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Some upcoming
Basic Pediatric Intensive Care Course (BPICC)
Courses
Bhubneshwar, Raipur -December 2014
PEDICON 2015, Delhi
CRITICARE 2015, Bengaluru

To Organize a BPICC in your area, please contact:

Dr Madhu Otiv
Chairperson IAP Intensive Care Chapter
M: 09822040950 • Email: madhu_otiv@hotmail.com

Dr Rajiv Uttam
National Co Convener BPICC
M: 9810055670 • Email: rajivuttam@hotmail.com

Dr Anil Sachdev
Chair Elect IAP Intensive Care Chapter
M: 9810098360 • Email: anilcriticare@gmail.com

Regional Conveners:
Dr Vikas Taneja (Gurgaon)
Dr Anjul Dayal (Hyderabad)
Dr Gnanam (Bengaluru)
Dr Parthsarathi Bhattacharya (Kolkotta)
Dr Vinay Joshi (Mumbai)
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¹Johns Hopkins Hospital, Baltimore, MD, ²Fortis Hospital, Bombay, India, ³Medanta Hospital, Delhi, India, ⁴KD Ambani Hospital, Bombay, India, ⁵Sai Children’s Hospital, New Panvel, India, ⁶Seth GS Medical College, Bombay, India, ⁷Rainbow Children’s Hospital, Vijaywada, India, ⁸BLK Superspecialty Hospital, New Delhi, India

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Comments by International Reviewers

Critical Thinking: PICU Quiz
Praveen Khilnani
Director, Pediatric Critical Care and Pulmonology, BLK Superspeciality Hospital, New Delhi
From Editors Desk

Dear Colleagues,

Fourth issue of IAP intensive care chapter journal: Journal of Pediatric Critical care (JPCC) is in your hands. National conference of Pediatric critical care is on in Delhi and abstracts for presentation and posters are published in this issue. As a highlight of this issue, symposium on monitoring in the PICU is presented by various authors from allover the country.

Website www.journalofpediatriccriticalcare.com is now fully functional and all issues of the journal may be downloaded. Please visit the journal page on facebook for comments. Any suggestions are welcome.

Articles from many regions of India as well as other countries have begun to pour in. Original articles from Pakistan, Canada and India are published in this issue.

We do have an ISSN number assigned: ISSN 2349-6592

With a continued regularity and publication of peer reviewed articles we should get indexed in pub med soon.

Thanks for your continued support and efforts to publish original articles as well as review the articles in a timely fashion.

Praveen Khilnani MD FAAP, FCCM
Editor in Chief
Journal of Pediatric critical care
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<td>Dr Banani Poddar</td>
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<td>Dr Ebor Jacob</td>
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<td>Dr Jhuma Sankar</td>
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<td>Dr Urmila Jhamb</td>
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<td>Dr Meera Ramakrishnan</td>
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<tr>
<td>Dr Maninder Dhamiwal</td>
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<td>Dr Vinay Patki</td>
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<td>Dr Rachna Sharma</td>
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<td>Dr Sanjeev Kumar</td>
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<td>Dr Niranjan Kissoon</td>
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<td>Dr M P Jain</td>
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For JPCC (Journal of Pediatric Critical Care) Manuscript Submission

Manuscript submission will be possible using our online submission system shortly.
All submissions should be made by email until further announcement regarding the online submission details and the journal website: Khilnanip@hotmail.com

Journal of Pediatric Critical Care is published quarterly (January, April, July and October) by IAP intensive care chapter. Manuscripts are judged by reviewers solely on the basis of their contribution of original data and ideas, and their presentation. All articles will be critically reviewed within 2 months, but longer delays are sometimes unavoidable. All manuscripts must comply with Instructions to Authors.

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ETHICS Investigations on human subjects should conform to accepted ethical standards. Fully informed consent should be obtained and noted in the manuscript. For all manuscripts dealing with experimental work involving human subjects, specify that informed consent was obtained following a full explanation of the procedure(s) undertaken. Patients should be referred to by number; do not use real names or initials. Also the design of special scientific research in human diseases or of animal experiments should be approved by the ethical committee of the institution or conform to guidelines on animal care and use currently applied in the country of origin.

STYLE OF MANUSCRIPTS All contributions should be written in English. Spelling should be American English. In general, manuscripts should be prepared according to International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. JAMA 1997; 269: 927-934. Manuscript should be as concise and clear as possible. Manuscripts not following Instruction to Authors will be returned to the authors.

LANGUAGE Only English articles will be accepted. Prior to submission, manuscripts prepared by authors whose native language is not English should be edited for proper spelling, grammar, and syntax by a professional editor or colleague fluent in English.

MANUSCRIPTS CATEGORIES Materials reviewed for publication in JOURNAL OF PEDIATRIC INTENSIVE CARE include the following:

Editorials
Editorials will present the opinions of leaders in pediatric intensive care
**Original articles**
Original clinical or laboratory investigation of clinical subjects should be reported. The material should be presented as concisely as possible.

**Review articles**
Reviews should document and synthesize current information on timely subjects.

**Case reports**
A case report should describe a new disease, or confirmation of a rare or new disease; a new insight into pathogenesis, etiology, diagnosis, or treatment; or a new finding associated with a currently known disease.

**Rapid communications**
These should be short papers, brief laboratory investigations and preliminary communications, which report new and exciting results requiring rapid publication.

**Letters**
These should be submitted in response to material published in the journal to make small clinical points or to introduce a point of view. Letters do not carry an abstract.

**Book reviews**
Reviews of newly published literature of interest.

**MANUSCRIPT**
Manuscript submission should be made by e-mail. Manuscripts should be submitted with text and tables, preferably in a recent Word or Word Perfect for Windows format. If article is submitted electronically, there is no need to send a hard copy. The Copyright Status Form should also be sent by e-mail or fax or regular mail.

Manuscripts should be clearly in double spacing on one side of good quality A4 paper (30 x 21 cm), using 2.5 cm margins. Pages should be numbered consequently in the top right-hand corner, commencing with the Title Page and including those containing Acknowledgements, References, Tables, and Figures.

**Conventional Manuscript** The manuscript should be arranged as follows, with each section beginning on a separate page, except in the category of Rapid communications.

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**Title page**
The category of manuscripts (as listed above) should appear on the title page. The title on the title page should contain no more than 80 letters and spaces. A running title of no more than 40 letters and spaces should be supplied. Each author’s first and last name as well as middle initial, highest academic degree, name of department(s) and institutions to which the work should be attributed, and address should appear. The author to whom communications will be directed should be designated and his or her telephone and FAX number and E-mail addresses (obligatory for submission) provided.

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Results should be presented in a logical sequence the text.

Tables and figures should not include material appropriate to the discussion.

Discussion
The new and important aspects of the study and the conclusions should be emphasized, without repeating data in detail. This section should consider the implications of the finding and their limitations. Link the conclusions with the goals of the study, and relate the observations to other relevant studies. New hypotheses and recommendations, when appropriate, may be included. Acknowledgement should be made only to persons who have made genuine contributions and who endorse the data and conclusions.

References
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Tables
Limit the number of tables. Data in tables should not be repeated in graphs. Do not use vertical lines to separate information within the table. Tables should be double-spaced and numbered consequently corresponding to in-text citation. A table title and number must be provided at the top. Headings should be concise and use Arabic numbers. Tables should be restricted to one manuscript page unless absolutely necessary. If a table continues past one page, repeat all sequence in heads and the stub (left-hand) column. All non-standard abbreviations should also be explained in the footnotes. Footnotes should be indicated by*, **. Statistical measures such as mean ± SD (standard deviation) should be identified in headings.

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Number figures as Fig. 1, Fig. 2, etc and refer to all of them in the text.
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Photographs are only acceptable if they have good contrast and intensity.

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Manuscript should be in metric units. Standard abbreviations may be used and should be defined in the Abstract and on the first mention in the text. In general, a term should not be abbreviated unless it is used repeatedly and the abbreviation is helpful to the reader.

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All articles will be critically evaluated by at least three reviewers of the editorial board (or known experts in the field) within 2 months, but longer delays are sometimes unavoidable.

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Proofs are sent to the corresponding author, together with a reprint order form approximately 6 weeks prior to the publication. Authors should retain a copy of the original manuscript. Only printer’s errors may be corrected; no changes in, or additions to, the edited manuscript will be allowed at this stage, unless in reply to specific editorial queries or requests. Corrected proofs must be returned within 48 hours of receipt, preferably by e mail or fax. If the publisher has not received a reply after 15 days, the assumption will be made that there are no errors to correct, and the article will be published after in-house correction. The reprint order form (with number of reprints requested, invoice and delivery address) should be returned with the corrected proof. Reprints may be ordered prior to publication on the form provided. The designated reviewing author will be responsible for ordering reprints for all authors. Reprints ordered after publication of the journal can be ordered at increased cost by special arrangement.

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# 16th National Conference of Pediatric Critical Care 2014

**Annual Conference of Indian Academy of Pediatric-Intensive Care Chapter**

**Venue:** Hotel Le Meridien, Janpath, New Delhi • **Date:** 6th to 9th November 2014

**Hosted by:**
IAP Intensive Care Chapter, Delhi & Indian Academy of Pediatrics - Delhi Branch

## Day 1: 8th November, 2014

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<th>Speaker(s)</th>
<th>Chairpersons</th>
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<td>Meet The Experts</td>
<td>Shekhar Venkataraman, Mohan Mysore, Utpal Bhalala, Soonu Udani (Anchor)</td>
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<tr>
<td>09.00am - 09.30am</td>
<td>Key Note Address</td>
<td>Jerry Zimmerman</td>
<td>Chairpersons: Soonu Udani, Madhu Otive, Praveen Khilnani, Anil Sachdev</td>
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<td>09.30am - 10.00am</td>
<td>Clinically meaningful outcomes after critical illness</td>
<td>Joe Carillo</td>
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<td>10.00am - 10.30am</td>
<td>How to assess volume responsiveness in 2014</td>
<td>Ravi Thiagarajan</td>
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<td>10.30am - 11.00am</td>
<td>Failing heart: Support beyond vasopressors</td>
<td>Vinay Nadkarni</td>
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<td>11.00am - 11.30am</td>
<td>Goal directed therapy in critical care</td>
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<td>08.00am - 11.00am</td>
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<td>Chairpersons: Satish Deopujari, Nameet Jerath, Shruti Agarwal, Prabhat Maheshwari</td>
<td>Chairpersons: Suneel Pooboni, Uma Ali, Anita Bakshi, N Ravishankar</td>
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<td>11.30am - 11.50am</td>
<td>Is NIV the first line therapy for acute respiratory failure</td>
<td>Mohan Mysore</td>
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<td>HFOV- Current status in PICU</td>
<td>Anil Sachdev</td>
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<td>Dopamine in septic shock- Current status</td>
<td>Utpal Bhalala</td>
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<td>12.30pm - 12.50pm</td>
<td>Ventilator induced lung injury- How to minimize it</td>
<td>Madhu Otiv</td>
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<td>02.00pm - 03.00pm</td>
<td>Free Paper Presentation</td>
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<td>Judges: Jerry Zimmerman, Rakesh Lodha, Sandeep Kumar</td>
<td>Judges: Vinay Nadkarni, Urmila Jhamb, Ebor Jacob</td>
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<td>PRO-CON Debate</td>
<td>ARDS- Role of corticosteroids</td>
<td>VSV Prasad</td>
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<td>Role of ECHO in titrating vasopressors</td>
<td>Pro-Con Debate Anuj Dayal/Sachin Shah</td>
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<td>03.40pm - 04.00pm</td>
<td>Akashdeep Arora</td>
<td>Should I use antipyretics aggressively in critical patient</td>
<td>Dhiren Gupta</td>
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<td>04.00pm - 04.20pm</td>
<td>Pro-Con Debate Banani</td>
<td>Vitamin D in critical care</td>
<td>Pro-Con Debate Vinay Joshi/Rashmi Kapoor</td>
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<tr>
<td>04.20pm - 05.00pm</td>
<td>Panel Discussion Moderators: Krishan Chugh, Panelists-Satish Deopujari,</td>
<td>Resistant infections in PICU</td>
<td>Critical care delivery in India</td>
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<td></td>
<td>Meera Ramakrishnan, Kundan Mittal, Gnanam, Jhuma Sankar</td>
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<td>Discussion Time 10 minutes</td>
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<td>05.30pm-06.00pm</td>
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<td>06.00pm-06.15pm</td>
<td>Tea</td>
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<td>06.15pm</td>
<td>Annual General Body Meeting</td>
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<tr>
<td>07.30pm Onwards</td>
<td>Banquet</td>
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</tbody>
</table>
### Day 2: 9th November, 2014

**08.00am - 09.00am**  
Meet the Experts: Vinay Nadkarni, Shruti Aggarwal, Suchitra Ranjit, Madhu Otiv (Anchor)

**Key note Address**

Chairpersons- Vinay Nadkarni, Mohan Mysore, Rajiv Uttam, Vikas Taneja

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Topic</th>
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<tbody>
<tr>
<td>09.00am - 09.30am</td>
<td>Shekhar Venkataranam</td>
<td>Common myths in clinical practice in PICU</td>
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<tr>
<td>09.30am - 10.00am</td>
<td>Praveen Khilnani</td>
<td>Pediatric intensive care in India- Past, Present and Future</td>
</tr>
<tr>
<td>10.00am - 10.30am</td>
<td>Jerry Zimmerman</td>
<td>Steroids in critical illness: Where is the Pendulum</td>
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<td>10.30am - 11.00am</td>
<td>Krishan Chugh</td>
<td>Evidence based medicine in PICU- Always practical?</td>
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<tr>
<td>11.00am - 11.30am</td>
<td>Mahendra Singh</td>
<td>Tea</td>
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**HALL A**

<table>
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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>11.30am - 11.50am</td>
<td>M Jayashree</td>
<td>CPP directed therapy in nontraumatic brain insult</td>
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<tr>
<td>11.50am - 12.10pm</td>
<td>Santosh Soans</td>
<td>Sedation and muscle relaxants in mechanically ventilated child-</td>
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<tr>
<td>12.10pm - 12.30pm</td>
<td>Suneel Pooboni</td>
<td>Acute severe respiratory failure-Is ECMO the answer</td>
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<tr>
<td>12.30pm - 12.50pm</td>
<td>Arun Bansal</td>
<td>Pittfalls of ScVO2 and blood Lactate levels in critical illness</td>
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<td>12.50pm - 01.00pm</td>
<td>Discussion</td>
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<td>01.00pm - 02.00pm</td>
<td>LUNCH</td>
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</table>
| 02.00pm - 03.00pm | Chairpersons:  
P. Bhattacharya, Basavraj, Meera Ramakrishnan, Mahesh Mohite |                                                                                                    |
| 02.00pm - 02.20pm | Baia Ramachandran | Utility of High Flow Nasal Cannula in PICU                                                         |
| 02.20pm - 02.40pm | BP Karunakara | IV Immunoglobulins in severe sepsis                                                                |
| 02.40pm - 03.00pm | Pro-Con Debate Rakesh Lodha / Puneet Pooni | Weaning from mechanical ventilation Protocollized vs Clinical Judgement                           |

**HALL B**

<table>
<thead>
<tr>
<th>Time</th>
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<tbody>
<tr>
<td>11.30am - 11.50am</td>
<td>Vinay Nadkarni</td>
<td>Berlin definition of ARDS Relevance for Pediatric Patient</td>
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<tr>
<td>11.50am - 12.10pm</td>
<td>Uma Ali</td>
<td>CRRT in sepsis-Timing and outcome</td>
</tr>
<tr>
<td>12.10pm - 12.30pm</td>
<td>Ravi Thilagarajan</td>
<td>Septic cardiomyopathy</td>
</tr>
<tr>
<td>12.30pm - 12.50pm</td>
<td>Shekhar Venkataranam</td>
<td>Bedside measurement of alveolar recruitment</td>
</tr>
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**02.00pm - 02.20pm**  
Chairpersons:  
P. Bhattacharya, Basavraj, Meera Ramakrishnan, Mahesh Mohite

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<tr>
<th>Time</th>
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<tr>
<td>02.00pm - 02.10pm</td>
<td>Shruti Agarwal</td>
<td>NIRS</td>
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<tr>
<td>02.10pm - 02.20pm</td>
<td>Dhiren Gupta</td>
<td>Meningococcal infection-What’s new?</td>
</tr>
<tr>
<td>02.20pm - 02.40pm</td>
<td>Satish Deopjari</td>
<td>Non-infectious causes of fever in PICU</td>
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<tr>
<td>02.40pm - 02.50pm</td>
<td>Sanjay Ghorpade</td>
<td>Anti fungal drugs</td>
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<tr>
<td>02.50pm - 3.00pm</td>
<td>J B Fink</td>
<td>Aerosol therapy in PICU</td>
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**03.00pm - 03.20pm**  
Chairpersons:  
Anupam Sachdeva, BB Aggarwal, Manish Sharma, Kundan Mittal

<table>
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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Topic</th>
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<tbody>
<tr>
<td>03.00pm - 03.20pm</td>
<td>Shekhar Venkataranam</td>
<td>How to get an article published in a critical care journal</td>
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<tr>
<td>03.20pm - 03.40pm</td>
<td>Nameet Jerath</td>
<td>Emerging diagnostic methods in sepsis and severe infections</td>
</tr>
<tr>
<td>03.40pm - 04.00pm</td>
<td>Vikas Taneja</td>
<td>Organ transplantation- Role of Intensivist</td>
</tr>
<tr>
<td>04.00pm - 04.20pm</td>
<td>Ebor Jacob</td>
<td>Abdomen-Neglected organ system in ICU</td>
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<tr>
<td>04.20pm - 05.00pm</td>
<td>Panel Discussion Moderator- Rajiv Uttam</td>
<td>Vasoactive drugs in PICU</td>
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<tr>
<td>05.00pm - 05.30pm</td>
<td>Vote of thanks</td>
<td>Summing it up! What have you learnt in NCPCC 2014?</td>
</tr>
</tbody>
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Alterations of Thyroid Function in Critically Ill Children

Vinayak K. Patki *, Jennifer V Antin**
*Pediatric Intensivist **Jr Consultant, Department of Pediatrics, Wanless Hospital, Miraj, Dist Sangli, Maharashtra

ABSTRACT

Title-Alterations of thyroid function in critically ill children
Aims & Objective- To study thyroid hormonal changes in critically ill children and correlate them with outcome.
Methods-In this prospective study total serum T3, T4 and TSH levels were estimated at admission and at discharge or prior to death in fifty critically ill cases admitted to PICU. Fifty healthy children were taken as controls. PRISMII score was used to predict outcome. Hormone levels were compared between cases and control and then between survivors and non survivors.
Results- Mean T3 (59.86±16.09 vs123.04±26.21)and T4 levels (5.38±1.30vs8.70±1.82) in cases were significantly (P-0.000) lower than that of controls,however no significant difference in the mean TSH values (2.21±1.91 vs2.18±1.06) were noted. Fourteen (28%) cases expired. Admission T3 level (44.71±13.35 Vs65.75±13.01) was significantly (p-0.000) lower in non survivors than survivors but there was no significant difference in T4 (4.86±1.57Vs5.57±1.15) and TSH(2.17±1.69 Vs 2.28±2.12 ) levels. Serum T3 (65.75±13.01vs96.36 ±25.48),T4 (5.57±1.15vs8.52±3.19) and TSH levels(2.28±2.12 vs3.06±1.61) improved in survivors but failed to improve in non survivors. LowT3 and T4 at admission were associated with high risk of mortality (odds ratio 14.8, p-0.000). PRISMII score and T4 in second sample were significant predictors of death.
Conclusion- In critically ill children T3, T4 levels are low, while TSH values may not change. T3 levels reflect patient’s clinical status and T4 levels can predict death.
Key words- thyroid hormone, critically ill children, PRISMII

Introduction

Altered thyroid function in nonthyroidalillness(NTI) is a well-recognized finding.(1,2)The term euthyroid sick syndrome (ESS) identifies abnormalities in thyroid function tests observed in patients with systemic nonthyroidal illnesses (NTIs). ESS has been classified as Type 1- low T3 syndrome, Type 2-low T4&low T3 syndrome and Type 3-low TSH syndrome. The severity and the nature of changes in thyroid function test have implications for the prognosis of the systemic illness.(3,4) These abnormalities result from variable, usually reversible, disturbances in the hypothalamo-pituitary-thyroid axis, thyroid hormone binding to serum proteins, tissue uptake of thyroid hormones, and/or thyroid hormone metabolism.(5) The production of thyroxine (T4) by the thyroid gland is regulated by the classic hypothalamus-pituitary-thyroid axis, in which the anterior pituitary releases thyroid stimulating hormone (TSH) thyrotropin as a result of the stimulation by hypothalamic thyrotropin-releasing hormone (TRH). The biological activity of thyroid hormone (i.e. the availability of the active hormone 3,5,3 V-triiodothyronine [T3]), is largely regulated by the iodothyroninedeiodinases D1, D2, and D3 which convert T4 to either T3 or to the inactive metabolite reverse T3 (rT3). Both T4 and T3 have an inhibitory effect on TRH and TSH secretion by way of a negative feedback loop mechanism.(5,6)

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Low serum total T3 is the most common abnormality...
in NTI. It is observed in about 70% of hospitalized patients.\(^{(7)}\) Serum total T\(_3\) may vary from undetectable to normal in patients with systemic illness. Within a few hours after the onset of disease, plasma T\(_3\) decreases and plasma rT3 increases, and the magnitude of these reciprocal changes is related to the severity of the disease.\(^{(7-9)}\) Altered expression of thyroid hormone transporters, impairment of 5’ deiodinaseactivity due to reduced availability of the enzyme co-factor glutathione due to reduced intake of carbohydrates, stress induced elevated steroids and free fatty acids as inhibitor of extra-thyroidal T\(_4\) to T\(_3\) conversion are some of the postulated mechanisms.\(^{(10-13)}\)

T\(_4\) decreases as well with T\(_3\) in severely ill patients and both low T\(_4\) and low T\(_3\) are associated with a poor prognosis.\(^{(14-16)}\) Suppression of thyroid releasing hormone (TRH) from hypothalamus due to dysregulation or inhibitory action of somatostatin, decreased pituitary response to TRH, decreased pituitary secretion of TSH due to cortisol, growth hormone, dopamine, opiate peptides secreted in response to stress, decreased responsiveness of pituitary TSH to low T\(_3\) or T\(_4\) and reduced plasmabinding of T4 are suggested reasons for low T\(_4\).\(^{(17-20)}\)

Majority of the studies till date on thyroid function test and its correlation with outcome in critically ill patients are mainly conducted in surgical ICUs especially in adults. There is paucity of data available in pediatrics ICUs, especially in India on this subject. Hence present study was conducted to evaluate the alteration of thyroid hormone function in critically ill children and to assess its correlation with their outcome.

Materials and Methods

In this prospective study fifty critically ill children admitted in Pediatric intensive care unit (PICU) were studied over a period of 1.5 years (August 2010 to February 2012). Critical illness was defined as any condition leading to malfunction of one or more organ system requiring support to maintain vital functions either with mechanical or pharmacological aids. PRISMII score (Pediatric risk of mortality score) was used to predict the outcome in critically ill patients at 0 and 24 hours. Data was collected within first hour of admission to pediatric ICU. Data collection pertinent to the analysis included ICU admission diagnosis, categorized by primary physiologic instability and outcome (survival or death). Total serum T\(_3\), T\(_4\), TSH levels were estimated twice in critically ill patients, first sample at admission to PICU and second sample at discharge or prior to death (depending on the outcome of patient). Fifty age and sex matched healthy children were taken as controls.

Admissions for post procedure recovery, cases with maternal or family history of thyroid illness, clinical evidence of thyroid dysfunction, or patients on any thyroid medication or on long term glucocorticoids, patient on drugs like radiographic agents, amiodarone and propranolol which affect directly thyroid function were also excluded from the study. The data was recorded on standardized sheet and included demographic variables such as age, sex, outcome, T\(_3\), T\(_4\), TSH levels and 14 physiological variables used in PRISMII score. Estimation of variable parameters was done. Blood pressure was recorded with noninvasive multipara monitors and oxygen saturation measured with pulse oximeter at admission. The Fio2 required for maintaining oxygen saturation above 90% was noted with oxygen monitor. Radial artery sampling was used for determining PaO\(_2\), Paco\(_2\) and bicarbonate levels. Standard lab techniques were utilized to measure blood levels of total bilirubin, protein, potassium, calcium, glucose, prothrombin time and partial thromboplastin time. Clinical assessment of heart rate, respiratory rate and pupillary reaction for each patient was made. The children were followed up during the hospital stay and the outcome measures were recorded as death or survived at the end of hospital stay. Serum total T\(_3\), T\(_4\) & TSH levels were estimated by solid-phase competitive luminescence immunoassay (CLIA). T\(_3\) values less than 60 ng/dl, T\(_4\) values less than 4.5 mcg/dl & TSH values less than 0.3 uU/ml was considered as low T\(_3\), T\(_4\) & TSH values respectively. Cases were also classified as Type I, Type II & Type III Euthyroid sick syndrome (ESS) accordingly. Only low T\(_3\) as ESS Type I, both Low T\(_3\) & Low T\(_4\) as ESS Type II & Low TSH as ESS Type III.
The hospital ethics and review board’s approval and informed consent from relatives was taken before undertaking the study. Statistical analysis of data was done by using IBM SPSS 19.0 Statistics software. Normally distributed continuous variables were compared with Student’s t-test and categorical variables were compared with Chi-square test or Fisher’s exact test. Pearson Correlation coefficient was used to study bivariate correlation. After determination of individual factors with mortality by univariate analysis, a binary logistic regression model of significant factors associated with mortality was developed. The results of regression model were presented as adjusted odds ratio. Wald’s chi square value was used to test unique contribution of each predictor. Regression model adequacy was tested by Omnibus test of model coefficients, Negelkerke $R^2$ and Hosmer & Lameshow chi square test. Receiver Operating Characteristic Curve analysis was used to find out the cut-off values for T, T4 and TSH and for PRISM II score to validate predicted probabilities of death. P< 0.05 was considered statistically significant.

### Results

Mean age of fifty critically ill children in the case group was 78.92±40.78 months (range 14 to 156 months). There was no significant difference in mean values of T3(60.28±17.69 Vs.57.12±12.71ng/dl), T4(5.64±1.05 Vs. 5.41±1.25mcg/dl) and TSH (2.53±1.25 Vs 2.24±1.61) between males and females. The distribution of cases according to diagnosis is mentioned in Table 2. Mean total protein levels (5.49±1.67 vs. 6.01±0.66 gm) were comparable between cases & controls. Fourteen (28%) children died and 36 (72%) survived. The means and SD of thyroid profile for given sample size and alpha (0.05,2 tailed), power of study was 1.00. The average duration between the first and second sample in survivors was 7.64±2.08 days and in non survivors cases was 6.29±2.28 days.

Mean serum T3 and serum T4 levels were significantly lower in cases than that in controls. However serum TSH levels were not significantly different between two groups (Table 1). At admission there was no significant difference in the serum levels of T4 and TSH between survivor and non survivors. However serum T3 level was significantly lower in non survivors (Table 3). Among survivors T3, T4 and TSH levels at discharge showed significant (p<0.000) rise as compared to their admission levels. However T3, T4 and TSH levels in the non survivors failed to improve (Table 4). There was no significant difference in mean total protein levels (5.78±0.62 Vs 5.38±0.66) between survived and expired children.

### Table 1: Comparativedemography in cases verses controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases ($n=50$)</th>
<th>Controls ($n=50$)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>37/13</td>
<td>38/12</td>
<td>0.817</td>
</tr>
<tr>
<td>Age in months</td>
<td>78.92±40.78</td>
<td>81.02±41.17</td>
<td>0.798</td>
</tr>
<tr>
<td>Serum proteins</td>
<td>5.49±1.67</td>
<td>6.01±1.66</td>
<td>0.126</td>
</tr>
<tr>
<td>T3</td>
<td>59.86±16.09</td>
<td>123.04±26.21</td>
<td>0.000</td>
</tr>
<tr>
<td>T4</td>
<td>5.38±1.30</td>
<td>8.70±1.82</td>
<td>0.000</td>
</tr>
<tr>
<td>TSH</td>
<td>2.21±1.91</td>
<td>2.18±1.06</td>
<td>0.928</td>
</tr>
</tbody>
</table>

### Table 2: Distribution of cases according to diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases ($n=50$)</th>
<th>Deaths ($n=14$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral encephalitis</td>
<td>7 (14%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>3 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>8 (16%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>Severe acute asthma</td>
<td>7 (14%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>3 (6%)</td>
<td>1 (7.14%)</td>
</tr>
<tr>
<td>gastroenteritis</td>
<td>6 (12%)</td>
<td>1 (7.14%)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>10 (20%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>6 (12%)</td>
<td>2 (14.3%)</td>
</tr>
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</table>

### Table 3: Comparison of thyroid profile between survivors & non survivors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Survivors ($n=36$)</th>
<th>Non survivors ($n=14$)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>First T3</td>
<td>65.75±13.01</td>
<td>44.71±13.35</td>
<td>0.000</td>
</tr>
<tr>
<td>First T4</td>
<td>5.57±1.15</td>
<td>4.86±1.57</td>
<td>0.085</td>
</tr>
<tr>
<td>First TSH</td>
<td>2.28±2.12</td>
<td>2.17±1.69</td>
<td>0.093</td>
</tr>
<tr>
<td>Second T3</td>
<td>96.36±25.48</td>
<td>42.57±11.94</td>
<td>0.000</td>
</tr>
<tr>
<td>Second T4</td>
<td>8.52±3.19</td>
<td>3.58±1.74</td>
<td>0.000</td>
</tr>
<tr>
<td>Second TSH</td>
<td>3.06±1.61</td>
<td>2.23±1.67</td>
<td>0.113</td>
</tr>
<tr>
<td>PRISM II at admission</td>
<td>7.17±1.78</td>
<td>8.64±1.73</td>
<td>0.011</td>
</tr>
<tr>
<td>PRISM II at 24hrs</td>
<td>7.50±1.75</td>
<td>10.79±1.72</td>
<td>0.000</td>
</tr>
<tr>
<td>Serum proteins</td>
<td>5.78±1.62</td>
<td>5.38±1.34</td>
<td>0.416</td>
</tr>
</tbody>
</table>

PRISMII: Pediatric Risk of Mortality Score II
Low T3 alone (type I ESS) was seen in 32 (64%) children, mortality in this group was 37.5% (12 out of 32) (odds ratio 4.1, p=0.056) while a combination of low T3 and T4 (type II ESS) was seen in 13 (26%) cases with mortality of 69.23% (9 out of 13) in this group and demonstrated almost 15 times more risk of mortality (odds ratio 14.9, p<0.000). Only 3 (6%) cases had isolated low TSH (type III ESS) & 2 (4%) had low T4 alone. There was no death in Type III ESS group.

**Table 4:** Comparison between the thyroid parameters in the first and second samples

<table>
<thead>
<tr>
<th>Parameter</th>
<th>survivors</th>
<th>P value</th>
<th>Non survivors</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First T3</td>
<td>65.75±13.01</td>
<td>0.000</td>
<td>44.71±13.35</td>
<td>0.000</td>
</tr>
<tr>
<td>Second T3</td>
<td>96.36±25.48</td>
<td></td>
<td>42.57±11.94</td>
<td></td>
</tr>
<tr>
<td>First T4</td>
<td>5.57±1.15</td>
<td>0.000</td>
<td>4.86±1.57</td>
<td>0.000</td>
</tr>
<tr>
<td>Second T4</td>
<td>8.52±3.19</td>
<td></td>
<td>3.58±1.74</td>
<td></td>
</tr>
<tr>
<td>First TSH</td>
<td>2.28±2.12</td>
<td>0.000</td>
<td>2.17±1.69</td>
<td>0.065</td>
</tr>
<tr>
<td>Second TSH</td>
<td>3.06±1.61</td>
<td></td>
<td>2.23±1.67</td>
<td></td>
</tr>
</tbody>
</table>

PRISMII score at 24 hrs. was significantly higher in patients who expired (10.79±1.72 Vs 7.50±1.75, p=0.000). PRISM score at 24 hours did not correlate with T3, T4 or TSH levels at admission, but had negative correlation with T4 levels of the second sample (Table 5). Age, sex, duration of PICU stay, ventilation and inotropic support did not show any correlation with patient outcome or thyroid hormone profile.

**Table 5:** Correlation of Thyroid Profile with PRISMII score & duration of PICU stay

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PRISMII at 24hrs</th>
<th>PICU stay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
</tr>
<tr>
<td>First T3</td>
<td>-0.037</td>
<td>0.953</td>
</tr>
<tr>
<td>First T4</td>
<td>-0.734</td>
<td>0.068</td>
</tr>
<tr>
<td>First TSH</td>
<td>-0.046</td>
<td>0.931</td>
</tr>
<tr>
<td>Second T3</td>
<td>-0.129</td>
<td>0.806</td>
</tr>
<tr>
<td>Second T4</td>
<td>-0.864</td>
<td>0.038</td>
</tr>
<tr>
<td>Second TSH</td>
<td>-0.090</td>
<td>0.864</td>
</tr>
</tbody>
</table>

r=correlation coefficient

**Table 6:** Multivariate analysis of factors associated with mortality by logistic regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald</th>
<th>S.E</th>
<th>df</th>
<th>P value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second T4</td>
<td>5.338</td>
<td>0.252</td>
<td>1</td>
<td>0.021</td>
<td>0.558</td>
</tr>
<tr>
<td>PRISMII at 24 hrs</td>
<td>4.192</td>
<td>0.290</td>
<td>1</td>
<td>0.041</td>
<td>1.811</td>
</tr>
<tr>
<td>constant</td>
<td>-0.3186</td>
<td>0.963</td>
<td>1</td>
<td>0.327</td>
<td>0.041</td>
</tr>
</tbody>
</table>

PRISMII: Pediatric Risk of Mortality Score II, SE-standard error, df: Degree of freedom

The area under Receiver Operating Characteristic (ROC) curve for the various thyroid hormone parameters, PRISMII score at admission and 24 hrs. with death as classification variable, along with the sensitivity and specificity is listed in table 7. The values for Area under curve (AUC) for second T4 (0.932) was comparable for PRISMII score (0.907) [Table 7] [Fig 1]. As AUC for second T4 for had highest sensitivity & specificity closely matching with respective value of PRISMII score, T4 as an

**Table 7:** ROC curve analysis of factors associated with mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>AUC</th>
<th>SE</th>
<th>P value</th>
<th>95%CI</th>
<th>sensitivity</th>
<th>specificity</th>
<th>criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>First T3</td>
<td>0.883</td>
<td>0.0724</td>
<td>0.001</td>
<td>0.761 to 0.956</td>
<td>85.7%</td>
<td>91.7%</td>
<td>≤ 51</td>
</tr>
<tr>
<td>First T4</td>
<td>0.705</td>
<td>0.0986</td>
<td>0.032</td>
<td>0.560 to 0.826</td>
<td>64.3%</td>
<td>88.9%</td>
<td>≤ 4.45</td>
</tr>
<tr>
<td>First TSH</td>
<td>0.526</td>
<td>0.0905</td>
<td>0.779</td>
<td>0.380 to 0.669</td>
<td>57.1%</td>
<td>63.9%</td>
<td>&gt;1.91</td>
</tr>
<tr>
<td>Second T3</td>
<td>0.867</td>
<td>0.0873</td>
<td>0.001</td>
<td>0.741 to 0.946</td>
<td>78.6%</td>
<td>94.4%</td>
<td>≤ 46</td>
</tr>
<tr>
<td>Second T4</td>
<td>0.932</td>
<td>0.0431</td>
<td>0.000</td>
<td>0.823 to 0.984</td>
<td>92.9%</td>
<td>83.3%</td>
<td>≤ 4.4</td>
</tr>
<tr>
<td>Second TSH</td>
<td>0.679</td>
<td>0.1000</td>
<td>0.742</td>
<td>0.532 to 0.804</td>
<td>42.9%</td>
<td>75.4%</td>
<td>&gt;0.91</td>
</tr>
<tr>
<td>PRISMII at 24hrs</td>
<td>0.735</td>
<td>0.0795</td>
<td>0.002</td>
<td>0.591 to 0.850</td>
<td>71.3%</td>
<td>66.7%</td>
<td>&gt; 7</td>
</tr>
<tr>
<td>PRISMII admission</td>
<td>0.735</td>
<td>0.0795</td>
<td>0.002</td>
<td>0.591 to 0.850</td>
<td>71.3%</td>
<td>66.7%</td>
<td>&gt; 7</td>
</tr>
</tbody>
</table>

ROC-receiver operating characteristic, AUC-area under curve, SE-standard error, CI-confidence interval
independent risk factor for mortality was studied by multivariate analysis using forward stepwise method of binary logistic regression. PRISM score at 24 hrs. And T4 levels in second sample were found to be significant predictors of mortality; (Table 6). Values of Omnibus model coefficient(33.58, p=0.000 at df=2) Nagelkerke R square (0.704) and Hosmer & Lemeshow test (chi-square 9.11 at df=8, sig.0.333) indicated strong predictive value & overall fitness of the regression model. Other thyroid hormone parameters were not found to predict mortality significantly.

Figure 1: Comparison of ROC curve

Discussion

Present study demonstrated lower mean T3 and T4 levels in the critically ill children. The commonest change seen was reduced serum T3 level (64% of cases). Low T4 levels were seen in 30% of cases, while low serum TSH level in only 6% of cases. Similar pattern was observed by Suvarna et al.(25) Many studies reported a higher incidence of low T3 levels in critically ill patients(14,22,24,25) but Bermudez et al.(7) in their study on adult patients and Anand et al(21) in their study on critically ill infants failed to demonstrate significant lower serum T4 levels. The combination of low T3 & low T4 was associated with almost 15 times risk of mortality in the present study. Similar observation was demonstrated in Zargar et al & Suvarna et al. (14,25) However, further multi-centric studies with larger sample size may throw more light on this aspect. The serum T3 levels at admission has been considered as baseline discriminator between survivors and non-survivors, which can prognosticate the clinical status of critically ill patients. (15) In the present study the mean serum T3 levels at admission was lower in nonsurvivors. Though Zucker et al & Suvarna et al (24,25) had similar observation, Anand et al & Uzel et al failed to demonstrate the same in infants. (21,22) It was also noted that serum T3 level improved in patients discharged from the PICU and did not improve in those who expired. This implies that serum T3 level closely follows the clinical status of the patients and persistently low serum T3 level may reflect poor outcome.

Although serum T4 level at admission did not discriminate between survivors and non-survivors, it decreased in patients prior to death reflecting the seriousness of the disease. It is postulated that when an illness is severe but less than life threatening, T4 levels are maintained due to increased secretion rate to match the accelerated T4 disposal. However, in very severe illness, the T4 level fails to keep up pace with the accelerated turnover and decreases. (17) We could not demonstrate any cut-off value for T4 to correlate with patient’s outcome. Zucker et al too failed to show this relationship. (24) Serum T4 levels at discharge from PICU or just prior to death and PRISMII score at 24 hours of admission to the PICU were found to be significant predictor of mortality with highest sensitivity & specificity. Similar finding was observed by Suvarna et al. (25) Type II ESS is reported with more severe illness and indicates a very poor prognosis. (15,16) In 26% cases it demonstrated almost 15 times increased risk of mortality. Suvarna et al(25) reported 30 times risk of mortality in such patients. These patients have inappropriately normal or low TSH inspite of low T3 and T4 and are considered to be clinically euthyroid. Glutathione and selenium are postulated to be co-factors for both enzymes: deiodinase (needed for T4 to T3 conversion) and glutathione peroxidase (defense strategy of the body to combat oxidative stress). Stress (critical illness) decreases the activity of deiodinase, thus sparing the co-factors for glutathione peroxidase activity (to combat stress). (1) Also low T3 decreases catabolism, thus decreasing mitochondrial free radical generation, and allowing.
energy to be expended for the defense processes. Thus ESS maybe considered as an adaptive process. \(7,8,24,29\)

We observed that in patients who survived, TSH levels increased significantly while it failed to improve in patients who expired. Similar observation was found by Suvarna et al.\(^{(25)}\) The transient increase in serum TSH during recovery from NTI suggests that TSH is suppressed in an illness. Pituitary TSH suppression may be related to the stress of an illness, and the resulting elevated cortisol and catecholamine levels and associated caloric deprivation.\(^{(4)}\)

Almost in all critical illness, there is a decrease in plasma concentration of proteins that bind thyroid hormone [albumin, thyroid binding pre albumin (TBPA) & thyroid binding globulin (TBG)]. As binding proteins decrease, total levels of T4 and to lesser degree of T3 decline.\(^{(1,3,5)}\) The free thyroxine index (FT4I) is an estimate of the amount of circulating free thyroxine which doesn’t get affected by levels of TBG or TBPA and can be used as sensitive indicator to diagnose ESS.\(^{(2,3,6)}\) We have not estimated FT4I ,TBPA or TBG in our study due to high cost involved, butas there was no significant difference in total serum protein levels of either cases and controls or between survived and expired, we can presume that changes in thyroid profile were reflecting critical phase of illness and not hypoproteinemia.

‘Is there any role of T3, T4 supplementation in critically ill patients in improving survival?’ The improvement of T3 levels in patients who survived and non-improvement in those who expired raises this important question. Most studies perceive low T3 without increased TSH as an adaptively protective response (metabolically protective) not warranting administration of T3 or T4 in NTI.\(^{(20,23,24,28)}\) Moreover decreased deiodinase activity in NTI may hamper peripheral conversion of T4 to T3.\(^{(28)}\) T4 therapy may in fact suppress thyroid function normalization during recovery by inhibiting TSH secretion.\(^{(28)}\) Administration of T3 in severe burn did not affect survival.\(^{(17)}\) However T3 infusion in patients with septic shock showed elevation of systolic blood pressure, reduced vasopressor requirement and improvement in renal function.\(^{(28)}\) Recent reports showed cardiac surgery patients with ESS tolerated T3 replacement therapy well and showed hemodynamic improvements in form of increase in cardiac index, reduced need of inotropic agents and mechanical device and decreased incidence of myocardial ischemia\(^{(27)}\) The therapeutic role of thyroid hormones in the management of NTI is still not very clear and awaits further well controlled randomized trials.

**Conclusions**

In critically ill children, mean T3, T4 levels are low, while TSH values may not change. At any given point T3 level reflects the patient’s clinical status and persistent low serum T3 levels with non-improvement would predict bad prognosis. Low T3 & T4 values at admission are associated with very high risk of mortality. T4 levels independently can predict mortality with high sensitivity & high specificity like PRISMIIscore at 24 hours. Children with combined low T3 and T4 levels need more close observation and aggressive therapeutic intervention.

**Limitations:**

Confounding bias related to effect of inotropic agents (dopamine, dobutamine) or exogenous steroid used in critical illness on thyroid hormones could not be eliminated. Estimation of rT3 and free T4 was not done in this study which would have given us an additional thyroid indicator of prognostic value. The thyroid hormone profile was done only twice i.e. at admission and at recovery or death in this study. More frequent estimation to assess the trend of changes in the thyroid hormone profile in the sick children can give us better information and help us to identify seriously ill patients much earlier.

**Conflict of Interest:** None

**Role of Funding Source:** None

**Acknowledgement:** Dr Nathaneal Sase, Director, Wanless Hospital, Miraj

**References:**


Full reference details:

Knowledge of Pediatric Sepsis among Trainees
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Abstract

Introduction: Sepsis is one of the leading causes of death in children in the developing world. Several studies have shown that the knowledge and implementation of current American College of Critical Care Medicine-Pediatric Advance Life Support (ACCM-PALS) guidelines on recognition and initial management of sepsis in children leads to significant improvement in outcomes. There is little known about the knowledge of current guidelines on recognition and initial management of pediatric sepsis among healthcare providers in Pakistan. Objectives: To assess the retention of knowledge among trainees of pediatrics after a 30 minutes didactic session on recognition and initial management of pediatric severe sepsis and septic shock.

Materials and Methods: We conducted 1-hr educational session, which consisted of 30-min lecture, 20-min for assessment through 20 single best multiple choice questions and 10-min of debriefing for pediatric residents at seven academic institutions in Pakistan. The key components of this exercise were recognition, initial five-minute management, fluid resuscitation, inotrope, antibiotics and steroid.

Results: Of the 222 residents who participated, 42% (91/222) correctly answered >60% of questions with a median score of 10/20 and IQR of 18. Recognition was done correctly by 41.2% (93/222); 54% (121/222) knew about fluid resuscitation, and 27.7% (62/222) about inotropic support. Eighty % (177/222) and 70.8% (158/222) had knowledge of steroid and antibiotic use respectively.

Conclusion: The knowledge of the recognition and initial management of sepsis in children among pediatric residents is suboptimal, even after a 30 minutes didactic session on the subject.

Key Words:
Sepsis, Septic shock, Knowledge, Residents, Mortality

Introduction:
Sepsis is one of the leading causes of childhood deathscially. Its incidence and mortality is particularly high in developing world, where 60 - 80% of under-five year mortality is attributed to sepsis-related illness. Recent advances over the last three decades reveal that sepsis is a dynamic process of continuum when shock, which is not reversed in early stages, progresses to multi-organ dysfunction syndrome, andwhich results in high mortality rate. Previous published reports show that the mortality in children from septic shock in pediatric intensive care units of developing countries is about 50%-7. The American College of Critical Care Medicine-Pediatric Advanced Life Support (ACCM-PALS) published time-sensitive, goal-directed and step-wise clinical practice guidelines for recognition and initial management of severe sepsis and septic shock in children in 2002 and revised in 20078,9. Use of these recommendations resulted in significant reduction in mortality in children with such conditions from various countries10,11. These guidelines were published in Journal of Critical Care Medicine which is not freely available12. Khilnani et al published guidelines for resource-limited countries13.
Therefore, many pediatricians are not aware of these guidelines in developing countries, which results in delayed recognition and treatment of sepsis and are associated with high mortality rates.
In Pakistan, little is known about knowledge
of current guidelines on recognition and initial management of severe sepsis and septic shock in children among healthcare providers. Post graduate trainees (residents) are generally the front-line physicians in the early care of sick children in Pakistan. Several studies have shown positive impact of educational intervention in recognition and treatment of sepsis both in adult and pediatric clinical practices globally\textsuperscript{10, 11, 13-15}. In this study, we aim to determine the effectiveness of a brief educational intervention aimed towards pediatrics resident physicians in Pakistan in improving their knowledge about the recognition and initial management of pediatric severe sepsis and septic shock.

**Materials and Methods:**
Pediatric residents from seven teaching institutions participated in this program. The educational sessions were conducted at seven teaching institutions where pediatric residency program is recognized by the College of Physicians and Surgeons of Pakistan. All pediatrics residents of these institutions were eligible for participation. Each educational session was of one hour, and consisted of three parts:

a. A 30-minutes didactic power point presentation on the recognition and management of pediatric sepsis based on ACCM-PALS 2007 guidelines and Pediatric Sepsis guidelines for resource-limited country delivered by a trained pediatric intensive care physician\textsuperscript{8,13}.

b. 20-minutes for knowledge assessment of participants through a multiple choice questionnaire. The assessment included five questions covering the domain of sepsis recognition, three questions covering vascular access and respiratory management, six questions covering fluid therapy, four questions covering inotropes and vaspressors and one question each covering antibiotics and corticosteroid use.

c. 10-min for debriefing.

The half hour talk was delivered emphasizing the recognition and initial management of severe sepsis and septic shock in children based on ACCM-PALS guidelines. Following the talk, all participants were asked to answer 20 MCQ questions in 20 minutes. Each correct answer was given one score and the overall score was expressed from 0 to maximum of 20. Data was analyzed on SPSS V 19, along with the median, mean and IQR score, frequency and percentages of total correct answers as well as correct answers in each domain is reported.

**Results:**
A total of 222 pediatric residents participated in this program. Out of 7 teaching institutions, two belonged to private sector while the rest were in public sector. Median number of participants in these sessions was 25 (IQR 46). The median test score on the knowledge of pediatric sepsis was 10 out of 20, with IQR of 18. Half of the residents answered fewer than half of the questions correctly and 42% (91/222) were able to correctly respond to >60% of questionnaires. The performance of residents on specific test items is shown in figure 1. The components of systemic inflammatory response syndrome (SIRS) were correctly recognized by 47.3% (105/222). The definition of severe sepsis and septic shock was identified correctly by 46% (102/222) and 32% (71/222) respectively. The overall response rate of recognition of sepsis was 41.8% (93/222). The correct response about initial management of sepsis in first five-minutes was 48% (106/222). Fifty-four percent (121/222) residents responded correctly for the fluid-resuscitation management. Twenty eight percent (62/222) correctly answered the questions regarding the use of inotropes. Question about steroids use was correctly answered by 80% of the responders (177/222) while 70.8% (158/222) of the participants correctly answered regarding the use of antibiotics.

**Discussion:**
Our study demonstrates that pediatric residents have suboptimal knowledge about diagnosis of sepsis and its immediate management, even after a thirty minutes didactic session on the subject. Published literature has reported few studies on the knowledge about sepsis among physicians and nurses\textsuperscript{16-21}. Most of the
studies have similar results. Zilgam et al showed that 48% and 67% of young doctors correctly identified severe sepsis and septic shock in their reports\textsuperscript{16}. We found that 46% and 32% of our pediatric trainees correctly identified severe sepsis and septic shock respectively. Assuncao et al also found inadequate physicians’ knowledge of severe sepsis (56.7%) \textsuperscript{18}. Fernandez et al showed that only 31.4 % were able to identify SIRS in study of physician’s knowledge in Surviving Sepsis Campaign\textsuperscript{22}. This is close to our study, in which 47.3% participants correctly identified SIRS. We found a particular deficiency in knowledge of correct use of inotropes in pediatric septic shock (27.7%) in our participants.

This study highlights very low level of knowledge of pediatric sepsis recognition and management from a developing country like Pakistan where sepsis-related death rate is still very high. Even though our 30 minute didactic session did not lead to optimal knowledge in the residents, Larsen \textit{et al} and Cruz \textit{et al} have shown that implementation of an educational program based on ACCM-PALS guidelines improves the survival of children with severe sepsis and septic shock. Perhaps a longer and more intense training workshop than the current 30 minute didactic session is needed to improve the knowledge related to pediatric sepsis in our trainee physicians.

Our study has few particular strengths and limitations. Limitations include that we did not perform a pre-educational intervention assessment of knowledge, which would have allowed us to determine the impact of our educational intervention more robustly. Secondly, the number of questions to check a particular domain was small, which could lead to lower precision of our assessment of knowledge of our participants. The strengths of the study include that this is the first study from Pakistan which highlights lack of critical, life-saving knowledge regarding pediatric sepsis management in the trainee physicians of Pakistan. We also show that just a brief 30 minutes didactic session is not enough to raise the awareness of the ACCM-PALS guidelines, and more robust workshops and training sessions are required, which should be conducted on regular basis.

**Conclusion:**

The knowledge of the recognition and initial management of sepsis in children among pediatric residents is suboptimal in Pakistan. Residency programs should emphasize evidence-based learning objectives to improve the recognition and initial management of pediatric sepsis to decrease the mortality rate in children from sepsis.

**References:**

2006; 129(2); 225-32.
Development and Implementation of Pediatric Critical Care Focused Simulation Workshop and Program in India

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Abstract:
Simulation-based learning has become a part of residency and fellowship training in many training programs in the United States. But, it has not been incorporated into the pediatric critical care medicine training in the developing countries like India. Simulation-based training allows rapid and repetitive learning of skills necessary to provide a high quality and safe care to critically ill children. There is a need to explore simulation as a tool to train pediatric and pediatric critical care medicine practitioners in the developing world. This is particularly pertinent to Indian subcontinent in which pediatric critical care medicine has grown by leaps and bounds over last decade. We hereby present one of the earliest reports of development and implementation of pediatric critical care focused simulation workshop and program in India.

Key Words: Simulation, Critical Care, Child, Training, India

This abstract was presented as a poster at American Academy of Pediatrics, National Conference & Exhibition, San Diego, California, USA, 2014.

Introduction:
Simulation training incorporates didactics, case-based learning and hands-on skill training.₁ Simulation based training programs geared towards pediatric critical care medicine have been successfully developed and implemented in western world². But, simulation based training of pediatric healthcare providers is underutilized in developing countries like India. Also, simulation-based, Pediatric Critical Care Medicine (PCCM) courses must focus on basic and advanced PCCM training in keeping with some of the known challenges of delivery of critical care unique to the developing world. The challenges involved with care of critically ill children in the developing world are limitation of resources, fulminant infections unique to the developing world, transportation of critically ill children to higher level of care and teamwork and communication. We sought to evaluate development and implementation of one of the earliest PCCM focused simulation workshop and program in India. We hereby describe one of the first PCCM simulation workshops which was successful in providing training in basic and advanced PCCM including fulminant infectious cases pertinent to Indian subcontinent.

Objectives:
To develop and implement a PCCM focused simulation workshop and program in India.

Methods:
A group of pediatricians and pediatric intensivists
from different institutions of India collaborated with a simulation expert and pediatric intensivist of USA to develop and implement a PCCM simulation workshop and program in India.

Need Assessment: The group first performed an informal need assessment. Since pediatric critical care medicine is often practiced by general pediatricians not formally trained in pediatric critical care medicine, a need assessment was crucial to determine overall structure of the workshop. Also, it was important to assess the needs to characterize the cases, the objectives of the cases, design and on-site resources.

Planning: Since one of the major regional suppliers of the simulation equipment was Laerdal Medical India Private Limited, the US-based faculty reached out to them and discussed about the workshop program, their willingness to participate and provide simulation resources (mannequins, simulation technicians and simulation software to run the scenario). The subsequent step was to design the workshop program and prepare the cases with the objectives geared towards the participant needs in keeping with the common critical care scenarios and the key challenges of the practice of critical care medicine in India. While designing the workshop, the organizers discussed about 1) The balance of didactic sessions, hands-on sessions and cases scenarios, 2) The objectives of Pediatric Advanced Life Support (PALS) scenarios, 3) The time allotment for each session, each case and time allotment for debriefing of each case. Since most the participants were anticipated to be PALS trained, the objectives of the PALS scenarios for the workshop were directed towards high-quality CPR, teamwork and communication. During the workshop planning phase, the organizers, faculty and members of Laerdal Medical India Pvt. Ltd. communicated on a frequent basis via email, teleconference and smart phone messenger (WhatsApp Inc, Mountain View, California, USA). The workshop faculty collected the latest guidelines on common critical care scenarios like difficult airway management guidelines, traumatic brain injury guidelines and circulated amongst the participants. The US-based simulation expert provided just-in-time “training of the trainer” course to the workshop faculty with dry runs of the case scenarios. The team utilized simulation resources and hospital-based resources to run the workshop. The team also designed skill stations for hands-on skill training in PCCM. The team evaluated the workshop and program through a just-in-time debriefing and post-session survey of the workshop participants.

Results:
The collaboration of pediatricians and pediatric intensivists from different parts of India with simulation expert from USA led to the development and implementation of a successful 2-day simulation-based PCCM workshop. A total of 12 Indian faculties and 1 US faculty participated in the workshop as simulation facilitators. The years of experience of pediatric practice beyond the basic pediatric training among the faculty ranged from 5-20 years. The entire faculty had in-depth knowledge and experience of PCCM and 10 out of 12 Indian faculties had PCCM training at centers of excellence abroad.

Figure 1. Faculty, nurses and hospital administrator at the inauguration of PCCM simulation workshop at Fortis Hospital, Mumbai, India. From left to right (in front) – Preeti (PICU charge nurse, Fortis Hospital, Mumbai), Vishal Baldua, MD (Pediatric Intensivist, Fortis Hospital, Mumbai), Jesal Sheth, MD (Pediatric Intensivist, Fortis Hospital, Mumbai), Utpal Bhalala, MD, FAAP (Assistant Professor and Simulation Faculty, Johns Hopkins Hospital, Baltimore, Maryland, USA), ArunaBhoy, MD (Director, Fortis Hospital, Mumbai), Praveen Khilnani, MD, FAAP (ChiefPediatric Intensivist, BLK Hospital, Delhi), Mahesh Mohite, MD (Pediatric Intensivist, Sai Children’s Hospital, New Panvel), Chandrahas Deshmukh, MD (Head of Pediatrics, KEM Hospital, Mumbai), Preetha Joshi, MD (Pediatric Intensivist, KDA Hospital, Mumbai); From left to right (in the back) – Maninder Dhaliwal, MD (Medanta Hospital, Gurgaon), Sameer Sadawarte, MD (Pediatric Intensivist, Fortis Hospital, Mumbai); Not in picture – Rakshay Shetty, MD (Pediatric Intensivist, USA).
Rainbow Children’s Hospital, Vijaywada), Swati Garekar, MD (Pediatric Cardiologist, Fortis Hospital, Mumbai), Vinay Joshi, MD (Pediatric Intensivist, KDA Hospital, Mumbai), Rahul Pandit, MD (Senior Intensivist, Fortis Hospital, Mumbai).

Based on the needs assessment, the organizers were able to design the workshop program, the cases, the objectives of the cases in keeping with the day-to-day critical care scenarios and challenges unique to the practice of critical care medicine in India. The didactics were restricted to 3 lectures - Simulation in healthcare, Cardiac Arrest and quality of CPR and Role of simulation in PCCM. A significant proportion of the workshop time was allotted to the case scenarios, bedside debriefing and hands-on training.

The first case scenario enacted by the faculty in front of the participants and displayed on the screen through a live video was aimed at highlighting the importance of the teamwork and communication in management of critically ill child. The remaining case scenarios for the participants were spread evenly over 2 days and intermixed with hands-on sessions to avoid monotony. There were 16 case scenarios run over 2 days and they comprised of rapid sequence intubation, difficult airway cases, septic shock, dengue hemorrhagic shock, Dengue with abdominal compartment syndrome, acute meningitis, acute myocarditis, ARDS, status epilepticus, cardiac triage, transport of critically ill child, polytrauma, cardiac tamponade, Pulseless Electrical Activity (PEA), Supraventricular Tachycardia (SVT) and Ventricular Fibrillation (VF).

Figure 2. Utpal Bhalala, MD, FAAP (USA faculty) going over the hands-on training on the use of glidescope in difficult airway cases.

Figure 3. Faculty showing effective bag-mask ventilation during resuscitation case scenario.

There were 4 simulation technicians who followed the instructions for running the case scenarios using structured case files which were prepared, revised and finalized by the faculties before the workshop. For running the cases, the workshop used 1 sim junior, 1 sim man 3G, 1 resuscitation baby with CPR feedback, 1 adult resuscitation simulator with CPR feedback and rhythm generating system; for hands-on training, the workshop used airway trainer, Ultrasound machine and intravenous line tissue blocks. The critical care ultrasound experts first went over the basic knobology. The hands-on training on use of critical care ultrasound for 4-view cardiac echocardiography, evaluation of inferior vena cava, evaluation of vessels for arterial and venous line placement and lung assessment was provided on a volunteer subject. Additional hands-on training on use of critical care ultrasound for peripheral intravenous line placement was provided on IV task trainer.

Of the 34 workshop participants, 11 were pediatric residents/pediatricians, 2 anesthesia trainees, 2 emergency medicine trainees and 19 nurses with interest in PCCM. The workshop cases focused on the learning objectives of teamwork and communication skills. The pediatric advanced life support cases focused on delivering high-quality resuscitation training. The program evaluation and debriefing at the end of the workshop revealed very high participant satisfaction with comments like – “Dedicated and knowledgeable faculty, Case based practical approach, Interactive format, Every Query answered, Excellent quality of the dummies, Hands on experience”.
Discussion:
Simulation-based training is rapidly becoming a standard of medical training in the western part of the globe. In 2011, a survey conducted by American Academy of Medical Colleges (AAMC) reported that all 90 medical schools and 64 teaching hospitals that responded to the survey indicated that they use simulation during medical school. There are well established institutional, regional and national simulation programs and training courses in the US. In the developing world, the simulation in health care is in its developing phase. Over last 5-7 years, a handful of centers have begun simulation-based medical training in India - a few notable names being - TACT (The Academy for Clinical Training), The Apollo Learning and Medical Simulation Center and SRM/STRATUS Centre for Medical Simulation. A group of physicians have been successful in introducing simulation-based training in emergency medicine in India. Also, inception of Pediatric Simulation Society of India (pediSTARS India) has marked the introduction of simulation training in pediatric medicine.

Pediatric critical care training programs in north-east region of the US have successfully established a rigorous, two day, multi-institutional, high-fidelity simulation-based “boot camp” for junior and senior level pediatric intensive care fellows. Unfortunately, the applications of simulation training focused towards common critical care scenarios and critical care challenges of India.

Conclusions:
A successful PCCM focused simulation training workshop and program were developed and implemented through collaboration of faculty from different parts of India under guidance of simulation expert from US. Simulation has a huge potential for improving PCCM training in developing countries like India.

Acknowledgements:
We are thankful to the administrators of Fortis Hospital, Mulund, Mumbai for providing us the necessary support for the workshop and Laerdal Medical India Pvt. Ltd. for providing simulation resources for the workshop at no cost.

References:


Special Neurocritical Care Review Article

Pediatric Intracranial Aneurysms and Subarachnoid Hemorrhage: Review

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Introduction
Intracranial aneurysms (ICA) are rare in the pediatric population (age< 18 years). German pathologist Eppinger first reported a case of childhood aneurysm in a 15-year-old boy who collapsed during strenuous gymnastics. His postmortem examination revealed a ruptured saccular aneurysm of the right anterior cerebral artery. After several years Edward Bull described the first ante mortem case in a 17-year-old girl who presented with severe headache and her diagnosis of a ruptured posterior communicating artery aneurysm was subsequently confirmed on autopsy. In the current era, modern neuro-imaging techniques and availability of angiography has greatly enhanced the ability of physicians to diagnose cerebral aneurysms. However, even today timely diagnosis of a pediatric aneurysm and aneurysmal subarachnoid hemorrhage continues to be challenging.

Incidence
Intracranial aneurysms are extremely uncommon in the pediatric population with a reported prevalence ranging from 0.5% to 4.6%. There is an overall male predominance (male: female ratio 1.75:1).

Location of Intracranial Aneurysms
More than 80% of the pediatric ICA are located in the anterior circulation while about 15% are located in the posterior circulation. The most common site in the anterior circulation is the internal carotid artery bifurcation (26%), followed by the anterior communicating artery complex (19%) and middle cerebral artery bifurcation (17%). Multiple aneurysms in children are uncommon and seen in less than 5% of all pediatric cases.

Etiology/Pathophysiology
The ICA can be congenital or acquired. The congenital (also known as berry or sacular) aneurysms are found in about 30% of cases. The exact pathophysiology of congenital ICA is debatable. It is likely due to a combination of congenital and degenerative factors. The pathological specimens show an absence of internal elastic lamina and tunica media at the site of aneurysm formation. The consensus view is that the transition zone from normal vessel into the aneurysmal sac is characterized by a congenital defect of the internal elastic lamina and tunica media. This site undergoes additional degenerative changes throughout life and turbulent blood flow can cause a saccular out pouching at the area of defect. This combined effect of underlying congenital defect on the vessel wall along with additional degenerative factors is responsible for the rarity of aneurysms in children and their increasing incidence in adulthood.

Acquired causes of ICA in children include trauma, infection and dissection. According to Krings et al. dissecting aneurysms are the most often encountered pediatric aneurysm and may account for up to 50% of all aneurysms in this age group. Traumatic aneurysms account for 14 to 39% of all pediatric aneurysms in different case series, and may occur after both penetrating and nonpenetrating trauma. Infectious aneurysms account for up to 2 to 10% of all pediatric aneurysms. They are most often of bacterial origin and are rarely caused by fungal infections. The most common organism is staphylococcal aureus, followed by streptococcus viridians and other gram-negative organisms.

Other conditions associated with increased risk of ICA are polycystic kidney disease, coarctation of aorta, sickle cell anemia, Ehlers-Danlos syndrome type 4, collagenopathy, and pseudoxanthoma elasticum.

Clinical Presentation
The most common presentation of ICA in children is an acute aneurysmal rupture with subarachnoid
hemorrhage (SAH). The signs and symptoms of SAH in neonates or infants are nonspecific and include irritability, drowsiness, poor oral intake, or vomiting. Symptoms in older children are similar to those in adults, such as acute headache, nausea, vomiting, photophobia, neck stiffness, loss of consciousness and neurological deficits. Seizures are common in both infants and older children.

An unruptured aneurysm may be asymptomatic and present as an incidental finding on neuroimaging or may cause symptoms due to mass effect such as partial complex seizures, cranial nerve palsies, or focal neurological deficit. These symptoms are more frequently seen in children than in adults.

Aneurysms presenting with SAH tend to re-bleed. If left untreated, 2 to 4 percent bleed again within the first 24 hours after the initial episode, and approximately 15 to 20 percent bleed a second time within the first two weeks. The risk of rupture of an ICA that is found incidentally is much less certain.

**Diagnosis**

The timely diagnosis of an ICA and SAH depends on high index of suspicion. If SAH is suspected, urgent computed tomography (CT) scan of the head without the administration of contrast material should be performed to confirm the clinical impression. Patients with a negative CT but a high index of suspicion should be considered for lumbar puncture. In those with SAH, the red blood cell (RBC) count is usually >100,000 cells/mm³ in the third tube of the cerebrospinal fluid (CSF) collection, and xanthochromia is present. The more sensitive and specific test to diagnose SAH is the measurement of excess bilirubin content in the CSF sample.

The next step after making a definitive diagnosis of a SAH should be to determine the etiology and to see whether an aneurysm is the cause of SAH in this patient. To do so, there are different imaging modalities currently used in clinical practice. The three imaging techniques to rule out an intracranial aneurysm and to delineate its size and morphological features are CT angiography (CTA), magnetic resonance angiography (MRA), and conventional catheter angiography.

The sensitivity and specificity of CTA to diagnose ICA varies from 0.77 to 0.97 and 0.87 to 1.00 respectively. However, the sensitivity for aneurysms less than 3 mm is low and is estimated to be 0.40 to 0.91. Its drawback is that it involves the use of intravenous contrast medium and thus it is contraindicated in patients with renal failure or in those who are allergic to iodinated contrast dye. (Fig 1-shows left terminal internal carotid artery aneurysm)

![Figure 1: CTA showing lobulated aneurysm arising from left terminal Internal carotid artery.](image-url)

Magnetic resonance angiography (MRA) produces images of the intracranial vasculature by detecting a specific range of blood flow velocities allowing the isolation of intracranial arteries. It is highly sensitive (0.69 to 0.99) and specific (1.00) in detecting aneurysms >3 mm in diameter. Its advantage is that it does not require intravenous contrast agent, however, it takes considerably longer time than CTA and thus is more difficult to use in critically ill patients.

Conventional cerebral angiography is the “gold standard” for imaging of ICA. It provides exceptional resolution, can detect small aneurysms and demonstrate dynamic flow of cerebral vasculature and of the aneurysm itself. It is a safe diagnostic modality in infants and children with low risks particularly in the hands of an experienced operator.

**SAH Grading scales**

Numerous SAH grading scales have been proposed in the past, with the aim to stratify the patients into various risk categories based on their presenting signs and symptoms. The most commonly used are Hunt and Hess scale and Fisher scale. Hunt and Hess scale (Table 1) is used to describe the neurological
condition on admission and is considered a good predictor of ultimate outcome\(^7\). The Fisher grade (Table 2) uses a four-point scale to describe the amount of blood on non-contrast-enhanced CT of the head and has been shown to correlate with the development of vasospasm\(^8\).

### Table 1: Hunt and Hess grading system for patients with SAH

<table>
<thead>
<tr>
<th>Grade</th>
<th>Neurological status</th>
<th>Percent risk of death as reported originally</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asymptomatic or mild headache and slight nuchal rigidity</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>Severe headache, stiff neck, no neurological deficit except cranial nerve palsy</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>Drowsy or confused, mild focal neurological deficit</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>Stuporous, moderate or severe hemiparesis</td>
<td>71</td>
</tr>
<tr>
<td>5</td>
<td>Coma, decerebrate posturing</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table 2: Fisher grade of cerebral vasospasm risk in SAH

<table>
<thead>
<tr>
<th>Group</th>
<th>Subarachnoid blood distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Thin distribution with vertical layers &lt; 1mm</td>
</tr>
<tr>
<td>3</td>
<td>Thick localized clots or vertical layers &gt; 1mm</td>
</tr>
<tr>
<td>4</td>
<td>Diffuse or no SAH, but with intracerebral or intraventricular hemorrhage</td>
</tr>
</tbody>
</table>

### Management

A multidisciplinary team including neurosurgeon, interventional neuroradiologist, neurologist and pediatric intensivist best manage pediatric ICA. The initial treatment of a child with ruptured ICA focuses on maintenance of adequate ventilation, hemodynamic stabilization, maintenance of cerebral perfusion, preventing intracranial hypertension and minimizing the risk of re-bleeding. The unconscious patients or those with a falling Glasgow Coma Scale (GCS) should be intubated and ventilated. Prior to securing the aneurysm, blood pressure should be adequately maintained, as hypertension increases the risk of re-bleeding while excessive fall in blood pressure increases risk of cerebral ischemia. Some of the patients may develop hydrocephalus as a result of aneurysmal SAH and may need external ventricular drain placed for initial stabilization before aneurysm obliteration. The ruptured ICA should be secured as soon as possible after initial stabilization as the greatest risk of re-bleeding occurs within the first 24 hours.

### Securing the aneurysm:

There are three options for treating ICA: observation, clipping and endovascular coiling. The management of unruptured aneurysms that are discovered incidentally depends on the patient’s clinical condition, and size and location of the aneurysm. Depending upon their size and location, they can be either observed with routine periodic follow-up imaging or treated electively. All ruptured aneurysms should be secured as early as possible by either clipping or coiling.

Clipping of aneurysms requires craniotomy and placement of MRI compatible permanent clips across the neck of the aneurysm, excluding it from the circulation (Fig 2 A). During the last decade endovascular procedures have been increasingly used to treat ICA. An interventional neuroradiologist usually performs endovascular coiling. With the use of angiographic techniques, a microcatheter is advanced into the aneurysm, and detachable coils of various sizes are deployed to decrease the amount of blood or to stop blood from filling the aneurysm (Fig 2 B).
Clipping or Coiling

Both the techniques have their own advantages and disadvantages. Though successful clipping is generally associated with definitive protection against re-rupture, it has risks associated with craniotomy. Endovascular coiling does not need craniotomy but aneurysms treated with coiling may reoccur and there is a risk of rupture of the aneurysm during catheter advancement into the aneurysm or during coil placement.

The International Subarachnoid Aneurysm Trial (ISAT) was a large, multicenter prospective study in adults comparing endovascular and surgical techniques for aneurysms presenting with SAH. Though the trial was criticized for many reasons, it showed an improvement in early survival in selected patients receiving endovascular therapy\(^9\). There are very few pediatric studies comparing both modalities of treatment. In the study by Agid et al, 77% of the patients in the endovascular group had good recovery as compared to 45% of the patients in surgical group\(^10\). In their study Sanai et al, had shown that patients treated with clipping had more complete obliteration of their aneurysm and significantly lower recurrence risk as compared to patients in coiling group\(^11\). Stiefel et al, found no difference in outcome of patients treated with either clipping or coiling\(^12\).

On the basis of literature, it remains controversial whether a given ICA should be treated surgically or managed endovascularly. However, recent American Heart Association (AHA) guidelines for the management of SAH in adults have recommended that in patients with ruptured aneurysms who are technically amenable to endovascular coiling and surgical clipping, the former should be considered\(^13\). However, there are no pediatric guidelines and the decision to do surgical clipping or endovascular coiling should be taken after discussion with multidisciplinary team.

Medical management of aneurysmal subarachnoid hemorrhage

The medical management of pediatric patients with aneurysmal SAH is as important as the surgical or endovascular intervention in ensuring a favorable outcome. Following securing of the aneurysm, management of SAH involves close neuromonitoring, prevention or treatment of vasospasm and other complications. Most of these patients need admission to the intensive care unit.

Vasospasm and Delayed Cerebral Ischemia

Vasospasm causing delayed cerebral ischemia (DCI) is defined as any neurological deterioration, including focal neurological deficits and altered consciousness, of which no other cause can be identified by radiographic, laboratory or electrophysiological investigations. It is very common in adult population with an incidence of about 30% but incidence of both radiographic and symptomatic vasospasm in pediatric population is much less. It usually happens between days four and ten after initial hemorrhage and persists for several days.

Diagnosis and monitoring for Vasospasm

All patients with aneurysmal SAH should be closely monitored clinically. Reduction in the level of consciousness with or without focal neurological deficit should raise suspicion of vasospasm. Digital subtraction angiography remains the diagnostic gold standard however CTA and MRA can be helpful at initial suspension (Fig 3). Transcranial Doppler Ultrasonography measures blood flow in basal cerebral arteries and is a useful noninvasive method to detect vasospasm.
Treatment of Vasospasm

Several pharmaceutical agents like magnesium, anti-fibrinolytics, anti-platelets, and statins have been tried for the prevention and treatment of vasospasm but none has any proven benefits except Nimodipine. Nimodipine is the only agent that has been shown to reduce the incidence of vasospasm and DCI and improve neurological outcome\(^1\). The AHAGuidelines recommend that oral nimodipine should be administered to all the patients with aneurysmal SAH immediately after diagnosis. The recommended dose in adults is 60 mg every four hours and is usually continued for 21 days. Although intravenous nimodipine is sometimes used, this route of administration remains unproven.

Another therapy that has been widely used to prevent and treat vasospasm is Triple H (hypertension, hypervolemia and hemodilution) therapy. However, this combination therapy has never been clinically proved to be useful and hypervolemia can be potentially harmful to critically ill patients. As per the recent guidelines, euvolemia rather than hypervolemia is recommended for both prophylaxis and treatment of vasospasm, and that hemodilution is not recommended\(^1\). Hypertensive therapy (induction of hypertension with vasopressors) is only recommended in patients with symptomatic vasospasm. Patients with symptomatic cerebral vasospasm, particularly those who have no response to medical treatment should undergo cerebral angioplasty of the narrowed vessels and/or selective intra-arterial vasodilator therapy\(^1\).

Management of other complications

Seizures

Seizures occur commonly in patients after aneurysmal SAH. The routine long term use of anticonvulsants is not recommended but the use of prophylactic anticonvulsants may be considered in the immediate post hemorrhagic period\(^1\). Levetiracetam is preferred and phenytoin should be avoided because of associated cognitive effects and poor outcome\(^1\).

Fever

Fever occurs in up to two-third of patients with aneurysmal SAH. Although the cause of fever can be related to the hypothalamic effects of subarachnoid blood, an infective cause should always be ruled out. Fever should be aggressively controlled with a target to achieve normothermia by the use of standard or advanced temperature modulating systems.

Dysnatraemia

Both hypernatremia and hyponatremia can occur in patients after aneurysmal SAH. Hyponatremia can develop from different mechanisms after SAH. It can be related to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), cerebral salt wasting syndrome or iatrogenic hemodilution. It is important to monitor and diagnose hyponatremia as treatment varies with etiology.

Anemia

Anemia is common after aneurysmal SAH and may compromise brain oxygen delivery. Current guidelines recommend that the use of packed red cell transfusion to maintain hemoglobin concentration between 8-10 g/dl is reasonable in patients with SAH\(^1\).

Cardiac dysfunction

Left ventricular dysfunction requiring inotropic support can occur in patients after SAH. It results from excessive catecholamine release in response to intracranial hemorrhage. In most cases it is temporary and resolves spontaneously after a variable period.

Outcome

Outcomes after aneurysm surgery and aneurysmal SAH are much better and favorable in children as
compared to adults. In general, children have a lower incidence of vasospasm, which accounts for most of the morbidity and mortality associated with aneurysmal rupture. Overall, in different case series 90-95% of pediatric patients has good outcome with Glasgow coma outcome scale of 4 or 5.

References:
Case Report

Pulmonary Tuberculosis with ARDS and Hemophagocytic Syndrome
– A case report


* RMO Cum Clinical Tutor, Institute of Child Health, **Associate professor, Institute of Child Health, ***Professor of Pediatrics, Institute of Child Health, Kolkata

ABSTRACT:
Hemophagocytic lymphohistiocytosis (HLH) is a heterogeneous group of clinical syndromes, either familial or genetic in origin or secondary, characterised by uncontrolled non-malignant proliferation of T-lymphocytes, histiocytes and macrophages leading to a cytokine storm and manifest as prolonged fever, organomegaly, cytopenia, hyperferritenemia and demonstrable hemophagocytosis in the bone marrow. Secondary infection associated HLH (IAHLH) can be triggered by many infections, mostly viral. Here we present a case of Pulmonary tuberculosis complicated by ARDS and HLH.

Introduction
Tuberculosis continues to be an important cause of morbidity and mortality for children worldwide. Very rarely it can manifest as diffuse bilateral X-ray changes suggestive of Acute Respiratory Distress Syndrome (ARDS). ARDS is an emergency and mostly need mechanical ventilation, non-invasive or invasive. ARDS can be a pulmonary manifestation of HLH. But tuberculosis complicated by both ARDS and HLH is extremely rare and till date there is no case report. Our case, 11 year old boy, presented with PUO, developed ARDS and HLH and ultimately diagnosed to be having tuberculosis.

Case Report
10yr old boy admitted with history of fever for 14 days. Clinical examination revealed only a just palpable liver. Investigation showed Hb 11.2gm%, TLC 6400/cmm, DLC - N 54 L38 M02 E03 B 02, Malaria Parasite not found, SGPT 220 IU/dl, Widal 1:320, chest x-ray noncontributory. Assuming a clinical diagnosis of enteric fever, iv ceftriaxone was started. Over next few days his fever decreased in intensity but did not subside. Mantoux test and blood culture were negative.

On day 5 of admission, he suddenly developed severe respiratory distress. Respiratory rate was 86/min, SPO2 in room air was 56%, with 12 litres of O2 it was only 88-90%. There was no accessory sounds in the chest, B/L VBS was there and air entry was good. Chest x ray showed B/L diffuse patchy opacities suggestive of ARDS. (figure 1) ABG revealed severe hypoxemia and so he was intubated and ventilated. Investigations showed a raised CRP with pancytopenia (TLC-3200, PLATELET 80,000, HB 8.2). HRCT showed features of ARDS with cavity and nodules in left upper lobe. (figure 2)

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Because of the sudden deterioration with development of cytopenia, HLH was thought of and corresponding tests showed Ferritin 7568ng/dl, TG 423mg/dl, LDH 2543IU/dl, Fibrinogen 123gm/L, FDP 7800. IV Immunoglobulin (2gram/kg) with IV dexamethasone 10mg/m2 /day was started following bone marrow aspiration.

Bronchoalveolar lavage showed acid fast bacilli and it was positive for Mycobacterium Tuberculosis Complex by DNA amplification (TB PCR Qualitative). Bone marrow revealed plenty of hemophagocytes.

Following initiation of therapy, blood parameters improved in the next 72 hours and he was extubated on day 5 of Mechanical ventilation and discharged on day 26 of admission with 4 antitubercular drugs (HRZE) and steroid. Dexamethasone was given for 8 weeks in tapering doses as per HLH 2004 protocol, but no other chemotherapeutic drugs like Cyclosporine or Etoposide was used.

He is on regular follow up for last 2 years and remains asymptomatic.

Discussion

Children contribute a significant proportion of the disease burden of tuberculosis and suffer severe disease-related morbidity and mortality, particularly in endemic areas. Pulmonary tuberculosis can manifest in various way in pediatric population. Symptomatic primary complex, progressive primary disease, endobronchial tuberculosis, tubercular pleural effusion and miliary tuberculosis are the commonest modes of presentation whereas gross fibrosis or cavitating lung lesions are uncommon.

ARDS (Acute respiratory distress syndrome) can result from either a direct lung injury or from a downstream inflammatory process manifested by profound hypoxemia and respiratory failure. ARDS has been traditionally described as: the acute onset of respiratory failure with bilateral infiltrates on chest radiograph associated with hypoxemia as defined by a PaO2/FiO2 ratio ≤200 mmHg, and there should be no evidence of left atrial hypertension or a pulmonary capillary pressure should be <18 mmHg (if measured) to rule out cardiogenic edema. In pediatric age group, ARDS is largely secondary to lung infections.

ARDS as a manifestation of pulmonary tuberculosis in children is extremely rare. Hemophagocytic lymphohistiocytosis (HLH) occurs due to uncontrolled proliferation and activation of macrophages, cytotoxic t cells and antigen presenting cells resulting in a state of hypercytokinemia. Any infection can trigger HLH, though most are triggered by viral infections.

Pulmonary tuberculosis manifesting as ARDS has rarely been reported in adults. Miliary tuberculosis is an uncommon but important treatable cause of ARDS. Mohan et al reported 6 cases of miliary TB who developed ARDS in the course of their disease. Agarwal et al also demonstrated that nine (4.9%) out of 187 adult patients had ARDS secondary to tuberculosis. But tubercular ARDS in pediatric population is extremely rare and limited to few case reports only.

Tuberculosis is considered a rare cause for infection associated secondary HLH. Wen su et al reported a case of tuberculosis induced HLH in a 58 year old patient under hemodialysis. Gupta et al presented a case of generalised lymphadenopathy, hepatosplenomegaly and progressive cytopenias in a 17-year-old male who was simultaneously diagnosed to have HLH and Tuberculosis as AFB was demonstrated from the lymph node aspirates. Deshpande et al also reported a case of miliary tuberculosis with hemophagocytosis in a 2 months old infant.

The most common pulmonary manifestation of HLH is Acute lung injury or ARDS. Lahm et al reported a case of Adenovirus associated HLH with ARDS. Roxana Mansour Ghanaiee et al also reported few cases of HLH in pediatric population in Iran who developed ARDS.

But, Pulmonary tuberculosis with ARDS with secondary HLH is yet to be reported in literature. IAHLH does not always need full HLH 2004 therapy protocol; they can often be treated successfully with low intensive therapy depending upon the severity, and the initial response to steroids. Many of them can be treated with steroid only protocol as this child received only steroid in a tapering dosage over 8 weeks.

Reference

1. Banu Rekha, Soumya Swaminathan. Childhood tuberculosis


Respiratory monitoring in Pediatric Intensive Care Unit (PICU) is an essence of critical care. Be it clinical, invasive or noninvasive, monitoring remains crucial in overall assessment of a critically ill child with cardio-respiratory problems. A functioning knowledge of the various tools of monitoring is essential in applying their use to patient care. This chapter discusses traditional methods of evaluation of respiratory system and newly established gold standard techniques as well. Attention is also given to newer modalities, including those that are investigational or currently limited to bench application, that give promise for future application in PICU clinical practice. Pulse oximetry and Capnography are the most commonly employed monitoring modalities, which have transformed the practice of critical care in last 10 years. Arterial blood gases and calculated oxygen indices have been most commonly used and form essential part of monitoring in PICU. However may be the excellent information provided by respiratory monitors it cannot replace careful bedside clinical examination.

Essentially respiratory monitoring consists of:
1. Physical examination
2. Non-invasive monitoring
3. Invasive monitoring

**Physical Examination**

Measuring the respiratory rate (Table 1) is easy and has a got good accuracy in prediction of lower respiratory tract infection. Presence of increased work of breathing is suggested by flaring of alae nasi, suprasternal, intercostal and subcostal retractions, use of accessory muscles of respiration and paradoxical breathing.

<table>
<thead>
<tr>
<th>Normal Respiratory Rates…….. (Table1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Infant (birth–1 year)</td>
</tr>
<tr>
<td>Toddler (1–3 years)</td>
</tr>
<tr>
<td>Preschooler (3–6 years)</td>
</tr>
<tr>
<td>School-age (6–12 years)</td>
</tr>
<tr>
<td>Adolescent (12–18 years)</td>
</tr>
</tbody>
</table>

Cyanosis of tongue and oral mucosa indicate oxygen saturation (SaO\textsubscript{2}) of less than 80 percent. However, there is significant inter-observer variability and difficulty in SaO\textsubscript{2} interpretation.

Let’s take a moment to review the Silverman-Anderson Index related to the assessment of the neonates with suspected or diagnosed RDS. When a neonate is a premature, or has underlying pathology, then expiratory grunting, retraction of the chest wall muscles and other signs of respiratory distress may be readily seen. The Silverman – Anderson Index, commonly referred to as the Silverman retraction score, was developed as a systematic means of assessing newborn respiratory status, particularly when respiratory distress is suspected.

<table>
<thead>
<tr>
<th>Silverman- Anderson Index (Table 2)</th>
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</thead>
<tbody>
<tr>
<td>Feature</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Chest movement</td>
</tr>
<tr>
<td>Intercostal retractions</td>
</tr>
<tr>
<td>Xiphoid retraction</td>
</tr>
<tr>
<td>Nasal Flaring</td>
</tr>
<tr>
<td>Expiratory Grunt</td>
</tr>
</tbody>
</table>

The parameters assessed by inspection and auscultation of the upper and lower chest and nares on a scale of 0,1,or 2. As it is observed in the table 2, the higher the score, the more severe is the respiratory distress.
Non-Invasive Respiratory monitoring

History
Oximetry measures the percentage of hemoglobin saturated with oxygen by passing specific wavelengths of light through the arterial blood. In 1875 a German physiologist named Karl von Vierofdt demonstrated that the oxygen in his hand was consumed when a tourniquet was applied. This was done utilizing transmitted light waves, but the development of the pulse oximeter was still a long way off. In 1936 Karl Matthes developed the first ear saturation meter that used two wavelengths of light. This compensated for the variations in tissue absorption. This idea was improved upon in 1940 when Glen Millikin developed a lightweight oximeter to help the military to solve their aviation hypoxia problem. The modern pulse oximeter was developed in 1972 by Takuo Aoyagi while he was working in Tokyo developing a noninvasive cardiac output measurement, using dye dilution and an ear densitometer. He noticed a correlation in the difference between unasorbed infrared and red light and the oxygen saturation. This led to the clinical application of the pulse oximeter. It was not until 1980 that Nellcor produced the first commercial pulse oximeter that was reliable, robust, and affordable. In 1988 the use of a pulse oximeter during anesthesia and recovery room became mandatory in Australia. Since then, its use has become mandated in many areas from pre-hospital treatment to intensive care units.

Pulse oximetry is now an integral part of PICU monitoring which helps in the assessment of the patient’s cardio-respiratory (oxygenation) status. It is a simple, non-invasive and continuous method of monitoring the oxygen saturation of arterial blood (SaO2) and now widely accepted as the fifth vital sign. The pulse oximeter is a convenient, cost-effective way to monitor the patient’s oxygenation status (and thereby O2 content) and determine the changes before they are clinically apparent. It is important to know how oximeters work in order to maximize their performance and avoid errors in the interpretation of results.

Pulse oximetry is based on principles of spectrophotometry governed by Beer-Lambert law. The mandatory condition for interpretation of SaO2 is the presence of a pulsatile arteriolar blood flow.

How pulse oximeter works? Interpretation of SaO2 is based on the fact that oxygenated hemoglobin (HbO2) and deoxygenated hemoglobin (Hb) have different absorption spectra. Currently available pulse oximeters use two light-emitting diodes (LEDs) that emit light at the 660 nm (red) and the 940 nm (infrared) wavelengths. These two wavelengths are used because HbO2 and Hb have different absorption spectra at these particular wavelengths. In the red region, HbO2 absorbs less light than Hb, while the reverse occurs in the infrared region. The ratio of absorbencies at these two wavelengths is calibrated empirically against direct measurements of SaO2 in volunteers, and the resulting calibration algorithm is stored in a digital microprocessor within the pulse oximeter. During subsequent use, the calibration curve is used to generate the pulse oximeter’s estimate of arterial saturation (SpO2). In addition to the digital readout of O2 saturation and pulse rate, most pulse oximeters display a plethysmographic waveform which can help clinicians to distinguish an artifactual signal from the true signal.

There are two techniques of measuring SaO2: transmission and reflectance. In the transmission method the emitter and photodetector are opposite of each other with the measuring site in-between. The light can then pass through the site. In the reflectance method, the emitter and photodetector, is next to each other on top the measuring site. The light bounces from the emitter to the detector across the site. The transmission method is the most common type of method of choice in use. The normal SpO2 value for adolescents and elders is greater than 95%, and for children, a level greater than 90-92% is normal. SpO2 can be misleading as other factors must be considered when determining whether this SpO2 is normal for the particular patient.

Critical discussion on Pulse oximetry (SpO2 = SaO2)
- SaO2 gives fairly good idea of not only saturation but also of oxygen content (CaO2) provided Carboxyhemoglobin (COHb) and methemoglobin (MetHb) are expected in normal amounts. Since 98% of CaO2 is contributed by saturated hemoglobin, hence it is a good idea that one should always calculate CaO2, every time, after observing SpO2 since CaO2 is the better indicator of oxygenation.
  \[ CaO_2 = \text{SaO}_2 (98\%) + \text{PaO}_2 (2\%). \]
  \[ [\text{CaO}_2 = 1.34\text{HbLSaO}_2 + \text{PaO}_20.003] \]

Interpretation SpO2 should always be done in context of ODC. Since conditions causing Left shift can have normal saturation but patient may be hypoxic (low PaO2). Similarly conditions causing Right shift may have low SaO2 but patient may not be hypoxic.
Limitations of Pulse oximetry Oximeters have a number of limitations which may lead to inaccurate readings. Shape of oxygen dissociation curve, Carboxyhemoglobin, Methemoglobin Anemia, Dyes, Nail polish, Ambient light, motion artifact, Skin pigmentation and Low perfusion states are other causes as well.

Pulse oximeters measure SpO\textsubscript{2} that is physiologically related to arterial oxygen tension (PaO\textsubscript{2}) according to the oxyhemoglobin dissociation curve (ODC). Because the ODC has a sigmoid shape, oximetry is relatively insensitive in detecting the development of hypoxemia in patients with high baseline levels of PaO\textsubscript{2} (upper flat portion of ODC curve).

Since pulse oximeters use only two wavelengths of light and, thus, it can distinguish only two substances, Hb and HbO\textsubscript{2}. When COHb and MetHb are also present, four wavelengths are required to determine the ‘fractional SaO\textsubscript{2}’: i.e., \((\text{HbO}_2 \times 100)/ (\text{Hb} + \text{HbO}_2 + \text{COHb} + \text{MetHb})\) and this can be measured by Co-oximetry. In the presence of elevated COHb levels, oximetry consistently over-estimates the true SaO\textsubscript{2} by the amount of COHb present since it has got same absorption spectrum as of HbO\textsubscript{2}. Elevated MetHb levels also may cause inaccurate oximetry readings.

Anemia does not appear to affect the accuracy of pulse oximetry even in non-hypoxemic patients with acute anemia; pulse oximetry was accurate in measuring O\textsubscript{2} saturation. Severe hyperbilirubinemia (mean bilirubin, 30.6 mg/dl) does not affect the accuracy of pulse oximetry.

Intravenous dyes such as methylene blue, indocyaninegreen, and indigocarmine can cause falsely low SpO\textsubscript{2} readings. Nail polish, if blue, green or black, causes inaccurate SpO\textsubscript{2} readings, whereas acrylic nails do not interfere with pulse oximetry readings. Falsely low and high SpO\textsubscript{2} readings occur with fluorescent and xenon arc surgical lamps.

Motion artifact continues to be a significant source of error and false alarms. In a recent, prospective study in an intensive care unit setting, SpO\textsubscript{2} signals accounted for almost half of a total of 2525 false alarms.

Inaccurate oximetry readings have been observed in pigmented patients, but not by all investigators. Low perfusion states, such as low cardiac output, vasoconstriction and hypothermia may impair peripheral perfusion and may make it difficult for a sensor to distinguish a true signal from background layers.

An under-recognized and worrisome problem with pulse oximetry is that many users have a limited understanding of how it functions and the
implications of its measurements. In a recent survey, 30% of physicians and 93% of nurses thought that the oximeter measured PaO\textsubscript{2}. Some clinicians also have a limited knowledge of the ODC, and they do not recognize that SpO\textsubscript{2} values in the high 80s represent seriously low values of PaO\textsubscript{2}. In the above survey, some doctors and nurses were not especially worried about patients with SpO\textsubscript{2} values as low as 80% (equivalent to PaO\textsubscript{2} \leq 45 mm of Hg).

Conventional pulse oximetry has problems during ambient light, abnormal hemoglobin, pulse rate and rhythm, vasoconstriction and cardiac function, physical motion and low perfusion and that has great impact on when making critical decisions. Arterial blood gas tests have been used to supplement or validate pulse oximeter readings. The advent of “Next Generation” pulse oximetry technology has demonstrated significant improvement in the ability to read through motion and low perfusion; thus making pulse oximetry more dependable to take decisions during critical period.

It is important to remember that pulse oximeters assess oxygen saturation only and thereby Oxygenation status and gives no indication of the level of CO\textsubscript{2} and thereby Ventilation status. For this reason they have a limited benefit in patients developing respiratory failure due to CO\textsubscript{2} retention.

The pulse oximeter may be used in a variety of situations that require monitoring of oxygen status and may be used either continuously or intermittently. It is not a substitute for an ABG, but can give clinicians an early warning of decreasing arterial oxyhemoglobin saturation prior to the patient exhibiting clinical signs of hypoxia. The pulse oximeter is a useful tool but the patient must be treated—not the numbers. As with all monitoring equipment, the reading should be interpreted in association with the patient’s clinical condition. If a patient is short of breath and bluish with a saturation reading of 100%, check for possible causes due to artifact. Never withhold therapeutic oxygen from a patient in distress while waiting to get a reading. If the patient appears to be in perfect health and the saturation is reading 70%, this should alert you to the possibility of interference. Never ignore a reading which suggests the patient is becoming hypoxic. The main disadvantage of pulse oximeter is its inability to use in cases of hyperoxia at saturations between 90-100%.

Masimo pulse oximetry - a new promising way of measuring SpO\textsubscript{2} !!

What makes Masimo pulse oximetry different from conventional pulse oximetry?

Conventional pulse oximetry assumes that arterial blood is the only blood moving (pulsating) in the measurement site. During patient motion, the venous blood also moves, which causes conventional pulse oximetry to under-read because it cannot distinguish between the arterial and venous blood. Masimo signal technology identifies the venous blood signal, isolates it, and cancels the noise and extracts the arterial signal, and then reports the true arterial oxygen saturation and pulse rate.

Following setbacks of Conventional Pulse Oximetry for inaccurate monitoring or signal dropout during the reading are rectified by Masimo technology

- Patient Motion or Movement
- Low Perfusion (low signal amplitude)
- Intense Ambient Light (lighting or sunlight)
- Electrosurgical Instrument Interference

Capnography

End-tidal CO\textsubscript{2} (EtCO\textsubscript{2}) monitoring is an exciting non-invasive technology that is more commonly used in the emergency department, intensive care units and in the pre-hospital settings. Its main use has been in verifying endotracheal tube position, during mechanical ventilation and cardio-pulmonary resuscitation, but it is being studied and used for other purposes as well. The American Heart Association new guidelines states the secondary confirmation of proper endotracheal tube placement in all patients by exhaled CO\textsubscript{2} immediately after intubation and during transport is essential.

EtCO\textsubscript{2} monitoring is an exciting new technology that measures CO\textsubscript{2} in the exhaled breath continuously and non-invasively. CO\textsubscript{2} is produced during cellular metabolism, transported to the heart and exhaled via the lung and so EtCO\textsubscript{2} reflects ventilation, metabolism and circulation. If any two systems are kept constant then changes in the third system reflect...
changes in EtCO2. This was first studied clinically by Smallhout and Kalenda in the 1970’s, and in the late 1980’s – 1990’s this methodology has been studied extensively in various clinical settings. The most common use of EtCO2 is to verify endotracheal tube (ETT) position. It is being increasingly studied and used during cardiopulmonary resuscitation (CPR) and other clinical settings.

**What is Capnography?**

*It is a graphical representation of noninvasive, continuous measurement of exhaled carbon dioxide (EtCO2) concentration over time accompanied by digital display that provides EtCO2 value and distinct waveform (tracing) for each respiratory cycle.*

Some definitions: **Capnometry**

- Capnometer: Provides only a numerical measurement of carbon dioxide
- Capnogram: Is a waveform display of carbon dioxide over time
- Capnography: A numerical value of the EtCO2 and a waveform of the concentration of CO2 present in the airway. And Respiratory rate detected from the actual airflow

Normal Capnogram (Fig)

![Normal Capnogram](image)

The Capnogram is divided into four distinct phases:

1. Phase I (A-B) is the beginning of exhalation. It represents most of the anatomical dead space. CO2 is almost zero.
2. Phase II (B-C) is where the alveolar gas begins to mix with the dead space gas and the CO2 begins to rapidly rise.
3. Phase III (C-D) represents the alveolar gas, usually has a slight increase in the slope as “slow” alveoli empty. The “slow” alveoli have a lower V/Q ratio and therefore have higher CO2 concentrations. In addition, diffusion of CO2 into the alveoli is greater during expiration. *This is more pronounced in infants.* EtCO2 is measured at the maximal point of Phase III (D)
4. Phase IV (D-E) is the inspirational phase

**Types of CO2 Monitors**

There are two types of CO2 monitors: 1) Mainstream and 2) Sidestream.

**Mainstream...... salient features are.......**

- The infrared sensor is located in the airway adapter, between the ET tube and the breathing circuit tubing.
- Response time is faster and may be as little as 40msec
- Water cannot be drawn-in to disrupt sensor function, and since no mixing of gases in the sample tube it is nearly a very accurate one.
- Difficult to calibrate without disconnecting (makes it hard to detect rebreathing)
- More prone to the reading being affected by moisture.
- Sensor device is larger in size hence can kink the tube.
- Adds dead space to the airway.
- Bigger chance of being damaged by mishandling.

**Sidestream...... salient features are.....**

- Can be used with in intubated or non-intubated patients thus have wider applications.
- The airway adapter is positioned at the airway (whether or not the patient is intubated) to allow aspiration of gas from the patient’s airway back to the sensor, which lies either within or close to the monitor, thus gas is sampled through a small tube
- Analysis is performed in a separate chamber
Clinical Applications of CO₂ Monitoring

The EtCO₂ level read on the display of the monitor depends upon the proper functioning of the following:

- Lungs and airways
- Patient ventilation system
- Respiratory mechanism
- Patient’s metabolism and circulation

Malfunctions of the lungs and airway OR the patient’s ventilation system can be depicted as follows:

- Upper airway obstruction – reflected by an increased EtCO₂
- Apnea – reflected by a sudden cessation of EtCO₂ readings
- Improper ventilator operation – reflected by either high or low EtCO₂ readings
- Hyperventilation – reflected by a decreased EtCO₂
- Hypoventilation – reflected by an increase in EtCO₂
- A faulty one-way valve – reflected by an increased inspired CO₂ and increased EtCO₂
- Esophageal intubation – reflected by no EtCO₂ reading
- Respiratory depression (from anesthesia) – reflected by a decreased EtCO₂
- Increased level of muscle relaxation – reflected by a decreased EtCO₂
- Reversal of muscle relaxant and resulting improvement in muscle tone – reflected by an increased EtCO₂
- Malignant hyperthermia – reflected by an increased EtCO₂

PaCO₂-EtCO₂ gradient

- It is usually < 6 mm Hg
- EtCO₂ is usually less
- Difference depends on the number of underperfused alveoli
- Tend to mirror each other if the slope of Phase III is horizontal or has a minimal slope

LIMITATIONS

1. Critically ill patients often have rapidly changing dead space and V/Q mismatch
2. Higher rates and smaller tidal volumes can increase the amount of dead space ventilation
3. High mean airway pressures and PEEP restrict alveolar perfusion, leading to falsely decreased readings
4. Low cardiac output will decrease the reading.

Indications for Capnography are:

1. Confirm and verify tracheal intubation placement.
2. Evaluate ventilator settings and circuit integrity.
3. Assess cardiopulmonary status and changes in pulmonary blood flow.
4. Assess airway management and changes in airway resistance.
5. Monitor effectiveness of CPR.
8. Monitor the effectiveness of ventilator weaning process, and response to changes in ventilator settings (i.e., respiratory rate, flow and/or volume).
9. Reduce the number and/or frequency of arterial blood gas drawings.
10. Aids in the treatment of neurological patients and the possibility of increasing intracranial pressures.

Other uses…….

- Metabolic
  - Assess energy expenditure
- Cardiovascular
  - Monitor trend in cardiac output
  - Can use as an indirect Fick method, but actual numbers are hard to quantify
  - Measure of effectiveness in CPR
  - Diagnosis of pulmonary embolism by measuring measure gradient
Microstream technology
It is 3rd generation technology which can be used with intubated or non-intubated patients and requires low sample flow rate - 50 ml/min. It allows its use in neonate & pediatric patients. In this technology sampling lines not flooded with moisture
Microstream improves upon conventional Sidestream sampling based upon the principle that CO₂ molecules absorb IR radiation at specific wavelengths

Advantages
1. No sensor at airway
2. Intubated and non-intubated patients (neonatal through adult)
3. No routine calibration
4. Automatic zeroing
5. Accurate at small tidal volumes and high respiratory rates
6. Superior moisture handling

Pulmonary Function Tests
Few of the numerous pulmonary function tests currently available have an impact upon clinical management of the critically ill child, particularly if the patient has to be moved to a laboratory. A number of other tests require highly specialized equipment and fulfill a predominant research role.
**Clinical relevant tests**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Tests</th>
<th>Common clinical use</th>
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<tr>
<td>PaO$_2$, SaO$_2$, PaCO$_2$</td>
<td>Arterial blood gases</td>
<td>Oxygenation, Ventilation status</td>
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<tr>
<td>SpO$_2$</td>
<td>Pulse oximetry</td>
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<tr>
<td>End-tidal PCO$_2$</td>
<td>Capnography</td>
<td>Ventilation status</td>
</tr>
<tr>
<td>Vital capacity, tidal volume</td>
<td>Spirometry, electronic flowmetry.</td>
<td>Serial measurement of borderline function (VC &lt; 10-15ml/kg) e.g. Gullain –Barré syndrome</td>
</tr>
<tr>
<td>Peak expiratory flow rate</td>
<td>Wright peak flow meter,</td>
<td>(Spontaneous ventilation) asthma</td>
</tr>
<tr>
<td>FEV$_1$, FVC</td>
<td>Spirometry, electronic flowmetry.</td>
<td>(Spontaneous ventilation) asthma, obstructive / restrictive disease.</td>
</tr>
<tr>
<td>Lung/chest wall compliance</td>
<td>Pressure- volume curve</td>
<td>Ventilator adjustments, monitoring disease progression.</td>
</tr>
<tr>
<td>Flow volume loop, pressure volume loop</td>
<td>Pneumotachograph* manometry</td>
<td>Ventilator adjustment</td>
</tr>
</tbody>
</table>

*(Pneumotachograph: an apparatus for recording the rate of airflow to and from lungs)*

**Research tests (examples)**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Tests</th>
<th>Research use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaphragmatic strength (transdiaphragmatic pressure)</td>
<td>Gastric and esophageal manometry</td>
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<tr>
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<td>Functional residual capacity</td>
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<td>Ventilation-perfusion relationship</td>
<td>Multiple inert gas elimination technique, isotope technique</td>
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</tr>
<tr>
<td>Pulmonary diffusing capacity</td>
<td>Carbon monoxide uptake</td>
<td>Pulmonary gas exchange.</td>
</tr>
</tbody>
</table>

**Notes**

- Compliance equals the change in pressure during a linear increase in volume above FRC.
- The Bohr equation calculates physiological deadspace (V$_D$); normally it is less than 30%.
- The shunt equations estimates the proportion of blood shunted past poorly ventilated alveoli (Qs) compared to total lung blood flow (Q$_T$).

These useful equations are supplement to assess pulmonary function, and ventilation/perfusion mismatch...

- V/Q = 1, Ventilation and perfusion are well matched.
- V/Q>1, increased deadspace (where alveoli are poorly perfused but well ventilated)
- V/Q<1, increased venous admixture or shunt (where alveoli are well perfused but poorly ventilated)

1. Alveolar gas equation: \( \text{PAO}_2 = \text{FiO}_2 \times (\text{PB} - \text{PH}_2\text{O}) - (\text{PaCO}_2 / \text{RQ}) \) [RQ=0.8]

2. Calculating the alveolar: arterial oxygen gradient: (A-a) DO$_2$, normal is 10-15 mm of Hg.
3. Bohr equation: \( V_D/V_T = (\text{PaCO}_2-\text{expired PCO}_2)/\text{PaCO}_2 \)
4. Shunt equation: \( \text{Qs/Q}_T = (\text{C}_2\text{O}_2-\text{CaCO}_2)/ (\text{C}_2\text{O}_2-\text{CvO}_2) \) where CCO$_2$ = end capillary O$_2$ content, a = arterial, v= mixed venous.
5. Expected PaO$_2 = \text{FiO}_2 \times 5$. A very useful equation with limitations.
1. P-V curve be obtained in fully relaxed and ventilated patient.
2. Both static (chest) and dynamic (lung) respiratory system compliance
   can be determined.
3. The lower inflection point represents appropriate setting for external
   Positive End Expiratory Pressure (PEEP).
4. The upper inflection point represents the maximum setting for PEAK
   AIRWAY PRESSURE (PAP).

X ray
A very commonly ordered investigation in PICU which has diagnostic, therapeutic and prognostic value is x-ray
chest. (This has been discussed detailed in other chapter
in this book)

Invasive monitoring
Arterial blood gas analysis
The term arterial blood refers to a specific set of tests performed on arterial blood sample. It provides four
key point information: pH, PO2, [HCO3] and PCO2.
The name blood gas is really a partial misnomer since H+ and HCO3 are not gases. It is a gold standard
investigation to assess pulmonary functions and cardiac as well.

Basic Concepts
• Arterial Blood Gas
• Gas Exchange
• Acid-Base Disturbances

Systematic Analysis of Arterial Blood Gases
1. Oxygenation
2. Stepwise approach to Acid-Base Disorders

Basic Introduction of Arterial Blood Gases
The term hypoxia refers to reduced O2 delivery to tissues. The term hypoxemia refers to reduced O2
content in arterial blood. A normal arterial pressure of O2 is dependent on the atmospheric pressure,
temperature, inspired O2 content, and the patient’s age.
Hypoxemia can be for two basic reasons; oxygen may not be delivered to the alveolar air sacs (hypoventilation) or oxygen in the alveoli may not enter into the blood stream. A patient can be hypercarbic (high levels of CO2) Or hypocarbic (low level of CO2) which is due to an inability to normally

exchange gas in the lungs.
The terms acidemia and alkalemia refer to alterations in blood pH, and are the result of underlying disturbance(s) (metabolic and/or respiratory). The terms acidosis and alkalosis refer to the processes that alter the acid-base status. There can be (and often are) more than one of these processes simultaneously in a patient

Diseases that alter the acid-base status of a patient can be divided….
1. Metabolic
2. Respiratory

Metabolic processes are those that primarily alter the HCO3 concentration in the blood. A decrease in
serum HCO3 (an alkali or base) leads to a metabolic acidosis, while an increase in serum HCO3 leads to a
metabolic alkalosis.
Respiratory processes alter the pH by changing the CO2 levels. CO2 accumulation causes an acid state in
the blood (through carbonic acid), and as respirations (respiratory rate and/or tidal volume) increase, the
body eliminates more CO2 (acid) and is left with a respiratory alkalosis. In other words, a decrease in
ventilation leads to retention and increased levels of CO2, and thus a respiratory acidosis.
In conclusion, pH altering processes can be one of four types:
1. Metabolic acidosis,
2. metabolic alkalosis,
3. Respiratory acidosis,
4. Respiratory alkalosis.

Again, one or more of these processes may be present in a patient with an abnormal acid-base status.

Systematic Analysis of Arterial Blood Gases
Arterial blood gases are obtained for two basic purposes:
1. To determine oxygenation and
2. To determine acid-base status.
Let’s elaborate now, how to determine oxygenation, and then evaluate the acid-base status systematically.

Determining Oxygenation i.e. Alveolar: arterial oxygen gradient: (A-a) DO2
(Age and FiO2 dependent derivative)
An important part of interpreting blood gases is to assess oxygenation. An arterial oxygen concentration
(PaO₂) of less than 60 mm Hg, associated with an oxygenation (SaO₂) of less than 90%, is poorly tolerated in humans; therefore a PaO₂ of less than 60 is termed hypoxemic. However, “normal” oxygenation decreases with age as the lungs become less efficient at diffusing oxygen from the alveolus to the blood. Again, normal oxygenation for age can be estimated as…PaO₂ = 104.2 - (0.27 x age) Or more crudely, normal oxygenation for age is roughly 1/3 of the patient’s age subtracted from 100. Using this estimation for example a 60-year-old patient should have a PaO₂ of 80 and 15-year-old patient should have a PaO₂ of 95. Values less than this would be considered hypoxemic for age.

Calculating the alveolar: arterial oxygen gradient:
(A-a) DO₂ can determine if hypoxia is a reflection of hypoventilation (in other words, decreased because of a rise in PaCO₂) or due to deficiency in oxygenation. Unlike oxygen (for which alveolar concentrations are higher than arterial concentrations) CO₂ freely diffuses across the lung such that the arterial and alveolar concentrations are identical. As a patient hypoventilates, CO₂ will accumulate in the body (more CO₂ is produced through metabolism than can be eliminated) and thus in the blood (where we measure it as PaCO₂). The carbon dioxide displaces the oxygen in the alveolus. This reciprocal relationship between oxygen and carbon dioxide in the alveolus is described by the alveolar gas equation:

\[ PAO_2 = 150 - 1.25 \times (PaCO_2) \]

\[ Pa = \text{partial pressure of a gas in the arterial blood.} \]

\[ PA = \text{partial pressure of a gas in the alveolus.} \]

This equation assumes that the patient is breathing room air (21% O₂) at atmospheric pressure.

Where do 150 come from? :
• (Atmospheric P - water vapor P) x FIO₂. At room temperature, at sea level,
• Atmospheric pressure = 760 mm Hg;
• In the lung, the air is fully saturated with water, giving a water vapor pressure of about 47.
• Room Air is about 21%, thus at room air, the PAO₂ = 0.21(760-47) = 149.7, or about 150.

AND…Where does 1.25 come from?
This is a fudge factor which is derived from the respiratory quotient. The formula actually requires that the PACO₂ be divided by the respiratory quotient, which is defined as the ratio of CO₂ produced to O₂ consumed (and which depends on diet and metabolism). We estimate the RQ to be 0.8, and the reciprocal of 0.8 is 1.25.

This value is the partial pressure of O₂ within the alveolus. Because the CO₂ freely diffuse from arterial blood to alveolar airspaces, the PACO₂ is equal to the PaCO₂, which is measured in the arterial blood gas. The above equation can then be rewritten as

\[ PAO_2 = 150 - 1.25 \times (PaCO_2) \]

Thus…A-a DO₂ = PAO₂ - PaO₂ Or

\[ A-a DO_2 = [150-1.25 \times (PaCO_2)] - PaO_2 \]

A normal A-a gradient is 10-20 mm Hg, with the normal gradient increasing within this range as the patient ages. An increased A-a gradient identifies decreased O₂ in the arterial blood compared to the O₂ in the alveolus. This suggests a process that interferes with gas transfer, or in general terms, suggests ventilation-perfusion mismatch. A normal A-a gradient in the face of hypoxemia suggests the hypoxemia is due to hypoventilation and not due to underlying lung disorders.

When the patient is not breathing room air then…

\[ A-a \text{ gradient} = \{(FI0₂)(760-47)-(1.25)(PaCO₂)\} - PaO₂ \]
Stepwise Approach to Diagnosing Acid-Base Disorders

In order to understand the various processes that can co-exist in a patient, one must systematically evaluate blood gases and serum electrolytes. The simple method of six steps to analyze the acid-base status of the patient is presented here.

**Steps in Acid-Base Analysis**

- Step 1. Consider the clinical settings! Anticipate the disorder!
- Step 2. Look at the pH?
- Step 3. Who is the culprit for changing pH?... Metabolic / Respiratory process
- Step 4. If respiratory...... acute and/or chronic And Is metabolic compensation appropriate?
- Step 5. If metabolic acidosis, Is respiratory compensation appropriate? Anion gap’ed and/or normal or both?
- Step 6. Is more than one disorder present? Mixed one?

**STEP 1**: Clinical assessment based on clinical settings is an essential first step. From the history, examination and initial investigations make a clinical decision as to what is the most likely acid-base disorder(s).

This is very important but be aware that in some situations, the history may be inadequate, misleading or the range of possible diagnoses large. Mixed disorders are often difficult: the history and examination alone are usually insufficient in sorting these out.

1. Vomiting.............. Metabolic alkalosis
2. Diarrhoea ............. Metabolic acidosis
3. Septicemia ............ Lactic acidosis
4. Hypotension, Hypoxemia, Shock ........ Lactic acidosis
5. Diabetes mellitus... Ketoacidosis
6. Pneumonia ............ Respiratory alkalosis/acidosis
7. Bronchial asthma ... Respiratory alkalosis/acidosis
8. Hepatic failure ...... Respiratory alkalosis, Metabolic alkalosis
9. CNS disorders ...... Respiratory alkalosis
10. Renal disorders ...... Metabolic acidosis

*KEY POINT: Metabolic alkalosis and acidosis can exist together with any respiratory either acidosis or alkalosis. Both two respiratory disorders can’t occur simultaneously*

**STEP 2**: Look at the pH

The pH of the arterial blood gas measurement identifies the disorder as alkalemic or acidemic. pH > 7.4 .... Alkalosis, pH < 7.4 ............ Acidosis, pH = 7.4 .......... Normal or mixed disorder (Only Chronic Respiratory alkalosis can have normal value of pH)

**STEP 3**: Who is responsible for this change in pH? Who is the CULPRIT?

HCO₃... METABOLIC PCO₂ ...... Respiratory > 26 ...... Met. Alkalosis > 45 ...... Resp. Acidosis
< 22 ...... Met. Acidosis < 35 ...... Resp. Alkalosis

It is essential to determine whether the disturbance affects primarily the arterial PaCO₂ or the serum HCO₃.
- ...... Respiratory disturbances alter the arterial PaCO₂ (normal value 35-45)
- ...... Metabolic disturbances alter the serum HCO₃ (normal value 22-26)

If the pH is low (i.e., the primary and controlling disturbance is acidosis causing acidemia) either the PaCO₂ is high or the HCO₃ is low. (These are the only ways in which the pH can be low). A high PaCO₂ defines a primary respiratory acidosis and a low HCO₃ defines a primary metabolic acidosis.

Conversely, if the pH is high (i.e., the primary and controlling disturbance is alkalosis causing alkalemia) either the PaCO₂ is low or the HCO₃ is high. (These are the only ways in which the pH can be high). A low
\( \text{PaCO}_2 \) defines a primary respiratory alkalosis and a high \( \text{HCO}_3 \) defines a primary metabolic alkalosis.

**STEP 4**: If it is a primary respiratory disturbance, Is it acute? And/OR Chronic.

*For 10 mm change in \( \text{pCO}_2 \), pH changes as:

- Acidosis (↑\( \text{CO}_2 \)) .... pH ↓ ... acute .... by 0.08, chronic .... by 0.03
- Alkalosis (↓\( \text{CO}_2 \)) .... pH ↑ ... acute .... by 0.08, chronic .... by 0.03
*\( \text{HCO}_3 \) Compensates as ....

- Acidosis (↑\( \text{CO}_2 \)) .... \( \text{HCO}_3 \)↑....... Acute .... by 1, Chronic .... by 3
- Alkalosis (↓\( \text{CO}_2 \)) .... \( \text{HCO}_3 \)↓.......Acute .... by 2, Chronic .... by 5

For example,

- In an acute respiratory acidosis, if the \( \text{PCO}_2 \) rises from 40 to 50, you would expect the pH to decline from 7.40 to 7.32.
- In an acute respiratory alkalosis, if the \( \text{PCO}_2 \) falls from 40 to 30, you would expect the pH to rise from 7.40 to 7.48.

In chronic respiratory disturbances, there are renal mediated shifts of bicarbonate that alter and partially compensate for the pH shift for a change in the \( \text{PaCO}_2 \).

- In a chronic respiratory acidosis, if the \( \text{PCO}_2 \) rises from 40 to 50, you would expect the pH to decline from 7.40 to 7.37.
- In a chronic respiratory alkalosis, if the \( \text{PCO}_2 \) falls from 40 to 30, you would expect the pH to rise from 7.40 to 7.43.

Remember: to suspect if

- compensated \( \text{HCO}_3 \) is > expected: additional metabolic alkalosis is there
- compensated \( \text{HCO}_3 \) is < expected: additional metabolic acidosis is there

**STEP 5**: If it is a primary metabolic disturbance, whether respiratory compensation appropriate?

*For metabolic acidosis: Expected \( \text{PCO}_2 \) = \((1.5 \times [\text{HCO}_3]) + 8 + 2 \) ... Winter’s formula

*OR* Expected \( \text{CO}_2 \) is equal to Last two digits of pH (important & easy to remember.)

For metabolic alkalosis: Expected \( \text{PCO}_2 \) = 6 mm for 10 mEq rise in Bicarb.

.........UNCERTAIN COMPENSATION

Remember: to suspect if

- Compensated \( \text{PCO}_2 \) is > expected: additional respiratory acidosis is there
- Compensated \( \text{PCO}_2 \) is < expected: additional respiratory alkalosis is there.

Processes that lead to a metabolic acidosis can be divided into

1) Increased anion gap and 2) Normal anion gap.

The anion gap is the difference between the measured serum cations (positive) and the measured serum anions (negative). *(Of course, there is no real gap; in the body the numbers of positive and negative charges are balanced. The gap refers to the difference in positive and negative charges among cations and anions which are commonly measured.) The commonly measured cation is sodium. (Some people also use potassium to calculate the gap; that results in a different range of normal values.) The measured anions include chloride and bicarbonate. Thus the anion gap can be summarized as: \( \text{AG} = [\text{Na}^+] - ([\text{Cl}] + [\text{HCO}_3^-]) \).

The normal anion gap is 12. An anion gap of > than 12 is increased. Anion gap > 25 has got distinct value having significant ACIDOSIS. This is important, because it helps to significantly limit the differential diagnosis of a metabolic acidosis. The most common etiologies of a metabolic acidosis with an increased anion gap include:

- Commonest pediatric causes are Lactic acidosis, diabetic ketoacidosis and renal failure.
- Aspirin, Ketones (starvation, alcoholic and diabetic ketoacidosis)
- Uremia (renal failure), Lactic acidosis, Ethanol, Paraldehyde and other drugs
- Methanol other alcohols, and ethylene glycol intoxication

**Key point**: The true anion gap is underestimated in hypoalbuminemia (fall in unmeasured anions); \( \text{AG} \) must be adjusted. Remember to adjust \( \text{AG} \): For every 1.0 fall in albumin, increase the \( \text{AG} \) by 2.5

**STEP 6**: Is more than one DISORDER present?

- Proper Clinical history
- pH normal, and \( \text{PCO}_2 \) and \( \text{HCO}_3 \) out of range
- PCO₂ and HCO₃ moving in opposite directions
- Degree of compensation for primary disorder is inappropriate.

**Key messages**

1. Respiratory monitoring helps in the early diagnosis of change in a physiological parameter of oxygenation and ventilation, and provides guidelines towards institution of appropriate therapy.
2. Basic knowledge of the principles of monitoring tools and correct interpretation of data is important since failure to do so can result in misdirected therapy.
3. Pulse oximetry and Capnography are the essential monitors in PICU which need clinical correlation.
4. Arterial blood gas analysis is an integral part of respiratory monitoring in PICU.
5. No amount of monitoring, though excellent information provided by monitors, however, can replace careful bedside clinical signs.

**Reference**

4. Lawrence Martin. In : All you really need to know to interpret arterial Blood gases 1992
The ability to intensively, continuously, and routinely monitor both usual vital signs and more specialized metrics forms one of the cornerstones of modern critical care. Monitoring should be selected and applied to detect pathophysiologic abnormalities in patients at high risk of developing them and to aid in the titration of therapy to appropriate physiologic end points. This area of medicine not only requires a detailed knowledge of patient physiology, but demands an understanding of the physical principles that underpin the technology and awareness of the limitations and potential errors of the information gathered.

The monitoring and diagnostics specifically addressed in this chapter include those related to the haemodynamic, respiratory and neurological systems of the body.

A. Hemodynamic Monitoring:
At the bedside, haemodynamic monitoring can be approached in a series of steps aimed at assessing global and regional perfusion:

**Initial steps**
1. Clinical assessment
2. Basic monitoring and assessment of global perfusion
3. Preload monitoring and fluid responsiveness

**Advanced monitoring measures**
1. Cardiac output monitoring
2. Assessment of cardiac contractility
3. Assessment of tissue perfusion.

**Step 1: Clinical assessment**
A clinical examination is the fastest and least invasive haemodynamic monitor available. Cold extremities, poor peripheral pulses and impaired capillary refill are useful immediate indices of hypoperfusion. A patient with inadequate global perfusion often presents with one or several of these features: tachypnoea, tachycardia, confusion, toe to core temperature gap, altered skin perfusion and oliguria. We can at bedside easily monitor three areas for end organ perfusion:

1. **CRT: Capillary refill time** – Assessment of CRT is almost universally done by pediatricians particularly in emergency room, neonatal ICU and pediatric ICU setting. There seems little agreement on the methods described for carrying out this simple assessment amongst the practitioners who follow various practices. It seems best to follow the below mentioned method:
   i. “Pediatric Advanced Life Support Providers manual 2011” guide lines for eliciting CRT in children, which states To evaluate the CRT, lift the extremity slightly above the level of the heart, press on the skin, and rapidly release. A CRT of less than 2 is normal.
   ii. “The facility based IMNCI participants manual-2009” guidelines for eliciting CRT in young infants. To assess the child’s capillary refill, grasp the child’s thumb or big toe between finger and thumb. Look at the pink of the nail bed. Apply minimal pressure necessary for 3 s to produce blanching of the nail bed. Time the capillary refill from the moment of release until total return of the pink color. A CRT of less than 3 is considered normal.

2. **Urine Output** – Recognize acute kidney injury by AKIN staging in children

3. **Sensorium** - An awake, adequately talking patient is the best indicator of adequate cerebral perfusion. Careful attention should be made to detecting skin mottling. It has been shown to independently predict mortality in septic shock in adults (2). Mottling usually begins at the knees, and can be quantified according to a mottling score (scored 0-5, with a higher score correlating with increased mortality). High doses of vasopressors can make skin mottling more severe and lead to purpuric changes. (Figure 1)
Figure 1. Mottling Score
Score 0 = no mottling
Score 1 = small area of mottling, localised to centre of knee
Score 2 = modest mottling area that does not extend beyond superior border of kneecap
Score 3 = mild mottling area that does not extend beyond the mid-thigh
Score 4 = severe mottling area, not going beyond the groin fold
Score 5 = extremely severe mottling area, extending beyond groin fold

Step 2: Basic monitoring and assessment of global perfusion

Concept of upstream & downstream markers:
The concept of tissue dysfunction in shock, has led to the concept of “upstream” and “downstream” indicators of organ perfusion. Upstream markers assess flow and pressure in the heart, vena cava, pulmonary artery, and aorta. These are the traditional variables that have been used to assess the hemodynamic status of critically ill patients. However, shock with end-organ dysfunction occurs at the capillary and tissue levels. Tools have therefore been developed that follow alterations in the microvasculature of critically ill patients. These techniques are known as the “downstream” markers. Since patients’ oxygen and metabolic needs vary with different stressors and at different times, monitoring downstream variables can be helpful. The current concept is to use these downstream markers to ensure that interventions that alter upstream variables are improving tissue oxygenation. Downstream markers therefore provide a guide to upstream therapy.

1. **Upstream markers** include systemic blood pressure, heart rate, central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and cardiac output
2. Currently available **downstream markers** include urine output, blood lactate, base excess, tissue carbon dioxide levels, and mixed venous oxygen and carbon dioxide levels.

A. Blood Pressure
Blood pressure measurement is integral in the support of the critically ill patients. Cardiac output and systemic vascular resistance determine the mean blood pressure. *It is very important to remember that pressure does not equal flow.* When cardiac output falls, normal blood pressure is maintained by compensatory vasoconstriction causing high systemic vascular resistance. Hypotension is therefore a late sign of cardiovascular decompensation. Hence as clinicians one must not feel reassured by the presence of a normal blood pressure.

Non-invasive BP Monitoring (NIBP): The oscillometric technique is the most commonly used technique to measure arterial pressure. Mean arterial pressure (MAP) is most accurate by this method and diastolic pressure is the least accurate. The blood pressure readings are influenced by cuff size and placement and flow in the limb. Accurate blood pressure measurement requires the use of a proper sized cuff. Current recommendations require the use of a cuff that covers 40% of the mid upper arm circumference.

*The major limitations of NIBP are:*
- readings can be fallacious in presence of hypoperfusion or peripheral vasoconstriction
- It gives intermittent readings
- Accuracy of readings are dependent on appropriate cuff size and placement
Invasive hemodynamic monitoring: Invasive BP monitoring is considered the gold standard for arterial pressure monitoring in an ICU. It is indicated in situations where there is need for continuous, reliable BP recording along with the need for frequent arterial sampling. The BP measured by this method is unaffected by poor flow or perfusion in the limb(3). IBP is a relatively safe procedure. Some of the complications include hemorrhage, hematoma, arterial thrombosis, vasospasm, ischemia and infection.

- The equipment required for invasive BP monitoring includes an arterial cannula with a heparinized saline column and flushing device, a transducer, an amplifier, and a monitor. A continuous column of fluid from the blood vessel lumen to the transducer diaphragm transmits variations in intraluminal pressure; causing changes in resistance and current those are converted into an electrical signal, which is amplified to display a waveform and digital pressure on the bedside monitor. Disposable transducers have diaphragms that contain silicon crystals that undergo change in electrical resistance in proportion to the pressure applied to the diaphragm. The arterial pressure waveform is a complex sine wave that is a summation of a series of simple sine waves of different frequencies.

- Pressure is usually measured with a transducer, which is a device that coverts pressure in a fluid filled system to electric waveform. Three factors have to be considered when using a transducer: (1) calibration (2) zero setting and (3) leveling.

  - Calibration: In this process, a known pressure is applied to the membrane and change in current is related to the applied pressure. The precision and accuracy of arterial pressure system depends on meticulous calibration that must be carried out each shift.

- Zero setting: Why is zeroing important? The process of eliminating the atmospheric pressure is called “zeroing,” and what is essentially being done is opening the fluid column on the measuring device to atmosphere and adjusting the electronics so that atmospheric pressure is the starting value or zero.

- Leveling: Leveling eliminates the influence of hydrostatic pressure on the transducer. A transducer that is positioned below the patient’s heart will produce falsely elevated pressure and a transducer positioned above the patient’s heart will produce falsely low pressure. Pressure measurements in a fluid-filled system are relative to a reference point. A widely used reference point is the phlebostatic axis which corresponds to the midpoint of the right atrium, because this is where blood comes back to the heart and this is also the pressure that provides the preload for the heart as a whole. The phlebostatic axis is determined by the junction of the two lines, a transverse line along the fourth intercostals space and a vertical line midway between the anterior and posterior chest wall.

- The system should be arranged such that the reference stopcock of the transducer (that is opened for zeroing the transducer) must be leveled to the phlebostatic axis.

- Pressure versus Flow:

  - Clinicians caring for sick children must remember that BP and heart rate often do not reflect blood flow. The distinction between pressure and flow is very important. This is most commonly seen during use of vasoconstrictor agents in the management of clinical shock. In this setting, an increase in blood pressure is often assumed to indicate an increase in systemic blood flow, but the opposite effect (a decrease in flow) is also possible. Few pointers:

    - Check if system is optimally damped
      - Damping is the tendency of the oscillation to die down; anything that takes energy out of system dampens the system. (Figure 2, Table 1 & 2)

Figure 2: The arterial waveforms – normal, over damped and under damped waveforms.
Table 1: Characteristic of Underdamped Waveforms

<table>
<thead>
<tr>
<th>Nature of waveform</th>
<th>Effect on measurements</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrow, peaked tracing</td>
<td>Overestimates SBP, Underestimates DBP, MAP remains unchanged</td>
<td>Long tubing, Increased vascular resistance</td>
</tr>
</tbody>
</table>

With too much damping (an "overdamped" system), however, frictional forces impede the arterial waveform such that it loses energy. Note the widened and slurred waveform characteristic of an overdamped pressure waveform (Figure 2). This waveform tends to underestimate SBP and overestimate DBP (Table-2).

In both setting, mean arterial pressure (MAP) remains same, hence rely on MAP when system optimization is in doubt.

Table 2: Characteristic of Overdamped Waveforms

<table>
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<tbody>
<tr>
<td>Widened and slurred pressure tracing</td>
<td>Underestimates SBP, Overestimates DBP, MAP remains unchanged</td>
<td>Air bubbles, Overly compliant tubing, Blood clots / Fibrin, Catheter kinks, Stopcocks / Injection ports, No fluid in flush bag / Low flush bag pressure</td>
</tr>
</tbody>
</table>

Although damping seems to be a solely a theoretical issue, under damped and over damped waveforms are encountered on a daily basis during arterial pressure monitoring in the intensive care unit. The ability to recognize when these potential sources of error or "dynamic response artifacts" are present is essential to being able to effectively analyze and apply haemodynamic measurements in the care of the critically ill and avoid potentially detrimental therapy based upon erroneous data.

- **Damping can be checked by square wave test**
  A “fast-flush” or “square wave test” is performed by opening the valve of the continuous flush device such that flow through the catheter-tubing system is acutely increased to 30 mL/hr from the usual 1-3 mL/hr. This generates an acute rise in pressure within the system such that a square wave is generated on the bedside monitor. With closure of the valve, a sinusoidal pressure wave of a given frequency and progressively decreasing amplitude is generated.
  - Optimally damped - one to two oscillations before return to tracing
  - Underdamped – more than 2 oscillations before returning to tracing
  - Overdamped – less than 3 oscillations before returning to zero.

- **Check arterial waveform and interpret**

Figure 3. Arterial waveform
A wave = anacrotic limb  B wave = systolic pressure  
C wave = dicrotic notch  D wave = diastole

Figure 4. Changes of the arterial pressure waveform configuration throughout the arterial tree. Note the increasing steepness and amplitude of the systolic upstroke and the changing location of the dicrotic notch. This phenomenon is also called Distal pulse wave amplification.
- The farther into the periphery blood pressure is measured the waveform appears narrower, systolic and pulse pressure increase and the diastolic pressure decrease. But MAP always remains same.
- Systolic blood pressure variations seen in hypovolemia
- Steep slope of upstroke suggests good contractility
- Position of dicrotic notch – low (low systemic vascular resistance) and high (high afterload)
- Slope of decent – steep (low systemic vascular resistance) (Figure 3&4)

• Optimize natural frequency of system
- Use wide-bore, high-pressure tubing no longer than 122 cm (48 in)
- Avoid tubing extensions and minimize stopcocks
- Ensure that all connections are tightened
- Eliminate air from the fluid and air bubbles from the tubing system
- Keep continuous flush bag filled and keep external pressure cuff at 300 mm Hg pressure
- Keep cannulated extremity in a neutral or slightly extended position to prevent catheter kinking.

B. SpO2 monitoring
Continuous SpO2 monitoring enables almost immediate detection of even a small reduction in arterial oxygen saturation, which is an integral part of oxygen delivery. However, based on the sigmoid shape of the dissociation curve there is a time delay of the detection of acute oxygenation failure. Taking into account the shape of the O2 dissociation curve, SpO2 should be maintained >92% in most critically ill patients. The SpO2 signal is often inaccurate in the presence of altered skin perfusion. The inability to measure SpO2 is an indicator of abnormal peripheral perfusion.

C. Lactate
Blood lactate concentration is commonly used as a global “downstream” marker of tissue perfusion and the adequacy of resuscitation. The normal serum lactate level in resting humans is approximately 1 mmol/L (0.7-2.0). The value is the same whether measured in venous or arterial blood (in the absence of a tourniquet). Elevated serum lactate levels may represent poor tissue perfusion. The association of increased lactate levels with circulatory failure, anaerobic metabolism and the presence of tissue hypoxia have led to its utility as a monitor of tissue perfusion in critically ill patients.

Lactate metabolism
Lactate is a byproduct of glycolysis. In the energy producing metabolism of glucose two distinct processes occur. The first series of enzymatic reactions (Enoden-Mierhoff pathway), occurring in the cytoplasm of cells, anaerobically transforms 1 molecule of glucose into 2 molecules of pyruvate, generating 2 molecules of ATP. This is the primary energy process for all cells functioning in a low oxygen environment, such as in poorly perfused tissues. Pyruvate may either be converted to lactate, producing one additional molecule of ATP, or move into the second series of reactions. The second series of enzymatic reactions (Krebs cycle) takes place in the mitochondria and requires oxygen: pyruvate is oxidized into CO2 and H2O producing 18 ATP molecules. In the absence of oxygen, pyruvate cannot enter the Krebs cycle and is preferentially transformed into lactate to maintain ATP production. This causes the lactate to pyruvate ratio to increase (normal ratio 10/1). Once molecular oxygen is again available, assuming that mitochondrial function is preserved, the excess lactate is rapidly metabolized back through pyruvate into CO2 and H2O via the Krebs cycle. Some cells, such as red blood cells, do not have mitochondria and thus are primary lactate producers. Since lactate is rapidly metabolized by liver and skeletal muscle, these functional anaerobic cells result in minimal blood lactate levels.

Lactate in the blood is metabolized mainly by the liver (50%) and kidneys (20%). Liver function and liver blood flow influence hepatic lactate clearance, but extreme conditions of pH can also decrease lactate clearance.

Types: Hyperlactaemia (>5 mmol litre−1) is conventionally divided into
Type A, in which tissue hypoxia results in faster production than removal
Type B, in which overt tissue hypoxia does not play a role. Type B has been further sub-divided depending on whether it is caused by underlying disease (B1), drugs and toxins (B2) or inborn errors of metabolism (B3).

Factors that may contribute to hyperlactataemia:
• Increased production of lactate: tissue hypoxia
• Increased aerobic glycolysis
• Inhibition of pyruvate dehydrogenase (in sepsis)
• Methanol/ethylene glycol/propofol toxicity
• Decreased clearance of lactate: liver dysfunction or failure, cardiopulmonary bypass (minor reduction in clearance)
• Acute hyperventilation can elevate blood lactate levels, perhaps secondary to increased splanchnic release of lactate during hyperventilation
• Exogenous sources of lactate:
  • Lactate buffered solutions used in continuous veno-venous haemodiafiltration (CVVHDF)
  • Medications (metformin, nucleosidic reverse transcriptase inhibitors, long-term linezolid use, intravenous lorazepam, valproic acid)
  • Haematologic malignancies.

While an elevated lactate may be a marker of illness severity and an important prognostic marker, this variable has not been studied as an end point of resuscitation. Lactate clearance lags by many hours following therapeutic interventions and is therefore not suited for goal-directed resuscitation. But, the rate of lactate clearance has been demonstrated to be a good marker of outcome (4).

D. Venous Oximetery

Oxygen saturation of the venous blood can be measured either at the level of the pulmonary artery: mixed venous oxygen saturation (SvO2), the level of the inferior vena cava, superior vena cava, or right atrium (RA); central venous oxygen saturation (ScVO2). Although hemodynamic assessment using clinical signs and symptoms, CVP, and urinary output can fail to detect early septic shock, tissue hypoxia suggested by ScVO2 or SVO2, and arterial blood lactate concentration can be an early marker of sepsis or marginal circulation. It is important, however, to remember that venous oxygen saturation like cardiac output is a marker of global tissue hypoxia and does not yield information on oxygen reserves or adequate tissue oxygenation of individual organs.

Physiology of mixed venous oxygen saturation
The transport system for oxygen is separated into 4 compartments:

• Blood oxygen content
• Oxygen delivery
• Oxygen consumption from the microcirculation
• Oxygen extraction ratio

Oxygen content The oxygen carried in arterial blood (CaO2) is in 2 forms:
Dissolved in plasma PO2 - <2%
Combined with hemoglobin SO2 - >98%.

Oxygen saturation is the ratio of the amount of oxygenated hemoglobin to the total hemoglobin in 100 ml of blood.

\[ \text{SaO2} = \frac{\text{HbO2} \times 100}{\text{Hb} + \text{HbO2}} \]

Oxygen saturation in arterial blood is normally 95 - 98% (ie nearly 98% of the heme groups in the hemoglobin are loaded with oxygen) whereas the saturation of venous blood is typically 60 - 80%. SvO2 is an averaged reflection of the saturation of venous blood from various organs. As a result it does not give indication of adequacy of oxygenation of individual vascular bed rather; it is global indicator of oxygen balance between oxygen consumption (VO2) and its delivery (DO2). Generally, the tissues utilise approximately 25% of the available oxygen leaving a luxury reserve of 75% for periods of increased requirements. Since >98% of all the circulating oxygen is bound to haemoglobin, oxyhaemoglobin saturation is a direct indicator of the oxygen content of blood.

\[ \text{CaO2} = (0.003 \times \text{PaO2}) + (1.34 \times \text{Hb} \times \text{SaO2}) \]

0.003 - solubility coefficient of oxygen in plasma - this fraction is negligible and insignificant 1.34 mls oxygen carried / gm of Hb

Note:
Changes in hemoglobin have a larger impact on arterial oxygenation than changes in PaO2
Hypoxemia (reflected by a decrease in PaO2) has a relatively minor impact on arterial oxygenation if the accompanying change in SaO2 is small. PaO2 influences oxygenation only to the extent that it influences saturation, depending on the position on the oxygen dissociation curve.

Oxygen delivery (DO2)
This is the amount of oxygen delivered to the tissues every min (ml/min) O2 delivery is
dependent on 2 factors - oxygen content of arterial blood and the blood flow to tissues as reflected by the cardiac output (Q).

\[ \text{DO2} = \text{CaO2} \times Q = (1.34 \times \text{Hb} \times \text{SaO2}) \times Q \]

In this analogy, the blood is compared to a train (Figure 5) consisting of boxcars (hemoglobin molecules). These boxcars have been filled (saturated) with a valuable product (oxygen) at the loading station (the lungs).

**Figure 5. Oxygen Delivery explained in analogy**

**Oxygen consumption (VO2)**

As the train progresses along the track, it stops at multiple depots. A portion of the product carried by the train is unloaded at each of these depots. Similarly, as blood flows from the left ventricle through the capillaries, oxygen is needed to meet the metabolic needs of the tissues. The difference between the amount of oxygen carried to the tissues (arterial oxygen delivery) and the amount of oxygen returned to the heart (venous oxygen delivery) indicates the total amount of oxygen consumed by the tissues (Figure 6). Mixed venous oxygen saturation reflects the amount of oxygen returning to the pulmonary capillaries, since it was not needed by the tissues to support metabolic function.

**Figure 6. Oxygen transport & consumption**

SvO2 represents the end result of both oxygen delivery and consumption at the tissue level.

\[ \text{SvO2} = \text{Oxygen Delivered} - \text{Oxygen Consumed} \]

\[ \text{SvO2} = (\text{SaO2}, \text{Hb}, \text{CO}) \times (\text{VO2}) \]

When a threat to normal oxygen supply/demand occurs, the body attempts to compensate, and its success is immediately reflected by SvO2. If the SvO2 value is normal, there is sufficient oxygen supply available to the tissues. However, if the SvO2 value is low, then either the oxygen supply is insufficient or the oxygen demand is elevated (Table 3 & 4). Regardless of the cause, a decrease in SvO2 indicates that the body has called upon its one of the last line of defense to preserve oxygen balance and therapeutic interventions may be appropriate.

**Oxygen Extraction ratio (O2 ER)**

The ratio of O2 uptake to O2 delivery, it is the fraction of oxygen delivered to the microcirculation that is taken up by the tissues.

\[ \text{O2 ER} = \frac{\text{VO2}}{\text{DO2}} \]

Normally 0.2 - 0.3 or 20 - 30 %, only this small a fraction is required to support aerobic metabolism under normal circumstances i.e. 25% of delivered oxygen and thus theoretically has a reserve of 75% oxygen. (Normal oxygen flux is 1000 ml and the oxygen consumption is 250 ml) However 100% oxygen extraction is not possible and beyond SvO2 of 30%, anaerobic metabolism will start. The fall or rise in SvO2 can be due to increased demands or decreased supply or increased supply or decreased demand respectively. Table 3 lists the clinical conditions in which these changes in SVO2 are likely to occur.
Table 3. Clinical conditions and their effects on O2 delivery and O2 consumption and on venous oximetry

<table>
<thead>
<tr>
<th>Decrease in SvO2/ScvO2</th>
<th>Increase in SvO2/ScvO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>O2 consumption ↑</td>
<td>O2 delivery ↓</td>
</tr>
<tr>
<td>O2 consumption ↓</td>
<td>O2 delivery ↑</td>
</tr>
<tr>
<td>Stress pain</td>
<td>Analgesia</td>
</tr>
<tr>
<td>hyperthermia</td>
<td>sedation</td>
</tr>
<tr>
<td>shivering</td>
<td>mechanical ventilation</td>
</tr>
<tr>
<td>anemia</td>
<td>hypoxia</td>
</tr>
<tr>
<td>low CO</td>
<td>hypothermia</td>
</tr>
<tr>
<td>high CaO2</td>
<td>high CO</td>
</tr>
<tr>
<td>high CO blood</td>
<td>transfusion</td>
</tr>
<tr>
<td>blood transfusion</td>
<td>maintain MAP</td>
</tr>
</tbody>
</table>

During exercise SvO2 normally decreases despite increasing DO2. Therefore a drop in SvO2 or ScvO2 does not necessarily mean that tissue hypoxia occurs. The magnitude of the decrease indicates the extent to which the physiological reserves are stressed. In healthy individuals, anaerobic metabolism may occur when SvO2 drops below 48%, its normal value of 75% to 30–40%, table 4 lists the correlation between values of mixed venous oxygen saturation status of oxygen supply and demand.

Table 4. Limits of SvO2 (& ScvO2) and clinical correlates

<table>
<thead>
<tr>
<th>SvO2 Value</th>
<th>Clinical Correlate</th>
</tr>
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<tbody>
<tr>
<td>SvO2 &gt;75%</td>
<td>Normal extraction, O2 supply &gt;O2 demand</td>
</tr>
<tr>
<td>75% &gt;SvO2 &gt;50%</td>
<td>Compensatory extraction, Increasing O2 demand or decreasing O2 supply</td>
</tr>
<tr>
<td>50% &gt;SvO2 &gt;30%</td>
<td>Exhaustion of extraction, Beginning of lactic acidosis O2 supply &lt;O2 demand</td>
</tr>
<tr>
<td>30% &gt;SvO2 &gt;25%</td>
<td>Severe lactic acidosis</td>
</tr>
<tr>
<td>SvO2 &lt;25%</td>
<td>Cellular death</td>
</tr>
</tbody>
</table>

What is the relationship is between the (ScvO2) and (SvO2), and can ScvO2 be substituted for SvO2? The problems with the use of mixed venous oximetry as a monitoring tool or as a therapeutic goal are: obtaining SvO2 needs insertion of a pulmonary artery catheter which requires particular skill, a lot of time and may be associated with complications. On the other hand, central venous catheter insertion is part of standard management of most critically ill patients, is an essential skill for the intensivist, and can be done rapidly. The tip of the central venous catheter usually lies at the junction of the superior vena cava and the right atrium or in the superior vena cava. The sample drawn from here represents not the mixed venous blood but the venous blood from upper body and neglects blood from the lower body. In normal conditions, the blood in inferior vena has higher oxygen saturation than that in superior vena cava. This is because of lower O2 extraction in many vascular circuits draining in the inferior vena cava, as these organs use blood flow for nonoxidative phosphorylation needs (e.g., renal blood flow, portal flow, hepatic blood flow). A normal value for SvO2 is in the range of 70-80%. Thus ScvO2, in normal individuals, is usually lower by 2-3% than the SvO2. This relationship changes during periods of cardiovascular instability. Figure 7 shows normal arterial and venous oxygen saturations in various vascular beds. In pathologic states, such as severe sepsis, circulatory shock, cardiogenic shock, heart failure, etc, the blood flow to the vital organs, including the brain and heart, is maintained. At the same time, there is decreased blood flow to the kidneys and splanchnic circulations. This reduced blood flow also results in increased oxygen extraction in the splanchnic circulation. This causes a decrease in the oxygen saturation of blood that is returning from the lower body (IVC), and results in ScvO2 being greater than SvO2. While monitoring ScvO2 thus, if there is a fall in SCvO2, this suggests even lower values of SvO2. The absolute values of SvO2 and ScvO2 may differ, however the changes in SvO2 are accompanied by parallel changes in ScvO2.

Figure 7. Arterial and Venous oxygen saturation in various vascular organs
Clinical utility of mixed venous saturation:
In the clinical setting, a decrease in SvO$_2$ of 5% from its normal value (65%-77%) represents a significant fall in DO$_2$ and/or an increase in O$_2$ demand. The ScVO$_2$ can be used in 2 ways:
1. Relating the absolute ScVO$_2$ value to the OER (eg, a low ScVO$_2$ value [< 70%] accompanied by a high OER [> 0.25] could indicate relatively low CO)
2. Changes in ScVO$_2$ might guide hemodynamic therapy, although it is difficult in hyperdynamic conditions (5).

In adult patients with sepsis, restoring ScVO$_2$ to > 70% might improve outcome (6). This might also be true for children with septic shock(7). Unfortunately, studies in septic adults have shown that many patients already have a ScVO$_2$ value of> 70% at the start of therapy, although they might still need hemodynamic improvement.

At present, the additional value of ScVO$_2$ measurement in pediatric clinical practice is not clear. Nevertheless, ScVO$_2$ monitoring is already incorporated in the surviving sepsis campaign algorithm for both adults and children. If ScVO$_2$ is used, it should preferably be combined with CO measurement or markers of insufficient oxygen perfusion such as lactate levels.

Note: Occasionally, normal or increased SvO$_2$ values are observed in a patient, who, by all other criteria, demonstrates compromised tissue oxygenation. Three etiologic mechanisms have been postulated for this observation: arterial admixture, abnormalities in distribution of blood flow, and histotoxic hypoxia.

Step 3: Preload and fluid responsiveness
In the presence of hypotension, an important step is the assessment of preload and fluid responsiveness. Preload is defined as end-diastolic myocardial stretch (wall tension) and is often estimated at the bedside by a single/static measurement e.g. central venous pressure, CVP. More recently, assessment of fluid responsiveness (e.g. pulse pressure variation PPV, systolic pressure variation, SPV) has been utilised in the care of critically ill patients. (Figure 9)

Clinically, preload may be separated into right ventricular (RV) and left ventricular (LV) preload. Jugular venous pressure (JVP) and CVP are used as surrogate estimates of RV preload. Pulmonary artery occlusion pressure (obtained using pulmonary artery catheter, see below) is used as a surrogate estimate of LV preload. Dynamic measures such as SPV are more accurate than static measurements for assessing fluid responsiveness in mechanically ventilated patients. In simple terms, assessing fluid responsiveness asks the question: will the cardiac output increase with fluid administration? The principle behind dynamic measures is that swings in intrathoracic pressure, imposed by mechanical ventilation, affect venous return and as a consequence cardiac output (8). These swings in cardiac output are exaggerated in hypovolaemia indicating that the heart is operating on the ascending limb of the Frank-Starling (FS) curve (Figure 8).

Figure 8 Frank-Starling relationship: Once the ventricle is functioning on the steep part of the Frank-Starling curve, there is a preload reserve. Volume expansion (VE) induces a significant increase in stroke volume. The pulse pressure (PPV) and stroke volume (SVV) variations are marked and the passive leg raising (PLR) and end-expiratory occlusion (EEO) tests are positive. By contrast, once the ventricle is operating near the flat part of the curve, there is no preload reserve and fluid infusion has little effect on the stroke volume. There is a family of Frank-Starling curves depending upon the ventricular contractility.
Central Venous Pressure

Central venous pressure is the intravascular pressure in the great thoracic veins, measured relative to atmospheric pressure. It is conventionally measured at the junction of the superior vena cava and the right atrium and provides an estimate of the right atrial pressure.

Interpretation of central venous pressure

Normal mean CVP is 5 to 3 mm Hg. Clinicians often assume that low values indicate hypovolemia and high values indicate hypervolemia or heart failure. However, isolated single CVP measurements are of limited utility. Instead, trends in CVP measurement over time or changes in CVP in response to therapy are better indicators of a patient's intravascular volume status. For example, a rapid fluid bolus (eg, 500 mL) administered to a hypovolemic patient with good ventricular function will increase CVP minimally (1-2 mm Hg), with a return to baseline within 10 to 15 minutes due to circulatory reflexes and stress relaxation of the vessels. The combination of a minimal rise in CVP and an associated increase in arterial blood pressure indicates a “volume-responsive” patient who may be hypovolemic.

In contrast, the same fluid bolus given to a patient who responds with a large increase in CVP without an accompanying improvement in blood pressure, suggests that additional volume loading is not indicated. Therefore, under most clinical circumstances, a trend in CVP values or its change with therapeutic maneuvers is more reliable than a single measurement. CVP is measured in the superior vena cava close to the right atrium, and for clinical purposes is assumed to equal right atrial pressure and right ventricular end-diastolic pressure. This pressure is monitored as a surrogate for right ventricular filling volume, which is proportional to muscle fiber length or preload, the major determinant of stroke output of the right ventricle for any given level of contractility. When using a filling pressure, such as CVP, as a surrogate for estimating cardiac volume, one must take into consideration several points:

- The diastolic-pressure–volume relationship in cardiac muscle is not linear, but rather curvilinear, with a progressively steeper slope at higher volumes.
- Ventricular compliance may change independent of end-diastolic volume (eg, as a consequence of ischemia). The same effective preload may be represented by two different CVP values if...
ventricular compliance changes (Figure 10).

- CVP measurements are referenced to atmospheric pressure, but physiologically, it is transmural pressure (the difference between intracardiac and intrathoracic-extracardiac pressure) that determines ventricular preload. Increased intrathoracic or high intrapericardial pressure (e.g., high positive end-expiratory pressure levels, cardiac tamponade, large pleural effusion) may attenuate venous return but, at the same time, paradoxically increase measured CVP (Figure 11).

In summary, changes in CVP over time or in response to fluid administration are more useful clinically than reliance on absolute numeric values. Central venous pressure must be considered to be the result of the complex interaction between intravascular volume status, ventricular compliance, and intrathoracic pressure.

Normal central venous pressure waveform morphology

The CVP has three prominent positive waves: the ‘a,’ ‘c,’ and ‘v’ waves and two prominent negative waves, the ‘x’ and ‘y’ descents. The ‘a’ wave is due to atrial contraction, the ‘c’ wave is due to the backward buckling of the tricuspid valve at the onset of systole, and the ‘v’ wave is due to atrial filling during diastole. The ‘x’ descent is due to the fall in atrial pressure during relaxation of the atrial contraction. The ‘y’ descent is due to the sudden decrease in atrial pressure at the onset of diastole when the atrioventricular valve opens and allows the atrium to empty into the ventricle. (Table 5)

Table 5. Central Venous Pressure Waveform Components

<table>
<thead>
<tr>
<th>Waveform Component</th>
<th>Phase of Cardiac Cycle</th>
<th>Mechanical Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>a wave</td>
<td>End diastole</td>
<td>Atrial contraction</td>
</tr>
<tr>
<td>c wave</td>
<td>Early systole</td>
<td>Isovolumic ventricular contraction, tricuspid motion toward the right atrium</td>
</tr>
<tr>
<td>v wave</td>
<td>Late systole</td>
<td>Systolic filling of the atrium</td>
</tr>
<tr>
<td>h wave</td>
<td>Mid to late diastole</td>
<td>Diastolic plateau</td>
</tr>
<tr>
<td>x descent</td>
<td>Mid systole</td>
<td>Atrial relaxation, descent of the base, systolic collapse</td>
</tr>
<tr>
<td>y descent</td>
<td>Early diastole</td>
<td>Early ventricular filling, diastolic collapse</td>
</tr>
</tbody>
</table>

Electronic measurement of central venous pressure

Prominent ‘a’ and ‘v’ waves raise the question where one should make the measurement on the tracing: at the top of the waves, the bottom, or the middle (Figure 12). As in all pressure measurements, there is an arbitrariness of the measurement; however, the

Figure 10. Pressure–volume relationship in a ventricle with normal or abnormal compliance. When ventricular compliance is normal, a 20-mL increase in right ventricular end-diastolic volume (RVEDV) produces a 2-mm-Hg rise in CVP (point A to point B) when RVEDV is 80 mL, but an 8-mm-Hg rise in CVP (point B to point C) when RVEDV is 100 mL. When ventricular compliance changes, as with ischemia or ventricular hypertrophy, higher filling pressures are required to generate the same RVEDV (point A to point D).

Figure 11. CVP changes during positive-pressure mechanical ventilation. Mean CVP increases at onset of each positive-pressure breath (arrows), but venous return decreases when the measured CVP increases.

Figure 12: Normal CVP and its temporal relationship to the ECG.
most common reason for assessing CVP is likely the assessment of cardiac preload. For this purpose, the best place for the measurement is the ‘z’ point, which is at the leading edge of the ‘c’ wave, for this gives the final pressure in the atrium and thus the ventricle just before ventricular contraction. This value is often not easy to identify, however, in which case it can be closely approximated by the base of the ‘a’ wave.

Although three distinct CVP peaks (a, c, v) and two troughs (x, y) are discernible in the normal venous pressure trace, heart rate changes and conduction abnormalities alter this pattern. A short ECG PR interval causes fusion of the a and c waves, and tachycardia reduces the length of diastole and the duration of the y descent, which causes the v and a waves to merge. In contrast, bradycardia causes each wave to become more distinct, with separate x and x' descents visible and a more prominent h wave. Although there are circumstances in which other pathologic waves may be evident in the CVP trace, one should resist the temptation to assign physiologic significance to each small pressure peak because many will arise as artifacts of fluid-filled tubing-transducer monitoring systems. It is more useful to search for the expected waveform components, including those characteristic of the pathologic conditions suspected (Table 6).

### Table 6. Central Venous Pressure Waveform Abnormalities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>Loss of a wave</td>
</tr>
<tr>
<td></td>
<td>Prominent c wave</td>
</tr>
<tr>
<td>Atroventricular dissociation</td>
<td>Cannon a wave</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>Tall systolic c-v wave</td>
</tr>
<tr>
<td></td>
<td>Loss of x descent</td>
</tr>
<tr>
<td>Tricuspid stenosis</td>
<td>Tall a wave</td>
</tr>
<tr>
<td></td>
<td>Attenuation of y descent</td>
</tr>
<tr>
<td>Right ventricular ischemia</td>
<td>Tall a and v waves</td>
</tr>
<tr>
<td></td>
<td>Steep x and y descents</td>
</tr>
<tr>
<td></td>
<td>M or W configuration</td>
</tr>
<tr>
<td>Pericardial constriction</td>
<td>Tall a and v waves</td>
</tr>
<tr>
<td></td>
<td>Steep x and y descents</td>
</tr>
<tr>
<td></td>
<td>M or W configuration</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>Dominant x descent</td>
</tr>
<tr>
<td></td>
<td>Attenuated y descent</td>
</tr>
<tr>
<td>Respiratory variation during</td>
<td>Measure pressures at</td>
</tr>
<tr>
<td>spontaneous or positive-pres-</td>
<td>end-expiration</td>
</tr>
<tr>
<td>sure ventilation</td>
<td></td>
</tr>
</tbody>
</table>

### Utility of CVP to Predict the Volume Responsive Patient

During the optimization of cardiovascular function, an important decision is whether to attempt to increase cardiac output by giving additional fluid or whether to administer inotropic drugs. A desirable characteristic, therefore, of any index of preload is that it should be able to predict whether or not the heart is fluid responsive, i.e., whether a further increase in preload will result in an increase in stroke volume. The majority of studies of the predictive value of CVP for fluid responsiveness have been unable to demonstrate a relationship between the baseline CVP and the response to filling; those studies where a relationship between low CVP and fluid responsiveness has been demonstrated found such an overlap of CVP values between the responder and non-responder groups that to threshold value which would discriminate between the two groups could be determined. Patients can be volume limited at CVP values as low as 2 mm Hg (based on sternal angle referenced values), whereas others may respond at CVP values greater than 18 mm Hg. We recently found that 40% of patients with a CVP below 6 mm Hg did not respond to fluids. Use of CVP measurements to assess whether or not a patient’s cardiac output will increase significantly in response to an infusion of intravenous fluid cannot therefore be recommended.

### Dynamic Changes in CVP

Recently there has been interest in using the dynamic changes in CVP with respiration to predict fluid responsiveness. Two studies from the same group [23, 24], both involving spontaneously breathing patients, have shown that an inspiratory fall in CVP by ≥ 1 mmHg is highly predictive of a fluid responsive cardiac index (9).

#### ‘y’ descent

Another indicator that there will not be an increase in cardiac output with a volume infusion is the magnitude of the ‘y’ descent. Although the number of patients was small, we found that a ‘y’ descent greater than 4 mmHg indicated that there would be no increase in cardiac output in response to fluid infusion. An explanation is that the ‘y’ descent is due...
to emptying the atrial volume during early diastole, and a steep fall means that volume must have started on the steep part of the diastolic pressure–volume curve (10)

**Hepatojugular reflux**

Another useful test is the hepatojugular reflux. The application of pressure to the abdomen can increase the return function and increase CVP. If the heart is functioning on the ascending portion of the cardiac function curve, the increase in preload will increase cardiac output, and the CVP will return to baseline in less than 10 seconds. If the heart is functioning on the flat part of the function curve, however, the rise in CVP will be sustained. This test thus indicates a limitation function of the right side of the heart(11)

**Pulmonary artery pressures**

Though the CVP is a reasonable measure of right ventricular preload, its utility in clinical care has been limited by the concern that it may not be a true reflection of left ventricular performance. As a consequence, with the emergence of technology that allows pulmonary artery catheterisation at the bedside, there has been increasing use of right heart pressures and more importantly of the PAoP to evaluate left ventricular preload. The Swan-Ganz pulmonary artery catheter, which has been in clinical use since 1970, is a flow-directed, balloon floatation catheter that is placed without radiographic assistance in the intensive care unit. Access is obtained via the internal jugular, subclavian or femoral vein.

Why are filling pressures inaccurate measures of preload?

The lack of correlation between measured CVP and PAoP on the one hand and diastolic volume and fluid-responsiveness on the other, springs from a multitude of causes. Broadly they fall in one of two categories; those affecting the reliable measurement of these pressures and those related to the physiological assumptions made in measuring these pressures.

**a. Factors limiting reproducible measurement**

Inaccuracies in measuring low pressures: One of the major issues in using fluid filled transducing systems for the measurement of low pressures like the CVP and PAoP is the need to filter out all hydrostatic errors. Accurate levelling of the transducer after zeroing to the atmosphere is crucial. A small shift of 1.36 cms in the levelling of the transducer can alter the measured pressure by 1 mm Hg, which is quite relevant in the range of values being measured. (Figure 12)

There seems to be confusion even amongst researchers about the physical principles underlying the measurement of pressures with fluid filled external transducers especially in reference to the importance of levelling to the top of a fluid column and the irrelevance of the relative position of the catheter tip. Based on these considerations one recent recommendation suggests “that in the routine clinical setting external transducers be positioned approximately 5 cm below the left sternal border at the fourth intercostal space” (“H” in Figure 12). It is also important to recognise that the external landmarks are best identified in supine patients. Lateral rotation of the patients, as is often done in the ICU, confounds accurate and reproducible identification of appropriate levelling landmarks

Pleural pressure: Ventilation, spontaneous or mechanical, can cause significant changes in the pleural pressure (Ppl) that can influence the measurement of vascular pressures. In order to annul the effect of these swings of Ppl, vascular pressures are measured at end exhalation (atmospheric pressure). This would be represented as the highest point in the pressure tracing during a spontaneous breathing cycle and as the lowest point during positive pressure ventilation. Unfortunately this point is far more difficult to measure in tachypneic patients with expiratory muscle recruitment either on the ventilator or during spontaneous breathing. Sedation to minimise patient effort or maintenance of a
mechanical rate high enough to override spontaneous breathing will allow better identification of the end-expiratory point in critically ill patients.

**b. Failure of assumptions** Besides the factors that may result in mismeasurement of vascular pressures, the poor correlation of CVP and PAoP with other estimates of preload is probably due to the lack of robustness of the physiological assumptions we make prior to measuring these pressures. Inter-individual differences may further confound the interpretation of CVP and PAoP.

In conclusion for static pressure indices, it is wrong to believe that the CVP and PAoP are foolproof measures of preload, as there are many limitations to accurate measurement. A full understanding of limitations will minimize errors in estimation and interpretation and allow these parameters to be used more effectively in clinical practice.

**Dynamic indices for preload assessment**

If absolute measures of cardiovascular values cannot be used effectively as parameters describing cardiovascular status or responsiveness, then more provocative maneuvers need to be employed to improve the utility of these measures. Cavallaro has proposed a useful classification of dynamic indices that predict volume responsiveness (8).

- **Group A** consists of indices based on cyclic variation in SV or SV-related hemodynamic parameters determined by mechanical ventilation induced cyclic variation in intrathoracic pressure, and includes such metrics as pulse pressure variation (PPV), its derivatives, and aortic blood flow.

- **Group B** is made up of indices based on cyclic variations of non-stroke volume-related hemodynamic parameters determined by mechanical ventilation, and includes vena cava diameter or ventricular pre-ejection period.

- **Group C** consists of indices based on preload redistribution maneuvers; mechanical ventilation is not required, and group C includes passive leg raising and Valsalva maneuvers.

Group A and B techniques are based on the physiologic interaction of the heart and lungs within a closed thoracic cavity, and rely on the phasic changes in SV created by changing intrathoracic pressure due to positive pressure mechanical ventilation. During positive pressure inspiration, preload to the right heart is decreased because of increased intrathoracic pressure, both from compression of the vena cava (decreased venous return) and increased right atrial pressure. This decrease in right ventricular (RV) preload leads to a decrease in RV output, which subsequently leads to a decrease in pulmonary artery blood flow, LV filling, and LV output. Other mechanisms postulated to increase LV SV variation with PPV include the following changes during inspiration, caused by increased transpulmonary pressure:

  - Increased RV afterload
  - Increased LV preload
  - Decreased LV afterload.

The end result of these pressure changes is that LV SV increases, while RV SV decreases during positive pressure inspiration. The delay of pulmonary blood transit time results in decreased RV SV translating to a decreased LV SV a few heartbeats later (ie, usually during expiration). These phasic differences are exaggerated in the setting of hypovolemia for several reasons:

  - The underfilled vena cava is more collapsible
  - The underfilled right atrium is more susceptible to increased intrathoracic pressure

More of the lung demonstrates the physiology of West Zones 1 and 2 (in West Zone 1 the alveolar pressure is greater then the arteriolar pressure, which is greater than venous pressure; in West Zone 2 the arteriolar pressure is greater than alveolar pressure, which is greater than venous pressure), which effectively increases RV afterload. Larger changes are seen when operating on the steeper portion of the Frank-Starling curve. This increased variation in pressures between the inspiratory phase and the expiratory phase can be used to identify hypovolemia and volume responsiveness, and is the basis for Cavallaro’s group A and B indices, including stroke volume variation (SVV) and pulse pressure variation.

**Stroke Volume Variation**

SVV examines the difference between the SV during
the inspiratory and expiratory phases of ventilation, and requires a means to directly or indirectly assess SV. This eliminates arterial compliance as a variable, but until recently, has required invasive monitoring such as aortic flow probes. Now, the PiCCO (Pulsion Medical Systems, Germany), LiDCCO (LiDCCO Group PLC, England) and FloTrac sensor (Edwards Lifesciences, USA) monitors uses pulse contour analysis through a proprietary formula to measure cardiac output and SVV. SVV of ≥10% has also been shown to be a specific and sensitive predictor of fluid responsiveness.

Systolic Pressure Variation (Figure 13)

Systolic pressure variation (SPV) is the difference between the maximum and the minimum systolic pressure over a single respiratory cycle and can be expressed in millimeters of mercury (SPmax - SPmin) or as a percent SPV(%) = 100 X (SPmax - SPmin)/ [(SPmax + SPmin)/2]). Increased SPV was the first of these indices to be recognized to correlate with hypovolemia and was later shown to have a sensitivity of 82%, specificity of 86%, and area under the receiver operator characteristic (ROC) curve (AUC) of 0.92, using a threshold of 8.5 mm Hg. SPV can be broken down into delta up (dUp) and delta down (dDown). These two components are calculated using a reference systolic pressure measured during an end–expiratory pause according to the following equations:

dUp = SPmax - SPref

dDown = SPref - SPmin

where SPmax is the maximum systolic pressure in a single respiratory cycle; SPref is the reference systolic pressure at end–expiration, and SPmin is the minimum systolic pressure measured in a single respiratory cycle. dUp reflects the inspiratory increase in systolic pressure, resulting from an increase in extramural aortic pressure (increase in diastolic pressure) and an increase in LV SV. As the extramural aortic pressure component seems more significant in many patients, increased dUp is not a reliable indicator of fluid responsiveness. dDown reflects the expiratory decrease in LV SV related to the inspiratory decrease in RV SV.

Pulse Pressure Variation (Figure 14)

Arterial pulse pressure is the difference between arterial systolic and diastolic pressure. This difference is influenced by SV and the arterial compliance. Comparison of the pulse pressure during inspiration with pulse pressure during expiration demonstrates the degree to which the pulse pressure is preload-limited. As comparison is being made during a single respiratory cycle, change in arterial compliance theoretically should be minimal. Prerequisites for the adequate use of PPV include sinus rhythm, absence of spontaneous ventilatory effort (sedated), absence of right heart failure and a tidal volume ≥8 mL/kg. Analysis of the PPV thus can be used to predict volume responsiveness, and is expressed as a percentage:

\[ PPV(\%) = 100 \times \frac{(PP_{max} - PP_{min})}{(PP_{max} + PP_{min})/2} \]

A PPV of ≥13% has been shown to be a specific and sensitive indicator of preload responsiveness (12).
Respiratory variability of the superior and inferior vena cava

The inferior and superior venae cavae are distensible blood vessels whose diameters and flow vary with respiration. These variations are reflected by changes in aortic flow within a few beats of the heart.

In PPV, the increase in pleural pressure is transmitted fully to the right atrium, and partially transmitted to the abdomen via depression of the diaphragm, causing an overall increase in transmural pressure of the IVC. Because the IVC is distensible, this increase in pressure causes an increase in diameter of the IVC. Unlike the IVC, the course of the SVC is mainly intrathoracic. Positive pressure ventilation then should cause a decrease in transmural pressure, and subsequent decrease in the diameter of the SVC, especially in hypovolemic patients.

Barbier and colleagues determined that the distensibility index of the IVC (dIVC), defined as (Dmax - Dmin)/Dmin and expressed as a percentage, was predictive of fluid responsiveness with a sensitivity of 90% and a specificity of 90%. They concluded that a dIVC above 18% was predictive of an increase in cardiac index of at least 15% with fluid loading(13). Viellard-Baron studied the effect of PPV on the SVC and the ability to predict volume responsiveness. They studied 66 mechanically ventilated patients in septic shock with acute lung injury. An SVC collapsibility index (maximum diameter on expiration – minimum diameter on inspiration) threshold of 36% allowed discrimination between non-responders and responders with sensitivity of 90% and specificity of 100%(14).

Cautions Regarding Cavallaro Group A and B Indices

There are several important caveats to keep in mind when using these dynamic indices to predict fluid responsiveness:

- Positive pressure, controlled ventilation is required to obtain meaningful values for any of the Cavallaro group A or B indices. Spontaneous respiratory efforts, even when supported by the ventilator, alter the mechanics such that these numbers lose their reliability.
- Sinus rhythm is required. Arrhythmia or frequent extra systoles result in altered SV and invalidate these tools to predict volume responsiveness.
- Many of these techniques require invasive arterial blood pressure monitoring with a catheter, and as such, they are prone to the same errors in measurement associated with invasive blood pressure monitoring: air bubbles in the catheter tubing, excessive tubing length, kinks in the tubing, excessively compliant tubing, and other errors.
- A single value never should replace clinical judgment. A high PPV value in a normotensive patient with evidence of normal tissue perfusion does not mean that person requires volume expansion.
- Further investigation of these techniques in the setting of vasoactive medications is needed.
- How extremes of ventilation (ie, low tidal volume, high respiratory rate, high positive end-expiratory pressure [PEEP]) affect group A and B indices is not yet clear. Most of the early data came from patients ventilated with at least 10 mL/kg tidal volumes.

Passive Leg Raising (gure 15)

Passive leg raising (PLR) is a form of reversible volume challenge that can be used to evaluate which patients will benefit from intravenous fluid and increased preload. Elevating a patient’s legs allows a passive transfer of blood from the lower part of the body toward the central circulation. The amount of blood transferred from the legs is variable and has been estimated to be between 150 to 750 mL (equivalent approximately to 4.3 ml/kg) depending on technique and patient. Importantly, PLR can be used in spontaneously breathing patients and in patients not in sinus rhythm. The increase in preload from the maneuver is reversed completely when the legs are returned to horizontal, meaning it is safe even in cases in which increasing blood volume may be harmful, such as ARDS. International consensus guidelines now recommend PLR to evaluate fluid responsiveness in patients with shock. Using esophageal Doppler measurements of aortic blood flow as a surrogate of cardiac output, Monnet found that an increase in
aortic blood flow of at least 10% with PLR predicted volume responsiveness with a sensitivity of 97% and specificity of 94% (15). Changes in aortic blood flow were rapid (within 30 seconds of PLR) and transient. The authors found that the PLR-induced changes in aortic blood flow and arterial pulse pressure variation were predictive of volume responsiveness, but the former was more accurate than the latter. Jabot and colleagues confirmed that maximal fluid shifts, and therefore better predictive value, are obtained when patients are shifted from the semirecumbent (chair) position to supine with legs elevated. Elevating the legs of a horizontal supine patient may still be helpful, but sensitivity is decreased. In the largest study to date, Thiel and colleagues measured SV changes with PLR, using a transthoracic Doppler device, they determined that a greater than or equal to 15% increase in SV with PLR predicted. Vasoconstrictors, increased intra-abdominal pressures, and elastic compression stockings all may have an impact on validity of PLR; further studies are needed to clarify these issues. It would be prudent to avoid PLR in patients with increased intracranial pressure.

Figure 15. Postural change during PLR

Respiratory Systolic Variation Test (figure 16)
The respiratory systolic pressure variation (RSVT) is a technique whereby three or four consecutive pressure-controlled breaths of increasing peak inspiratory pressures are administered over a brief period of time to intubated, sedated patients. The minimum systolic blood pressure (SBP) value following each of these breaths is recorded, and the results plotted against their respective airway pressures. A steeper slope (ie, larger decrease in SBP with increasing tidal volume) implies that the patient will be fluid-responsive, whereas less of a slope implies the patient’s ventricles are on the flat part of the Frank-Starling curve, and the patient will not increase cardiac output with fluid loading.

Figure 16. Response of the arterial blood pressure (BP) to the RSVT. Three consecutive mechanical pressure-controlled breaths are delivered with inspiratory pressures of 10, 20, and 30 cm H2O. Minimal values of SBP in response to each breath are recorded, and then the slope of the relationship between the decrease in BP and inspiratory pressure is calculated.

End-expiratory occlusion test (EEOT)
It is hypothesized that upon interrupting mechanical ventilation at the end of expiration for a period of 15 sec, the preload increases due to an increase of the venous return in such a way sufficient to predict a fluid response. Recently, Monnet et al. validated this hypothesis in patients with circulatory failure. Responsive patients demonstrated an increase of the pulse pressure and cardiac index with this maneuver. It is also possible to apply this test to patients with arrhythmia in whom a partial ventilatory modality is being used or in patients with ARDS with low pulmonary compliance where the use of the PPV and SVV do not present greater usefulness.

Cardiac Preload Evaluation Using Echocardiographic Techniques
In short, using echocardiographic and Doppler parameters, low volume status is often characterized by a small inferior vena cava size and large diameter respiratory changes, large respiratory movements of the interatrial septum, small LV size, E/A ratio < 1, DTE > 150 ms, TDA > 60 ms, A/a > 1, SF > 55 %, E/Em < 8 and E/Vp < 2.5, low cardiac output and
large respiratory variations of aortic flow or stroke volume (16).

**Conclusion:** Dynamic indices repeatedly have been shown to be superior to static measures for determining preload responsiveness in critically ill patients. The number of options for assessing fluid responsiveness available to the clinician is increasing; however, few have been evaluated in large, multicenter trials. Currently there are no data on whether managing patients using dynamic indices affects outcomes. It is important to remember that preload responsiveness does not equate to needing more preload. Healthy individuals are preload-responsive, and will increase their cardiac output in response to a fluid challenge, but they do not require increased blood volume. Therefore even with accurate measures of preload responsiveness, clinical judgment remains essential.

**Step 4: Cardiac output monitoring**
Cardiac output (CO) monitoring plays an essential role in critical care. Direct measurement of CO should be considered when a patient remains hypotensive despite adequate fluid resuscitation or when there is ongoing evidence of global tissue hypoperfusion. There are many CO monitoring devices available today. These include devices which use methodologies based on indicator dilution, thermodilution, pulse pressure analysis, Doppler principles, and also Fick principle. Patient status dictates the type of CO monitoring required. These systems can be easily listed in order of degree of invasiveness, from the highly invasive PAC to the completely non-invasive bioimpedance/bioreactance technique and transthoracic echo-doppler.

Methods of cardiac output measurements:

<table>
<thead>
<tr>
<th>A. Invasive</th>
<th>B. Non-invasive/ Minimal Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dilution techniques</td>
<td>• Indirect Fick using CO2</td>
</tr>
<tr>
<td>• Dye dilution</td>
<td>• Bioimpedance</td>
</tr>
<tr>
<td>• Pulmonary artery thermodilution</td>
<td>• Echocardiography</td>
</tr>
<tr>
<td>• Transpulmonary thermodilution</td>
<td>• Transoesophageal Doppler</td>
</tr>
<tr>
<td>• Lithium dilution</td>
<td>• Pulse contour analysis</td>
</tr>
<tr>
<td>• Direct - Fick</td>
<td></td>
</tr>
</tbody>
</table>

In general, dilution techniques deliver a reliable CO measurement for children from 3.5 kg, but all require insertion of central venous and arterial catheters. Less invasive methods are often less reliable. At present the transpulmonary thermodilution method is considered to be the clinical gold standard for children (17). The transpulmonary thermodilution technology also offers the measurement of global enddiastolic volume, reflecting preload, and extravascular lung water (EVLW), which reflects pulmonary edema. In general, the bedside CO techniques cannot be used in patients with intracardiac and extracardiac shunts. However, the transpulmonary thermodilution technology and the modified CO2 Fick methods might be feasible in this situation. Nonetheless, in adults there is no evidence that the use of a pulmonary artery catheter improves morbidity and/or mortality rates (18). Likewise, the evidence that CO monitoring improves outcome in critically ill children is also missing. CO monitoring does provide the clinician with important hemodynamic information and provides a physiologic value that can be used to determine and guide therapy. Clinical studies of CO-guided hemodynamic therapy in children, therefore, are warranted.

**Basic principles of thermodilution and indicator dilution methods**
The principles underlying these techniques are essentially the same (Table 7). An indicator is injected into a central vein, and cardiac output is calculated by measuring the change in blood indicator concentration over time at a point downstream of the injection. The method for sensing the indicator varies according to the injectate and may utilize a thermistor (temperature), densitometry or oximetry (dye), or an ion-selective electrode (lithium charge) (Figure 17).
Three principle phases of indicator dilution: 

(a) Injection 

(b) Indicator mixes with the bloodstream (mixing and dilution) 

(c) Detection

The change in concentration of indicator over time produces an indicator dilution curve (Figure 18).

Figure 17. Three principle phases of indicator dilution: (a) an indicator is brought into the circulation (injection), (b) the indicator mixes with the bloodstream (mixing and dilution), and (c) the concentration of the indicator is determined downstream (detection).

The shape of the curve will differ according to where it is measured relative to the site of injection. For example, the transit time is brief when the indicator is measured within the pulmonary artery, resulting in peaked curves with a relatively short tail. However, if the indicator is measured in a systemic artery, it must first pass through the pulmonary circulation and left heart, resulting in a longer transit time and producing a curve that is less peaked with a prolonged tail (Figure 19&20).

For thermodilution methods (e.g. pulmonary artery catheter, PiCCO, VolumeView) a drop in temperature is used instead of an injected indicator. A temperature–time curve is thus produced.

The temperature–time curves for the PAC and PiCCO/VolumeView will look slightly different because of the different sites where the change in temperature is measured (pulmonary artery for PAC; femoral artery for PiCCO/VolumeView).

Figure 18. Indicator dilution curve

Figure 19. The transpulmonary thermodilution curve, with the characteristic delay in the peak temperature change compared to the PAC thermodilution. Based on the same principle as the PAC thermodilution, the transpulmonary method obviates the need for a PAC.

Figure 20. Demonstrates site of injection & temperature measurement
The Direct Fick Method

The Fick method was first described by Adolph Fick in 1870(19), who applied the concept of mass balance to the measurement of blood flow. As such, it remains one of the most technically challenging, yet useful techniques for measuring cardiac output, not least because of its applicability to patients with anatomic shunts. The Fick principle involves adding (or removing) an indicator and measuring the change in indicator concentration upstream and downstream of the point of indicator addition (or removal); flow can then be calculated via the formula:

\[
\text{Flow (volume/time)} = \frac{\text{indicator added (mass/time)}}{\text{change in indicator concentration (mass/volume)}}
\]

For calculation of cardiac output, the most common measured indicator is oxygen consumption, although carbon dioxide production can also be utilized. A valuable aspect of the Fick principle is that it allows cardiac output to be calculated separately for the systemic (\(Q_s\)) and pulmonary (\(Q_p\)) circulations. The Fick technique requires a method for measuring oxygen consumption or carbon dioxide production, as well as access to the arterial and mixed venous circulations. Traditional methods for measuring oxygen consumption, such as the Douglas bag or spirometry, preclude measurement in the intensive care environment. However, these techniques have been advanced with portable metabolic monitors and/or mass spectrometry. As the Fick technique is vulnerable to many sources of error at each measurement step, attention to detail is vital.

Continuous cardiac output measurement: Minimal/Non-invasive:

Arterial pressure waveform analysis

The PiCCO and LiDCO and Flotrac/Vigileo systems provide continuous CO measurement using the arterial pressure waveform. These systems analyse the arterial waveform and use algorithms to calculate the CO. The newer versions LiDCO (LiDCOrapid) and Flotrac/Vigileo do not require calibration (20). The main advantage of the arterial pressure trace-derived systems is that they are less invasive than the PAC. However they have weaknesses which limit their use in certain clinical situations.

The way in which the arterial pressure waveform is analysed is slightly different with each device (Figure 21). PiCCO analyses the systolic portion of the arterial waveform. LiDCO analyses the waveform with what is called pulse power analysis. Flotrac/

---

Table 7. Dilution methods for determining cardiac output

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Additional variables measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermodilution: (pulmonary artery sampling)</td>
<td>Proven track record; semicontinuous mode available</td>
<td>Variations in cardiac output with respiratory cycle; difficult access in small patients; inaccurate at low flow; low but significant morbidity: infection, bleeding, catheter knotting</td>
<td>Pulmonary pressure; wedge pressure; mixed venous oxygen saturation</td>
</tr>
<tr>
<td>Thermodilution: Transpulmonary (systemic artery sampling)</td>
<td>Easy access in small patients; repeatable; continuous if device is combined with arterial pulse contour method (combination commercially available)</td>
<td>Requires dedicated arterial line, safe length of insertion time unknown, frequent recalibration required if used in conjunction with pulse contour method</td>
<td>Intrathoracic blood volume (preload); cardiac function index (contractility); extravascular lung water; stroke volume variability (if used with pulse contour method)</td>
</tr>
<tr>
<td>Dye dilution</td>
<td>Accurate</td>
<td>Sequential measurements limited by dye clearance; commercial availability of dye and devices</td>
<td></td>
</tr>
<tr>
<td>Lithium chloride dilution</td>
<td>Utilizes preexisting central venous and arterial lines; continuous if device is combined with arterial pulse contour method (combination commercially available)</td>
<td>Sequential measurements limited by lithium clearance; theoretical risk of toxicity; requires blood sample with each measurement; unlicensed in &lt;40 kg; frequent recalibration required if used in conjunction with pulse contour method</td>
<td>Stroke volume variability (if used with pulse contour method)</td>
</tr>
</tbody>
</table>
Vigileo analyses the waveform 100 times/second over 20 seconds, capturing 2000 data points for analysis. This is then incorporated into a proprietary formula to calculate CO.

**Echocardiography and Doppler technology to measure cardiac output**

Echocardiography has become an important diagnostic and monitoring tool in critical care. Cardiac output can be measured by 2D echocardiography and Doppler technology, using either a transthoracic (TTE) or transoesophageal (TOE) technique. TTE has the advantage of being rapid and non-invasive, but images may sometimes be limited in ventilated ICU patients. TOE provides high quality images but is more invasive than TTE.

Stroke volume is calculated using Doppler to measure the velocity time integral (VTi) of the flow signal at a given site, and 2D echo to measure the cross sectional area of the same site. These measurements of flow and diameter are usually obtained at the level of the left ventricular outflow tract (LVOT), and then used to calculate CO. Many modern machines will compute this information automatically when measurements are entered. Echo-Doppler calculation of CO is operator dependent, and continuous measurement of CO cannot be performed using this technique.

Continuous transoesophageal echocardiography is a miniaturised TOE probe which allows continuous qualitative haemodynamic assessment from a transverse plane, allowing visual assessment of cardiac performance and fluid status. It consists of a disposable probe (licensed for use up to 72 hours) which is connected to the echocardiography machine. Although smaller than a conventional TOE probe, some of the contraindications to TOE use may still apply with this device. There has been limited evaluation of this technique to date in critically ill patients.

Oesophageal Doppler monitoring Oesophageal Doppler (ODM) measures blood flow velocity in the descending aorta by using a Doppler transducer at the tip of a probe, which is inserted into the oesophagus via the mouth or nose.

**CO2 rebreathing**

CO2 rebreathing systems, based on the Fick principle, use a CO2 sensor, a disposable airflow sensor and a disposable rebreathing loop. CO2 production is calculated from minute ventilation and its CO2 content, and the arterial CO2 content is estimated from end-tidal CO2. Partial rebreathing reduces CO2 elimination and increases the end-tidal CO2. By combining measurements taken during and without rebreathing, venous CO2 content can be eliminated from the Fick equation. However, intrapulmonary shunting of blood and rapid hemodynamic changes affect the accuracy of the measurement, so that this technique is not considered to be reliable in acutely ill patients.

**Bioimpedance and bioreactance**

Bioimpedance is based on the fact that the conductivity of a high-frequency, low-magnitude alternating current passed across the thorax changes as blood flow varies with each cardiac cycle. These changes can be measured using electrodes placed on a patient’s chest and used to generate a waveform from which cardiac output can be calculated. Bioreactance has developed out of bioimpedance and measures changes in the frequency of the electrical currents traversing the chest, rather than changes in impedance, potentially making it less sensitive to noise. These techniques are non-invasive and
can be applied quickly. They have been used for physiological studies in healthy individuals and may be useful in perioperative applications, but are less reliable in critically ill patients. Electrical interference may also occur in the ICU environment.

**Volume clamp method**

This newer non-invasive technique uses an inflatable finger cuff. Photoelectric plethysmography in combination with a volume clamp technique (inflatable finger cuff) is used to produce a brachial arterial waveform, allowing continuous CO to be measured. Data to date on the usefulness of this technique in the critically ill is limited.

**Step 5: Assessment of cardiac contractility**

Assessing cardiac contractility is important in establishing the aetiology of shock, and in guiding further therapy. For example, a patient in cardiogenic shock with poor LV function is likely to require inotropy with adrenaline or dobutamine infusion, whereas a septic patient with a hyperdynamic heart is more likely to benefit from a vasopressor infusion such as noradrenaline.

**Echocardiography**

Cardiac performance may be rapidly assessed at the bedside using transthoracic echocardiography (TTE). A visual assessment of LV function will often reveal any significant abnormality. Formal estimation of LV contractility can be performed by measuring ejection fraction (EF). The EF is the percentage of LV diastolic volume ejected with each heart beat (normal >55%) (Table 8).

\[
\text{EF} (\%) = \frac{(\text{EDV} - \text{ESV})}{\text{EDV}} \times 100
\]

**Table 8. Left Ventricular ejection fraction range**

<table>
<thead>
<tr>
<th>Ejection fraction (EF) Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥55%</td>
</tr>
<tr>
<td>Mild impairment</td>
<td>45–54%</td>
</tr>
<tr>
<td>Moderate impairment</td>
<td>30–44%</td>
</tr>
<tr>
<td>Severe impairment</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>

The utility of echocardiography as a haemodynamic monitor is far greater than assessment of LV function. It is the test of choice in critically ill hypotensive patients to identify or exclude a ‘cardiac’ cause of shock as it is portable to the bedside, safe and can provide an immediate diagnosis. Left ventricular contractility can also be estimated by analysis of the arterial waveform. It is derived from the maximum speed of the arterial pressure curve (dP/dtmax) during the ejection phase.

Echocardiography should not be viewed simply in the context of cardiac output or ejection fraction. It can provide an assessment of preload and diagnose potentially reversible ventricular or valvular pathologies, cardiac tamponade, or massive pulmonary embolism or congenital shunt defects.

**Step 6: Assessment of microcirculation / regional tissue perfusion**

Measuring the adequacy of microcirculatory blood flow as a direct indicator of the success of the cardiovascular system to provide adequate oxygen and nutrients to the cells, can be regarded as an important extension of the measurement of systemic hemodynamic variables [21,22]. However several issues need to be addressed. These are:

1. The reliability and reproducibility of the measurement
2. The identification of the most relevant microcirculatory parameters which need to be determined; and
3. The prognostic value of these parameters in guiding therapy

**A. Orthogonal polarisation spectral (OPS) and sidestream dark field (SDF) imaging devices**

Orthogonal polarization spectral (OPS) imaging is the first hand-held imaging device that allows bedside visualization of the microcirculation. OPS imaging is based on the optical technique introduced by Slaaf et al, in which green polarized light is used to illuminate the tissue area of interest, which at the bedside is usually the buccal or sublingual mucosa. The green light is absorbed by hemoglobin within the red blood cells (RBCs) in the microcirculation. The reflected light is detected by an orthogonally placed analyzer which filters out surface reflections in order to
produce a high contrast reflected light image of flowing RBCs within the microcirculation. Sidestream darkfield (SDF) imaging is the improved successor to OPS imaging and is based on the dark field illumination technique introduced by Sherman et al. In this technique, the micro circulation can be observed without the need to use transillumination (Figure 22). Instead SDF imaging uses a stroboscopic light emitting diode ring-based imaging device so it provides better image quality of the microcirculation.

What can be measured with these techniques and what is important? Different variables can be measured, including vascular density, heterogeneity of perfusion, and microvascular blood flow (Table 9). Several limitations should be acknowledged. Secretions and movement artifacts may impair image quality. In addition, movement artifacts can spuriously interrupt flow in some microvessels. Finally, the investigation of the sublingual area is only feasible in sedated or cooperative patients. It is also impossible to evaluate the sublingual microcirculation in hypoxemic patients who are being treated with noninvasive mechanical ventilation.

B. NIRS (Near-infrared spectroscopy)

Near-infrared spectroscopy (NIRS) is a technique that utilizes near-infrared light to measure chromophores (oxy- and deoxyhemoglobin, myoglobin, and cytochrome aa3) in tissues. The fractions of oxy- and deoxyhemoglobin are used to calculate tissue O2 saturation (StO2). In addition, total light absorption is used to compute total tissue hemoglobin (HbT) and the absolute tissue hemoglobin index (THI), two indicators of blood volume in the region of microvasculature sensed by the probe.

According to Beer’s law, the NIRS signal is limited to vessels that have a diameter less than 1 mm (arterioles, capillaries, and venules), but, as 75% of the blood in a skeletal muscle is venous, NIRS StO2 measurements mostly represent local venous hemoglobin O2 saturation. This represents the aggregate of O2 saturations in the sampling volume and this technique is not suitable in conditions of heterogeneous blood flow. Indeed, even though StO2 is slightly lower in septic patients compared to healthy volunteers, there
is a huge overlap between the groups. StO2 also differs from ScvO2 saturation in sepsis. The analysis of changes in StO2 during a brief episode of forearm ischemia enables quantification of microvascular dysfunction. This technique, which can easily be repeated, is particularly promising as it provides quantitative information on microvascular function within a few minutes. One should bear in mind that NIRS does not measure microcirculatory blood flow, making interpretation of the absolute StO2 value in terms of tissue oxygenation difficult. As StO2 represents the balance between O2 delivery and O2 consumption, any change in StO2 can reflect a change in flow in the same direction and/or a change in metabolism in the opposite direction. More importantly, proportional changes in flow and metabolism may be associated with unchanged StO2.

Table 9: Parameters for the evaluation and scoring of the microcirculation by SDF.

<table>
<thead>
<tr>
<th>Microcirculation parameter</th>
<th>Information provided</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microvascular flow index (MFI)</td>
<td>Perfusion quality (for small, medium, and large vessels)</td>
<td>The image is divided into four quadrants; a number is assigned for each quadrant according to the predominant type of flow (0 = no flow; 1 = intermittent; 2 = sluggish; 3 = continuous). The MFI results from the averaged values.</td>
</tr>
<tr>
<td>De Backer score (n/mm)</td>
<td>Vessel density</td>
<td>The image is divided by 3 vertical and 3 horizontal lines; the De Backer score is calculated as the number of vessels crossing the lines divided by the total length of the lines.</td>
</tr>
<tr>
<td>Total vessel density (mm/mm²)</td>
<td>Vessel density (for small, medium, and large vessels)</td>
<td>Total length of vessels is divided by the total surface of the analyzed area.</td>
</tr>
<tr>
<td>Perfused vessel density (mm/mm²)</td>
<td>Functional vessel density (for small, medium, and large vessels)</td>
<td>Total length of perfused vessels (sluggish or continuous) is divided by the total surface of the analyzed area.</td>
</tr>
<tr>
<td>Proportion of perfused vessels (%)</td>
<td>Perfusion quality (for small, medium, and large vessels)</td>
<td>100 number of perfused vessels is divided by the total number of vessels.</td>
</tr>
<tr>
<td>Flow heterogeneity index (FHI)</td>
<td>Perfusion heterogeneity</td>
<td>The difference between the highest MFI and the lowest MFI is divided by the mean MFI. MFI is intended as the averaged MFI of each site.</td>
</tr>
</tbody>
</table>

*Vessel diameter classification: <20 μ = small; 20–50μ = medium; 50–100 μ = large. Three or five sites are evaluated. MFI of small vessels can be calculated separately.

Figure 23. Portable near infrared spectroscopy (NIRS) monitor in use. The probe is placed over the thenar eminence.

Figure 24. Schematic illustration of the StO2 changes during VOT.

In addition, the vasoreactivity test evaluates a different aspect of microvascular function than flow: it evaluates microvascular reserve more than actual microvascular perfusion (23). NIRS-derived measurements are influenced by adipose tissue thickness as well as the presence of edema; hence, in the majority of studies, the thenar eminence has been used because the thickness of skin and adipose tissue covering this muscle is less influenced by any increase in fluid content or body mass index (Figure 23 & 24). The influence of temperature and vasoactive substances on NIRS-derived variables obtained in the thenar eminence need to be evaluated. Likewise, the relationship between peripheral and more central microvascular beds need to be further studied in critically ill patients. Finally, NIRS devices vary in
terms of wavelength and number of wavelengths, optode spacing, and algorithms. Accordingly, the data reported with the different devices may vary somewhat and this absence of standardization may limit comparisons of results from different trials (Table 10).

**Table 10. Summary of techniques used to evaluate the microcirculation at the bedside**

<table>
<thead>
<tr>
<th>Variable measured</th>
<th>Main limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Techniques measuring microvascular perfusion</strong></td>
<td></td>
</tr>
<tr>
<td>Laser Doppler</td>
<td>Flow (relative), hemoglobin content/microvascular reactivity test</td>
</tr>
<tr>
<td>Nailfold videomicroscopy</td>
<td>Vascular density, heterogeneity, flow</td>
</tr>
<tr>
<td>OPS and SDF</td>
<td>Vascular density, perfusion heterogeneity, flow</td>
</tr>
<tr>
<td><strong>Techniques measuring tissue oxygenation</strong></td>
<td></td>
</tr>
<tr>
<td>SvO2</td>
<td>Adequacy of perfusion to flow</td>
</tr>
<tr>
<td>O2 electrodes</td>
<td>Tissue PO2</td>
</tr>
<tr>
<td>NIRS</td>
<td>Tissue O2 saturation</td>
</tr>
<tr>
<td>Reflectance spectroscopy</td>
<td>O2 saturation/microvascular reactivity test</td>
</tr>
<tr>
<td>Gastric tonometry</td>
<td>Tissue CO2 (reflects inadequate perfusion and/or anaerobic metabolism)</td>
</tr>
<tr>
<td>Sublingual capnometry</td>
<td>Tissue CO2 (reflects inadequate perfusion and/or anaerobic metabolism)</td>
</tr>
</tbody>
</table>

These devices have been used in clinical research to evaluate the microcirculation but have not yet found a definite role in clinical practice.

**References**

Intracranial Pressure and its Monitoring: A review
Suresh Panda, Rakshay Shetty
Rainbow Childrens Hospital, Hyderabad

Evidence suggests that the mortality and morbidity of acquired brain injury could be reduced if clinicians used an aggressive intracranial pressure guided approach to care. Despite nearly 50 years of evidence that intracranial pressure monitoring benefits patient care, only about half of the patients who could benefit are monitored. Some clinicians express concerns regarding risks such as bleeding, infections, and inaccuracy of the technology. Others cite cost as the reason. This article discusses the risks and benefits of intracranial pressure monitoring and the current state of evidence of why patients should be monitored.

Keywords: intracranial pressure, cerebral perfusion pressure, monitoring devices, drift, infections, hemorrhage

Background
Elevated intracranial pressure (ICP) is seen in head trauma, hydrocephalus, intracranial tumors, metabolic encephalopathy, intracranial bleeds and CNS infections. Increased ICP is an important cause of secondary brain injury, and its degree and duration is associated with outcome after TBI.\textsuperscript{1,2} Intractable intracranial hypertension can lead to death or devastating neurological damage either by reducing cerebral perfusion pressure (CPP) and causing cerebral ischemia or by compressing and causing herniation of the brainstem or other vital structures. Prompt recognition is crucial in order to intervene appropriately. The association between the severity of intracranial hypertension and poor outcome after severe head injury is well recognized. Outcomes tend to be good in patients with normal ICP, whereas those with elevated ICP are much more likely to have an unfavorable outcome. Elevated ICP carries a mortality rate of around 20%.

The rapid recognition of elevated ICP is therefore of obvious and paramount importance so that it can be monitored and so that therapies directed at lowering ICP can be initiated. Continuous ICP monitoring is important both for assessing the efficacy of therapeutic measures and for evaluating the evolution of brain injury.

Although some investigators have questioned invasive ICP monitoring in improving patient outcomes, numerous retrospective have favored the use of this technique.

The goal of ICP monitoring is to ensure maintenance of optimal CPP. The ICP also forms a basis for medical or surgical intervention in cases of increased ICP in cases of intractable ICP elevation that do not respond to conservative management.

ICP monitoring may be discontinued when the ICP remains in the normal range within 48-72 hours of withdrawal of ICP therapy or if the patient’s neurological condition improves to the point where he or she is following commands.

Pathophysiology
Physiology of ICP was described by Professors Munroe and Kellie in the 1820s. In essence, they noted that, in adults, the brain is enclosed in a rigid case of bone and that the volume of its contents must remain constant if ICP is to remain constant. The intracranial compartment consists of brain approximately 83%, cerebrospinal fluid (CSF) approximately 11%, and blood approximately 6%.

Under normal conditions there are two main components of ICP namely CSF and vasogenic.\textsuperscript{3} The former is derived from the circulation of CSF and is responsible for baseline ICP. It may be deranged in pathologic states, causing an increase in ICP, because of resistance to CSF flow between intracerebral compartments secondary to brain swelling or expansion of intracranial mass lesions, or because CSF outflow is obstructed.
The vasogenic component of ICP is associated with continuous, small fluctuations of cerebral blood volume (CBV). Vasogenic increases in ICP may be caused by high PaCO2, increase in cerebral metabolism, and cerebral hyperemia. An increase in the volume of one of the components of the intracranial cavity (e.g., brain) requires a compensatory reduction in another (e.g., CSF) to maintain a constant pressure.

Brain tissue is essentially incompressible, so any increase in ICP due to brain swelling initially results in extrusion of CSF and (mainly venous) blood from the intracranial cavity, a phenomenon known as "spatial compensation." CSF plays the largest role in spatial compensation because it can be expelled from the intracranial cavity into the reservoir of the spinal theca.

![Figure 1. Intracranial pressure (ICP) volume curve. The curve has three parts: a flat part representing good compensatory reserve (A-B), an exponential part representing reduced compensatory reserve (B-C) and a final flat part representing terminal derangement of cerebrovascular responses at high ICP (C-D).](image)

The relationship between ICP and intracranial volume is described by the pressure-volume curve that comprises of three parts (Fig. 1). The first part of the curve is flat because compensatory reserves are adequate and ICP remains low despite increases in intracerebral volume (A–B in Fig. 1). When these compensatory mechanisms become exhausted, the pressure-volume curve turns rapidly upwards in an exponential fashion. Intracranial compliance is now critically reduced and a small increase in intracerebral volume causes a substantial increase in ICP (B–C in Fig. 1). At high levels of ICP, the curve plateaus as the capacity of cerebral arterioles to dilate in response to a reduction in CPP become exhausted. The high brain tissue pressure results in collapse of these dysfunctional vessels as cerebrovascular responses become terminally disrupted (C–D in Fig. 1).

Increased ICP causes a critical reduction in CPP and CBF and may lead to secondary ischemic cerebral injury. A number of studies have shown that high ICP is strongly associated with poor outcome, particularly if the period of intracranial hypertension is prolonged. Increased ICP can also cause actual shift of brain substance resulting in structural damage to the brain and to herniation through the tentorial hiatus or foramen magnum. The latter results in pressure on the brainstem causing bradycardia and hypertension (the classic Cushing reflex) and, if untreated, respiratory depression and death.

**Interaction with blood pressure and cerebral blood flow**

Cerebral perfusion pressure (CPP), defined as the mean arterial pressure (MAP) minus ICP, is a critical determinant of cerebral blood flow (CBF) and plays an important role in ICP management. Normally CBF is "autoregulated" at a constant level over a wide range of CPPs (from 50 to 150 mmHg in adults) (Fig 2).

Pressure auto regulation of this type is mediated by changes in arteriolar diameter and cerebrovascular resistance. The auto regulatory curve is shifted to the left in children and shifted to the right in patients with chronic hypertension. In pathologic states with impaired auto regulation, such as TBI and subarachnoid hemorrhage, CBF may approximate a linear relationship with CPP, which creates a smaller range of optimal CPP (Fig 2). Reduction of CPP below the lower limit of autoregulation can
lead to ischemia, whereas CPP elevation above the upper limit of autoregulation can be associated with hyperemia, exacerbation of vasogenic edema, and increased ICP. Although the optimal CPP for any particular patient may vary, as a rule of thumb CPP should be maintained above 70 mmHg to avert ischemia and below 110 mmHg to avoid breakthrough hyperperfusion in adults.

CBF also depends upon Paco2 and Pao2 level. In general, the cerebral vessels are less responsive to changes in PaO2 than to those in PaCO2. Arteriolar diameter and CBF progressively increase as PaCO2 rises from 20 to 80 mmHg, whereas hypoxemia leads to vasodilatation and increased CBF only when PaO2 falls below 50 mmHg.

![Fig 2: Cerebral autoregulation curve.](image)

**Normal and Pathologic ICP**

**Table 2:** Normal intracranial pressure values

<table>
<thead>
<tr>
<th>Age group</th>
<th>Normal range (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>&lt;10–15</td>
</tr>
<tr>
<td>Children</td>
<td>3–7</td>
</tr>
<tr>
<td>Term infants</td>
<td>1.5–6</td>
</tr>
</tbody>
</table>

The definition of intracranial hypertension depends on the specific pathology and age, although ICP >15 mm Hg is generally considered to be abnormal. However, treatment is instituted at different levels depending on the pathology. For example, ICP <15 mm Hg warrants treatment in a patient with hydrocephalus, whereas after TBI, treatment is indicated when ICP exceeds 20 mm Hg. Thresholds vary in children and it has been recommended that treatment should be initiated during TBI management when ICP exceeds 15 mm Hg in infants, 18 mm Hg in children up to 8-yr-of-age and 20 mm Hg in older children and teenagers.

ICP is not evenly distributed in pathologic states because CSF does not circulate freely and intracranial CSF volume may be low because of brain swelling. The assumption of one, uniform, ICP is therefore questionable and intraparenchymal pressure may not be indicative of “real” ICP, i.e., ventricular CSF pressure. In the injured brain, there may be intraparenchymal pressure gradients between the supra and infra-tentorial compartments and bilateral monitoring has revealed differential pressures across the midline in the presence of hematomas and also in the absence of space-occupying lesions.

**Causes of Raised Intracranial Pressure**

**Table 3**

<table>
<thead>
<tr>
<th>Pathological process</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized mass lesions</td>
<td>Traumatic hematomas (extradural, subdural, intracerebral) neoplasm (glioma, meningioma, metastasis) Abscess Focal edema secondary to trauma, infarction, tumor</td>
</tr>
<tr>
<td>Disturbance of CSF circulation</td>
<td>Obstructive hydrocephalus, Communicating hydrocephalus</td>
</tr>
<tr>
<td>Obstruction to major venous sinuses</td>
<td>Depressed fractures overlying major venous sinuses Cerebral venous thrombosis</td>
</tr>
<tr>
<td>Diffuse brain edema or swelling</td>
<td>Encephalitis, meningitis, diffuse head injury, subarachnoid hemorrhage, Reye’s syndrome, lead encephalopathy, water intoxication, near drowning</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Benign intracranial hypertension</td>
</tr>
</tbody>
</table>

**Methods of ICP Monitoring**

ICP cannot be reliably estimated from any specific clinical feature or computed tomography (CT) finding and must actually be measured.
Intraparenchymal Pressure Transducers

The pressure transducer in these disposable devices is incorporated into the tip of a thin fiber optic cable (the Camino device) or within a strain-gauge micro sensor at the tip of a flexible catheter (the Codman device). These catheters can be placed into either the brain parenchyma or the ventricle via a small burr hole and screw. With intraparenchymal placement, the infection rate is exceedingly low (approximately 1%). When combined with a ventricular catheter, the system allows simultaneous CSF drainage and continuous ICP measurement. These devices only need to be calibrated once prior to insertion, and the accuracy of ICP measurements is generally superior to those provided by subarachnoid bolts or epidural transducers. A new version of the Codman monitor also provides measurements of brain temperature. A third intraparenchymal monitor recently approved by U.S. Food and Drug Administration (FDA) (the Spielberg device) features a small air filled balloon at the tip of a flexible catheter; it has the advantage of providing measurements of intracranial compliance (calculated as a pressure/volume index) as well as ICP.

Intraventricular Catheters

The “gold standard” technique for ICP monitoring is a catheter inserted into the lateral ventricle, usually via a small right frontal burr hole. This can be connected to a standard pressure transducer via a fluid filled catheter. The reference point for the transducer is the foramen of Munroe, although, in practical terms, the external auditory meatus is often used. Ventricular catheters measure global ICP and have the additional advantages of allowing periodic external calibration, therapeutic drainage of CSF, and administration of drugs (e.g., antibiotics). However, placement of the catheter may be difficult if there is ventricular effacement or displacement due to brain swelling or intracranial mass lesions. The use of intraventricular Catheters is complicated by infection in up to 11% of cases. This is a serious complication resulting in significant morbidity and mortality. The risk of infection increases after 5 days and this has been presumed to be related to retrograde colonization of the catheter. However, recent data suggest that CSF infection is also likely to be acquired during introduction of the catheter in a significant number of cases. Intraventricular catheters may become blocked, especially in the presence of subarachnoid blood or increased CSF protein. Although the patency of catheters can often be restored by gentle flushing, repeated attempts significantly increase the risk of infection.

Regular microbiological analysis of CSF samples to permit early diagnosis of ventriculitis is recommended by some, whereas others believe that routine sampling may actually predispose to higher infection rates because of the repeated opening of the closed drainage system. The use of antibiotic-impregnated catheters is associated with a lower infection rate, although catheters coated with hydrogel to impede bacterial adherence are not associated with reduced infection rates.

Different methods of monitoring ICP are depicted in figure 3. Intraventricular catheter and intraparenchymal micro transducer systems are the most common monitoring devices used in practice. Subarachnoid and epidural devices have much lower accuracy and are now rarely used. Measurement of lumbar CSF pressure does not provide a reliable estimate of ICP and may be dangerous in the presence of increased intracranial hypertension. Advantages and disadvantages of each monitoring method are summarized in Table 4.

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Subarachnoid Bolts
This is another fluid-coupled system which connects the intracranial space to an external transducer at the bedside via saline-filled tubing\(^{33}\). The subarachnoid bolt is actually a hollow screw that is inserted via a burr hole. The dura at the base of the bolt is perforated with a spinal needle, allowing the subarachnoid CSF to fill the bolt. Pressure tubing is then connected to establish communication with a pressure monitoring system. Although the infection risk is low, these devices are prone to error, including underestimation of ICP, screw displacement, and occlusion by debris\(^{34}\).

Epidural Transducers
These devices (the Gaeltec device) are inserted deep into the inner table of the skull and superficial to the dura\(^{35}\). In most of these devices, pressure is transduced by an optical sensor. They have a low infection rate (approximately 1\%)\(^{29}\), but are prone to malfunction, displacement, and baseline drift that can exceed 5±10 mmHg after more than a few days of use. Much of the inaccuracy results from having the relatively inelastic dura between the sensor tip and the subarachnoid space.

Noninvasive ICP Monitoring
At present there is no noninvasive method that can provide accurate continuous online measurement of ICP. However, optic nerve sheath diameter (OPNSD)\(^{38,39}\) and transcranial Doppler (TCD) Ultrasonography are promising modalities. TCD measures the velocity of blood flow in the basal cerebral arteries, shows characteristic changes with increasing ICP\(^{36}\). As CPP falls, diastolic velocity decreases and pulsatility increases, reflecting increased distal vascular resistance to flow. Though this finding is specific for severe intracranial hypertension, TCD is not sensitive to mild to moderate ICP elevations. Lateralized asymmetries in TCD pulsatility correlate with lesion volume in intracerebral hemorrhage, and are believed to reflect compartmentalized ICP gradients\(^{37}\).

Indication
The most common use of continuous ICP monitoring is in the management of severe closed head injury. Bullock and colleagues reviewed the published evidence base for the indications for ICP monitoring. They concluded that there were insufficient data to support standard treatment guidelines (no class I evidence). There was, however sufficient class II and III evidence to support the following indications summarized in Table 5.

Table 5: Indications of ICP Monitoring

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe head injury</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Central nervous system infections</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
</tr>
</tbody>
</table>

Contraindication
No absolute contraindications. However, caution should be exercised in following conditions
- Coagulation defects
- Anticoagulant therapy
- Scalp infection

Complications
- Intracranial infection
- Intracerebral hemorrhage
- Air leakage into the ventricle or subarachnoid space
- CSF leakage
- Over drainage of CSF leading to ventricular collapse and herniation
- Loss of monitoring or drainage capabilities due to the occlusion of the catheter with brain tissue or blood
- Inappropriate therapy because of erroneous ICP readings due to dampened waveforms, electromechanical failure, or operator error (i.e. inappropriate leveling)

Analysis of ICP Wave Form
Four major waveforms are of clinical importance: normal, A, B, and C.
**Normal:** Normal ICP waves have a steep upward systolic slope followed by a downward diastolic slope with a dicrotic notch. In most cases, this waveform occurs continuously and indicates that the ICP is between 0 and 15 mm Hg.

**“A” waves or “plateau” waves**
These are steep increases in ICP from baseline to peaks of 50–80 mm Hg that persist for 5–20 min. These waves are always pathologic and may be associated with early signs of brain herniation, such as bradycardia and hypertension. They occur in patients with intact autoregulation and reduced intracranial compliance and represent reflex, phasic vasodilatation in response to reduced cerebral perfusion. The development of plateau waves leads to a vicious cycle, with reductions in CPP predisposing to the development of more plateau waves, further reductions in CPP and irreversible cerebral ischemia.

**“B” waves**
These are rhythmic oscillations occurring at 0.5–2 waves/min with peak ICP increasing to around 20–30 mm Hg above baseline. They are related to changes in vascular tone, probably due to vasomotor instability when CPP is at the lower limit of pressure autoregulation.

**“C” waves**
These are oscillations occurring with a frequency of 4–8/min and are of much smaller amplitude than B waves, peaking at 20 mm Hg. They occur synchronously with ABP, reflect changes in systemic vasomotor tone, and are of no pathologic significance.


**Why Monitor ICP?**
Four lines of evidence support the use of ICP monitoring in children with severe TBI.
1. Frequently reported high incidence of intracranial hypertension.
2. A widely reported association of intracranial hypertension and poor neurological outcome.
3. Concordance of protocol driven intracranial hypertension and best reported clinical outcome.
4. Improved outcome associated with successful ICP lowering therapies

There is a large body of evidence to indicate that ICP monitoring is of benefit to the patient by the following ways:

1. **Early detection of developing pathology**
   Patients at high risk of developing raised ICP usually are drowsy or sedated and ventilated, and the first clinical indication of an increase of edema or a hematoma might be signs of herniation. By alerting the medical team prior to this deterioration, monitoring enables early intervention and improved outcome. Intervention when a small rise in IC occurs has also been shown to prevent later profound intracranial hypertension. A management protocol based solely on repeated CT scans is economically not feasible for most of our patients, and has been shown to be less accurate than actual monitoring. There is also evidence that time-bound repetition of CT scans does not contribute to patient management. In addition to the lack of benefit, transporting a critically ill patient for investigation increases the risk for the patient and imposes a logistical strain on the ICU. ICP monitoring can indicate the need for a repeat imaging and avoid routine protocol-based investigation. ICP monitoring should never be at the expense of clinical examination.

2. **Limit avoidable therapy**
   Empirical therapy for presumed raised intracranial
pressure runs the risk of inflicting unnecessary iatrogenic complications on patients who either had only mild or no intracranial hypertension. These include unnecessary prolongation of ventilation, brain ischemia induced by hyperventilation, fluid-electrolyte imbalance induced by mannitol and diuretics and even at times unnecessary surgery.

3. Cerebral perfusion pressure
The CPP can be calculated only if the ICP is measured. The importance of maintaining an adequate CPP has been discussed earlier in this review.

4. Safety factor
ICP monitoring can help in revealing shortcomings in other treatment modalities like head positioning, adequacy of sedation, analgesia or paralysis, and even draws attention to other abnormalities such as hyponatremia. Most raised ICP alarms are in fact due to one of these causes, and therefore the monitoring provides an additional layer of safety for the patient.

5. Decision on surgery
The decision to operate on the brain when the clinical and radiological features are ambiguous is extremely difficult. Knowledge of the ICP can help in decision-making regarding surgery in these cases. ICP monitoring also provides essential information for the timing of decompressive craniectomies in stroke, subarachnoid hemorrhage and severe head injury.

6. CSF drainage
The use of an intraventricular catheter to monitor ICP also provides the option of venting CSF, which directly lowers the pressure without any of the systemic effects associated with all other means of ICP control.

7. Prognostication
Refractory raised pressure intuitively indicates a bad prognosis which has been demonstrated in all studies from the 1970s to the present. There is also data to show that even transient, controllable rises in ICP indicate a worse prognosis in head injury.

Opinions against ICP monitoring
The arguments against ICP monitoring are generally negative and much fewer than those of proponents of monitoring.

1. Lack of evidence
There has not been a randomized controlled trial on the efficacy of ICP monitoring in improving outcome, and there most likely will never be one because the utility of monitoring is so widely accepted that a trial where ICP is not monitored for a group of patients is considered unethical. Even if a trial were to be attempted, the sample size required to prove the benefit would be over 750 patients, which would be logistically and financially extremely difficult.

2. Outcome without monitoring
Recent Trial on Intracranial Pressure Monitoring in Traumatic Brain Injury by Randall M, Chesnut et al showed no significant between-group difference in the primary outcome, a composite measure based on percentile performance across 21 measures of functional and cognitive status (score, 56 in the pressure-monitoring group vs. 53 in the imaging–clinical examination group; P = 0.49). Six-month mortality was 39% in the Pressure-monitoring group and 41% in the imaging–clinical examination group (P = 0.60). The median length of stay in the ICU was similar in the two groups (12 days in the pressure-monitoring group and 9 days in the imaging–clinical examination group; P = 0.25), although the number of days of brain-specific treatments (e.g., administration of hyperosmolar fluids and the use of hyperventilation) in the ICU was higher in the imaging–clinical examination group than in the pressure-monitoring group (4.8 vs. 3.4, P = 0.002). The distribution of serious adverse events was similar in the two groups.

3. Clinical deterioration
Temporal lobe hematomas and swelling can theoretically cause uncal herniation and brainstem
compression without raising the ICP to alarm threshold values – there is a report of herniation taking place at an ICP of 18 mmHg.

4. Choice of patients to monitor
The debate on which patients will benefit from ICP monitoring is nowhere near settled, the closest approach to agreement being with regard to trauma. There is not sufficient data on other disease conditions for the establishment of guidelines.

Conclusion
ICP monitoring is safe, has relatively low complications rates, and has been shown to improve patient outcomes by giving the clinician a tool to evaluate both the patient and the effectiveness of treatment. Proper training for the clinician who is inserting the device, whether neurosurgeon or non-neurosurgeon, will minimize complication and facilitate accurate information being obtained. It is important to remember the strengths and limitations of each system when choosing the placement of the monitor (intraparenchymal, intraventricular, or surface monitor), the technology (fluid-filled versus advanced technology), and as well as cost. With proper education of all staff regarding the care, management, and troubleshooting of ICP, monitoring ICP will enhance the care we give our brain-injured patients.

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Intracranial Pressure and its Monitoring: A review


Introduction
The diagnosis of Brain Death in children is generally regarded as being more difficult than in adults and there is considerable variation in the exact protocol followed in different countries, and even between different states in the same country. Nevertheless, the diagnostic procedure is essentially by clinical examination.

The following guidelines are based on multiple sources, including the American Academy of Pediatrics Guidelines for the determination of brain death in children\textsuperscript{1,4}, the American Academy of Neurology evidence based guideline update 2010\textsuperscript{2}, the Australian and New Zealand Intensive Care Society statement on death and organ donation, 2008\textsuperscript{3} and the general consensus of the Guidelines committee of experts from India listed at the end of this article (Guidelines group was chaired and coordinated by Dr Balaramachandran in year 2011 and this consensus was compiled by him on behalf of the Guidelines group).

Definition
Brain death is defined as irreversible cessation of all functions of the entire brain, including the brain stem.

Pre-requisites
The following conditions must be met before brain death can be determined:
1. There must be a recognized cause of coma sufficient to explain the irreversible cessation of all brain function. Both coma and apnea must coexist to declare brain death.
2. Potentially reversible causes of coma must be excluded
   a. Hypothermia – core body temperature must be $>35^\circ\text{C}$, since severely hypothermic patients may appear brain dead
   b. Uncontrolled hypotension – the blood pressure must be normal for age (systolic BP not $<2$ SD below norm for age)
   c. Sedatives and other CNS depressant drugs / toxins – sufficient time must be allowed for any CNS depressant agents to be metabolized. If this cannot be assured, a drug level may be obtained, if possible, to show that the drug in question does not exceed the normal therapeutic levels.
   d. If neuromuscular blocking agents have been administered, a peripheral nerve stimulator should be used to show that there is no residual neuromuscular blockade
   e. Severe metabolic derangements must be excluded, including markedly abnormal plasma concentrations of glucose, sodium, potassium, phosphate, magnesium, calcium
   f. Any other sign that suggests a potentially reversible cause of coma

3. Neurological assessment may be unreliable immediately following cardiopulmonary resuscitation or acute brain injury – brain death evaluation should be deferred by 24 hours in these circumstances.

Clinical Examination
The diagnosis of brain death is essentially clinical. There must be absence of higher brain function – lack of consciousness
There must be absence of brain stem functions

NOTE
Observations that are compatible with brain death
- The following observations can be present in brain death

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• Spinal reflexes in response to stimulation
  • These may include movements of the upper limbs, deep tendon reflexes, plantar reflexes, respiratory like movements and head turning
• Sweating, blushing or tachycardia
• Normal blood pressure without pharmacological support
• Absence of diabetes insipidus

**Observations that are incompatible with brain death**
The following observations are incompatible with brain death:
• Decerebrate or decorticate posturing
• True extensor or flexor responses to painful stimuli
• Seizures

**Number of tests and who should perform them**
Two examinations (including two apnea tests) should be performed, separated by an interval. A different Consultant Physician who is taking care of the child should perform each clinical examination. These physicians should have specific expertise and experience in performing such assessment and can include Pediatric Intensivists, Neurologists, Anesthesiologists, Neurosurgeons or Pediatricians. The same individual may perform the apnea tests. In case the testing is being performed for the purposes of organ harvesting, additional requirements from the individual State Governments may apply (such as pre-registration and authorization of the physician performing the tests).

**Demonstration of apnea**
The role of the apnea test has been questioned recently\(^5\). Nevertheless, it continues to be a part of

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<table>
<thead>
<tr>
<th>Clinical testing</th>
<th>Test procedure and response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma</td>
<td>Apply noxious stimuli in the cranial nerve distribution and all four limbs and trunk. There should be no motor response</td>
<td>See note below</td>
</tr>
<tr>
<td>Pupillary light reflex – cranial nerves II &amp; III</td>
<td>Shine a bright light into each eye and look for pupillary constriction. There should be no pupillary constriction</td>
<td>Pupils must be ≥ 4 mm in diameter. A magnifying glass may be used, if required. Use of anti-cholinergic drugs, such as Atropine, can cause pupillary dilatation</td>
</tr>
<tr>
<td>Corneal reflex – cranial nerves V &amp; VII</td>
<td>Touch the corneas with soft cotton wool. There should be no blinking or withdrawal reflex</td>
<td>Touch only the lateral aspect of the cornea to avoid damage</td>
</tr>
<tr>
<td>Absence of movement of the bulbar musculature – cranial nerves V &amp; VII</td>
<td>Apply deep pressure over the condyles at the temporomandibular joints and over the supra-orbital ridges. There should be no grimacing or facial muscle movement</td>
<td></td>
</tr>
<tr>
<td>Oculo-vestibular reflex – cranial nerves III, IV, VI &amp; VIII</td>
<td>Inspect the external auditory meatus with an otoscope to make sure that the ear drum is visible and intact – if required, clean any cerumen before proceeding. Elevate head to 30° and place in the neutral position. Instill 20 – 50 ml of iced water into the ear canal with a syringe. Hold both eyes open and observe for at least 1 minute. There should be no response – both eyes should remain in the mid-position. Wait 5 minutes and repeat test in the other ear</td>
<td>Fracture of the skull base or petrous temporal may obliterate the response on the side of the fracture.</td>
</tr>
<tr>
<td>Gag reflex – cranial nerves IX &amp; X</td>
<td>Stimulate the posterior pharyngeal wall on both sides with a tongue depressor. There should be no gag response</td>
<td>May be difficult to examine in orally intubated patients</td>
</tr>
<tr>
<td>Cough reflex - cranial nerve X</td>
<td>Stimulate the trachea with a suction catheter. There should be no cough</td>
<td></td>
</tr>
<tr>
<td>Flaccidity</td>
<td>Evaluate all extremities by passive range of motion (unless contra-indicated). There should be flaccid tone and no spontaneous or induced movements</td>
<td>See note below</td>
</tr>
</tbody>
</table>
the Brain Death testing protocol in most countries at
this time. The apnea test must be performed twice (as
part of each clinical exam), but may be performed by
the same individual – preferably the physician who
is managing the patient’s ventilator. The following
section describes how to perform the apnea test.
The same pre-requisites apply as for performing
the clinical tests – i.e. the patient should not
be hypothermic, hypotensive or have a serious
metabolic or endocrine disturbance. Additional
contraindications include a high cervical spinal cord
injury or very high oxygen / ventilatory requirements
that will result in the inability to disconnect safely
from the ventilator. If the apnea tests cannot be
performed safely, then an ancillary test must be
performed to determine brain death.
1. Pre-oxygenate the patient for 5 minutes with
   100% oxygen.
2. The physician involved in certifying brain death
   should be physically present at the bedside during
   the test to attest to the presence of apnea.
3. Manipulate the ventilator to allow the PaCO
   to rise to > 40 mm Hg –– this baseline arterial CO
   should be confirmed by blood gas analysis or end
tidal CO
4. Monitor the patient during the test (ECG, blood
   pressure and SpO
   ) and stop the test if there is
   significant hypotension, desaturation or cardiac
arrhythmia
5. Disconnect the patient from the mechanical
   ventilator and insert an appropriately sized oxygen
catheter into the endotracheal tube. Adjust the
   oxygen flow to deliver 100% oxygen at a flow rate
   between 2 – 6 L/min. Use only the minimum flow
   required to maintain adequate oxygen saturation.
   A T-piece or CPAP circuit can also be used to
   supply oxygen to the patient when disconnected
   from the ventilator.
6. After a period of apnea of between 5 – 10 minutes
   (depending on the PaCO
   at the beginning of the
test), perform an arterial blood gas. The PaCO
   on
the ABG should be ≥ 60 mm Hg and ≥ 20 mm Hg
more than the baseline level. If the PaCO
   does not
meet these parameters, the test may be continued
   and the ABG repeated after 5 minutes, provided
   the patient continues to be stable.
7. Observe the patient continuously for the presence
   of any respiratory efforts. If any respiratory efforts
   are noted, abandon the test immediately. If there
   is complete apnea, note the duration of apnea and
   the PaCO
   at the end of the test.
8. Reconnect the patient to the mechanical ventilator.
Response: In a brain dead patient, no respiratory
efforts should be seen during the period of apnea.
Ancillary Tests
Ancillary tests are not routinely required to determine
brain death and are not a substitute for the clinical
examination. However, they may be used in specific
situations:
a. When the apnea test cannot be performed safely
b. If there is uncertainty regarding the results of the
   neurological examination
c. If a medication may be present that would preclude
   declaration of brain death
d. In order to reduce the waiting period between the
two sets of tests
A number of ancillary tests are available.
EEG
A digital EEG should be performed by a technician
who has experience in performing EEG’s for the
purposes of determining brain death. In general,
the sensitivity should be increased to 2 μV, the high
frequency filter should be set above 30 Hz and the
low frequency filter set not above 1 Hz. A minimum
of eight scalp electrodes should be used. The EEG
should demonstrate a lack of reactivity to intense
somatosensory and audiovisual stimulation.
Tests to Assess Intracranial Blood Flow
The purpose of these tests is to show that there is no
flow in the intracerebral vessels, due to occlusion
of the vasculature by cerebral edema. The various
techniques by which intracranial blood flow can be
assessed include four vessel cerebral angiography,
Radionuclide imaging, CT angiography, Magnetic
Resonance angiography and Trans Cranial Doppler
ultrasonography. Of these techniques, four-vessel
cerebral angiography is regarded as the gold standard
and involves direct injection of contrast medium into both Carotid arteries and both Vertebral arteries. Of all the confirmatory tests mentioned above, EEG is the most easily available test. Radionuclide cerebral blood flow assessment is also acceptable – the remainder are time consuming, not easily available, not always standardized, may require shifting an unstable patient and, in some cases, expensive.

Any one of the following tests may be used (depending on availability) when an ancillary test is required:

i. EEG
ii. Radionuclide cerebral blood flow assessment
iii. Four vessel cerebral angiography.

**Time Course of Tests for Brain Death**
- The clinical tests are performed twice, each time by a different physician
- The apnea test is performed twice – may be performed by the same physician
- Death is declared when the second neurological examination and apnea test confirm that the results of the first tests are unchanged and the changes are irreversible
- If an ancillary test performed after the first clinical examination/apnea test is consistent with brain death, then the second clinical examination/apnea test can be performed at any time

Table 1 below gives the time gap between the clinical tests.

<table>
<thead>
<tr>
<th>Age</th>
<th>Clinical tests</th>
<th>Interval between tests</th>
<th>Ancillary tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term new born (&gt; 37 weeks gestational age to 30 days)</td>
<td>As adult</td>
<td>24 hrs</td>
<td>If required</td>
</tr>
<tr>
<td>31 days – 18 years</td>
<td>As adult</td>
<td>12 hrs</td>
<td>If required</td>
</tr>
</tbody>
</table>

**References**

**Pediatric Braindeath Guidelines Group 2011**
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NCPCC 2014 Abstracts (Oral)

High-frequency Oscillatory Ventilation (HFOV) for Acute Pediatric Respiratory Failure - A tertiary care centre experience of 62 cases

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Background & Aims: The present article reports our experience with high-frequency oscillatory ventilation (HFOV) in pediatric patients with acute respiratory failure who deteriorated on conventional mechanical ventilation.

Methods: In this analysis of retrospective data, we analyzed the chart records of 62 consecutively ventilated pediatric patients with HFOV from October 2011 to August 2014 in our pediatric intensive care unit. The demographics, cause of respiratory failure, Pediatric Index of Mortality (PIM II) Score, oxygenation index, PaCO₂, and complications if any, were recorded and calculated at various time points before and after the start of HFOV, along with patient outcome and cause of death.

Results: There were 39 male subjects while 23 were female. The median age of the subjects was 54 (1.5-192) months. All patients received conventional ventilation before HFOV. Mean oxygenation index (OI) at the start of HFOV was 28 and mean PCO₂ was 67 mmHg with significant respiratory acidosis in all. After initiation of HFOV, there was an immediate and sustained improvement in ventilation with significant decrease in PCO₂ (p ≤ 0.003) and improved oxygenation with increase in PaO₂/FiO₂ ratio in most subjects except 4. Oxygenation Index (OI) was decreased significantly after 6 hours of HFOV and maintained for at least 48 hours (p < 0.05) except in patients who developed complications (pneumothorax – 5, hemodynamic compromise – 3 & oxygenation failure – 4). Overall survival rate was 33%. Mean PIM II risk of mortality was 63% with no mortality benefit with use of HFO in our series of patients.

Conclusions: HFOV rescue therapy was associated with a significant improvement in ventilatory & oxygenation parameters without any benefit on mortality. Future studies are necessary to evaluate whether the outcome of patients may be improved if HFOV is applied earlier in the course of disease.

Occurrence and Outcome of Acute Kidney Injury Amongst Patients Admitted in Paediatric Intensive Care Unit (PICU)

Urmila Jhamb, Jyoti
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Objective: To study the occurrence and progression of acute kidney injury (AKI) IN Children in paediatric intensive care unit (PICU), as defined by PRIFLE criteria and to study its association with mortality and length of stay in PICU.

Design: Prospective cohort study.

Setting: PICU, Maulana Azad Medical College

Patients: The study included 250 patients, aged 1 month to 12 years, admitted to PICU, from May 2012 to Jan 2013.

Intervention: For all Patients pRIFLE stage was checked at admission, every 2nd day if normal and daily if any abnormality was found.

Main outcome measures: Patients were subsequently divided into AKI and no AKI groups, progression/improvement of various AKI stages was recorded and effect of AKI on mortality and Length of stay in PICU was analyzed.

Result: 34.4% of total patients developed AKI. 24.8% had an initial p-rifle Score of risk (R), 7.2% had injury (I) and 2.4% had failure (F). Out of children who had initial score of R, 14.5% progressed to I while 89% were detected with AKI within 7 days of PICU stay. Mortality in max pRIFLE score of R, I, F was 45.8%, 62.3%, 62.5% respectively, compared with 18.9% for patients without AKI. Children with AKI had a higher mean (1.64 times) length of stay in PICU than children with no AKI.

Conclusion: In our PICU population acute kidney injury, as defined by the pRIFLE classification, is associated with increased mortality and length of stay.

Predictors of Extubation Success in Mechanically Ventilated Children in PICU

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Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Aim: To evaluate the significance of parameters affecting extubation in children.

Methods: Data was collected prospectively on all children between age group of one month to 17 year, admitted to pediatric ICU over a period of one year. Patients admitted with respiratory failure at admission or during hospitalization were included. Pre-extubation clinical, ventilator and laboratory parameters were evaluated. Their significance in relation to extubation success was determined by student’s t test and chi-square test.

Results: A total of 53 patients underwent 62 extubation trials (n = extubation trials). Patients who were successfully extubated had significantly better nutritional status (weight > 3rd centile) and lower PRISM score (< 10). Most common etiology amongst patients who were being mechanically ventilated was primary pulmonary pathology. Extubation success was significantly higher in this group (p-value=0.0039). Laboratory parameters (pre-extubation ABG, hematocrit, serum K+) were not found to be significantly associated with extubation success. Pre-extubation ventilator parameters-PEEP (< 3), DPIP (8-11), ventilator rates (< 25) and FiO₂ (< 0.35) were found to be associated with significantly higher extubation success. Stridor, accidental extubation, VAP (ventilator associated pneumonia) and duration of mechanical ventilation (> 7 days) had statistically
Impact of Multifaceted Quality Improvement Intervention on Device Related Infections in Pediatric Intensive Care Unit-A single centre experience
Ramachandran Rameshkumar, Anbazhagan Jagadeesh, Manju Kedarnath, Subramanian Mahadevan, Parameshwaran Narayanan, Kelamangalam Neelakantakurup Harikrishnan, Sujatha Sistla
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Background and Aims: Health care associated infections (HAI) are a significant problem in PICU. Surveillance and prevention of HAI by multifaceted quality improvement intervention remains a part of standard of care.

Methods: Study was conducted in 19 bedded-PICU of a tertiary care referral academic institute. Data regarding VAP and CLABSI from the above mentioned factors. 77.8% had good neurological outcome. Multivariate logistic regression analysis showed prolonged CFT, combined (metabolic& respiratory) acidosis and altered coagulation profile during pre-arrest period, need for multiple doses (> 3) of adrenaline during intra-arrest period and low GCS at 24 hrs post ROSC were also predictive of non survival apart from the above mentioned factors. 77.8% had good neurological outcome (with PCPC score of 1 or 2 at hospital discharge). All these parameters were compared between the survivors (discharged after an in-hospital cardiac arrest) and non survivors.

Results: Among 5049 children admitted during study period, 382 (7.5%) children had an episode of in-hospital cardiac arrest. Of these, 225 children had to be excluded. 137 children were included for study and results of these were analysed. ROSC was achieved in 82 children (59.8%) but only 27 children (19.7%) survived till hospital discharge (survivors). Most common rhythm during arrest was bradycardia (72.9%) followed by asystole (19%) and VT/VF (5.8%). Presence of low blood pressure, prolonged capillary refilling time, low saturation and hypothermia at 4 hours, 12 hours and 24 hours post cardiac arrest were associated with poor outcome. Multivariate logistic regression analysis showed prolonged CFT, combined (metabolic& respiratory) acidosis and altered coagulation profile during pre-arrest period, need for multiple doses (> 3) of adrenaline during intra-arrest period and low GCS at 24 hrs post ROSC were also predictive of non survival apart from the above mentioned factors. 77.8% had good neurological outcome (with PCPC score of 1 or 2 at hospital discharge).

Conclusion: Survival after cardiac arrest can be reliably predicted using certain pre-arrest parameters and blood investigations and post cardiac arrest hemodynamic parameter monitoring.

Assessment of Volume Responsiveness by Passive Leg Raising Test in Pediatric Patients with Shock - Preliminary observations
Priyavarthini V, Sathish kumar K, Suchitra Ranjita, Rajeshwari Nataraj
Pediatric Intensive Care Unit, Apollo Children’s Hospital, Chennai, Tamilnadu.

Background and Aims: Passive leg raising (PLR) test to assess fluid responsiveness (FR) has been validated extensively in adults higher association with extubation failure.

Conclusions: This study demonstrates that close attention towards etiology, clinical assessment, PRISM Score, respiratory mechanics, duration of mechanical ventilation and ventilator related complications, may help predict extubation success. Thus improving patient care and final outcome.

Factors Affecting Survival After in-Hospital Cardiac Arrest Among Pediatric Patients in a Tertiary Care Hospital in South India
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and has been found to be very useful in assessment of the same. However, paediatric literature is limited. The objective of this study was to determine if PLR induced changes in hemodynamics predicted FR in children with shock.

**Methods:** This is an ongoing prospective observational study in a tertiary care paediatric centre, done after ethics committee approval. Children with tachycardia plus any other sign of shock were included. Hemodynamic parameters including heart rate, systolic BP, stroke volume and cardiac index (CI) were assessed at baseline, after PLR and after volume loading using Ultrasound Cardiac Output Monitor (USCOM). An increase in CI > 10% with PLR was considered as predictor of fluid response.

**Results:** Of 17 patients, only 3 patients (17.6%) had >10% increase in CI after PLR and 5 (29.4%) had an increase after fluid challenge. The sensitivity and specificity of PLR in predicting fluid responsiveness were 40% and 91.7% respectively. The positive predictive value of PLR was 66.7% and the negative predictive value 78.6%.

**Conclusions:** The preliminary results of this ongoing study indicate that PLR may not be as good a predictor of FR as in adults. However, the negative predictive value may be significant. Certainly, the sample size was small and larger numbers are required to validate these findings.

### Retrospective Analysis of Levosimendan in Pediatric Post Cardiac Surgery Patients

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**Background and Aim:** Levosimendan is a new inodilator with calcium sensitizing and K-ATP channel opening properties. Our aim was to demonstrate its safety and efficacy in post cardiac surgery patients.

**Methods:** Ethical clearance was obtained. Retrospective analysis of 20 children who received levosimendan infusions between March 2013 and August 2014. Cases included were TGA, TAPVC, AVCD, TOF, Ebstein’s anomaly etc. Levosimendan was administered without bolus dose, as a continuous infusion of 0.1 to 0.2 μg/kg/min over 24 to 48 hours duration. Mean time of initiation was 6.5 days (1-17 days). Hemodynamic parameters, inotropic score and ECHO findings were analysed from 48 hours before and up to 5 days after levosimendan infusion. Adverse effects during levosimendan infusion were studied.

**Results:** Mean inotropic score (IS) for patients improved from 14.72 to 9.63 (median value before infusion 14 (range 1.25-42.3) and after infusion 8.6 (range 1.6-51)) 14 out of 20 (70%) patients had improvement in the IS within 72 hours. ECHO showed marginal improvement for 6 patients (30%) in terms of biventricular function. HR, systolic BP, diastolic BP, mean BP, and CVP were largely unchanged. No adverse effects were noticed.

**Conclusions:** This study shows levosimendan is safe in postoperative period and its use resulted in a significant reduction in inotrope score. Further prospective studies in children are required to determine its efficacy early in post cardiac surgery children with LCOS.

### Long Term Effects of Mechanical Ventilation on Pulmonary Functions in Children

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**Aim:** To determine effect and factors affecting pulmonary function tests in mechanically ventilated children on follow up.

**Method:** Mechanically ventilated children (> 5 yrs) admitted in PICU of a tertiary care, multispecialty hospital over a period of 15 months were included. PFT were done using spirometer at time of discharge, 3 months and 6 months later. Values were compared to expected norms at each visit and deficit improvement noted.

**Results:** 20 patients completed 6 month follow up (male: female 3:1) with mean age of 9 years. Reason for ventilation was pulmonary condition (45%), CNS (35%) and miscellaneous (20%), mean duration of ventilation 8.3 days. 75% (n = 15) and 65% (n = 13) patients at 3 months, 6 months respectively had restrictive pattern of lung function. No patient had significant deficit in tidal volume. Significant improvement was seen in inspiratory volume, PEFR at 3 and 6 months though normal values were not achieved. Nearly 65% and 60% children had deficit in FVC at 3 and 6 months respectively. Significant increase in FEV1 occurred on follow up. Patients with neurological causes, low PRISM III scores had better results, while longer duration of ventilation, high peak pressures and high FiO2 had worse outcome. Vital Capacity, FEV1 and FVC showed greatest deficits.

**Conclusion:** Mechanically ventilated patients develop significant defects in long term lung function, most common was restrictive lung disease. Many factors may affect the same. Longer follow up studies are needed.

### Comparison of 0.45% vs. 0.22% Normal Saline in 5% Dextrose as Intravenous Maintenance Therapy in Children Admitted in Pediatric ICU

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**Background and Aims** – Due to concerns regarding occurrence of hyponatremia with use of hypotonic maintenance solutions (0.22% normal saline (NS) in 5% dextrose) in critically ill children, we did a study to compare the change in serum sodium levels in children receiving i.v. maintenance fluids as 0.22% NS in 5% dextrose or 0.45% NS in 5% dextrose.
Methods- An open labeled RCT was conducted in 140 children aged 3 months-12 years in PICU. One group received 0.22% NS in 5% dextrose and the other received 0.45% NS in 5% dextrose. We studied the change in serum sodium levels from baseline at 24 & 48 hours and occurrence of dysnatremia. Ethical approval was obtained from institutional ethical committee.

Results- 68 children received 0.22% NS in 5% dextrose and 72 received 0.45% NS in 5% dextrose. Mean change in serum sodium levels from baseline between two groups (0.22% saline vs. 0.45% saline) was statistically significant (At 24 hrs: -2.75±4.61 vs. +0.61±4.58, p=0.0001; At 48 hrs: -2.68±3.99 vs. +0.68±4.23, p = 0.0157). The number of patients with hyponatremia was significantly higher in the 0.22% saline group at 24 hrs (Moderate hyponatremia (125-129 mEq/l) - 5 vs. 0, p=0.025; MILD hyponatremia (130-134 mEq/l) - 31 vs. 11, p=0.000). No hypernatremia was observed with 0.45% dextrose saline.

Conclusions- With the use of 0.22% dextrose saline, fall in serum sodium was significantly higher and there was more severe hyponatremia. 0.45% dextrose saline caused a minimal increase in mean serum sodium and no hyponatremia making it a more appropriate maintenance fluid.

Competing interests- None.

**Effect of Estimated Glomerular Filtration Rate (eGFR) & Fluid Balance on Clinical Course and Outcomes of Children Admitted with Severe Dengue**

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Background and aims: To measure estimated glomerular filtration rate (eGFR) at admission and fluid balance in the first 36 hours of ICU stay and assess their effect on disease course and outcomes in severe dengue. This was designed as a retrospective descriptive study in a tertiary level pediatric intensive care unit in South India.

Methods: Case records of all children fulfilling the WHO case definition of severe dengue were included, those who received intravenous fluid for less than 12 hours were excluded. Primary parameters measured included fluid balance in first 36 hours measured every 12 hours, durations of oxygen requirement, mechanical ventilation, ICU stay and total hospital stay.

Results: 26 children were enrolled, 14 boys and 12 girls. The median duration of ICU stay was 60 hours, and that of hospital stay 109 hours. eGFR was less than 60 mL/min in 6 patients (83.3% expired and 16.7% survived). eGFR, measured by modified Schwartz’s formula, at the time of admission correlated inversely with requirement of oxygen therapy and mechanical ventilation (p<0.05) and fluid balance in first 36 hours. Positive fluid balance (FO > 15%) in the first 36 hours was significantly higher in children who expired (p<0.011). eGFR>90 mL/min at admission had 100% sensitivity and 79% specificity to predict the possible occurrence of fluid overload >15% (Area under curve - 0.882)

Conclusion: Fluid balance in the first 36 hours had a significant positive correlation with mortality and negative correlation with eGFR. Children with admission eGFR<90 mL/min may require restrictive fluid therapy to improve survival.
Flexible Fibreoptic Bronchoscopy in Critically Sick Indian Children
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Background: Flexible fibreoptic bronchoscopy (FFB) remains a modality occasionally used in critically sick Indian children for a variety of reasons. This modality, however, is safe and helpful for both diagnosis as well as guidance of treatment. This study is a brief description of our experience with this modality.

Materials and Methods: This observational study was conducted in the PICU over a 15 month period from March 2012 till June 2013. Children requiring a bronchoscopy for predefined indications were enrolled in the study. A record was maintained for the indication for the procedure, the patient’s clinical status, ventilator parameters, etc. The procedure was performed under continuous cardiorespiratory monitoring. A lavage sample was collected when indicated. Patient’s vital parameters and ventilator settings, if any, were recorded before, during and up to 6 hours post procedure. The success in achieving objectives, both diagnostic and therapeutic was noted.

Results: FFB was performed in a total of 43 PICU patients during the study period. The mean age ranged between 1 month to 12 years. Of the 43 children studied 36 were males (83.7%).

The common indications were persistent radiographic shadows in the form of pneumonia (27.9%) or collapse (20.9%), suspected airway foreign body (20.9%) and acute stridor (16.3%). One patient was intubated using flexible bronchoscopy. The route for scope insertion was through the nostril in 26 patients (60.5%), patient was intubated using ventilator parameters, etc. The procedure was performed under continuous cardiorespiratory monitoring. A lavage sample was collected when indicated. Patient’s vital parameters and ventilator settings, if any, were recorded before, during and up to 6 hours post procedure. The success in achieving objectives, both diagnostic and therapeutic was noted.

Conclusion: Flexible fibreoptic bronchoscopy in PICU patients has a high diagnostic yield, is safe and well tolerated.

Bedside Sonographic Measurement of the Inferior Vena Cava Diameter Correlate With Central Venous Pressure in the Assessment of Intravascular Volume in Children
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Background: Volume status assessment is an important aspect of patient management in the pediatric intensive care unit (PICU). Echocardiologist-performed measurement of IVC distensibility index (IVC-DI) provides useful information about filling pressures, but is limited by its portability, cost, and availability. Intensivist-performed bedside ultrasonography (INBU) examinations have the potential to overcome these impediments. We used INBU to evaluate hemodynamic status of PICU patients, focusing on correlations between IVC-DI and CVP.

Methods: 201 children were included. The difference in the mean daily fluid balance (ml/kg) between survivors and non-survivors was maximum at 48 hours (32.3 ± 2.9 vs 46.7 ± 5.0, p =0.01). Patients who developed > 20% FO at 48 hours had significantly higher mortality (25/45;
Effect of Pre-hospital Transport and Patient Related Factors on Rates of PICU Admission Among Patients Presenting to the Pediatric Emergency Department of a Tertiary Care Centre

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Background and Aims: Data on the transport practices prevalent among patients presenting to the Pediatric emergency department (PED) of resource limited countries is scarce. Moreover, effect of these and other patient related factors on rates of ICU admission has also not been well studied. The aim of this study was therefore to evaluate the prevailing pre-hospital transport practices and study the effect of these and other patient related factors on rates of admission to the PICU.

Methods: Children presenting to the PED of our hospital over a period of 6 months (Jan-Jun 2013) were evaluated. We collected information on details pertaining to pre-hospital transport, and, their clinical parameters, and need for PICU admission. The study was approved by the IRB.

Results: A total of 319 patients presented to the PED during the study period. Nearly 61% (196) of the patients used public transport systems such as autorickshaw and bus to transport the children to the health care facility. Fifty four children (17%) required PICU admission and 19 (6%) were admitted to the wards. Severe sepsis/septic shock (26, 48%) was the commonest cause for PICU admission, followed by respiratory illnesses such as pneumonia and asthma (13, 24%). On univariable analysis, we found factors such as nature of illness (septic shock/pneumonia), Pediatric Index of mortality (PIM) 2 score and duration of illness before presentation to be significantly associated with need for PICU admission.

Conclusion: Public transport systems were commonly used to transport patients from home/hospital to our centre. Nature of illness and the admission PIM2 scores predicted the need for PICU admission.

Key words: Pre-hospital transport; PICU admission; public transport; autorickshaw

Continuous Renal Replacement Therapy (CRRT) in Children With Sepsis and Multi Organ Dysfunction Syndrome - Indian Scenario

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Background: Sepsis with multi organ dysfunction syndrome (MODS) is a common occurrence in Pediatric Intensive Care Unit (PICU) in sick children. Unfortunately scanty literature is available regarding CRRT utility in sepsis with MODS from developing countries.

Objectives: To report our experience and emphasize the initiation of early CRRT in managing children with sepsis and MODS in a developing nation.

Materials and methods: Medical records of children required CRRT in PICU at Sir Ganga Ram Hospital from September 2010 to August 2014 were retrospectively analyzed to obtain data on demographic factors, mode of CRRT & its prescription, probable effect of CRRT on inotropic score, plateau pressures, P/F ratio, hemodynamic stability while on CRRT, anticoagulants, feasibility and complications.

Results: During the study period 23 children required CRRT (male-15). The median age was 11 years (13 months to 16 years) and median weight 39 kg (7.5 kg to 65 kg). 18 had primary diagnosis of sepsis with MODS, while 5 had severe Dengue fever with sepsis. At initiation of CRRT, all patients were receiving mechanical ventilation and inotropic support. 11 children (47.8%) had fluid overload (FO) of >10% at the time of initiation of CRRT. 8 out of 11 survivors (72%) received CRRT within 48 hours of admission while in 7 out of 12 (58.4%) non-survivors CRRT was initiated after 48 hours. The median FO among survivors and non survivors was 9.1% (2.9%-12.5%) and 7.4% (2.4%-14%) respectively but the mean serum creatinine in survivors and non survivors were 2.5±0.8SD and 3.5±1.1SD (p<0.03) respectively. There was no statistically significant difference in the duration of ICU stay and CRRT, change in inotropic score and P/F ratios between the survivor and non-survivor. Total of 30 CRRT sessions amounting to 1142.4 hours were given. CVVHDF was preferred in all patients. The mean lifespan of filter was 47.62 hours. One patient had Intracranial bleed secondary to heparin usage as an anticoagulant. Manageable electrolyte abnormalities like hypokalemia, hypophosphatemia, hypomagnesaemia, hypocalcaemia were observed in 75%, 55%, 40%, 10% patients respectively. Clotting was the most common circuit related complication.

Conclusion: Early initiation of CRRT in children with sepsis and MODS may improve the survival but large sample size is required for validation in Indian scenario.
Infection Risk From Femoral vs Jugular Venous Catheters
Critical Care Medicine - December 30, 2013 - Vol. 19 - No. 8

Femoral venous catheters may carry the same risk of infection as jugular venous catheters in critically ill patients.

Article Reviewed

Objective
To evaluate the risk of infection and catheter-tip colonization with femoral versus internal jugular central venous catheters.

Design
Secondary analysis from 2 previous studies designed to assess the effect of chlorhexidine-impregnated dressings on the incidence of catheter-related bloodstream infections (CR-BSI).

Methods
Both studies enrolled ICU patients from hospitals in France. The present study analyzed data only from internal jugular and femoral vein sites. Catheters were managed via a protocol similar to that of Centers for Disease Control guidelines for catheter maintenance. Catheters were removed when no longer needed or if CR-BSI was suspected. Catheter-tip culture was performed with a quantitative culture technique. Insertion-site skin colonization was assessed semiquantitatively by pressing an agar-coated, chlorhexidine-neutralizing plate to the skin. If a CR-BSI was suspected, peripheral blood cultures were obtained. A special blinded committee classified the event as a CR-BSI or colonization. A Cox model for clustered data was constructed to determine the effect of catheter site on colonization and CR-BSI.

Results
2128 patients involving 2527 catheters and 19,481 catheter-days were analyzed (55.4% femoral, 44.6% internal jugular). Patients with femoral catheters were sicker, and median time of catheter duration was longer (7 vs 5 days). There was no difference in CR-BSI. Catheter colonization was not different between the femoral and internal jugular vein sites overall, although there was an increase in femoral site colonization after the fourth day. There was a decrease in colonization for females at the internal jugular site. Dressing disruptions were higher at the femoral site. Skin colonization at catheter removal was higher at the internal jugular vein site. There was no difference between sites when impregnated dressings were used.

Conclusions
Internal jugular and femoral central venous catheters carry a similar risk of CR-BSI and skin colonization.

Reviewer’s Comments
The subclavian site is clearly preferred for central venous access, but fewer than half of ICU patients receive subclavian catheters because of either real or perceived disadvantages (risk of pneumothorax, bleeding, etc). We are often forced to choose “the lesser of 2 evils,” namely, internal jugular or femoral. There are a number of factors that must be weighed in this decision, and risk of infection is high on the list. The present study suggests that infectious risk may be similar between the sites, especially if the catheter remains in place <5 days. Use of chlorhexidine-impregnated dressings may also reduce skin colonization and, perhaps ultimately, infection. The overall rate of infection in this study was low (0.8%), so it may have been underpowered.
to detect a difference. This study did not assess the risks of other complications with the femoral site (reduced mobility, deep venous thrombosis), so it must be interpreted in the broader context of site selection.(Reviewer–Brian T. Garibaldi, MD).

The Bad Blood of Transfusion Medicine
Critical Care Medicine - December 30, 2013 - Vol. 19 - No. 8

A restrictive, compared to a more liberal, transfusion strategy has been shown to decrease the number of blood transfusions in elderly mechanically ventilated patients without worsening clinical outcomes.

Article Reviewed

Background
A restrictive transfusion strategy improves outcomes in critically ill patients, but elderly patients with respiratory failure may need extra oxygen-carrying capacity to supply adequate oxygen to their tissues.

Objective
To compare the effect of a restrictive versus liberal transfusion strategy on outcomes in elderly critically ill ventilated patients.

Design
Open-label randomized trial.

Participants
100 patients in 6 ICUs aged >55 years already ventilated for >4 days, needing at least another 24 hours of ventilation, and having a hemoglobin (Hgb) <9.0 g/dL.

Methods
The primary endpoint was difference in Hgb levels between groups. Clinical outcomes, such as mortality and ventilator-free days, were secondary outcomes.

Interventions
Patients in the liberal arm received single-unit transfusions when their Hgb fell <9.0 g/dL with a target of 9.0 g/dL to 11.0 g/dL compared to a transfusion threshold of 7.0 g/dL and a goal of 7.0 g/dL to 9.0 g/dL for the restrictive group. The strategy was continued for the longer of either 14 days or ICU discharge. With significant bleeding, clinicians could transfuse as clinically indicated.

Results
Almost one-third of the patients had ischemic heart disease and two-thirds had already received at least 1 transfusion prior to enrollment. The restrictive group received a median of 1 less unit of red-blood cell (RBC) transfused (2 units vs 3 units; \( P =0.002 \)), with 9% fewer patients receiving a transfusion (40% vs 49%). The mean Hgb was almost 1.5 g/dL higher in the liberal strategy group (9.6 g/dL vs 8.2 g/dL; \( P <0.0001 \)). There was no difference in any of the secondary outcomes, including ICU length of stay, hospital length of stay, ventilator-free days, or change in sequential organ failure assessment score. Hospital mortality was numerically lower in the restrictive strategy group, but it was not statistically significant (19% vs 24%; relative risk, 0.76; 95% confidence interval, 0.48 to 1.2).

Conclusions
A restrictive transfusion strategy resulted in lower mean Hgb values and less transfusions but similar clinical outcomes as a more liberal transfusion strategy in older, mechanically ventilated patients.

Reviewer’s Comments
Despite new blood preparation and storage techniques, the results of this study, although limited to elderly mechanically ventilated patients, are very similar to those from the Transfusion Requirements in Critical Care study, which was completed more than a decade ago. Once again, a higher transfusion threshold did not improve outcomes, and it may have worsened them. This has now been shown in general ICU patients, in patients following cardiac surgery, and in critically ill patients with upper gastrointestinal bleeds. Limitations to this study include its small size and the definition of “elderly” extending to as young
as 55 years; however, all available data indicate transfusing PRBCs to optimize oxygen delivery in all critically ill patients is not beneficial. The real advance in transfusion medicine will occur when we obtain the ability to measure the oxygen delivery and/or demand in each individual patient at the bedside. (Reviewer—Todd W. Rice, MD, MSc).

**Induced Hypothermia Not Beneficial in Severe Bacterial Meningitis**

Critical Care Medicine - December 30, 2013 - Vol. 19 - No. 8

Induced hypothermia for 48 hours fails to improve neurological outcomes in patients with bacterial meningitis and may worsen mortality.

**Article Reviewed**


**Background**

The morbidity and mortality of bacterial meningitis remain high, with about 20% of patients dying and another large proportion surviving with significant neurological injury. Induced hypothermia has benefit in other conditions with global cerebral ischemia, but its effect in bacterial meningitis remains unknown.

**Objective**

To determine if induced hypothermia would improve the functional outcome of comatose patients with bacterial meningitis.

**Design**

Open-label, multicenter, randomized controlled trial.

**Participants**

98 adults with suspected or proven meningitis with a Glasgow Coma Scale score of < 9 from 49 ICUs in France.

**Methods**

The primary endpoint was Glasgow Outcome Scale score 3 months after randomization assessed by a blinded physician via telephone. Only mild or no disability was scored as a favorable outcome. Three-month mortality, hearing impairment, and muscle strength were secondary outcomes.

**Interventions**

Induced-hypothermia patients were cooled to 32 degrees Celsius to 34 degrees Celsius for 48 hours followed by passive rewarming. Patients in both groups were treated with appropriate antibiotics, tight glycemic control, and mean arterial pressure >70 mm Hg. A total of 87% of patients in both groups received steroids.

**Results**

After enrollment of 98 of a planned 276 patients, the data and safety monitoring board stopped the study due to higher mortality in the hypothermia group (51% vs 31%; $P = 0.04$). Streplococcus pneumoniae was the causative agent in 77% of cases. A total of 37% of patients in the hypothermia group had shock at baseline compared to only 20% in the control group ($P = 0.14$). Mean temperatures 24 hours after randomization were 33.3 degrees Celsius versus 37.0 degrees Celsius in the hypothermia and control groups, respectively. At 3 months, an unfavorable neurological outcome occurred in 42 of 49 patients in the hypothermia arm (86%) compared to 36 of 49 (73%) in the control ($P = 0.13$). After multivariable adjustment, mortality remained higher in the hypothermia group at 3 months, although not statistically significant (hazards ratio, 1.76; $P = 0.10$).

**Conclusions**

Induced hypothermia did not improve favorable neurological outcomes in patients with severe bacterial meningitis and may have worsened mortality.

**Reviewer’s Comments**

Given its success in post-cardiac arrest patients, hypothermia has become an exciting treatment modality. Its use has started to spread to other disease processes, including some studies looking at its use in neurological injuries, drownings, and fulminating hepatic failure. In the not-so-distant
past, sepsis represented a relative contraindication to hypothermia, but recently this has thought to be less of an issue. This study in patients infected with bacterial meningitis demonstrated no benefit, and even potential harm, with hypothermia. The fact that patients who underwent cooling overall had worse outcomes is concerning that maybe this is sepsis related. These data demonstrate that although hypothermia may be good post-cardiac arrest, it clearly is not a panacea, and we should exercise caution implementing it in patients who are infected. (Reviewer–Todd W. Rice, MD, MSc).

Lung Ultrasound Frequently Changes Management in Mechanically Ventilated Patients
Critical Care Medicine - December 30, 2013 - Vol. 19 - No. 8

When performed for specific clinical questions or unexplained alterations in arterial blood gas results, lung ultrasound has an impact on clinical decision-making in critically ill patients receiving mechanical ventilation.

Article Reviewed

Background
Lung ultrasound (LU) is a noninvasive tool that provides rapid and accurate diagnostic information in mechanically ventilated patients. The impact of this modality on medical decisions in the ICU has not been examined.

Objective
To examine the impact of LU on decision-making among critically ill patients receiving mechanical ventilation.

Design
Single-center, prospective, interventional trial.

Participants
189 mechanically ventilated patients in a combined medical-surgical ICU.

Methods
Patients were enrolled when a single operator was available and the primary physician requested LU due to unexplained alteration in arterial blood gas or suspicion of 1 of 5 specific pathologic conditions (pneumothorax, significant pleural effusion, unilateral atelectasis, pneumonia, diffuse interstitial syndrome). The LU operator reported imaging findings, but he/she did not play a role in decision-making. LU was performed using a validated protocol. The clinical yield of LU for the specific diagnosis was calculated as the percentage of studies that confidently excluded the suspected diagnosis or revealed positive findings with diagnostic implications. The primary physician labeled findings as expected or unexpected. Impact of LU on decision-making was assessed by calculating a net reclassification improvement.

Results
LU was performed 253 times in 189 patients. A total of 108 (42.7%) studies were performed due to unexplained change in blood gas and 145 (57.3%) due to a suspected pathologic condition. The net reclassification improvement was 85.6%, and management changed directly due to LU findings in 119 cases (47%). LU findings supported diagnoses not suspected by the primary physician in 53 (21%) cases.

Conclusions
LU impacts clinical decision-making when performed for specific clinical questions or unexplained alterations in arterial blood gas results in critically ill patients receiving mechanical ventilation.

Reviewer’s Comments
Although prior research has demonstrated the diagnostic utility of bedside LU in critically ill patients, this study attempts to evaluate the impact of LU on medical decision-making. The high percentage of management changes reported to be due to ultrasound findings is impressive, and the frequent findings consistent with unsuspected diagnoses are very intriguing. In addition, performing
LU for 5 specific suspected diagnoses or blood-gas abnormalities is a unique characteristic of this study design, as compared to routine LU in patients with respiratory failure. The non-randomized design and uncontrolled nature of the study, however, are major limitations that cannot be overlooked. In addition, this study was performed at a single center with significant experience using LU, such that routine chest x-rays are no longer obtained in this ICU. Therefore, these results are not generalizable to other centers. Although LU is a powerful bedside tool in experienced hands, the results of this study must be taken in the context of these major limitations. (Reviewer--Jakob I. McSparron, MD).

**Using Prone Positioning at High PEEP Levels**
Critical Care Medicine - December 30, 2013 - Vol. 19 - No. 8

Using prone positioning at high positive end-expiratory pressure levels protects against marked rises in tidal hyperinflation, decreases cyclic recruitment/derecruitment, and increases alveolar recruitment.

**Article Reviewed**

**Background**
A recent large randomized controlled trial reported that prone positioning markedly improved mortality in mechanically ventilated patients with acute respiratory distress syndrome (ARDS). The mechanisms by which this led to better outcomes is unclear.

**Objective**
To examine how the combination of prone positioning and positive end-expiratory pressure (PEEP) in mechanically ventilated patients with ARDS impacts alveolar recruitment, tidal hyperinflation, and cyclic recruitment/derecruitment.

**Participants**
24 adult mechanically ventilated patients (for 24 to 72 hours) who fulfilled ARDS criteria.

**Methods**
Measurements were obtained in both the ICU and in the CT scanner. All patients were paralyzed, deeply sedated, and underwent lung-protective ventilation ($V_{t}=6$ mL/kg). In the ICU, respiratory mechanics and oxygenation were measured after 20 minutes of ventilation at a PEEP of 5 and 15 cm H$_2$O. A recruitment maneuver (RM) of 45 cm H$_2$O was performed to standardize volume history before each change in PEEP. In the CT scanner, static images to assess alveolar recruitment were taken in both prone and supine positions at PEEP 5 and 15 and during an RM. Dynamic images (to assess tidal hyperinflation and cyclic recruitment/derecruitment) were taken both supine and prone at 5 and 15 cm H$_2$O PEEP. The various lung compartments were categorized by CT density, and “high recruitability” was defined as having >14% of potentially recruitable lung volume in the supine position. The sequencing of positions and PEEP levels were randomized.

**Results**
Raising PEEP to 15 cm H$_2$O in either position improved oxygenation and overall compliance while decreasing nonaerated tissue at the expense of increased tidal hyperinflation. Compared to supine, prone positioning resulted in significantly less tidal hyperinflation and nonaerated tissue at PEEP 15. The combination of prone positioning and PEEP 15 led to significantly decreased cyclic recruitment/derecruitment. In the supine position, a PEEP of 15 cm H$_2$O increased tidal hyperinflation significantly, and this was significantly attenuated by prone positioning. A total of 14 of 24 patients had high lung recruitability. They responded better to increasing PEEP to 15 (better compliance, less cyclic recruitment/derecruitment). For low recruitability patients, prone positioning significantly reduced nonaerated tissue.

**Conclusions**
Using prone positioning at high PEEP levels reduces tidal hyperinflation, decreases cyclic recruitment/derecruitment, and increases alveolar recruitment.
Reviewer’s Comments
This study supplements our understanding of the physiologic effects of prone positioning on lung mechanics and ventilator-induced lung injury in ARDS patients. One criticism on ARDS trials is that patients are often very heterogeneous. In trials looking at an open lung strategy, there were concerns that the final results were negative because there was a subpopulation of PEEP-responsive patients and another group of nonresponders. Perhaps prone positioning makes these groups more homogeneous and, thus, amplifies the effects of an open lung strategy. (Reviewer–Timothy J. Scialla, MD).

Does Arterial Line Infection Rate Rival Frequency of Central Line Infection?
Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

Arterial catheter-related bloodstream infections occur with a similar frequency to that of central venous catheter-related bloodstream infections.

Article Reviewed

Background
Despite widespread arterial catheter use, limited data report the risk of arterial catheter-related bloodstream infection (CRBSI) or provide insight into its pathogenesis.

Objective
To examine the epidemiology, microbial pathogenesis, and risk factors surrounding arterial CRBSI.

Design
Prospective study.

Participants
542 patients (834 arterial catheters, 3273 catheter-days) who also participated in 2 prospective randomized trials of CRBSI prevention methods (a chlorhexidine-alcohol solution for cutaneous antisepsis or a chlorhexidine-impregnated sponge dressing).

Methods
Investigators routinely obtained quantitative cultures of insertion site skin, catheter segments, hub, and infusate at the time of catheter removal. Restriction-fragment DNA subtyping defined concordance between catheter and peripheral blood organisms. A univariate analysis explored risk factors for arterial CRBSI.

Results
109 catheters (13%) were colonized, and causative bacteremia occurred in 11 cases (1.3%; 3.4 per 1000 catheter-days). Extraluminal colonization caused 63% of CRBSIs. Univariate analysis identified duration of catheter placement > 6 days as a risk factor for CRBSI (RR, 4.3; 95% CI, 1.2 to 15.6). The rate of arterial CRBSI was similar to the rate of non-cuffed central venous (CV) CRBSI in the contemporaneous randomized trials (2.7%, 5.9 per 1000 catheter-days).

Conclusions
Arterial CRBSIs occur with comparable frequency to CV CRBSIs and should be included in the differential diagnosis of sepsis or bacteremia. Extraluminal colonization is an important pathogenic mechanism of arterial CRBSI. Arterial catheters should be removed as early as possible.

Reviewer’s Comments
Arterial CRBSIs may be underappreciated in the ICU. When they do occur, CRBSIs increase ICU length of stay and carry a high attributable mortality. This prospective study used rigorous microbiological methodology to determine that the risk of arterial CRBSI is on par with the risk of CV CRBSI. The authors report a point estimate for arterial CRBSI risk but do not provide a confidence interval (CI); based on their figures, a 95% CI of 0.7% to 2.4% surrounds the arterial CRBSI incidence estimate of 1.3% (modified Wald method). It should be noted that the reported risk of CV CRBSI (2.7%; 5.9 per 1000 catheter-days) is on the high end of published values. Only 11 arterial CRBSIs occurred in their sample, which precluded multivariate analysis. Their
univariate data have wide CIs and do not inform which risk factors for arterial CRBSI are most prominent other than duration of catheter placement >6 days. Their finding that extraluminal colonization caused the majority of arterial CRBSI confirms that an alternative anatomic site should be selected when replacing arterial catheters. This article contradicts the notion that arterial catheters are an uncommon cause of bacteremia, although more robust data are still needed. Arterial catheters should be a suspected source in cases of sepsis or bacteremia without another compelling etiology and should be removed as soon as possible. (Reviewer–Benjamin D. Singer, MD).

Is It Time to Throw Away Gowns in the UCI?

Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

Universal contact isolation does not reduce acquisition of methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant Enterococcus, but it may decrease MRSA acquisition in ICUs with a high incidence of MRSA colonization.

Article Reviewed


Background

Nosocomial infections with methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant Enterococcus (VRE) are associated with poor patient outcomes and high costs of care.

Objective

To determine if universal contact isolation (UCI; gown and gloves for all patients in the ICU) reduces acquisition of MRSA and VRE colonization during an ICU stay.

Design

Cluster randomized, prospective controlled trial.

Methods

20 ICUs (medical, surgical, and medical-surgical) were compared. MRSA and VRE swabs were obtained from patients at admission and at discharge. Primary (combined) end point was acquisition of either MRSA or VRE. Secondary end points were acquisition of MRSA or VRE, a health care-associated infection (HAI), and adverse events.

Results

Use of UCI did not decrease the combined end point of acquisition of either MRSA or VRE, but it decreased rates of MRSA acquisition alone. No difference in the development of HAI was observed in either group. UCI increased the frequency of handwashing, but it decreased entry into each patient’s room.

Conclusions

Despite a high compliance with UCI, routine use of gowns and gloves did not reduce the acquisition of either MRSA or VRE (as a composite end point), but it did reduce MRSA colonization (as a single end point).

Reviewer’s Comments

Hospitals, regulatory agencies, and advocates for health care improvement have been searching for the magic bullet to reduce HAIs, especially those associated with resistant organisms such as VRE and MRSA. This study asks whether routine use of gowns and gloves in all patients reduces the acquisition of VRE or MRSA during an ICU stay. Routine use of gowns and gloves did not reduce acquisition of VRE or MRSA. This seems like a victory for those of us who hate donning gowns and gloves. However, UCI did reduce MRSA acquisition alone. While there were no differences in rates of HAIs, the study may not have been powered to detect these differences. Since intervention groups had higher baseline rates of MRSA than did control groups, this finding may more generalizable to ICUs with higher rates of admission MRSA colonization. Also, the reduction in rates of MRSA acquisition may have been related to decreased contact with providers/hour or increased compliance with hand washing, both of which might affect acquisition of MRSA as an isolated intervention. There were no cost/benefit analyses of costs associated with implementation of...
UCI or patient/family/provider satisfaction analyses. These factors might also affect implementation of UCI, particularly with studies demonstrating that use of gowns and gloves increase a patient’s sense of isolation. While I’d like to throw out routine use of gowns and gloves in favor of efforts aimed at increased hand washing in ICUs with modest to high rates of MRSA colonization, that move is premature. (Reviewer—Alison S. Clay, MD).

De-Escalation of Broad-Spectrum Antibiotics Decreases Mortality in Sepsis

Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

De-escalating broad-spectrum antibiotics based on culture results decreases mortality in septic patients.

Article Reviewed

Background
The Surviving Sepsis Campaign 2012 guidelines recommend empiric broad-spectrum antibiotics in the initial management of patients with severe sepsis or septic shock, and de-escalation of antibiotics to the most targeted regimen based on culture data. These recommendations are not based on robust clinical evidence, however, as randomized controlled trials have not been performed to rigorously assess their risks and benefits.

Objective
To assess the effects of de-escalating antibiotics on short- and longer-term mortality after culture results were available in patients with severe sepsis or septic shock.

Discussion
712 patients with severe sepsis (n=278) or septic shock (n=434) were evaluated during the 4-year study period. In total, 84 patients died before culture results were available and were excluded from analyses. Culture results were available for 76.7% of the 628 patients included in analysis. After culture results were available (on average 72 hours after admission), de-escalation of antibiotics was done for only 219 (34.9%) of patients. The respective in-hospital mortality rates for patients for whom antibiotics were de-escalated, not changed, or escalated were 27.4%, 32.6%, and 42.9% (P =0.006 for between-group differences). These differences were similar for ICU mortality and 90-day mortality. After correcting for potential confounders, de-escalation was found to be associated with decreased mortality as compared to not de-escalating antibiotic therapy (adjusted OR, 0.58; 95% confidence intervals [CI], 0.36 to 0.93). This association was also true for patients who received adequate initial empiric antibiotic therapy (403 patients), as de-escalation carried an adjusted OR of 0.54 (CI, 0.33 to 0.89). Propensity score-adjusted logistic regression corroborated these results, as the propensity score-adjusted OR for de-escalation was 0.57 (CI, 0.38 to 0.94).

Conclusions
De-escalation of antibiotics when culture results are known is safe and may result in decreased mortality for patients with severe sepsis and septic shock.

Reviewer’s Comments
Overuse of broad-spectrum antibiotics increases health care costs and encourages drug resistance. However, it is unexpected that it might also kill the patients being treated. Knowledge of these adverse effects has not substantively changed practice, and overuse of broad-spectrum antibiotics remains common. Perhaps this study can lead some to change their practice and rationally de-escalate antibiotics when culture results indicate it is safe to do so. Although this study is an observational trial with risk of unmeasured confounders, it does add to the growing literature demonstrating increased mortality associated with failure to de-escalate antibiotics.
in patients with severe sepsis and septic shock. Considered from a different perspective, this and other studies demonstrate that failure to de-escalate may cause harm and increase mortality in our critically ill patients with sepsis. (Reviewer—Jeremy B. Richards, MD, MA).

**High Intraoperative Fluid Balance Associated With Increased Postoperative Mortality**

Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

High intraoperative fluid balance is associated with increased frequency of postoperative complications, including mortality.

**Article Reviewed**

**Background**
The optimal strategy for intraoperative fluid management is unknown. Since the type and means of administering fluids has been shown to affect outcomes in other clinical settings, determining the effects of intraoperative fluid balances on postoperative outcomes is important.

**Objective**
To determine the effects of intraoperative fluid balance on postoperative clinical outcomes, including organ dysfunction and mortality.

**Design/Methods**
This was a multicenter prospective study in 4 ICUS at 3 hospitals in Brazil. Exclusion criteria included palliative surgery, limited life expectancy, renal disease, advanced congestive heart failure (NYHA class IV heart failure or an ejection fraction of <30%), and diabetes, among others.

**Results**
479 patients who underwent surgery and were admitted to an ICU were enrolled in the study. Patients who died after surgery (8.7% of the cohort) had a higher intraoperative fluid balance than patients who did not die (non-survivors 1.95 L) (range of 1.4 to 3.4 L) versus survivors 1.4 L [1.0 to 1.6 L]). Not unexpectedly, patients who died were in general sicker than patients who survived, with higher ASA and SAPS-3 scores, both of which were statistically significantly higher in patients who died. In addition, patients with an intraoperative fluid balance of >2.0 L had a statistically significantly longer ICU length of stay than patients who received <2.0 L (P<0.001). Postoperative infectious, neurological, respiratory, and cardiovascular complications were also statistically significantly higher in patients who received >2.0 L intraoperatively. These unadjusted observations were confirmed by multivariate regression analyses, as a high intraoperative fluid balance was associated with an adjusted OR for death of 1.024 (confidence intervals, 1.007 to 1.041; P =0.006).

**Conclusions**
High intraoperative fluid balance is associated with increased mortality, increased ICU length of stay, and increased postoperative complications.

**Reviewer's Comments**
This study is interesting, as the authors assessed intraoperative fluid balance and not the total quantity of fluid provided during surgery. The specific calculation was the sum of crystalloids and/or colloids infused, minus urine output and estimated insensible losses (based on the type and duration of surgery performed.) Of note, estimated blood loss was explicitly not included in the determination of intraoperative fluid balance due to “variations that may occur among observers in computing blood loss.” Not including estimated blood loss both makes sense (there is wide variation in this value between practitioners) and limits the study’s results (massive hemorrhage would be nice to know about in considering intraoperative fluid balance.) There are other issues with this study, including the exclusion of several patient populations such as diabetics, and the universal use of colloids, as all patients received approximately 500 cc of colloids intraoperatively for unclear reasons. Acknowledging this and other
limitations, this is still an intriguing study, and further work to more rigorously characterize best practices for optimal intraoperative fluid management strategies are clearly needed. (Reviewer – Jeremy B. Richards, MD, MA).

**Rapid Fingerprinting of Pathogens With Mass Spectrometry**

Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

Partnering rapid identification of pathogens by mass spectrometry with an antimicrobial stewardship team may improve clinical outcomes in bloodstream infection.

**Article Reviewed**


**Background**

Rapid identification of pathogens during bloodstream infection (BSI) is associated with improved patient outcomes. Emerging technologies, including mass spectrometry by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF), have shown promise for providing accelerated pathogen identification. Antimicrobial stewardship teams (ASTs) that provide real-time advice to clinicians on positive cultures are also reported to yield better outcomes than standard laboratory reporting.

**Objective**

To determine whether rapid MALDI-TOF identification of pathogens, partnered with AST intervention, yields better microbiological and clinical outcomes in BSI than conventional laboratory reporting.

**Design**


**Participants**

501 adult patients with bacteremia or candidemia.

**Methods**

Patients with BSI identified by MALDI-TOF over a 3-month period (September to November 2012) were compared to a historical control group with conventional pathogen identification from the same 3 calendar months during the previous year. Positive gram stains were reported in real-time for both groups; during the MALDI-TOF period, an AST provided real-time culture alerts and antibiotic recommendations.

**Results**

The MALDI-TOF with AST strategy was associated with a reduction in time to pathogen identification (55.9 vs 84.0 hours; \( P < 0.001 \)), as well as in time to effective (20.4 vs 30.1 hours; \( P = 0.021 \)) and optimal (47.3 vs 90.3 hours; \( P < 0.001 \)) antibiotic therapy. On univariate analysis, there were also reductions in mortality (14.5% vs 20.3%), recurrent bacteremia (2.0% vs 5.9%), and length of intensive care unit stay (8.3 vs 14.9 days).

**Conclusions**

MALDI-TOF mass spectrometry identification of pathogens, partnered with AST intervention, decreased time to pathogen identification and to effective antibiotic therapy, and improved clinical outcomes.

**Reviewer’s Comments**

Similar to other emerging methods for rapid pathogen identification, such as peptide nucleic acid-fluorescence in situ hybridization (PNA-FISH) and nucleic acid microarrays, MALDI-TOF mass spectrometry shows great promise for improving microbiologic and clinical outcomes during infection. While PNA-FISH has been more extensively studied, MALDI-TOF is much less labor-intensive and allows facile identification of a much broader array of pathogens, suggesting it may be the more easily acquired technology. The findings of the present study are consistent with those of 3 prior observational studies of MALDI-TOF. It is difficult to know the relative degree to which MALDI-TOF versus AST affected outcomes in this trial; indeed
the investigators found that clinician acceptance of an AST intervention was independently associated with a trend toward reduced mortality on multivariate analysis. In addition, this non-randomized, historically controlled trial is subject to several possible biases. Nonetheless, taken together with past reports, this study strongly suggests that AST initiatives, partnered with best practices for rapid pathogen identification, should be optimized and strongly encouraged as standard of care. (Reviewer—Michael B. Fessler, MD).

Focused US Increases Diagnostic Accuracy for Acute Respiratory Symptoms
Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

Focused ultrasonography aids in diagnosing potentially life-threatening illness in patients presenting to the emergency department.

Article Reviewed

Background
In patients with acute but nonspecific respiratory symptoms, diagnostic accuracy is essential to quickly institute appropriate therapy. Moreover, delayed diagnosis slows therapy and worsens outcomes. Sonography might be a useful extension of the initial clinical exam in such patients.

Objective
To evaluate the ability of focused ultrasonography (US) to identify potentially life-threatening illnesses at presentation of acute respiratory illness.

Design
Prospective observational study.

Participants
Patients presenting to a single university medical center in Denmark over a 6-month period.

Methods
Emergency department (ED) patients with tachypnea, hypoxia, dyspnea, cough, and chest pain were eligible if they were aged >18 years and had focused US within 1 hour of presentation. ED physicians made a primary assessment based on routine history, physical, and diagnostic testing. Subsequently, all included patients underwent 3 US evaluations: focused assessed transthoracic echocardiography, focused lung US, and limited compression ultrasonography whose descriptions are outlined in the paper. The US exams were performed by a single investigator. Primary assessment was compared to US assessment diagnoses, and the gold standard was a chart audit after discharge.

Results
139 of 342 screened patients were included. Primary assessment yielded the correct diagnosis 59.6% of the time. Isolated focused US identified 44.3% of the correct diagnoses; however, the focused US also identified 26 patients (19%) with a predefined potentially life-threatening diagnosis that was missed on the primary assessment. In total, 73% of these potentially life-threatening diagnoses were confirmed by chart audit. The focused US was performed in 12 minutes (interquartile range, 11 to 14 minutes), and a complete exam was achieved on 96% of patients. For focused US, the positive predictive value was 76.7% and the negative predictive value was 100% in determining predefined life-threatening diagnoses.

Conclusions
Focused US of the heart, lungs, and deep veins is a fast, accurate way to determine potentially life-threatening illnesses in patients with acute respiratory illness.

Reviewer’s Comments
This is another study that supports the use of ultrasonography in patients with acute illness. Although the single test does not perform as well as a primary clinical assessment, focused US was able to diagnose significant illness where recognition otherwise may have been delayed. The US test was fast to perform, but the single operator had extensive
experience. This may limit generalizability of the findings, which are critically dependent on the skill of the ultrasonographer and perhaps the lack of skill of the ED physicians. This investigation suggests that, with proper training and experience, focused US as part of a primary assessment of patients with acute respiratory illness augments diagnostic accuracy and may identify potentially life-threatening illness early. However, it was an uncontrolled and purely observational study. The conclusions are limited; US was fast and accurate. Its impact on clinical outcomes remains speculative. (Reviewer–Jeffrey B. Hoag, MD, MS).

Can We Afford ECMO?
Critical Care Medicine - January 30, 2014 - Vol. 19 - No. 9

Extracorporeal membrane oxygenation is an extremely resource-intensive salvage therapy that remains in clinical practice without the support of good clinical evidence.

Article Reviewed

Background
Extracorporeal membrane oxygenation (ECMO) is a well-established but expensive salvage therapy for respiratory failure. The costs and trends in use warrant consideration.

Objective
To examine the temporal trends and costs associated with ECMO use in the U.S.

Design
Health insurance database study.

Participants

Methods
The Nationwide Inpatient Sample (NIS) database was examined for trends in ECMO use over study period. The NIS provides insurance-based data on approximately 20% of all U.S. admissions.

Results
The study included 8753 admissions involving ECMO. Costs associated with ECMO increased from $109 million in 1998 to $765 million in 2009. The per-patient charges and length of stay increased over this time as well as in-hospital mortality, which rose from 33% in 1998 to 53% in 2009. These changes seemed related to changes in case-mix, a lower proportion of post-cardiomyotomy cases, and more cases involving cardiogenic shock, respiratory failure, and lung transplant. Mean post-cardiomyotomy hospital charges were $273,429 ± $31,361 whereas charges in the setting of heart transplant were $722,123 ± $57,494 and lung transplant were $702,973 ± $50,502. Overall in-hospital mortality associated with ECMO cases was 51% and discharges to location other than home were common at 58.6%, and were highest at 78.9% in association with lung transplantation.

Conclusions
The dramatic increase in health care expenditures associated with ECMO was not entirely attributable to increases in volume. Changes in case-mix have resulted in higher costs and worse outcomes.

Reviewer’s Comments
In light of the Affordable Care Act, there is increasing attention paid to the costs of health care. The current study is timely; ECMO may be unaffordable care. Enthusiasm for ECMO as a salvage therapy for refractory lung failure surged after the controversial CESAR trial was published in 2009. It is therefore likely that the temporal trends described in this paper continued or accelerated. Currently, ECMO should be considered a very expensive therapy outside of evidence-based medicine. While potentially promising, the optimal role of ECMO remains to be determined. (Reviewer–Robert Michael Reed, MD).
Question 1:
Which of the following effects is least likely to be mediated by atrial natriuretic peptide on the kidneys?
A) A direct increase in efferent arteriolar resistance with a net increase in glomerular filtration
B) Direct natriuresis resulting from inhibition of sodium transport in the medullary collecting duct
C) Indirect natriuresis resulting from inhibition of aldosterone release from the zona glomerulosa of the adrenal gland
D) A direct decrease in afferent arteriolar resistance resulting in an increase in renal blood flow
E) An indirect increase in efferent arteriolar resistance via activation of the renin-angiotensin system

Question 2:
A 14-year-old boy sustains significant blunt abdominal trauma when hit by a motor vehicle while riding his bicycle. Following adequate resuscitation with multiple blood products and crystalloid, he has significant abdominal distension and oliguria with increasing serum potassium on serial measurements. Which of the following is the least likely to be a cause of hyperkalemia?
A) Decreased glomerular filtering of potassium due to an overall decrease in the glomerular filtration rate
B) Hypoxemic injury to the renal tubule and impaired potassium excretion
C) Activation of the renin-angiotensin-aldosterone axis with increased tubular reabsorption of potassium
D) Metabolic acidosis with cellular exchange of intracellular potassium for hydrogen ion
E) Increased potassium load from tissue catabolism

Question 3:
A 9-month-old boy presents with difficulty breathing. His mother states that he has been treated for croup twice already with similar symptoms. He has had 2 days of upper respiratory tract infection symptoms and now has expiratory stridor on examination. Which of the following is correct?
A) Croup (viral laryngotraceobronchitis) is typically characterized by expiratory stridor
B) Intrathoracic airway obstruction is typically worse during inspiration
C) Extrathoracic airway obstruction is typically worse during inspiration
D) Croup (viral laryngotraceobronchitis) is typically characterized by intrathoracic airway obstruction

Question 4:
A 12-year-old boy with acute respiratory distress syndrome is being mechanically ventilated in synchronized intermittent mandatory ventilation pressure control/pressure support mode with peak inspiratory pressures of 28 mm Hg, positive end-expiratory pressure of 12 mm Hg, FIO2 of 0.60, and rate of 15/min. Arterial blood gas analysis shows PaCO2 of 60 mm Hg, and PaO2 of 60 mm Hg. His respiratory quotient is 0.8, core body temperature is 37°C (98.5°F), and barometric pressure is 747 mm Hg. What is this patient’s PAO2-PaO2 difference?
A) 285 mm Hg
B) 300 mm Hg
C) 345 mm Hg
D) 360 mm Hg
E) Cannot be determined

Question 5:
A patient with acute respiratory distress syndrome has been managed with high-frequency oscillatory ventilation for the past 2 hours. A blood gas study shows pH of 7.48, PaCO2 of 30 mm Hg, PaO2 of 70 mm Hg, bicarbonate level of 22 mEq/L, and oxygen saturation of 97% on a FIO2 of 60%. Which of the following is the most appropriate intervention?
A) Wean the mean airway pressure.
B) Increase the delta P.
C) Decrease the frequency.
D) Increase the mean airway pressure.
E) Increase the frequency.

**Question 6:**
A patient is admitted following an elective posterior spinal fusion. Besides kyphoscoliosis, the only pertinent history is sulfamethoxazole/trimethoprim allergy. In the operating room, he received packed red blood cells, 3 U; platelets, 4 U; and crystalloid fluid, 6 L, with only 2.4 L of urine output. He is admitted to the pediatric ICU on mechanical ventilation due to persistent hypoxemia. His admission chest radiograph shows diffuse pulmonary edema, so he is given a dose of furosemide. In the next 30 minutes he develops tachycardia, bronchospasm, and diffuse flushing. Which of the following is the most likely cause of his decompensation?
A) Inadvertent administration of an aminoglycoside for postoperative wound prophylaxis
B) Allergic reaction to furosemide
C) Transfusion reaction
D) Worsening pulmonary edema from transfusion-related acute lung injury
E) Aspiration pneumonia

**Question 7:**
A 2-year-old, acyanotic infant with tetralogy of Fallot undergoes elective repair with ventricular septal defect closure and right ventricle-to-pulmonary artery conduit placement, but a restrictive patent foramen ovale is not addressed. Four hours after being admitted postoperatively, she develops tachycardia with hypotension despite a central venous pressure of 20 mm Hg and hypoxemia. Her arterial blood gas analysis shows pH of 7.28, PaCO2 of 55 mm Hg, PaO2 of 50 mm Hg, bicarbonate level of 23 mEq/L, and base excess of –0.1 mEq/L. The most appropriate next maneuver is:
A) Sedation with fentanyl, 2 µg/kg
B) Opening her sternotomy incision
C) Initiation of cooling and administration of amiodarone
D) Giving 5% albumin solution, 20 mL rapid IV push
E) Hyperventilation with 100% oxygen

**Question 8:**
A 6-month-old infant is admitted to the pediatric ICU with the confirmed diagnosis of Klebsiella pneumoniae meningitis. Antibiogram profile shows the organism to be an extended-spectrum betalactamase-positive strain that is sensitive to extended-spectrum penicillins, second-generation and third-generation cephalosporins, and aminoglycosides. The most appropriate long-term course of antibiotic therapy would include:
A) Gentamicin
B) Ceftazidime
C) Clindamycin
D) Cefuroxime

**Question 9:**
An obtunded, 2-year-old boy presents to the emergency department with a BP of 70/20 mm Hg, HR of 200/min, and temperature of 40.1°C (104.1°F). He has the ecchymotic lesions pictured in the Figure on his trunk and extremities.
Which of the following statements is incorrect?
A) Absence of meningitis (>20 WBCs/µL in cerebrospinal fluid) is associated with a poorer outcome.
B) Carriage of the organism in the nasopharynx is common.
C) Presence of petechiae for less than 12 hours prior to admission is associated with a favorable outcome.
D) Prior infections with influenza A or B have been associated with increased susceptibility to this organism.
E) Association of thrombocytopenia is common.

**Question 10:**
A child with acute respiratory distress syndrome is receiving mechanical ventilation with the following settings: mode, pressure-regulated; volume control, 8 mL/kg; plateau pressure, 30 cm H2O; mean airway pressure, 20 cm H2O; positive end-expiratory pressure, 10 cm H2O; FiO2, 0.5; rate, 22/min; inspiratory time, 0.7 seconds. The associated arterial blood gas measurements are pH, 7.36; Paco2, 106 mm Hg; PaCO2, 45 mm Hg; bicarbonate, 25 mEq/L.
Which of the following will most adversely affect the oxygenation index?
A) Need to increase mean airway pressure to 25 cm H$_2$O to generate the same blood gas data
B) Drop in PaO$_2$ to 80 mm Hg with no changes in ventilator settings
C) Need to increase the ventilator rate to 30/min to generate the same blood gas data
D) Need to increase FIO$_2$ to 0.60 to generate the same blood gas data
E) Increase in PaCO$_2$ with no changes in ventilator settings

QUIZ Answers and explanations

1. Answer E
   Rationale:
   Atrial natriuretic peptide directly decreases the afferent arteriolar resistance and inhibits the activity of the renin-angiotensin axis, thereby indirectly resulting in decreased afferent arteriolar resistance and an increase in renal blood flow. Increased efferent arteriolar resistance is a direct effect of atrial natriuretic peptide that somewhat counteracts the increase in renal blood flow, but results in increased glomerular pressures and increased glomerular filtration rate. Natriuresis is accomplished directly by the action of atrial natriuretic peptide on sodium reabsorption in the medullary collecting duct, and indirectly by the inhibition of aldosterone release from the adrenal gland.

2. Answer C
   Rationale:
   Activation of the renin-angiotensin-aldosterone axis may occur due to decreased renal blood flow or reduced tubular effluent flow; however, the activity of aldosterone in the intact kidney is to reabsorb sodium ion at the expense of potassium ion, thereby resulting in hypokalemia. The most common causes of hyperkalemia in acute renal failure are as follows:
   - Reduction in the glomerular filtration rate, thereby limiting the glomerular filtration of potassium ion
   - Decreased secretion of potassium due to direct injury to the renal tubular cells (acute tubular necrosis)
   - Metabolic acidosis due to azotemia or lactic acid, resulting in the exchange of intracellular potassium ion for extracellular hydrogen ion
   - Increased tissue catabolism or tissue necrosis with the resultant release of potassium ion
   - Exogenous administration of potassium ion, such as may occur with transfusion of multiple blood products

3. Answer C
   Rationale:
   Intrathoracic airway (ie, distal trachea, bronchi, bronchioles) obstruction is typically worse during expiration. Therefore, tracheobronchomalacia and bronchiolitis are characterized by expiratory stridor and wheezing, respectively. In contrast, extrathoracic airway (ie, larynx, proximal trachea) obstruction is typically worse during inspiration. Croup is therefore characterized by inspiratory stridor.

4. Answer A
   Rationale:
   PAO$_2$ is calculated using the alveolar gas equation (PB, barometric pressure; PH$_2$O, water vapor pressure; RQ, respiratory quotient):
   \[ \text{PAO}_2 = \text{FIO}_2 \times (\text{PB} - \text{PH}_2\text{O}) - \frac{\text{PaCO}_2}{\text{RQ}} \]
   The water vapor pressure (PH$_2$O) at a temperature of 37°C (98.5°F) is 47 mm Hg. Therefore,
   \[ \text{PaO}_2 = 0.60 \times (747 - 47) - 60/0.8 = 420 - 75 = 345 \text{ mm Hg} \]
   The PAO$_2$ – PaO$_2$ difference is then 345 mm Hg – 60 mm Hg, or 285 mm Hg.

5. Answer E
   Rationale:
   High-frequency oscillatory ventilation (HFOV) has become an increasingly utilized tool in the management of severe hypoxemic respiratory failure. A modest number of variables are under control of the practitioner that allow support for oxygenation and/or ventilation. The blood gas analysis demonstrates a respiratory alkalosis (pH will decrease by 0.08 for every 10 mm Hg change in PaCO$_2$ from a normal value). As a result, the patient is currently being overventilated, and an alteration that results in decreased ventilation is indicated. It is important to recall that ventilation is inversely proportional to the frequency (Hz). Therefore, to decrease ventilation, one would increase the frequency. Increasing the delta P would increase the ventilation further. Changing the mean airway pressure (MAP) would have little
influence on ventilation. The patient continues to have a marginally accepted PaO2 (70 mm Hg) while on an FIO2 of 60%; therefore, it is premature to consider weaning the MAP at this time. Since the patient has only been managed for 2 hours and the PaO2 remains acceptable, increasing the MAP is not indicated at this time. High-frequency oscillatory ventilation is used predominantly for hypoxemic respiratory failure and persistent, severe air leaks. Its effect on ventilation is often unpredictable.

Two parameters regulate oxygenation:
• FIO2
• MAP: increase MAP to increase PaO2

Two parameters regulate ventilation:
• Delta P or amplitude: increase delta P to increase carbon dioxide.
• Frequency: increase frequency to DECREASE ventilation/carbon dioxide.
• Remember that frequency goes in the direction you want your carbon dioxide to go.

\[
CvO_2 = (13.5 \times 1.36 \times 0.56) + (0.003 \times 30) = 10.37 \text{ mL/dL}
\]

Recall that respiratory quotient (RQ) is the ratio of VCO2 to VO2 such that,

\[
VO_2 = \frac{VCO_2}{RQ} \text{ or here: } VO_2 = 236 \text{ mL/min}/0.76 = 310 \text{ mL/min}
\]

As a result: cardiac output = 310 mL/min/([17.52 – 10.37 mL/dL]) × 100 = 4.3 L/min

Fick principle is frequently used to measure cardiac output using oxygen content differences in systemic and pulmonary circulations:
• Cardiac Output = Oxygen Uptake/(Arterial Oxygen – Venous Oxygen)

Remember conversion of units is crucial here: CaO2 and CvO2 are most commonly calculated as mL/dL, so to convert to L/min, the product must be multiplied by 100 (number of dL in L).

6. Answer B
Rationale:
Recall that furosemide is a member of the sulfa family of drugs (similar to cotrimoxazole). The timing of the reaction (within 30 minutes of drug administration) is typical for allergic reactions. The symptomatology is consistent with acute release of histamine from triggered mast cells causing flushing, vasodilation (hence the tachycardia), and bronchospasm. Transfusion-related acute lung injury can manifest with pulmonary edema and persistent hypoxemia, though this is rarely associated with the allergic manifestations described in this case. Acute transfusion reactions can present with these manifestations, but the timing is much more proximate to the timing of the blood product transfusion. There would be no reason that an aminoglycoside should trigger an allergic reaction in a sulfa-allergic patient.

7. Answer E
Rationale:
It is imperative to familiarize oneself with anticipated postoperative complications following specific repairs of congenital heart lesions. Bleeding with tamponade and arrhythmias can potentially complicate every postoperative course. In the setting of acyanotic (so-called “pink”) tetralogy, the pulmonary vasculature is under both increased pressure and flow due to the ventricular septal defect-like physiology with little obstructive physiology. These patients are at risk for acute pulmonary hypertensive crises (PHCs) characterized by acute hypotension with concurrent elevation in the central venous pressure (and pulmonary artery pressure, if being monitored). Several causes can trigger an acute PHC, including hypovolemia, agitation, hypoxia, and/or hypercapnia. In this case, the patient’s arterial blood gas analysis shows a respiratory acidosis, which can profoundly effect pulmonary vascular resistance by increasing it. The quickest maneuver one can perform in this setting that may be of substantial benefit is to reverse this with hyperventilation. Also, the addition of 100% oxygen is a potent vasodilator, which may acutely aid in decreasing pulmonary vascular resistance. Opening the chest may be indicated ultimately, but would not be the first thing to attempt. Fluid administration to increase right ventricular preload will help with PHC, but this too will take time to obtain and intravenously push. Junctional ectopic tachycardia can be a frequent complication following repairs of congenital lesions associated with right ventricular hypertrophy. Sedation, cooling, and amiodarone can control the rate of junctional ectopic tachycardia; however, this diagnosis and therapy will take additional inquiry of the electrocardiographic strips and time. While all these maneuvers may be
necessary and/or indicated, the first response should be immediate reversal of the respiratory acidosis and provision of 100% oxygen, which can be achieved almost immediately.

8. Answer A
Rationale:
Appropriate antibiotic coverage is critical to successful treatment of acute bacterial meningitis. Gram-negative meningitis may require an antibiotic course as long as 3 weeks. Antibiotic resistance has become a real issue in both community and hospital clinical settings. The Klebsiella strain described in this scenario is noted to be extended-spectrum beta-lactamase positive. Although its antibiogram shows sensitivity to beta-lactam antibiotics, it is at high risk for becoming a resistant strain. Aminoglycosides are not affected by beta-lactamases. Clindamycin is not appropriate for gram-negative infections.

9. Answer C
Rationale:
Neisseria meningitidis sepsis can produce rapidly developing septic shock. The pictured patient had classic purpura fulminans caused by N meningitidis. This organism is usually endemic and is commonly carried in the nasopharynx. Infection is more common in males and following influenza infections.

10. Answer B
Rationale:
Oxygenation Index = \( \text{FIO}_2 \times \text{mean airway pressure (MAP)/PaO}_2 \) has been used to assess risk of ventilator-associated injury associated with barotraumas and oxygen toxicity and to identify appropriate candidates for extracorporeal life support. Baseline oxygenation index above \( (0.5 \times 20 \times 100)/106 = 9.4 \)

- a. \( (0.5 \times 25 \times 100)/106 = 11.8 \)
- b. \( (0.5 \times 20 \times 100)/80 = 12.5 \)
- c. \( (0.5 \times 20 \times 100)/106 = 9.4 \)
- d. \( (0.6 \times 20 \times 100)/106 = 11.3 \)
- e. \( (0.5 \times 20 \times 100)/106 = 9.4 \)
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