Anaesthesiologists Congress, 2012 Critical Care Society of Southern Africa Congress, 2010 Emergency Medicine in the Developing World, Cape Town, 2009

References

1 Cohen JE, Small C. Hypsographic demography: the distribution of human population by altitude. *Proc Natl Acad Sci U S A* 1998; **95**: 14009-14

2 Moon RE. Oxygen in Acute Illness: More or Less? *Crit Care Med* 2015; **43**: 1547-8

3 James MF, Hofmeyr R, Grocott MP. Losing concentration: time for a new MAPP? *Br J Anaesth* 2015; **115**: 824-6

4 Ehrenwerth J, Eisenkraft JB, Berry JM. *Anesthesia equipment : principles and applications*. Second edition. Edn. Philadelphia, PA: Saunders, 2013

5 James MF, White JF. Anesthetic considerations at moderate altitude. *Anesth Analg* 1984; **63**: 1097-105

6 Andrews JJ, Johnston RV, Jr. The new Tec6 desflurane vaporizer. *Anesth Analg* 1993; **76**: 1338-41

7 Windsor J, van der Kaaij J, Ellerton J, Oxer H, Hillebrandt D, Rodway G. Methoxyflurane as an analgesic for prehospital use at high altitude. *High Alt Med Biol* 2009; **10**: 201-2

8 Venticinque. #160. *MFMJ* 2015

9 Bosco G. Anesthesia at High Altitudes. In: Ehrenwerth J, Eisenkraft J, Berry J, eds. *Anaesthesia Equipment: Principles and Applications*: Elseview Health Sciences, 2013