6th GUJARAT CRITICAL CARE CONFERENCE 2018

CONTROVERSIES IN CRITICAL CARE
BACK TO BASICS

28/29/30 SEPTEMBER 2018

PANDIT DINDAYAL UPADHYAY AUDITORIUM, AHMEDABAD
WWW.GUJARATCRITICON.IN
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• Top 101 Critical care papers in intensive care medicine
  Dr. Manoj Singh
Dear Friends

It gives me immense pleasure to get in touch with you!

I’m very happy to know that the Gujarat Criticon Critical Care Conference is been held at Ahmedabad on 29-39 September 2018!

Critical care in India is growing fast and spreading its wings across the length and breadth of India which is our aim, taking critical care to places!

This conference has an excellent scientific program and involves the best critical care faculty in the Country!

I’m sure the scientific content will benefit all students and fellow colleagues; and will make them updated with what’s new in the field of critical care!

I congratulate Dr Jigar Mehta, Dr Manoj Singh, Dr Anish Joshi, Dr Raj Rawal, Dr Gopal Raval and Dr Vivek Dave for arranging this academic feast in the lovely buzzing city of Ahmedabad and support our mission to spread knowledge!

Wish the conference a great success!

Best wishes to you all

Dr. Subhal Dixit
President Elect ISCCM
It is a matter of pride to host the 6th Gujarat Criticon 2018 at Ahmedabad from 28th to 30th September 2018.

Critical Care Medicine evolved in our state at jet speed in last decade. The infrastructure developments, corporate sector growth, medical tourism and 108 ambulance service play major role in it. Now all advanced monitoring, all life supporting measures, accurate drug delivery system and trained staff are within reach of Common Man.

Critical Care Units undoubtedly are backbone of any small scale hospital or major institutes. The consultants, fellows, medical officers and all para medical staffs are working round the clock to deliver better outcome. This is the only branch of Medicine which works 24 by 7.

Indian Society of Critical Care Medicine Ahmedabad branch in association with Bhavnagar, Baroda, Karamsad, Rajkot, Surat and Valsad Branch have set the Scientific Agenda based on theme Controversies in Critical Care. This was chosen deliberately to clarify the practicing Physician in Intensive Care about the common day to day Clinical Issues in this fast-growing Science.

In coming years to come, there will be more numbers of high end infrastructure, more penetration in peripheries, more training centres and more awareness in community. We give you assurance of 'Savings MORE lives through critical care'. This is a matter of pride that we have crossed 900 plus registration, a dream which we dared to achieve few months ago.

Jay Garvi Gujarat, Jay Hind

Dr. Jigar Mehta
Chairman
Gujarat Criticon 2018
From the Secretarial Desk……

I welcome you to the World Heritage City ‘ Ahmedabad’ for the 6th State level Gujarat Criticon 2018 which is being held at the same city from which the 1st State level critical care conference started. Gujarat Criticon has now become a major face of the intensivists of Gujarat & has brought all ISCCM branches of Gujarat under one roof. The unique concept of this conference when it was started in 2013 was that it should have active participation of the entire state branches & not just the host branch is being fulfilled & followed year on year.

Critical Care is now a well established speciality & is now a mandatory requirement for care of ICU patients. The new ICUs which are coming up either in cities or in peripheries are now recruiting intensivists as full timers which shows the strength this branch has developed. There has been a marked improvement in the infrastructure & critical care facilities which are now being provided in Gujarat ICUs like ECMO, CRRT etc. Gujarat is proud to have heart transplants done where intensivists played a vital role in explaining, coordinating, caring & transporting organs from one place to another. Organ shortage is a major challenge that we are facing in today’s world so to increase awareness among the medical fraternity & to make them proactive we are first time organizing an Organ donation workshop in this state level conference.

Ahmedabad branch has grown significantly from a small group to now a bigger number of members which is still growing day by day. The number of critical care seats has gone significantly higher giving better academic prospects to the young budding doctors to fulfil their dreams.

“Gujarat Criticon” a brand is successful due to the untiring efforts of many people whose names I cannot mention here as the list is very long. I thank all my colleagues, mentors, office bearers, organizing committee, pharma industry, event management company & last but not the least our delegates for making this conference a grand success.

I will be glad to hear your feedbacks about the conference on isccmahmedabad@gmail.com or our facebook page of isccmahmedabad.

Dr. Anish Joshi
Org. Secretary
Gujarat Criticon 2018

We have selected all the topics in line of current burning topics in Intensive care. Unlike other updates in our Branch, this gives different twists to same topic by solving the practical aspects of Acute Medicine. Even the workshops are designed in such a way that we will get in-depth hands on knowledge in Airway, Ultrasound, Ventilator and Obstetrics by National and International Faculty. Even the most talked about topic on Organ Donation with its Medicolegal aspects has been covered in entire days programme.

The latest guidelines and interventions will be discussed by experts in this field along with super-specialist. We have Dr Jesus Ortega coming from Spain, Dr Brendan Madden from UK and Dr Muhammed Assaduzzaman from Bangladesh as International Faculty. They will be joined by our eminent National Faculty from Indian College of Critical Care Medicine. The scientific content has been already appreciated by the core committee. Come and let us be a part of this academic feast during 28-30th September 2018.

Dr. Manoj Singh
Chairmen Scientific Committee
Gujarat Criticon 2018
Its gives me a immense pleasure to welcome you on 6th GUJRAT CRITICON 2018 at Ahmedabad. A conference not only brings under a roof many intellectuals but also provide an outstanding arena for exchanging ideas.

Many new developments are emerging in the field of Critical care medicine. I hope, this conference will open new era to understand of problem and provide suitable solution for Critical illness.

I assure all the delegates that this conference will update you with all scientific and technological advancements in Critical Care medicine.

Lastly, I again welcome you all hoping that the ideas and information exchanged during this conference will significantly benefit our society and help improve the treatment of our patients.

Dr. Gopal Raval
Treasurer
Gujarat Criticon 2018
Dear ISCCM colleagues and delegates of Gujarat Criticon 2018

Warm welcome and Greetings from "Souvenir Editorial Team" Gujarat Criticon 2018.

It is a great pleasure to present first E-Souvenir as a conference companion in a new technology. This as part of our “Go Green” initiative. The soft copy will remain a means for easy access to the delegates for quick reference.

As per our conference theme along with abstract of our esteemed guest speakers, this time we have included "Current controversies in Critical care" topics which gives a practical guidelines regarding present recommendations for controversial therapies. We hope it will be very useful in your day to day practice. All the topics has been selected with current Evidence based Medicine references and Internationally recognized journals.

We has also included a compilation of top 101 papers in critical care courtesy Dr. Manoj Singh. This will come as a handy reference to the critical care practitioners.

Once again a warm welcome from Souvenir Team Gujarat Criticon 2018 and we hope this souvenir will be a good memory of this academic Feast.

As the editors of this souvenir, we hope that we have made justice to needs and aspirations of critical care practitioners.

Dr. Maharshi Desai
Dr. Harendra Thakker
Dr. Rajesh Thosani
Dr. Bhavik Shah
Editorial Team
Gujarat Criticon 2018
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In the Management of Invasive Fungal Infections caused by Candida and Aspergillus

**MYCAMINE®**
(micafungin sodium) for injection

**Power... Simplified**

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<th>Indications and dosage of MYCAMINE® (micafungin sodium)</th>
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<td>Treatment of Candidemia, Acute Disseminated Candidiasis, Candida peritonitis and abscesses*</td>
<td>100 mg</td>
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<td>Treatment of Esophageal Candidiasis ¹</td>
<td>150 mg</td>
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<td>Prophylaxis of Candida and Aspergillus Infections in Hematopoietic Stem Cell Transplant (HSCT) Recipients ¹</td>
<td>50 mg</td>
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<td>Treatment of Aspergillus Infections (Fungemia, respiratory mycosis, gastrointestinal mycosis) ³</td>
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1. **Effective**
2. **Well Tolerated**
3. **FEW DDI**
4. **Convenient to Use**

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**Abbreviated Prescribing Information of Micafungin**

**In 1 mg/mL vials:**

**MICAFUNGIN SODIUM FOR INJECTION** 50 mg/mL (Micafungin Sodium for Injection)

**INDICATIONS:** Treatment of candidemia, acute disseminated candidiasis, Candida peritonitis and abscesses, esophageal candidiasis, prophylaxis of Candida and Aspergillus infections in hematopoietic stem cell transplant recipients and treatment of fungemia, respiratory mycosis, gastrointestinal mycosis caused by Aspergillus. **DOSEAGE AND ADMINISTRATION:** Do not mix co-infective with other medications. **DOSAGE:** In Adults: Treatment of candidemia, acute disseminated candidiasis, Candida peritonitis and abscesses: 100 mg once daily. Use of esophageal candidiasis: 150 mg once daily. Prophylaxis of Candida and Aspergillus infections in HSCT recipients: 15 mg once daily. **Prophylaxis of Micafungin sodium:** Use dose 100-150 mg daily for severe and refractory acute myeloid leukemias or 300 mg daily for recipients of HSCT. **ADMINISTRATION:** Dilute and reconstitute solution: 0.9% Sodium Chloride solution for injection (0.9% solution for infusion) for injection (0.9% solution for infusion). **ADVERSE REACTIONS:** Gastrointestinal disorders, infection, renal disorders, neoplasms and related conditions, dermatologic disorders, allergy, other disorders, adverse-reactions, other. **CONTRAINDICATIONS:** Hypersensitivity to any of its ingredients or other echinocandins. **SPECIAL WARNINGS AND PRECAUTIONS:** Hypersensitivity reactions: Isolated cases of serious reactions reported. **NURSE:** Body mass index (BMI) and BMI-related information: A healthy volunteer: Isolated cases of significant hypotension and bronchial asthma also reported. **Reference:** Treatment of patients developing clinical or laboratory evidence of hemolysis or hematuria: amanita for screening, evaluate risk/benefit of continuing therapy. Hematologic: Laboratory abnormalities in liver function tests in severe healthy volunteers. **INTERACTIONS:** Increased AUC of Cimetidine, AUC and Cmax of Clopidogrel, Cmax of Erythromycin, monitor for toxicity and reduce dosage of clopidogrel. **PREGNANCY AND LACTATION:** No data available and no animal studies. **OVERDOSAGE:** Not reported. **HOW SUPPLIED/STORED:** Injection: 1 mg/mL vials. **FULL PRESCRIBING INFORMATION Available at:**

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**Reference:**

3. Mycamin® prescribing information (MYCIPIN/IN) dated 7th May 2012

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**MICAFUNGIN SODIUM FOR INJECTION** 1 mg/mL vials

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**ASTELLAS PHARMA INDIA LTD., 301, 3rd Floor, C & S Square,127 Anuradha Kiru Road, Chakala, Andheri (E), Mumbai-400099, India, Tel: +91-22-61576003**

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**MICAFUNGIN SODIUM FOR INJECTION** 100 mg/mL (Micafungin Sodium for Injection)
Patients with invasive fungal infections (IFI) are pluri-pathological and have severe underlying conditions. IFI is, frequently, a consequence of a weak immune system of patients and an iatrogenic medicine. However, it is out of doubt that IFI poses a high mortality for patients and antifungal resistance is one more driver playing a role in the prognosis. Increasing antifungal resistance in Candida and Aspergillus to azoles and echinocandins and the emergence of intrinsically antifungal resistant fungal pathogens – p. e. Candida auris – are challenging physicians when facing patients with IFI due to the limited drug options. New drugs belonging to different families of antifungals with alternative mechanisms of action is part of the solution but this is not a reality yet. Therefore rapid detection of antifungal resistance in the clinical microbiology laboratory is a matter of concern. Microdilution is the gold standard for the study of antifungal resistance; commercial methods, such as the E-test or Sensititre YeastOne, are designed to be tested in the clinical microbiology laboratory. Testing a number of isolates using microdilution procedures is key to spot the actual rate of antifungal resistance and guide accurate empirical treatment.

The high mortality of patients with invasive fungal infections (IFIs) and the limitations of the classical microbiological IFI diagnosis have led to a widespread use of empirical antifungal treatment based on clinical suspicion. This strategy results in advantage for some patients who receive early antifungal treatment but in turn translates into an overuse of antifungals in others who may never benefit from that treatment. Moreover, empirical treatment poses a high economic burden for hospitals, promotes antifungal resistance, and causes toxicity for patients. Rational use of antifungals should be “a must” in modern hospitals nowadays and there is a need for detecting, from the group of patients at IFI risk, those who may benefit from antifungal treatment. New microbiological procedures for the diagnosis of IFI are based on the detection of circulating biomarkers in biological fluids; biomarker detection has improved the sensitivity and specificity of classic fungal culture and can be used for using antifungals in a more rational way. Antifungal stewardship programs are addressed to decrease the unnecessary use of antifungal agents assuring the treatment in those patients with evidence of IFI. The use of mycological diagnostic procedures with high negative predictive value is key for making decisions in these programs. Implementation of antifungal stewardship programs must involve a multidisciplinary team including microbiologists, infectious diseases consultants, pharmacists, epidemiologists, and those clinicians from any specialty dealing with patients with IFI.
**Introduction:** Because timing is crucial in injured patient, a systematic approach that can be rapidly and accurately applied is essential.

**Preparation**
- Prehospital Phase – intimation & initial management
- Hospital Phase – bed, medications, monitors & personals to be available.

**Triage**
- Multiple Casualties
- Mass Casualties – where numbers exceed the capacity of treating centre.

**Primary Survey with Simultaneous Resuscitation**
- Airway Maintenance with Restriction of Cervical Spine Motion
- Breathing and Ventilation
- Circulation with Hemorrhage Control
- Disability (Neurologic Evaluation)
- Exposure and Environmental Control

**Adjuncts to the Primary Survey with Resuscitation**
- ECG Monitoring
- Pulse Oximetry
- Ventilatory Rate, Capnography, and Arterial Blood Gases
- Urinary and Gastric Catheters
- X-ray Examinations and Diagnostic Studies

Consider Need for Patient Transfer – even after primary survey & initial stabilization

Special Populations – children, obese, elderly and pregnant women

**Secondary Survey**
- History – AMPLE
  - Allergies
  - Medications currently used
  - Past illnesses/Pregnancy
  - Last meal
  - Events/Environment related to the injury
• Physical Examination
  Adjuncts to the Secondary Survey –
  includes CT scan, contrast urography and angiography; transesophageal ultrasound, bronchoscopy,
esophagoscopy, etc

Definitive Care –as per evaluation & inter-hospital transfer protocol to be followed

Records and Legal Considerations
• Records – meticulous & in chronological order.
• Consent prior to Treatment except in life threatening condition.
• Forensic Evidence – Photographs, clothing, bullet or Alcohol level

Teamwork
  One team leader should be there who assign roles to other members so the care is wholesome.

REFERENCES:
1. Advanced trauma life support, American College of Surgeons Committee on Trauma; 2018.
2. American College of Surgeons Committee on Trauma. Resources for Optimal Care of the Injured
  Patient. Chicago, IL: American College of Surgeons Committee on Trauma; 2006.
5. Guidelines for field triage of injured patients: recommendations of the Na

CHANGING STROKE OUTCOMES
Dr. Khusrav Bajan

In 2015, there were an estimated 42 million prevalent cases of cerebrovascular disease worldwide,
including an estimated 5.39 (95% uncertainty interval [UI]: 5.02–5.73) million acute first ischemic strokes,
and 3.58 (95% UI 3.34–3.82) million acute first haemorrhagic and other strokes. Estimates from the Global
Burden of Diseases, Injuries, and Risk Factors Study ranked stroke as the second most common cause of
deaths.

The timely evaluation and initiation of treatment for acute ischemic stroke (AIS) is critical to optimize
patient outcomes. Existing literature suggests that appropriate identification of symptoms within the
window period if presented to the emergency department is very vital. Time is tissue and outcomes of
acute ischemic stroke patients receiving thrombolytic therapy are optimized when door-to-needle times are less than 60 minutes. Prehospital Cincinnati score is one of the valuable tools of recognition of stroke in prehospital setup. To date Tissue Plasminogen Activator (tPA) is the most preferred thrombolytic therapy improving clinical outcomes. IV tPA should be administered to all eligible acute stroke patients within 3 hours of last known normal and to a more selective group of eligible acute stroke patients (based on ECASS III exclusion criteria) within 4.5 hours of last known normal. Centres should attempt to achieve door-to-needle times of <60 minutes in ≥ 50% of stroke patients treated with IV tPA.

Newer researches has shown that Endovascular thrombectomy for ischemic stroke within 6 to 24 hours plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion and a region of tissue that was ischemic but not yet infarcted. The updated guidelines considers NIHSS score, ASPECT score, Causative occlusion artery involvement and patient age, for patients where thrombectomy could be considered.

In cases of haemorrhagic strokes, the correct management of blood pressure has been found to have a U shaped association with mortality, indicating extremes of BP to have a much worse prognosis and outcome.

REFERENCES:
The quest for finding an ideal anticoagulant that can replace the commonly used VKA (warfarin) continues. There is now a plethora of data regarding the safety and efficacy of newer oral anticoagulants (NOAC) compared to warfarin for wide ranging clinical indications. These NOACs fall into 2 distinct categories due to their specific targeted action - Factor Xa Inhibitors and Thrombin Inhibitors. Rivaroxaban, Apixaban and Edoxaban belong to the group of Factor Xa Inhibitors while Dabigatran remain the sole Thrombin Inhibitor. Nonvalvular atrial fibrillation (NVAF) is a common cardiac rhythm disorder that is associated with up to a 5-fold increase in stroke risk. Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common cause of vascular disease-related death. NVAF and VTE affect several million people in the U.S. and are associated with significant morbidity and substantial healthcare resource utilization and costs. It was estimated in 2008 that the annual direct medical cost of NVAF was $6 billion for NVAF-related costs only and $26 billion when including other concomitant cardiovascular and noncardiovascular costs. VTE was estimated in 2011 to cost between $13.5 and $27.2 billion annually in the U.S.

To reduce stroke risk of patients with NVAF warfarin therapy has been used for decades; however, warfarin has several disadvantages in that it has a slow onset of action, narrow therapeutic range, interacts with food and other medications, and its use requires frequent monitoring and dose adjustments. Because of these reasons and others, such as increased bleeding risk, there is reluctance to prescribe warfarin therapy to many NVAF patients and for patients to remain adherent to therapy. Warfarin therapy, succeeding low molecular weight heparin (LMWH), is also commonly used among VTE patients, who experience similar disadvantages as NVAF patients on warfarin therapy. The suboptimal use of warfarin therapy among NVAF and VTE patients can lead to poor patient outcomes and higher healthcare costs, which may potentially be prevented with better alternative therapies.

Recently, the targeted-specific oral anticoagulants (TSOACs), dabigatran, rivaroxaban, apixaban, and edoxaban have been approved by the FDA for treatment of NVAF and VTE. All of the TSOACs have been shown to be efficacious for the treatment of NVAF and VTE in randomized phase III clinical trials. In addition to being efficacious for the treatment of NVAF and VTE, TSOACs offer pharmacologic advantages over other anticoagulation therapies in that they are orally administered, have a rapid onset of action, few drug-drug or drug-food interactions, and predictable pharmacokinetics, thereby eliminating the need for regular monitoring. In the TSOAC vs. warfarin clinical trials clinical event rates, including stroke and systemic embolism, recurrent VTE, and bleeding, differed among NVAF and VTE patients treated with the different TSOACs vs. warfarin. As clinical event rates differed among NVAF and VTE patients treated with the different TSOACs vs. warfarin it is important to determine which of the TSOACs may provide the best clinical and economic benefits so that healthcare providers, healthcare policy makers, and payers have the information for decision-making processes. Therefore, several studies undertaken so far have shown, the potential savings in medical costs associated with use of each of the TSOACs vs. warfarin for the treatment of NVAF and VTE. It has been estimated that when any of the four TSOACs are used instead
of warfarin medical costs are reduced for patients with NVAF and VTE, with apixaban being associated with the greatest reductions in medical costs for both patient groups.

In patients with nonvalvular atrial fibrillation and an increased risk of stroke prophylaxis, apixaban 5 mg, dabigatran 150 mg, and rivaroxaban 20 mg were all cost-effective alternatives to warfarin.

One has to take into account other factors (INR monitoring, stroke burden, and major bleeding) when looking at cost-effectiveness. Using data, derived from the RE-LY trial, these studies have shown that Dabigatran is cost-effective when the anticipated savings from differences in clinical outcomes (incidence of stroke and bleeding events) are taken into consideration. Definite conclusions regarding the cost-effectiveness of the NOACs will only be possible with further studies designed to specifically answer this question.

ECMO IN SEVERE ARDS

Dr. Amit Mandal

ARDS is a life-threatening form of respiratory failure characterized by inflammatory pulmonary edema resulting in severe hypoxemia associated with substantial morbidity and mortality.

ARDS management remains largely supportive, with mechanical ventilation forming the cornerstone of therapy. Management of ARDS is clinically challenging because some approaches to mechanical ventilation exacerbate lung injury (ventilator-induced lung injury - VILI) and increase mortality.

There is substantial evidence of efficacy for several therapies for ARDS and for the diseases that cause ARDS:

**Mechanical ventilation with**

- Lower tidal volumes of 4 to 8 mL/kg per breath, calculated using predicted body weight (PBW) (1)
- Lower inspiratory pressures, targeting a plateau pressure <30 cm H2O (1)
  - Neuromuscular blockade in ARDS patients with Pao2/Fio2 < 150 (2)
  - Prone positioning in ARDS patients with Pao2/Fio2 < 150 (3)
  - Rapid administration of antibiotics in patients with severe infections (4)
  - Conservative fluid strategy for ARDS patients not in shock (5)

Extra-corporeal membrane oxygenation (ECMO) offers an opportunity to maintain arterial oxygenation within normal limits without resorting to high Fio2s or PEEPs. Moreover, it can maintain Paco2 within normal limits without generous tidal volumes or rapid respiratory rates. With ECMO, we can maintain acceptable gas exchange while resting the lung with small tidal volumes, low respiratory rates, and small-to-moderate PEEPs which can “buy time” for other treatments such as antibiotics and for natural healing processes. Thus, there may be a strong physiologic rationale for ECMO in ARDS.

Critical care treatments have favorable risk-benefit ratios, only if the risk of the therapy is negligible. ECMO, however, is a complex, invasive, and risky therapy. Complications are as follows:
Though some consider that CESAR study of 2009 was a positive trial supporting ECMO in ARDS, in actuality it was a trial comparing management of patients at community hospitals with management at a high-volume specialty center capable of ECMO (only 75% of patients in the group managed at the tertiary center actually received ECMO). (15)

ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial was a RCT designed to determine the effect of early initiation of ECMO in patients with the most severe forms of ARDS. The conclusions were that in patients with very severe ARDS, 60day mortality was not significantly lower with ECMO than with a strategy of conventional mechanical ventilation that included ECMO as rescue therapy. (16)

Beyond CESAR, the ECMO dataset consists of uncontrolled case series (12) and propensity-matched observational cohorts (13, 16). Uncontrolled case series, while supporting the feasibility of ECMO in severe ARDS, do not demonstrate equivalence or superiority to conventional management.

Medical history is full of examples of treatments, which had strong rationale but were ultimately proved ineffective or harmful. ECMO should be considered only in patients who deteriorate after proven therapies have been attempted or in patients with contraindications for these therapies and should be used in a research context to determine if ECMO is truly efficacious for reducing mortality and improving other important clinical outcomes in severe ARDS patients.

In the absence of convincing evidence for ECMO, ECMO should not be considered a first-line therapy for severe ARDS.

### Risk and liabilities of ECMO

<table>
<thead>
<tr>
<th>Complication</th>
<th>Rate</th>
</tr>
</thead>
</table>
| Cannulation complications occur in 6% of patients and can be catastrophic (7) | • Vascular injuries, (8)  
• Retroperitoneal hematoma, (8)  
• Right ventricular perforation, (8)  
• Pericardial tamponade, (8)  
• Hemothorax, (8) |
| Cannula site or bloodstream infection on VV-ECMO (6, 9) | Up to 35% |
| Bleeding patients on VV-ECMO (6) | In nearly 30% |
| Venous thromboembolism is common (10) | In more than 50%  
Risk varies inversely with the intensity of systemic anticoagulation |
| Neurologic injury (11,12,13,14) | Intra-cerebral hemorrhage, is the most feared and consequential complication of ECMO support and affects up to 12% of patients on VV ECMO |
| Patients who sustain neurologic complications on ECMO have a nearly 80% mortality. | |

Risk and liabilities of ECMO

- Complication rate of 40% in patients receiving veno-venous (VV) for ARDS (6)

- Cannulation complications occur in 6% of patients and can be catastrophic (7)
  - Vascular injuries, (8)
  - Retroperitoneal hematoma, (8)
  - Right ventricular perforation, (8)
  - Pericardial tamponade, (8)
  - Hemothorax, (8)

- Cannula site or bloodstream infection on VV-ECMO (6, 9) Up to 35%

- Bleeding patients on VV-ECMO (6) In nearly 30%

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- Patients who sustain neurologic complications on ECMO have a nearly 80% mortality.
REFERENCES:


CONTROVERSIES IN INTERPRETING CULTURE REPORTS
Dr. Jesús Vicente Guinea Ortega

Fungal infections (IFI) are featured by posing a high mortality for patients infected. Clinical presentation of IFI is mostly unspecific and the microbiological tools are key to make clinical decisions, but unfortunately they are hindered by a low sensitivity and specificity. Mycological diagnosis of IFI has historically relied on fungal culture of clinical samples. Cultures are a cheap and easy-to-do microbiological procedure, allowing species identification and antifungal susceptibility testing as well. However, patients with positive cultures do not necessarily have IFI and, conversely, IFI cannot be ruled out in those patients with negative results. Therefore, non-culture based techniques to improve the limitation of cultures have been developed in the last few years. The detection of biomarkers such as Aspergillus galactomannan, Candida mannan/anti-mannan, panfungal beta-d-glucan, Aspergillus lateral flow device, and fungal DNA has considerably improved the yield of microbiological diagnosis of IFI. Coupling fungal cultures with biomarkers detection may help to make better clinical decisions. However, even these new tools, are far
Acute respiratory failure remains a common problem for the intensivist. After a proper history is taken, clinical examination done & early laboratory tests sent, every patient will require an imaging for proper diagnosis & management. Traditionally this imaging has been a chest XRay, followed by an echocardiogram. Later CT scan & sometimes MR scan have been added to our repertoire. In fact CT scan along with echocardiography remain the gold standard for most of the diseases causing acute respiratory failure. The problems of CT scan remain, its availability (not available in all set ups), portability (its not portable), the risk of radiation & also the cost. Lung ultrasound has progressed in a big way in the last two decades, to become a very necessary tool for imaging in this situation.

Lung was thought to be not well visualized by the ultrasound because of its high air content. The difference in the acoustic impedance between the soft tissues & air makes 99% of the ultrasound waves get reflected. This makes penetration of the ultrasound waves into the lung, difficult. Rather than viewing the structures actually, ultrasound of the lung gives rise to several artifacts. However, these artifacts can be recognized & valuable information can be obtained out of them.

It is to be noted, that lung ultrasound is mostly a point of care ultrasonography (POCUS), with very defined protocols, trying to identify some very specific syndromes. It is mostly done by the intensivist/ internist/ pulmonologist. Some point of care examination protocols have been developed by Lichtenstein & Volpicelli. To mention the important ones: Bedside Lung Ultrasound in the Emergency (BLUE) protocol & Fluid Administration Limited by Lung Sonography (FALLS) protocol. Another protocol – Sequential Emergency Sonography Assessing Mechanism (SESAME), uses the same machine for a sequential echocardiogram, lung ultrasound, Doppler of the thigh veins & abdominal ultrasound for a rapid diagnosis of shock.

As already mentioned, lung ultrasound is a very result oriented technic & it can be imparted to physicians without formal radiology training. One study showed that about ten supervised LUS procedures can make a medical student reasonably proficient in the procedure.
<table>
<thead>
<tr>
<th>Disorder</th>
<th>LUSG finding</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>Absent lung sliding, Barcode pattern in M mode</td>
<td>Sensitivity 89%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specificity 99%</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>Anechoic fluid. “Quad” sign</td>
<td>Sensitivity 93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specificity 95%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>B’ profile, AB profile, Air bronchograms</td>
<td>Sensitivity 93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specificity 94%</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>Bilateral B profile.</td>
<td>Sensitivity 93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specificity 89%</td>
</tr>
<tr>
<td>ARDS</td>
<td>B lines with heterogeneous distribution +/- lung sliding</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>Intact lung sliding, A profile.</td>
<td>Sensitivity 93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specificity 89%</td>
</tr>
</tbody>
</table>

The chart above is showing the common syndromes which can be diagnosed by LUS, & compares its sensitivity & specificity with CT scan of the chest - which is taken as the gold standard. The figure below shows a schematic representation of the step by step approach to diagnose a patient with suspected lung pathology.
To conclude, lung ultrasound is poised to become a very useful & easily accessible tool for the intensivist & the internist in bedside diagnosis of several acute lung problems. When combined with other modalities like echocardiogram, abdominal ultrasound etc, it is a powerful tool to assess many of the critical illnesses like respiratory failure, shock etc.

**INTERPRETATION OF CULTURE REPORTS**

Dr. Amit Mandal

Appropriate use and interpretation of blood microbiology results may be one of the most challenging and one of the most important functions of routine clinical care. Effective implementation of this function requires careful consideration of specimen collection (and processing), pathogen detection techniques, and prompt and precise reporting of identification and susceptibility results.

The treating physician should give an appropriate analytical request and provide the laboratory with complete and precise patient information, which are inevitable prerequisites of a proper testing and interpretation. The clinical microbiologist can offer advice concerning the differential diagnosis, sampling techniques and detection methods to facilitate diagnosis.

Rapid detection methods are essential, since the sooner a pathogen is detected, the better chance the patient has of getting cured. Besides the gold-standard blood culture technique, microbiologic methods that decrease the time in obtaining a relevant result are more and more utilized today. In the case of certain pathogens, the pathogen can be identified directly from the blood culture bottle after propagation with serological or automated/semi-automated systems.

Bacteraemia/fungaemia can induce a systemic inflammatory response syndrome and as a clinical continuum can fall into life-threatening severe sepsis or septic shock. Clinical outcomes in severe sepsis and septic shock hinge upon the optimized selection, dosing, and delivery of highly potent antimicrobial therapy. Identification of the causative agent is one of the most important aspects determining the eventual outcome.

Appropriate sample collection, volume of blood required, blood-to-broth ratio, formulation of the analytical request, and transportation are prerequisites to a good microbiology report. Sending of representative samples for processing (for example – a skin swab will on grow colonizers and not true infective organisms, rather deep tissue should be sent) is vital for interpretation and treatment. Differentiating between contaminant and true infection requires a discussion between the clinician and microbiologist to appropriately interpret the microbiology report and eventually treat the patient.
The MIC is a key component of the relationship between antimicrobials and microorganisms. It is defined as the lowest antimicrobial concentration that inhibits the growth of bacteria/fungi and is a measure of the susceptibility of the pathogen to an antimicrobial. However, the interpretation of the MIC value is highly dependent on both the antimicrobial and the pathogen (for example, in the treatment of a cerebral spinal fluid infection, a low MIC for Streptococcus pneumoniae and ceftriaxone can still be considered as resistant because of likely reduced antimicrobial penetration of the brain barrier).

The MIC value allows the clinician to:

- Select the most appropriate antimicrobial: a direct relationship between MIC and patient outcome has been demonstrated in many studies.
- Customize antimicrobial dosing taking into account the susceptibility of the pathogen (MIC) combined with patient profile and the PK parameters of the drug through use of TDM. The MIC helps to define the target exposure that an optimized antimicrobial dosing regimen should reach.

The MIC helps in the selection of the most appropriate antimicrobial.

- A low MIC (lower than the susceptible breakpoint) indicates that an antimicrobial will most likely be effective and is therefore an appropriate choice for treatment.
- A high MIC (higher than the susceptible breakpoint i.e., intermediate or resistant) means that an antimicrobial may have limited or no effectiveness for treatment.

PK/PD is central to antimicrobial dosing optimization. Predicting altered PK is vital to determine if target concentration/MIC ratios can be achieved in patients, thereby maximizing the chances of clinical cure.

LEGAL ASPECTS OF ORGAN DONATION AND TRANSPLANTATION IN INDIA
Dr. Sumana Navin, Course Director, MOHAN Foundation, Chennai

INTRODUCTION
After years of exploitative practices in living unrelated transplants the Transplantation of Human Organs Act was passed in India in 1994 to put a stop to commercial dealings in organs. It also accepted the concept of brain-stem death and deceased organ donation and transplantation. Living unrelated donation is still permissible under the Act, but it has to be established that such a donation is altruistic in nature.

This article summarises the points relevant to deceased organ donation in the Transplantation of Human Organs Act, 1994, Transplantation of Human Organs Rules, 1995 (amended 2008), Transplantation of Human Organs and Tissues Act, 2011 (Amendment) and the Transplantation of Human Organs and Tissues Rules, 2014.
The Act itself lays down the broad legal framework, while the Rules are about the practical working of the Act (the required ‘Forms’ and other documents). Since Health is a state subject, each state has to adopt the Act by passing legislation. Government Orders/Resolutions have also been brought out by some state governments for clarity on procedures to be followed.


- To regulate removal, storage and transplantation of human organs for therapeutic purposes.
- Prevent commercial dealings in organs.
- Brain-stem death defined – Stage at which all functions of the brain stem have permanently and irreversibly ceased.
- Procedure for brain-stem death certification laid out.
- Consent for deceased organ donation:
  - Self when alive, 2 witnesses (Form 5 – “Donor card”)
  - Person in lawful possession of body (Form 6)
  - Parents, in case of minors (Form 9)
  - Unclaimed bodies, > 48 hours, hospital / prison in-charge
- Regulatory / Enforcement bodies:
  - Appropriate Authority: State appointed for granting and renewing hospital transplant license, monitoring of hospitals
  - Authorisation Committee: clearance of unrelated living donor transplants
- Board of Medical Experts (panel comprising four doctors for certifying brain death)
  - Hospital medical administrator
  - Independent specialist from panel authorised by Appropriate Authority (Doctor No. 2)
  - Neurologist / Neurosurgeon (Doctor No. 3)
  - Treating medical officer

Doctors No. 2 and No. 3 will be co-opted by the Administrator in-charge of the hospital from the panel of experts approved by the Appropriate Authority.

- Brain-stem death certification - The format for brain-stem death certification is laid out in Form 8 (Brain-stem death certificate). Two independent certifications have to be carried out at least six hours apart. While the brain-stem death certificate requires the doctors to document the results of testing for brain-stem reflexes and the apnoea test, there are no guidelines in the Rules about how the apnoea test should be done.
TRANSPLANTATION OF HUMAN ORGANS AND TISSUES ACT, 2011 (AMENDMENT) &
TRANSPLANTATION OF HUMAN ORGANS AND TISSUES RULES, 2014

• Tissues also included (except blood).

• Human Organ Retrieval Centre defined. This is a hospital which has adequate facilities for treating seriously ill patients who can be potential donors of organs in the event of death. These hospitals need to be registered for retrieval of human organs and tissues (Form 13 – Application for registration of hospital to carry out organ/tissue retrieval other than eye/cornea retrieval).

• Transplant coordinator defined. This is a person appointed by the hospital for coordinating all matters relating to removal or transplantation of human organs or tissues.

• Required request – It is the duty of the registered medical practitioner (RMP) in consultation with the transplant coordinator if available to make known to the family of a brain-stem dead person the option of organ and tissue donation. Whether donation is authorized or declined needs to be documented in Form 8 (Declaration cum consent Form) – Annexure 1.

• Expansion of brain-stem death certification panel – Anaesthetist / Intensivist nominated by the head of the hospital and duly empanelled by the Appropriate Authority may certify brain death as a member of the Board of Medical Experts.

• Brain-stem death certificate is Form 10 (Annexure 2) as per the Rules of 2014. It is essentially the same as Form 8 of the Rules of 2008 with two additions – i) an Anaesthetist or Intensivist can be a part of the panel. ii) In case of children 6 to 12 years of age, 1 to 5 years of age and infants, the time interval between the first and second testing shall increase depending on the opinion of the panel of experts.

• Deceased donor maintenance cost - Can be borne by recipient, institution, government or NGO/Society.

• Procedure for donation of organ or tissue in medicolegal cases – After the authority for removal of organs or tissues, as also the consent to donate organs from a brain-stem dead donor are obtained, the RMP of the hospital shall make a request to the Station House Officer or Superintendent of Police or Deputy Inspector General of the area either directly or through the police post located in the hospital to facilitate timely removal of organs or tissue from the donor and a copy of such a request should also be sent the designated post-mortem doctor of the area simultaneously.
The Governments of Tamil Nadu and Kerala have brought out Government Orders (GOs) laying down the procedure for brain-stem death certification. This includes the Brain-stem death certificate (Form 8 as per the Rules 2008) and, in addition, the guidelines for Apnoea test. The Tamil Nadu GO mentions that Intensivists can be a part of the panel certifying brain death, while the Kerala GO does not.

Revised guidelines for brain-stem death certification were issued by the Government of Kerala in 2017. This included obtaining written consent for performing the apnoea test as well as videography of the procedure from the relatives by the hospital in which the patient is admitted. Real time (time and date stamped) videography of the brain-stem death certification for both the apnoea tests must be produced. A peripheral nerve stimulation is to be carried out to rule out residual neuromuscular blockade through pharmacology agents.

The guidelines for Apnoea test that are a part of Tamil Nadu GO No. 75 on ‘Procedure for declaration of brain death’ is given as Annexure-3.

The Government of Andhra Pradesh’s GO and the Government of Maharashtra’s Resolution both say that Intensivists can be a part of the panel certifying brain death. Form 8 is used for brain-stem death certification. There are no guidelines for Apnoea test.

For more details on the Gos - Tamil Nadu (www.transtan.tn.gov.in), Kerala (www.knos.org.in), Telangana (www.jeevandan.gov.in), Maharashtra (www.ztccmumbai.org)
ANNEXURE 1 - FORM 8 (Rules 2014)

For Declaration cum consent

(To be filled by near relative or lawful possessor of brain-stem dead person)

[See rules 5(1)(b), 5(4)(b) and 5(4)(d)]

DECLARATION AND CONSENT FORM

I…………………………………………………...S/o,D/o,W/o…………………………………………………...aged………………resident of .................................................................in the presence of persons mentioned below, hereby declare that:

1. I have been informed that my relative (specify relation) ..........................................................................
S/o,D/o,W/o…………………………………………………aged………………has been declared brain stem dead / dead.

2. To the best of my knowledge (Strike off whichever is not applicable):
   a. He/She. (Name of the deceased)..................................................... had / had not, authorised before his/her death, the removal of ......................................(Name of organ/tissue/both) of his/her body after his/her death for therapeutic purpose. The documentary proof of such authorisation is enclosed / not available
   b. He/She. (Name of the deceased)........................................... had not revoked the authority as at No. 2 (a) above (If applicable).
   c. There are reasons to believe that no near relative of the said deceased person has objection to any of his/her organs/tissue being used for therapeutic purposes.

3. I have been informed that in the absence of such authorisation, I have the option to either authorise or decline donation of organ/tissue/both including eye/cornea of ...........................................(Name of the deceased) for therapeutic purposes. I also understand that if corneas/eyes are not found suitable for therapeutic purpose, then may be used for education/research.

4. I hereby authorise / do not authorize removal of his/her body organ(s) and/or tissue(s), namely (Any organ and tissue/ Kidney /Liver /Heart /Lungs /Intestine /Cornea /Skin /Bone /Heart Valves /Any other; please specify).............................................................................................................................. for therapeutic purposes. I also give permission for drawing of a blood sample for serology testing and am willing to share social/behavioural and medical history to facilitate proper screening of the donor for safe transplantation of the organs/ tissues.

Date…………………. Signature of near relative /person in lawful possession of the dead body, and address for correspondence*

Place…………………… Telephone No.………………………… Email: …..............................................

* in case of the minor the declaration shall be signed by one of the parent of the minor or any near relative authorised by the parent. In case the near relative or person in lawful possession of the body refuses to sign this form, the same shall be recorded in writing by the Registered Medical Practitioner on this Form.
(Signature of Witness 1)
Shri/Smt./Km. .......................................................... , S/o, D/o, W/o .................................................................
aged .........................................................., resident of .................................................................
Telephone No .........................................................., Email: ............................................................................

(Signature of Witness 2)
Shri/Smt./Km. .......................................................... , S/o, D/o, W/o .................................................................
aged .........................................................., resident of .................................................................
Telephone No .........................................................., Email: ............................................................................
ANNEXURE 2 - FORM 10 (Rules 2014)
For certification of brain stem death
(To be filled by the board of medical experts certifying brain-stem death)

[See rules 5(4)© and 5(4)(d)]

We, the following members of the Board of medical experts after careful personal examination hereby certify that Shri/Smt./Km…………………………………………………………………………….....aged about …………………… son of /wife of / daughter of …………………………………………………. Resident of …………………………………………………………………………………………………………………...is dead on account of permanent and irreversible cessation of all functions of the brain-stem. The tests carried out by us and the findings therein are recorded in the brain-stem death Certificate annexed hereto.

Dated………………
Signature……………………………..

1. R.M.P.- Incharge of the Hospital                            2. R.M.P. nominated from the panel of
   In which brain-stem death has occurred.                     Names sent by the hospitals and approved
   (where Neurologist/Neurosurgeon is not available, any Surgeon or Physician and Anaesthetist or
   Intensivist, nominated by Medical Administrator Incharge from the panel of names sent by the hospital
   and approved by the Appropriate Authority shall be included)

BRAIN-STEM DEATH CERTIFICATE
(A) PATIENT DETAILS

1. Name of the patient:     Mr./Ms……………………………………...................................................…...
   S.O./D.O./W.O             Mr./Ms……………………………………......................................................…
   Sex…………………………...…..Age……………………

2. Home Address: .................................................................................................................................
   ............................................................................................................................................................
   ............................................................................................................................................................

3. Hospital Patient Registration Number (CR No.): .............................…………...........……………………

4. Name and Address of next of kin or person .................................................……………………………………..
   responsible for the patient ......................................................................................................................
   (if none exists, this must be specified) .................................................................................................

5. Has the patient or next of kin agreed.................................................……………………………………..
   to any donation of organ and/or tissue?

6. Is this a Medico-legal Case? Yes………………….No…………………..
(B) PRE-CONDITIONS:
1. Diagnosis: Did the patient suffer from any illness or accident that led to irreversible brain damage?
   Specify details…………………………………………………………………………………………………………………
   …………………………………………………………………………………………………………………………….
   …………………………………………………………………………………………………………………………….
Date and time of accident/onset of illness…………………………………………………………
Date and onset of non-reversible coma…………………………………………………………
2. Findings of Board of Medical Experts:

First Medical Examination Second Medical Examination
1. The following reversible causes of coma have been excluded:
   Intoxication (Alcohol)
   Depressant Drugs
   Relaxants (Neuromuscular blocking agents) Primary Hypothermia
   Hypovolaemic shock
   Metabolic or endocrine disorders
   Tests for absence of brain-stem functions
2. Coma
3. Cessation of spontaneous breathing
4. Pupillary size
5. Pupillary light reflexes
6. Doll’s head eye movements
7. Corneal reflexes (Both sizes)
8. Motor response in any cranial nerve distribution, any responses to stimulation of face, limb or trunk.
9. Gag reflex
10. Cough (Tracheal)
11. Eye movements on caloric testing bilaterally.
12. Apnoea tests as specified.
13. Were any respiratory movements seen?

Date and time of first testing: …………………………………………………………………………………………….
Date and time of second testing:………………………………………………………………………………………….
This is to certify that the patient has been carefully examined twice after an interval of about six hours and on the basis of findings recorded above, Mr./Ms…………………………………………………………………………...is declared brain-stem dead.

Date:
Signatures of members of Brain Stem Death (BSD) Certifying Board as under:
Note:

1. Where Neurologist/Neurosurgeon is not available, then any Surgeon or Physician and Anaesthetist or Intensivist, nominated by Medical Administrator Incharge of the hospital shall be the member of the board of medical experts for brain-stem death certification.

2. The minimum time interval between the first and second testing will be six hours in adults. In case of children 6 to 12 years of age, 1 to 5 years of age and infants, the time interval shall increase depending on the opinion of the above BSD experts.

3. No.2 and No.3 will be co-opted by the Administrator Incharge of the hospital from the Panel of experts (Nominated by the hospital and approved by the Appropriate Authority).
Guidelines for Apnoea Tests:

Patient should have a temperature of more than 35 centigrade euvoletic and with Systolic pressure =/> 90 mm of Hg.

1. The first Apnoea test should be performed only after 4 hours of Coma associated with absence of brain stem reflexes. In the case of Anoxic brain damage, this period should be extended to 12 hours.

2. The Physician involved in certifying Brain death shall be present during Ventilator removal to attest the presence of apnoea if found.

3. Ventilator manipulation is performed to raise the PaCo2 =/> 40 mmHg.

4. The patient should be hyper oxygenated with 100% oxygen for 15 minutes, while still on the ventilator, prior to the apnoea test.

5. Either a blood gas or trending of ETCO2 should be used to determine the adequacy of the baseline prior to the test. SPO2 should be monitored during apnoea test.

6. Place the patient on 100% oxygen through a tracheal catheter with the tip towards the end of the tube with a continuous 6L/min O2 flow.

7. The patient is taken off the ventilator in the presence of the physician certifying brain death. The patient is kept off the Ventilator for a variable period of time (usually 3 to 8 minutes) to allow the PaCo2 to rise =/> 55 mmHg or =/> 15 mmHg over baseline. During this time the patient is observed for respiratory movements.

8. Test interpretations:
   a. Positive test – implying apnea despite adequate stimulation
      i. Patient remains apneic, without respiratory movements
      ii. PaCo2 is =/> 55 mmHg or =/> 15 mmHg from baseline

   b. Negative test – Implying apnea is not present
      i. Respiratory efforts noted at any time during the test

   c. Indeterminate test
      i. PaCo2 < 55 mm Hg or there is less than 15 mm Hg increase over baseline.

   d. Indeterminate tests can either be repeated or another confirmatory test utilized.

9. Apnoea test should be aborted if the patient develops hypotension, or significant cardiac arrhythmias.

10. These norms will vary for patients less than 12 years and patients with major chest trauma.
INTRODUCTION

The Transplantation of Human Organs Act was passed in India in 1994 to regulate the removal, storage and transplantation of human organs for therapeutic purposes as well as prevent commercial dealings in organs. It also accepted the concept of brainstem death and deceased organ donation and transplantation. The major cause of brainstem death in India is catastrophic brain injury sustained in a road traffic accident which is a medico-legal case (MLC). When families agree to organ donation in such a case, the procedure to be followed involves two groups who play pivotal roles - the police and the doctors who perform the post-mortem (primarily Forensic Medicine experts).

The Transplantation of Human Organs Act, 1994, did not offer much clarity on this procedure. This sometimes resulted in a peculiar situation where the post-mortem report read ‘organs missing’! The Transplantation of Human Organs and Tissues Rules, 2014 sought to clarify this. Health is a state subject, so Government Orders have been brought out by some states on the procedure to be followed for organ donation in medico-legal cases.

LEGAL FRAMEWORK

Formalities in Road Traffic Accidents and Medico-Legal Cases

When an accident victim is brought to a hospital for emergency treatment, a First Information Report (FIR) has to be filed by the family in the nearest police station. Such cases are called medico-legal cases. Also, any medical treatment (for suicide, assault, poisoning or fall) which requires the police to be notified becomes a medico-legal case. Road Traffic Accidents (RTA) are booked under Indian Penal Code (IPC) 304A.

In case of an unnatural death preliminary inquiry into the cause of death (inquest) is done by the police. The inquest is held by a police officer - Investigating Officer (IO) not below the rank of Senior Head Constable as per the provisions outlined in section 174 of the Code of Criminal Procedure. The IO prepares the inquest report (Panchanama) which takes about 1 to 2 hours. After the inquest, the IO prepares a request to the doctors to conduct the post-mortem. A registered medical practitioner (RMP) from allopathic stream is authorised to conduct post-mortem. After the post-mortem, the body is handed over to the police who then gives it to the family.

This in itself is a time-consuming process, but in deceased donation there are even more formalities involving the brainstem death certification panel, police, Forensic Medicine experts as well as multiple teams involved in organ retrieval thus increasing the timeline. In such a situation, there is a possibility that the relatives may withdraw consent for organ donation. It is therefore imperative for health care professionals to explain the procedure in its entirety to the family members.
Framework for organ donation in medico-legal cases as per Transplantation of Human Organs Act (THO), 1994

The Forensic Medicine expert needs to authorise the retrieval of organs in an MLC. Since the police has to conduct the inquest they have to give a ‘No Objection’ for organ donation to proceed. This has been laid out in the following sections of the THO Act 1994:

Chapter II, Section 4: No facilities shall be granted under sub-section (2) of section 3 and no authority shall be given under sub-section (3) of that section for the removal of any human organ from the body of a deceased person, if the person required to grant such facilities or empowered to give such authority has reason to believe that an inquest may be required to be held in relation to such body in pursuance of the provisions of any law for the time being in force.

Chapter II, Section 6: Where the body of a person has been sent for post-mortem examination -
1. for medico-legal purposes by reason of the death of such person having been caused by accident or any other unnatural cause; or
2. for pathological purposes, the person competent under this Act to give authority for the removal of any human organ from such dead body may, if he has reason to believe that such human organ will not be required for the purpose for which such body has been sent for post-mortem examination, authorise the removal, for therapeutic purposes, of that human organ of the deceased person provided that he is satisfied that the deceased person had not expressed, before his death, any objection to any of his human organs being used, for therapeutic purposes, after his death or, where he had granted an authority for the use of any of his human organs for therapeutic purposes after his death, such authority had not been revoked by him before his death.”

Framework for organ donation in medico-legal cases as per Transplantation of Human Organs and Tissues Rules, 2014

Section 6 lays down the procedure for donation of organ or tissue in medico-legal cases -

1. After the authority for removal of organs or tissues, as also the consent to donate organs from a brain stem dead donor are obtained, the RMP of the hospital shall make a request to the Station House Officer or Superintendent of Police or Deputy Inspector General of the area either directly or through the police post located in the hospital to facilitate timely removal of organs or tissue from the donor and a copy of such a request should also be sent the designated post-mortem doctor of the area simultaneously.
2. It shall be ensured that, by retrieving organs, the determination of the cause of death is not jeopardised.
3. The medical report in respect of the organs or tissues being retrieved shall be prepared at the time of retrieval by retrieving doctor (s) and shall be taken on record in post-mortem notes by the registered medical practitioner doing post-mortem.
Wherever it is possible, attempt should be made to request the designated post-mortem registered medical practitioner, even beyond office timing, to be present at the time of organ or tissue retrieval. In case a private retrieval hospital is not doing post mortem, they shall arrange transportation of body along with medical records, after organ or tissue retrieval, to the designated post-mortem centre and the post mortem centre shall undertake the post-mortem of such cases on priority, even beyond office timing, so that the body is handed over to the relatives with least inconvenience.

State Government Procedures

Some state governments have formalised procedures (Tamil Nadu and Delhi), while others have a more informal system. The Tamil Nadu Government Order (GO) No.86 outlines the procedure for post-mortem examination in medico-legal cases of organ donation (Annexure 1 – GO, Form I, II and III). The salient points (as illustrated in the flow chart) are:

1. Role of the police (Investigating Officer): Form I - Police Intimation Form
2. Role of the treating doctor in the ICU: Form II - Organ Functional Status Certificate
3. Role of the doctor performing the post-mortem: Form 3 - Organ Retrieval Authorisation Form
4. Permitting private hospitals where organ retrieval is taking place to have post-mortem performed in a designated area by a doctor with the necessary expertise.

In Delhi, the police give a No Objection Certificate (NOC) stating that they have no objection to the organ retrieval taking place (Annexure 2 – Form I, II, III).

CONCLUSION:

In India, the number of road traffic accident deaths was 1,50,785 in the year 2016 as per the Accidents India 2016 Report released by the Ministry of Road Transport and Highways. Uttar Pradesh topped the list with a percentage share of 12.8 per cent followed by Tamil Nadu (11.4 per cent) and Maharashtra (8.6 per cent).

In Tamil Nadu preliminary data from the Transplant Authority of Tamil Nadu estimates the number of deceased donors from April 2017 to March 2018 to be 143, while the number of donations from medico-legal cases was 123 out of which 108 cases were a result of road traffic accidents. It underscores the importance of streamlining and standardising the procedure for organ donation in medico-legal cases. This will expedite the process and alleviate the agony of waiting for families who have chosen to donate the organs of their loved ones. Critical care physicians are first line caregivers and their understanding of the medico-legal procedure relating to deceased organ donation will help them support families in this most difficult of situations.
REFERENCES:

PROTOCOL BASED SEPSIS MANAGEMENT
Dr. Khusrav Bajan

Sepsis remains a significant public health problem, with increasing incidence but decreasing mortality worldwide.

The first working definition of sepsis was developed in 1991: the concept of systemic inflammatory response syndrome (SIRS), which is characterized by a cluster of symptoms triggered by an inflammatory response that may or may not be due to an infectious process.

The **Sepsis-3 task force**, convened in 2014 by the SCCM and the ESICM, introduced a new definition which mainly focuses on organ dysfunction and hypoperfusion along with a dysregulated host response in the presence of infection, rather than on inflammation. Septic shock is now defined as a subset of sepsis in which the patient has profound hypoperfusion.

The Surviving Sepsis Campaign Bundle: 2018 Update mentioned a revision of the SSC bundles, in that the 3-hr and 6-hr bundles have been combined into a single “**hour-1 bundle**” with the explicit intention of beginning resuscitation and management immediately with the time of presentation in the emergency department taken as **‘Time Zero’** and to

- a) Measure lactates, remeasure if the initial lactate is > 2mmol/l.
- b) Obtain blood cultures prior to administration of antibiotics.
- c) Administer broad spectrum antibiotics.
- d) Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate ≤ 4mmol/l.
- e) Apply vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain MAP ≤ 65 mm Hg.
A Randomized Trial of Protocol-Based Care for Early Septic Shock conducted in 2014 stated mortality was markedly lower among those who were treated according to a 6-hour protocol of early goal-directed therapy (EGDT), in which intravenous fluids, vasopressors, inotropes, and blood transfusions were adjusted to reach central hemodynamic targets, than among those receiving usual care.

Protocol driven Fluid resuscitation, Sedation use and Transfusion of blood and products have shown to have better outcomes.

A protocolized ventilator and weaning methods are also desirable in Sepsis induced or Primary ARDS. Protocols and bundles however well executed, should be individualized and tailored depending upon the institutional practices and the host conditions.

REFERENCES:

• Levy et al. The Surviving Sepsis Campaign Bundle: 2018 Update. Critical Care Medicine June 2018 ; 46(6).

PULMONARY EMBOLISM : THE RIGHT VENTRICULAR SPIRAL OF DEATH?
Dr. Jose Chako

Traditionally, the assessment of ventricular function has focussed mainly on the left ventricle. However, the right ventricle (RV) fails acutely in pulmonary embolism, in contrast to chronic dilatation and dysfunction that may occur in long-standing pulmonary arterial hypertension. Abrupt decompensation of the RV may occur in acute pulmonary embolism, leading to high mortality. It is important to recognize the early warning signs RV failure and initiate appropriate therapy in a timely manner. There is a wide spectrum of severity of RV involvement in acute pulmonary embolism, which often makes risk stratification difficult. Anticoagulation alone may be adequate in segmental or subsegmental emboli; however, in acute massive pulmonary embolism, thrombolytic treatment is the preferred therapeutic modality. In patients who remain hemodynamically unstable, catheter-directed thrombectomy or operative pulmonary embolectomy must be considered.
Maternal illness during pregnancy is not uncommon and sometimes requires radiographic imaging for proper diagnosis and treatment. The patient and her physician may be concerned about potential harm to the fetus from radiation exposure. In reality, however, the risks to the developing fetus are quite small. The accepted cumulative dose of ionizing radiation during pregnancy is 5 rad,

no single diagnostic study exceeds this maximum. For example, the amount of exposure to the fetus from a chest x-ray of the mother is only 0.00007 rad. The most sensitive time period for central nervous system teratogenesis is between 10 and 17 weeks of gestation.

Non urgent radiologic testing should be avoided during this time. Rare consequences of prenatal radiation exposure include a slight increase in the incidence of childhood leukemia and, possibly, a very small change in the frequency of genetic mutations. Such exposure is not an indication for pregnancy termination.

Many women become ill while pregnant and require acute medical care, including radiographic imaging with ionizing radiation. Exposure of a fetus to radiation can be alarming to parents and is dealt with by the general public with less objectivity than is evident with exposure to almost any other agent.

Even physicians are at times known to approach this topic in a biased and unscientific manner, leading to poor patient care and inappropriate advice. It is important for primary care doctors to have a clear perception of the actual risks and benefits of radiographic studies during pregnancy.

Ionizing radiation (x-ray) is composed of high-energy photons that are capable of damaging DNA and generating caustic free radicals. A patient's dose of photons is measured in the gray (Gy) and the rem, or in the older and more commonly recognized unit, the rad. The range of doses provided by common radiographs is outlined in Table
## Estimated Fetal Exposure for Various Diagnostic Imaging Methods

### Estimated fetal dose per examination (rad)

<table>
<thead>
<tr>
<th>Examination type</th>
<th>Estimated fetal dose per examination (rad)</th>
<th>No. of examinations required for a cumulative 5 rad dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plain films</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Skull</td>
<td>0.004</td>
<td>1,250</td>
</tr>
<tr>
<td>2 Dental</td>
<td>0.0001</td>
<td>50,000</td>
</tr>
<tr>
<td>3 Cervical spine</td>
<td>0.002</td>
<td>2,500</td>
</tr>
<tr>
<td>4 Upper or lower extremity</td>
<td>0.001</td>
<td>5,000</td>
</tr>
<tr>
<td>5 Chest (two views)</td>
<td>0.00007</td>
<td>71,429</td>
</tr>
<tr>
<td>6 Mammogram</td>
<td>0.020</td>
<td>250</td>
</tr>
<tr>
<td>7 Abdominal (multiple views)</td>
<td>0.245</td>
<td>20</td>
</tr>
<tr>
<td>8 Thoracic spine</td>
<td>0.009</td>
<td>555</td>
</tr>
<tr>
<td>9 Lumbosacral spine</td>
<td>0.359</td>
<td>13</td>
</tr>
<tr>
<td>10 Intravenous pylogram(IVP)</td>
<td>1.398</td>
<td>3</td>
</tr>
<tr>
<td>11 Pelvis</td>
<td>0.040</td>
<td>125</td>
</tr>
<tr>
<td>12 Hip (single view)</td>
<td>0.213</td>
<td>23</td>
</tr>
</tbody>
</table>

| **CT scans (slice thickness: 10 mm)**                  |                                            |                                                       |
| 1 Head (10 slices)                                    | < 0.050                                    | > 100                                                 |
| 2 Chest (10 slices)                                   | < 0.100                                    | > 50                                                  |
| 3 Abdomen (10 slices)                                 | 2.600                                      | 1                                                     |
| 4 Lumbar spine (5 sliceS)                             | 3.500                                      | 1                                                     |
| 5 Pelvi metry (1 slice with scout film)                | 0.250                                      | 20                                                    |

| **Fluroscopic Y**                                     |                                            |                                                       |
| 1 Upper GI series                                     | 0.056                                      | 89                                                    |
| 2 Barium swallow                                      | 0.006                                      | 833                                                   |
| 3 Barium enema                                        | 3.986                                      | 1                                                     |
Much of our information regarding the effects of radiation in humans has come from the study of atomic bomb survivors who were irradiated with high doses while in utero in Nagasaki and Hiroshima, Japan.

Understanding outcomes after high-dose exposure can help physicians understand potential effects from low-dose medical x-rays.

These effects can be grouped into three categories: teratogenesis (fetal malformation), carcinogenesis (induced malignancy) and mutagenesis (alteration of germ-line genes).

RADIATION-INDUCED TERATOGENESIS
The fetal malformations most commonly caused by high-dose radiation are central nervous system (CNS) changes, especially microcephaly and mental retardation. Many Japanese bomb victims who were exposed in utero to doses greater than 10 to 150 rad developed microcephaly. A linear, dose-related association between severe mental retardation and radiation was also found, with the important caveat that most cases followed exposure during weeks 10 to 17 of gestation. This trend reaches 40 percent at 100 rad, although it is not statistically significant at doses generated by diagnostic radiographs. Nevertheless, until more data are available delineating potential fetal risk, it is prudent to delay non-urgent radiographs during the sensitive period of 10 to 17 weeks of gestation.

RADIATION-INDUCED MALIGNANCY
Exposure to as little as 1 or 2 rad has also been associated with a slight increase in childhood malignancies, especially leukemia. For example, the background rate of leukemia in children is about 3.6 per 10,000, Exposure to one or two rad increases this rate to 5 per 10,000. While these doses do fall within the range of that supplied by some radiographic studies, the absolute increase of risk (about one in 10,000) is very small. Nevertheless, physicians should carefully weigh the risks and benefits of any radiographic study and include the mother in the decision-making process whenever possible.

RADIATION-INDUCED GENE MUTATION
Radiation can cause germ-line mutations, potentially affecting future generations. Although radiation is commonly believed to create bizarre new mutations, data show that usually it merely increases the frequency of mutations occurring naturally in the general population. The dosage required to double this baseline mutation rate is between 50 and 100 rad, far in excess of the radiation doses occurring in common radiographic studies. Put another way, it is believed that if 10,000 persons were exposed to 1 rad, 10 to 40 new genetic mutations would be induced.
Statements on Diagnostic Imaging Modalities During Pregnancy

X-ray imaging
1. “No single diagnostic procedure results in a radiation dose that threatens the well-being of the developing embryo and fetus.”- American College of Radiology
2. “[Fetal] risk is considered to be negligible at 5 rad or less when compared to the other risks of pregnancy, and the risk of malformations is significantly increased above control levels only at doses above 15 rad.”- National Council on Radiation Protection
3. “Women should be counseled that x-ray exposure from a single diagnostic procedure does not result in harmful fetal effects. Specifically, exposure to less than 5 rad has not been associated with an increase in fetal anomalies or pregnancy loss.”- American College of Obstetricians and Gynecologists.

Magnetic resonance imaging
“Although there have been no documented adverse fetal effects reported, the National Radiological Protection Board arbitrarily advises against its use in the first trimester.”- American College of Obstetricians and Gynecologists and National Radiological Protection Board

Ultrasound imaging
“There have been no reports of documented adverse fetal effects for diagnostic ultrasound procedures, including duplex Doppler imaging.” “There are no contraindications to ultrasound procedures during pregnancy, and this modality has largely replaced x-ray as the primary method of fetal imaging during pregnancy.”- American College of Obstetricians and Gynecologists

Now a day use of ultrasound is increase and its like point of care in ICU & ER, with this modality you can diagnosed many thing like effusion /pneumothorax/consolidation/cardiac function /deep vein thrombosis/abdominal pathology/

Safety Counseling
When an expectant mother considers any radiation exposure, the most prominent question in her mind is likely to be, “Is this safe for my baby?” To answer this question, the clinician must carefully choose words that will help a patient understand the real, although very small, risks of exposure. Careful attention must also be given to the parents' potential emotional turmoil at the thought of placing their infant at any increased risk, however small.

“Safe” is a relative term, but one that physicians should not be afraid to use. When a radiographic study is needed for appropriate management of a pregnant patient, the American College of Radiology recommends that “health care workers should tell patients that x-rays are safe and provide patients with a clear explanation of the benefits of x-ray examinations.”
Diagnostic x-rays during pregnancy are considered safe, yet physicians should use reasonable caution while remaining sensitive to patients' fears and concerns. As with all patient care, good communication promotes a trusting relationship. Unexpected outcomes often lead to anger and legal action. Thus, a factual discussion of the nature of the planned examination and its potential outcomes, and documenting consent are appropriate steps before ordering a study. Asking nonpregnant women with child-bearing potential about the possibility of pregnancy is also an important way to avoid unpleasant surprises.

Women exposed to radiation exceeding a cumulative dose of 5 rad and those with particular concerns about their infant's health may require further evaluation or referral. A radiation physicist can calculate the estimated dose of radiation to the fetus to assist in patient counseling.

A physician's caution should not become unreasonable. Concerns of medico legal liability may lead some caregivers to inappropriately withhold needed x-rays, thus jeopardizing the health of both mother and fetus. Yet legal liability with exposures less than 5 rad should be minimal and, in fact, many key organizations have declared such exposures to be safe. Furthermore, it would be difficult to prove that a given radiograph caused harm in light of the high baseline rate of malformations. Ensuring that radiographs are truly indicated and are ordered in accordance with applicable published guidelines will give further support to a physician's course of action at any review.

If a mother's illness necessitates x-rays, there should usually be no hesitation in ordering the needed study. A reasonable guideline has been proposed by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (ACOG) that balances these issues.

**Abortions Counselling**

A woman may fear radiation so much that she believes she should abort a fetus after exposure. Up to 25 percent of exposed women believe their infants are at risk for major malformation. Timely counselling can often correct such a misunderstanding. It is important that patients and physicians not confuse social issues with medical ones. Medically, the additional risk imposed by diagnostic radiation is simply too small to justify terminating a pregnancy.

For example, one risk associated with lower-dose radiation is childhood leukemia. Yet it would be necessary to abort 1,999 exposed fetuses to prevent one case of leukemia. Guidelines from ACOG clearly support this understanding: “Exposure to x-ray during pregnancy is not an indication for therapeutic abortion.”
TAKE HOME MESSAGE

1. A pregnant woman who is ill and requires radiographic imaging faces potential risks from her disease to her own health as well as that of her developing infant's. These risks almost always outweigh the minor hazards posed by low-dose radiation exposure. Physicians should not hesitate to order a study if an appropriate work-up of the mother requires a specific test to guide diagnosis and treatment.

2. Non urgent x-rays should be avoided in weeks 10 to 17, the period of greatest CNS sensitivity.

3. Ultrasonography may represent an alternative to ionizing radiation and is considered safe throughout pregnancy. Its point of care and provide diagnosis at bed site

4. Patient counseling before radiation exposure will help alleviate anxiety and misunderstandings. Proper communication may also reduce unnecessary litigation in the event of an unexpected outcome.

TELEMEDICINE: A LUXURY OR A NECESSITY?

Dr. Raymond Savio

Telemedicine is defined by the WHO as “The delivery of healthcare services, where distance is a critical factor, by all healthcare professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation and for the continuing education of healthcare providers, all in the interests of advancing the health of individuals and their communities”. Many years since its inception and perhaps its execution now, isn’t half as complex as the definition itself! Telemedicine was likely adopted by NASA as early as in the 1960s to monitor physiologic changes in astronauts, but it wasn’t until the year 2000 that the government of India took special note of this technology-based delivery of healthcare. With close to 70% of the Indian population residing in rural areas with limited healthcare facilities, it is rather high time that telemedicine had taken off as a widespread and efficient means of healthcare delivery.

While overcoming hurdles arising from distance happens to be one of the primary objectives, timely identification of critical signs, prioritizing patients who may benefit from urgent referral to a tertiary centre and knowledge transfer are other noteworthy advantages. The availability of real-time tele conferencing has further made this service quicker and cost efficient to the patient. Over the years, telemedicine has further expanded to include several other applications such as tele-education, tele-proctoring, disaster management and home-care which have rather become the norm in many parts of the country. Despite this, its growth has not kept pace with demand. The potential of this technology is still to be explored to its fulness.
Healthcare providers often quote issues with infrastructure, implementation, acceptance and viability as reasons for delay in progress in this field. Furthermore, legal and ethical challenges and privacy concerns are other impediments to headway. Nevertheless, telemedicine is expected to make a big wave in near future with improvements in digital, analog and wireless technology. Currently, there are only a few players affiliated to tertiary hospitals, offering telemedicine technology in India. With time, this situation is expected to improve and create a favourable impact on cost and access to healthcare across India. This has rather become the need of the hour and not luxury in this country of 1.35 billion population and a doctor to people ratio of 1:11082 as highlighted by the central bureau of health intelligence in 2018!

REFERENCES:


THROMBOCYTOPENIA IN PREGNANCY
Dr Rajal Thaker

Normal pregnancy is associated with a physiologic fall in the platelet count. The reason for this decline is not known, although it has been speculated that these changes may reflect dilution, decreased platelet production, or increased platelet turnover during pregnancy and increased platelet aggregation driven by increased levels of thromboxane A2.

Thrombocytopenia is defined as a platelet count < 150 × 10⁹/L, is second only to anemia as the most common hematologic abnormality encountered during pregnancy.

- Mild: 100 to 150 × 10⁹ /L
- Moderate: 50 to 100 × 10⁹ /L
- Severe: Less than 50 × 10⁹ /L
- Most of the decrease in occurs platelet occurs in third trimester of pregnancy
- Platelet count may also be lower in women with twins as compared with singleton pregnancies, perhaps due to a greater increase in thrombin generation
- Prevalence at the end of pregnancy is between 6.6% and 11.6%
- The overall incidence of thrombocytopenia in pregnancy is 8%, but when patients with obstetric or medical conditions are excluded, the incidence drops to 5.1%
Thrombocytopenia in pregnancy may result from several etiologies, which include those, that are unique to pregnancy and others, which may occur, in non-pregnant settings. They include gestational thrombocytopenia (70-75%), hypertensive disorders of pregnancy (21%) like preeclampsia, eclampsia and HELLP syndrome, liver diseases including acute fatty liver of pregnancy, drug induced thrombocytopenia, immune thrombocytopenia (4%), thrombocytopenia due to viral infections, SLE, APLA syndromes.

Thrombocytopenia can have a wide range of prognostic implications, from completely benign to life threatening. Awareness of these causes facilitates proper diagnosis and management of thrombocytopenia in the pregnant women. These conditions, however, can cause considerable morbidity and mortality, and they must be managed closely.

**CAUSES OF THROMBOCYTOPENIA IN PREGNANCY**

**Pregnancy-specific**

*Isolated thrombocytopenia*

Gestational thrombocytopenia (70%-80%)

**Thrombocytopenia associated with systemic disorders**

Preeclampsia (15%-20%)

HELLP syndrome (< 1%)

Acute fatty liver of pregnancy (< 1%)

**Not pregnancy-specific**

- Primary immune thrombocytopenia – ITP (1%-4%)
- Secondary immune thrombocytopenia due to viral infections (e.g., HIV, Hep C, H pylori, CMV, EBV) (< 1%)
- Autoimmune conditions such as SLE, APLS (Antiphospholipid antibody syndrome)
- Bone marrow disorders such as MDS, myelofibrosis
- Disseminated intravascular coagulation
- Drugs Heparin induced thrombocytopenia
- Hypersplenism
- Inherited thrombocytopenia, Type IIB vWD
- Nutritional deficiencies B12, folate
- Thrombotic microangiopathies: Thrombotic Thrombocytopenic Purpura (TTP)/Hemolytic Uremic Syndrome(HUS)
- Splenic sequestration (liver diseases, portal vein thrombosis, storage disease etc
**Gestational thrombocytopenia** occurs in approximately 8% of all pregnancies and accounts for more than 70% of cases with thrombocytopenia in pregnancy. In this condition however platelet counts usually remain above 100×10⁹/L, but can fall to 70×10⁹/L. This condition usually occurs in the late second or third trimesters of pregnancy. A diagnosis of gestational thrombocytopenia unlikely if the platelet count is <50 x 10⁹/L, with very few cases having been described with counts 40-50 x 10⁹/L. The aetiology may be due to increased peripheral consumption of platelets. It is usually a diagnosis of exclusion. It usually requires routine prenatal care and monitoring of platelet count every 4 weeks. Mode of delivery is as per maternal and fetal indications. Epidural anaesthesia is safe at counts above one lakh. Recurrence of gestational thrombocytopenia in subsequent pregnancies is common and patient should be properly counseled about this. It has features overlapping ITP. The existence of pre-pregnancy thrombocytopenia should rule out gestational thrombocytopenia. However, previous pregnancies complicated by thrombocytopenia would favor gestational thrombocytopenia. Gestational thrombocytopenia resolves spontaneously after delivery within 6 weeks postpartum and there is absence of thrombocytopenia in newborn.

**Immune thrombocytopenia** due to production of IgG antiplatelet antibodies against own platelet membrane glycoprotein’s is characterized by, moderate thrombocytopenia, is an early gestation platelet count below one lakh, and increased megakaryocyte level on bone marrow biopsy. History of thrombocytopenia before 28 weeks and a platelet count less than 50×10⁹/L is highly suggestive of ITP. In ITP most often there is a history of bleeding outside pregnancy and low platelet counts prior to pregnancy. Management in ITP is directed towards raising platelet counts to prevent spontaneous bleeding and ensure safe delivery. Treatment of ITP in pregnancy is mainly steroids and IVIG though the response is lesser in pregnant than non-pregnant patients. Generally treatment is required only in the third trimester and aim is to keep the values above 50×10⁹/L. Due to the increased risk of neonatal thrombocytopenia instrumental delivery should be avoided in cases of maternal ITP. Platelet transfusions may be less effective in view of ongoing platelet destruction.

**Preeclampsia** is a common cause of thrombocytopenia in third trimester of pregnancy. The risk of development of thrombocytopenia is about 18% in preeclampsia, 10-12% in DIC and 4-15% in HELLP syndrome. The general approach in these cases would be medical stabilization and expeditious delivery after 34 weeks. If earlier then maternal well-being has the priority.

Thrombocytopenia may be related to **liver disease and hypersplenism** in pregnancy. Most liver disease in pregnancy is attributable to 1 of the 5 liver diseases unique to pregnancy: hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy. Of these disorders, only HELLP, preeclampsia, and acute fatty liver of pregnancy are associated with thrombocytopenia. A recent study showed that 47% of patients had platelet count less than 100×10⁹ /L. Management of AFLP is immediate termination of pregnancy. Coagulation studies should be optimized by transfusion prior to delivery.
Systemic lupus erythematosus (SLE) predominantly affects women of childbearing age. Disease flares during pregnancy and pose challenges with respect to distinguishing physiologic changes related to pregnancy from disease related manifestations. So a multidisciplinary approach with close medical, obstetric, and neonatal monitoring is necessary to optimize both maternal and fetal outcomes. Thrombocytopenia less than $100 \times 10^9 /L$ is one of the diagnostic criteria of SLE. The thrombocytopenia of SLE rarely becomes severe. If treatment is required in severe thrombocytopenia, patients may respond to hydroxychloroquine, glucocorticoids, or other immunosuppressive medications used for other manifestations of SLE.

A rare inherited cause of thrombocytopenia is type IIB von Willebrand disease (VWD). Women with this condition may develop thrombocytopenia, for the first time, in pregnancy and be misdiagnosed with ITP. Platelet counts may occasionally fall to levels as low as $10-20 \times 10^9 /L$ at term, typically with nadir value 1-3 days before delivery, but they rapidly improve after delivery.

Heparin induced thrombocytopenia (HIT) occurs in 1% to 5% of patients receiving unfractionated heparin within the previous 5 to 10 days. HIT is an extremely thrombotic process, despite the low platelet count.

Analgesics like aspirin, acetaminophen, antibiotics like penicillin and drugs like heparin, methyldopa, digitalis, and cyclosporine may cause thrombocytopenia. It is recommended to obtain a baseline platelet count before starting therapy, then repeat platelet counts on Days 7 and 14 of therapy. HIT should be suspected if the platelet count falls by approximately 50% or more. If the repeat platelet counts are normal, no further testing is necessary.

Chronic infection with HIV and HCV are frequent causes of chronic thrombocytopenia. Treatment of HIV and HCV related thrombocytopenia should be directed toward antiviral therapy with highly active antiretroviral therapy regimens.

The antiphospholipid antibody syndrome is an autoimmune disorder, which associates clinical thromboembolism with obstetric manifestations. Antiphospholipid antibodies cause obstetric accidents by a thrombocytopenia phenomenon.

Other etiologies for moderate to severe thrombocytopenia in pregnancy are malaria and dengue as they are endemic in our area. Pregnancy increases susceptibility to malaria and is associated with profound alterations in the fibrinolytic and coagulation systems. Both plasmodium falciparum and plasmodium vivax can cause thrombocytopenia in pregnancy, and more chances with repeated infections. If these infections are treated appropriately, there are fewer chances of complications but complicated malaria is associated with poor feto-maternal outcomes.
Thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) are collectively referred to as thrombotic microangiopathies and are not pregnancy specific, although they occur with increased frequency during pregnancy, with an incidence of 1 in 25,000. The incidence is greater in the second and third trimesters. The differentiation between TTP, HUS and HELLP can be difficult or even impossible, especially when the onset is during the second and third trimesters. Delivery leads to resolution of preeclampsia but not TTP/HUS. If suspected preeclampsia/HELLP does not improve within 48-72 hours after delivery, TTP/HUS should be considered.

REFERENCES:

WHEN WOULD YOU NOT USE CORTICOSTEROIDS IN THE CRITICALLY ILL
Dr. Jose Chako

Corticosteroid therapy in critically ill patients is often deeply entrenched in controversy. There are several clear indications for its use, including acute adrenal insufficiency, anaphylactic reactions, and acute exacerbation of bronchial asthma. Administration prior to antibiotic therapy has been shown to be of benefit in meningitis due to Streptococcus pneumoniae. There is conflicting evidence of benefit in septic shock, acute respiratory distress syndrome, and airway edema. There is conclusive evidence that corticosteroid therapy is not beneficial in traumatic brain injury and Guillain Barre syndrome. The possibility of serious adverse effects including hyperglycemia, hypernatremia, ICU-acquired weakness, and flare-up of septic complications need to considered in patients who receive steroids. It is important to consider whether these side effects may outweigh any presumed benefit from corticosteroid therapy. There is an ever-growing body of knowledge regarding the rational use of corticosteroids that will help clinicians make a considered decision on appropriate use.
### Anti-infectives Product Range

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
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<tr>
<td>RUAJ</td>
<td>Meropenem Injection 2 gm / 1 gm</td>
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<tr>
<td>RUAJ-S-1.5</td>
<td>Meropenem and Sulbactam for Injection 1.5 gm</td>
</tr>
<tr>
<td>ZOACT</td>
<td>Cefoperazone and Sulbactam Injection 1.5 gm</td>
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<tr>
<td>ZOACT FORTE</td>
<td>Cefoperazone and Sulbactam Injection 3 gm</td>
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<tr>
<td>IMIREN</td>
<td>Imipenem and Cilastatin Injection 1 gm/0.5 gm</td>
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<td>Sulbactam for Injection 2 gm / 1 gm</td>
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<tr>
<td>TIZIREN</td>
<td>Tigecycline for Injection 50 mg</td>
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<tr>
<td>MYXITIN</td>
<td>Colistimethate Sodium For Injection 4.5 MIU / 3 MIU / 2 MIU / 1 MIU</td>
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<tr>
<td>TAZOREN</td>
<td>Piperacillin and Tazobactam Injection 4.5 gm</td>
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<td>TEICOGRESS</td>
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### Clinical Nutrition Product Range

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<th>Product</th>
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<tr>
<td>GLUTAHENZ-IV/SACHET</td>
<td>L-Glutamine - 15 gm sachet/ L-Alanyl-L-Glutamine Infusion 20%</td>
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<tr>
<td>OTSKI-IV</td>
<td>Trace elements Injection U.S.P. ( Copper, Chromium, Manganese, Selenium, Zinc )</td>
</tr>
<tr>
<td>LAMINO-8%</td>
<td>Amino Acids Infusion 8% w/v</td>
</tr>
<tr>
<td>LAMINO-10% PLUS</td>
<td>Amino Acids Infusion 10% w/v with electrolytes</td>
</tr>
<tr>
<td>LAMINO RESPI</td>
<td>Food Supplement for Respiratory Care</td>
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</table>
Acetylcysteine and Sodium Bicarbonate in contrast nephropathy: To give or not to give

**BACKGROUND:** Intravenous sodium bicarbonate and oral/IV acetylcysteine are widely used to prevent acute kidney injury and associated adverse outcomes after angiography without definitive evidence of their efficacy.

Radiocontrast media may cause acute kidney injury (AKI) among high-risk patients. Earlier studies have been inconsistent but indicated that the administration of oral acetylcysteine may decrease the risk of AKI, and led to suggestion to administer acetylcysteine before and the day of angiography to patients at risk of contrast nephropathy. A recent randomized trial in over 5000 patients at increased risk for nephropathy who were undergoing scheduled angiography found that oral acetylcysteine, compared with placebo, did not prevent death, need for dialysis, or decline in kidney function [1]. The trial was a 2 by 2 factorial design and also compared intravenous sodium bicarbonate with isotonic saline.

Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine.


**METHODS:** Using a 2-by-2 factorial design, we randomly assigned 5177 patients at high risk for renal complications who were scheduled for angiography to receive intravenous 1.26% sodium bicarbonate or intravenous 0.9% sodium chloride and 5 days of oral acetylcysteine or oral placebo; of these patients, 4993 were included in the modified intention-to-treat analysis. The primary end point was a composite of death, the need for dialysis, or a persistent increase of at least 50% from baseline in the serum creatinine level at 90 days. Contrast-associated acute kidney injury was a secondary end point.

**RESULTS:** The sponsor stopped the trial after a prespecified interim analysis. There was no interaction between sodium bicarbonate and acetylcysteine with respect to the primary end point (P=0.33). The primary end point occurred in 110 of 2511 patients (4.4%) in the sodium bicarbonate group as compared with 116 of 2482 (4.7%) in the sodium chloride group (odds ratio, 0.93; 95% confidence interval [CI], 0.72 to 1.22; P=0.62) and in 114 of 2495 patients (4.6%) in the acetylcysteine group as compared with 112 of 2498 (4.5%) in the placebo group (odds ratio, 1.02; 95% CI, 0.78 to 1.33; P=0.88). There were no significant between-group differences in the rates of contrast-associated acute kidney injury.

**CONCLUSIONS:** Among patients at high risk for renal complications who were undergoing angiography, there was no benefit of intravenous sodium bicarbonate over intravenous sodium chloride or of oral acetylcysteine over placebo for the prevention of death, need for dialysis, or persistent decline in kidney function at 90 days or for the prevention of contrast-associated acute kidney injury.
RECOMMENDATION: For patients undergoing angiography who are at increased risk for contrast nephropathy, acetylcysteine not be given, either orally or intravenously (Grade 2B).

Give isotonic saline rather than sodium bicarbonate prior to angiography.

Balanced crystalloids versus isotonic saline in critically ill and noncritically ill patients

BACKGROUND: Many of the intravenous solutions used for fluid resuscitation in critically-ill patients are hyperchloremic (eg, isotonic saline) relative to plasma, such that large volume resuscitation using isotonic saline may be associated with the development of hyperchloremic metabolic acidosis. This has led to suggestions that isotonic fluids with lower chloride concentration (also known as buffered or balanced crystalloids including lactated-Ringers solution, lactated-Hartmann solution, 0.45 percent saline solution with 75 mmol/L of sodium bicarbonate, or Plasma-lyte) be used instead of isotonic saline for large volume resuscitation.

The administration of balanced crystalloids (eg, Plasma-Lyte or Ringer's lactate) versus isotonic saline for large volume resuscitation is controversial, hampered by conflicting data and the lack of an ideal crystalloid solution. One randomized trial in over 15,000 critically ill patients [1] and another in over 13,000 noncritically ill patients in the emergency department [2] found that, compared with isotonic saline, balanced crystalloids reduced the composite outcome of death from any cause at 30 days, new renal replacement therapy, or persistent renal dysfunction. Patients who received larger volumes (eg, >2 liters) benefited the most.

1 Balanced Crystalloids versus Saline in Critically Ill Adults.


BACKGROUND: Both balanced crystalloids and saline are used for intravenous fluid administration in critically ill adults, but it is not known which results in better clinical outcomes.

METHODS: In a pragmatic, cluster-randomized, multiple-crossover trial conducted in five intensive care units at an academic center, we assigned 15,802 adults to receive saline (0.9% sodium chloride) or balanced crystalloids (lactated Ringer's solution or Plasma-Lyte A) according to the randomization of the unit to which they were admitted. The primary outcome was a major adverse kidney event within 30 days - a composite of death from any cause, new renal replacement therapy, or persistent renal dysfunction (defined as an elevation of the creatinine level to ≥ 200% of baseline) - all censored at hospital discharge or 30 days, whichever occurred first.
RESULTS: Among the 7942 patients in the balanced-crystalloids group, 1139 (14.3%) had a major adverse kidney event, as compared with 1211 of 7860 patients (15.4%) in the saline group (marginal odds ratio, 0.91; 95% confidence interval [CI], 0.84 to 0.99; conditional odds ratio, 0.90; 95% CI, 0.82 to 0.99; P=0.04). In-hospital mortality at 30 days was 10.3% in the balanced crystalloids group and 11.1% in the saline group (P=0.06). The incidence of new renal replacement therapy was 2.5% and 2.9%, respectively (P=0.08), and the incidence of persistent renal dysfunction was 6.4% and 6.6%, respectively (P=0.60).

CONCLUSIONS: Among critically ill adults, the use of balanced crystalloids for intravenous fluid administration resulted in a lower rate of the composite outcome of death from any cause, new renal replacement therapy, or persistent renal dysfunction than the use of saline.

2 Balanced Crystalloids versus Saline in Noncritically Ill Adults.


BACKGROUND: Comparative clinical effects of balanced crystalloids and saline are uncertain, particularly in noncritically ill patients cared for outside an intensive care unit (ICU).

METHODS: We conducted a single-center, pragmatic, multiple-crossover trial comparing balanced crystalloids (lactated Ringer’s solution or Plasma-Lyte A) with saline among adults who were treated with intravenous crystalloids in the emergency department and were subsequently hospitalized outside an ICU. The type of crystalloid that was administered in the emergency department was assigned to each patient on the basis of calendar month, with the entire emergency department crossing over between balanced crystalloids and saline monthly during the 16-month trial. The primary outcome was hospital-free days (days alive after discharge before day 28). Secondary outcomes included major adverse kidney events within 30 days - a composite of death from any cause, new renal-replacement therapy, or persistent renal dysfunction (defined as an elevation of the creatinine level to 200% of baseline) - all censored at hospital discharge or 30 days, whichever occurred first.

RESULTS: A total of 13,347 patients were enrolled, with a median crystalloid volume administered in the emergency department of 1079 ml and 88.3% of the patients exclusively receiving the assigned crystalloid. The number of hospital-free days did not differ between the balanced crystalloids and saline groups (median, 25 days in each group; adjusted odds ratio with balanced crystalloids, 0.98; 95% confidence interval [CI], 0.92 to 1.04; P=0.41). Balanced crystalloids resulted in a lower incidence of major adverse kidney events within 30 days than saline (4.7% vs. 5.6%; adjusted odds ratio, 0.82; 95% CI, 0.70 to 0.95; P=0.01).
CONCLUSIONS: Among noncritically ill adults treated with intravenous fluids in the emergency department, there was no difference in hospital-free days between treatment with balanced crystalloids and treatment with saline.

Although well-conducted, both of these studies were criticized for issues including small median volumes of infusion, heterogeneity of the populations studied, and a response in a composite outcome that was marginal. Nonetheless, it is unlikely that further well designed trials will be conducted in the near future to help the clinician choose isotonic saline or balanced crystalloids for fluid resuscitation.

RECOMMENDATION: The clinician should have a low threshold to re-evaluate the type of fluid administered depending on the patient's response and development of adverse effects. The rationale for this recommendation is based upon the lack of an ideal standard resuscitation solution, data from randomized trials that have not shown a consistent benefit in hospital mortality or preservation of kidney function with balanced crystalloids as compared with saline (particularly for patients in whom smaller volumes are administered [eg, <2L]), and cumulative evidence from subgroup analyses that suggest potential benefit from balanced crystalloids in those in whom large volumes of fluids are administered (eg, > 2 liters).

Fecal Microbiota transplantation for treatment of recurrent C. difficile infection

The gastrointestinal tract harbors a highly complex community of micro-organisms that exist in symbiosis with the host. The human gut microbiota is estimated to consist of at least $10^{14}$ bacteria and as many as 1000 to 1200 bacterial species, most of which reside in the colon.

Administration of antibiotics can significantly alter the composition of the microbiota, which can lead to selective removal of bacteria that serve as a barrier to pathogen colonization. Antibiotic-mediated changes in the composition of the gut microbiota may also lead to homeostatic imbalance through alterations in the gut barrier functions and result in mucosal immune defects, which would predispose the host to enteric infections such as C. difficile by allowing environmentally acquired spores to germinate and successfully colonize the gut.

Recurrence of C. difficile infection (CDI) is an increasing problem following antimicrobial therapy world over and in India also. Patients with recurrent CDI have been observed to have reduced diversity of the intestinal microbiome and diminished numbers of bacteria relative to healthy individuals. Transplantation of stool microbiota from healthy individuals to patients with recurrent C. difficile can restore these missing strains and break the cycle of CDI recurrence.(1)

Fecal microbiota transplantation (FMT) instillation of processed stool collected from a healthy donor into the intestinal tract of a patient with recurrent CDI is effective for treatment of recurrent CDI. FMT protocols vary between institutions, and comparative efficacy studies are few and underpowered.
Candidates for FMT - FMT is the preferred management approach for patients with third or subsequent nonsevere CDI recurrence despite appropriate antibiotic therapy. (Grade 1B)

Choice of delivery route

Delivery routes and efficacy - The optimal approach to FMT administration is uncertain. FMT may be administered via oral capsules, lower gastrointestinal (GI) tract procedure (colonoscopy, retention enema), or upper GI tract procedure (nasojejunal [NJ]/nasoduodenal [ND] tube)

Patients with nonsevere CDI treated with FMT typically have resolution of abdominal discomfort and diarrhea in 36 to 48 hours.

1 Duodenal infusion of donor feces for recurrent Clostridium difficile.


BACKGROUND: Recurrent Clostridium difficile infection is difficult to treat, and failure rates for antibiotic therapy are high. We studied the effect of duodenal infusion of donor feces in patients with recurrent C. difficile infection.

METHODS: We randomly assigned patients to receive one of three therapies: an initial vancomycin regimen (500 mg orally four times per day for 4 days), followed by bowel lavage and subsequent infusion of a solution of donor feces through a nasoduodenal tube; a standard vancomycin regimen (500 mg orally four times per day for 14 days); or a standard vancomycin regimen with bowel lavage. The primary end point was the resolution of diarrhea associated with C. difficile infection without relapse after 10 weeks.

RESULTS: The study was stopped after an interim analysis. Of 16 patients in the infusion group, 13 (81%) had resolution of C. difficile-associated diarrhea after the first infusion. The 3 remaining patients received a second infusion with feces from a different donor, with resolution in 2 patients. Resolution of C. difficile infection occurred in 4 of 13 patients (31%) receiving vancomycin alone and in 3 of 13 patients (23%) receiving vancomycin with bowel lavage (P<0.001 for both comparisons with the infusion group). No significant differences in adverse events among the three study groups were observed except for mild diarrhea and abdominal cramping in the infusion group on the infusion day. After donor-feces infusion, patients showed increased fecal bacterial diversity, similar to that in healthy donors, with an increase in Bacteroidetes species and clostridium clusters IV and XIVa and a decrease in Proteobacteria species.
CONCLUSIONS: The infusion of donor feces was significantly more effective for the treatment of recurrent C. difficile infection than the use of vancomycin.

2. Frozen vs Fresh Fecal Microbiota Transplantation and Clinical Resolution of Diarrhea in Patients With Recurrent Clostridium difficile Infection: A Randomized Clinical Trial.


IMPORTANCE: Clostridium difficile infection (CDI) is a major burden in health care and community settings. CDI recurrence is of particular concern because of limited treatment options and associated clinical and infection control issues. Fecal microbiota transplantation (FMT) is a promising, but not readily available, intervention.

OBJECTIVE: To determine whether frozen-and-thawed (frozen, experimental) FMT is noninferior to fresh (standard) FMT in terms of clinical efficacy among patients with recurrent or refractory CDI and to assess the safety of both types of FMT.

DESIGN, SETTING, AND PARTICIPANTS: Randomized, double-blind, noninferiority trial enrolling 232 adults with recurrent or refractory CDI, conducted between July 2012 and September 2014 at 6 academic medical centers in Canada.

INTERVENTIONS: Patients were randomly allocated to receive frozen (n=114) or fresh (n=118) FMT via enema.

MAIN OUTCOMES AND MEASURES: The primary outcome measures were clinical resolution of diarrhea without relapse at 13 weeks and adverse events. Noninferiority margin was set at 15%.

RESULTS: A total of 219 patients (n=108 in the frozen FMT group and n=111 in the fresh FMT group) were included in the modified intention-to-treat (mITT) population and 178 (frozen FMT: n=91, fresh FMT: n=87) in the per-protocol population. In the per-protocol population, the proportion of patients with clinical resolution was 83.5% for the frozen FMT group and 85.1% for the fresh FMT group (difference, -1.6% [95% CI, -10.5% to]; P=.01 for noninferiority). In the mITT population the clinical resolution was 75.0% for the frozen FMT group and 70.3% for the fresh FMT group (difference, 4.7% [95% CI, -5.2% to]; P<.001 for noninferiority). There were no differences in the proportion of adverse or serious adverse events between the treatment groups.
Intraosseous (IO) infusion, a technique for vascular access, was described first in 1922 and was widely used for drug administration in children in the 1940s. It fell out of favor during the 1950s and 1960s, when disposable intravenous catheters were developed and techniques for insertion improved. In the 1980s, after the publication of numerous clinical reports of its effective use in children and animal models, the practice of IO infusion increased. Use in adults has also grown, especially in the prehospital setting. Today, the procedure is reserved for acute, life-threatening or medically necessary situations when standard venous access methods cannot be rapidly achieved and as the first attempt at vascular access in cardiopulmonary arrest or severe shock in selected patients.

Intraosseous (IO) cannulation provides intravascular access via the medullary sinuses in the bone marrow of long bones. These veins, supported by the bony matrix, do not collapse in patients with shock or hypovolemia.

CONCLUSIONS AND RELEVANCE: Among adults with recurrent or refractory CDI, the use of frozen compared with fresh FMT did not result in worse proportion of clinical resolution of diarrhea. Given the potential advantages of providing frozen FMT, its use is a reasonable option in this setting.

3. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA).

McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, Dubberke ER, Garey KW, Gould CV, Kelly C, Loo V, Shaklee Sammons J, Sandora TJ, Wilcox MH
Clin Infect Dis. 2018;66(7):e1
The following list provides the site and draining vessels for the most commonly used sites:

- Proximal tibia – Popliteal vein
- Femur – Branches of the femoral vein
- Distal tibia (medial malleolus) – Great saphenous vein
- Proximal humerus – Axillary vein
- Manubrium (upper sternum) – Internal mammary and azygos veins

**TRAINING:** Intraosseous (IO) cannulation is likely to be used by the emergency care provider during resuscitation. The patient’s life may well depend upon the clinician’s ability to secure vascular access. Thus, emergency physicians and others who may need to perform IO cannulation emergently should learn to do so well in advance of the immediate need.

**FLUID AND DRUG ADMINISTRATION:** Any intravenous drug or routine resuscitation fluid can be administered safely by the IO route. Examples include epinephrine, dopamine, dobutamine, adenosine, digitalis, heparin, lidocaine, atropine, sodium bicarbonate, phenytoin, neuromuscular blocking agents, antibiotics, crystalloids, colloids, and blood products. Drug and fluid dosing is the same as for intravenous administration. However, for adenosine, the IO route may not be as effective as upper extremity peripheral intravenous access for the treatment of supraventricular tachycardia.

**RAPID FLUID ADMINISTRATION AND VISCOUS DRUGS:** Crystalloid fluids (eg, normal saline) for rapid volume expansion and viscous drugs and solutions should be administered under pressure using an infusion pump, pressure bag, or manual injection through a syringe and stopcock. These approaches overcome the resistance of emissary veins that lead from the intramedullary cavity to the general circulation. The IO site and extremity should be monitored frequently for infiltration during rapid fluid administration.

Infusion rates equivalent to a 21 gauge peripheral intravenous catheter are typically achieved.

- For adults in cardiopulmonary arrest or with severe shock in whom peripheral venous access cannot be obtained, placement of an IO cannula for medication administration, fluid therapy, and diagnostic studies pending percutaneous central venous line placement or surgical venous cutdown is advised (Grade 2B). IO needle be flushed before and after medication administration if fluids are not already infusing.
- IO cannulation may also be appropriate in patients with emergency conditions where reliable venous access cannot be achieved quickly (eg, shock, sepsis, status epilepticus, extensive burns, multiple trauma) or in patients for whom intravascular access is medically necessary and cannot be achieved by other means.
- IO cannulation should not be performed in fractured bones, bones with a prior failed IO placement attempt, or in extremities with vascular disruption. IO access also should be avoided in patients with osteogenesis imperfecta, osteopetrosis, right to left congenital cardiac shunts, or those with burns or infection near the access site.
• All patients who undergo IO placement for life-threatening illnesses (eg, cardiac arrest) have the first attempt made at the proximal tibial site, unless otherwise contraindicated (Grade 1B). A battery powered or impact driven device is typically required to accomplish IO placement in the proximal tibia of patients over six years of age. If such a device is not available, the clinician should attempt manual placement at the medial or lateral malleolus in older patients.

• In critically ill adults who require immediate vascular access (eg, patients in arrest or severe shock), IO placement is performed without analgesia. These patients may receive systemic analgesia (eg, fentanyl intraosseously) or infusion of preservative-free lidocaine, if they become responsive to pain once the IO is placed and as tolerated by their clinical condition.

• In awake patients for whom IO placement is in response to difficulty with peripheral venous access and whose condition is not emergent, analgesia for IO placement be provided by local infiltration of anesthetic at the IO site and administration of preservative-free lidocaine through the IO cannula prior to infusion of medications, fluids, or blood products (Grade 2C).

• Analgesia for the pain associated with the IO infusion itself may be obtained by slowly administering 0.5 mg/kg preservative-free lidocaine 2 percent (20 mg/mL, maximum dose: 40 mg) over one minute through the IO catheter prior to flushing and drug administration. Systemic analgesia (eg, fentanyl intraosseously, as tolerated) is an alternative method of analgesia for IO infusion and can be provided to patients with persistent pain during infusion despite administration of intravenous lidocaine. Local infiltration of anesthetic at the IO insertion site may not be necessary in adolescents and adults when using a battery-powered driver.


Intravenous thrombolysis in patients with an unknown stroke onset time

BACKGROUND: Under current guidelines, intravenous thrombolysis is used to treat acute stroke only if it can be ascertained that the time since the onset of symptoms was less than 4.5 hours. However, many patients do not qualify because more than 4.5 hours have passed since they were last known to be without stroke symptoms. A trial was done to determine whether patients with stroke with an unknown time of onset and features suggesting recent cerebral infarction on magnetic resonance imaging (MRI) would benefit from thrombolysis with the use of intravenous alteplase.

The placebo-controlled Wake-Up Stroke trial selected 500 adults with unwitnessed stroke onset (most awoke from sleep with stroke symptoms) who had an ischemic parenchymal brain lesion on magnetic resonance imaging (MRI) diffusion-weighted imaging but no corresponding hyperintensity on fluid-attenuated inversion recovery (FLAIR) [1]. This imaging constellation correlates with a stroke onset time of 4.5 hours or less. At 90 days, a favorable outcome was more likely for patients assigned to intravenous alteplase compared with those assigned to placebo (53 versus 42 percent). However, the mortality rate and the rate of symptomatic intracranial hemorrhage were both nonsignificantly higher in the alteplase group. Although this approach seems promising, additional trials are needed to determine the efficacy and safety of intravenous alteplase for patients with unknown stroke onset time and a mismatch pattern on imaging.

METHODS: In a multicenter trial, we randomly assigned patients who had an unknown time of onset of stroke to receive either intravenous alteplase or placebo. All the patients had an ischemic lesion that was visible on MRI diffusion-weighted imaging but no parenchymal hyperintensity on fluid-attenuated inversion recovery (FLAIR), which indicated that the stroke had occurred approximately within the previous 4.5 hours. We excluded patients for whom thrombectomy was planned. The primary end point was favorable outcome, as defined by a score of 0 or 1 on the modified Rankin scale of neurologic disability (which ranges from 0 [no symptoms] to 6 [death]) at 90 days. A secondary outcome was the likelihood that alteplase would lead to lower ordinal scores on the modified Rankin scale than would placebo (shift analysis).

RESULTS: The trial was stopped early owing to cessation of funding after the enrollment of 503 of an anticipated 800 patients. Of these patients, 254 were randomly assigned to receive alteplase and 249 to...
receive placebo. A favorable outcome at 90 days was reported in 131 of 246 patients (53.3%) in the alteplase group and in 102 of 244 patients (41.8%) in the placebo group (adjusted odds ratio, 1.61; 95% confidence interval [CI], 1.09 to 2.36; \( P=0.02 \)). The median score on the modified Rankin scale at 90 days was 1 in the alteplase group and 2 in the placebo group (adjusted common odds ratio, 1.62; 95% CI, 1.17 to 2.23; \( P=0.003 \)). There were 10 deaths (4.1%) in the alteplase group and 3 (1.2%) in the placebo group (odds ratio, 3.38; 95% CI, 0.92 to 12.52; \( P=0.07 \)). The rate of symptomatic intracranial hemorrhage was 2.0% in the alteplase group and 0.4% in the placebo group (odds ratio, 4.95; 95% CI, 0.57 to 42.87; \( P=0.15 \)).

CONCLUSIONS: In patients with acute stroke with an unknown time of onset, intravenous alteplase guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia resulted in a significantly better functional outcome and numerically more intracranial hemorrhages than placebo at 90 days.

RECOMMENDATION: In hospitals with appropriate facility, benefit of intravenous alteplase can be extended to patients after ischemic stroke who would otherwise be ineligible for this therapy.

MALDI-TOF mass spectrometry an emerging technology for microbial identification and diagnosis

Until recently, microbial identification in clinical diagnostic laboratories has mainly relied on conventional phenotypic and gene sequencing identification techniques. The development of matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) devices has revolutionized the routine identification of microorganisms in clinical microbiology laboratories by introducing an easy, rapid, high throughput, low-cost, and efficient identification technique. This technology has been adapted to the constraint of clinical diagnostic laboratories and has the potential to replace and/or complement conventional identification techniques for both bacterial and fungal strains. Using standardized procedures, the resolution of MALDI-TOF MS allows accurate identification at the species level of most Gram-positive and Gram-negative bacterial strains with the exception of a few difficult strains that require more attention and further development of the method. Similarly, the routine identification by MALDI-TOF MS of yeast isolates is reliable and much quicker than conventional techniques. Recent studies have shown that MALDI-TOF MS has also the potential to accurately identify filamentous fungi and dermatophytes, providing that specific standardized procedures are established for these microorganisms. Moreover, MALDI-TOF MS has been used successfully for microbial typing and identification at the subspecies level, demonstrating that this technology is a potential efficient tool for epidemiological studies and for taxonomical classification.

Overall, a MALDI-TOF MS will be soon present in most diagnostic laboratories as, despite the significant cost of the instrument and for maintenance, running costs and consumables are much lower than those for other conventional methods, rendering this technology a worthy quantum leap tool.
Osmotic therapy in traumatic brain injury

Osmotic therapy - Osmotic therapy (mannitol or hypertonic saline) is generally utilized in TBI patients who are clinically symptomatic from cerebral edema or have documented ICP elevation that does not respond to initial measures such as CSF drainage, analgesia, and sedation.

Dose: Infusion of 3 percent NaCl to achieve a sodium goal of 145 to 155 mEq/L in patients with elevated ICP. Mannitol is an acceptable alternative. Mannitol has also been shown to reduce ICP and improve CBF. Mannitol is administered in boluses of 0.25 to 1 g/kg every four to six hours as needed.

Intravascular injection of hyperosmolar agents (mannitol, hypertonic saline) creates an osmolar gradient, drawing water across the blood-brain barrier. This leads to a decrease in brain volume and a decrease in ICP. The effect of hyperosmolar therapy diminishes with time, as a compensatory increase in brain osmoles occurs within 24 hours. Thus, hyperosmolar agents should be weaned slowly after initiation to prevent a reversal in the osmotic gradient and consequent rebound cerebral edema.

Monitoring of serum osmolality (maintained <320 mmol/L to minimize complications), fluid balance, renal function, and electrolytes is required. There are several concerns with the scheduled administration of mannitol. As an osmotic diuretic, mannitol may cause dehydration and acute kidney injury.

The more serious theoretical concern with mannitol use is leakage into brain tissue in patients with disruption of the blood-brain barrier, with consequent reversal of the osmolar gradient and rebound cerebral edema. Judicious administration of mannitol, on an as-needed basis for elevations in ICP, is advisable to minimize this risk.

Hypertonic saline is an effective hyperosmolar agent for the control of elevated ICP. This agent has been used as 3 percent, most commonly used as a continuous infusion. When used as a continuous infusion, 3 percent NaCl may be titrated to a sodium goal of approximately 145 to 155 mEq/L. Hypertonic saline should be administered via a central venous catheter because of the risk of extravasation injury when used with peripheral intravenous (IV) access. Short-term use via peripheral IV access is permissible in the setting of acute ICP elevation, however, while central access is obtained.

Hypertonic saline has several theoretical advantages over mannitol. In particular, volume depletion and hypovolemia do not occur, which makes this agent safer in the trauma patient with ongoing blood loss, hypovolemia, or hypotension. Hypertonic saline has a reflection coefficient of 1.0 (compared with 0.9 for mannitol), and is therefore less likely to leak into brain tissue. Potential adverse effects include circulatory overload and pulmonary edema, and an increased chloride burden, which may result in a non-anion gap metabolic acidosis.

REVIEW OF LITERATURE: In the aggregate, multiple observational studies [1,2], small randomized clinical trials [3,4,5,6], meta-analyses [7], and systematic reviews [8] have not found compelling evidence
to suggest superiority of either agent to improve outcomes such as mortality or functional recovery. The majority of studies do suggest improved ICP control with hypertonic saline, along with possible improvements in cerebral perfusion and brain tissue oxygenation.

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4. Isovolume hypertonic solutes (sodium chloride or mannitol) in the treatment of refractory posttraumatic intracranial hypertension: 2 mL/kg 7.5% saline is more effective than 2 mL/kg 20% mannitol
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Restrictive versus liberal perioperative fluid therapy for open abdominal surgery

Maintenance of tissue perfusion by maintaining euvolemia is the goal for intraoperative monitoring of intravascular fluid volume and administration of intraoperative fluid therapy. Both hypovolemia and hypervolemia are associated with postoperative morbidity.
Absolute or relative hypovolemia is common in the perioperative period due to preoperative dehydration, vasodilation caused by anesthetic and adjuvant drugs, and surgical bleeding. The most common cause of perioperative tissue edema is retention of fluid administered during surgery.

While physiological parameters such as blood pressure (BP), heart rate (HR), central venous pressure (CVP), and urine output (UO) are monitored during surgery, significant intraoperative reduction in tissue perfusion may not be recognized even with continuous monitoring of these static parameters.

Restrictive (zero-balance) strategy -
With a restrictive zero-balance approach, only the fluid that is lost during surgery is replaced, including the following strategies [10]:

- During the intraoperative period, patients receive a balanced electrolyte crystalloid solution administered at a rate of 1 to 3 mL/kg per hour to replace sensible and insensible losses [9].

- For blood loss, additional fluid may be administered. Studies suggest that the optimal crystalloid-to-blood volume ratio is approximately 1.5:1.0, and that the optimal colloid-to-blood ratio is 1:1, until a threshold for red blood cell (RBC) transfusion is reached [101-104].

- Patients do not receive "preloading" of crystalloids prior to a neuraxial block or induction of general anesthesia.

Whether a restrictive fluid therapy regimen (ie, zero balance), which is associated with lower rates of pulmonary complications following major abdominal surgery, is safe and effective in high-risk patients is unknown.

The REstrictive versus LibEral Fluid therapy (RELIEF) trial randomly assigned nearly 3000 high-risk patients (>70 years of age, heart disease, diabetes, renal dysfunction, morbid obesity) to a restrictive or liberal fluid therapy regimen during and after abdominal surgery [1].

**Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery.**

BACKGROUND: Guidelines to promote the early recovery of patients undergoing major surgery recommend a restrictive intravenous-fluid strategy for abdominal surgery. However, the supporting evidence is limited, and there is concern about impaired organ perfusion.

METHODS: In a pragmatic, international trial, we randomly assigned 3000 patients who had an increased risk of complications while undergoing major abdominal surgery to receive a restrictive or liberal intravenous-fluid regimen during and up to 24 hours after surgery. The primary outcome was disability-free survival at 1 year. Key secondary outcomes were acute kidney injury at 30 days, renal-replacement therapy at 90 days, and a composite of septic complications, surgical-site infection, or death.

RESULTS: During and up to 24 hours after surgery, 1490 patients in the restrictive fluid group had a median intravenous-fluid intake of 3.7 liters (interquartile range, 2.9 to 4.9), as compared with 6.1 liters (interquartile range, 5.0 to 7.4) in 1493 patients in the liberal fluid group (P<0.001). The rate of disability-free survival at 1 year was 81.9% in the restrictive fluid group and 82.3% in the liberal fluid group (hazard ratio for death or disability, 1.05; 95% confidence interval, 0.88 to 1.24; P=0.61). The rate of acute kidney injury was 8.6% in the restrictive fluid group and 5.0% in the liberal fluid group (P<0.001). The rate of septic complications or death was 21.8% in the restrictive fluid group and 19.8% in the liberal fluid group (P=0.19); rates of surgical-site infection (16.5% vs. 13.6%, P=0.02) and renal-replacement therapy (0.9% vs. 0.3%, P=0.048) were higher in the restrictive fluid group, but the between-group difference was not significant after adjustment for multiple testing.

CONCLUSIONS: Among patients at increased risk for complications during major abdominal surgery, a restrictive fluid regimen was not associated with a higher rate of disability-free survival than a liberal fluid regimen and was associated with a higher rate of acute kidney injury.

One of the major limitations of this study is its pragmatic design, wherein the perioperative care is not standardized and there is a wide variation in the anesthetic and analgesic techniques, including use of use of epidural analgesia, variable intraoperative hemodynamic management, and variable postoperative care. The total fluid volume administered during and up to 24 hours after surgery was 3.7 versus 6.1 L in the restrictive and liberal groups, respectively. These volumes were lower than traditional liberal fluid strategy totals, and balanced electrolyte solutions were used in both groups.

INTERPRETATION: Rates of disability-free survival at one year, pulmonary edema, and duration of mechanical ventilation were similar for both approaches, but restrictive fluid therapy resulted in higher rates of acute kidney injury, need for renal replacement therapy, and surgical site infection. These findings suggest that that administration of a total volume of balanced electrolyte solutions that modestly exceeds zero fluid balance is not harmful. However, excessive perioperative administration of intravenous fluid, which was common in traditional liberal or fixed-volume approaches to fluid therapy, should be avoided.
**Methylprednisolone infusion in early severe ARDS:**

**OBJECTIVE:** Current status of steroids in severe ARDS

Despite the recent advances in the care of critically ill patients, ARDS is still a clinical condition associated with high mortality rates.

Corticosteroids have been used for the treatment of ARDS for the last 20 years. However, their benefits are still unproven. Discrepancy of results from clinical trials may be explained by different doses and duration of administration as well as patient selection and excess of morbidity imposed by steroid related side effects. However, the recent study by Meduri and co-workers sheds some new light on ARDS pharmacotherapy by demonstrating clinical improvement based on possible immune-modulatory effects of steroid infusion, thus hastening the resolution of lung injury and organ failure. Common aspects among all studies showing benefits of steroids were the use of relatively lower doses, easy infusion and selection of an extremely severely ill population. Moreover, these “successful” prospective studies had also similar limitations, the foremost one being a relatively small sample size with limited power for the detection of important outcomes (e.g. hospital mortality). Therefore, these results must be viewed with caution, because the morbidity burden associated with corticosteroids cannot be underestimated and a recent large multi-centric trial failed to show any significant improvement in the outcome of patients with ARDS and severe sepsis.

In Dr. Meduri’s recently published study on value of methylprednisolone infusion in early severe ARDS, the patients were randomized in a 2:1 fashion in favour of methylprednisolone. The incidence of catecholamine dependent shock in the placebo group was nearly twice that of methylprednisolone group. (46.4% Vs 23.8%; p=0.03) Ten of the 15 control patients (67%) who remained on MV on day 9 received methylprednisolone because their lung injury scores had not improved. The proportion of patients requiring MV at 28 days was not statistically different between the two groups. The likelihood of surviving till hospital admission was also not different between the two groups.

**CONCLUSIONS:** The use of glucocorticoids cannot be widely recommended as a “standard of care” for patients with ARDS.

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What’s new in the extra-corporeal treatment of sepsis?

OBJECTIVE: Current status of extra-corporeal treatment of sepsis

The high incidence and morbidity, mortality and associated costs of septic shock illustrate that the medical need for an adjuvant treatment is still unmet. Endotoxin, one of the most potent mediators of sepsis, is found in high levels in approximately half of patients with septic shock. Polymyxin B (PMX) hemoperfusion has been shown in numerous studies to successfully remove endotoxin and potentially improve outcomes. Although numerous case series and small studies suggest that these beneficial effects may also be present in sepsis patients.

In the recently finalized Euphrates Trial (evaluating the use of polymyxin B hemoperfusion in a randomized controlled trial of adults treated for endotoxaemia and septic shock), PMX perfusion was applied in blinded manner in patients with septic shock and confirmed endotoxaemia as measured by endotoxin activity array (EAA). The trial conducted in USA and Canada was powered to enroll 360 patients to detect an effect on 28 day all cause mortality. Similar to the previous trials, treatment consisted of 2 sessions of PMX hemoperfusion 24 hours apart. Unique features of this trial included patient enrichment by use of EAA to confirm endotoxaemia (EAA > 0.6) and use of detailed “façade” hemoperfusion event as a blinding mechanism. Following the second interim analysis, the study was resized to 650 patients. However, after 446 evaluable patients were included, the trial was terminated. The study has not yet been published, but Spectrum, the company of EAA has stated that it failed to meet its primary end point. There was a non-significant 5% mortality reduction in the per protocol population and it is mentioned that “other positive benefits” were observed in treated septic shock patients compared to standard treatment.

New developments are emerging. Coupled plasma filtration adsorption is another extra-corporeal blood purification therapy for sepsis, which adsorbs both pro-inflammatory and anti-inflammatory mediators from filtered plasma. Effects on clinical outcome are awaited. The ‘CytoSorb’ filter with polymer beads that have pores that can adsorb hydrophobic molecules in a size range of approximately 10-55 KD (sufficient to remove almost all cytokines including HMGB 1, but not endotoxin) has a huge absorption area of 40,000 sq.m. and several case series have been published. The ‘Oxiris-filter’ is designed to adsorb endotoxin as well as cytokines, but no adequately powered human study is cuttenrly available.

While removal of endotoxin/ cytokines is theoretically seen as a beneficial effect, other potentially detrimental effects may also occur. As both pro-and anti-inflammatory cytokines may decrease, the net effect is uncertain. In addition, other nutrients and therapeutic drugs (including antibiotics) may also be removed from the circulation, with potential negative impact on organ function and recovery.

CONCLUSIONS: Blood purification in sepsis is a valid approach, the potential efficacy of LPS/cytokine elimination using these membranes currently cannot be estimated without positive clinical data from RCTs.
Prevention of stress ulceration - current trends in critical care

Gastric anti-secretory therapies for the prevention of stress related mucosal bleeding (SRMB) are frequently administered in intensive care unit settings. The pathogenesis of stress ulcers in critical illness is linked to many factors, such as hypovolaemia, depressed cardiac output, increased vasoconstriction and importantly splenchnic hypoperfusion, which contributes to acid-back diffusion and reduction in bicarbonate secretion, mucosal blood flow and gastro-intestinal motility. Although, mechanical ventilation is regarded as the most frequent risk factor, several other disease states related to critical illness that contribute to gut ischemia and acute organ failure have also been implicated.

OBJECTIVE: to identify the level of current intensivist’s knowledge regarding risk assessment and intensive care unit (ICU) clinical practice pertaining to SRMB including pharmacologic approaches for stress ulcer prevention.

DESIGN: A nation-wide survey of critical care physicians.

Study population: 2000 random physician members of the Society of Critical Care Medicine

Measurement and main results: The response rate was 519 (26%) of 2000 with data analysis from 501 (25.1%) usable surveys. Respondents were affiliated with internal medicine (44.3%), Surgery (42.3%) and anaesthesiology (12.6%). Gut ischemia was indicated as the perceived major cause of stress ulceration (59.7%). The estimated incidence of clinically important bleeding was 2% or less by 62% respondents; however, 28.6% of the physicians surveyed initiate stress ulcer prophylaxis in all ICU patients, regardless of bleeding risk. Respiratory failure was most frequently indicated as a reason for stress ulcer prophylaxis (68.6%), followed by shock/hypotension (49.4%), sepsis (39.4%) and head injury/major neurologic insult (35.2%). The first line agents selected for stress ulcer prophylaxis include histamine 2 receptor antagonists (63.9%), followed by Proton pump inhibitors (23.1%) and sucralfate (12.2%). Concern for nosochomial pneumonia was regarded as more prevalent with anti-secretory therapies in those who chose sucralfate (61%) as initial therapy compared with overall respondents (26.9%) (p<0.001)
CONCLUSIONS: The majority of intensivists surveyed recognized stress related mucosal bleeding as a relatively infrequent event; however, implementation of a stress ulcer prophylaxis risk stratification scheme for ICU patients is necessary. Histamine 2 receptor antagonists are consistently perceived as appropriate initial agents, although proton pump inhibitors have become first line therapy in an increasing percentage of critical care patients, despite limited data regarding their use in this population.

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Advance Hemodynamic Monitoring

A Hemodynamic monitoring is useful to know the cardiovascular performance and essential guideline in diagnostic and therapeutic guidance in critically ill patient under going for tissue hypo perfusion.

Till now hemodynamic monitoring was limited by CVP line or Pulmonary Artery Catheter (PAC) to know the status of Pre Load, Mixed Venous Oxygen Saturation and serum lactate level.

But now a days it’s very essential to identify differential diagnosis of shock, to know the response of fluid therapy and to decide for the use of vasopressor or ionotropic support in ICU.

An advanced hemodynamics monitoring include continuous cardiac output monitoring (CCO), stroke volume variation, pulse pressure variation, SVR, SVRI, PVR, PVRI and cardiac index.

Clinical evaluation for hemodynamic variables-

anaesthesiology (12.6%). Gut ischemia was indicated as the perceived major cause of stress ulceration (59.7%). The estimated incidence of clinically important bleeding was 2% or less by 62% respondents; however, 28.6% of the physicians surveyed initiate stress ulcer prophylaxis in all ICU patients, regardless of bleeding risk. Respiratory failure was most frequently indicated as a reason for stress ulcer prophylaxis (68.6%), followed by shock/hypotension (49.4%), sepsis (39.4%) and head injury/major neurologic insult (35.2%). Th
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<th>Type of hemodynamic variable</th>
<th>Parameter</th>
<th>Comments</th>
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<tr>
<td>Solitary</td>
<td>Blood pressure</td>
<td>Hypotension is always pathological</td>
</tr>
<tr>
<td></td>
<td>Central venous pressure (CVP)</td>
<td>CVP is only elevated in disease</td>
</tr>
<tr>
<td></td>
<td>Pulmonary artery occlusion pressure (Ppao)</td>
<td>Ppao is the back-pressure to pulmonary blood flow</td>
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<tr>
<td></td>
<td>Cardiac output</td>
<td>There is no normal cardiac output, only an adequate or inadequate one</td>
</tr>
<tr>
<td></td>
<td>Mixed venous oxygen saturation (SvO2)</td>
<td>Decreasing SvO2 is a sensitive but nonspecific marker of cardiovascular stress</td>
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<th>Type of hemodynamic variable</th>
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<tbody>
<tr>
<td>Dynamic</td>
<td>Volume challenge</td>
<td>Positive response defined as an increase in any of blood pressure, CVP, Ppao, cardiac output and/or SvO2, or a decrease in heart rate</td>
</tr>
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<td>Echocardiographic analysis of vena cavae collapse during positive pressure inspiration identifies CVP &lt;10 mmHg if it detects</td>
<td>Complete inferior vena caval collapse</td>
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<td>&gt;36% collapse in superior vena caava</td>
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<td></td>
<td>Defining preload responsiveness</td>
<td>&gt;13% pulse pressure variation during positive pressure ventilation</td>
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<td>&gt;1 mmHg decrease in CVP during spontaneous inspiration</td>
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BACKGROUND:
Advanced hemodynamic monitoring is recommended in patients with complex circulatory shock.

OBJECTIVES:
To evaluate the current attitudes and beliefs among German intensivists, regarding advanced hemodynamic monitoring, the actual hemodynamic management in clinical practice, and the barriers to using it.

MATERIALS AND METHODS:
Web-based survey among members of the German Society of Medical Intensive Care and Emergency Medicine.

RESULTS:
Of 284 respondents, 249 (87%) agreed that further hemodynamic assessment is needed to determine the type of circulatory shock if no clear clinical diagnosis can be made. In all, 281 (99%) agreed that echocardiography is helpful for this purpose (transpulmonary thermodilution: 225 [79%]; pulmonary artery catheterization: 126 [45%]). More than 70% of respondents agreed that blood flow variables (cardiac output, stroke volume) should be measured in patients with hemodynamic instability. The parameters most respondents agreed should be assessed in a patient with hemodynamic instability were mean arterial pressure, cardiac output, and serum lactate. Echocardiography is available in 99% of ICUs (transpulmonary thermodilution: 91%; pulmonary artery catheter: 63%). The respondents stated that, in clinical practice, invasive arterial pressure measurements and serum lactate measurements are performed in more than 90% of patients with hemodynamic instability (cardiac output monitoring in about 50%; transpulmonary thermodilution in about 40%). The respondents did not feel strong barriers to the use of advanced hemodynamic monitoring in clinical practice.

CONCLUSIONS:
This survey study shows that German intensivists deem advanced hemodynamic assessment necessary for the differential diagnosis of circulatory shock and to guide therapy with fluids, vasopressors, and inotropes in ICU patients.
Hemodynamic monitoring in the critically ill: an overview of current cardiac output monitoring methods

Johan Huygh, Yannick Peeters, Jelle Bernards, and Manu L. N. G. Malbrain

Abstract
Critically ill patients are often hemodynamically unstable (or at risk of becoming unstable) owing to hypovolemia, cardiac dysfunction, or alterations of vasomotor function, leading to organ dysfunction, deterioration into multi-organ failure, and eventually death. With hemodynamic monitoring, we aim to guide our medical management so as to prevent or treat organ failure and improve the outcomes of our patients. Therapeutic measures may include fluid resuscitation, vasopressors, or inotropic agents. Both resuscitation and de-resuscitation phases can be guided using hemodynamic monitoring. This monitoring itself includes several different techniques, each with its own advantages and disadvantages, and may range from invasive to less- and even non-invasive techniques, calibrated or non-calibrated. This article will discuss the indications and basics of monitoring, further elaborating on the different techniques of monitoring.

CONCLUSIONS:
Critically ill patients are often hemodynamically unstable (or at risk of becoming unstable), and advanced hemodynamic monitoring is recommended in complex situations or in patients with shock who do not respond to initial fluid resuscitation. Pulse contour analysis, in particular, with the added functional variables SVV and PPV, can be of significant value in the assumption that the patient is in regular sinus rhythm and fully sedated under controlled mechanical ventilation.

Methylprednisolone in acute spinal cord injuries:
Methylprednisolone is the only treatment that has been suggested in clinical trials to improve neurologic outcomes in patients with acute, nonpenetrating TSCI. However, the evidence is limited, and its use is debated.

Efficacy — The evidence regarding the efficacy of glucocorticoids in acute TSCI is limited and, to many, unconvincing.

Two blinded, randomized controlled trials have studied the efficacy of glucocorticoid therapy in patients with acute TSCI:

• The National Acute Spinal Cord Injury Study (NASCIS) II compared methylprednisolone (30 mg/kg IV, followed by 5.4 mg/kg per hour over 23 more hours), naloxone, and placebo in 427 acute TSCI patients [1]. At one year, there was no significant difference in neurologic function among treatment groups.
The National Acute Spinal Cord Injury Study (NASCIS) II compared methylprednisolone (30 mg/kg IV, followed by 5.4 mg/kg per hour over 23 more hours), naloxone, and placebo in 427 acute TSCI patients [1]. At one year, there was no significant difference in neurologic function among treatment groups. However, within the subset of patients treated within eight hours, those who received methylprednisolone had a modest improvement in motor recovery compared with those who received placebo. Wound infections were somewhat more common in patients who received methylprednisolone.

NASCIS III compared three treatment groups: methylprednisolone administered for 48 hours, methylprednisolone administered for 24 hours, and tirilazad mesylate (a potent lipid peroxidation inhibitor) administered for 48 hours in patients with acute complete or incomplete TSCI [2]. All 499 patients received an initial IV bolus of 30 mg/kg methylprednisolone and were treated within eight hours of TSCI. For patients treated within three hours, there was no difference in outcomes among treatment groups at one year. For patients treated between three to eight hours, 48 hours of methylprednisolone was associated with a greater motor but not functional recovery compared with other treatments. Patients who received the longer duration infusion of methylprednisolone had more severe sepsis and severe pneumonia compared with the shorter duration of infusion; mortality was similar in all treatment groups [3].

In 2013, based upon the available evidence, the American Association of Neurological Surgeons and Congress of Neurological Surgeons stated that the use of glucocorticoids in acute spinal cord injury is not recommended [4]. Position statements from the Canadian Association of Emergency Physicians, endorsed by the American Academy of Emergency Medicine, concur that treatment with glucocorticoids is a treatment option and not a treatment standard [5-6]. A Consortium for Spinal Cord Medicine similarly concluded that "no clinical evidence exists to definitely recommend" the use of steroid therapy.

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2 Methylprednisolone or tirilazad mesylate administration after acute spinal cord injury: 1-year follow up. Results of the third National Acute Spinal Cord Injury randomized controlled trial.


**Bronchial blocker**

One lung ventilation is a need of surgical and medical condition for treatment related to lung disease and recently it's also helpful for minimal invasive coronary artery bypass surgery for lung isolation.

It’s an alternative to double lumen endobronchial tube (DLT) and this is used for both adult and pediatric patient even smallest size DLT is possible to insert.

There are various bronchial blockers are available like- Arndt bronchial blocker, Cohens bronchial blocker, Coopdech bronchial blocker, EZ bronchial blocker which is inserted with help of fiber optic bronchoscope on selected side.

The Univent endotracheal tube is also an alternative in which there is separate y channel to insert bronchial blocker.
Routine double tube

**INDICATION:**
- Pneumonectomy or Lobectomy
- Isolation of lung like- Broncho pleural Fistula, prevention of Contamination and spillage material to healthy side,
- MICS (CABG)
- Bronchiectasis
ADVANTAGES OVER DLT:

• Repeated intubation or changeover of endotracheal tube is avoided.
• Minimum chances of airway injury.
• Isolation of individual segment is possible.
• Technically simple
• Use in pediatric patient also.

COMPLICATION:

• Misplacement of Bronchial blocker which can give rise to respiratory arrest.
• Rupture of Balloon and malposition.
• An accidental injury to airway if forcefully handed for insertion.

Effective Use of Bronchial Blockers in Lung Isolation Surgery: An Analysis of 130 Cases

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BACKGROUND:

One-lung ventilation (OLV) is necessary for selected surgical settings and medical conditions. Different methods have been described and used to isolate 1 lung, including the double-lumen endotracheal tube (DLT) and a variety of bronchial blockers (Bbs). This selection is often based on the preferences and experiences of the anesthesiologist and surgeon. Complications associated with OLV isolation tubes have been previously described, but complications specifically associated with the Cohen BB (CBB) (Cook Medical, Bloomington, IN) have not been investigated. The purpose of this retrospective review was to determine the incidence of vocal cord injury, tracheobronchial injury, and hoarseness in adult patients who underwent OLV with the CBB.

METHODS:

We reviewed electronic anesthesia records, operative dictation, and inpatient progress notes to collect information about vocal cord injury, bronchial injury, hoarseness, and sore throat for adults who underwent surgical and diagnostic procedures requiring OLV. Secondary endpoints were types of surgical procedures, degree of difficulty with orotracheal intubation, ability of the patient to tolerate extubation in the operating room, and whether the thoracic surgeon deemed the lung separation adequate. P< 0.05 was considered significant.
RESULTS:
Of 130 patients, 113 underwent OLV with a CBB, and 17 patients underwent OLV with a DLT. The thoracic surgeon deemed the lung isolation adequate in all cases. Airway injury occurred in 2 patients with a CBB and none with a DLT ($P = 0.86$). Both airway injuries were attributed to surgical technique. Two cases of postoperative hoarseness occurred in the CBB group ($P = 0.86$). One injury was attributed to vagus nerve transection, and the other injury was diagnosed as vocal cord paralysis of unknown etiology. In 1 case, orotracheal intubation with a DLT was unsuccessful because of intubation difficulty and required conversion to a regular endotracheal tube and CBB for successful lung isolation. Conclusion: This study demonstrates that the use of CBB can be successful in a wide variety of thoracic operations, has minimal complications, eliminates the need for tracheal tube exchange when postoperative mechanical ventilation is required, and effectively isolates the lungs of critically ill patients.

Article- 2

The EZ-blocker for one-lung ventilation in patients undergoing thoracic surgery: clinical applications and experience in 100 cases in a routine clinical setting

Andreas Moritz1*, Andrea Iroushek2, Torsten Birkholz3, Johannes Pröttengeier4, Horia Sirbu5 and Joachim Schmidt6

BACKGROUND:
In certain clinical situations the insertion of a double-lumen tube (DLT) for one-lung ventilation (OLV) is not feasible or unfavorable. In these cases, the EZ-Blocker (EZB) may serve as an alternative. The aim of our analysis was to report on the clinical applications and our experience with the EZB for one-lung ventilation in 100 patients undergoing thoracic surgery.

METHODS:
All anesthetic records from patients older than 18 years of age undergoing general anesthesia in the department of thoracic surgery with intraoperative use of an EZB for OLV at the University Hospital of Erlangen in four consecutive years were analyzed retrospectively.

RESULTS:
Most frequently, EZB was used in difficult airway (27%) and for surgical procedures with high risk for left recurrent laryngeal nerve injury (21%), followed by application in intubated (12%) or tracheostomized (11%) patients. 11% of the patients had an increased risk of gastric regurgitation. Almost all EZBs were placed free of complications (99%). Clinically sufficient lung collapse was achieved in all patients. No serious airway injuries or immediate complications were documented.
**CONCLUSIONS:**
The EZB is an efficient, easy-to-use and safe airway device and enables OLV in several clinical situations, when conventional DLTs are not feasible or less favorable. Three major applications were depicted from the data: expected difficult airway, surgical procedures with necessity of intraoperative recurrent laryngeal nerve monitoring and already intubated or tracheostomized patients.

**Association of RBC transfusion with morbidity and mortality in patient undergoing cardiac surgery**

A coronary artery disease is a leading disease in society due to modification in life style, stress, smoking, hypertension and diabetes and sedentary life style.

This disease is treated with coronary artery bypass surgery or angioplasty. In the time of early 1990, the CABG was totally performed with use of cardio pulmonary bypass pump or perfusion technology which was called on pump surgery.

But now a days, due to advancement of monitoring technology, skill and expertise to surgeon and anesthetist, availability of safe and efficient pharmacological medication majority of CABG is conducted by off CPB (without pump) which has exhibited lots of benefits over on pump CABG like- less blood transfusion and product, less chances of neurological and renal injury as well as early and fast recovery has change the scenario of post-operative outcome. Because of that the patient acceptance ratio has increase for cardiac treatment.

**Article- 1**


**Blood transfusion in cardiac surgery is a risk factor for increased hospital length of stay in adult patients.**


**BACKGROUND:**
Allogeneic red blood cell (RBC) transfusion has been proposed as a negative indicator of quality in cardiac surgery. Hospital length of stay (LOS) may be a surrogate of poor outcome in transfused patients.
METHODS:
Data from 502 patients included in Transfusion Requirements After Cardiac Surgery (TRACS) study were analyzed to assess the relationship between RBC transfusion and hospital LOS in patients undergoing cardiac surgery and enrolled in the TRACS study.

RESULTS:
According to the status of RBC transfusion, patients were categorized into the following three groups: 1) 199 patients (40%) who did not receive RBC, 2) 241 patients (48%) who received 3 RBC units or fewer (low transfusion requirement group), and 3) 62 patients (12%) who received more than 3 RBC units (high transfusion requirement group). In a multivariable Cox proportional hazards model, the following factors were predictive of a prolonged hospital length of stay: age higher than 65 years, EuroSCORE, valvular surgery, combined procedure, LVEF lower than 40% and RBC transfusion of >3 units.

CONCLUSIONS:
RBC transfusion is an independent risk factor for increased LOS in patients undergoing cardiac surgery. This finding highlights the adequacy of a restrictive transfusion therapy in patients undergoing cardiac surgery.

Articles- 2

Blood Transfusion and Increased Perioperative Risk in Coronary Artery Bypass Grafts
Igor C. Campos1, MD; Valessa Tanganelli1, MD; Hugo P. Maues1, MD; Marcio C. M. Coelho1, MD; Fernanda A. Martins1, MD; Giovana Munhoz1, MD; Julyana G. T. Egito1, MD; Hayala C. C. Souza2; Cássio M. C. Giannini3, MD; Pedro S. Farsky4, MD, PhD
Braz J Cardiovasc Surg 2017;32(5):394-400

OBJECTIVE:
To correlate blood transfusions and clinical outcomes during hospitalization in coronary artery bypass grafting surgery (CABG).

METHODS:
Transfusion, clinical and hematological data were collected for 1,378 patients undergoing isolated or combined CABG between January 2011 and December 2012. The effect of blood transfusions was evaluated through multivariate analysis to predict three co-primary outcomes: composite ischemic events, composite infectious complications and hospital mortality. Because higher risk patients receive more transfusions, the hospital mortality outcome was also tested on a stratum of low-risk patients to isolate the effect of preoperative risk on the results.
RESULTS:
The transfusion rate was 63.9%. The use of blood products was associated with a higher incidence of the three coprimary outcomes: composite infectious complications (OR 2.67, 95% CI 1.70 to 4.19; P<0.001), composite ischemic events (OR 2.42, 95% CI 1.70 to 3.46; P<0.001) and hospital mortality (OR 3.07, 95% CI 1.53 to 6.13; P<0.001). When only patients with logistic EuroSCORE 2% were evaluated, i.e., low-risk individuals, the mortality rate and the incidence of ischemic events and infectious complications composites remained higher among the transfused patients [6% vs. 0.4% (P<0.001), 11.7% vs. 24.3% (P<0.001) and 6.5% vs. 12.7% (P=0.002), respectively].

CONCLUSION:
The use of blood components in patients undergoing CABG was associated with ischemic events, infectious complications and hospital mortality, even in low-risk patients.

Article-3

The impact of blood transfusion on morbidity and mortality after cardiac surgery.

Dorneles Cde C1, Bodanese LC, Guaragna JC, Macagnan FE, Coelho JC, Borges AP, Goldani MA, Petracco JB.

OBJECTIVES:
To analyze the impact of blood transfusion on the incidence of clinical outcomes postoperatively (PO) from cardiac surgery.

METHODS:
Retrospective cohort study. We analyzed 4028 patients undergoing coronary artery bypass grafting (CABG), valve (TV), or both, in Brazilian tertiary university hospital between 1996 and 2009. We compared the postoperative complications between patients with blood transfusion (n = 916) and non-blood transfusion (n = 3112). Univariate analysis was performed using the Student t test, and multivariate logistic regression bivariate (stepwise forward). Were considered significant variables with P <0.05.

RESULTS:
Patients who received blood transfusions had more infectious episodes as mediastinitis (4.9% vs. 2.2%, P <0.001), respiratory infection (27.8% vs 17.1%, P <0.001) and sepsis (6.2% vs. 2.5%, P <0.001). There were more episodes of atrial fibrillation (AF) (27% vs. 20.4%, P <0.001), acute renal failure (ARF) (14.5% vs 7.3%, P <0.001) and stroke (4.8% vs. 2.6%, P = 0.001). The length of PO hospital stay was higher in transfused (13 ± 12.07 days vs. 9.72 ± 7.66 days, P <0.001). However, mortality didn't differ between
groups (10.9% vs. 9.1%, P = 0.112). The transfusion was shown to be a risk factor for: respiratory infection (OR: 1.91, 95% CI 1.59-2.29, P <0.001), AF (OR: 1.35, 95% CI 1.13-1.61, P = 0.01), sepsis (OR: 2.08, 95% CI 1.4-3.07, P <0.001), mediastinitis (OR: 2.14, 95% CI: 1.43-3.21, P <0.001), stroke (OR: 1.63, 95% CI 1.1-2.41, P = 0.014) and ARF (OR 1.8, 95% CI: 1.39-2.33, P <0.001).

CONCLUSIONS:
The blood transfusion is associated with increased risk of infectious events, episodes of AF, ARF and stroke, as well as the increased length of hospital stay but not mortality.

Therapeutic Hypothermia

The normal human body temperature range is typically stated as 36.5–37.5 °C (97.7–99.5 °F) and this range is maintain by thermos regulation. It’s also called as Targeted temperature management (TTM).

The hypothermia mean the decrease in body temperature 32° to 34° C (89.6° to 93.2° F) in patients who don’t regain consciousness after return of spontaneous circulation following a cardiac arrest.

Hypothermia also is used to treat newborns with perinatal asphyxia.

This is also useful in patients with anoxic neurological injury due to stroke, spinal cord injury.

Mechanisms of action:
The effect of hypothermia on the injured brain is complex and not fully understood. It has been established that induced hypothermia has the following mechanisms of action that lead to its neuroprotective effect:

1. Reduction in cerebral metabolism (CMRO2) by approximately 7% per 1°C. This leads to less oxygen and glucose consumption.
2. Promotion of cerebral vasoconstriction, which can directly decrease ICP. Also vascular permeability and therefore oedema formation is decreased.
3. Prevention of neuronal injury leading to programmed cell death (apoptosis) mainly by inhibition of caspase activation.
4. Suppression of the inflammatory cascade and decreased nitric oxide, cytokine and leukotriene production. Leukocyte migration from the damaged endothelium is diminished.
5. Improved ionic homeostasis and blockage of the destructive neuroexitotoxic cascade consequent to glutamate accumulation and receptor activation, and subsequent intracellular calcium overload.
6. Decreased free radical formation
7. It allows for the cerebral regional temperature differences of 2–3°C that are known to exist (cerebral thermo-pooling). Thus, the likelihood of some areas of the brain being hyperthermic (which is known to worsen outcome) is reduced.
INDICATION:
• Traumatic head injuries
• Newborn hypoxic–ischaemic encephalopathy
• Neurosurgery
• Cerebrovascular accident (stroke)
• Cardiac arrest survivors

Article-1

Overview of Therapeutic Hypothermia
Shlee S. Song, M.D. and Patrick D. Lyden, M.D., FAAN, FAHA


ABSTRACT:
Therapeutic Hypothermia has proven neuroprotective effects in global cerebral ischemia. Indications for hypothermia induction include cardiac arrest and neonatal asphyxia. The two general methods of induced hypothermia are either surface cooling or endovascular cooling. Hypothermia should be induced as early as possible to achieve maximum neuroprotection and edema blocking effect. Endovascular cooling has the benefit of shorter time to reach target temperature but catheter insertion requires expertise and training, which may be a barrier to widespread availability. The optimum method of cooling is yet to be determined but a multimodal approach is necessary to address three phases of cooling: induction, maintenance, and re-warm. Specifying core practitioners who are well-versed in established guidelines can help integrate the multidisciplinary team that is needed to successfully implement cooling protocols. Reducing shivering to make heat exchange more efficient with tighter temperature control enables quicker time to target temperature and avoids re-warming which can lead to inadvertent increase in intracranial pressure and cerebral edema. Promising applications but yet to be determined is whether hypothermia treatment can improve outcomes in acute ischemic stroke or traumatic brain injury.

CONCLUSIONS:
Hypothermia improves neurologic outcome and decreases mortality in patients with global cerebral ischemia, such as cardiac arrest patients and infants with hypoxic ischemic encephalopathy. To provide effective treatment, optimal induction and safe rewarming methods need to be determined. Hypothermia has not been proven to show benefit in patients with stroke and traumatic brain injury. Therefore, hypothermia should only be used in randomized controlled trials in this patient population.
Therapeutic Hypothermia for Neuroprotection
History, Mechanisms, Risks, and Clinical Applications
Lioudmila V. Karnatovskaia, MD,1 Katja E. Wartenberg, MD, PhD,2 and William D. Freeman, MD
Originally published 8 Jul 2003 Circulation. 2003;108:118–121

ABSTRACT:
The earliest recorded application of therapeutic hypothermia in medicine spans about 5000 years; however, its use has become widespread since 2002, following the demonstration of both safety and efficacy of regimens requiring only a mild (32°C-35°C) degree of cooling after cardiac arrest. We review the mechanisms by which hypothermia confers neuroprotection as well as its physiological effects by body system and its associated risks. With regard to clinical applications, we present evidence on the role of hypothermia in traumatic brain injury, intracranial pressure elevation, stroke, subarachnoid hemorrhage, spinal cord injury, hepatic encephalopathy, and neonatal peripartum encephalopathy. Based on the current knowledge and areas undergoing or in need of further exploration, we feel that therapeutic hypothermia holds promise in the treatment of patients with various forms of neurologic injury; however, additional quality studies are needed before its true role is fully known.

CONCLUSIONS:
Despite several millennia of reported sporadic use, the “dark ages” of hypothermia appear to have ended, and it has now entered a period of renaissance where recognition of its medical benefits and applications is expanding rapidly, once mild cooling was shown to be beneficial without many of the feared side effects. Nonetheless, body cooling requires an intensive care unit setting with protocolized implementation and close monitoring. Understanding the mechanisms by which hypothermia affects body systems, particularly the brain, is paramount to the advancement of its application into the promising novel areas especially in areas those where treatment options are limited. Therapeutic hypothermia holds promise in the treatment of patients with various forms of neurologic injury; however, additional quality studies are needed before its true role is fully known.
A blood transfusion is the most essential as well as dangerous medicine. So it is very important to take decision for blood and transfusion of blood product depend upon the condition of critically ill patient under guideline.

Nowadays the indication of blood and its component like- Fresh Frozen Plasma, Platelet Rich Concentrate, Single donor Platelet and Red Cell Concentrate or PCV- is used according to the need and indication of the patient.

Article-1


Indications for blood and blood product transfusion

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ABSTRACT:
Transfusion of blood products carries certain inherent risks and hence it should be undertaken only if it improves patient outcome. A review of the literature was carried out to find the indications and effects of transfusion on morbidity and mortality of patients. There is high-quality evidence showing that restrictive blood transfusion with a transfusion trigger of haemoglobin of 7-8 g/dl or the presence of symptoms of anaemia is safe and not associated with increased mortality compared with liberal transfusion. Thus, restrictive strategy is strongly recommended in surgical and critically ill-patients. There is moderate evidence for the use of plasma and platelet transfusion in patients receiving massive blood transfusion. There is not enough evidence to support the use of plasma, platelets and cryoprecipitate in any other clinical setting. Retrospective studies show improved survival after high plasma and platelet to red blood cell ratio of 1:1:1, but this has not been confirmed in randomised trials.

CONCLUSION:
Blood and its components are life-saving drugs with inherent risks. Therefore, they should be used optimally and prudently to maximise patient outcomes. Current evidence shows that restrictive transfusion of blood is safe in stable post-operative and normovolaemic critically ill-patients with the trigger for transfusion being Hb of 7-8 g/dl or symptoms of anaemia. The transfusion trigger for patients with acute coronary syndrome is not known. There is recent evidence that in both septic shock and head injury, a lower transfusion trigger of 7 g/dl is better. There is not enough scientific evidence to guide the use of plasma, platelets and cryoprecipitate. Prospective randomised studies are required to determine the thresholds for transfusion of these products.
ABSTRACT:
Sepsis is very common and lethal. Sepsis is the leading cause of death in non-coronary Intensive Care Units, and the tenth leading cause of death overall. Red blood cell transfusion is one of the most commonly used interventions in the ICU to treat severe anemia, which often occurs in sepsis. Several problems were documented with RBC transfusions and will be reviewed, such as infection, pulmonary complications such as TRALI and Transfusion-Associated Circulatory Overload (TACO), Transfusion-Related Immunomodulation (TRIM) and multiorgan failure, and increased mortality. Most of these complications are partially explained by volume of the unit of blood as well as pathogenic factors of stored RBCs related to 2,3 BPG concentration, inflammatory mediators, nitric oxide, ATP concentration and RBC rheology, and RBC adhesion characteristics. These same factors are present in RBCs of septic patients as well. Until better evidence is available, a “restrictive” strategy of RBC transfusion (transfuse when Hb < 7 g/dL) is recommended except in acute hemorrhage, or in patients with acute myocardial ischemia when a hemoglobin trigger of 8 g/dl is reasonable.

CONCLUSION:
Red blood cell transfusion is one of the most commonly used interventions in the ICU to treat severe anemia, which often occurs in sepsis. Several problems were documented with RBC transfusions, such as infection, pulmonary complications such as TRALI and transfusion-associated circulatory overload (TACO), transfusion-related immunomodulation (TRIM) and multiorgan failure, and increased mortality. Until better evidence is available, a “restrictive” strategy of RBC transfusion (transfuse when Hb < 7 g/dL) is recommended except in acute hemorrhage, or in patients with acute myocardial ischemia when a hemoglobin trigger of 8 g/dl is reasonable.

ABSTRACT:
Blood transfusion refers to the perioperative administration of blood and blood components. Adherence to proper indications for blood component therapy is essential because of its potential adverse effects and
costs of transfusion. Over the years, the significance of blood components in treating certain diseases or conditions has been recognized. In this article, the most commonly used blood components along with the new developments in component therapy have been discussed. Recommendations by different academic and clinical trials and studies have been presented for quick reference. The individual coagulation factors are discussed in brief.

CONCLUSION:
Inappropriate blood component transfusion use has been decreased by audits, discussions with ordering physicians, ward rounds, computer-based decision-support systems and comprehensive educational outreach programs. The lack of data from prospective, randomized studies with adequate sample size, control groups, clinical outcome measurements and other features of well-designed clinical effectiveness research impedes the development of evidence-based clinical practice guidelines for blood component therapy. As our understanding of how the immune system functions and as technology has progressed, specialized components or manufactured products such as blood substitutes have been advanced as remedies to some of the complications with component transfusion. Most importantly, transfusion decisions should be based on sound physiologic principles and a comprehensive assessment of the patient's risk factors.
A WORLD OF EXPERIENCE IN ONE ANTICOAGULANT

CLEXANE® (Enoxaparin Sodium Injection)

THERAPEUTIC CATEGORY Antithrombotic

COMPOSITION Each pre-filled cartridge contains Enoxaparin 30mg / 0.3mL, 40mg / 0.4mL, 60mg / 0.6mL, 80mg / 0.8mL

THERAPEUTIC INDICATIONS Prophylaxis of recurrent thromboembolism (RTE) disease in particular those which may be associated with orthopedic or general surgery. Prophylaxis of VTE in medical patients hospitalised due to acute illnesses, inducing cardiac insufficiency, respiratory failure, severe infections, rheumatic diseases. Treatment of deep vein thrombosis with or without pulmonary embolism. Prevention of thrombus formation in atrioventricular catheterisation during haemodialysis. Treatment of unstable angina and non-Q-wave myocardial infarction administered concurrently with aspirin. Treatment of acute ST Segment Elevation Myocardial Infarction (STEMI) including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).

DOSEAGE AND ADMINISTRATION Prophylaxis of VTE in medical patients: Initial dose: 2mg/kg or 40mg sc ed or 7 to 10 days: 50 to 60mg sc ed. Prophylaxis of VTE in medical patients: 40mg sc ed or daily, once daily for 3 days, then 10mg sc ed or daily. Doseage for a patient with body weight over 100kg: 1mg/kg sc ed or daily. Doseage for a patient with body weight less than 50kg: 0.5mg/kg sc ed or daily. Treatment of acute STEMI: 5mg kg sc ed or daily for 5 days followed by 5mg kg sc ed 1 to 3 days.

SAFETY-RELATED INFORMATION

Contraindication: Contraindicated in patients with known hypersensitivity to enoxaparin sodium, heparin or other low molecular weight heparins (LMWHs). History of immune mediated heparin-induced thrombocytopenia (HIT) within the past 100 days or in the presence of circulating antibodies. Active major bleeding and conditions with a high risk of uncontrolled hemorrhage including recent hemorrhagic stroke.

Precautions & Warnings: Do NOT administer by INTRAVASCULAR ROUTE. Bleeding occurs in the skin of the injection site should be investigated and appropriate treatment instituted. Use with caution in conditions associated with increased potential bleeding (e.g., heparin-induced thrombocytopenia, history of peptic ulcer, recent abdominal surgery, stroke, uncontrolled severe arterial hypertension, diabetic retinopathy, recent sudden or orthopedic surgery, or conditions that increase the risk of bleeding). If bleeding occurs in the skin of the injection site, heparin-induced thrombocytopenia should be monitored. Elderly patients (especially those with age and sex) may be at increased risk for bleeding complications with the therapeutic dose range. Increased risk of bleeding in patients with renal impairment. Increased risk of bleeding in severe liver disease. Women and pregnancy with prophylactic dosages. Other patients (especially those of higher risk of thromboembolism). Patients should be observed closely for signs and symptoms of thromboembolism. Bleeding in some patients may occur due to the risk of anti-factor antibodies. LMWH should not be used interchangeably. There have been cases of necrotising myositis reported with the use of enoxaparin sodium and similar start of treatment resulting in long term or permanent paralysis. Use with caution in patients with a history of enoxaparin-induced thrombocytopenia (HIT) with or without thrombosis. To minimise the risk of bleeding following vascular instrumentation during treatment of unstable angina and non-Q-wave myocardial infarction and acute ST-segment elevation myocardial infarction, advise patients to follow the thrombosis recommended advise. Clexane injection doses, Use of Clexane injection for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been adequately studied. Pregnant women with mechanical prosthetic heart valves may be at higher risk of thromboembolism. At higher doses, increase in aPTT and ACT may occur. Increase in aPTT and ACT are not linearly correlated with increasing enoxaparin sodium antithrombotic activity and therefore are unsuitable and unreliable for monitoring enoxaparin sodium activity.

Preparations & Solutions: These are used during pregnancy only if the physician has indicated a need. Lasting mothers receiving enoxaparin sodium should be advised to avoid breast-feeding.

Adverse Reactions: Common (≥1/100 to <1/10): Hypersensitivity, thrombocytopenia, allergic reactions, hepatic enzymes increase (mainly transaminases). Rare (≥1/1000): Urticaria, pruritus, angioedema, injection site haemorrhage, injection site pain, other injection site reactions, Post marketing experience (frequency not known): asthenia, headache, rash, dizziness, oedema, upper respiratory tract infections, otitis externa (or nasoorbitoethmoiditis). Have been reported with the combined use of enoxaparin sodium with aspirin, selective vascular smooth muscle or pharmacological drugs, hepatic dysfunction, coagulation disorders, with thrombocytopenia, upper respiratory tract infections, otitis externa, or nasoorbitoethmoiditis. The frequency was generally occurring at the injection site, injection site nodules, digestive, haemorrhagic and cholestatic liver injury, oesophageal perforation following long-term therapy (≥1/10000).

For updated information please contact Sanofi India Ltd., Sanofi House, CTS No. 117-8, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400 072 - India.

Sanofi India Limited: Sanofi House, CTS No. 117-8, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400 072 - India.

Revised: April 2017
In a randomized controlled trial of 861 patients with ARDS, mechanical ventilation with a tidal volume of 6 ml/kg and plateau pressure \(<\ 30\ \text{cmH}_2\text{O}\), in comparison with tidal volume of 12 ml/kg and plateau pressure \(<\ 50\ \text{cmH}_2\text{O}\), was associated with a 9% absolute mortality decrease (31% vs 40%, \(P=0.007;\ \text{NNT}=11\)) and a 2 day increase in ventilator-free days (12±11 vs. 10±11; \(P=0.007\)).

In a multicenter, randomized, double-blind trial comparing 0.9% saline or 4% albumin for fluid resuscitation in 6997 critically ill patients in the ICU, there was no difference in mortality (729 v 726, RR 0.99; 95 CI 0.91 to 1.09; \(P=0.87\)), new single-organ and multiple-organ failure (\(P=0.85\)), mean (SD) numbers of ICU days (6.2±6.2 v 6.5±6.6, \(P=0.44\)), hospital days (15.6±9.6 v 15.3±9.6; \(P=0.30\)), days of mechanical ventilation (4.3±5.7 v 4.5±6.1; \(P=0.74\)), or days of renal-replacement therapy (0.4±2.0 v 0.5±2.3) respectively.

In a randomized controlled trial comparing a red cell transfusion trigger of 7 g/dL versus 10 g/dl in 838 critically ill resuscitated patient, there was no difference in either total 30 day mortality (18.7% vs 23.3%, \(P=0.11\), respectively) or mortality in those with clinically significant cardiac disease (20.5% vs 22.9%; \(P=0.69\)). The restrictive transfusion policy was superior for mortality outcome in patients with APACHE II scores of <20 (8.7% vs 16.1%;\(P=0.03\)), in patients < 55 years of age (5.7% vs 13.0%; \(P=0.02\)), and during hospitalization (22.2% vs 28.1%; \(P=0.05\)).

In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Voluven) with 0.9% saline for fluid resuscitation in 7000 critically ill patients, this colloid therapy was associated with a 21% increased risk of the requirement for renal replacement therapy (HES RRT requirement 7.0% versus saline 5.8%; relative risk 1.21; 95% CI 1.00 to 1.45; \(P=0.04\) and no mortality benefit (HES mortality 18.0% versus saline mortality 17.0%; relative risk in the HES group, 1.06; 95% CI 0.96 to 1.18; \(P=0.26\)). Starch therapy was also associated with increased rates of hepatic failure, rash and pruritus.

In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Tetraspan) with Ringer’s acetate for fluid resuscitation in 804 patients with severe sepsis, at 90 days the use of HES was associated with an 8% absolute increase in mortality (51% v 43%; relative risk: 1.17; 95% CI: 1.01 to 1.36; P=0.03) and a 6% absolute increase in renal replacement therapy (22% v 16%; relative risk: 1.35; 95% CI 1.01 to 1.80; P=0.04).


In a single centre, randomised, controlled trial comparing daily sedation hold with continuous sedation in 128 critically ill mechanically ventilated adults, sedation hold decreased the median durations of mechanical ventilation (4.9 days versus 7.3, p=0.004) and ICU length of stay (6.4 days versus 9.9 days, p = 0.02) as well as the requirement for diagnostic testing for changes in mental status (9% versus 27%, p = 0.02). There were no significant differences in adverse events, including self extubation (intervention group 4% versus control group 7 %, p = 0.88).


In a multicentre, randomized controlled trial comparing intensive glucose control (81-108 mg/dL / 4.5 6.0 mmol/L) with conventional glucose control (≤180 mg/dL / ≤ 10.0 mmol/L) in 6,104 adult medical and surgical patients, intensive glucose control increased mortality (27.5% vs 24.9%; odds ratio 1.14; 95% CI 1.02 to 1.28; P=0.02). There was no significant difference between medical and surgical patients (odds ratio 1.31 and 1.07 respectively; P=0.10). Severe hypoglycaemic episodes (blood glucose level ≤40mg/dL / 2.2 mmol/L) were more common in the intensive glucose control group (6.8% vs 0.5%; P<0.001). There were no significant differences in the median number of days of mechanical ventilation (P=0.56) or renal-replacement therapy (P=0.39), or days in ICU (P=0.84) or hospital (P=0.86).


In a multicentre, randomised, controlled, double-blind study comparing low-dose dopamine (2μg/kg/min) infusion with placebo in 328 patients with at least two SIRS criteria and early renal dysfunction, there were no differences in peak serum creatinine concentration (dopamine 245 vs placebo 249 μmol/L; p=0.93), increase in serum creatinine from baseline to highest value (62 vs 66 μmol/L; p=0.82), patients whose serum creatinine concentration exceeded 300 μmol/L (56 vs 56; p=0.92), requirement for renal replacement therapy (35 vs 40; p=0.55), duration of ICU stay (13 vs 14 days; p=0.67), duration of hospital stay (29 vs 33 days; p=0.29), or mortality (69 deaths versus 66 deaths).
In a multicenter, randomized, control trial, comparing temperature management at 33°C with 36°C in 939 comatose patients after out-of-hospital cardiac arrest of presumed cardiac cause, there was no difference in mortality at the end of the trial (33°C group 50% vs 36°C group 48%; hazard ratio with 33°C, 1.06; 95% CI 0.89 to 1.28; P = 0.51), 180-day composite of mortality and poor neurological function (54% vs. 52%, respectively; RR 1.02; 95% CI 0.88 to 1.16; P = 0.78), or serious adverse events (93% vs. 90%, respectively; RR 1.03; 95% CI 1.00 to 1.08; P = 0.09).

Prasad et al reviewed 2,044 original articles published from 2001 to 2010 in the New England Journal of Medicine, and found of 1,344 articles which investigated a medical practice, 73.0% examined a new medical practice, and 27.0% tested an established practice; while 70.5% had positive findings, and 29.5% had negative findings. Of the 1,344 articles addressing a medical practice, 56% demonstrated a new practice surpassed a standard of care, 12% demonstrated a new practice was no better than current practice, 11% showed an existing practice was no better than a lesser therapy, 10% showed an existing practice was better than a lesser standard, while 10% were inconclusive. Of the 363 articles testing standard of care, 146 (40.2%) reversed that practice, whereas 138 (38.0%) reaffirmed it.

In a multicentre, double-blind, randomized placebo-controlled trial comparing hydrocortisone (50mg IV 6 hourly, then tapered) with placebo in 499 patients with septic shock, there was no significant difference in 28-day mortality (hydrocortisone group 34.3% vs placebo group 31.5%; P=0.51). Subgroup analyses of 28-day mortality based on response to corticotropin also showed no difference between study groups. Hydrocortisone hastened reversal of shock compared to placebo, however, with more episodes of superinfection, including new sepsis and septic shock.

In a multicentre, randomised control trial, comparing prolonged periods of prone position ventilation with ongoing supine position ventilation, in 466 patients with moderate-to-severe ARDS, prone positioning was associated with reduced 28 day mortality (16% versus 32.8%, hazard ratio 0.39, 95% CI 0.25 to 0.63, P<0.001), reduced 90 day mortality (23.6% versus 41%, HR 0.44, 95% CI 0.29 to 0.67, P<0.001), and less cardiac arrests (31 patients versus 16 patients, P=0.02), with no difference in other complications.

In an unblinded, single center, randomized control trial comparing selective digestive tract decontamination (oral and enteral polymyxin E, tobramycin, and amphotericin B combined with an initial 4-day course of intravenous cefotaxime) with standard treatment in 934 critically ill patients, SDD was associated with reductions in ICU mortality (15% versus 23%, P=0.002), hospital mortality (24% versus 31%, P=0.02) and colonization with resistant gram-negative bacteria (16% versus 26%, P=0.001), with equal colonization of vancomycin resistant enterococcus (1% versus 1% p=1.0) and absence of methicillin resistant staphylococcus aureus colonization.


In a multicenter, randomized control trial comparing critical care management with a pulmonary artery catheter to management without a pulmonary artery catheter in 1,014 general ICU patients, there was no difference in hospital mortality (68% versus 66%, hazard ratio 1.09, 95% CI 0.94 to 1.27, P=0.39) or complications, with the incidence of non-fatal complications secondary to pulmonary artery catheterization being 9.5%.

Maitland et al performed a stratified (severe hypotension or not), multicenter, randomized control trial, in a resource-limited setting in sub-Saharan Africa, comparing a fluid bolus (20 to 40 ml of 5% albumin or 0.9% saline) with no fluid bolus at admission to hospital in 3,141 children with febrile illness and impaired perfusion, and found fluid bolus therapy was associated with a higher mortality at 48 hours (albumin 10.6%, saline 10.5%, no bolus 7.3%; relative risk bolus therapy versus no bolus 1.45, 95% CI 1.13 to 1.86, P=0.003), and 28 days (12.2%, 12.0% & 8.7%, respectively; RR bolus therapy versus no bolus p=0.004), with similar incidences of pulmonary oedema, increased intracranial pressure (2.6%, 2.2% versus 1.7% P=0.17), and neurological sequelae in the three groups (P=0.92).

In a blinded, multicenter, randomized control trial, comparing noradrenaline plus dobutamine with adrenaline in 330 patients with septic shock, aiming to maintain mean arterial pressure at 70 mmHg, there were no significant differences in 28 day mortality (34% vs. 40%, relative risk 0.86, 95% CI 0.65 to 1.14, P=0.31), ICU mortality (47% vs 75, p=0.69), hospital mortality (52% vs 49%, p=0.51), 90 day mortality (52% vs 50%, p=0.73), time to haemodynamic success (p=0.67), time to vasopressor withdrawal (p=0.09), or rates of serious adverse events.

In a multicenter, randomized control trial, comparing ongoing conventional mechanical ventilation in a non-ECMO centre with transfer to an ECMO centre for respiratory support with either conventional mechanical ventilation or ECMO in 180 patients with severe hypoxic respiratory failure, ECMO centre management, where only 75% of the transferred patients actually received ECMO, was associated with increased 6-month survival (63% vs. 47%, relative risk 0.69, 95% CI 0.05 to 0.97, P=0.03) and a gain of 0·03 quality-adjusted life-years at 6-months, with a lifetime model predicting the cost per QALY of ECMO to be £19 252 (95% CI 7622—59 200) at a discount rate of 3·5%


In a blinded, multicenter, randomized, control trial, comparing activated protein C (24 µg/kg/hr for 96 hours) with a placebo, in 1,697 adults with septic shock, there were no significant differences in mortality at 28 (26.4% vs. 24.2%, relative risk with APC 1.09, 95% CI 0.92 to 1.28 P=0.31) or 90 days (34.1% versus 32.7%, relative risk with APC 1.04, 95% CI 0.90 to 1.19, P=0.56), including those with initially low levels of APC (28 day mortality 28.7% vs. 30.8%, RR 0.93, 95% CI 0.74 to 1.17; p=0.54), or difference in serious bleeding (APC 10 patients versus placebo 8 patients, P=0.81).


In a blinded, international, multicenter, randomized control trial, largely in resource limited healthcare systems, comparing administration of tranexamic acid (TXA) within 8 hours of traumatic injury (1g over 10 min, then infusion of 1g over 8 hours) with placebo in 20,211 adult patients, with or at risk of significant haemorrhage (SBP <90 mmHg or HR >110 bpm, or both), TXA was associated with reduced mortality (14.5% versus 16.0%; relative risk 0.91, 95% CI 0.85 to 0.97; p=0.0035), including reduced bleeding-related mortality (4.9% versus 5.7%; RR 0.85, 95% CI 0.76 to 0.96; p=0.0077), despite no difference in requirement for blood transfusions (50.4% vs. 51.3%) or vascular-occlusive events. In a subsequent post hoc analysis, the bleeding-related mortality reduction with TXA was time dependent, and actually reversed with late administration after 3 hours of injury (TXA 4.4% vs. placebo 3.1%, p=0.004).


23. Casaer. Early versus Late Parenteral Nutrition in Critically Ill Adults. NEJM 2011;365:506-517

In a multicenter, randomized trial comparing early parenteral nutrition (within 48 hours of ICU admission) with late parenteral nutrition (within day 8 of ICU admission) to supplement inadequate...
enteral nutrition, in 4,640 critically ill patients, late parenteral nutrition was associated with multiple improvements, including shorter durations of ICU (3 days vs. 4 days; p=0.02) and hospital (14 vs. 16 days, p=0.004) stay, fewer ICU infections (22.8% vs. 26.2%, P=0.008), lower incidence of cholestasis (P<0.001), reduced requirement for ventilation for > 2 days (36.3% vs. 40.2%, P=0.006), less duration of renal-replacement therapy (7 vs. 10 days, P=0.008) and mean reduction in health care costs of £910 (P=0.04).

Doig et al performed a multicenter, randomized trial comparing standard care with early parenteral nutrition in 1,372 critically ill patients with relative contraindications to enteral nutrition remaining in ICU for > 2 days, and found no difference in 60 day mortality (standard care 22.8% vs. early PN 21.5%; risk difference -1.26%; 95% CI -6.6 to 4.1; P = 0.60). Early parenteral nutrition patients required fewer days of mechanical ventilation (7.73 versus 7.26, risk difference -0.47; 95% CI -0.82 to -0.11; P = 0.01), less muscle wasting based on subjective global assessment (0.43 versus 0.27; mean difference -0.16; 95% CI -0.28 to -0.038; P = 0.01) and less fat loss (0.44 versus 0.31; mean difference -0.13; 95% CI -0.25 to -0.01; P = 0.04). Day-60 quality of life (RAND-36 General Health Status) was statistically higher in the early PN group, which was not clinically meaningful. (45.5 versus 49.8;mean difference 4.3; 95% CI 0.95 to 7.58; P = 0.01).


In a multicentre, randomised controlled trial comparing paired daily sedation hold plus daily spontaneous breathing trial (intervention) versus uninterrupted sedation plus a daily spontaneous breathing trial (control) in 336 sedated, mechanically ventilated patients, the intervention was associated with more days breathing without assistance (14·7 vs 11·6 days; 95% CI 0·7 to 5·6; p=0·02), earlier discharge from both intensive care (median time in ICU 9·1 days vs 12·9 days; p=0·01) and the hospital (median time in the hospital 14·9 days vs 19·2 days; p=0·04), and reduced one-year mortality (HR 0·68; 95% CI 0·50 to 0·92; p=0·01; NNT 7.4, 95% CI 4·2 to 35·5). More patients in the intervention group self-extubated, but with similar rates for both reintubation after self-extubation and total reintubation.


   In a single centre, randomized controlled trial comparing semirecumbent with supine body position in 86 mechanically ventilated medical patients, the semirecumbent group had a lower frequency of suspected noscomial pneumonia (8% vs 34%; 95% CI for difference 10·0 to 42.0; P=0·003) and microbiologically confirmed pneumonia (5% vs 23%; 95% CI 4.2 to 31.8; p=0·018). Supine body position (odds ratio 6.8; 95% CI 1.7 – 26.7; P=0·006) and enteral nutrition (odds ration 5.7; 95% CI 1.5 – 22.8; P=0·013) were independent risk factors for nosocomial pneumonia.


   In a multicentre, double-blind, randomized controlled trial comparing 48 hours of cisatracurium besylate with placebo in 340 patients with early severe ARDS, neuromuscular blockade was associated with a trend for reduced crude 90-day mortality (31.6% (95% CI 25.2 – 38.8) vs 40.7% (95% CI 33.5 – 48.4)) (P=0.08). After adjustment for baseline PaO2:FiO2, plateau pressure and Simplified Acute Physiology II scores, neuromuscular blockade reduced the adjusted hazard ratio for death at 90 days (HR 0.68, 95% CI 0.48 to 0.98; P=0.04). There was no difference in the rate of ICU acquired paresis.

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In a multicentre, blinded, randomized, controlled trial comparing therapeutic hypothermia (32°C to 34°C for 24 hours) with normothermia in 273 comatose survivors of out-of-hospital VF/VT, hypothermia improved favourable neurological outcomes (55% vs 39%; RR 1.40, 95% CI 1.08 to 1.81) and 6 month mortality (41% vs 55%; RR 0.74, 95% CI 0.58 to 0.95). The complication rate did not differ significantly between the two groups.

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