SYLLABUS

SIXTEENTH INTERNATIONAL CONFERENCE ON
CONTINUOUS RENAL REPLACEMENT THERAPIES

CRRT 2011

February 22-25, 2011

San Diego, California Hilton San Diego Bayfront

Endorsed by the
International Society of Nephrology
and Acute Kidney Injury Network

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WEDNESDAY AFTERNOON, FEBRUARY 23

11:45am-1:10pm *Conference Waterfront Luncheon - **Sapphire Terrace** (Rain Back-up - Sapphire CDGH)*

Indigo A **NURSING FORUM LUNCHEON**
End of Life Care: Dilemmas and Solutions
Lynette Cederquist, MD

FOCUS GROUP LUNCHEONS *(see Final Program for descriptions)*
Sapphire 410 **GAMBRO** - Is Your Critically Ill AKI Patient Drowning?
Sapphire 400 **Alere San Diego, Inc. -** The Promising Role of NGAL in the Intensive Care Unit & Emergency Department

SESSION I: PATIENT CHARACTERISTICS (OPENING SESSION)

1:10-3:35 **Plenary 1**
MINI-SYMPOSIA
Organ Dysfunction in the Critically Ill Patient: Emerging Concepts
Co-chairs: Michael Joannidis, MD
John A. Kellum, MD

1:10-1:15 **Opening Remarks**
Ravindra L. Mehta, MBBS, MD, DM, FACP

1:15-1:30 **Mitochondrial Injury and the Microcirculation** 21
Can Ince, PhD

1:30-1:45 **Endotoxemia Induced Inflammation** 23
Peter Pickkers, MD, PhD

1:45-2:00 **Augmented Renal Clearance**.....24
Jeffrey Lipman, MD

2:00-2:15 **Adipose Tissue Alterations in Critical Illness: A Protective Response?** .....*
Miet Schetz, MD, PhD

2:15-2:30 **Anesthesia and the Microcirculation** 25
Andrew D. Shaw, MD FRCA FCCM

2:30-2:45 **Dysnatremias In The ICU: Cause For Concern?** 26*
Mitchell H. Rosner, MD

2:45-3:00 **The Neuroenteric Axis and Distant Organ Dysfunction**
Raul Coimbra, MD, PhD, FACS

3:00-3:30 **SPECIAL LECTURE**
AKI To CKD Progression: Mechanisms, Pathways and Targets 27
Joseph V. Bonventre, MD, PhD

3:30-3:45 **Panel Discussion**

3:45-4:15 *Coffee Break: Exhibits Open*

NOTES:
1. "*" means presentation slides are available on online.
3. Workshop outlines and/or slides may have been submitted by one faculty member for use by others in the same workshop.

WEDNESDAY AFTERNOON, FEBRUARY 23 *(continued)*

4:15-6:00 **Plenary 2**
MINI-SYMPOSIA
Acute Kidney Injury (AKI): Pathophysiology

Co-chairs: Joseph V. Bonventre, MD, PhD
Can Ince, PhD

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Mark D. Okusa, MD

4:30-4:45 **Oxygen, Hydrogen and Carbon Monoxide Gases with Therapeutic Potential?** 29
Anupam Agarwal, MD

4:45-5:00 **Liver Kidney Interactions Deranged Physiology or Auto Regulatory Success?**
Tarek Hassanein, MD

5:00-5:15 **Worsening Renal Function in Heart Failure: Predictive Factors**
Alan Maisel, MD

5:15-5:30 **Cardio Renal Syndrome It's Time to Use Biomarkers**....30*
John L. Jefferies, MD

5:30-5:45 **Do Genes Matter in Acute Kidney Injury?** 31
Andrew D. Shaw, MD FRCA FCCM

5:45-6:00 **Panel Discussion**

6:00-6:30 **SPECIAL SESSION**
Critical Care Nephrology Jeopardy 32
Moderator: Noel Gibney, MD
Nephrology Team: Ashita Tolwani, Emil Paganini, Claudio Ronco
Itensivists Team: John Kellum, Andrew Shaw, Miet Schetz

6:30-8:00 **EXHIBIT RECEPTION AND POSTER SESSION**

THURSDAY MORNING, FEBRUARY 24

SESSION II: EMERGING CONCEPTS IN AKI AND CRITICAL CARE

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7:30- 9:45 **Plenary 3**
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Co-chairs: Claudio Ronco, MD

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John A. Kellum, MD

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Ravindra L. Mehta, MBBS, MD, DM, FACP

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Bruce A. Molitoris, MD

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Prasad Devarajan, MD

9:00-9:30 **SPECIAL LECTURE**
Smart Medical Environments: The Role of Informatics
Lucila Ohno-Machado, MD, PhD

9:30-9:45 **Panel Discussion**

9:45-10:15 *Coffee Break - Exhibits Open*

THURSDAY MORNING, FEBRUARY 24 *(continued)*

10:15-1:00 **Plenary 4**
MINI-SYMPOSIA
Challenges and Controversies in Renal Support and CRRT

Co-chairs: Ashita Tolwani, MD
David M. Ward, MD, FRCP

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Jeffrey Lipman, MD

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Ian Baldwin, RN, PhD, ACCCN

10:45-11:00 **Combination Therapies for Renal Support: The Japanese Experience** ……44*
Kazo Kaizu, MD

11:00-11:15 **Combined Extracorporeal Lung and Renal Support**
Claudio Ronco, MD

11:15-11:30 **Peritoneal Dialysis in AKI: A Viable Alternative** ……45*
Daniela Ponce, MD

11:30-11:45 **Prolonged Dialysis: 24 hr SLED is it CRRT?** ……46*
Balazs Szamosfalvi, MD

11:45-12:00 **Managing The Cardiorenal Syndrome: The Role Of PD**……47*
Rajasekara Chakravarthi, MD, DNB (Nephrology)

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Oliver Joannes-Boyau, MD

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Ravindra L. Mehta, MBBS, MD, DM, FACP

12:35-12:50 **Panel Discussion**

12:50-1:00 **Top Abstract Awards**

1:00-2:30 *Lunch Hosted by Conference - **Waterfront Park** (Rain Back-up: Indigo AE)*

FRIDAY MORNING, FEBRUARY 25

SESSION III: TECHNIQUE CHARACTERISTICS

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7:30-10:10 **Plenary 5**
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Kianoush Kashani, MD

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Andrew Lewington, MD

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9:00-9:15 **KDIGO AKI Guidelines: How Can We Use Them?**
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9:15-9:30 **Biomarkers in AKI: Ready for Clinical Care?**
Patrick T. Murray, MD

9:30-9:45 **Contrast Nephropathy: What Do We Know Now?**.....56
Richard Solomon, MD

9:45-10:0 **Panel Discussion**

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FRIDAY MORNING, FEBRUARY 25 *(continued)*

SESSION IV: FUTURE TRENDS IN CRRT AND CRITICAL CARE

10:30-1:00 **Plenary 6**
MINI SYMPOSIA
Emerging Strategies in AKI and Extracorporeal Support

10:30-10:55 **SPECIAL LECTURE**
Development of CRRT in Infants and Children: From Origin to the Future
Claudio Ronco, MD

10:55-11:10 **Advances with Therapeutic Apheresis** ……*
David M. Ward, MD, FRCP

11:10-11:25 **Alkaline PO4 Trial** ……57*
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Ian Baldwin, RN, PhD, ACCCN

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Tarek Hassanein, MD

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12:40-12:55 **Critical Care Nephrology: Literature Review** ……64*
Noel Gibney, MD

12:55-1:00 **Closing Remarks**
Ravindra L. Mehta, MD, FACP
Chairman

1:00 **Conference Adjourns**

WEDNESDAY MORNING, FEBRUARY 23

NOTE: Please see Final Program page 7 for **Industry Workshop** list and locations, separate handouts will be provided for **A01 A09 A18 & A26**. **CME CREDITS DO NOT APPLY TO A01 A09 A18 & A26.**

8:30-10:00 SIMULTANEOUS WORKSHOPS GROUP 1

A01 ***Separate handouts will be provided for this workshop***

B02 Vascular Access /Membrane and Circuit 1 (C,N,AP)
Principles of catheter choice, placement, maintenance, recognition and management of complications, selection and use of membranes for different applications, circuit design, setup and monitoring.

Michael Joannidis, MD ……65
Miet Schetz, MD, PhD……*

C03 Dialysis Dose Prescription and Delivery (C,N,AP)
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William R. Clark, MD
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Claudio Ronco, MD

D04 Critical Care Pharamacology: Vasopresors, and Ionotropes (A,N,AP)
Pathophysiology of shock and the principles and practical use of vasopressors, ionotropes, vasodilators in critically ill patients.

Thomas A. Golper, MD ……68*
Jeffrey Lipman, MD

E05 Biomarkers 1: Principles and Applications (C,N,AP)
Principles and classification of biomarkers and their application for diagnosis and management of diseases. Criteria for using biomarkers as surrogate end points.

Joseph V. Bonventre, MD, PhD
William L. Macias, MD, PhD
Chirag Parikh, MD, PhD ……69

F06 Extracorporeal Techniques for Sepsis 1: Pathophysiology and Targets (A)
Pathophysiology of sepsis and rationale for use of extracorporeal support in treatment of sepsis.
Experimental models for high permeability membranes, HVHF, VHVHF and hybrid therapies.

Patrick M. Honoré, MD ……70*
Peter Pickkers, MD, PhD……*

G07 Competency Assessment in CRRT (C,N)
Description on training requirements, core curriculum and skills assessment for CRRT care delivery.

Ian Baldwin, RN, PhD, ACCCN ……72*
Patty Graham, RN, MS, CCRN, CS
Eileen Lischer, MA, BSN, RN, CNN ……73*

H08 Fluids and Solutions in the Critically Ill 1
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Patrick T. Murray, MD
Andrew D. Shaw, MD FRCA FCCM

10:00-10:15 *Coffee Break*

WEDNESDAY MORNING, FEBRUARY 23 *(continued)*

10:15 - 11:45 SIMULTANEOUS WORKSHOPS GROUP 2

A09 ***Separate handouts will be provided for this workshop***

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Michael Joannidis, MD ……74
Ashita Tolwani, MD ……75*

C11 Fluid Management (C,N,AP)
Principles of volume assessment, fluid removal and fluid regulation with different CRRT equipment.
Ravindra L. Mehta, MD, FACP ……76*

D12 Critical Care Management: Nutrition Assessment and Delivery (I,N,AP)
Pathophysiology of malnutrition in critically ill patients. Principles of nutritional assessment and support and adjustments for RRT.
Oliver Joannes-Boyau, MD ……78
Miet Schetz, MD, PhD ……*

E13 Biomarkers 2: Application in AKI (I,N,AP)
Development and qualification of structural and functional biomarkers for AKI. Current performance characteristics and application for diagnosis, management and prognostication in AKI.
Joseph V. Bonventre, MD, PhD
Prasad Devarajan, MD ……*
Patrick T. Murray, MD ……79

F14 Liver and the Kidney 1: Principles of Hepatic Dysfunction (A,N))
Pathophysiology of hepatic failure and rationale for use of different techniques for extracorporeal support techniques (Cell based systems, MARS, CRRT) for hepatic support.
Tarek Hassanein, MD

G15 Therapy Modalities: IHD, SLED, PD
Comparisons of operational characteristics including anticoagulation, membranes, solutions and flows and approaches for ongoing and future research.
Rajasekara Chakravarthi, MD, DNB ……80
Mark R. Marshall, MBChB, FRACP, MPH
Daniela Ponce, MD ……81*

H16 Pediatric CRRT: The Basics (I,N,AP) ……82*
Technique requirement and application for use in children excluding neonates. Topics covered will include the epidemiology of pediatric acute kidney injury, and a focus on the pediatric CRRT prescription (anticoagulation, fluid composition, modality, and nutrition provision), as well as outcome in pediatric CRRT.
Steven R. Alexander, MD
Patrick D. Brophy, MD
Geoffrey Fleming, MD
Jordan M. Symons, MD
Michael Zappitelli, MD, MSc

I17 Preventing and Managing Complications of Dialysis: Intradialytic Hypotension
Definitions and pathophysiology of intradialytic hypotension. Strategies for prevention and management.
Andrew Davenport, MD, FRCP ……83*

11:45am-1:00pm *Lunches Hosted by Conference - See page 5*

THURSDAY AFTERNOON, FEBRUARY 24

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A18 ***Separate handouts will be provided for this workshop***

B19 Drug Management in CRRT (C,N,AP)
Drug Dosing principles for critically ill patients and adjustments in extracorporeal support techniques.
Jeffrey Lipman, MD
Bruce A. Mueller, PharmD, FCCP, FASN 84*

C20 Starting and Stopping RRT for AKI: Principles and Practice (A)
Principles of determining when to start and stop RRT. Case based discussion of various approaches.
Etienne Macedo, MD, PhD 85
Ravindra L. Mehta, MD, FACP 86*

D21 Acid Base and Electrolyte Problems in the Critically Ill 1 (I)
Principles for evaluating and managing acid base and electrolyte problems in critically ill patients using case studies.
Eric AJ Hoste, MD, PhD
John A. Kellum, MD 88
Mitchell H. Rosner, MD 89*

E22 Ensuring Patient Safety and Quality Measures for RRT in AKI 1: Water Standards, Infection Control (C,N,AP)
Discussion of the recent developments in ensuring quality and patient safety for acute dialysis delivery.
Thomas A. Golper, MD 90*
Eileen Lischer, MA, BSN, RN, CNN 91*

F23 Heart Failure and Cardio-renal Syndrome 1: Pathophysiology (I)
Pathophysiology, recognition and management strategies for cardiac and renal failure in the critically ill patient.
Dinna Cruz, MD, MPH 92*
Alan Maisel, MD 93*
Claudio Ronco, MD

G24 Extracorporeal Techniques for Sepsis 2 (A)
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Oliver Joannes-Boyau, MD 96

H25 Fluids and Solutions in the Critically Ill 2: Solutions for CRRT (I,N,AP)
Currently available solutions for CRRT and dialysis. Practical approaches for achieving metabolic, acid-base, electrolyte and divalent ion control with RRT techniques.
Andrew Davenport, MD, FRCP 97*
Michael Joannidis, MD 98

4:00-4:30 *Break - Exhibits Open*

THURSDAY AFTERNOON, FEBRUARY 24 *(continued)*

4:30-6:00 SIMULTANEOUS WORKSHOPS GROUP 4

A26 ***Separate handouts will be provided for this workshop***

B27 Assessing the Microcirculation (A)
Techniques of monitoring and interpretation of microcirculatory alterations in critical illness as measured by direct sublingual observation. Strategies to assess microcirculatory alterations in the critically ill patients will be presented and discussed.

Rolando Claure, MD ……99
Can Ince, PhD ……101
Etienne Macedo, MD, PhD

C28 Plasma Exchange Therapy and Hybrid Techniques (A,N)
Principles of plasma exchange, sorbent based and hybrid therapies for extracorporeal support. Case based discussion of practical application of plasma exchange, sorbent based and hybrid therapies for extracorporeal support.

Andre A. Kaplan, MD ……102*
David M. Ward, MD, FRCP……*

D29 Acid Base and Electrolyte Problems in the Critically Ill 2 (I)
Principles for evaluating and managing acid base and electrolyte problems in critically ill patients using case studies.

Eric AJ Hoste, MD, PhD
Andrew Lewington, MD ……103*
Mitchell H. Rosner, MD……104*

E30 Ensuring Patient Safety and Quality Measures for RRT in AKI 2: Dialysis Adequacy, Monitoring, Nursing Issues (C,N,AP)
Discussion of the principles of a systems based approach to implementing and monitoring quality to reduce errors in therapy prescription and delivery.

Eileen Lischer, MA, BSN, RN, CNN ……105*
Ashita Tolwani, MD ……106*

F31 Heart Failure and Cardio-renal Syndrome 2: Management Strategies and Case Studies (A,N)
Technical considerations, practical application and results of different methods to treat heart failure and cardio-renal syndrome.

Dinna Cruz, MD, MPH ……*
Alan Maisel, MD ……107*
Emil P. Paganini, MD, FACP, FRCP ……108

G32 Liver and Kidney 2: Hepatic Support (A,N)
Technical considerations, practical application and results of different methods of hepatic support for patients with hepatic failure and hepatorenal syndrome.

Andrew Davenport, MD……109*
Tarek Hassanein, MD

H33 CRRT in the Newborn: Principles and Practical Issues (C,N,AP) ……110*
Pathophysiology and management of metabolic disorders, neonatal AKI and intoxications with CRRT.

Steven R. Alexander, MD
David Askenazi, MD
Jordan M. Symons, MD

I34 Withdrawing & Withholding Support for AKI: Ethical Issues in the ICU
Factors influencing decisions for withholding and withdrawing dialysis in the management of critically ill patients. General principles for ethical decisions and how an approach can be developed to manage patients requiring dialysis.

Lynette Cederquist, MD
Noel Gibney, MD ……111*

6:00 Adjourn

Technique Characteristics

Poster Number

CRRT Applications

Targeted Interventions

RRT Research

Epidemiology and Patient Characteristics

Research in AKI

UC San Diego
SCHOOL OF MEDICINE

CONFERENCE DESCRIPTION AND LEARNER OBJECTIVES

The CRRT conference is designed to provide an up-to-date review of the latest developments and research in the field of ICU medicine, acute kidney injury and CRRT. The conference is structured to promote multidisciplinary interaction among specialists in nephrology, critical care, nursing support personnel and industry involved in the care of the critically ill patient. A combination of invited lectures, lively debates, panel discussions, interactive workshops, oral and poster presentations will be utilized for CME credits.

At the end of this conference attendees should be able to:

1. Discuss the pathophysiology of critical illness and acute kidney injury
2. Describe the principles and practice of CRRT techniques and their application
3. Recognize key features for fluid management, hemodynamic monitoring and resuscitation for critically ill patients
4. Obtain hands on experience with different CRRT machines

NEEDS ASSESSMENT

Acute kidney injury (AKI) is a common, heterogeneous and detrimental clinical condition that has significant attributable morbidity and mortality. Despite major advances in understanding the epidemiology, pathogenesis and outcomes of AKI, the preventive measures remain inadequate and therapeutic approaches (except for renal replacement therapy) have largely proven futile so far. Recent publications from several international consensus conferences including the Acute Kidney Injury network (AKIN) (CJASN May 2008 vol. 3 no. 3 887-894)); the American Thoracic Society (ATS), European Respiratory Society (ERS) , European Society of Intensive Care Medicine (ESICM), Society of Critical Care Medicine (SCCM), and the Société de Réanimation de Langue Française (SRLF) (Am J Respir Crit Care Med. 2010 May 15;181(10):1128-55) have highlighted several gaps in our knowledge particularly in the following areas:

1. Pathophysiology and diagnosis of AKI in critically ill patients
2. Management strategies for prevention, treatment and follow up of patients with AKI
3. Optimal strategies for initiating and delivering dialysis with continuous renal replacement therapies (CRRT), intermittent hemodialysis (IHD) and peritoneal dialysis (PD) for the support of patients with AKI and multiple organ failure.

The 16th International CRRT conference addresses these needs focusing on the recent advances in our understanding of mechanisms, pathways of AKI and its effects on other organs, pathophysiology of critical illness, acute kidney injury, emerging strategies in the management of sepsis, multiorgan failure, development and use of biomarkers, technical advances in CRRT and the appropriate utilization of these techniques.

TARGET AUDIENCE

The CRRT target audience includes: MD/DOs, NP/PA/Nurses, Dieticians, Industry, Pharmacists, Residents and Fellows. Specialties include: Anesthesiology, Cellular & Molecular Medicine, Critical Care, Emergency Medicine, Family & Preventative Medicine, Geriatrics, and Internal Medicine.

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the University of California, San Diego School of Medicine and CRRT, Inc. The University of California, San Diego School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The University of California, San Diego School of Medicine designates this live activity for a maximum of 34 *AMA PRA Category 1 Credits™* . Physicians should only claim credit commensurate with the extent of their participation in the activity.

BRN: For the purpose of recertification, the American Nurses Credentialing Center accepts 34 *AMA PRA Category 1 Credits™* issued by organizations accredited by the ACCME. For the purpose of relicensure, the California Board of Registered Nursing accepts 34 *AMA PRA Category 1 Credits™* (report up to 34 hours of credit and list "CME Category 1" as the provider number).

CULTURAL AND LINGUISTIC COMPETENCY

California Assembly Bill 1195 requires continuing medical education activities with patient care components to include curriculum in the subjects of cultural and linguistic competency. It is the intent of the bill, which went into effect on July 1, 2006, to encourage physicians and surgeons, CME providers in the state of California, and the Accreditation Council for Continuing Medical Education to meet the cultural and linguistic concerns of a diverse patient population through appropriate professional development. The planners, speakers and authors of this CME activity have been encouraged to address issues relevant in their topic area. In addition, a variety of resources are available that address cultural and linguistic competency, some of which are included in your syllabus or handout materials. Additional resources and information about AB1195 can be found on our website at http://cme.ucsd.edu.

Faculty Disclosure

16th International Conference on Continuous Renal Replacement Therapies
February 22-25,2011

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	Satellite Dialysis	Consultant
Joseph Bonventre, MD,PhD	Partners HealthCare System	Holder of Patent Rights to KIM-1 which has been licensed to J and J, Genzyme, BiogenIdec, R and D, BioassayWorks
Jorge Cerda, MD, FACP, FASN	Gambro	Advisory Board Consultant
Lakhmir Chawla, MD	Astute Medical	Consultant/ Research
	Covidien Medical	Consultant
	NxStage Medical	Consultant
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William Clark, MD	Gambro	Full-time Employee
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Noel Gibney, MD	Gambro	Member,Expert Panel
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Richard Solomon, MD	PLC Med	Consultant
	Bracco Diagnostics	Consultant
Ashita Tolwani, MD	Gambro Renal Products	Expert Panel Member
Christof Westenfelder, MD	Allocure, Inc	Consultant until Dec 6, 2010

The following speakers have no relevant financial relationships to disclose:

Anupan Agarwal, MD	Raul Coimbra, MD, PhD, FACS	Kambiz Kalantarinia, MD,MS	David Perkins, MD
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Mitochondrial Injury and the Microcirculation

Can Ince PhD
1:15-1:30
Wednesday, February 23

Educational Objectives:
1. Understand mitochondrial oxygen utilization and oxyidative phosphyrilation
2. Theories regarding the role of mitochondrial dysfunction in critical illness (oxygen conformance theory and cytopathic hypoxia)
3. Techniques for assessment of mitochondrial and microcirculatry oxygenation

Content Description:
Being able to assess mitochondrial function in patients represents one of the holy grails of intensive care medicine because preservation of mitochondrial function to produces ATP by oxidative phosphorylation is essential to sustain life. In states of sepsis and shock it is thought that mitochondrial dysfunction may form an important contributing factor in the pathogenesis of MOF. Indeed Brealey et al. showed in clinical study by taking muscle biopsies from patients that mitochondrial failure is prevalent in sepsis.

The redox state of mitochondrial NADH/NAD+ is the main source of energy transfer from the citric acid cycle to the respiratory chain and is considered as the gold standard for mitochondrial energy state. The fluorescent properties of NADH has allowed imaging modalities to be used to investigate the spatial and temporal properties of changes in mitochondrial energy state in situ in experimental studies of sepsis. These studies have shown the highly heterogeneous nature of dysoxia during sepsis and have identified microcirculatory weak units as underlying the hypoxic state associated with sepsis and shock. It also demonstrated that it is the heterogeneous nature of the microcirculation which determined the heterogeneous availability of oxygen to meet the needs of the tissue mitochondria.

Measurement of quantitative values of mitochondrial oxygen tension (mitpO2) in vivo has an unattained aim in mitochondrial physiology. Early experiments using myoglobin spectroscopy estimated mitpO2 to be around 2 to 5 mmHg and this has been the generally accepted paradigm in the literature. Schumacker and and co-workers later introduced the so-called oxygen conformance theory whereby mitpO2 levels adapted to microcirculatory pO2 (μpO2) levels and were expected to be much higher than earlier supposed, close in value to μpO2 values. In vivo confirmation of such higher mitpO2 value were lacking however due to lack of available techniques. We recently identified the oxygen dependent properties of endogenously present mitochondrial protoporphyrin IX for quantitative measurement of mitpO2 in vivo by use of a quenching of delayed fluorescence technique. This was an important development because it confirmed the predictions of the oxygen conformance theory where mitpO2 values instead being less than 5 mmHg were found to be much higher (between 20 and 30mmHg) following closely μpO2 . Our development of delayed PiX now opens the way to investigate the role of mitochondrial oxygenation in conditions of sepsis, shock and resuscitation in vivo for the first time in great detail.

Suggested Reading:

Singer M (2007) Mitochondrial function in sepsis: acute phase versus multiple organ failure. Crit Care Med. 35(9 Suppl):S441-8.

Ince C, Sinaappel M (1999) Microcirculatory oxygenation and shunting in sepsis and shock. Crit Care Med 27:1369-1377.

Brealey D, Brand M, Hargreaves I, Heales S, Land J, Smolenski R, Singer M (2002) Association between mitochondrial dysfunction and severity and outcome of septic shock. Lancet 360(9328):219-23.

continued

Ait-Oufella H, Maury E, Lehoux S, Guidet B, Offenstadt G.(2010) The endothelium: physiological functions and role in microcirculatory failure during severe sepsis. Intensive Care Med. 36(8):1286-98.

Porta F, Takala J, Weikert C, Bracht H, Kolarova A, Lauterburg B, Borotto E, Jakob S (2006) Effects of prolonged endotoxemia on liver, skeletal muscle and kidney mitochondrial function Critical Care 2006, 10:R118

Schumacker, P. T., N. Chandel, and A. G. Agusti. 1993. Oxygen conformance of cellular respiration in hepatocytes. Am. J. Physiol. 265:L395–L402.

Mik EG, Stap J, Sinaasappel M, Beek JF, Aten JA, van Leeuwen TG, Ince C. (2006) Mitochondrial PO2 measured by delayed fluorescence of endogenous protoporphyrin IX. Nature Methods (11):939-45.

Mik EG, Johannes T, Zuurbier C, Heinen A, Houben-Weerts JH, Balestra GM, Stap J, Beek JF, Ince C. (2008). In vivo mitochondrial oxygen tension measured by a delayed fluorescence lifetime technique. Biophys J. ;95(8):3977-90

Balestra GM, Legrand M, Ince C. (2009) Microcirculation and mitochondria in sepsis: getting out of breath. Curr Opin Anaesthesiol. 22(2):184-90.

Endotoxemia-Induced Inflammation

Peter Pickkers
1:30-1:45
Wednesday, February 23

Educational Objectives
1. Learn about the possibilities to investigate the innate immune response and inflammation-associated organ injury in humans in vivo.
2. Describe the pathophysiological changes that occur during experimental endotoxemia.
3. Describe the effects of experimental endotoxemia on the kidneys.

Content Description
The healthy human model of endotoxin administration (systemic or endobronchial) has been used to great advantage for gaining insight into mechanisms of disease and for determination of therapeutic signal strength. Today, controlled endotoxin infusion has been widely used as a model system to study new therapeutic agents for inflammation before wider clinical studies are undertaken, and to delineate better the multifaceted human innate and adaptive immune responses to endotoxin. Of all the animals studied, man is the most sensitive to the effects of endotoxin. The responses of human subjects to endotoxin infusion are remarkably similar. Typically, within 50–90 min following endotoxin infusion, subjects describe flu-like symptoms such as fatigue, malaise, arthralgias, myalgias, headache, nausea, and often chills that resolve within 3–4 h. After a latent period up to 120 min, there is a monophasic increase in fever which peaks at 1–2°C above baseline. The fever may last up to 3–4 h (depending on dose) and resolves without residual effect. Experimental endotoxemia is associated with subclinical organ dysfunction. There is a depression of left ventricular function that is independent of changes in left ventricular volume or vascular resistance, and similar to changes observed in septic shock. Also subclinical renal injury occurs during experimental endotoxemia. Healthy endotoxemia volunteers had a higher excretion of nitric oxide (NO) metabolites compared with control subjects and this was correlated with proximal tubule injury (based on urinary cytosolic glutathione-S-transferase-A1). Since this injury was reduced by an inhibitor of inducible NO synthase (aminoguanidine), it appears that up-regulation of iNOS and subsequent NO production is be responsible for the LPS-induced renal proximal tubule damage. These studies illustrate that the experimental endotoxemia model can be used for the evaluation of anti-inflammatory reagents as well as to address basic scientific questions of endotoxin biology.

Suggested Reading
1. From therapy to experimental model: a hundred years of endotoxin administration to human subjects. Marjan Bahador, Alan S. Cross. J Endotoxin Res 2007; 13; 251.
2. Lowry SF. Human endotoxemia: a model for mechanistic insight and therapeutic targeting. Shock 2005; 24 (Suppl. 1): 94–100.
3. Upregulation of renal inducible nitric oxide synthase during human endotoxemia and sepsis is associated with proximal tubule injury. Heemskerk S, Pickkers P, Bouw MP, Draisma A, van der Hoeven JG, Peters WH, Smits P, Russel FG, Masereeuw R. Clin J Am Soc Nephrol. 2006 Jul;1(4):853-62.

Augmented Renal Clearance

Jeffrey Lipman MD
1:45-2:00
Wednesday, February 23

Educational Objectives:
1. What a "normal" serum creatinine means
2. What is meant by the term "Augmented Renal Clearance"
3. The clinical spectrum of patients it occurs in and the clinical implications of ARC

Content Description:
We regularly use serum creatinine concentrations as an index of renal function. When this value is raised we assume (most often correctly so) that there is renal dysfunction. There are a number of equations that have been derived in this population group (ie those patients with raised serum creatinine) to equate abnormal creatinine concentrations with diminished creatinine clearance, and hence the level of renal dysfunction. Typically we adjust downwards the dosage of renally excreted drugs accordingly.

It has been assumed until very recently that a "normal" serum creatinine concentration infers "normal creatinine clearance" and hence we prescribe "normal" doses of renally excreted drugs.

There is a group of patients however, where a normal creatinine concentration is concurrent with a very high creatinine clearance – a phenomenon we have termed Augmented Renal Clearance (ARC). Patients with ARC often manifest an underlying inflammatory and hyperdynamic circulatory response, coupled with "normal" baseline renal function (examples include young trauma patients or patients with haematological malignancies). In ICU we compound this problem by administering fluid and/or inotropic agents to defend a blood pressure.

"You only find what you look for". In this group of patients unless creatinine clearance is actually measured this phenomenon can be missed, and the equations produced for abnormal renal function are insensitive in predicting such high creatinine clearance.

The clinical effects of ARC are predominantly manifested in renally excreted drugs. Of particular importance here are antibiotics, and specifically those that need an adequate trough level for optimal efficacy ie non-concentration dependent or time dependent antibiotics. The beta-lactam group of antibiotics are of extreme importance here, as patients with ARC are at risk of under-dosing, predisposing to treatment failure and development of resistant organisms. Therapeutic drug monitoring is one way to avoid such under-dosing.

Suggested Reading:
1. Udy AA, Roberts JA, Boots RJ, Paterson DL, Lipman J. ARC - Augmented Renal Clearance: Implications for Antibiotic Dosing in the Critically Ill. Clin Pharmacokinet 2010;49:1-16.
2. Udy AA, Boots R, Senthuran S, Stuart J, Deans R, Lassig-Smith M, Lipman J. Augmented creatinine clearance in traumatic brain injury. Anesth Analg 2010;111:1505-1510.
3. Udy A, Roberts JA, Boots RJ, Lipman J. You only find what you look for: the importance of high creatinine clearance in the critically unwell. Anaesth Intens Care 2009;37:11-13.
4. Martin JH , Fay MF, Udy A, Roberts JA, Kirkpatrick CMJ, Ungerer J, Lipman J. Pitfalls of using estimations of glomerular filtration rate in an intensive care population. Intern Med J 2011 ; in press
5. Udy AA, Putt MT, Shanmugathasan S, Roberts JA, Lipman J. Augmented renal clearance in the Intensive Care Unit: an illustrative case series. Int J Antimicrob Agents 2010;35:606-608.
6. Roberts JA, Lipman J Pharmacokinetic issues for antibiotics in the critically ill patient. Crit Care Med 2009;37:840-851.
7. Roberts JA, Kruger P, Paterson D, Lipman J. Antibiotic Resistance – What's dosing got to do with it? Crit Care Med 2008;36:2433-2440
8. Roberts JA, Ulldemolins M, Roberts MS, McWhinney B, Ungerer J, Paterson DL, Lipman J. Therapeutic drug monitoring of ,-lactams in critically ill patients: proof of concept. Int J Antimicrob Agents 2010;36:332-339.

Anesthesia and the Microcirculation

Andrew D. Shaw MD FRCA FCCM
2:15-2:30
Wednesday, February 23

Educational Objectives:
1. Understand the effect of anesthetic drugs on the microcirculation.
2. Discuss goal directed fluid therapy as a technique for optimizing surgical outcomes.
3. Discuss the implications of this technique for surgical ICU patients.

Content Description:
The microcirculation is a relatively new space in which the effects of drug therapy and other interventions may be considered. Until recently, direct monitoring of the microcirculation was impossible, and investigators relied on indirect assessment and inference from measurements made in the macrocirculation. The advent of Laser Doppler Flowmetry (LDF), Orthogonal Polarization Spectral (OPS), and Sidestream Dark-Field (SDF) imaging have changed this such that it is now possible to monitor the microcirculation in humans, in real time. Anesthetic drugs and techniques are known to affect microcirculatory physiology, and the importance of microvascular integrity is increasingly appreciated in the field of perioperative medicine. This short talk will establish the thesis that anesthetic drugs and perioperative goal directed fluid therapy are able to protect microcirculatory flow characteristics, and that this in turn translates into preserved perioperative organ function and reduced morbidity in surgical patients.

Dysnatremias In The ICU: Cause For Concern?

Mitchell H. Rosner MD
2:30-2:45
Wednesday, February 23

Educational Objectives:
1. Describe the pathogenesis of acute and chronic hyponatremia
2. Understand the complications associated with hyponatremia and its treatment
3. Describe the role of hypertonic saline and vasopressin receptor antagonists in the therapy of hyponatremia

Content Description:
Hyponatremia is the most common electrolyte abnormality encountered in hospitalized patients. The condition itself as well as improper therapy can lead to serious complications. Recent data also underscores the fact that hyponatremia itself is a powerful indicator of increased morbidity and mortality as well as increased hospital length of stay and costs. The manifestations of hyponatremia are related to changes in cellular volume and function and are largely seen as neurological symptoms ranging from mild encephalopathy to coma. Proper therapy of hyponatremia requires an understanding of the physiology of renal water handling as well as the action of arginine vasopressin. Recent advances in the therapy of hyponatremia include the introduction of drugs that specifically antagonize the actions of vasopressin at the vasopressin receptor located on the cortical collecting duct of the kidney. This session will discuss: (1) the epidemiology and consequences of hyponatremia; (2) the pathogenesis of acute and chronic hyponatremia and (3) the therapy of acute and chronic hyponatremia with a focus on the avoidance of over-correction.

Suggested Reading:
1. Rosner MH. Hyponatremia in heart failure: The role of arginine vasopressin. Cardiovasc Drugs Ther. 2009; 23(4):307-15.

2. King J, Rosner MH. Osmotic demyelination syndrome. Am J Med Sci. 2010;339(6):561-7

3. Ferguson-Myrthil N. Novel agents for the treatment of hyponatremia: A review of Conivaptan and Tolvaptan. Cardiol Rev. 2010;18(6):313-21

4. Sterns RH, Hix JK, Silver S. Treatment of hyponatremia. Curr Opin Nephrol Hypertens. 2010;19(5):493-8.

SPECIAL LECTURE
AKI To CKD Progression: Mechanisms, Pathways and Targets

Joseph V. Bonventre MD, PhD
3:00-3:30
Wednesday, February 23

Educational Objectives:
1. Review the epidemiologic data for effects of AKI on progression of renal disease.
2. Describe the differences in development of fibrosis in a number of models of AKI.
3. Describe how fibrosis is correlated with failure of the surviving proximal tubule cell to progress through the cell cycle and how this results in a pro-fibrotic secretory phenotype.
4. Describe signaling pathways that link cell cycle arrest in G2/M with fibrosis.

Content Description:
After injury the kidney can repair itself. With mild injury this repair can result in return to a functional and structural state that closely reflects the baseline state of the kidney prior to the injury. With severe injury, however, repair can result in chronic inflammation and fibrosis which can ultimately lead to chronic kidney disease. This later outcome may be particularly prominent if there is baseline renal disease prior to the development of AKI. Epidemiological studies have shown that patients with AKI is a powerful force in leading to progression of kidney disease. Recent data have led to a new paradigm of how surviving epithelial cells can potentiate the development of fibrosis and attributes myofibroblast expansion to perivascular and interstitial fibroblasts rather than epithelial to mesenchymal transition (EMT). After severe injury, the proximal tubule cellular proliferative response is abnormal due to cell cycle arrest at the G2/M phase of the cell cycle, resulting in generation of profibrotic factors including cytokines, growth factors and matrix proteins. Dissection of cell signaling pathways points to new targets to therapies to block fibrosis.

Suggested Reading:
1.Bonventre JV. Dedifferentiation and proliferation of surviving epithelial cells in acute renal failure. J Am Soc Nephrol 2003;14(Suppl 1) S55-61.

2. Humphreys BD, Valerius MT, Kobayashi A, Mugford JW, Soeung S, Duffield JS, McMahon AP, Bonventre JV. Intrinsic epithelial cells repair the kidney after injury. Cell Stem Cell 2008;2(3):284-91.

3. Humphreys BD, Lin SL, Kobayashi A, Hudson TE, Nowlin BT, Bonventre JV, Valerius MT, McMahon AP, Duffield JS. Fate tracing reveals the pericyte and not epithelial origin of myofibroblasts in kidney fibrosis. Am J Pathol 2010;176(1):85-97.

4. Yang L, Besschetnova TY, Brooks CR, Shah JV, Bonventre JV. Epithelial cell cycle arrest in G2/M mediates kidney fibrosis after injury. Nat Med 2010;16(5):535-43, 1p following 143.

5.Hsu CY, Chertow GM, McCulloch CE, Fan D, Ordonez JD, Go AS. Nonrecovery of kidney function and death after acute on chronic renal failure. Clin J Am Soc Nephrol 2009;4(5):891-8.

6.Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, Collins AJ. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol 2009;20(1):223-8.

Human AKI: Do We Understand Mechanisms?

Mark D. Okusa MD
4:15-4:30
Wednesday, February 23

Educational Objectives:
1. Describe the pathology of human AKI
2. Discuss experimental models of AKI

Content Description:
The pathogenesis of acute kidney injury (AKI) is complex. A variety of molecular responses occur that are 'maladaptive' and stereotypical. These responses lead to endothelial and epithelial cell injury following the onset of reperfusion. Pathogenic factors such as, vasoconstriction, leukostasis, vascular congestion, apoptosis, and abnormalities in immune modulators and growth factors have formed the basis of rational therapeutic interventions. However, many of these targeted therapies have failed, or are inconclusive. There are a number of factors that have been contributed to these failed human trials including: patient factors and clinical trial design. In addition to these concerns, there is a long-standing concern as to what we really know about human AKI. This presentation will discuss what we know about human AKI and its relation to animal models of AKI.

Suggested Reading:
1. Olsen TS, Hansen HE, Olsen HS. Tubular ultrastructure in acute renal failure: alterations of cellular surfaces (brush-border and basolateral infoldings). Virchows Arch A Pathol Anat Histopathol 1985;406:91-104.
2. Olsen S, Burdick JF, Keown PA, Wallace AC, Racusen LC, Solez K. Primary acute renal failure ("acute tubular necrosis") in the transplanted kidney: morphology and pathogenesis. Medicine (Baltimore) 1989;68:173-87.
3. Lieberthal W, Nigam SK. Acute renal failure. I. Relative importance of proximal vs. distal tubular injury. Am J Physiol 1998;275:F623-31.
4. Ramaswamy D, Corrigan G, Polhemus C, et al. Maintenance and recovery stages of postischemic acute renal failure in humans. Am J Physiol Renal Physiol 2002;282:F271-80.
5. Solez K, Morel-Maroger L, Sraer JD. The morphology of 'acute tubular necrosis' in man: analysis of 57 renal biopsies and a comparison with the glycerol model. Medicine (Baltimore) 1979;58:362-76.
6. Myers BD, Miller DC, Mehigan JT, et al. Nature of the renal injury following total renal ischemia in man. J Clin Invest 1984;73:329-41.
7. Byrick RJ, Rose DK. Pathophysiology and prevention of acute renal failure: the role of the anaesthetist. Can J Anaesth 1990;37:457-67.

Oxygen, Hydrogen and Carbon Monoxide Gases with Therapeutic Potential?

Anupam Agarwal MD
4:30-4:45
Wednesday, February 23

Educational Objectives:

1. Describe the pathways that lead to generation of gaseous molecules with potential for therapy in acute kidney injury.
2. Discuss the pathogenetic mechanisms of protection offered by gaseous mediators in acute kidney injury.
3. Discuss therapeutic potential of gaseous mediators in acute kidney injury.

Content Description:
Gases such as oxygen, hydrogen and carbon monoxide are intricately associated with the environment. However, these mediators are also produced or degraded endogenously to produce molecules with potent biological properties. The breakdown of oxygen leads to the generated of a variety of reactive oxygen species such as superoxide and hydrogen peroxide. Molecular hydrogen, the most abundant molecule in the universe, has potent protective effects in kidney injury models, actions that are mediated through scavenging effects on reactive oxygen species. Carbon monoxide is produced through the enzymatic reaction catalyzed by the heme oxygenase-1 enzyme during heme degradation and has shown to be protective in numerous models of inflammation, ischemia-reperfusion injury and immune-mediated rejection. This presentation will discuss the pathways through which these gases molecules are generated or broken down and their biological functions in the context of acute kidney injury.

Suggested Reading:
George JF, Agarwal A. Hydrogen: another gas with therapeutic potential. Kidney Int. 2010 Jan;77:85-7.

Cardinal JS, Zhan J, Wang Y, Sugimoto R, Tsung A, McCurry KR, Billiar TR, Nakao A. Oral hydrogen water prevents chronic allograft nephropathy in rats. Kidney Int. 2010 Jan;77(2):101-9.

Jarmi T, Agarwal A.cHeme oxygenase and renal disease. Curr Hypertens Rep. 2009 Feb;11(1):56-62.

Vera T, Henegar JR, Drummond HA, Rimoldi JM, Stec DE. Protective effect of carbon monoxide-releasing compounds in ischemia-induced acute renal failure. J Am Soc Nephrol. 2005 Apr;16(4):950-8.

Ryter SW, Choi AM. Heme oxygenase-1/carbon monoxide: novel therapeutic strategies in critical care medicine. Curr Drug Targets. 2010 Dec;11(12):1485-94.

Abid MR, Razzaque MS, Taguchi T. Oxidant stress in renal pathophysiology. Contrib Nephrol. 2005;148:135-53.

Cardio Renal Syndrome It's Time to Use Biomarkers

John L. Jefferies MD
5:15-5:30
Wednesday, February 23

Educational Objectives:
1. Describe the currently used biomarkers in heart failure and kidney injury
2. Describe the current utility of biomarkers in heart failure and kidney injury
3. Describe the practical issues of using biomarkers for clinical decision making and research trials

Content Description:
The cardiorenal syndrome is an intricate clinical interplay between the heart and the kidneys which may be from acute or chronic insult primarily in the heart, the kidneys, or systemic processes. The cardiac contributions are often secondary to myocardial dysfunction resulting in the clinical findings of heart failure. Heart failure is a complex clinical syndrome that results in significant neurohormonal and inflammatory upregulation. Evidence of this upregulation can be measured clinically through the use of biomarkers such as B-type natriuretic peptide (BNP) and troponins. Similarly, kidney injury results in biomarkers that are easily measured such as neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C. These biomarkers have significant clinical implications regarding screening, timing of appropriate interventions, and prognosis. Furthermore, these biomarkers serve as very sensitive tests that allow them to play important roles in clinical trials in both adult and pediatric investigation.

Suggested Reading:
1. Ronco C, Ronco F: Cardio-renal syndromes: a systematic approach for consensus definition and classification. Heart Fail Rev. 2011 Jan 1.

2. Maisel AS, Katz N, Hillege HL, Shaw A, Zanco P, Bellomo R, Anand I, Anker SD, Aspromonte N, Bagshaw SM, Berl T, Bobek I, Cruz DN, Daliento L, Davenport A, Haapio M, House AA, Mankad S, McCullough P, Mebazaa A, Palazzuoli A, Ponikowski P, Ronco F, Sheinfeld G, Soni S, Vescovo G, Zamperetti N, Ronco C, Acute Dialysis Quality Initiative consensus group: Biomarkers in kidney and heart disease. Nephrol Dial Transplant. 2011 Jan:26(1)62-74.

3. Devarajan P:Biomarkers for the early detection of acute kidney injury. Curr Opin Pediatr. 2011 Jan 19.

4. Braunwald E: Biomarkers in heart failure. N Engl J Med. 2008 May 15;358(20)2148-59.

5. Seta Y, Shan K, Bozkurt B, Oral H, Mann DL: Basic mechanisms in heart failure: the cytokine hypothesis. J Card Fail. 1996 Sep;2(3):243-9.

6. Bennett MR, Devarajan P:Proteomic analysis of acute kidney injury: Biomarkers to mechanisms. Proteomics Clin Appl. 2011 Feb;5(1-2):67-77.

7. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michi K, Oates JA, Rahko PS, Silver MR, Stevenson LW, Yancy CW; American College of Cardiology Foundation; American Heart Association: 2009 Focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the International Society for Heart and Lunch Transplantation. J Am Coll Cardiol. 2009 Apr 14;53(15):e1-e90.

Do Genes Matter in Acute Kidney Injury?

Andrew D. Shaw MD FRCA FCCM
5:30-5:45
Wednesday, February 23

Educational Objectives:
1. Discuss the methods available for understanding complex trait genetic associations.
2. Review positive GWAS findings in CKD and their relevance for AKI.
3. Review the role of MCP 1 variants in susceptibility to AKI.

Content Description:
The common disease-common variant paradigm for complex trait genetic association has dominated the field of human genetics for a decade or more. However, GWAS investigations have failed to explain the genetic determinants of the majority of heritable traits. This has lead some investigators to suggest that in fact it is rare variants with relatively large effects (inherited within families) that are actually responsible, and that these cannot be fully appreciated without fine sequencing regions of interest.

In kidney disease, there have been positive reports of genetic determinants of glomerular filtration rate in CKD, and susceptibility to other chronic renal diseases. There has not been a positive GWAS in AKI however, despite some early positive (but subsequently unreplicated) candidate studies.

New biomarker discovery studies are pointing to previously unappreciated targets, such as MCP 1, in AKI, and the expression levels of some of these have been shown to be affected by genetic variation.

In this short lecture we will review the complex trait investigator's toolkit, the positive GWAS data (and what they mean for AKI), and the newly described place of MCP 1 in AKI susceptibility.

SPECIAL SESSION
Critical Care Nephrology Jeopardy

Noel Gibney MD
6:00-6:30
Wednesday, February 23

Educational Objectives:
To review and answer a variety of knowledge testing questions on Critical Care Nephrology.

Content Description:
This first episode of Critical Care Nephrology Jeopardy will see a team of 3 nephrologists and 3 intensivists square off against each other and answer questions on critical care nephrology.

Nephrology Team:
Ashita Tolwani, Emil Paganini, Claudio Ronco

Intensivists Team:
John Kellum, Andrew Shaw, Miet Schetz

NOTES

Renal Angina: A New Paradigm for AKI

Stuart L. Goldstein MD
7:30-7:45
Thursday, February 24

Educational Objectives:

1. Highlight the challenges of early modifiable acute kidney (AKI) diagnosis given the lack of actionable signs or symptoms of early AKI
2. Describe the concept of Renal Angina in terms of an AKI risk-stratification system to direct evaluation and management
3. Present the published empiric Renal Angina tranches, a set of testable hypothesis for risk stratification to direct AKI biomarker assessment
4. Present preliminary pediatric data assessing the Renal Angina tranches to predict AKI development

Content Description:

Small elevations in serum creatinine may reflect significant kidney damage and be associated with poor patient outcomes, thus rendering creatinine to be a late marker of acute kidney injury (AKI). AKI researchers refer to the AKI biomarker quest as the "search for the renal troponin I," implying that such putative earlier AKI biomarker use could allow for earlier intervention. The analogy to troponin I and its acceptance to prompt evaluation and therapeutic intervention to treat myocardial ischemia and prevent myocardial infarction an informative and potentially applicable model to the AKI field. Because AKI does not hurt, there is no validated equivalent of chest pain or anginal equivalent to increase suspicion for AKI presence on the part of the clinician. So, although biomarkers may ultimately be validated to detect AKI early, unless nephrologists and intensivists can define "renal angina" to initiate "renal troponin I" assessments, AKI biomarkers may never realize their full potential to improve patient care and outcomes. This presentation will review the data leading to the Renal Angina tranche development and review an initial study testing the Renal Angina construct.

Suggested Reading:

1. Goldstein SL, Chawla LS. Renal angina. Clin J Am Soc Nephrol 2010;5:943-9.
2. Chawla LS, Seneff MG, Nelson DR, et al. Elevated plasma concentrations of IL-6 and elevated APACHE II score predict acute kidney injury in patients with severe sepsis. Clin J Am Soc Nephrol 2007;2:22-30.
3. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int 2007;71:1028-35.
4. Levy MM, Macias WL, Vincent JL, et al. Early changes in organ function predict eventual survival in severe sepsis. Crit Care Med 2005;33:2194-201.
5. Sutherland SM, Zappitelli M, Alexander SR, et al. Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 2010;55:316-25.

Recovery From AKI: Determinants and Predictors - Lessons from the ATN Trial

John A. Kellum MD
7:45-8:00
Thursday, February 24

Educational Objectives:
1. To review the clinical course of AKI and recovery
2. To discuss mechanisms of renal recovery
3. To review evidence on the role of clinical and biomarker data on clinical risk prediction for recovery after AKI

Content Description:
Sepsis is a leading cause of acute kidney injury (AKI) in hospitalized patients,1-5 and development of AKI is associated with increased risk of death.3, 5 Recent studies of patients with AKI in which sepsis was the main contributing factor for AKI, demonstrated that a large number of survivors failed to recover renal function. First, the Beginning and Ending Supportive Therapy for the kidney study showed that 13.8% of patients with severe AKI require renal replacement therapy at hospital discharge.1 Second, the Acute Renal Failure Trial Network study revealed that only 16% of participants were alive and free of renal replacement therapy by hospital discharge, and only 25% by day 60.6 These findings emphasize the need for exploring interventions to improve outcomes following AKI.

However, in order to design interventions for AKI it is important to distinguish patients at risk for failure to recover kidney function from those who are likely to spontaneously recover renal function. Such early risk stratification has important therapeutic implications such as to enroll a homogenous group of patients in clinical trials of AKI, to determine the timing of initiation of renal replacement therapy in those with severe AKI, and withdraw care in those who are likely to have poor prognosis. However existing clinical severity scores for AKI,7-12 have neither high levels of discrimination nor calibration to predict renal recovery.13 On the other hand emerging newer biomarkers of AKI could aid in risk stratification analogous to biomarkers of cardiovascular disease.14, 15

Neutrophil gelatinase-associated lipocalin (NGAL) is emerging as an important biomarker for early detection of AKI in various settings,16-31 including sepsis-induced AKI,24 and would be a logical choice to evaluate for prediction of recovery. In addition, our prior work has suggested that plasma interleukin (IL)-6, a proinflammatory molecule, was strongly associated with sepsis-induced AKI.32 However, neither plasma NGAL (pNGAL) nor IL-6 has been evaluated as a marker of outcome following AKI. Therefore, we examined whether pNGAL or IL-6 is a useful biomarker for predicting failure to recover in a multicenter, prospective cohort study of patients with severe AKI associated with community-acquired pneumonia. We chose community-acquired pneumonia because it is a leading cause of AKI and a common infectious cause of hospitalization.33
Using the widely validated Risk, Injury and Failure (RIFLE) criteria to define AKI, we performed the following analyses. First, among patients with severe AKI (RIFLE-F), we performed an outcome-stratified analysis of baseline characteristics of patients who recovered renal function from those who did not. Recovery was defined as alive and neither requiring renal replacement therapy during hospitalization, nor having persistent RIFLE-F at hospital discharge. Second, we examined differences in pNGAL and IL-6 concentration by recovery status. Third, we examined whether pNGAL predicted failure to recover after adjusting for differences in demographics, severity of illness, process of care and within the strata of risk categories for non-recovery. Fourth, we assessed the contribution of pNGAL to a clinical model in reclassifying recovery using net reclassification index (NRI) and tested the percentage of correct reclassification for each risk category.

Suggested Reading:
1. Uchino, S, Kellum, JA, Bellomo, R, Doig, GS, Morimatsu, H, Morgera, S, Schetz, M, Tan, I, Bouman, C, Macedo, E, Gibney, N, Tolwani, ARonco, C: Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA, 294: 813-8, 2005.

2. Bagshaw, SM, Uchino, S, Bellomo, R, Morimatsu, H, Morgera, S, Schetz, M, Tan, I, Bouman, C, Macedo, E, Gibney, N, Tolwani, A, Oudemans-van Straaten, HM, Ronco, CKellum, JA: Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clin J Am Soc Nephrol, 2: 431-9, 2007.

3. Palevsky, PM, Zhang, JH, O'Connor, TZ, Chertow, GM, Crowley, ST, Choudhury, D, Finkel, K, Kellum, JA, Paganini, E, Schein, RM, Smith, MW, Swanson, KM, Thompson, BT, Vijayan, A, Watnick, S, Star, RAPeduzzi, P: Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med, 359: 7-20, 2008.

4. Mehta, RL, Pascual, MT, Gruta, CG, Zhuang, SChertow, GM: Refining predictive models in critically ill patients with acute renal failure. J Am Soc Nephrol, 13: 1350-7, 2002.

5. Uchino, S, Bellomo, R, Morimatsu, H, Morgera, S, Schetz, M, Tan, I, Bouman, C, Macedo, E, Gibney, N, Tolwani, A, Doig, GS, Oudemans van Straaten, H, Ronco, CKellum, JA: External validation of severity scoring systems for acute renal failure using a multinational database. Crit Care Med, 33: 1961-7, 2005.

6. Cruz, DN, de Cal, M, Garzotto, F, Perazella, MA, Lentini, P, Corradi, V, Piccinni, PRonco, C: Plasma neutrophil gelatinase-associated lipocalin is an early biomarker for acute kidney injury in an adult ICU population. Intensive Care Med, 36: 444-51.

7. Murugan, R, Karajala-Subramanyam, V, Lee, M, Yende, S, Kong, L, Carter, M, Angus, DC, Kellum, JA: Acute kidney injury in non-severe pneumonia is associated with an increased immune response and lower survival. Kidney Int, 77: 527-35, 2010

How Should We Define Recovery from AKI?

Ravindra L. Mehta MBBS, MD, DM, FACP
8:00-8:15
Thursday, February 24

Educational Objectives:
1. Understand current concepts of renal recovery

2. Define parameters that should be considered for renal functional recovery and identify factors influencing renal functional recovery after AKI

3. Describe various approaches and practical aspects for defining recovery form AKI and key issues to be addressed in future trials

Content Description:
Renal recovery after acute kidney injury (AKI) is an important outcome, most commonly defined as dialysis independence at hospital discharge. Currently there is no standardized definition of renal recovery following an episode of AKI. In most studies, renal recovery has been linked to a return of renal function to "baseline". However, this is strongly conditioned by underlying kidney disease and what is considered "baseline". Additionally the magnitude of renal recovery is usually linked to arbitrary cut points ranging from dialysis dependence to achieving serum creatinine levels within a few percent points of baseline. Current studies have also been limited to evaluating GFR changes as the pertinent criteria for recovery without consideration of additional elements of renal function. Finally, the time to recovery and patterns of recovery are not well described. This lecture focuses on the epidemiology of renal recovery after AKI and provides a framework for determining renal recovery after AKI and defining the relationship of a lack of renal recovery and subsequent outcomes including the development of chronic kidney disease.

Suggested Reading:
1. Siew ED, Matheny ME, Ikizler TA, Lewis JB, et al. Commonly used surrogates for baseline renal function affect the classification and prognosis of acute kidney injury. Kidney Int 2009.
2. Endre ZH, Pickering JW. Outcome definitions in non-dialysis intervention and prevention trials in acute kidney injury (AKI). Nephrol Dial Transplant 25: 107-118.
3. Palevsky PM, O'Connor TZ, Chertow GM, Crowley ST, et al. Intensity of renal replacement therapy in acute kidney injury: perspective from within the Acute Renal Failure Trial Network Study. Crit Care 2009; 13: 310.
4. Waikar SS, Liu KD, Chertow GM. Diagnosis, epidemiology and outcomes of acute kidney injury. Clin J Am Soc Nephrol 2008; 3: 844-861.
5. Waikar SS, Bonventre JV. Creatinine kinetics and the definition of acute kidney injury. J Am Soc Nephrol 2009; 20: 672-679.
6. Liu KD, Glidden DV. Clinical trials for acute kidney injury: design challenges and possible solutions. Curr Drug Targets 2009; 10: 1190-1195.
7. Mehta RL. Outcomes research in acute renal failure. Semin Nephrol 2003; 23: 283-294.
8. Macedo E, Bouchard J, Mehta RL. Renal recovery following acute kidney injury. Curr Opin Crit Care 2008; 14: 660-665.
9. Bagshaw SM, Uchino S, Cruz D, Bellomo R, et al. A comparison of observed versus estimated baseline creatinine for determination of RIFLE class in patients with acute kidney injury. Nephrol Dial Transplant 2009; 24: 2739-2744.
10. Bagshaw SM, Mortis G, Godinez-Luna T, Doig CJ, et al. Renal recovery after severe acute renal failure. Int J Artif Organs 2006; 29: 1023-1030.
11. Bell M. Acute kidney injury: new concepts, renal recovery. Nephron Clin Pract 2008; 109: c224-228.
12. Block CA, Schoolwerth AC. Acute renal failure: outcomes and risk of chronic kidney disease. Minerva Urol

Nefrol 2007; 59: 327-335.
13. Franzen D, Rupprecht C, Hauri D, Bleisch JA, et al. Predicting outcomes in critically ill patients with acute kidney injury undergoing intermittent hemodialysis--a retrospective cohort analysis. Int J Artif Organs 33: 15-21.
14. Goldberg R, Dennen P. Long-term outcomes of acute kidney injury. Adv Chronic Kidney Dis 2008; 15: 297-307.
15. Hayes LW, Oster RA, Tofil NM, Tolwani AJ. Outcomes of critically ill children requiring continuous renal replacement therapy. J Crit Care 2009; 24: 394-400.
16. Hsu CY, Chertow GM, McCulloch CE, Fan D, et al. Nonrecovery of kidney function and death after acute on chronic renal failure. Clin J Am Soc Nephrol 2009; 4: 891-898.
17. Liu KD, Brakeman PR. Renal repair and recovery. Crit Care Med 2008; 36: S187-192.
18. Mehta RL, Pascual MT, Soroko S, Savage BR, et al. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney Int 2004; 66: 1613-1621.
19. Schiffl H, Fischer R. Five-year outcomes of severe acute kidney injury requiring renal replacement therapy. Nephrol Dial Transplant 2008; 23: 2235-2241.
20. Schmitt R, Coca S, Kanbay M, Tinetti ME, et al. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. Am J Kidney Dis 2008; 52: 262-271.
21. Swaminathan M, Hudson CC, Phillips-Bute BG, Patel UD, et al. Impact of early renal recovery on survival after cardiac surgery-associated acute kidney injury. Ann Thorac Surg 89: 1098-1104.
22. Thakar CV, Christianson A, Freyberg R, Almenoff P, et al. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. Crit Care Med 2009; 37: 2552-2558.

Severity of AKI and Progression to CKD: Can We Intervene?

Lakhmir S. Chawla MD
8:15-8:30
Thursday, February 24

Educational Objectives:
1. Describe the risk of progression to chronic kidney disease in survivors of acute kidney injury
2. Describe the patients who are at greatest risk for progression to AKI
3. Understand the potential pathophysiologic mechanisms of progression

Content Description:
Acute Kidney Injury (AKI) has been shown to be associated with progression to chronic kidney disease (CKD). Multiple studies have shown that subsets of AKI survivors are at high risk for progression to advanced stage CKD and death. Risk factors associated with AKI survivors progressing to CKD have been identified and include: advanced age, diabetes mellitus, decreased baseline eGFR, severity of AKI, and a low concentration of serum albumin. These risk factors can be utilized to identify those patients at highest risk for progression. Because the progression to CKD in these AKI survivors typically occurs months after the initial AKI insult, a common injury pathway of CKD progression is probable, and therapeutic interventions that have been shown to forestall CKD progression are likely to be effective in patients who suffer AKI and then progress to CKD.

Suggested Reading:

1. Amdur RL, Chawla LS, Amodeo S, et al. Outcomes following diagnosis of acute renal failure in U.S. veterans: focus on acute tubular necrosis. Kidney Int 2009; 76: 1089-1097.

2. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. JAmSocNephrol 2009; 20: 223-228.

3. Lo LJ, Go AS, Chertow GM, et al. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. Kidney Int 2009; 76: 893-899.

4. Wald R, Quinn RR, Luo J, et al. Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. JAMA 2009; 302: 1179-1185.

5. Chawla LS, Amdur, RL, Amodeo, S, Kimmel, PL, Palant C. Severity of Acute Kidney Injury Predicts Progression to Chronic Kidney Disease: Validation of a Risk Score. in press Kidney International 2011.

6. Chawla LS, Seneff MG, Nelson DR, et al. Elevated plasma concentrations of IL-6 and elevated APACHE II score predict acute kidney injury in patients with severe sepsis. ClinJAmSocNephrol 2007; 2: 22-30.

7. Liu KD, Glidden DV, Eisner MD, et al. Predictive and pathogenetic value of plasma biomarkers for acute kidney injury in patients with acute lung injury*. Crit Care Med 2007.

8. Sutton TA, Mang HE, Campos SB, et al. Injury of the renal microvascular endothelium alters barrier function after ischemia. Am J Physiol Renal Physiol 2003; 285: F191-198.

Minimizing the Effect of AKI on CKD Progression

Bruce A. Molitoris MD
8:30-8:45
Thursday, February 24

Educational Objectives:
1. Discuss how CKD is the most important risk factor for developing AKI
2. Indicate how AKI likely leads to CKD and its progression.
3. Discuss how preventing AKI in CKD patients undergoing proceedures at risk of causing AKI may provide important protection for limiting progression.

Content Description:
Recent evidence from experimental and clinical investigations indicates repeated AKI episodes trigger CKD and accelerate its progression to ESRD. Thus, prevention of AKI may minimize CKD development and reduce its progression to ESRD. As we have previously shown that siRNA against P53 (siP53) minimized ischemia/reperfusion AKI, we assessed whether its use during repeated AKI would limit CKD progression. First, we tested whether siP53 was capable of preventing CKD development caused by recurrent ischemia. Male SD rats underwent 5 recurrent (at monthly interval) 45 min bilateral renal pedicle clamp followed by i.v. injection of siP53. Each consecutive AKI cycle resulted in higher SCr levels in untreated rats but not in siP53 treated rats. Ten days after the fifth AKI, untreated AKI rats displayed lower 24 hr GFR ($p<0.01$) and more advanced proteinuria and histological signs of CKD than siP53-treated ($p< 0.01$). We next investigated the efficacy of siP53 in minimizing AKI exacerbation of CKD with pre-existing CKD. CKD was induced in SD rats by unilateral nephrectomy, followed by 3-4 bimonthly cycles of AKI with rats on high salt diet. When CKD was confirmed (high SCr, proteinuria and low GFR), rats were subjected to AKI (40 min clamp) followed by treatment with either control siRNA or siP53. Dynamics of post-AKI changes of SCr indicated treatment with siP53 markedly attenuated AKI and lead to a rapid return of increased SCr levels to baseline. In contrast, SCr levels in control siRNA treated CKD rats reached 2-fold higher levels of SCr as a result of AKI and SCr remained elevated for at least one week. Histopathological evaluation showed less signs of both AKI and CKD in siP53-treated rats($p< 0.01$). Thus, prevention of AKI minimized the development of CKD and progression of CKD in a proteinuric CKD model. These data have important clinical implications regarding preventative strategies for AKI especially in CKD patients.

Suggested Reading:
1. Preexisting chronic kidney disease: a potential for improved outcomes from acute kidney injury. Khosla N, Soroko SB, Chertow GM, Himmelfarb J, Ikizler TA, Paganini E, Mehta RL; Program to Improve Care in Acute Renal Disease (PICARD). Clin J Am Soc Nephrol. 2009 Dec;4(12):1914-9. Epub 2009 Nov 25.

2. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. Lo LJ, Go AS, Chertow GM, McCulloch CE, Fan D, Ordoñez JD, Hsu CY. Kidney Int. 2009 Oct;76(8):893-9. Epub 2009 Jul 29

3. Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, Collins AJ: Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol. 2009 Jan;20(1):223-8.

4. Xue JL, Daniels F, Star RA, Kimmel PL, Eggers PW, Molitoris BA, Himmelfarb
J, Collins AJ: Incidence and Mortality of Acute Renal Failure in Medicare Beneficiaries, 1992 to 2001. J Am Soc Nephrol 17:1135-42, 2006.

AKI to CKD in Children, They Grow Up to be Adults with CKD

Prasad Devarajan MD
8:45-9:00
Thursday, February 24

Educational Objectives:
1. Discuss the evidence for AKI to CKD transition in animal models
2. Discuss the evidence for AKI to CKD transition in children
3. Discuss the role of biomarkers for prediction of AKI to CKD transition

Content Description:
This presentation will discuss the evidence for progression from AKI to CKD in animal models and in children. The presentation will then explore some of the emerging mechanisms, and the role of biomarkers in predicting this transition.

Suggested Reading:
1. Devarajan P. The use of targeted biomarkers for chronic kidney disease. Adv Chronic Kidney Dis. 2010;17(6):469-79.
2. Goldstein SL, Devarajan P. Acute kidney injury in childhood: should we be worried about progression to CKD? Pediatr Nephrol. 2010 Oct 10. [Epub ahead of print]
3. Venkatachalam MA, Griffin KA, Lan R, Geng H, Saikumar P, Bidani AK. Acute kidney injury: a springboard for progression in chronic kidney disease. Am J Physiol Renal Physiol. 2010 Mar 3. [Epub ahead of print]

Drug Dosing in RRT: Do We Under Deliver?

Jeffrey Lipman MD
10:15-10:30
Thursday, February 24

Educational Objectives:

1. Understand that CRRT encompasses different modalities and is not standardised across centres

2. Understand that drug elimination across the artificial kidney can be predicted, but due to differing CRRT modalities in the ICU is not always accounted for and often difficult to quantify,

3. Understand the factors in the critically ill relating to drug movement across membranes.

Content Description:

The systems and technology for Intermittent Hemo Dialysis (IHD) across the world have been relatively well defined, as have the prescriptions for the patient with chronic renal failure (CRF). What happens in one place is relatively similar to that in another.

The basic principles of movement of drugs across the artificial kidney include membrane characteristics, drug size and the sieving co-efficient of the drug for that circuit .Drug dosing before and after IHD has a relatively well validated set of rules.

Whilst drug and patient variables tend to be constant in the populations with CRF neither is the circuitry nor are the patients in the ICU similar.

Importantly pharmacokinetic variables in the critically ill patient such as volume of distribution and protein binding complicate any prescription and this is particularly important for antibiotic prescriptions where drug cannot be titrated to a measurable endpoint like blood pressure or heart rate.

The various modalities in which CRRT have been used (CVVH vs CVVHD vs CVVHDF vs SLED) makes a one size fits all cookbook recipe impossible to prescribe.

Until we can routinely use therapeutic drug monitoring the best we have are predictive models for drug prescribing. Only by understanding critical illness pathophysiology, drug pharmacokinetics and artificial membrane characteristics we can we expect to improve the accuracy of these models. Unless there is titratable endpoint of a drug during CRRT,currently the best cookbook recipe we have are complicated predictive algorithms.

Suggested Reading:

1. Gibney RT, Kimmel PL, Lazarus M. The Acute Dialysis Quality Initiative--part I: definitions and reporting of CRRT techniques. Adv Ren Replace Ther 2002;9:252-254
2. Cerda J, Ronco C. Modalities of continuous renal replacement therapy: technical and clinical considerations. Semin Dial 2009;2:114-122.
3. Roberts JA, Lipman J Pharmacokinetic issues for antibiotics in the critically ill patient. Crit Care Med 2009;37:840-851.
4. Choi G Gomersall CD, Tian Q, Joynt GM, Freebairn RC, Lipman J. Principles of antibacterial dosing in continuous renal replacement therapy. Crit Care Med 2009;37:2268-2282.
5. Roberts JA, Kruger P, Paterson D, Lipman J. Antibiotic Resistance – What's dosing got to do with it? Crit Care Med 2008;36:2433-2440.
6. Ulldemolins M, Roberts JA, Rello J, Paterson DL, Lipman J. The effects of hypoalbuminaemia on optimizing antibiotic dosing in critically ill patients. Clin Pharmacokinet 2011;50:99-110.

Large RCT's in RRT: What Can Be Learned for Nursing

Ian Baldwin RN, PhD, ACCCN
10:30-10:45
Thursday, February 24

Educational Objectives:

1. To review the key demographic and other findings of large CRRT trials effect of investigation 'dose'.
2. To consider these study findings as useful to compare or assess unit performance.
3. To reveal key areas of interest for CRRT nursing and how these may further improve application of CRRT in the future.

Content Description:

The relationship between 'dose' (effluent mL/kg/hr) and patient mortality has been assessed in several large randomized controlled trials. Methods used and findings from large randomized controlled CRRT trials can provide useful information and a focus for improving nursing application of therapies in the ICU. The RRT dose studies whether alone, or after meta-analysis enable benchmarking for a number of variables related to the application of CRRT in the ICU. For example, patient age, diagnosis, weight, illness score, treatment start time and duration, recovery, baseline biochemistry etc. can be useful to review and compare to your centre's best practice. Critical analysis of these studies reveals difficulties achieving prescribed dose, hypotensive episodes, and hypophosphataemia. All of these problems can be minimized by skilled nursing management and are useful targets for protocol revision and improving CRRT in the future.

Accurate patient weight was important for prescription and was estimated in many centers even though it is known to correlate poorly with measured weight. Patient weight measurement should now become a daily nursing procedure; in many centers this variable was previously unknown or estimated. Adverse outcomes have been reported from undetected weight gain during CRRT suggesting daily weight should be recorded along with the daily prescription orders. In addition, as dose was also measured by effective treatment time, hours of filter/circuit function is also an important variable to measure and report routinely. This can also be a measure for success of anticoagulation methods and nursing expertise especially when associated with the 'off time' or time to change and restart a treatment. Interruptions to CRRT occur due to procedures in and out of the ICU. When poor planning and scheduling occurs, 'off time' for these can reduce treatment time and dose significantly. Related to this variable is the definition of clotting or circuit failure. This is determined by the bedside nurse managing the CRRT and is often poorly or loosely defined or assessed by study protocols. Determining the best indicator of this event for a study protocol and nurses using CRRT is an important quality improvement step.

Hypotension was also reported as an adverse event, may have influenced outcome findings, and has many possible causes in the critically ill. However hypotension can be caused by CRRT and is more likely if cardiac failure exists. Other factors contribute to RRT hypotension such as rapid fluid loss prescription, inappropriate extracorporeal circuit and blood flow settings, starting a treatment to quickly, poor patient and therapy fluids temperature management, poor access catheter placement, and suboptimal vasoactive infusions use. Skilled use of CRRT can reduce hypotensive events from the above causes.

Low phosphate levels was a further finding, more prevalent in the high intensity treatment groups. This may have also influenced study findings unless corrected. As with potassium management, nurses can also prevent this during CRRT with monitoring and appropriate replacement protocols.

As reflected in the publications it is also evident that different machines were used, in different centers and that terminology to describe a treatment prescription varied. In the dose studies, fluid removal rate as effluent (mL/kg/Hr) was the independent variable, but how this was achieved with a CRRT machine, and within the existing protocols and culture of an ICU varied considerably. No doubt start up meetings to clarify the application of the study protocol was done on initiation of the study in every centre. This highlights the need to review

nomenclature and increase understanding of how a prescription, and language used needs to match the machines settings and terminology used; e.g. effluent, ultra filtrate, turnover, exchange, dia-filtrate, waste flow, waste volume. Unless these terms are clarified, errors can occur.

A more positive perspective is to acknowledge that for the five large trials completed and reviewed for this abstract (2 multicentre and 3 single centre) devoted to dose, effectively using low and high volume haemofiltration, 3628 critically ill patients were treated with a low complication rate. This is a testament to the advances in nursing expertise, and machine technology in the field of CRRT.

Suggested Reading:

1. Bouchard J, Macedo E and Mehta R. 2010. Dosing of Renal Replacement Therapy in Acute Kidney Injury: Lessons learned from clinical trials. American Journal of kidney Diseases. Vol. 55. No. 3 pp. 570 – 579.
2. Cerda J, Sheinfeld G and Ronco C. 2010. Fluid overload in Critically Ill Patients with Acute Kidney Injury. Blood Purif. 29; 331-338.
3. Fülöp, Tibor Pathak, Minesh B, Schmidt, Darren W, Lengvárszky, Zsolt Juncos, Julio P Lebrun, Christopher J, Brar, Harjeet, Juncos, Luis A. 2010. Volume-Related Weight Gain and Subsequent Mortality in Acute Renal Failure Patients Treated With Continuous Renal Replacement Therapy. ASAIO Journal; Volume 56 - Issue 4 - pp 333-337.
4. Schiffl H. 2010. The dark side of high-intensity renal replacement therapy of acute kidney injury in critically ill patients. International Urol. Nephrology. 42: 435-440.
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6. Saudan P, Niederberger M, De Seigneux S, et al. 2006. Adding a dialysis dose to continuous hemofiltration increases survival in patients with acute renal failure. Kidney Int. 70: 1312-1317.
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8. Bellomo R, Ronco C, Mehta R. 1996. Nomenclature for continuous renal replacement therapies. Am J Kidney Dis;28(suppl 3):S2-S7.
9. RENAL Replacement Therapy Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lo S, McArthur C, McGuinness S, Myburgh J, Norton R, Scheinkestel C, Su S. 2009. Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med. Oct 22;361(17):1627-38.
10. Palevsky PM, O'Connor TZ, Chertow GM, Crowley ST, Zhang JH, Kellum JA; US Department of Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network. 2009. Intensity of renal replacement therapy in acute kidney injury: perspective from within the Acute Renal Failure Trial Network Study. Crit Care.;13(4):310. Epub 2009 Aug 11.
11. Ostermann M, Chang RW. 2010. Intensity of continuous renal-replacement therapy. N Engl J Med. Feb 4;362(5):466; author reply 467-8.

Combination Therapies for Renal Support: The Japanese Experience

Kazo Kaizu MD
10:45-11:00
Thursday, February 24

Educational Objectives:
1. Describe the number of blood purification therapy (BPT) performed and disease treated with BPT in hospitals with both more than 200 beds and intensive care units in a year of 2009 in Japan.
2. Describe efficacy and mortality of BPT in each mode of BPT and disease.
3. Describe efficacy and mortality of BPT in each stage of AKIN classified by RIFE criteria.

Content Description:
1. The number of doctors who receive questionnaires was 50 in all over Japan (Recovery rate 53.8%).
2. The number of patients treated with BPT was 2010 (M/F : 1266 / 738).
3. The number of BPT performed was 2,561.
4. The number of each mode of BPT were as follows :
   - CRRT : 1,357 (53.0%)
   - Plasma exchange : 175 (7.0%)
   - Direct hemoperfusion : 380 (16.0%)
   - PMX-DHP(DHP with polymixin-B coated textile) : 373 (16.0%)
   - AC-DHP(DHP with activated carbon) : 17 (1.0%)
5. The number of disease treated with BPT were as follows :
   - MOF : 117
   - ARF : 426
   - Sepsis : 188
   - Acute hepatic failure : 49
6. 28-days of survival rates of patients with different organ-failure were as follows :

No of organ-failure	Survival rate (%)
1	73.5
2	72.1
3	59.1
4	36.4
5	42.9
6	33.3

7. 28-days of survival rate of CRRT in each stage of AKI were as follows :

Stage	%
Risk	27.3
Injury	46.2
Failure	40.0

Peritoneal Dialysis in AKI: A Viable Alternative

Daniela Ponce MD
11:15-11:30
Thursday, February 24

Educational Objectives:
1. To understand the scientific rational for indications and no indications of PD in AKI
2. To discuss different PD types and doses for AKI patients and to compare it to other dialysis methods
3. To define the role of PD in AKI patients

Content Description:
PD is and can be utilized with success for the treatment of a selected group of AKI patients. There is still a rationale for the use of PD in critically ill patients, especially in those countries where more sophisticated technologies are not available.
To overcome PD limitations, as the risk of peritoneal infection, occurrence of protein losses and a limited capacity to modulate fluid and solute removal, an adequate prescription of high volume continuous PD, with a dwell time of approximately 1 hour, using a flexible PD catheter, an automated PD cycler and higher glucose concentrations may contribute to providing adequate treatment in AKI patients, who have not presented absolute or relative contra-indications for PD use.
These techniques might help to maintain PD as a suitable alternative for the treatment of AKI, comparable to other dialysis method.

Presentation Outline

1. Is PD used? Where?
2. Can PD be used in AKI? Why?
4. When to indicate it? For whom patients?
5. How to prescribe it?
6. Is it better or worsen than other methods?
7. What is the real role of PD in AKI patients?

Suggested Reading:
1.Ronco R. Can peritoneal dialysis be considered an option for the treatment of acute kidney injury? Perit Dial Int 2007; 27: 251–3
2. Gabriel DP, Ribeiro do Nascimento GV, Teixeira CJ, Cuadrado ML, Barretti P, Balbi AL. High volume peritoneal dialysis for acute renal failure. Perit Dial Int 2007; 27:277–82.
3. Gabriel DP, Caramori JT, Martim LC et al: High volume peritoneal dialysis vs daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. Kidney Int Suppl 2008:S87– S93
4. Passadakis PS, Oreopoulos GD. Peritoneal dialysis in patients with acute renal failure. Adv in Perit Dial 2007: 23
5. Chionh CY, Ronco C, Finkelstein FO, Soni SS et al. Acute peritoneal dialysis: what is the adequate dose for acut kidney injury? Nephrol Dial Transplant 2010; 1-6
6. Ponce D, Balbi AL. Peritoneal Dialysis: a viable alternative. Perit Dial Int, 2011 (in press)

Prolonged Dialysis: 24 hr SLED is it CRRT?

Balazs Szamosfalvi, MD
11:30-11:45
Thursday, February 24

Educational Objectives:
1. Briefly review the traditional application of sustained low efficiency dialysis (SLED) for CRRT
2. Explain the principles of safe, near-automated regional citrate anticoagulation (RCA) during 24-hour SLED and the rationale for the development of this therapy
3. Appraise the performance of our novel 24-hour SLED-RCA program in contrast to traditional CRRT

Content Description:
Due to technical features of intermittent hemodialysis (iHD) machines, SLED is usually implemented as an 8-16-hour shift therapy to avoid clotting and delivering very high daily small solute clearance. RCA during SLED allows a new approach and may be easier and safer to perform than during traditional CRRT with pre-packaged fluids. We developed a 24-hour SLED-RCA program using a very low blood flow in iHD mode with 9-hour 59-minute back-to-back sessions with online clearance (OLC) measurements. To eliminate errors, RCA prescriptions are generated from and archived on a secure web-server. We use a 1.5 m2 high-flux hemodialyzer; a zero calcium, 140 Na and 32 bicarbonate dialysate with optional phosphate supplement 3.2 mg/dL; and an optical hematocrit (Hct) and O2 saturation sensor. Flow rates are QB=60 ml/min, QD=400 mL/min; Qcitrate=150 mL/h of Acid Citrate Dextrose-A; and net ultrafiltration is 0-500 ml/hour. The QCa is infused into the venous limb of the circuit and adjusted hourly based on the optical Hct and a < 24-hour-old albumin level. Systemic iCa is sampled every 6 hours. The high Qcitrate to QB ratio completely blocks circuit clotting without adverse electrolyte or acid-base effects. The >95% citrate extraction on the dialyzer prevents systemic citrate accumulation even in patients with severe liver dysfunction and after days of SLED-RCA. Predictive QCa dosing results in systemic iCa 0.9 to 1.3 mM for all patients. OLC is feasible and stable in the range of 40-55 mL/min. Clearance with ultrapure dialysate is in traditional CRRT range at 3 L/h with a convective component due to internal filtration on the dialyzer. Telemetry data collection with commercial software is feasible. Disposables cost 300 dollars less per day per patient then with traditional CRRT. Nurse satisfaction with the modality is very high. In summary, 24-hour SLED-RCA is CRRT, has novel features with empiric value, costs less than traditional CRRT, and may help expand the use of 24-hour CRRT in the ICU.

Suggested Reading:
1. Marshall, MR, Golper, TA, Shaver, MJ, et al. Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy. Kidney Int 2001; 60:777
2. Schlaeper, C; Amerling, R; Manns, M; Levin, NW. High clearance continuous renal replacement therapy with a modified dialysis machine. Kidney Int Suppl 1999: S20
3. Morath, C, Miftari, N, Dikow, R, et al. Sodium citrate anticoagulation during sustained low efficiency dialysis (SLED) in patients with acute renal failure and severely impaired liver function. NDT 2008; 23:421
4. Clark, JA, Schulman, G, Golper, TA. Safety and efficacy of regional citrate anticoagulation during 8-hour sustained low-efficiency dialysis. Clin J Am Soc Nephrol 2008; 3:736
5. Gotch, FA; Panlilio, FM; Buyaki, RA; Wang, EX; Folden TI; Levin, NW. Mechanisms determining the ratio of conductivity clearance to urea clearance. Kidney International (2004) 66, SS3–SS24
6. Messer, J; Mulcahy, B; Fissell, WH. Middle-Molecule Clearance in CRRT: In Vitro Convection, Diffusion and Dialyzer Area. ASAIO Journal 2009; 55(3): 224-226
7. Yamamoto, KI; Matsukawa, H; Yakushiji, T; Fukuda, M; Hiyoshi, T; Sakai, K. Technical Evaluation of Dialysate Flow in a Newly Designed Dialyzer. ASAIO Journal 2007 53(1): 36-40
8. Fiore, GB; Guadagni, G; Lupi, A; Ricci, Z; Ronco, C. A New Semiempirical Mathematical Model for Prediction of Internal Filtration in Hollow Fiber Hemodialyzers. Blood Purif Vol. 24, No. 5-6, 2006
9. Szamosfalvi, B; Frinak, S; Yee, J. Automated regional citrate anticoagulation: technological barriers and possible solutions. Blood Purif 2010;29(2): 204-9
10. Yang, Y. J., B. Szamosfalvi, J. Yee, S. Frinak and E. V. Anslyn (2011). "Development of an online citrate/Ca2+ sensing system for dialysis." Analyst 136(2): 317-320

Managing The Cardiorenal Syndrome: The Role Of PD

Rajasekara Chakravarthi M, DNB
11:45-12:00
Thursday, February 24

Educational Objectives:
1. To discuss the role of Ultrafiltration in the management of refractory heart failure.

2. Discuss advantages of Ultrafiltration done by peritoneal route as compared by the conventional Ultrafiltration done in the ICCU

3. Understand how bedside CAPD catheterisation can be done and Ultrafiltration initiated bedside in ICU immediately.

Content Description:

Patients who have refractory heart failure get admitted into the hospital repeatedly with little benefit as they will develop resistance to diuretics and ionotropes with time. Atleast three trials have looked at the role of early Ultrafiltration in ICCU in relieving the symptoms, making them diuretic sensitive, discharging early as early as in three days and also in reducing the number of hospitalizations in an year. We will discuss how ultrafiltration scores over the diuretics and ionotropes. We will learn how peritoneal route ultrafiltarion can be initiated in the ICCU immediately after introducing a peritoneal catheter bedside.

Suggested Reading:

1. Ultrfiltration versus intravenous diuretics for patients hospitalized for decompensated heart failure
Costanzo et al
J Am Coll Cardiol, 2007;49:675-683

2. The Relief for acutely fluid overloaded patients with decompensated congestive heart failure trial. RAPID CHF
Bart et al
J Am Coll Cardiol, 2005;46:2043-2046

3. Early ultrafiltration in patients with decompensated heart failure and obseraved resistance to intervention with diuretic resistance. EUPHORIA
Costanzo et al
J Am Coll Cardiol, 2005;46:2047-2051

High Volume Hemofiltration in Sepsis: Results from the IVOIRE Study

Oliver Joannes-Boyau MD
12:00-12:15
Thursday, February 24

Content Description:
Presentation and results from IVOIRE study.
Large multicentric international randomized controlled trial
High volume CRRT (70 ml/kg/h) versus standard CRRT (35 ml/kg/h) in septic shock patients with acute kidney injury.

How Do We Make Decisions for Initiating Dialysis?

Ravindra L. Mehta MBBS, MD, DM, FACP
12:15-12:35
Thursday, February 24

Educational Objectives:
1. Describe the components and factors influencing timing to initiate dialysis in AKI

2. Discuss the factors influencing physician decisions for initiating dialysis

3. Describe a practical framework for utilizing this information for improving decisions for dialysis initiation

Content Description:
Defining when to initiate dialysis continues to be one of the most controversial areas in management of patients with AKI. The optimal timing to initiate RRT in AKI is not defined. There is usually no hesitation in offering RRT in the presence of life threatening situations (e.g. severe hyperkalemia). However, in the absence of these factors there is generally a tendency to avoid RRT as long as possible, a thought process that reflects the decisions made for patients with end stage renal disease (ESRD), in whom the initiation of dialytic therapy signals its dependency. Two factors tend to discourage nephrologists from initiating RRT. First, there are well known risks of the procedure, including complications of vascular access placement, infection, hypotension, arrhythmia, among others. Second, there is a strong concern that some element of the RRT procedure may slow the recovery of renal function, and increase the risk of developing end-stage renal failure. Currently, there is wide variation in how decisions for initiating RRT are made. There is no comprehensive resource assessing how and why physicians make decisions. Thus, the current approach to timing of RRT initiation is based on arbitrary thresholds of traditional serum biomarkers (e.g. BUN and creatinine) or time from an event (e.g. (ICU) admission or AKI diagnosis) and these are relatively insensitive as target criteria. This lecture will discuss the factors influencing physician's decisions to initiate dialysis and describe a framework for assessing the relative contribution of these factors.

Suggested Reading:
1. Mehta RL, Letteri JM. Current status of renal replacement therapy for acute renal failure. A survey of US nephrologists. The National Kidney Foundation Council on Dialysis. Am J Nephrol 1999; 19: 377-382.
2. Mehta RL. Indications for dialysis in the ICU: renal replacement vs. renal support. Blood Purif 2001; 19: 227-232.
3. Bouchard J, Weidemann C, Mehta RL. Renal replacement therapy in acute kidney injury: intermittent versus continuous? How much is enough? Adv Chronic Kidney Dis 2008; 15: 235-247.
4. Gibney N, Hoste E, Burdmann EA, Bunchman T, et al. Timing of initiation and discontinuation of renal replacement therapy in AKI: unanswered key questions. Clin J Am Soc Nephrol 2008; 3: 876-880.
5. Perianayagam MC, Seabra VF, Tighiouart H, Liangos O, et al. Serum cystatin C for prediction of dialysis requirement or death in acute kidney injury: a comparative study. Am J Kidney Dis 2009; 54: 1025-1033.
6. Seabra VF, Balk EM, Liangos O, Sosa MA, et al. Timing of renal replacement therapy initiation in acute renal failure: a meta-analysis. Am J Kidney Dis 2008; 52: 272-284.
7. Waikar SS, Bonventre JV. Can we rely on blood urea nitrogen as a biomarker to determine when to initiate dialysis? Clin J Am Soc Nephrol 2006; 1: 903-904.
8. Bouchard J, Macedo E, Mehta RL. Dosing of Renal Replacement Therapy in Acute Kidney Injury: Lessons Learned From Clinical Trials. Am J Kidney Dis.
9. Bouchard J, Mehta RL. Acid-base disturbances in the intensive care unit: current issues and the use of continuous renal replacement therapy as a customized treatment tool. Int J Artif Organs 2008; 31: 6-14.
10. Bouchard J, Mehta RL. Fluid accumulation and acute kidney injury: consequence or cause. Curr Opin Crit Care 2009; 15: 509-513.
11. Bouchard JM, R and Mehta, RL. Stopping Acute Kidney Replacement Therapy

Critical Care Nephrology 2008 2008.
12. Mehta RL, Bouchard J. Dialysis dosage in acute kidney injury: still a conundrum? J Am Soc Nephrol 2008; 19: 1046-1048.
13. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, et al. Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury. J Crit Care 2009; 24: 129-140.
14. Bouchard J, Macedo E, Mehta RL. Renal support in critically ill patients with acute kidney injury. N Engl J Med 2008; 359: 1959-1960; author reply 1961-1952.
15. Macedo E, Bouchard J, Mehta RL. Renal recovery following acute kidney injury. Curr Opin Crit Care 2008; 14: 660-665.
16. Palevsky PM. Clinical review: timing and dose of continuous renal replacement therapy in acute kidney injury. Crit Care 2007; 11: 232.
17. Palevsky PM. Indications and timing of renal replacement therapy in acute kidney injury. Crit Care Med 2008; 36: S224-228.
18. Zamperetti N, Ronco C, Brendolan A, Bellomo R, et al. Bioethical issues related to continuous renal replacement therapy in intensive care patients. Intensive Care Med 2000; 26: 407-415.
19. Howard CS, Teitelbaum I. Renal replacement therapy in patients with chronic liver disease. Semin Dial 2005; 18: 212-216.
20. Draper H. Ethical aspects of withdrawing/withholding renal replacement therapies on patients in acute renal failure in an intensive care unit. EDTNA ERCA J 2002; Suppl 2: 39-42.
21. Lee CP, Chertow GM, Zenios SA. A simulation model to estimate the cost and effectiveness of alternative dialysis initiation strategies. Med Decis Making 2006; 26: 535-549.
22. Liu KD, Himmelfarb J, Paganini E, Ikizler TA, et al. Timing of initiation of dialysis in critically ill patients with acute kidney injury. Clin J Am Soc Nephrol 2006; 1: 915-919.
23. Bagshaw SM, Cruz DN, Gibney RN, Ronco C. A proposed algorithm for initiation of renal replacement therapy in adult critically ill patients. Crit Care 2009; 13: 317.
24. Bagshaw SM, Gibney RT. Ideal determinants for the initiation of renal replacement therapy: timing, metabolic threshold or fluid balance? Acta Clin Belg Suppl 2007: 357-361.

Urine Output: The Canary in the Mine?

Etienne Macedo MD, PhD
7:30-7:45
Friday, February 25

Educational Objectives:

1. Briefly review the physiology of urine flow, alterations in urine analysis and these characteristics in prerenal failure and tubular necrosis.
2. Comment on studies that applied the urine output criterion to diagnosis AKI and understand how differences in definitions may explain positive or negative associations of urine output criterion and outcomes.
3. Comment on prior studies that applied the urine analysis as a criterion to differentiate prerenal from AKI. Understand how different definitions may explain positive or negative associations of urine analysis to kidney recovery and outcomes.
4. Understand the difficulties associated with performing urine analysis, including microscopy and electrolyte studies. Comment on the reasons why most of the epidemiologic and clinical studies fail to investigate these aspects in AKI patients.
5. Discuss new proposed definitions of oliguria and urine analysis

Content Description:

Oliguria is a frequent event in ICU patients and urine output (UO) is a criterion for AKI diagnosis and staging in the RIFLE and AKIN classification systems. Most of the studies validating the RIFLE and AKIN have assessed exclusively serum creatinine (sCr) criterion and few studies have systematically assessed the UO as defined by RIFLE/AKIN classification.

Although some emphasis has been place on urine flow, urinalysis and urine microscopy has not been consistently used as a tool to diagnose and classify AKI patients. Some recent studies have emphasized the importance of urine analysis and urine microscopy as a non-invasive method to help determine the differential diagnosis and etiology of AKI, grade its severity and predict outcomes.

Coupled with other biomarkers for AKI, comprehensive clinical evaluation with urine-sediment and new biomarkers could distinguish the pathophysiology of AKI, permit early interventions to correct reversible elements and ultimately improve outcomes from this disease.

Suggested Reading:

1. Perazella MA, Coca SG, Hall IE, et al. Urine microscopy is associated with severity and worsening of acute kidney injury in hospitalized patients. Clin J Am Soc Nephrol 2010;5(3):402-408.
2. Barrantes F, Tian J, Vazquez R, et al. Acute kidney injury criteria predict outcomes of critically ill patients. Critical care medicine 2008;36(5):1397-1403.
3. Perazella MA, Coca SG, Kanbay M, et al. Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalized patients. Clin J Am Soc Nephrol 2008;3(6):1615-1619.
4. Chawla LS, Dommu A, Berger A, et al. Urinary sediment cast scoring index for acute kidney injury: a pilot study. Nephron Clin Pract 2008;110(3):c145-150.
5. Macedo E, Malhotra R, Claure-Del Granado R, et al. Defining urine output criterion for acute kidney injury in critically ill patients. Nephrol Dial Transplant.
6. Joannidis M, Metnitz B, Bauer P, et al. Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. Intensive care medicine 2009;35(10):1692-1702.
7. Haase M, Bellomo R, Matalanis G, et al. A Comparison of the RIFLE and Acute Kidney Injury Network classifications for cardiac surgery-associated acute kidney injury: A prospective cohort study. The Journal of thoracic and cardiovascular surgery 2009.
8. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: A systematic review. Kidney international 2008;73(5):538-546.
9. Bagshaw SM, Bellomo R. Urine abnormalities in acute kidney injury and sepsis. Contrib Nephrol;165:274-283.

AKI in The Developed and Developing World: Knowledge Gained and Applied?

Jorge Cerda MD, FACP, FASN
7:45-8:00
Friday, February 25

Educational Objectives:
1. Describe the contrasting characteristics of AKI in developed and developing countries
2. Propose solutions to the unique characteristics of AKI in the developing world

Content Description:

Introduction
Acute kidney injury (AKI) in developing countries demonstrates surprising commonalities between seemingly disparate regions.

We reviewed the recent world literature on AKI, contrasted differences and similarities between developed and developing countries, analyzed the practical implications of such differences and made evidence-based recommendations.

Methods
PubMed and MEDLINE searched yielding 23,074 results during the last 5 years. Redefined set yielded 4353 results; results were then restricted to developing countries. Resulting 653 publications were manually reviewed and results analyzed. Degree of regional development defined according to the United Nations 2006 Human Development Report.

Results and Conclusions
While in developed countries AKI predominantly occurs among older populations in the ICU with multiple organ failure, sepsis and high mortality, in developing countries AKI occurs in either rural or urban settings. Urban cases are similar to the developed world, but rural cases are due to a single disease and specific conditions (gastroenteritis) or infections (severe malaria, leptospirosis, HUS), and occur among young, otherwise healthy individuals. Most etiologies (diarrhea, poisonings, malaria, septic abortion) are preventable with individual, community and regional measures.

As in the developed world, in developing countries AKI is increasingly prevalent and associated with severe morbidity and mortality, especially in children. Uncertainty on the real incidence of AKI limits the visibility of the problem, thus reducing its political importance and hampering efforts to limit its occurrence. Dialysis is generally unavailable or too costly; effective measures must entail community-wide efforts to eradicate causes, achieve early diagnosis and aggressively manage pre-renal conditions and specific infections.

Suggested Reading:
Cerdá J, Lameire N, Eggers P, Pannu N, Uchino S, Wang H, Bagga A, Levin A. Epidemiology of Acute Kidney Injury. Clin J Am Soc Nephrol. 2008;3:881-6

Cerdá J, Bagga A, Kher V, Chakravarthi RM. The contrasting characteristics of acute kidney injury in developed and developing countries. Nature Clin Pract Nephrol. 2008;4(3):138-153

Biomarkers to Predict AKI in the ICU: Results from a Multicenter Study

Kianoush Kashani MD
8:00-8:15
Friday, February 25

Educational Objectives:
1- multicenter investigation to detect an early AKI marker-report
2- using biomarker panels in improving the efficacy of AKI early detection
3- New markers of early AKI detection

Content Description:
AKI based on the acute kidney injury network (AKIN) criteria is defined based upon a rise in serum creatinine and/or decrease in urine output. Early diagnosis of acute kidney injury can potentially provide a wider therapeutic window for the prophylaxis and treatment of AKI and its related complications. New biomarkers of AKI have been investigated. Unfortunately none of the current markers have proven to have enough sensitivity or specificity to be considered as new effective tool in early AKI detection.
In a multicenter investigation 324 patients who had risk factors for AKI were recruited. Urine and blood samples were collected at recruitment, 12, and 24 hours and then daily until hospital discharge or maximum of 7 days. more than 140 different potential makers were measured in the blood and urine samples. two markers were identified to have appropriate sensitivity and specificity. A two marker panel found to have Cstat of 0.8 in a multivariate logistic regression model. AUC of ROC curve for diagnosis of AKI 24 hours prior to diagnosis of AKI by AKIN criteria for marker #one found to be 0.77 and for marker #two was 0.76. In this cohort AUC of ROC curve for diagnosis of AKI 24 hours prior to diagnosis of AKI by AKIN criteria for urine NGAL was 0.72. Conclusion: a two marker panel for early diagnosis of AKI was identified. This panel needs to be validated in a multicenter trial.

Suggested Reading:
1. Bagshaw, S.M., C. George, and R. Bellomo, A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. Nephrol Dial Transplant, 2008. 23(5): p. 1569-74.
2. Himmelfarb, J., et al., Evaluation and Initial Management of Acute Kidney Injury. Clin J Am Soc Nephrol, 2008. 3(4): p. 962-967.
3. Parikh, C.R.M.D.P. and P.M.D. Devarajan, New biomarkers of acute kidney injury. Critical Care Medicine Acute Kidney Injury in the ICU, 2008. 36(4): p. S159-S165.
4. Haase, M., et al., Novel Biomarkers Early Predict the Severity of Acute Kidney Injury After Cardiac Surgery in Adults. The Annals of Thoracic Surgery, 2009. 88(1): p. 124-130.
5. Haase-Fielitz, A., et al., The predictive performance of plasma neutrophil gelatinase-associated lipocalin (NGAL) increases with grade of acute kidney injury. Nephrol. Dial. Transplant., 2009: p. gfp234.
6. Han, W.K., et al., Urinary Biomarkers in the Early Detection of Acute Kidney Injury after Cardiac Surgery. Clin J Am Soc Nephrol, 2009. 4(5): p. 873-882.
7. Koyner, J.L., et al., Urinary Biomarkers in the Clinical Prognosis and Early Detection of Acute Kidney Injury. Clinical Journal of the American Society of Nephrology, 2010. 5(12): p. 2154-2165.

Raising Awareness of AKI: Strategies and Results

Andrew Lewington MD
8:15-8:30
Friday, February 25

Educational Objectives:
1. Understand why we need to raise the awareness of AKI
2. Understand what strategies have been employed to raise the awareness of AKI
3. Consider what new strategies could be used to raise the awareness of AKI

Content Description:
The lecture will consider why it is necessary to raise the awareness of acute kidney injury (AKI). In particular it will draw reference to evidence that even small rises in serum creatinine portend a worse prognosis to both medical and surgical patients. It is therefore important to engage with different specialties and healthcare professionals to highlight the negative effects that AKI may have on patients that they care for. As nephrologists we see patients that are referred already with a diagnosis of AKI. There is evidence from the 2009 UK National Confidential Enquiry Into Patient Outcomes and Death (NCEPOD) adding insult to injury AKI study that the significant proportion of cases AKI could be both prevented and managed better. In 2010 the UK National Confidential Enquiry Into Patient Outcomes and Death (NCEPOD) an age-old problem study confirmed that a significant number of patients aged over 80 years who died within three months of having surgery developed AKI and had poor evaluation of volume status and appropriate fluid therapy.

Examples will be given of how the UK has tried to raise the awareness of AKI by engaging with other specialties and health care professionals including pharmacy and nursing colleagues. These efforts have been supported by the government with establishment of an AKI delivery board. Proposals have been made to the National Institute for Health and Clinical Excellence (NICE) and guidelines are planned for AKI over the next few years. International guidelines for AKI will be published later this year by KDIGO.

It remains important to identify the knowledge gaps that exist with respect to AKI across the whole range of health professionals and specialties. Once these knowledge gaps have been identified in educational resources may be targeted appropriately. A range of educational measures have been introduced which include the development of electronic educational resources and e-learning packages. World kidney Day would potentially provide an excellent opportunity to raise the awareness of AKI.

Suggested Reading:
1.www.akinet.org
2.www.ncepod.org
3.www.kdigo.org
4.www.nice.org.uk

Fluid Status in Heart Failure and Critically Ill AKI Patients

Dinna N Cruz, MD, MPH
8:45-9:00
Friday, February 25

Educational Objectives
1. Discuss fluid overload/ fluid status as a "biomarker" in the setting of AKI (in the ICU) and acute heart failure (AHF)
2. Briefly review studies related to fluid status and RRT initiation in critically ill AKI patients
3. Briefly review methods of assessing fluid overload/ fluid status in chronic and acute HF
4. Introduce bioimpedance as a method to assess fluid status in AHF

Content Description
In HF, fluid accumulation, defined as either a positive cumulative fluid balance or as an acute redistribution of fluid, represents a core precipitating mechanism of acute decompensation and is associated with worsening symptoms, hospitalization and death. Determining fluid balance in HF may be complex and depend largely on underlying pathophysiology; however, in addition to simple fluid balance (intake minus output) measurement, newer biomarkers (i.e. B-type natriuretic peptides) and novel technology (i.e. bioimpedance) are proving to be useful for detection and risk identification for acute decompensated HF that may allow earlier intervention and translate into improved clinical outcomes. Recent data have also emerged showing the importance of fluid balance in both adult and pediatric patients with AKI. In general, a positive cumulative fluid balance portends higher morbidity and an increased risk for worse clinical outcome. Fluid balance should be recognized as a potentially modifiable biomarker and determinant of clinical outcome in these patients.
To date, the impact of fluid balance in both of these syndromes, more so with AKI, has likely been underappreciated. There is little to no data specifically on fluid balance in the cardiorenal syndrome, where acute/chronic heart disease can directly contribute to acute/chronic worsening of kidney function that likely exacerbates fluid homeostasis. Additional investigations are needed.

References
1. Bagshaw SM, Cruz DN. Fluid overload as a biomarker of heart failure and acute kidney injury. Contrib Nephrol. 2010;164:54-68.
2. Bagshaw SM, Brophy PD, Cruz D, Ronco C. Fluid balance as a biomarker: impact of fluid overload on outcome in critically ill patients with acute kidney injury. Crit Care. 2008;12(4):169.
3. Bagshaw SM, Cruz DN, Gibney RN, Ronco C. A proposed algorithm for initiation of renal replacement therapy in adult critically ill patients. Crit Care. 2009;13(6):317.
4. Macedo E, Bouchard J, Soroko SH, Chertow GM, Himmelfarb J, Ikizler TA, et al. Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients. Crit Care. 2010;14(3):R82.
5. Piccoli A. Bioelectric impedance measurement for fluid status assessment. Contrib Nephrol. 2010;164:143-52.
6. Peacock WF, Soto KM. Current techniques of fluid status assessment. Contrib Nephrol. 2010;164:128-42.
7. Cruz DN, Soni S, Slavin L, Ronco C, Maisel A. Biomarkers of cardiac and kidney dysfunction in cardiorenal syndromes. Contrib Nephrol. 2010;165:83-92.

Contrast Nephropathy: What Do We Know Now?

Richard Solomon MD
9:30-9:45
Friday, February 25

Educational Objectives:
1. Describe the pathophysiology of contrast induced nephropathy.
2. Evaluate the use of various prevention strategies to prevent contrast induced nephropathy.
3. Discuss the importance of contrast induced nephropathy for long term adverse cardiovascular events.

Content Description:
Contrast induced nephropathy (CIN) continues to be an important concern. The pathogenesis involves generation of reactive oxygen species within the renal parenchyma as a result of medullary vasoconstriction (ischemia) and direct renal tubule cell toxicity. Strategies to reduce the incidence of CIN focus on identifying high risk patients and mitigating the effects of reactive oxygen species. New research studies have further clarified the efficacy of antioxidant strategies. The impact of CIN on long term cardiovascular events is well known but whether CIN is causally related is still unclear.

Suggested Reading:
[1] Heyman SN, Rosen S, Khamaisi M, Idee JM, Rosenberger C. Reactive oxygen species and the pathogenesis of radiocontrast-induced nephropathy. Invest Radiol 2010;45:188-195.
[2] Sendeski M, Patzak A, Persson PB. Constriction of the vasa recta, the vessels supplying the area at risk for acute kidney injury, by four different iodinated contrast media, evaluating ionic, nonionic, monomeric and dimeric agents. Invest Radiol 2010;45:453-457.
[3] Song K, Jiang S, Shi Y, Shen H, Shi X, Jing D. Renal replacement therapy for prevention of contrast-induced acute kidney injury: a meta-analysis of randomized controlled trials. Am J Nephrol 2010;32:497-504.
[4] Wiedermann C, Joannidis M. Increasing evidence base for sodium bicarbonate therapy to prevent contrast media-induced acute kidney injury: little role of unpublished studies. Nephrol Dial Transplant 2010;25:650-654.
[5] Ribichini F, Graziani M, Gambaro G, Pasoli P, Pighi M, Pesarini G, Abaterusso C, Yabarek T, Brunelleschi S, Rizzotti P, Llupo A, Vassanelli C. Early creatinine shifts predict contrast-induced nephropathy and persistent renal damage after angioplasty. Am J Med 2010;123:755-763.
[6] James M, Ghali WA, Knudtson ML, Ravani P, Tonelli M, Faris P, Pannu N, Manns BJ, Klarenbach SW, Hemmelgarn BR. Associations between acute kidney injury and cardiovascular and renal outcomes after coronary angiography. Circulation 2010;123:409-416.

Alkaline PO4 trial

Peter Pickkers
11:10-11:25
Friday, February 25

Educational Objectives
1. Describe the (patho)physiological role of alkaline phosphatase in the kidney and during sepsis-induced AKI.
2. To evaluate whether AP treatment improves renal function in septic patients with acute kidney injury (AKI).

Content Description
No current treatment is available for sepsis-induced acute kidney injury. Alkaline phosphatase is an endogenous dephosphorylation enzyme that is depleted in the kidney during an ischemic or inflammatory insult. Administration of alkaline phosphatase in animal models of sepsis attenuates the inflammatory response and improves survival.

The results of the recently completed prospective, double-blind, randomized, placebo-controlled study of the safety and efficacy of AP in septic patients with evidence of AKI will be discussed. Details to what extent administration of alkaline phosphatase attenuates the inflammatory response, reduces urinary excretion of markers of tubular injury and improves renal function in septic patients with acute kidney injury will be discussed.

Suggested Reading
1. Alkaline phosphatase treatment improves renal function in severe sepsis or septic shock patients. Heemskerk S, Masereeuw R, Moesker O, Bouw MP, van der Hoeven JG, Peters WH, Russel FG, Pickkers P; APSEP Study Group. Crit Care Med. 2009 Feb;37(2):417-23.
2. Clinical pharmacology of exogenously administered alkaline phosphatase. Pickkers P, Snellen F, Rogiers P, Bakker J, Jorens P, Meulenbelt J, Spapen H, Tulleken JE, Lins R, Ramael S, Bulitta M, van der Hoeven JG. Eur J Clin Pharmacol. 2009 Apr;65(4):393-402.

New Membranes at the Horizon

Patrick M. Honoré MD
11:25-11:40
Friday, February 25

Educational Objectives:
1) To show the great capabilities of New Membranes that are already on the Market.

2) Show the potential advantages but also the limitations of these new membranes.

3) Discuss the available literature regarding these most recent data about these new membranes.

Content Description:
Types of New Available Membranes in 2011:
New High Cut-Off Membranes:
Eg: Membranes exhibiting large pores such as SepteX® from Gambro™ & others..
New Adsoprtive Membranes:
Eg: Special focus on endotoxin adsorption (Toraymyxin® from Toray™ or Oxiris® from Gambro™) or specific immuno-adorsption (Prosorba® from Fresenius™) with promising results in recent studies (21) and the promise of RCTs in the near future.

High permeability hemofofiltration (HPHF) do offers to the clinician especially with the combined use of high volume hemofiltration (for Synergic action) a new tool in order to try to effectively combat septic shock with acute kidney injury (AKI).

Previous studies did show that HPHF especially with combined HVHF can removed much large quantities of mediators.

A preliminary study called the HICOSS study(High Cut-off in Septic Shock)was looking as pilot study in order to compare in 80 patients with Septic Shock plus AKI. 40 patients were assigned with conventional membrane and 40 patients were assigned with an hyperpermeable membrane (septex).Those patients were in septic shock plus AKI but also in multiple organ failure (MODS).The mode chosen was CVVD for 5 consecutive days.The principal aim was to evaluate the safety regarding albumin losses (cut-off of 60 kDa) and a 50 % reduction in catecholamine requirements.Mortality was a secondary end point.

The results shows a excellent safety as the membrane was not loosing albumin more than a classical membrane.Nevertheless, regarding vasopressors free days as well length of ICU stay and mortality , no differences could be seen between the two groups.This may be due the fact that the mode was only CVVD and perhaps the results would be very different if we were using CVVH at 35 ml/kg/h plus HPHF.Description will be done also regarding data for new adsorptive membranes.

In conclusion, the hyperpermeable membrane (septex) is safe and could be a important therapeutic tool in the future when associated with HVHF.Potential effect of highly adsorptive membranes need to be evaluated.

Suggested Reading:
1. Matson J R, Zydney AR, Honore,PM. Blood Filtration: New Opportunities and the Implications On System Biology.Critical Care and Resucitation 2004; 6:209-218.

2. Morgera S, Haase M, Kuss T, et al. Pilot study on the effects of high cutoff hemofiltration on the need for norepinephrine in septic patients with acute renal failure. Crit Care Med 2006;34:2099-104.

3. Honoré PM, Zydney LA, Matson JR : High volume and high permeability haemofiltration for sepsis : the evidence and the key issues. Review article. Care of Critically ill 2003;19:69-76.

4. Cruz DN, Antonelli M, Fumagalli R, et al. Early use of polymyxin B hemoperfusion in abdominal septic shock: the EUPHAS randomized controlled trial. JAMA 2009;301:2445-52.

5. Honore PM, Joannes-Boyau O, Dobbeleir N.Blood Purification in Sepsis & Acute Kidney Injury in Critically Ill Patients:New Insights & Potential Mechanisms with an Update on Recent Trials.Chapter of the Yearly Book in Intensive Care Medicine 2011
(31 th ISICEM March 2011)

6.Honore PM et al. Continuous Hemofiltration or Intermittent Dialysis for Septic Shock Patients in ICU with AKI :A Pragmatic Approach for Bedside Intensivists Summarizing the More Recent Advances.Annals of Intensive Care 2011: In Press.

Learning and Monitoring Clinical Development in the ICU:
Using "Avatar Interactive Software" and Web Based "Clinical Experience Portals"

Ian Baldwin RN, PhD, ACCCN
11:40-11:55
Friday, February 25

Educational Objectives:

1. To appreciate the difficulties providing learning and educational opportunities across a 24/7 large nursing team within Critical Care.
2. To introduce current terminology describing the context of advanced computer use for education and e-learning.
3. To consider the potential of web based education software and the concepts of clinical experience recording via web portal, and learning in the 'virtual world' hospital or ICU.
4. To review prototype examples of the above.

Content Description:

Providing learning opportunities across large staffing pools in the ICU, where a 24/7 day roster applies can be difficult. Traditional education approaches via classroom lectures have limitations in respect of access, interaction and feedback. The spread of the digital world in our lives with widespread access and use of email, the information 'superhighway' of internet search engines and use of web 2.0 functionality of social networking sites, Twitter, Blogs, Wikki's, You –Tube and Pod casts suggests education and training would ideally fit into this context. The role of the teacher and presenter would be different, learners not limited to accessing classes at set times, be cost efficient, and may provide interaction or immersion in artificial clinical environments yielding improved work competency in the real world. Games software is well advanced with dynamic, immersive, 3-D, interactive and virtual world settings with high quality graphics, but focused to different challenges and 'thrills' in artificial worlds. This software and context suggests many possibilities if suitable software was available for health care training. The ability of a user to take on a human shape or fictitious but unique self as an 'Avatar' means that interaction with others, clinical decision making and close to real life experience can occur with safety, repetition and may increase motivation to learn, truly making health care education effective and 'fun'.

The second aspect of providing education in the clinical context is to be able to review working experiences and hopefully see that knowledge and skills are transferred from the virtual, to the real world. This has been limited in the past to old approaches of providing set time intervals of experience in a ward or clinical area, mandating a minimum completion of procedures to be done or learnt, attendance at specific lectures or tutorials with no, or very loose records for ensuring this is actually achieved. Paper log books have been used in the past, and current trainees may not record procedures and experiences or use simple spread sheets, e-diaries or i-phone applications. However this limits the teacher or supervisor to monitor progress and more reliably mandate minimum competency achievement. With mobile wireless technology and or networked bedside computers more readily available in hospitals it is now feasible to provide suitable software to allow the recording of experience(s) and monitor this to a minimum 'set', provide feedback with enhancements such as quizzes, case studies and clinical learning tools; a shared clinical experience portal (CEP) with identifier log-in. Microsoft SharePoint® can be used to achieve this and is a collaboration and document-management platform that can be used to host web sites that access shared workspaces and documents, as well as specialized applications like wikis and blogs from a browser.

This presentation will provide an introductory and basic review of these two innovations in health care learning.

Suggested Reading:

1. Margaret M Hansen. 2008. Versatile, Immersive, Creative and Dynamic Virtual 3-D Healthcare Learning Environments: A Review of the Literature. J Med Internet Res. Jul–Sep; 10(3): e26. Published online 2008 September 1.

2. Leong JJ, Kinross J, Taylor D, Purkayastha S. 2008. Surgeons have held conferences in Second Life. BMJ. Jul 8;337:a683. doi: 10.1136/bmj.a683

3. Baumgart D. 2005. Personal digitial assistants in healthcare; eperienced clinicains in the palm of you hand? Lancet.;366(9492):1210-1223.

4. George L, Davidson L. 2005 . PDA use in nursing education: Prepared for today, poised for tomorrow. Online Journal of Nursing Informatics. 9(2).

5. Fischer S, Stewart T, Mehta S, Wax R, Lapinsky S. 2003. Handheld computing in medicine. Journal of the American Medical Informatics Association.;10(2):139-149.

6. Stroud SD, Erkel EA, Smith CA. 2005. The use of personal digital assistants by nurse practitioner students and faculty. Journal of the American Academy of Nurse Practitioners.;17(2):67-75.

7. Stott D. 2008. Attending Medical School in Virtual Reality. Student BMJ. Jul 12]. webcite http://student.bmj.com/issues/07/12/news/431.php.

8. The Virtual Clinical Learning Lab. PULSE!! 2008. Jul 11. webcite http://www.sp.tamucc.edu/pulse/home.asp

9. Kusumoto L, Shorrock D, Heinrichs WM, Dev P, Youngblood P. 2007. The integration of physiology models with avatars to expand the opportunities for high-fidelity medical training. SimTech 2007 Healthcare Simulation Conference; pp. 50–53.

10. Hansen M. 2008. Online virtual 3-D healthcare learning environments (presentation). First Education Meeting. Health Informatics Society of Australia, NSW; Sydney, Australia. Feb.

11. Hansen MM, Murray PJ, Erdley WS. 2009. The potential of 3-D virtual worlds in professional nursing education. Stud Health Technol Inform. 146:582-6.

12. John Wiecha, Robin Heyden, Elliot Sternthal, and Mario Merialdi. 2010. Learning in a Virtual World: Experience With Using Second Life for Medical Education J Med Internet Res. Jan–Mar; 12(1): e1. Published online 2010 January 23.

Surveillance and Early Recognition of AKI: The "Sniffer" Approach

Kianoush Kashani MD
11:55-12:10
Friday, February 25

Educational Objectives:
1- Designing an electronic surveillance tool for ICU syndromes
2- Use of Electronic Surveiullance tool in diagnosis of AKI (feasability)
3- AKI definition (AKIN) as a platform for electronic surveillance tools.

Hypothesis:
We designed and tested an electronic surveillance tool (AKI sniffer) to screen all the ICU admissions for the earlier diagnosis of AKI and improved outcome of ICU patients. We hypothesized that using AKI sniffer can detect diagnosis of AKI earlier than clinicians.

Methods:
Using advances in medical informatics, we developed and tested an AKI "sniffer". Our AKI sniffer is an automated screening tool which can identify patients with AKI in stage 1, 2 or 3. The first phase of designing the AKI sniffer conducted as a retrospective study in the adult medical ICU within our institution. Consecutive Olmsted county residents who were admitted to the medical ICU between January 2006 and December 2006 underwent electronic sniffer surveillance. A Microsoft SQL-based integrative near-real time database, Multidisciplinary Epidemiology and Translational Research in Intensive Care (METRIC) Data Mart, served as the main data source. Our SAS-based simulation sniffer engine retrospectively screened data on an hourly basis and recorded alerts when patients met criteria for any stage of AKI. AKI was defined according to the Acute Kidney Injury Network (AKIN) group classification. To identify patients with AKI, the algorithm utilized changes in hourly urine output, creatinine, and need for renal replacement therapy (figure 4). The primary outcome was diagnostic performance of the AKI sniffer in comparison to manual chart review conducted by a physician blinded to the sniffer results. After excluding patients who denied research authorization, we identified 1,872 patients between January 2006 and December 2006 who met criteria for inclusion in the study.

Conclusion:
Electronic surveillance tool (AKI sniffer) can be used as screening tool for early detection of AKI. Our current software needs improvement in sensitivity and specificity. Quality improvement of AKI sniffer is work in progress. Optimized sniffer needs to be validated clinically before generalization.

Suggested Reading:
1. Ali, T., et al., Incidence and outcomes in acute kidney injury: a comprehensive population-based study. J Am Soc Nephrol, 2007. 18: p. 1292 - 1298.
2. Barrantes, F., et al., Acute Kidney Injury Predicts Outcomes of Non-Critically Ill Patients. Mayo Clinic Proceedings, 2009. 84(5): p. 410-416.
3. Barrantes, F., et al., Acute kidney injury criteria predict outcomes of critically ill patients. Crit Care Med, 2008. 36: p. 1397 - 1403.
4. Chertow, G.M., et al., Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol, 2005. 16(11): p. 3365-70.
5. Mehta, R.L., et al., Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care, 2007. 11(2): p. R31.
6. Herasevich, V., et al., Informatics infrastructure for syndrome surveillance, decision support, reporting, and modeling of critical illness. Mayo Clin Proc. 85(3): p. 247-54.

The ASSESS-AKI Study

Chirag Parikh MD, PhD
12:25-12:40
Friday, February 25

Educational Objectives:
To discuss the study design and goals of the NIH sponsored ASSESS-AKI study

Content Description:
The incidence of acute kidney injury (AKI) has been increasing over time and is associated with a high risk of short-term death. Previous studies on hospital-acquired AKI have important methodological limitations, especially their retrospective study designs and limited ability to control for potential confounding factors.

The Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) Study was established to examine how a hospitalized episode of AKI independently affects the risk of chronic kidney disease development and progression, cardiovascular events, death, and other important patient-centered outcomes. This prospective study will enroll a cohort of 1100 adult participants with a broad range of AKI and matched hospitalized participants without AKI at three Clinical Research Centers, as well as 100 children undergoing cardiac surgery at three Clinical Research Centers. Participants will be followed for up to four years, and will undergo serial evaluation during the index hospitalization, at three months post-hospitalization, and at annual clinic visits, with telephone interviews occurring during the intervening six-month intervals. Biospecimens will be collected at each visit, along with information on lifestyle behaviors, quality of life and functional status, cognitive function, receipt of therapies, interim renal and cardiovascular events, electrocardiography and urinalysis. ASSESS-AKI will characterize the short-term and long-term natural history of AKI, evaluate the incremental utility of novel blood and urine biomarkers to refine the diagnosis and prognosis of AKI, and identify a subset of high-risk patients who could be targeted for future clinical trials to improve outcomes after AKI.

Suggested Reading:
The assessment, serial evaluation, and subsequent sequelae of acute kidney injury (ASSESS-AKI) study: design and methods.
Go AS, Parikh CR, Ikizler TA, Coca S, Siew ED, Chinchilli VM, Hsu CY, Garg AX, Zappitelli M, Liu KD, Reeves WB, Ghahramani N, Devarajan P, Faulkner GB, Tan TC, Kimmel PL, Eggers P, Stokes JB; Assessment Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury Study Investigators.

Critical Care Nephrology: Literature Review

Noel Gibney MD
12:40-12:55
Friday, February 25

Educational Objectives:
To review important and interesting publications in Critical Care Nephrology in 2010 and early 2011.

Content Description:
The following publications are recommended to the reader. Some of these will be discussed in detail in this presentation depending on prior discussions at the conference and time.

Suggested Reading:
Perazella MA, Coca SG, Hall IE, Iyanam U, Koraishy M, Parikh CR. Urine Microscopy Is Associated with Severity and Worsening of Acute Kidney Injury in Hospitalized Patients. Clin J Am Soc Nephrol 2010;5:402-8.

Endre ZH, Walker RJ, Pickering JW, Shaw GM, Frampton CM, Henderson SJ, Hutchison R, Mehrtens JE, Robinson JM, Schollum JB, Westhuyzen J, Celi LA, McGinley RJ, Campbell IJ, George PM.. Early intervention with erythropoietin does not affect the outcome of acute kidney injury (the EARLYARF trial). Kidney Int 2010;77: 1020-1030.

Gordon AC, Russell JA, Walley KR, Singer J, Ayers D, Storms MM, Holmes CL, Hébert PC, Cooper DJ, Mehta S, Granton JT, Cook DJ, Presneill JJ . The effects of vasopressin on acute kidney injury in septic shock. Intensive Care Med 2010;36:83-91.

Johansen KL, Smith MW, Unruh ML, Siroka AM, O'Connor TZ, Palevsky PM; VA/NIH Acute Renal Failure Trial Network. Predictors of health utility among 60-day survivors of acute kidney injury in the Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network Study. Clin J Am Soc Nephrol 2010;5;1366-1372.

Redfors B, Bragadottir G, Sellgren J, Swärd K, Ricksten SE. Acute renal failure is NOT an "acute renal success"--a clinical study on the renal oxygen supply/demand relationship in acute kidney injury. Crit Care Med. 2010;38:1695-701.

Vermeulen Windsant IC, Snoeijs MG, Hanssen SJ, Altintas S, Heijmans JH, Koeppel TA, Schurink GW, Buurman WA, Jacobs MJ. Hemolysis is associated with acute kidney injury during major aortic surgery. Kidney Int. 2010;77:913-20.

Kümpers P, Hafer C, Lukasz A, Lichtinghagen R, Brand K, Fliser D, Faulhaber-Walter R, Kielstein JT. Serum neutrophil gelatinase-associated lipocalin at inception of renal replacement therapy predicts survival in critically ill patients with acute kidney injury. Crit Care. 2010;14(1):R9.

Uchino S, Bellomo R, Bagshaw SM, Goldsmith D. Transient azotaemia is associated with a high risk of death in hospitalized patients. Nephrol Dial Transplant. 2010;25:1833-9.

Bagshaw SM, Bennett M, Haase M, Haase-Fielitz A, Egi M, Morimatsu H, D'amico G, Goldsmith D, Devarajan P, Bellomo R. Plasma and urine neutrophil gelatinase-associated lipocalin in septic versus non-septic acute kidney injury in critical illness. Intensive Care Med. 2010;36:452-61.

Lerolle N, Nochy D, Guérot E, Bruneval P, Fagon JY, Diehl JL, Hill G. Histopathology of septic shock induced acute kidney injury: apoptosis and leukocytic infiltration. Intensive Care Med. 2010;36:471-8.

Paragas N, Qiu A, Zhang Q, Samstein B, Deng SX, Schmidt-Ott KM, Viltard M, Yu W, Forster CS, Gong G, Liu Y, Kulkarni R, Mori K, Kalandadze A, Ratner AJ, Devarajan P, Landry DW, D'Agati V, Lin CS, Barasch J. The Ngal reporter mouse detects the response of the kidney to injury in real time. Nat Med. 2011 Jan 16. [Epub ahead of print]

B02
Vascular Access /Membrane and Circuit

Michael Joannidis MD
8:30-10:00
Wednesday, February 23

Educational Objectives:
1. Describe the differences in membrane properties and its effects on biocompatibilty and coagulation system in CRRT
2. Discuss effects and usage of pre- and postdilution in CVVH and CVVHDF
3. Describe effects of CRRT modalities (CVVH, CVVHD, CVVHDF) on filter survival and solute clearance

Content Description:
Biocompatibility is significantly influenced by membrane characteristics. Main determinants are electronegativity of membrane surface and its ability to bind plasma proteins, as well as complement activation, adhesion of platelets and sludging of erythrocytes. Modification of existing membranes to increase heparin binding (AN69ST) reduced clotting in intermittent hemodialysis. Newer membranes are being developed with various polyethersulfone coatings that reduce activation of coagulation.

In predilution CRRT, substitution fluids are administered before the filter, thus diluting the blood in the filter, decreasing hemoconcentration and improving rheological conditions.

Reduced filter down-time may compensate for the lower predilution clearance. Predilution particularly reduces middle molecular clearance, the clinical consequences of which are still unclear.

For several reasons continuous venovenous hemofiltration (CVVH) appears to be associated with shorter circuit life than - hemodialysis (CVVHD). First, for the same CRRT dose hemofiltration requires higher blood flows. Higher blood flows give more flow limitation and more frequent stasis of blood flow. Second, hemofiltration is associated with hemoconcentration, occurring as a consequence of ultrafiltration. Within the filter, hematocrit, platelet count and coagulation factors increase, enhancing the tendency to coagulation. Hemodiafiltration (CVVHDF) combines the possible advantages of hemofiltration higher middle molecular clearance) with less hemoconcentration. Higher solute clearances can be attained at relatively lower blood flows and may thus increase circuit survival.

Suggested Reading:
1: Joannidis M, Oudemans-van Straaten HM. Clinical review: Patency of the circuit in continuous renal replacement therapy. Crit Care. 2007;11(4):218. Review.

2. Ramesh Prasad GV, Palevsky PM, Burr R, Lesko JM, Gupta B, Greenberg A: Factors affecting system clotting in continuous renal replacement therapy: results of a randomized, controlled trial. Clin Nephrol 2000, 53: 55-60.

3. Ricci Z, Ronco C, Bachetoni A, D'amico G, Rossi S, Alessandri E et al.: Solute removal during continuous renal replacement therapy in critically ill patients: convection versus diffusion. Crit Care 2006, 10: R67.

4. Brophy PD, Somers MJ, Baum MA, Symons JM, McAfee N, Fortenberry JD et al.: Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT). Nephrol Dial Transplant 2005, 20: 1416-1421.

5. Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R: Pre-dilution vs. post-dilution during continuous veno-venous hemofiltration: impact on filter life and azotemic control. Nephron Clin Pract 2003, 94: c94-c98.

6. Van der Voort PH, Gerritsen RT, Kuiper MA, Egbers PH, Kingma WP, Boerma EC: Filter run time in CVVH: pre- versus post-dilution and nadroparin versus regional heparin-protamine anticoagulation. Blood Purif 2005, 23: 175-180.

7. Padrini R, Canova C, Conz P, Mancini E, Rizzioli E, Santoro A: Convective and adsorptive removal of beta2-microglobulin during predilutional and postdilutional hemofiltration. Kidney Int 2005, 68: 2331-2337.

8. hu LP, Zhang XX, Xu L, Du CH, Zhu BK, Xu YY: Improved protein-adsorption resistance of polyethersulfone membranes via surface segregation of ultrahigh molecular weight poly(styrene-alt-maleic anhydride). Colloids Surf B Biointerfaces 2007, 57: 189-197.

9. Chanard J, Lavaud S, Randoux C, Rieu P: New insights in dialysis membrane biocompatibility: relevance of adsorption properties and heparin binding. Nephrol Dial Transplant 2003, 18: 252-257.

10. Sperling C, Houska M, Brynda E, Streller U, Werner C: In vitro hemocompatibility of albumin-heparin multilayer coatings on polyethersulfone prepared by the layer-by-layer technique. J Biomed Mater Res A 2006, 76: 681-689.

C03
Dialysis Dose Prescription and Delivery

Rolando Claure MD
8:30-10:00
Wednesday, February 23

Educational Objectives:
1. Describe the influence of operational characteristics of different RRT techniques on solute control.
2. Discuss the methods for assessing dialysis dose delivered and the factors influencing this parameter. A description of different methods for comparing dose among different types of RRT will be provided.
3. To expand the concept of dialysis dose and which other markers should be consider for prescribing and assessing it.

Content Description:
Assessing and delivering dialysis dose in acute kidney injury has emerged as an important issue in the management of critically-ill patients. There is ongoing debate on how dose of dialysis should be expressed and measured. Most studies have focused on clearance of small molecules (blood urea nitrogen) as a marker of delivered dose and for establishing dose outcome relationships. Recent evidence has shown that other markers may also be important to consider as acid-base balance and fluid overload have emerged as important factors contributing to outcomes. This workshop will provide an evaluation of current approaches to prescribing and delivering dialysis dose in acute kidney injury, identify gaps in practice and propose an integrated approach to optimize dose delivery in dialysis with a goal to improve outcomes.

Suggested Reading:
1. Marshall MR. Current status of dosing and quantification of acute renal replacement therapy. Part 1: mechanisms and consequences of therapy under-delivery. Nephrology (Carlton) 2006; 11: 171-180.

2. Davenport A, Bouman C, Kirpalani A, Skippen P, et al. Delivery of renal replacement therapy in acute kidney injury: what are the key issues? Clin J Am Soc Nephrol 2008; 3: 869-875.

3. Gotch FA. The current place of urea kinetic modelling with respect to different dialysis modalities. Nephrol Dial Transplant 1998; 13 Suppl 6: 10-14.

4. Gotch FA. Is Kt/V Urea a Satisfactory Measure for Dosing the Newer Dialysis Regimens? Seminars in dialysis 2001; 14: 15-17.

5. Diaz-Buxo JA, Loredo JP. Standard Kt/V: comparison of calculation methods. Artificial organs 2006; 30: 178-185.

6. Casino FG, Lopez T. The equivalent renal urea clearance: a new parameter to assess dialysis dose. Nephrol Dial Transplant 1996; 11: 1574-1581.

7. Ratanarat R, Permpikul C, Ronco C. Renal replacement therapy in acute renal failure: which index is best for dialysis dose quantification? The International journal of artificial organs 2007; 30: 235-243.

8. Casino FG, Marshall MR. Simple and accurate quantification of dialysis in acute renal failure patients during either urea non-steady state or treatment with irregular or continuous schedules. Nephrol Dial Transplant 2004; 19: 1454-1466.

9. Ricci Z, Salvatori G, Bonello M, Pisitkun T, et al. In vivo validation of the adequacy calculator for continuous renal replacement therapies. Critical care (London, England) 2005; 9: R266-273.

10. Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney international 2009; 76: 422-427.

D04
Critical Care Pharamacology: Vasopresors, and Ionotropes

Thomas A. Golper MD
Jeffry Lipman, MD
8:30-10:00
Wednesday, February 23

Educational Objectives:
1. Understand why the differing pathophysiologies in the critically ill become the rationale for the use of specific agents.
2. Understand how the physiology of drug handling differs when critically ill.
3. Understand how renal replacement therapies alter physiology and drug handling.

Content Description: This workshop will discuss the use of vasopressors, inotropes and vasodilators in the critically ill. Since from one patient to another the pathophysiology differs, there will be differing rationales for the use of specific agents. Dr. Lipman as an intensivist will discuss why and how he selects specific agents. Dr. Golper as a nephrolgist will discuss how renal replacement therapies and acute kidney injury affect these decisions.

There will be short presentations (lectures) cases to discuss, plenty of audience participation and time for discussion.

Suggested Reading:
Russell JA, Walley KR, Singer J et al. Vasopressin versus norepinephrine infusion in patients with septic shock. N Engl J Med 2008;358:877-887.

Annane D, Vignon P, Renault A et al. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. Lancet 2007;370:676-684.

Myburgh JA, Higgins A, Jovanovska A et al. A comparison of epinephrine and norepinephrine inc critically ill patients. Intensive Care Med 2008;34:2226-2234.

Lehtonen et al Pharmacokinetics and pharmacodynamics of intravenous inotropic agents. Clin Pharmacokin43:187, 2004

DePaepe et al Pharmacokinetic and pharmacodynamic considerations when treating patients with sepsis and septic shock. Ibid 41:1135, 2002

Mann et al Pharmacokinetic and pharmacodynamics in critically ill patients World J of Surgery 11:210, 1987

E05
Biomarkers 1: Principles and Applications

Chirag Parikh MD, PhD
8:30-10:00
Wednesday, February 23

Educational Objectives:
1) To discuss biomarkers from regulatory point of view
2) To evaluate application of biomarkers in various clinical settings
3) To discuss the interpretation of biomarker studies when the biomarkers are being compared to a poor gold standard.

Content Description:
In this workshop, we will discuss the development and application of biomarkers from regulatory and clinical point of view. We will also present some cases to discuss how the biomarkers can help with management in our current clinical practice. Finally, we will discuss the interpretation of biomarker studies in the context of varying status of underlying baseline kidney function, non-steady state and comparison to poor gold standard.

Suggested Reading:
1. Biomarkers Definitions Working Group: Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clinical Pharmacology & Therapeutics 2001;69:89-95.
2. Parikh CR, Lu JC, Coca SG, et al: Tubular proteinuria in acute kidney injury: a critical evaluation of current status and future promise. Ann Clin Biochem 2010;47:301-312.
3. Coca SG, Parikh CR. Urinary biomarkers for acute kidney injury: perspectives on translation. Clin J Am Soc Nephrol. 2008 Mar;3(2):481-90. Epub 2008 Feb 6. Review. PubMed PMID: 18256377.
4: Wu I, Parikh CR. Screening for kidney diseases: older measures versus novel biomarkers. Clin J Am Soc Nephrol. 2008 Nov;3(6):1895-901. Epub 2008 Oct 15. Review. PubMed PMID: 18922990.
5. Waikar SS, Betensky RA, Bonventre JV: Creatinine as the gold standard for kidney injury biomarker studies? Nephrol Dial Transplant 2009;24: 3263-3265.
6. 1: Waikar SS, Bonventre JV. Creatinine kinetics and the definition of acute kidney injury. J Am Soc Nephrol. 2009 Mar;20(3):672-9. Epub 2009 Feb 25. PubMed PMID: 19244578; PubMed Central PMCID: PMC2653692.
7: Waikar SS, Sabbisetti VS, Bonventre JV. Normalization of urinary biomarkers to creatinine during changes in glomerular filtration rate. Kidney Int. 2010 Sep;78(5):486-94. Epub 2010 Jun 16. PubMed PMID: 20555318; PubMed Central PMCID: PMC3025699.

F06

Extracorporeal Techniques for Sepsis 1:
Pathophysiology and Targets

Patrick M. Honoré MD
8:30-10:00
Wednesday, February 23

Educational Objectives:
1)Review briefly the rationale of Hybrid therapy in sepsis regarding experimental issues.Special focus on Hybrid therapy regarding large bore membranes and highly adsoptive membranes.

2) Describe the New Possibilities given with the New Membranes for High permeability hemofiltration (HPHF) that do offers to the clinician especially with the combined use of high volume hemofiltration (for Synergic action) a new tool in order to try to effectively combat septic shock with acute kidney injury (AKI).
Previous studies did show that HPHF especially with combined HVHF can removed much large quantities of mediators.

3)Describe the new possibilities given with the New Membranes for Hybrid Therapies regarding High Adsorptive Hemofiltration doing at the same time, Endotoxin Adsorption and Cytokine Adsorption.

4)Review all animal & experimental data regarding this issue.

Content Description:
A few words has to be said about some new insides regarding the latest theory of “New Active Transportation between two Asymmetric Compartments” Hypothesis and New Insights into Rationale & Potential Mechanisms. Pro-mediators as well as mediators are removed at interstitial and tissue levels, following removal from the blood compartment, until a so-called threshold point is reached at which some pathways and cascades are stopped .At this level, the cascades are interrupted and no further harm can be done to the tissues.Until recently, this mechanism was taught to be a passive transportation pathway.As said in the introduction, effectiveness through only a passive transportation mechanism remains elusive.Indeed as demonstrated before and knowing that the surface of the central blood compartment (CEBC) is about 30 mÇ, which is much smaller than the surface of the capillary blood compartment (CABC)which is about 300 mÇand therefore passive transport between these two asymmetric compartments will not yield the same elimination rate on both sides.As a consequence, when a given technique is able to remove 40 % of the mediators of the CEBC side, it will only represents 4 % of the removal into the CABC side if the removal is only a passive mechanism.It is therefore easy to understand, that an other mechanism has to take place and this should be this time, an active transportation mechanism.

Previous studies did show that HPHF especially with combined HVHF can removed much large quantities of mediators.

A preliminary study called the HICOSS study(High Cut-off in Septic Shock)was looking as pilot study in order to compare in 80 patients with Septic Shock plus AKI. 40 patients were assigned with conventional membrane and 40 patients were assigned with an hyperpermeable membrane (septex).Those patients were in septic shock plus AKI but also in multiple organ failure (MODS).The mode chosen was CVVD for 5 consecutive days.The principal aim was to evaluate the safety regarding albumin losses (cut-off of 60 kDa) and a 50 % reduction in catecholamine requirements.Mortality was a secondary end point.

The results shows a excellent safety as the membrane was not loosing albumin more than a classical membrane.Nevertheless, regarding vasopressors free days as well length of ICU stay and mortality , no differences could be seen between the two groups.This may be due the fact that the mode was only CVVD and perhaps the results would be very different if we were using CVVH at 35 ml/kg/h plus HPHF.Description will be done also regarding data for new adsorptive membranes.

In conclusion, the hyperpermeable membrane (septex) is safe and could be a important therapeutic tool in the future when associated with HVHF.Potential effect of highly adsorptive membranes need to be evaluated.

Experimental studies are still under way.Those studies will need mechanistic steps, small RCT's steps and finally large RCT's at some point.

Suggested Reading:

1- Honoré PM, Joannes-Boyau O, Jacobs R,Solignac M .Blood Purification in Sepsis:Fiction or Fact for the Clinician. Reanimation 2010;19:7-12

2.- Honoré PM, Zydney AL, Matson JR. High volume and high permeability haemofiltration in sepsis. The evidences and the key issues. Care Crit ill 2003;3:69-76

3. Matson J R, Zydney AR, Honore,PM. Blood Filtration: New Opportunities and the Implications On System Biology.Critical Care and Resucitation 2004; 6:209-218.

4. Morgera S, Haase M, Kuss T, et al. Pilot study on the effects of high cutoff hemofiltration on the need for norepinephrine in septic patients with acute renal failure. Crit Care Med 2006;34:2099-104.

5. Cruz DN, Antonelli M, Fumagalli R, et al. Early use of polymyxin B hemoperfusion in abdominal septic shock: the EUPHAS randomized controlled trial. JAMA 2009;301:2445-52.

6. Honore PM, Joannes-Boyau O, Dobbeleir N.Blood Purification in Sepsis & Acute Kidney Injury in Critically Ill Patients:New Insights & Potential Mechanisms with an Update on Recent Trials.Chapter of the Yearly Book in Intensive Care Medicine 2011
(31 th ISICEM March 2011)

7.Honore PM et al. Continuous Hemofiltration or Intermittent Dialysis for Septic Shock Patients in ICU with AKI :A Pragmatic Approach for Bedside Intensivists Summarizing the More Recent Advances.Annals of Intensive Care 2011: In Press.

G07
Competency Assessment in CRRT

Ian Baldwin RN, PhD, ACCCN
8:30-10:00
Wednesday, February 23

Educational Objectives:
1. To review suitable core curriculum for CRRT when applied in the ICU.
2. To review suitable competency assessments and testing methods from the curriculum.
3. To consider measures of success following competency assessment.

Content Description:
This presentation will integrate with others in the workshop to provide a practical review of what competency means in a working shift for the ICU nurse and the background framework of a suitable CRRT curriculum. This is important because patients requiring CRRT therapy are associated with high mortality and are often the sickest patients within a nurses care. Reports of errors and mistakes linking CRRT use to patient harm and deaths have been a harsh reminder that the therapy is potentially dangerous and requires proper education (knowledge) and training (practical) for nurses. There may be an association between patient outcomes and CRRT nursing education/training ?

While many hospitals have developed significant 'local' expertise and skill providing CRRT, the research base for nursing and best practise is reflected in a lack of publications, and poor curriculum content within specialty nurse training programs. This suggests that much expertise is developed by trial and error at the bedside, with some devoted individuals championing the cause in isolation, but suboptimal care often evident in their absence. Appropriate undergraduate and post graduate curriculum content, followed by workplace training, experience and competency assessment is often the history for the success of other life support treatments in the ICU setting. Assessing the success of such teaching and assessment efforts is also necessary. So what should the CRRT curriculum include for ICU nurses?

A well used and tested approach to this will be presented and reviewed.

Suggested Reading:
1. Baldwin I and Fealy N. 2009 Nursing for renal replacement therapies in the Intensive Care Unit: historical, educational, and protocol review. Blood Purification. 27: 174 – 181.
2. Baldwin I and Fealy N. 2009 Clinical nursing for the application of renal replacement therapies in the Intensive Care Unit. Seminars in Dialysis. Vol. 22 No. 2. pp 189 – 193.
3. Baldwin I. 2007 Is there a need for a nurse emergency team for continuous renal replacement therapy ? in Contributions to Nephrology Vol. 156. pp. 191-196. C Ronco, R Bellomo, J Kellum editors. Basel, Karger.
4. Rauen C A. 2001. Using simulation to teach critical thinking skills. Critical care Nursing Clinical of North America. Vol. 13. No. 1. 93 – 103. March.
5. Baldwin I. 1997. Training Management and Credentialing for CRRT in Critical Care. American Journal of Kidney Diseases, Vol 30(5) S4.S112-116.
6. Boyle M and Baldwin I. 2010 Understanding the Continuous Renal Replacement Therapy circuit for Acute Renal failure support; A quality issue in the Intensive Care Unit. AACN Vol. 21 No. 4 pp. 365 - 75
7. Mehta R, Martin R. 1996. Initiating and implementing a continuous renal replacement therapy program: requirements and guidelines. Sem in Dialysis; 9:80-87.
8. Hagaman C, Ballard-Hernandez J, Cabaluna V. 2008 Developing Nursing Competency in Continuous Renal Replacement Therapy (CRRT). Abstract in Critical care Nurse; 28 (2) April e5
9. Barletta J F, Barletta G-M, Brophy P D, Maxvold N J, Hackbarth R M and Bunchman T E. 2006. Medication errors and patient complications with continuous renal replacement therapy. Pediatric Nephrology. Jun;21(6):842-5.

G07
Competency Assessment in CRRT

Eileen Lischer MA, BSN, RN, CNN
8:30-10:00
Wednesday, February 23

Educational Objectives:
1. Discuss the elements to be considered in developing a competency
2. Identify competency areas for CRRT
3. Discuss the evaluation process and techniques

Content Description:
CRRT possesses many complex processes with many options for equipment and procedures. Assessing competency is critical to determine performance excellence and ensure patient safety. Competency assessment is an ongoing process that requires continuing education and skill evaluation. The process is useful in designing and implementing a learning experience to facilitate the RN in achieving the required performance competencies. Competency evaluations identify areas of strength and developmental needs. A plan needs to be in place to routinely assess skill performance adequacy and supplement the individual's knowledge base with current information. While many organizations have developed Standards of Practice, each unit must determine what competency meets their individual setting. This lecture will offer examples of CRRT competencies as a guideline.

Suggested Reading:
Burrows-Hudson, Sally and Prowant, Barbara F., Nephrology Nursing Standards of Practice and Guidelines for Care, American Nephrology Nurse Association publication 2005 pp. 103-112. www.annanurse.org

Lancaster, Larry E, Core Curriculum for Nephrology Nursing, 5th edition, , American Nephrology Nurse Association publication , pp 231-278.

Continuous Renal Replacement Therapy, Nephrology Nursing Guidelines for Care, ANNA publication. 2005. (endorsed by the American Association of Critical Care Nurses)

Standards for the Acute and Critical Care Nurse. www.aacn.org

B10
Anticoagulation: Mechanisms and Techniques

Michael Joannidis MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
1. Describe the principles of conventional anticoagulation in CRRT (heparins).
2. Describe pathophysiology and clinical presentation of heparin induced thrombocytopenia (HIT)
3. Describe alternative anticoagulation in suspicion or in the presence of HIT.

Content Description:
Premature circuit clotting is a major problem in daily practice of continuous renal replacement therapy (CRRT), increasing blood loss, work load and costs. Early clotting is related to bioincompatibility, critical illness, vascular access, CRRT circuit and modality. This workshop focuses on measures to prevent circuit failure, comprising non-anticoagulant measures as well as systemic and regional anticoagulation. Non-anticoagulation measures include optimization of extracorporeal flow, CRRT settings and training of nurses. Anticoagulation is generally required. Systemic anticoagulation interferes with plasmatic coagulation, platelet activation or both, and should be kept at a low dose to mitigate bleeding complications. Under these conditions low molecular weight heparins have been shown to be more efficient than unfractionated heparins but require anti-Xa monitoring.

Anticoagulation with heparins bears significant risk of emerging heparin induced thrombocytopenia (HIT). In case of HIT any heparin administration has to be stopped and alternative immediately anticoagulation regimens must be applied. Currently available options in HIT are danaparoid or the direct thrombin inhibitor argatobran. For both substances limited experience for CRRT is reported in the literature.

Suggested Reading:
1: Schusterschitz N, Bellmann R, Stein M, Dunzendorfer S, Pechlaner C, Joannidis M. Influence of continuous veno-venous hemofiltration on argatroban clearance in a patient with septic shock. Intensive Care Med. 2008 Jul;34(7):1350-1. Epub 2008 Feb 23. PubMed PMID: 18297262.

2: Joannidis M, Oudemans-van Straaten HM. Clinical review: Patency of the circuit in continuous renal replacement therapy. Crit Care. 2007;11(4):218. Review. PubMed PMID: 17634148; PubMed Central PMCID: PMC2206533.

3: Link A, Girndt M, Selejan S, Mathes A, Böhm M, Rensing H. Argatroban for anticoagulation in continuous renal replacement therapy. Crit Care Med. 2009 Jan;37(1):105-10. PubMed PMID: 19050602.

4: Tolwani AJ, Wille KM. Anticoagulation for continuous renal replacement therapy. Semin Dial. 2009 Mar-Apr;22(2):141-5. Review. PubMed PMID: 19426417.

5: Joannidis M, Kountchev J, Rauchenzauner M, Schusterschitz N, Ulmer H, Mayr A, Bellmann R. Enoxaparin vs. unfractionated heparin for anticoagulation during continuous veno-venous hemofiltration: a randomized controlled crossover study. Intensive Care Med. 2007 Sep;33(9):1571-9. Epub 2007 Jun 12. PubMed PMID: 17563874.

6: Oudemans-van Straaten HM, van Schilfgaarde M, Molenaar PJ, Wester JP, Leyte A. Hemostasis during low molecular weight heparin anticoagulation for continuous venovenous hemofiltration: a randomized cross-over trial comparing two hemofiltration rates. Crit Care. 2009;13(6):R193. Epub 2009 Dec 3. PubMed PMID: 19958532; PubMed Central PMCID: PMC2811918.

7: Oudemans-van Straaten HM, Wester JP, de Pont AC, Schetz MR. Anticoagulation strategies in continuous renal replacement therapy: can the choice be evidence based? Intensive Care Med. 2006 Feb;32(2):188-202. Epub 2006 Feb 2. Review. PubMed PMID: 16453140.

B10
Anticoagulation: Mechanisms and Techniques

Ashita Tolwani MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
1. Discuss the mechanism of citrate anticoagulation and metabolic consequences
2. Describe the composition of commercially available citrate solutions and the different methods of citrate delivery
3. Discuss citrate circuit options and protocols for CVVH, CVVHD, CVVHDF, and SLED

Content Description:
This presentation describes the use of citrate anticoagulation for CRRT using a case-based approach. Several published citrate protocols for each CRRT modality will be discussed in detail, including the description of the technique,components, circuit, target parameters and dialyzer patency rates. Metabolic complications of citrate, including citrate toxicity, will be discussed.

Suggested Reading:
1. Davenport A, Tolwani A. Citrate anticoagulation for continuous renal replacement therapy (CRRT) in patients with acute kidney injury admitted to the intensive care unit. NDT Plus 2009;2:439-447.
2. Oudemans-van Straaten HM, Bosman RJ, Koopmans M et al. Citrate anticoagulation for continuous venovenous hemofiltration. Crit Care Med 2009; 37:545-552.
3. Tolwani A, Prendergast M, Speer R, Stofan B, Wille K. A practical anticoagulation CVVHDF protocol for metabolic control and high solute clearance. CJASN 2006;1:79-87.

C11
Fluid Management

Ravindra L. Mehta MBBS, MD, DM, FACP
10:15-11:45
Wednesday, February 23

Educational Objectives:
1. Describe the goals of fluid management in critically ill patients and identify complications of fluid resuscitation.
2. Discuss the principles of fluid management with CRRT techniques and discuss the practical issues in developing a strategy for using CRRT as a fluid regulatory device.
3. Describe the practical issues related to fluid regulation with CRRT based on different modalities and pumps.

Content Description:
Volume support is frequently required in critically ill patients exhibiting hypovolemia particularly in the setting of shock, systemic inflammatory response syndrome (SIRS) and sepsis. Often volume management results in a fluid overloaded state requiring diuresis or dialytic intervention. Achieving an appropriate level of volume management requires knowledge of the underlying pathophysiology, evaluation of volume status, selection of an appropriate solution for volume repletion and maintenance and modulation of the tissue perfusion and cellular injury. In the presence of a failing kidney, fluid removal is often a challenge and it is often necessary in this setting to institute dialysis for volume control rather than metabolic control. CRRT techniques offer a significant advantage over intermittent dialysis for fluid control, however, if not carried out appropriately it can result in major complications. In order to utilize these therapies for their maximum potential it is necessary to recognize the factors which influence fluid balance and have an understanding of the principles of fluid management with these techniques. This workshop will describe the current concepts of volume management in shock states and discuss the basic methods for fluid management with CRRT and provide an approach to targeted intervention in critically ill patients. We will use case studies to describe various approaches for fluid removal and regulation with CRRT.

Suggested Reading:
1. Bagshaw SM, Baldwin I, Fealy N, Bellomo R. Fluid balance error in continuous renal replacement therapy: a technical note. Int J Artif Organs 2007; 30: 434-440.
2. Bagshaw SM, Brophy PD, Cruz D, Ronco C. Fluid balance as a biomarker: impact of fluid overload on outcome in critically ill patients with acute kidney injury. Crit Care 2008; 12: 169.
3. Bellomo R. Bench-to-bedside review: lactate and the kidney. Crit Care 2002; 6: 322-326.
4. Bouchard J, Mehta RL. Fluid accumulation and acute kidney injury: consequence or cause. Curr Opin Crit Care 2009; 15: 509-513.
5. Bouchard J, Mehta RL. Volume management in continuous renal replacement therapy. Semin Dial 2009; 22: 146-150.
6. Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int 2009; 76: 422-427.
7. Gibney N, Cerda J, Davenport A, Ramirez J, et al. Volume management by renal replacement therapy in acute kidney injury. Int J Artif Organs 2008; 31: 145-155.
8. Gunnerson KJ, Kellum JA. Acid-base and electrolyte analysis in critically ill patients: are we ready for the new millennium? Curr Opin Crit Care 2003; 9: 468-473.
9. Jabara AE, Mehta RL. Determination of fluid shifts during chronic hemodialysis using bioimpedance spectroscopy and an in-line hematocrit monitor. ASAIO J 1995; 41: M682-687.
10. Kellum JA. Fluid resuscitation and hyperchloremic acidosis in experimental sepsis: improved short-term survival and acid-base balance with Hextend compared with saline. Crit Care Med 2002; 30: 300-305.
11. Mehta RL. Fluid management in CRRT. Contrib Nephrol 2001: 335-348.
12. Mehta RL. Fluid balance and acute kidney injury: the missing link for predicting adverse outcomes? Nat Clin Pract Nephrol 2009; 5: 10-11.

13. Mehta RL, Cantarovich F, Shaw A, Hoste E, et al. Pharmacologic approaches for volume excess in acute kidney injury (AKI). Int J Artif Organs 2008; 31: 127-144.
14. Mehta RL, Clark WC, Schetz M. Techniques for assessing and achieving fluid balance in acute renal failure. Curr Opin Crit Care 2002; 8: 535-543.
15. Murugan R, Venkataraman R, Wahed AS, Elder M, et al. Preload responsiveness is associated with increased interleukin-6 and lower organ yield from brain-dead donors. Crit Care Med 2009; 37: 2387-2393.
16. Naka T, Bellomo R, Morimatsu H, Rocktaschel J, et al. Acid-base balance during continuous veno-venous hemofiltration: the impact of severe hepatic failure. Int J Artif Organs 2006; 29: 668-674.
17. Ronco C. Fluid balance in CRRT: a call to attention! Int J Artif Organs 2005; 28: 763-764.
18. Ronco C, Ricci Z, Bellomo R, Baldwin I, et al. Management of fluid balance in CRRT: a technical approach. Int J Artif Organs 2005; 28: 765-776.
19. Sutherland SM, Zappitelli M, Alexander SR, Chua AN, et al. Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55: 316-325.
20. Bouchard J, Mehta RL. Acid-base disturbances in the intensive care unit: current issues and the use of continuous renal replacement therapy as a customized treatment tool. Int J Artif Organs 2008; 31: 6-14.
21. Bouchard J, Macedo E, Mehta RL. Dosing of Renal Replacement Therapy in Acute Kidney Injury: Lessons Learned From Clinical Trials. Am J Kidney Dis.
22. Cerda J, Sheinfeld G, Ronco C. Fluid overload in critically ill patients with acute kidney injury. Blood Purif 29: 331-338.
23. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, et al. Fluid balance and acute kidney injury. Nat Rev Nephrol 6: 107-115.
24. Prowle J, Bellomo R, Buckmaster J, Gutteridge G, et al. Continuous hemofiltration for anasarca: recovery of renal function after 71 liters of net ultrafiltration. Int J Artif Organs 2008; 31: 367-370.
25. Kugener L, Brasseur A, Fagnoul D, Vincent JL. High rate ultrafiltration in anasarca: 33 l of net negative fluid balance in 52 h! Intensive Care Med 37: 180-181.

D12
Critical Care Management: Nutrition Assessment and Delivery

Oliver Joannes-Boyau MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
- Nutritional impact of sepsis and CRRT
- Amino-Acid, vitamins and trace elements needs with and without CRRT
- Amino-Acid, vitamins and trace elements management during CRRT

Content Description:
Continuous renal replacement techniques as sepsis have an impact on nutritional status of patients in ICU. It is important to know the exact removal power of hemofiltration on amino-acids and trace elements and how we can counter this. There are some articles and small studies in the literature that focus on this subject, but with low level results and few recommendations. In the IVOIRE study amino-acids and trace elements were dosed at different times to follow the level of removal of these along time and to try to find simple tips to avoid nutritional deficit in the future. For septic patients, antibiotics are also crucial and we know that CRRT has a high potential of removal for these molecules. A review of literature and the results from IVOIRE study will be presented with new recommendations for good nutrition management given procedures in the future.

Suggested Reading:
1. Bouman CS, van Kan HJ, Koopmans RP, Korevaar JC, Schultz MJ, Vroom MB. Discrepancies between observed and predicted continuous venovenous hemofiltration removal of antimicrobial agents in critically ill patients and the effects on dosing. Intensive Care Med 2006;32(12):2013-9.
2. Bugge JF. Pharmacokinetics and drug dosing adjustments during continuous venovenous hemofiltration or hemodiafiltration in critically ill patients. Acta Anaesthesiol Scand 2001;45(8):929-34.
3. Roberts JA, Lipman J. Pharmacokinetic issues for antibiotics in the critically ill patient. Crit Care Med 2009;37(3):840-51; quiz 859.
4. Berger MM, Shenkin A, Revelly JP, et al. Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients. Am J Clin Nutr 2004;80(2):410-6.
5. Berger MM, Shenkin A. Vitamins and trace elements: practical aspects of supplementation. Nutrition 2006;22(9):952-5.
6. Marin A, Hardy G. Practical implications of nutritional support during continuous renal replacement therapy. Curr Opin Clin Nutr Metab Care 2001;4(3):219-25.
7. Valencia E, Marin A, Hardy G. Nutrition therapy for acute renal failure: a new approach based on 'risk, injury, failure, loss, and end-stage kidney' classification (RIFLE). Curr Opin Clin Nutr Metab Care 2009;12(3):241-4.

E13
Biomarkers 2: Application in AKI

Patrick T. Murray MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
1 .Describe the development and qualification of functional biomarkers of AKI, including current performance characteristics and application for diagnosis, management and prognostication in AKI.
2. Describe the development and qualification of and structural/damage biomarkers of AKI, including current performance characteristics and application for diagnosis, management and prognostication in AKI.
3 .Discuss the use of AKI biomarkers (functional and structural/damage markers) to detect drug nephrotoxicity in drug development.

Content Description:
In this workshop, we will provide an overview of the current inventory of AKI biomarkers that have been identified. We will separately review those markers that are functional (identifying changes in renal function) or structural (identifying renal damage). We will identify markers that are useful to assess AKI risk; to diagnose AKI earlier than current diagnostic tools; to differentiate between causes of AKI; to predict or quantify AKI severity; to predict clinical outcomes of AKI; and to assess the course (progression or recovery) of AKI. We will also specifically review the current status of AKI biomarkers to identify nephrotoxicity in drug development.

Suggested Reading:
1. Biomarkers Definitions Working Group: Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clinical Pharmacology & Therapeutics 2001;69:89-95.
2. Bellomo R, Ronco C, Kellum JA, et al.: Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8(4): R204-12.
3. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A: Acute Kidney Injury Network (AKIN): report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
4. P Murray, P Devarajan, A Levey, KU Eckardt, J Bonventre, R. Lombardi, S Herget-Rosenthal, A Levin: Criteria for AKI Diagnosis and Staging in Different Environments. Clinical Journal of the American Society of Nephrology 2008;3(3)864-8.
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6. Soto K, Coelho S, Rodrigues B, Martins H, Frade F, Lopes S, Cunha L, Papoila AL, Devarajan P: Cystatin C as a marker of acute kidney injury in the emergency department. Clin J Am Soc Nephrol. 2010 Oct;5(10):1745-54. Epub 2010 Jun 24
7. Nejat M, Pickering JW, Walker RJ, Endre ZH: Rapid detection of acute kidney injury by plasma cystatin C in the intensive care unit. Nephrol Dial Transplant. 2010 Oct;25(10):3283-9. Epub 2010 Mar 28.
8. Nickolas TL, O'Rourke MJ, Yang J, Sise ME, Canetta PA, Barasch N, Buchen C, Khan F, Mori K, Giglio J, Devarajan P, Barasch J: Sensitivity and specificity of a single emergency department measurement of urinary neutrophil gelatinase-associated lipocalin for diagnosing acute kidney injury. Ann Intern Med. 2008 Jun 3;148(11):810-9.
9. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A; NGAL Meta-analysis Investigator Group. Accuracy of neutrophil gelatinase-associated lipocalin (NGAL) in diagnosis and prognosis in acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis 2009; 54(6):1012– 1024. PMID 19850388.
10. Bonventre JV, Vaidya VS, Schmouder R, et al Next generation biomarkers for detecting kidney toxicity. Nature Biotechnol 2010; 21(5): 426-440.

G15
Therapeutic Modalities: IHD, SLED, PD

Rajasekara Chakravarthi MD, DNB (Nephrology)
10:15-11:45
Wednesday, February 23

Educational Objectives:

1.To discuss various options of dialytic modalities for patients with Acute kidney injury in the ICU

2.Discuss the advantages and disadvantages of PD vs SLED vs CRRT

3.Understand how these three modalities are complimentary to each other and how one can be used as a bridge to the other

Content Description:
Patients in the ICU are a heterogenous group. The dialytic modalities available at present may not address all their metabolic and haemodynamic needs.
Each modality like Peritoneal dialysis, SLED or CRRT will address the needs of some patients. It is necessary to choose a modality which helps the pt to come out of a clinical situation on that particular day. It may be necessary to choose a different modality of RRT the next day as the needs are different. All the three modalities of RRT have their advantages and disadvantages and actually compliment each other in the ICU. One can be a bridge to the other.

Suggested Reading:
1. Critical Care Nephrology
by Claudio Ronco
Rinaldo Bellomo
John Kellum

second edition. 2009 Elsevier Inc

2. Renal Replacement Therapy for Acute Renal FailureSeminars in Dialysis
1993, 9;6 (entire issue dedicated to RRT in ICU)

G15
Therapeutic Modalities: IHD, SLED, PD

Daniela Ponce MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
1. Review the role of Peritoneal Dialysis (PD) in Acute Kidney Injury (AKI).
2. Present different types and doses of PD for AKI including intermittent PD, tidal PD and high volume PD.
3. Discuss comparison of PD in AKI to other extracoporeal therapies (iHD, SLED, CRRT)

Content Description:
PD is an under-utilized modality worldwide for AKI, but is frequently used in developing countries due to its lower cost and minimal infrastructure requirements. Recently, there has been an increased interest in using PD to manage patients with AKI.
The use of cyclers, flexible catheter and high volume of dialysis fluid have been purposed to overcome some of the classic limitations of PD use in AKI, as low rate of ultrafiltration, high chance of infection and no metabolic control,
This workshop will provide an overview of that a careful prescription and accurate measurement of efficiency may contribute to providing adequate treatment in a selected group of AKI patients, comparing PD to other dialysis methods regarding its efficacy and patients outcome.

Presentation Outline
1. Case study
2. Is PD used?
3. Can it be used? Why?
4. For whom patients?
5. How to prescribe it?
6. Is it better or worsen than other methods?

Suggested Reading:
1. Gabriel DP, Ribeiro do Nascimento GV, Teixeira CJ, Cuadrado ML, Barretti P, Balbi AL. High volume peritoneal dialysis for acute renal failure. Perit Dial Int 2007; 27:277–82.
2.Daugirdas JT. Peritoneal dialysis in acute renal failure—why the bad outcome? N Engl J Med 2003; 347:933–5.
3. Phu NH, Hien TT, Mai NTH et al. Hemofiltration and peritoneal dialysis in infection associated acute renal failure in Vietnam. N Engl J Med 2002;347: 895-902.
4. Gabriel DP, Caramori JT, Martim LC et al: High volume peritoneal dialysis vs daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. Kidney Int Suppl 2008:S87– S93
5. Chionh CY, Soni SS, Cruz DN, Ronco C. Peritoneal dialysis for acute kidney injury: techniques and dose.Contrib Nephrol. 2009;163:278-84
6. Chionh CY, Ronco C, Finkelstein FO, Soni SS et al. Acute peritoneal dialysis: what is the adequate dose for acut kidney injury? Nephrol Dial Transplant 2010; 1-6

H16
Pediatric CRRT: The Basics

Jordan M. Symons MD
10:15-11:45
Wednesday, February 23

Educational Objectives:
Following this session, participants should be able to:

1. Recognize the various indications for continuous renal replacement therapy (CRRT) in the pediatric population
2. Describe the different methods and techniques available to provide CRRT to children
3. Understand the outcome for children who require CRRT and who receive CRRT

Content Description:
Continuous renal replacement therapy (CRRT) is now a well-established option for renal replacement in the critically ill pediatric patient. Providing CRRT to a child presents a series of challenges, some of which differ from those seen in the care of the adult patient. This session will present basic issues in pediatric CRRT, including:

• Epidemiology of pediatric acute kidney injury (AKI)

• Indications for CRRT, including AKI and other issues (e.g., fluid overload, metabolic disease)

• Methods for providing successful CRRT to the pediatric patient, with special emphasis on the unique characteristics of the critically ill child and how this may have an impact on the approach (vascular access, devices, prescription, anticoagulation, complications)

• Outcomes for pediatric patients who require CRRT

The session will include slide presentation and informal discussion; questions and interaction between faculty and participants is desired and strongly encouraged.

Suggested Reading:
Brophy PD et al. Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT). Nephrology Dialysis Transplantation 20: 1416-1421, 2005.

Goldstein SL et al. Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. Kidney International 67: 653-658, 2005.

Hayes LW et al. Outcomes of critically ill children requiring continuous renal replacement therapy. Journal of Critical Care 24: 394-400, 2009.

MacLaren G and Butt W. Controversies in paediatric continuous renal replacement therapy. Intensive Care Medicine 35: 596-602, 2009.

Southerland SM et al. Fluid overload and mortality in children receiving continuous renal replacement therapy: The Prospective Pediatric Continuous Renal Replacement Therapy Registry. American Journal of Kidney Diseases 56(2): 316-325, 2010.

Symons JM et al. Demographi characteristics of pediatric continuous renal replacement therapy: a report of the Prospective Pediatric Continuous Renal Replacement Therapy Registry. CJASN 2: 732-738, 2007.

Zappitelli M et al. Continuous renal replacement therapy amino acid, trace metal and folate clearance in critically ill children. Intensive Care Medicine. 35(4): 698-706, 2009.

I17
Preventing and Managing Complications of Dialysis: Intradialytic Hypotension

Andrew Davenport MD, FRCP
10:15-11:45
Wednesday, February 23

Educational Objectives:
1. To discuss the reactions which occur when blood passes through the extracorporeal circuit
2. The effects of different anticoagulants
3. Factors which affect intravascular volume and tone during dialysis treatments

Content Description:
Hypotension during treatment with an extracorporeal circuit typically occurs either due to a loss of vascular tone or due to a reduction in effective circulating volume. As such patient factors are an important determinant, with these reactions occurring more commonly in patients with reduced systemic vascular resistance (acute liver failure, severe sepsis), hypovolaemia and reduced cardiac output (cardiogenic shock).

Hypotensive reactions can be divided into those which occur at the start or shortly after connecting the patient to the extracorporeal circuit and those towards the end of the session. Early reactions are subdidved into acute anaphylactoid reactions to anticoagulants and sterilising agents, and extracorporeal reactions secondary to anaphylotoxin production (C3a & C5a), bradykin formation and nitric oxide generation.

Later episodes of hypotension are typically associated with reduction in the effective plasma volume, either due to changes in vascular tone or an imbalance between ultrafiltration rate and plasma refilling rate, or cardiac causes, predominantly arrhythmias. Excessive ultrafiltration rates may stem from inaccurate clinical assessment and prescription of fluid orders, staff errors in terms of machine programming or over riding machine alarms leading to unrecognised changes in ultrafiltration rates, and machine errors. Plasma refilling rate depends upon plasma osmolality, and vascular tone is affected by temperature.

Suggested Reading:

1 Kooman J, Basci A, Pizzarelli F, Canaud B, Haage P, Fouque D, Konner K, Martin-Malo A, Pedrini L, Tattersall J, Tordoir J, Vennegoor M, Wanner C, Ter Wee P, Vanholder REBPG guideline on haemodynamic instability. Nephrol Dial Transplant. 2007;22 Suppl 2:ii22-ii44
2 Davenport A. Sudden collapse during haemodialysis due to immune mediated heparin induced thrombocytopenia. Nephrol Dial Transplant 2006;21: 1721-1724
3 Davenport A. Intradialytic complications during hemodialysis. Hemodial Int. 2006;10:162-167
4 Maggiore Q, Pizzarelli F, Sisca S, Zocalli C, Parlongo S, Nicolo F, Creazzo G. Blood temperature and vascular stability during hemodialysis and hemofiltration. ASAIO Trans 1982; 28: 523-527
5 Andrulli S, Colzani S, Mascia F, Lucchi L, Stipo L, Bigi MC, Crepaldi M, Redaelli B, Albertazzi A, Locatelli F. The role of blood volume reduction in the genesis of intradialysis hypotension. Am J Kidney Dis. 2002 ;40:1244-1254
6 Mancini E, Mambelli E, Irpinia M, Gabrielli D, Cascone C, Conte F, Meneghel G, Cavatorta F, Antonelli A, Villa G, Dal Canton A, Cagnoli L, Aucella F, Fiorini F, Gaggiotti E, Triolo G, Nuzzo V, Santoro A. Prevention of dialysis hypotension episodes using fuzzy logic control system. Nephrol Dial Transplant. 2007;22:1420-1427

B19
Drug Management in CRRT

Bruce A. Mueller PharmD, FCCP, FASN
2:30-4:00
Thursday, February 24

Educational Objectives:
1. Given an actual patient case, formulate a drug therapy regimen.
2. Calculate a drug's dose if given the sieving coefficient of that drug and the CRRT parameters.

Content Description:
Case-based discussion of practical aspects for drug prescription, delivery and management of drug interactions in CRRT.

A case will be presented and dosing approaches will be shared with the audience. Questions are encouraged from the audience.

Suggested Reading:
Mueller BA, Pasko DA, Sowinski KM. Higher renal replacement therapy dose delivery influences on drug therapy. Artif Organs 2003;27(9):806-812.

Roberts JA, Lipman J. Pharmacokinetic issues for antibiotics in the critically ill patient. Crit Care Med 2009;37:840-851.

Decker BS, Mueller BA, Sowinski KM. Drug Dosing Considerations in Alternative Hemodialysis. Advances in Chronic Kidney Disease 2007; 14, No 3 (July): e17-e26.

C20
Starting and Stopping RRT for AKI: Principles and Practice

Etienne Macedo MD, PhD
2:30-4:00
Thursday, February 24

Educational Objectives:
1. Describe the factors affecting timing of initiation and stopping of RRT in critically ill patients.
2. Discuss the principles and evidence for early intervention with RRT in the ICU
3. Describe various approaches and practical aspects for initiating and stopping RRT

Content Description:
Several randomized studies have tried to delineate the best modality or the optimal dialysis dose to manage acute kidney injury (AKI), with inconsistent results. One important aspect of the management of critically ill patients which is still controversial is the timing of initiation and cessation of renal replacement therapy (RRT). The lack of consensus on what parameters should guide the decision to start dialysis has led to a wide variation in dialysis initiation. A contributing factor is the lack of studies in the modern era evaluating the relationship of timing of dialysis initiation and outcomes. Although listed as one of the top priorities in research on AKI, timing of dialysis initiation has not been included as a factor in large, randomized controlled trials in this area. Similarly, cessation of RRT has received little attention and has not been studied extensively. This workshop will utilize cases to illustrate the principles for determining optimal time for intervention and a strategy for stopping RRT in critically ill patients

Suggested Reading:
1. Palevsky PM, Zhang JH, O'Connor TZ, et al. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med 2008; 359: 7-20.
2. Liu KD, Himmelfarb J, Paganini E, et al. Timing of initiation of dialysis in critically ill patients with acute kidney injury. Clin J Am Soc Nephrol 2006; 1: 915-919.
3. Saudan P, Niederberger M, De Seigneux S, et al. Adding a dialysis dose to continuous hemofiltration increases survival in patients with acute renal failure. Kidney Int 2006; 70: 1312-1317.
4. Bouman C, Oudemans-Van Straaten H, Tijssen J, et al. Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: a prospective, randomized trial. Crit Care Med 2002; 30: 2205-2211.
5. Sugahara S, Suzuki H. Early start on continuous hemodialysis therapy improves survival rate in patients with acute renal failure following coronary bypass surgery. Hemodial Int 2004; 8: 320-325.
6. Demirkiliç U, Kuralay E, Yenicesu M, et al. Timing of replacement therapy for acute renal failure after cardiac surgery. J Card Surg 2004; 19: 17-20.
7. Elahi M, Asopa S, Pflueger A, et al. Acute kidney injury following cardiac surgery: impact of early versus late haemofiltration on morbidity and mortality. Eur J Cardiothorac Surg 2009; 35: 854-863.
8. Durmaz I, Yagdi T, Calkavur T, et al. Prophylactic dialysis in patients with renal dysfunction undergoing on-pump coronary artery bypass surgery. Ann Thorac Surg 2003; 75: 859-864.
9. Andrade L, Cleto S, Seguro A. Door-to-dialysis time and daily hemodialysis in patients with leptospirosis: impact on mortality. Clin J Am Soc Nephrol 2007; 2: 739-744.
10. Bagshaw SM, Uchino S, Bellomo R, et al. Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury. J Crit Care 2009; 24: 129-140.
11. Van Biesen W, Yegenaga I, Vanholder R, et al. Relationship between fluid status and its management on acute renal failure (ARF) in intensive care unit (ICU) patients with sepsis: a prospective analysis. J Nephrol 2005; 18: 54-60.
12. Bouchard J, Soroko SB, Chertow GM, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int 2009; 76: 422-427.
13. Gibney N, Hoste E, Burdmann EA, et al. Timing of initiation and discontinuation of renal replacement therapy in AKI: unanswered key questions. Clin J Am Soc Nephrol 2008; 3: 876-880.
14. Seabra V, Balk E, Liangos O, et al. Timing of renal replacement therapy initiation in acute renal failure: a meta-analysis. Am J Kidney Dis 2008; 52: 272-284.
15. Liangos O, Rao M, Balakrishnan V, et al. Relationship of urine output to dialysis initiation and mortality in acute renal failure. Nephron Clin Pract 2005; 99: c56-60.
16. Shiao C, Wu V, Li W, et al. Late initiation of renal replacement therapy is associated with worse outcomes in acute kidney injury after major abdominal surgery. Crit Care 2009; 13: R171.

C20
Starting and Stopping RRT for AKI: Principles and Practice

Ravindra L. Mehta MBBS, MD, DM, FACP
2:30-4:00
Thursday, February 24

Educational Objectives:
1. Describe the factors affecting timing of initiation and stopping of RRT in critically ill patients.

2. Discuss the principles and evidence for early intervention with RRT in the ICU

3. Describe various approaches and practical aspects for initiating and stopping RRT

Content Description:
Several randomized studies have tried to delineate the best modality or the optimal dialysis dose to manage acute kidney injury (AKI), with inconsistent results. One important aspect of the management of critically ill patients which is still controversial is the timing of initiation and cessation of renal replacement therapy (RRT). In recent publications, timing of initiation of RRT was listed as one of the top priority in research on AKI. Similarly, cessation of RRT has received little attention and has not been studied extensively. This workshop will utilize cases to illustrate the principles for determining optimal time for intervention and a strategy for stopping RRT in critically ill patients

Suggested Reading:
1. Mehta RL, Letteri JM. Current status of renal replacement therapy for acute renal failure. A survey of US nephrologists. The National Kidney Foundation Council on Dialysis. Am J Nephrol 1999; 19: 377-382.

2. Mehta RL. Indications for dialysis in the ICU: renal replacement vs. renal support. Blood Purif 2001; 19: 227-232.

3. Bouchard J, Weidemann C, Mehta RL. Renal replacement therapy in acute kidney injury: intermittent versus continuous? How much is enough? Adv Chronic Kidney Dis 2008; 15: 235-247.

4. Gibney N, Hoste E, Burdmann EA, Bunchman T, et al. Timing of initiation and discontinuation of renal replacement therapy in AKI: unanswered key questions. Clin J Am Soc Nephrol 2008; 3: 876-880.

5. Perianayagam MC, Seabra VF, Tighiouart H, Liangos O, et al. Serum cystatin C for prediction of dialysis requirement or death in acute kidney injury: a comparative study. Am J Kidney Dis 2009; 54: 1025-1033.

6. Seabra VF, Balk EM, Liangos O, Sosa MA, et al. Timing of renal replacement therapy initiation in acute renal failure: a meta-analysis. Am J Kidney Dis 2008; 52: 272-284.

7. Waikar SS, Bonventre JV. Can we rely on blood urea nitrogen as a biomarker to determine when to initiate dialysis? Clin J Am Soc Nephrol 2006; 1: 903-904.

8. Bouchard J, Macedo E, Mehta RL. Dosing of Renal Replacement Therapy in Acute Kidney Injury: Lessons Learned From Clinical Trials. Am J Kidney Dis.2010

9. Bouchard J, Mehta RL. Acid-base disturbances in the intensive care unit: current issues and the use of continuous renal replacement therapy as a customized treatment tool. Int J Artif Organs 2008; 31: 6-14.

10. Bouchard J, Mehta RL. Fluid accumulation and acute kidney injury: consequence or cause. Curr Opin Crit Care 2009; 15: 509-513.

11. Bouchard JM, R and Mehta, RL. Stopping Acute Kidney Replacement Therapy
Critical Care Nephrology 2008

12. Mehta RL, Bouchard J. Dialysis dosage in acute kidney injury: still a conundrum? J Am Soc Nephrol 2008; 19: 1046-1048.

13. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, et al. Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury. J Crit Care 2009; 24: 129-140.

14. Bouchard J, Macedo E, Mehta RL. Renal support in critically ill patients with acute kidney injury. N Engl J Med 2008; 359: 1959-1960; author reply 1961-1952.

15. Macedo E, Bouchard J, Mehta RL. Renal recovery following acute kidney injury. Curr Opin Crit Care 2008; 14: 660-665.

16. Palevsky PM. Clinical review: timing and dose of continuous renal replacement therapy in acute kidney injury. Crit Care 2007; 11: 232.

17. Palevsky PM. Indications and timing of renal replacement therapy in acute kidney injury. Crit Care Med 2008; 36: S224-228.

18. Zamperetti N, Ronco C, Brendolan A, Bellomo R, et al. Bioethical issues related to continuous renal replacement therapy in intensive care patients. Intensive Care Med 2000; 26: 407-415.

19. Howard CS, Teitelbaum I. Renal replacement therapy in patients with chronic liver disease. Semin Dial 2005; 18: 212-216.

20. Draper H. Ethical aspects of withdrawing/withholding renal replacement therapies on patients in acute renal failure in an intensive care unit. EDTNA ERCA J 2002; Suppl 2: 39-42.

21. Bagshaw SM, Cruz DN, Gibney RN, Ronco C. A proposed algorithm for initiation of renal replacement therapy in adult critically ill patients. Crit Care 2009; 13: 317.

22. Bagshaw SM, Gibney RT. Ideal determinants for the initiation of renal replacement therapy: timing, metabolic threshold or fluid balance? Acta Clin Belg Suppl 2007: 357-361.

D21
Acid Base and Electrolyte Problems in the Critically Ill 1

John A. Kellum MD
2:30-4:00
Thursday, February 24

Educational Objectives:
1- To review the quantitative physical chemical approach to acid-base
2- To compare and contrast quantitative and qualitative approaches to acid-base
3- To demonstrate how both approaches can be combined and used at the bedside

Content Description:
Clinicians working in the ICU spend much of their time managing problems related to fluids, electrolytes, and blood pH. Recent advances in the understanding of acid–base physiology have resulted from the application of basic physical-chemical principles of aqueous solutions to blood plasma. All changes in blood pH, in health and in disease, occur through changes in three variables: carbon dioxide, relative electrolyte concentrations, and total weak acid concentrations. However, while this quantitative approach has enjoyed widespread use among researchers, clinicians are reluctant to employ it. Recent advances have brought a measure of parity between the newer and the older, descriptive approach to acid-base physiology. This case-based lecture will illustrate how both approaches can be combined to result in a powerful bedside tool.

Suggested Reading:
Kellum JA. Disorders of acid-base balance. Crit Care Med. 2007 Nov;35(11):2630-6.

D21
Acid Base and Electrolyte Problems in the Critically Ill 1

Mitchell H. Rosner MD
2:30-4:00
Thursday, February 24

Educational Objectives:
1. To understand and treat patients with severe hyponatremia
2. To understand the pitfalls associated with common formulas used to treat patients with hyponatremia
3. To understand the various treatments and their efficacy for hyperkalemia

Content Description:
This workshop will consist of case-based presentations covering common issues in the diagnosis and therapy of patients with complex electrolyte and acid-base disorders. The presenters will use cases to discuss sodium and potassium disorders as well as complex acid-base problems. The session will be interactive and audience members will be encouraged to ask questions and discuss various approaches for diagnosis as well as therapy.

Suggested Reading:
1. Rose BD, Post T. Clinical Physiology of Acid-Base and Electolyte Disorders. Mc Graw Hill, New York
2. Palmer BF. A physiologic-based approach to the evaluation of a patient with hypokalemia. Am J Kidney Dis 2010; 56: 1184-1190
3. Palmer BF. A physiologic-based approach to the evaluation of a patient with hyperkalemia. Am J Kidney Dis 2010; 56: 387-393
4. Verbalis JG. Managing hyponatremia in patients with syndrome of inappropriate antidiuretic hormone. Endocrinol Nutr 2010; 57(suppl 2: 30-40)

E22
Ensuring Patient Safety and Quality Measures for RRT in AKI 1: Water Standards, Infection Control

Thomas A. Golper MD
2:30-4:00
Thursday, February 24

Educational Objectives:
1. Understand why water quality and safety is important to patient outcomes in hospital dialysis or other renal replacement therapies.
2. Understand where water safety problems occur and how to prevent them.
3. Understand an approach to continually reassessing delivery system safety and how to measure success in this area

Content Description:
This workshop will discuss how water systems work in the context of what can go wrong, jeopardizing patient safety. We will expand beyond just wate and infection control systems to discuss approaches to assess, measure and monitor systems in the context of reducing errors and creating a more safe delivery system for renal replacement therapies.

There will be short presentations (lectures) cases to discuss, plenty of audience participation and time for discussion

E22
Ensuring Patient Safety and Quality Measures for RRT in AKI 1:
Water Standards, Infection Control

Eileen Lischer MA, BSN, RN, CNN
2:30-4:00
Thursday, February 24

Educational Objectives:
1. Discuss the AAMI standards for water safety.
2. Identify nursing issues with each testing procedure
3. Discuss the performance improvement process for water safety

Content Description:
Water quality is essential for a safe dialysis therapy. AAMI is the regulatory organization in the US that determines water quality standards. It is imperative that water quality be taken seriously, staff trained and competent and continuing surveillance performed. This workshop session will discuss the various water tests required and nursing considerations in performing and monitoring water quality in an RRT program.

Suggested Reading:
ANSI/AAMI RD52:2004/A3:2009, Dialysate for Hemodialysis, Amendment 3-Annex E: Special Considerations for Acute Hemodialysis

Northwest Renal Network #16, Monitoring Your Dialysis Water Treatment System, 2005 p 1-30

F23
Heart Failure and Cardiorenal syndrome 1: Pathophysiology

Dinna N Cruz, MD, MPH
2:30-4:00
Thursday, Feb 24,

Educational Objectives
1. Briefly review studies related to selected biomarkers in CRS Type 1
2. Briefly review studies related to selected biomarkers in CRS Types 2/4
3. Discuss selected studies on NGAL as a cardiac biomarker which may give fresh insight to the pathophysiology of CRS

Content Description
Cardiorenal syndrome (CRS) refers to pathophysiologic interaction of the heart and kidney and is associated with acute kidney injury (AKI) and high mortality. Cardiac surgery or acute decompensated heart failure and radiocontrast-induced nephropathy are common clinical scenarios of CRS type 1. Unfortunately, established functional biomarkers of glomerular filtration rate such as serum creatinine, urea, and diuresis delay AKI diagnosis by 24 to 48 hours. Novel renal biomarkers indicating rather tubular injury are emerging and may have wide implications.

This review focuses on selected novel renal biomarkers with the most promising biologic characteristics and clinical evidence for their AKI predictive ability: neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, and interleukin 18. Studies of these biomarkers in specific CRS settings are reviewed. Because of time constraints, it is not possible to do a comprehensive discussion of all biomarker studies dne in CRS settings. Finally selected studies which suggest that NGAL is also a cardiac biomarker will be reviewed.

References
1. Cruz DN, Soni S, Slavin L, Ronco C, Maisel A. Biomarkers of cardiac and kidney dysfunction in cardiorenal syndromes. Contrib Nephrol. 2010;165:83-92.
2. Bagshaw SM, Cruz DN, Aspromonte N, Daliento L, Ronco F, Sheinfeld G, et al. Epidemiology of cardiorenal syndromes: workgroup statements from the 7th ADQI Consensus Conference. Nephrol Dial Transplant. 2010 May;25(5):1406-16.
3. Cruz DN, Goh CY, Haase-Fielitz A, Ronco C, Haase M. Early biomarkers of renal injury. Congest Heart Fail. 2010 Jul;16 Suppl 1:S25-31.
4. Hemdahl AL, Gabrielsen A, Zhu C, Eriksson P, Hedin U, Kastrup J, et al. Expression of neutrophil gelatinase-associated lipocalin in atherosclerosis and myocardial infarction. Arterioscler Thromb Vasc Biol. 2006 Jan;26(1):136-42.
5. Aghel A, Shrestha K, Mullens W, Borowski A, Tang WH. Serum neutrophil gelatinase-associated lipocalin (NGAL) in predicting worsening renal function in acute decompensated heart failure. J Card Fail. 2010 Jan;16(1):49-54.
6. Han WK, Waikar SS, Johnson A, Betensky RA, Dent CL, Devarajan P, et al. Urinary biomarkers in the early diagnosis of acute kidney injury. Kidney Int. 2008 Apr;73(7):863-9.
7. Han WK, Wagener G, Zhu Y, Wang S, Lee HT. Urinary biomarkers in the early detection of acute kidney injury after cardiac surgery. Clin J Am Soc Nephrol. 2009 May;4(5):873-82.
8. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A. Accuracy of neutrophil gelatinase-associated lipocalin (NGAL) in diagnosis and prognosis in acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis. 2009 Dec;54(6):1012-24.
9. Manzano-Fernandez S, Boronat-Garcia M, Albaladejo-Oton MD, Pastor P, Garrido IP, Pastor-Perez FJ, et al. Complementary prognostic value of cystatin C, N-terminal pro-B-type natriuretic Peptide and cardiac troponin T in patients with acute heart failure. Am J Cardiol. 2009 Jun 15;103(12):1753-9.
10. Yndestad A, Landro L, Ueland T, Dahl CP, Flo TH, Vinge LE, et al. Increased systemic and myocardial expression of neutrophil gelatinase-associated lipocalin in clinical and experimental heart failure. Eur Heart J. 2009 May;30(10):1229-36.

F23
Heart Failure and Cardio-renal Syndrome 1: Pathophysiology

Alan Maisel MD
2:30-4:00
Thursday, February 24

Educational Objectives:
to learn the pathophysiology of heart failure
to learn how BNP can be used for diagnosis
to learn how to manage chf

Content Description:
Heart failure is a complicated disease with a pathophysiology that involves activation of the renin, angiotensin, and aldosterone nervous system. In this day and age, one half of new heart failure is perserved systolic function usually eminating from hypertension or ischemic heart disease. Diagnosis of acute heart failure is difficult, as signs and symptoms are atypical and not always present. B-type natriuretic peptide (BNP) is release as a result of end-diastolic wall stress and rapidly release in the circulation as a way to combat the RAAS. A low BNP in patients with symptoms of HF essentually rules out heart failure as a diagnosis. bnp levels > 400pg/ml make the diagnosis likely. Caveats in bnp use include the concept of l"fry" and "wet" bnp, obesity and renal dysfunction.

G24
Extracorporeal Techniques for Sepsis 2

Patrick M. Honoré MD
2:30-4:00
Thursday, February 24

Educational Objectives:
1) Review briefly the rationale of Hybrid therapy in sepsis regarding experimental issues.Special focus on Hybrid therapy regarding large bore membranes and highly adsoptive membranes.

2) Describe the New Possibilities given with the New Membranes for High permeability hemofiltration (HPHF) that do offers to the clinician especially with the combined use of high volume hemofiltration (for Synergic action) a new tool in order to try to effectively combat septic shock with acute kidney injury (AKI).

Previous studies did show that HPHF especially with combined HVHF can removed much large quantities of mediators.

3) Describe the new possibilities given with the New Membranes for Hybrid Therapies regarding High Adsorptive Hemofiltration doing at the same time, Endotoxin Adsorption and Cytokine Adsorption.

4) Review all clinical data regarding this issue.

5) Try to see which clinical situation could fit the best with those new types of membranes.

Content Description:
Clinical use day by day for bedside intensivists need to be further established.Although some data can be show about safety issues regarding the use of some membranes.

A step by step approach will be needed before routine implementation.Nevertheless, some clinical scenarios can be outlined so far.
Briefly, we should describe new insides regarding the “New Active Transportation between two Asymmetric Compartments” Hypothesis and New Insights into Rationale & Potential Mechanisms. Pro-mediators as well as mediators are removed at interstitial and tissue levels, following removal from the blood compartment, until a so-called threshold point is reached at which some pathways and cascades are stopped .At this level, the cascades are interrupted and no further harm can be done to the tissues.Until recently, this mechanism was taught to be a passive transportation pathway.As said in the introduction, effectiveness through only a passive transportation mechanism remains elusive.Indeed as demonstrated before and knowing that the surface of the central blood compartment (CEBC) is about 30 mÇ, which is much smaller than the surface of the capillary blood compartment (CABC)which is about 300 mÇand therefore passive transport between these two asymmetric compartments will not yield the same elimination rate on both sides.As a consequence, when a given technique is able to remove 40 % of the mediators of the CEBC side, it will only represents 4 % of the removal into the CABC side if the removal is only a passive mechanism.It is therefore easy to understand, that an other mechanism has to take place and this should be this time, an active transportation mechanism. Previous studies did show that HPHF especially with combined HVHF can removed much large quantities of mediators.A preliminary study called the HICOSS study(High Cut-off in Septic Shock)was looking as pilot study in order to compare in 80 patients with Septic Shock plus AKI. 40 patients were assigned with conventional membrane and 40 patients were assigned with an hyperpermeable membrane (septex).Those patients were in septic shock plus AKI but also in multiple organ failure (MODS).The mode chosen was CVVD for 5 consecutive days.The principal aim was to evaluate the safety regarding albumin losses (cut-off of 60 kDa) and a 50 % reduction in catecholamine requirements.Mortality was a secondary end point.The results shows a excellent safety as the membrane was not loosing albumin more than a classical membrane.Nevertheless, regarding vasopressors free days as well length of ICU

stay and mortality , no differences could be seen between the two groups.This may be due the fact that the mode was only CVVD and perhaps the results would be very different if we were using CVVH at 35 ml/kg/h plus HPHF.Description will be done also regarding data for new adsorptive membranes.

Experimental & Clinical studies as well clinical evaluation (safety) are still under way.Those studies will need mechanistic steps, small RCT's and large RCT's at some point.

In conclusion, the hyperpermeable membrane (septex) is safe and could be a important therapeutic tool in the future when associated with HVHF.Potential effect of highly adsorptive membranes need to be evaluated.

As said and although further evaluation need to be done, some specific clinical scenarios can be identified in order to delineate the current use in clinical conditions of these new hybrid therapies by the bedside clinician.

Suggested Reading:

1- Honore PM, Joannes-Boyau O,Boer Willem, Collin V High Volume Haemofiltration for Sepsis & SIRS:Current Concepts & Future Prospects. In-Depth-Review. Blood Purif 2009;28;1-11.

2- Honore PM, Joannes-Boyau O, Boer W, Collin V,Jennes S. Continuous Haemofiltration in 2009 : What's New for Clinicians regarding : Pathophysiology , Technique to be Privileged and Dose to be Recommended . In-Depth-Review.Blood Purif 2009;28-135-143.

3- Honoré PM, Joannes-Boyau O, Jacobs R,Solignac M .Blood Purification in Sepsis:Fiction or Fact for the Clinician. Reanimation 2010;19:7-12

4.- Honoré PM, Zydney AL, Matson JR. High volume and high permeability haemofiltration in sepsis. The evidences and the key issues. Care Crit ill 2003;3:69-76

5. Matson J R, Zydney AR, Honore,PM. Blood Filtration: New Opportunities and the Implications On System Biology.Critical Care and Resucitation 2004; 6:209-218.

6. Morgera S, Haase M, Kuss T, et al. Pilot study on the effects of high cutoff hemofiltration on the need for norepinephrine in septic patients with acute renal failure. Crit Care Med 2006;34:2099-104.

7. Cruz DN, Antonelli M, Fumagalli R, et al. Early use of polymyxin B hemoperfusion in abdominal septic shock: the EUPHAS randomized controlled trial. JAMA 2009;301:2445-52.

8. Honore PM, Joannes-Boyau O, Dobbeleir N.Blood Purification in Sepsis & Acute Kidney Injury in Critically Ill Patients:New Insights & Potential Mechanisms with an Update on Recent Trials.Chapter of the Yearly Book in Intensive Care Medicine 2011
(31 th ISICEM March 2011)

9. Honore PM et al. Continuous Hemofiltration or Intermittent Dialysis for Septic Shock Patients in ICU with AKI :A Pragmatic Approach for Bedside Intensivists Summarizing the More Recent Advances.Annals of Intensive Care 2011: In Press.

G24
Extracorporeal Techniques for Sepsis 2

Oliver Joannes-Boyau MD
2:30-4:00
Thursday, February 24

Educational Objectives:
- Knowing the different techniques of blood purification
- The rational for the use of blood purification in sepsis
- New blood purification techniques in sepsis

Content Description:
The use of blood purification techniques are developing rapidly in the whole world , but the knowledge about these techniques remains low. A quick presentation of all the techniques currently available and the future in the field will be presented. We will also review the potential interest of specific technique of blood purification in sepsis. And we will finish by the last results and current researches.

Suggested Reading:
1. Cruz DN, Perazella MA, Bellomo R, et al. Effectiveness of polymyxin B-immobilized fiber column in sepsis: a systematic review. Crit Care 2007;11(2):R47.
2. Bengsch S, Boos KS, Nagel D, Seidel D, Inthorn D. Extracorporeal plasma treatment for the removal of endotoxin in patients with sepsis: clinical results of a pilot study. Shock 2005;23(6):494-500.
3. Bellomo R, Honore PM, Matson J, Ronco C, Winchester J. Extracorporeal blood treatment (EBT) methods in SIRS/Sepsis. Int J Artif Organs 2005;28(5):450-8.
4. Kellum JA, Song M, Venkataraman R. Hemoadsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor-kappaB DNA binding, and improves short-term survival in lethal endotoxemia. Crit Care Med 2004;32(3):801-5.
5. Kellum JA. Hemoadsorption therapy for sepsis syndromes. Crit Care Med 2003;31(1):323-4.
6. Kanno Y, Nemoto H, Nakamoto H, et al. Selection of hemoperfusion therapy for patients with septic shock on the basis of the primary disease. J Artif Organs 2003;6(3):205-10.
7. Tsuchida K, Takemoto Y, Sugimura K, Yoshimura R, Nakatani T. Direct hemoperfusion by using Lixelle column for the treatment of systemic inflammatory response syndrome. Int J Mol Med 2002;10(4):485-8.
8. Ronco C, Brendolan A, Lonnemann G, et al. A pilot study of coupled plasma filtration with adsorption in septic shock. Crit Care Med 2002;30(6):1250-5.
9. Schmidt J, Mann S, Mohr VD, Lampert R, Firla U, Zirngibl H. Plasmapheresis combined with continuous venovenous hemofiltration in surgical patients with sepsis. Intensive Care Med 2000;26(5):532-7.

H25
Fluids and Solutions in the Critically Ill 2: Solutions for CRRT

Andrew Davenport MD, FRCP
2:30-4:00
Thursday, February 24

Educational Objectives:

1. understand electrolyte composition of replacement fluids compared to plasma water, interstitial fluid and intracellular composition
2. difference in electrolyte transport between convective and diffusive modes
3. effect of choice of lactate and bicarbonate on acid-base control

Content Description:
Sodium is the predominant cation in plasma water and haemofiltration substitution fluids/dialysates, whereas potassium is the major intracellular cation. Whereas the plasma calcium concentration is greater than magnesium, magnesium concentration is greater in muscle.

During dialysis movement is mainly by diffusion, and besides moving along a concentration gradient, solute movement is also affected by charge and chemical or electrical binding. Thus the driving force for solute transfer during diffusion depends upon the effective free concentration. Whereas, with convection, solute movement follows water flux, so called solvent drag. Thus solutes bound in small complexes that are small enough to pass through the membrane pores can be lost in the ultrafiltrate. Similarly there are differences in solute clearances between pre and postdilutional haemofiltration, particularly when high volumes are used. For example sodium and calcium balance is more positive with postdilutional than with predilutional replacement.

For non citrate CRRT systems fluid replacements contain the anions lactate and/or bicarbonate and chloride. The exact composition varies from manufacturer to manufacturer, thus some fluids contain more lactate/bicarbonate and less chloride, and vice versa. If the rate of lactate metabolism is reduced, then hyperlacatemia may ensue, and if the rate of lactate conversion through to bicarbonate is less than losses of bicarbonate and lactate into the ultrafiltrate/dialysate, then hyperlactatemia with systemic acidosis develops.

Suggested Reading:
please limit to 10 referencesDavenport A. Replacement and dialysate fluids for patients with acute renal failure treated by continuous veno-venous haemofiltration and/or haemodiafiltration. Contrib Nephrol. 2004;144:317-28.

Davenport A. Dialysate and substitution fluids for patients treated by continuous forms of renal replacement therapy. Contrib Nephrol. 2001;(132):313-22

McLean AG, Davenport A, Cox D, Sweny P.Effects of lactate-buffered and lactate-free dialysate in CAVHD patients with and without liver dysfunction.
Kidney Int. 2000 Oct;58(4):1765-72.

Davenport A, Worth DP, Will EJ. Hypochloraemic alkalosis after high-flux continuous haemofiltration and continuous arteriovenous haemofiltration with dialysis. Lancet. 1988 Mar 19;1(8586):658.

H25
Fluids and Solutions in the Critically Ill 2: Solutions for CRRT

Michael Joannidis MD
2:30-4:00
Thursday, February 24

Educational Objectives:
1) Describe electrolyte clearance and associated dangers of respective disturbance during CRRT
2) Discuss the effects of citrate solutions of on acid base status in critically ill patients
3) Describe temperature effects on solubility

Content Description:
CRRT is also used for providing electrolyte and acid-base homeostasis in the setting of AKI. Whereas sodium and potassium are normally quite stable during CRRT significant removal of phosphate and magnesium have to be taken into account. Since hypophosphatemia and hypomagnesiemia carry the risk of muscle weakness and arrhythmias, respectively, regular control of respective serum levels is warranted and substitution often required. Usage of phosphate containing replacement fluids may diminish risk associated with depletion during CRRT.

Citrate, frequently used for anticoagulation, is metabolized to bicarbonate by the liver. Thus, citrate administration during CRRT provides buffer capacity. Overdosing citrate may result in metabolic alkalosis. On the other hand in the setting of severe liver dysfunction citrate accumulation may occur leading to metabolic acidosis. Varying citrate administration rate and/or clearance may be applied to adapt to respective metabolic needs.

Heating of substitution fluids though increasing solubility of small solutes may carry the danger of bubble generation in bicarbonate containing solutions. This may result in system dysfunction.

Suggested Reading:
1: Kraus MA. Selection of dialysate and replacement fluids and management of electrolyte and Acid-base disturbances. Semin Dial. 2009 Mar-Apr;22(2):137-40. Review. PubMed PMID: 19426416.

2: Celik JB, Topal A, Kartal E, Yosunkaya A. Clinical outcome following the use of inadequate solutions for continuous veno-venous hemodiofiltration. Ren Fail. 2008;30(10):959-64. PubMed PMID: 19016146.

3: Bouchard J, Mehta RL. Acid-base disturbances in the intensive care unit: current issues and the use of continuous renal replacement therapy as a customized treatment tool. Int J Artif Organs. 2008 Jan;31(1):6-14. Review. PubMed PMID: 18286450.

4: Aucella F, Di Paolo S, Gesualdo L. Dialysate and replacement fluid composition for CRRT. Contrib Nephrol. 2007;156:287-96. Review. PubMed PMID: 17464138.

5: Druml W, Kierdorf HP; Working group for developing the guidelines for parenteral nutrition of The German Association for Nutritional Medicine. Parenteral nutrition in patients with renal failure - Guidelines on Parenteral Nutrition, Chapter 17. Ger Med Sci. 2009 Nov 18;7:Doc11. Review. PubMed PMID: 20049069; PubMed Central PMCID: PMC2795369.

6 Broman M, Carlsson O, Friberg H, Wieslander A, Godaly G. Phosphate-containing dialysis solution prevents hypophosphatemia during continuous renal replacement therapy. Acta Anaesthesiol Scand. 2011 Jan;55(1):39-45.

B27
Assessing the Microcirculation

Rolando Claure MD
Etienne Macedo MD, PhD
4:30-6:00
Thursday, February 24

Educational Objectives:
1. Discuss the different methods for evaluating the microcirculation.

2. To review the different scores available for microcirculation analysis, and which measurements should be included.

3. Discuss how monitoring of the microcirculation may help us at the bedside.

Content Description:
Microvascular perfusion plays an important role in the development of organ failure in hospitalized patients. Although microcirculation is the primary site of oxygen and nutrient exchange, microvascular oxygen delivery cannot be predicted from global hemodynamic measurements. Hemodynamic assessment has been limited to measurements of cardiac output and oxygen delivery, which are indirect measurements of microcirculation. However, several observational studies and randomized controlled trials trying to improve these parameters based on information derived from pulmonary artery catheter have shown no benefits in outcomes.

In critically-ill patients improvement in microvascular perfusion should be to one of the major therapeutic goals. Recent advances in technology have allowed direct visualization of the microcirculation. The octagonal polarization spectral (OPS) and the side stream dark field (SDF) imaging devices provide high contrast images of the microvasculature. Experimental studies have shown alterations in the microcirculation common to different pathological process. OPS and SDF imaging have been used to assess microvascular alterations in many disease processes such as: sepsis, painful crises in sickle cell disease, bacterial infection in cirrhosis, leukostasis in patients with chronic myeloid leukemia, and changes in the volume status of hemodialysis patient. It has also been used to assess the effect of different therapies on microcirculation in experimental animal models and in septic patients. Additionally, in critically-ill patients with sepsis and septic shock, recent studies have correlated microcirculatory flow abnormalities with hemodynamics, oxygen transport and survival.

The introduction of OPS and SDF imaging has opened challenging new perspectives in in vivo research of microcirculatory alterations, and has highlighted the importance of microcirculatory alterations in multiple organ failure and sepsis.

Suggested Reading:
1. van Beers EJ, Goedhart PT, Unger M, Biemond BJ, Ince C. Normal sublingual microcirculation during painful crisis in sickle cell disease. Microvascular Research 76:57 60, 2008.

2. Sheikh, M. Y., U. Javed, et al. Bedside Sublingual Video Imaging of Microcirculation in Assessing Bacterial Infection in Cirrhosis. Dig Dis Sci, 2009

3. Boerma EC, van del Voort PHJ, Spronk PE, et al. Relationship between sublingual and intestinal microcirculatory perfusion in patients with abdominal sepsis. Crit Care Med 35:1055 1060, 2007.

4. Trzeciak S, Dellinger PR, Parrillo JE, et al: Early microcirculatory perfusion derangements in patients with severe sepsis and septic shock: Relationship to hemodynamics, oxygen transport, and survival. Ann Emerg Med 49:88-98, 2007.

5. Johannes T, Mik EG, Nohé B, et al: Influence of fluid resuscitation on renal microvascular PO2 in a normotensive rat model of endotoxemia. Crit Care 10:R88, 2006.

6. Sakr Y, Chierego M, Piagnerelli M, et al: Microvascular response to red blood cell transfusion in patients with severe sepsis. Crit Care Med 35:1639 1644, 2007.

7. De Backer D, Creteur J, MD, PhD; Dubois MJ, et al: The effects of dobutamine on microcirculatory alterations in patients with septic shock are independent of its systemic effects. Crit Care Med 34:403–408, 2006.

8. Verdant C, De Backer D. How monitoring of the microcirculation may help us at the bedside. Curr Opin Crit Care 11:240-244, 2005.

9. Dobbe JGG, Streekstra GJ, Atasever B, et al: Measurement of functional microcirculatory geometry and velocity distributions using automated image analysis. Med Biol Eng Comput 46:659-670, 2008.

10. Dubin A, Pozo M.O., Casabella Ch.A., et. Al. Increasing arterial blood pressure with norepinephrine does not improve microcirculatory blood flow: a prospective study. Crit Care 13:R92, 2009.

11. Bemelmans R.H.H., Boerma E.Ch., Barendregt J., et al. Changes in the volume status of haemodialysis patients are reflected in sublingual microvascular perfusion. Nephrol Dial Transplant. Advance access published June 10, 2009.

B27
Assessing the Microcirculation

Can Ince PhD
4:30-6:00
Thursday, February 24

Educational Objectives:

• Discuss the physiology of the microcirculation and the parameters which defines its function in different organs. Discuss the physiological determinants of perfusion and oxygenation of the microcirculation and how these can be measured in the clinical scenario
• Discuss the latest developments in the bed side assessment of the microcirculation and their meaning in terms of prognosis and response to therapy.
• Practical demonstration of the use of sublingual SDF imaging

Content Description:
In this lecture we will discuss the (patho)physiological significance of microcirculatory alterations in clinical states of sepsis, shock and resuscitation and how its monitoring at the bed side has played a central role in identifying its significance. Besides the clinical background of microcirculatory , the methods both in terms of hardware and analysis methods will be discussed. Following this recent improvements in the techniques of monitoring and interpretation of microcirculatory alterations in critical illness as measured by direct sublingual microcirculation observation. We will present our new developed software which gives instant evaluation of the images as well as improvements in the devices for reducing pressure artefacts. A new improved imaging device will be presented. Next a new internet platform will be presented for allowing international exchange of images and setting the scene for multi-central intervention trials with as goal the improvement of the microcirculation to be held. In this context the progress of epidemiological survey of microcirculatory alterations (perfusion as well oxygenation) in the critically ill patients will be presented.

Suggested Reading:
Goedhart PT, Khalilzada M, Bezemer, R, Merza J , Ince C (2007) Sidestream Dark Field (SDF) imaging: a novel stroboscopic LED ring-based imaging modality for clinical assessment of the microcirculation. Optics Express 15: 15101-15114

Sakr Y, Dubois MJ, De Backer D, Creteur J, Vincent JL present a study entitled (2004) Persistent microcirculatory alterations are associated with organ failure and death in patients with septic shock. Crit Care Med32:1825-31.

Trzeciak S, McCoy JV, Dellinger RP, Arnold RC, Rizzuto M et al (2008) Early increases in microcirculatory perfusion uring protocol-directed resuscitation are associated with reduced multi-organ failure at 24 h in patients with sepsis Intensive Care Med 34(12):2210-7

Dobbe JGG, Streekstra GJ, Atasever B, van Zijderveld R, Ince C (2008) Measurement of functional microcirculatory geometry and velocity distributions using automated image analysis. Medical & Biological Engineering & Computing Med Biol Eng Comput. 46(7):659-70.

Arnold RC, Parrillo JE, Phillip Dellinger R, Chansky ME, Shapiro NI, Lundy DJ, Trzeciak S, Hollenberg SM. (2009) Point-of-care assessment of microvascular blood flow in critically ill patients. Intensive Care Med. 35(10):1761-6.

Balestra GM, Bezemer R, Boerma EC, Yong ZY, Sjauw KD, Engstrom AE, Koopmans M, Ince C (2010) Improvement of Sidestream Dark Field Imaging with an Image Acquisition Stabilizer.BMC Med Imaging. 13;10(1):15.

C28
Plasma Exchange Therapy and Hybrid Techniques

Andre A. Kaplan MD
4:30-6:00
Thursday, February 24

Educational Objectives:
Particpants will be familiar with the kinetics of removing large molecules with therapeutic plasma exchange.

Participants will be familiar with clinical situations when plasma exchange would be beneficial.

Participants will understand how to prescibe plasma exchange

Content Description:
The Kinetics of Removing Large Molecules: Implication for the Rational Prescription of Plasma Exchange.

The proper prescription of plasma exchange requires an understanding of the movement of large molecules throughout the different compartments of the body. This presentation will examin the kinetics of immunoglobulin removal as an example of how to predict the chemical results of plasma exchange.

Suggested Reading:
Kaplan AA: Therapeutic Plasma Exchange: Core Curriculum 2008. Am J Kidney Dis 52:1180-96, 2008

D29
Acid Base and Electrolyte Problems in the Critically Ill 2

Andrew Lewington MD
4:30-6:00
Thursday, February 24

Educational Objectives:
1. Appreciation of the range of acid-base and electrolyte disorders that can occur in the critically ill
2. Interpretation of acid-base and electrolyte disorders
3. Management specific acid-base and electrolyte disorders

Content Description:
This session will present real clinical examples of acid-base and electrolyte disorders in critically ill patients. There will be an opportunity to interpret these acid-base and electrolyte disorders and propose appropriate causes and diagnoses. Attendees will be encouraged consider how these specific acid-base electrolyte disorders should be managed. The actual management and outcome of these cases will be presented and discussed. The clinical cases presented will include iatrogenic metabolic alkalosis and hypokalaemia, mixed metabolic alkalosis and acidosis, iatrogenic metabolic acidosis and severe hyponatraemia in the setting of acute kidney injury.

Suggested Reading:
1. Up-to-date
2. Comprehensive Clinical Nephrology. Floege, Johnson, Feehally

D29
Acid Base and Electrolyte Problems in the Critically Ill 2

Mitchell H. Rosner MD
4:30-6:00
Thursday, February 24

Educational Objectives:
1. To understand and treat patients with severe hyponatremia
2. To understand the pitfalls associated with common formulas used to treat patients with hyponatremia
3. To understand the various treatments and their efficacy for hyperkalemia

Content Description:
This workshop will consist of case-based presentations covering common issues in the diagnosis and therapy of patients with complex electrolyte and acid-base disorders. The presenters will use cases to discuss sodium and potassium disorders as well as complex acid-base problems. The session will be interactive and audience members will be encouraged to ask questions and discuss various approaches for diagnosis as well as therapy.

Suggested Reading:
1. Rose BD, Post T. Clinical Physiology of Acid-Base and Electolyte Disorders. Mc Graw Hill, New York
2. Palmer BF. A physiologic-based approach to the evaluation of a patient with hypokalemia. Am J Kidney Dis 2010; 56: 1184-1190
3. Palmer BF. A physiologic-based approach to the evaluation of a patient with hyperkalemia. Am J Kidney Dis 2010; 56: 387-393
4. Verbalis JG. Managing hyponatremia in patients with syndrome of inappropriate antidiuretic hormone. Endocrinol Nutr 2010; 57(suppl 2: 30-40)

E30
Ensuring Patient Safety and Quality Measures for RRT in AKI 2: Dialysis Adequacy, Monitoring, Nursing Issues

Eileen Lischer MA, BSN, RN, CNN
4:30-6:00
Thursday, February 24

Educational Objectives:
1. Identify the elements of a performance improvement process.
2. Discuss the role of every nurse in all steps of the PI process.

Content Description:
The nurse plays a critical role in the performance improvement process. The PDSA cycle mimics the nursing process and lends itself to an organized and systematic framework for assessing the quality of nursing interventions in an RRT program. In a comprehensive program, a multi-disciplinary approach to performance analysis and action plans are critical both for improved outcomes and program success. In this workshop, a model of performance improvement will be presented. Sample indicators and thresholds as well as tracking tools will be presented.

E30
Ensuring Patient Safety and Quality Measures for RRT in AKI 2: Dialysis Adequacy, Monitoring, Nursing Issues

Ashita Tolwani MD
4:30-6:00
Thursday, February 24

Educational Objectives:
1. Explore quality indicators for a successful CRRT program.
2. Discuss strategies for continuous education and training of health care professionals involved with CRRT.
3. Describe an interdisciplinary process for providing continuous quality improvement in CRRT.

Content Description:
This workshop focuses on using the principles and concepts of continuous quality improvement (CQI) to ensure CRRT efficacy and patient safety. Suggestions and examples are presented for the use of quality indicators in monitoring patient outcomes and identifying opportunities for improvement. Such quality indicators include achievement of desired solute clearance, acid-base homeostasis, electrolyte balance, appropriate fluid removal and balance, anticoagulation, temperature control, and avoidance of errors. This workshop will provide a framework for developing and implementing a comprehensive, systems based approach for optimizing CRRT care delivery in hospitalized patients.

Suggested Reading:
Boyle M, Baldwin I. Understanding the Continuous Renal Replacement Therapy Circuit for Acute Renal Failure Support: A Quality Issue in the Intensive Care Unit. AACN Advanced Critical Care Volume 21, Number 4, pp.367–375. 2010

Baldwin I, Bellomo R. Quality assurance for continuous renal replacement therapies. Continuous Renal Replacement Therapy. Eds. John Kellum, Rinaldo Bellomo, Claudio Ronco. pp. 247-251. 2010

F31
Heart Failure and Cardio-Renal Syndrome 2:
Management Strategies and Case Studies

Alan Maisel MD
4:30-6:00
Thursday, February 24

Educational Objectives:
how to treat acute heart failure

how to treat chronic heart failure

using bnp levels in titrating treatment

Content Description:
heart failure is a complicated disease with a pathophysiology that involves activation of the renin, angiotensin, and aldosterone nervous system. In this day and age, one half of new heart failure is perserved systolic function usually eminating from hypertension or ischemic heart disease. Diagnosis of acute heart failure is difficult, as signs and symptoms are atypical and not always present. B-type natriuretic peptide (BNP) is release as a result of end-diastolic wall stress and rapidly release in the circulation as a way to combat the RAAS. A low BNP in patients with symptoms of HF essentually rules out heart failure as a diagnosis. bnp levels > 400pg/ml make the diagnosis likely. Caveats in bnp use include the concept of l"fry" and "wet" bnp, obesity and renal dysfunction. maangement includes, diuretics vasodilators and inotropic agents. BNP levels can be used to guide therapy as it is a good surrogate of wedge pressure in volume overloaded patients

F31
Heart Failure and Cardio-Renal Syndrome 2:
Management Strategies and Case Studies

Emil P. Paganini MD, FACP, FRCP
4:30-6:00
Thursday, February 24

Educational Objectives:
1. Discuss alternative methods of fluid control in CHF

2. Review new data on Cardio-renal relationship with CHF patients

3. Explain potential payment for the procedure in both office and hospital situations

Content Description:
While there has been a number of studies where ultrafiltration techniques have shown some promise in the treatment of CHF, there lingers a concern over the morbidity incurred by the treatment itself. Other means of controling fluid have been used in the past and are regaining popularity as we have an increasing population of patients who are functional and yet hampered with CHF

The resurgence of peritoneal dialysis, the review of intra-abdominal pressure release, the rebirth of renal nerves and their association to both disease and treatment warrent further review and study.

The issue of cost is another hurtle to be overcome. There are not only clinical trials to offer a basis for effectiveness (something yet not determined to the satisfaction of the FDA) but also trial payments to see both the utility and effectiveness of total cast surrounding severe CHF therapy, including hospitalization and ED visit alternatives.

G32
Liver and Kidney 2: Hepatic Support

Andrew Davenport MD, FRCP
4:30-6:00
Thursday, February 24

Educational Objectives:
1. To understand why clotting occurs in extracorporeal circuits in patients with liver failure
2. To understand why some therapies can be complicated by hypoglycaemia
3. To understand the limitation of lactate and citrate as anionic buffers in patients with hyperacute liver failure

Content Description:
Patients with hyperacute liver failure are at increased risk of cerebral oedema and intracranial hypertension. Conventional haemodialysis leads to an acute fall in plasma urea and other small solute concentrations during the first hour of treatment. This rapid fall in osmolality leads to a gradient between the plasma and the brain, as water moves twenty times faster than urea, such that water can flow along a concentration gradient from the plasma into the brain, so increasing cerebral oedema, and resulting in brain stem coning in severe cases. Thus slower therapies such as CRRT are preferable in cases of hyperacute liver failure. However the Achilles heel of continuous dialysis/haemofiltration circuits is circuit clotting, so that they become intermittent therapies rather than continuous, In acute liver failure, the liver fails to sythesise some of the natural anticoagulants (antithrombin, proteins S & C), and hepatic necrosis leads to inflammatory reaction and increased release of tissue factor. So although these patients often have abnormal prothrombin times, they are often procoagulant, with increased risk of extracorporeal circuit clotting.

Patients with acute liver failure may be unable to maintain glucose homeostasis and are at risk of hypoglycaemia. Thus to prevent hypoglycaemia, dialysates and or replacement solutions should contain glucose.

Traditional aemofiltration and dialysates for CRRT have been lactate based, or more recently citrate has been introduced as an anticoagulant. Lactate and citrate are then indirectly converted through to bicarbonate and so correct metabolic acidosis. However if the rate of metabolism through to bicarbonate is reduced due to hepatic insufficiency, then the patient will become acidotic if the continued losses of bicarbonate and lactate/citrate by the dialyzer/haemofilter exceed the rate of conversion through to bicarbonate. Thus in cases of hyperacute liver failure bicarbonate based dialysates and reinfusion fluids are often required.

Suggested Reading:

Davenport A. Continuous renal replacement therapies in patients with liver disease. Semin Dial. 2009 Mar-Apr;22(2):169-72

Davenport A, Tolwani A. Citrate anticoagulation for continuous renal replacement therapy (CRRT) in patients with acute kidney injury admitted to the intensive care unit Nephrol Dial Transplant plus 2009; doi:10.1093/ndt-plus/sfp136
Agarwal B, Shaw S, Hari MS, Burroughs AK, Davenport A. Continuous renal replacement therapy (CRRT) in patients with liver disease: Is circuit life different?J Hepatol. 2009 Jun 24

Davenport A, Will EJ, Davison AM Hyperlactataemia and metabolic acidosis during haemofiltration using lactate-buffered fluids Nephron. 1991; 59(3):461-5

H33
CRRT in the Newborn: Principles and Practical Issues

David Askenazi MD
4:30-6:00
Thursday, February 24

Educational Objectives:
Due their low blood volume and small size, neonates present unique challenges when they require renal replacement therapy (RRT). During this interactive, state-of- art seminar on RRT in the newborn, we will discuss the epidemiology of different neonatal populations who require RRT. We will discuss specific techniques and RRT prescription, which will enable the team to provide efficient therapy, while reducing risks of potential complications. We will discuss specific challenge of RRT in a patient receiving extra-corporeal membrane oxygenation. We will complete the discussion by talking about the critically ill newborn born with inborn error of metabolism.

I34
Withdrawing & Withholding Support for AKI:
Ethical Issues in the ICU

Noel Gibney MD
4:30-6:00
Thursday, February 24

Educational Objectives:
Discuss and provide framework for decision to withhold or withdraw life support therapies including renal replacement therapy in critically ill patients.
Define what constitutes informed consent
Discuss the importance of prognostication, determination of medical futility, and conflict resolution.
Discuss the importance of advance care planning, including advance directivs and POLST
Discuss the process of withdrawal of life support and provision of palliative measures.

Content Description:
Although there are major differences across regions and countries, in general, the vast majority of patients who die in critical care units do so after either the withholding or withdrawal of life support therapies. Observational studies documenting physician behavior have noted changes in the modes of patient deaths and an earlier abandonment of life-sustaining treatments. Limitations are associated with patient age, diagnoses, ICU stay, and geographic and religious factors. In North America, medicine has moved from a paternalistic model to one that promotes autonomy and self-determination. Patient expectations and preferences now help shape end-of-life practices, limiting the use of technologies that may prolong dying rather than facilitate recovery. In other geographic regions, patient-physician relationships are still somewhat paternalistic. This can be difficult for patients, families and health care professionals. On the other extreme, active shortening of life is practiced in a small number of countries. Seriously ill patients and family members have defined the importance of various elements related to quality end-of-life care. The most important elements related to trust in the treating physician, avoidance of unwanted life support, effective communication, continuity of care and life completion. Variation in the perception of what matters the most indicates the need for customized or individualized approaches to providing end-of-life care. Determination of medical futility can sometimes result in conflicts regarding decisions to withdraw or withhold treatment. Such conflicts should be approached with efforts to resolve dispute and achieve consensus. There are established guidelines for withholding or withdrawal of renal replacement therapy in patients with AKI. These include estimating prognosis and addressing the issues of advance directives and patient and family preferences through the process of shared decision-making to clarify appropriate strategies for clinical management and interventions. Time-limited trials of dialysis may be an invaluable tool in this process.

Suggested Reading:
1.Prendergast TJ, Claessens MT, Luce JM. A national survey of end-of-life care for critically ill patients. Am J Respir Crit Care Med. 1998 Oct;158(4):1163-7.

2.Sprung CL, Maia P, Bulow HH, Ricou B, Armaganidis A, Baras M, Wennberg E, Reinhart K, Cohen SL, Fries DR, Nakos G, Thijs LG; Ethicus Study Group. The importance of religious affiliation and culture on end-of-life decisions in European intensive care units. Intensive Care Med. 2007 Oct;33(10):1732-9.

3.Sprung CL, Woodcock T, Sjokvist P, Ricou B, Bulow HH, Lippert A, Maia P, Cohen S, Baras M, Hovilehto S, Ledoux D, Phelan D, Wennberg E, Schobersberger W. Reasons, considerations, difficulties and documentation of end-of-life decisions in European intensive care units: the ETHICUS Study. Intensive Care Med. 2008 Feb;34(2):271-7.

4.Truog RD, Campbell ML, Curtis JR, Haas CE, Luce JM, Rubenfeld GD, Rushton CH, Kaufman DC; American Academy of Critical Care Medicine. Recommendations for end-of-life care in the intensive care unit: a consensus statement by the American College [corrected] of Critical Care Medicine. Crit Care Med. 2008 Mar;36(3):953-63.

5.Patel SS, Holley JL. Withholding and withdrawing dialysis in the intensive care unit: benefits derived from consulting the renal physicians association/american society of nephrology clinical practice guideline, shared decision-making in the appropriate initiation of and withdrawal from dialysis. Clin J Am Soc Nephrol. 2008 Mar;3(2):587-93.

6.Luce JM. A history of resolving conflicts over end-of-life care in intensive care units in the United States. Crit Care Med. 2010 Aug;38(8):1623-9.

7.Luce JM. End-of-life decision making in the intensive care unit. Am J Respir Crit Care Med. 2010 Jul 1;182(1):6-11.

Technique Characteristics

1. Regional Citrate Anticoagulation Using a Calcium-containing Replacement Solution for Continuous Venovenous Hemofiltration

Ling Zhang, Yujie Liao, Ping Fu, Yi Tang, West China Hospital of Sichuan University, Chengdu, Sichuan, China

Purpose: Regional citrate anticoagulation (RCA) is an effective and safe method for continuous renal replacement therapy (CRRT) but RCA is not widely used because of complex therapeutic modalities and specialized calcium-free replacement solution with the need of continuous intravenous calcium infusion. We firstly designed a simplified protocol for RCA by using an available calcium-containing replacement solution for continuous venovenous hemofiltration(CVVH). **Methods:** Fifteen patients, with acute or chronic renal failure in the intensive care unit of West China Hospital of Sichuan University, were treated with RCA-based pre-dilution CVVH using a calcium-containing replacement solution (ionized calcium 1.60mmol/L). We pumped the 4% tri-sodium citrate solution into the arterial line of extracorporeal circulation with a starting rate of 220ml/h, while adjusting the rate to achieve a post-filtered ionized calcium level of between 0.25 and 0.5mmol/L. Initial blood flow was set at 180ml/min. Calcium gluconate (10%) was infused intravenously to maintain the plasma ionized calcium > 0.95mmol/L on the basis of arterial blood gas analysis every 6 hours. The replacement solution was delivered at 2000-3000ml/h. Biochemical parameters, arterial blood gas analysis and whole blood activated clotting time (WBACT) were assessed. We also measured the serum citrate concentration during treatment. **Results:** We performed 48 sessions. Mean hemofilter survival was 46.4±16.2h (range, 16-82h). Mean 4% tri-sodium citrate solution pumped was 225.3±5.2ml/h, and mean pre-filtered and post-filtered ionized calcium level were 0.96±0.23 mmol/L and 0.38±0.15 mmol/L, respectively. Ninety-two percent, 63%, and 59% of hemofilters were patent at 24, 48, and 72h. The pre-filter WBACTs altered little ($P>0.05$)_but the WBACTs of post-filter significantly prolonged about 30% compared with that of pre-CVVH ($P<0.05$). The mean serum citrate concentration was not changed significantly at 24, 48, and 72h. No bleeding episodes were found, and no patient showed the symptoms and signs of hypocalcium or citrate toxicity. **Conclusions:** Our simplified RCA protocol using a calcium-containing replacement solution for CVVH is effective and safe and also obviates the need of continuous intravenous calcium infusion.

2. Nafamostat Mesilate for Anticoagulation in Continuous Renal Replacement Therapy

SY Yoon, SD Hwang , SC Lee, Kwandong University, Goyang, Korea

Purpose: During continuous renal replacement therapy (CRRT), anticoagulation of the extracorporeal circuit is generally required. Although heparin is the most common choice of anticoagulant, it is thought to be associated with bleeding complications, especially in high risk patients. Furthermore, heparin can cause thrombocytopenia. Therefore, several drugs have been used during CRRT as an alternative anticoagulant such as citrate and hirudin. We conducted retrospective observational study to assess the efficacy and adverse effect of nafamostat mesilate, a serine protease inhibitor, compared with heparin. **Methods:** we reviewed the medical record of the 138 patients who had treated with CRRT in the intensive care unit (ICU), Myongji hospital, Kwandong University, Goyang, Korea from January 2007 to December 2008. We excluded the patients who died within the first circuit use or ingested paraquat. **Results:** 121 patients with 593 circuits were included in this study. As an initial anticoagulation, heparin is used in 37 patients (30.6%), nafamostat mesilate in 11 (9.1%), and 8 patients were in systemic anticoagulation. There was no difference in age, sex, APACHE II score, SAPS II score, laboratory data and survival according to initial anticoagulation method. We excluded 23 circuits (3.9%) used in systemic anticoagulation. Among the 570 circuits, 337 circuits (59.1%) received no anticoagulation, 180 (31.6%) received heparin, and 53 (9.3%) received nafamostat mesilate. Overall median filter life span with nafamostat mesilate was significantly greater than heparin (19 vs 14 hours, $p<0.01$) and Kaplan-Meier survival plots revealed the longer survival of the circuits using nafamostat mesilate than heparin or without anticoagulation. Although nafamostat mesilate induced aPTT prolongation in 5 circuits (9.4%) contrast to 5 (2.7%) in heparin, bleeding episodes were not increased. **Conclusions:** Nafamostat mesilate anticoagulation was associated with prolonged filter survival

compared with heparin. These data suggests that nafamostat mesilate is a good choice for anticoagulant during CRRT in critically ill patients.

3. Continous Veno-Venous Hemodiafiltration (CVVHDF) with Sodium Citrate in Patients with Heparin Induced Thrombocytopenia – Case Report

Joanna Zbura, Wojciech Mielnicki, Piotr Garba, Zbigniew Sycz, *4th Clinical Military Hospital, Wroclaw, Poland*

Background and Aims: Acute renal failure (ARF) is a frequent disease in Intensive Care Unit patients. Among different methods of treatment, continuous veno – venous haemodiafiltration (CVVHDF) is a method closely related to physiologic conditions. It enables to provide more optimal haemodynamic conditions, small fluid shift in time, less arrhythmias and better control of fluid balance during treatment of critically ill patients. During CVVHDF continuous infusion of unfractionated heparin is a standard procedure (rarely low molecular weight heparin) with regular measurement of APTT or ACT. Usage of heparin is associated with high risk of bleeding and heparin induced thrombocytopenia. There are two types of heparin induced thrombocytopenia (HIT). Type I – nonimmunological, caused by direct interaction of heparin with thrombocytes. This type is a mild one leading to decrease in number of thrombocytes to 100 thousand, which goes back to normal after long usage – it is clinically not significant. Type II is caused by production of IgG against heparin and platelet factor (PF 4) complex. Immunoglobulins are built into the heparin – PF4 complex and cause platelet activation, increased thromboxane synthesis, release of platelet contents, platelet aggregation, endothelium damage and eventually tendency to thrombosis. This type leads to severe course of disease, and happens in 0,1 – 10% of patients usually 5 to 10 days after introduction of heparin. It can lead to decrease in number of platelets to less than 50 thousand. Alternative in such cases is continuous veno – venous haemodiafiltration with sodium citrate as anticoagulant. This therapy uses substitution fluids with sodium citrate (13,3 mmol/l) given as predilution fluid causing anticoagulation and providing bicarbonate buffer. Frequent control of calcium ions (Ca2+) is very important in this therapy along with substitution of calcium as an infusion of calcium chloride or calcium gluconate. We use CVVHDF in patients with acute renal failure as a method of choice. In this case report we tried to evaluate the role of sodium citrate in patients with HIT. CASE REPORT 45 year old man was admitted to ICU due to worsening of respiratory function in the course of pancreatitis. The patient has been treated for pituitary insufficiency for 9 years (tumour) and has been on chronic hormone substitution: Letrox, Testosterone, Hydrocortisone. Acute pancreatitis was probably caused by improper diet with accompanying lipid metabolism disorder. On admission to ICU patient's condition was moderately severe. He was conscious with limited contact, with respiratory insufficiency, intubated through mouth and mechanically ventilated on BILEVEL with FiO2 1,0 and subsequently 0,6. On auscultation: bilateral vesicular murmur decreased at the bases of lungs and on chest X-ray: atelectasis at the bases of lungs. The patient was haemodynamically stable with BP of 120/80 mmHg and heart rate of around 100/min. Sedation with midazolam and fentanyl was started. In the first few hours after admission oliguria and signs of renal failure were observed. In the second day of hospitalization circulatory failure developed requiring infusion of noradrenaline. Due to oliguria and worsening of renal function, decision was made to introduce dialysis catheter and start CVVHDF with heparin with regular control of ACT. Target for ACT was between 180 and 280 seconds. Because of bilateral pleural effusion chest drains were introduced bilaterally in the second day of ICU stay. In the seventh day of ICU stay percutanous tracheostomy was performed without complications. In the eighth day antibiotic therapy was modified according to antibiogram (Acinetobacter baumanii in bronchial tree). In the eleventh day abdominal CT scan was performed, and because of severe condition of the patient and abdominal CT scan result, decision was made to perform laparotomy. During operation a lot of necrotic tissue was evacuated from around pancreas, right kidney and gallbladder and surgical drains were inserted. Four units of red blood cells were transfused. In the fourteenth day of CVVHDF sudden fall in platelet count was observed (from 118 x 103 to 44 x 103). For the next three days CVVHDF was continued with heparin and platelet count fell to 7 x 103. In the eighteenth day of dialysis decision was made to substitute heparin with sodium citrate. In the first day of

dialysis with sodium citrate platelet count rose from 7 x 103 to 9 x 103 and in the next day to 15 x 103. The platelet count systematically improved in the following days of dialysis with sodium citrate. In the eight day of dialysis with sodium citrate (24th day of CVVHDF) platelet count was 106 x 103 and systematically improved. During CVVHDF with sodium citrate level of ionised calcium was monitored in arterial blood gasses (ABG). At the beginning ABG were taken every two hours, and after level of ionised calcium was stabilised (1,1 – 1,3 mmol/l) during infusion of calcium chloride, every four hours. Flow rate of particulate fluids during dialysis was chosen according to what producer suggested, and it was based on ongoing clinical trials: dialyzate fluid (PrismOcal) 1500ml/h, substitution fluid (post membrane) 100 ml/h, anticoagulant (Prismocitrate 10/2) 2500 ml/h, blood flow 130 – 150 ml/h. In 30th day after abdominal CT scan in early morning hours the patient was rushed to theatres. During laparotomy a large collection of pus and necrotic tissue were evacuated. A few hours after the operation the patient was rushed back to theatres because of severe postoperative bleeding. During laparotomy bleeding vessel was found near bladder and bleeding was surgically stopped. After the operation the patient was in critical condition. Flow rates of catecholamines were increased without haemodynamic response. In the evening hours patient developed bradycardia which eventually led to asystole. Patient died the same day.

CONCLUSIONS: In the reported case heparin induced thrombocytopenia was observed. It had probably immunological background, but presence of immunoglobulins against heparin – PF4 comlex was not examined. Diagnosis was based on clinical findings. Change of heparin to sodium citrate during CVVHDF resulted in rise of platelet count from the very first day of CVVHDF with sodium citrate.

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4. Is Regional Citrate Superior to Systemic Heparin Anticoagulation for Continuous Renal Replacement Therapies?

Rolando Claure-Del Granado, Etienne Macedo*, Sharon Soroko*, Glenn M. Chertow**, Jonathan Himmelfarb***, T. Alp Ikizler****, Emil P. Paganini*****, Ravindra L. Mehta*, *University of California San Diego, San Diego, ** Stanford University, Palo Alto, CA; ***University of Washington, Seattle, WA, USA; **** Vanderbilt University, Nashville, TN, USA; ***** Cleveland Clinic Foundation, Cleveland, OH, USA*

Objective: Continuous renal replacement therapies (CRRT) are increasingly utilized to treat critically-ill patients with acute kidney injury (AKI). Efficiency of CRRT depends on circuit longevity which is influenced by anticoagulation. We hypothesized that in critically-ill AKI patients treated with CRRT, regional citrate anticoagulation increases filter survival time and filter efficacy contributing to a higher delivered dose in comparison to systemic heparin. **Methods**: We analyzed data from 229 critically-ill patients from 5 centers in a prospective observational cohort (PICARD) with at least 48 hours on CRRT. Filter anticoagulation was determined by each center (systemic heparin or regional citrate). No anticoagulation used in patients with high risk of bleeding complications. In 590 sessions in which effluent urea nitrogen (FUN) was available, filter efficacy was assessed by calculating FUN/BUN ratios each 12 hours. Dose assessment was performed using Standard Kt/V (StdKt/V) adjusted for the different types of CRRT. **Results:** Of the 229 patients with AKI requiring CRRT, 57 were treated with regional citrate, 105 with systemic heparin, and 67 with saline flushes. Regional citrate or systemic heparin was used in 1037 (60%) of the 1730 treatments. Overall mean filter life with regional citrate was significantly greater than with heparin (54.5 vs. 21.1 hours; $p < 0.001$). In patients who received no anticoagulation, a mean of 6.0 filters were used for a mean of 25.9 hrs each; in patients who received heparin, a mean of 8.1 filters were used for a mean of 27.2 hrs each; and in patients who received citrate, a mean of 3.0 filters were used for a mean of 57.5 hours each. Median [IQR] filter efficacy with citrate was significantly higher than with heparin (FUN/BUN ratio of 0.91 [0.83 – 0.98] vs. 0.82 [0.74 – 0.87]; $p < 0.001$). Median [IQR] StdKt/V with citrate was also higher (8.1 [5.9 – 10.4] vs. 6.1 [4.4 – 8.1]; $p < 0.001$). **Conclusions:** Compared to the use of systemic heparin and saline flushes, regional citrate anticoagulation significantly increases filter survival time and maintains filter efficacy. Regional citrate anticoagulation provides the highest delivered dose. These data suggest that regional citrate seems to be a superior anticoagulant for CRRT.

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5. Hypophosphatemia In CRRT: Quantifying Phosphate Removal By A Fractional Effluent Collection Method

Shilpa Sharma, Sushrut Waikar, Brigham & Women's Hospital, Boston, MA, USA

Purpose: Hypophosphatemia is a frequent complication during continuous renal replacement therapy (CRRT), and may contribute to poor patient outcomes due to phosphate's critical role in energy metabolism in every organ system. We sought to quantify the clearance of phosphate during continuous hemofiltration, the main CRRT modality used in our institution. **Methods:** We modified the effluent line of the CRRT setup by adding a T-connector to divert approximately 1% of the total effluent volume to a collection bag over 24 hours. Estimated phosphate removal was calculated by multiplying the total effluent volume with concentration of phosphate in the effluent fraction. Results were verified by comparison to 4 hours complete collections in a subset of enrolled patients. **Results:** To date, eight 24-hr effluent collections were performed on 3 patients, all of whom were anuric and none of whom received intravenous or oral phosphate during the 24 hour period. Results are summarized in the table. **Conclusions:** CVVH results in a negative phosphate balance. Substantial amounts of phosphate may be cleared by CVVH before overt hypophosphatemia develops. Prophylactic replacement of phosphate in patients undergoing CVVH may be prudent. Our preliminary data suggests the need for future studies to examine the potential clinical consequences of intracellular phosphate depletion during CRRT.

	Patient 1	Patient 2	Patient 3
Serum phosphorus (mg/dl)	3	2.7	3.8
Infused phos (mg)	0	0	0
Estimated phos removed (mg)	1248	1512	1824
Phos mass balance (mg)	-1248	-1512	-1824

6. Choosing Between The Modalities: Is Sustained Low Efficiency Dialysis/Diafiltration (SLED/SLED-F) More Cost Effective Than Continuous Renal Replacement Therapy (CRRT)

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Anthony B. Williams, Department of Intensive Care Medicine, Middlemore Hospital, Counties Manukau District Health Board, Manukau, Auckland, New Zealand

Introduction: Renal replacement therapy in critically ill patients with acute kidney injury includes CRRT, SLED/SLED-F, and intermittent hemodialysis (iHD). Outcome studies do not show one modality to result in less mortality than the others. Modality choice therefore often comes down to logistics and cost-effectiveness. SLED/SLED-F is increasingly popular and involves the application of conventional iHD machinery with reduced Qb and Qd for prolonged periods. Preliminary studies from the US (Golper, Contributions to Nephrology,Vol 144:278-283) and Canada (Berbece et al, Kidney Int, Vol 70:963-968) have shown SLED/SLED-F to be more cost-effective than CRRT. In this study, we explored the same issue in Australia and New Zealand (NZ). **Methods:** Costs were calculated per 24 hours for SLED-F and CRRT (Table 1), assuming that treatments are performed by ICU nurses (the default practice in Australia and NZ). Modelled SLED-F treatments were for 8 hrs using Fresenius 5008 machines with Polysulfone (AV1000) filters, bicarbonate-based dialysate +/- on-line replacement fluid at a combined rate of 300 mls/min, blood flow at 250 mls/min, performed alternate-day ("low-dose" SLED-F) or daily ("high-dose" SLED-F), assuming no re-started treatments and one diafilter/line-pack/ 24hrs. Modelled CRRT treatments were continuous using Gambro Prismaflex, bicarbonate-based dialysate or substitution fluid (Hemosol-BO) with an effluent rate of 25mls/kg/hr ("low-dose" CRRT) and 40mls/kg/hr ("high-dose" CRRT), assuming no down-time and one filter/line-pack/24hrs. Costing was based on list prices, and included water-treatment, dialysate filters and water-testing for SLED-F. We assumed the same or very similar initial purchase costs for SLED-F and CRRT machines. We modelled marginal costs and assumed fixed costs such as personnel, vascular access, anticoagulation, and

miscellaneous consumables (syringes, gloves, etc) were the same or very similar between modalities. **Conclusion:** Our analysis in Australia and NZ is congruent with North American studies: SLED/SLED-F is more cost-effective than CRRT, and will often be the preferred modality.

Table 1: Cost of per 24 hours of SLED-F (sustained low-efficiency daily dialysis-diafiltration) and Continuous Veno-venous Haemodialysis (CVVHD) in Australia and New Zealand

	low dose SLED-F (alternate-day)	high dose SLED-F (daily treatments)	low dose CVVHD (25mls/kg/hr)	high dose CVVHD (40mls/kg/hr)
		Australia		
Diasafe	4.75	4.75	-	-
Water Testing	6.85	6.85	-	-
CVVHD replacement fluid-bicarbonate	-	-	294.00	470.40
CVVHD Haemofiltration Set*	-	-	300.00	300.00
SLED-F Consumables pack**	116.23	232.45	-	-
Total cost per 24 hours ($AUD)	127.82	244.04	594.00	770.40
		New Zealand		
Diasafe	3.44	3.44	-	-
Water Testing	6.85	6.85	-	-
CVVHD replacement fluid-bicarbonate	-	-	294.00	470.40
CVVHD Haemofiltration Set*	-	-	250.00	250.00
SLED-F Consumables pack**	80.95	161.90	-	-
Total cost per 24 hours ($NZD)	91.24	172.19	544.00	720.40

*includes: Filter, AV Bloodlines, Filtrate line, Substitution Line, Drain Bag, accessories

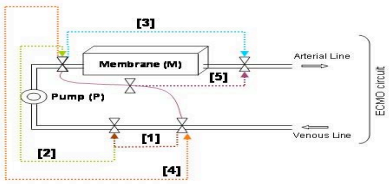
**includes: AV1000S filter, 5008 BVM blood line, 5008 900g bi-Bag, Potassium Modifier 100mL, CVC On/Off dressing packs with syringes, ARrT plus Part A Concentrate, Na+ 140, K+ 2.0, Ca+ 1.6, Citrosteril disinfection, Sen-Safe Chlorine Test Strips

7. An Experiment Using Commonly Used Continuous Renal Replacement Therapy Machines In Parallel With Extracorporeal Membrane Oxygenation

Sobhana T, CS Tan, M Kaushik, HL Choong, Singapore General Hospital

Background: Patients requiring extracorporeal membrane oxygenation (ECMO) often have concurrent acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT). Connecting CRRT circuits to the pre-existing ECMO circuit obviates the need for a separate vascular access but is hampered by the pressure limits of the CRRT machine. Current literature is predominantly in the pediatric population where lower blood flows for the ECMO circuit is required. The aim of the study was to explore various connections between CRRT and ECMO circuit at adult flow rates. **Methods:** Three CRRT machines were tested – Prisma, Prismaflex (Gambro, Lund, Sweden) and Aquarius (Edwards Lifesciences, Sydney, Australia). A mock ECMO circuit was set up using 1 liter of blood diluted in saline. ECMO blood flow was fixed at 4 liters/min. Each CRRT machine, primed in CVVHDF settings was connected in parallel to the ECMO circuits in a [1] Pre-pump(P)- Pre-P, [2] Pre-P-Post-P, [3] Post-P-Post-Membrane (M), [4] Post-P-Pre-P and [5] via an access port on a bridge created between Pre-P and Post-P with return Post-M. Pressure readings and patency of the CRRT circuits were recorded **Results**: Circuit showed favorable pressures and patency in connections [2] and [3] with the Prisma machine, and [3] with the Prismaflex machine. Connections [1] and [4] triggered return pressure alarms and subsequent circuit shut down. Alarms were triggered in all 4 connections with the Aquarius machine. No pressure alarms were triggered using connection [5] in all 3 CRRT machines. **Conclusions**: There is limited literature on CRRT connections to an ECMO circuit in the adult population. Each CRRT machine has its own operational pressure limits which restrict the connection of a low flow CRRT circuit to a high flow ECMO circuit. We have successfully identified potential connections with commonly used CRRT machines to overcome this obstacle. However, further clinical trials are needed to establish the ideal circuit for patients on ECMO with AKI.

Figure: (following page)



CRRT Applications

8. Different Modes of Blood Purification for Acute Kidney Injury following Multiple Bee Stings

Ling Zhang, Ping Fu, Yunying Shi, Li Zhou, West China Hospital of Sichuan University, Chengdu, Sichuan, China

Purpose: Multiple wasp stings are one of the common causes contributing to rhabdomyolysis and acute kidney injury (AKI). This study is to investigate the effect of different modes of blood purification for the treatment of acute kidney injury (AKI) following multiple wasp stings. **Methods:** 103 patients with wasp stings injury during 2001-2009 were retrospectively analyzed, in which 87 cases_84.5%_suffered from AKI and 60 cases (68.9%) complicated with multiple organs dysfunctional syndrome (MODS). Eighty-two cases with AKI (APACHE Scores:19.2±4.6) were recieved blood purification: (1)CVVH group:early intervention of continuous venovenous hemofiltration (CVVH) for at least 48h was performed, then CVVH was replaced by intermittent hemodialysis (IHD) when conditions of patients were stable. (2)CVVH+PE group: plasmapheresis was performed twice on Day 1 and Day 2 in addition to CVVH. (3)IHD group: IHD was performed three times per week. (4)PD group: continuous ambulatory peritoneal dailysis (CAPD) was performed. **Results:** (1)CVVH group: 33 cases (91.7%) discharged improved, but 3 case(8.3%) died. (2)CVVH+PE group: 9 cases (90%) discharged improved, but 1 case(10%) died. (3)IHD Group: 22 cases (73.3%) improved but 3 cases died(10.0%), 2 cases(6.7%) progressed to end stage renal disease(ESRD) and 3 cases(10.0%) withdrawed. (4)PD group: no patients improved, 2 cases(33.3%) died, 3 cases(50%) progressed to ESRD and 1 case withdrawed. Survival rate and recovery of the renal function in groups of CVVH, CVVH+PE and IHD groups were better than PD group. There was no significant differences of survival rate and recovery of the renal function among CVVH, CVVH+PE and IHD groups. But in the early stage, the decrease in total bilirubin, creatine kinase and white blood cells are more significant in groups of CVVH and CVVH+PE than IHD group ($P<0.05$). Adverse events (low blood pressure) in CVVH and CVVH+PE group were less than IHD group ($P<0.05$). Patients in CVVH+PE group progressed into polyuria (16.1±8.3 vs.23.2±11.2 days) and normal renal function (26.4±11.8 vs.34.2±16.1 days) earlier than CVVH group ($P<0.05$).

Conclusions: Results from this study indicate that early CVVH treatment might be helpful in patients with impaired organ function and might reduce hospitalization days. But whether it can increase the survival rate of patients is still nessasary to be confirmed by further studies. CVVH combined PE might represent as a novel approach. CAPD may not be the first choice because of the low clearance rate.

9. What Happened to a Patient Used Continuous Renal Replacement Therapy (CRRT) with Extra Corporeal Membrane Oxygenator (ECMO)? : A Case Review

Mimi Lee, Cheong Sook Yoo, Eunok Kwon, Seoul National University Hospital, Seoul, Korea

Purpose: The purpose of this case review is to show the problem appeared in CRRT using Venous-Arterial ECMO catheter. **Methods:** A Korean young man was 24 years old had suffered from idiopathic cardiomyopathy. V-A ECMO was applied to him while he waited for heart transplantation. The meantime, laboratory finding included blood nitrogen urea, creatinine, and myoglobin had more worsened. Hence, we applied the CRRT to a patient. Access line of the CRRT was connected arterial (perfusion) catheter of the ECMO and return line of the CRRT was connected venous (drain) catheter of the ECMO (figure 1). It means that CRRT and ECMO ran inversely each other. **Results:** After the CRRT started with the ECMO, drain blood of the ECMO pulled return blood of the CRRT like a vacuum because ECMO flow (3.5L/min) was greater than CRRT flow (150ml/min). As a result, return pressure of the CRRT had too negative and access pressure had too positive. To make matters worse, CRRT net balance was out of setting value due to abnormal pod pressure. Finally, we'd used a strategy that all CRRT lines

was used only perfusion catheter of the ECMO (figure 2). That is, access line of the CRRT was used distal perfusion catheter in ECMO and return line of the CRRT was used proximal one. Although sometimes we'd heard return pressure alarm because of its positive pressure, recurrent problem such as distorted pod pressures, uncorrected CRRT net balance had solved.
Conclusion: We should be monitor pod pressure of the CRRT at least every two hours. And if it will be happen some differences between actual removal fluid and setting value, it must check condition of CRRT and ECMO.
Figure:

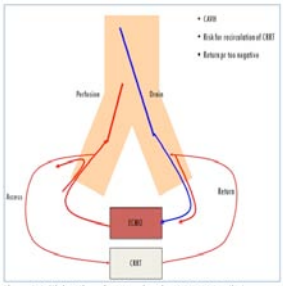


Figure 1. Initial setting of CRRT using the V-A ECMO catheter: Access line of the CRRT + Perfusion catheter of the ECMO, Return line of the CRRT + Drain catheter of the ECMO

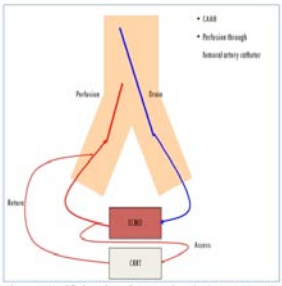


Figure 2. Modified setting of CRRT using the V-A ECMO catheter: Access line of the CRRT + Distal perfusion catheter of the ECMO, Return line of the CRRT + Proximal catheter of the ECMO

10. Continuous Renal Replacement Therapy (CRRT) and Plasma Adsorbtion Prior to and Following Liver Transplantation

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Purpose: Acute renal failure (ARF) and hyperbilirubinemia have poor prognosis in the setting of end-stage liver disease, unless liver transplantation is carried out. ARF and hyperbilirubinemia are common complications following liver transplantation also. We hereby present our results from a two-year study and treatment of these diseases by continuous renal replacement therapy (CRRT) and plasma adsorption. **Methods:** We have treated five patients, three of them prior to and two of them after liver transplantation for the period of year 2008 till 2010. All five patients have had ARF and hyperbilirubinemia. We have utilized an apparatus, allowing for subsequent application of CRRT and plasma pheresis techniques. CRRT has been performed as continuous venovenous haemodialysis (CVVHD) with high flux membrane. Plasma adsorption has been performed via hihly selective membrane for bilirubin adsorbtion. **Results:** We have repaired renal function and achieved for normal bilirubin rates in two patients - one of these prior to, and one after liver transplantation. We could not succeed in restoring the renal function in the other three patients and they have deceased.
Conclusions: Despite of high mortality rate in CRRT and plasma adsorption when applied for treating patients with ARF and hyperbilirubinemia, these therapies are justified efforts so as to prevent renal failure after liver transplantation.

11. Acute Kidney Injury, CRRT and Fluid Management in Patients with Septic Shock and Pre-existing Non-cardiac Pulmonary Hypertension

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Background: Appropriate volume management is a difficult task in patients with pulmonary hypertension (PH) complicated by septic shock (SS), particularly in those patients who developed AKI. We reviewed contemporary treatment and outcome of SS in patients with PH managed at a tertiary care institution. **Methods:** We identified 82 consecutive patients with an established diagnosis of non-cardiac (non-Group 2 by WHO Classification) PH who were treated for SS between July 2004 and July 2007. Patients with LVEF<50%, diastolic dysfunction, pericardial effusion and significant valve disease were excluded. Descriptive statistics were used to study the patient groups, causes and severity of PH, incidence of complications including AKI and utilization of specific treatment strategies including IV fluid administration, use of vasoactive medications and CRRT. RIFLE criteria were used to diagnose AKI. **Results:** The major cause of the PH was COPD (24 patients,29%), followed by ILD (14 patients, 17%) and ESLD (12 patients,15%). PH was mild in 46 patients (56%), moderate in 21(26%) and severe in 15(18%). Among all patients 27 had CKD (stage 3-5) and 6 more had ESRD. ESRD patients were excluded from analysis of AKI. In the first 48h 56(74%) patients developed AKI. CRRT was used in management of 33 patients: 28 with AKI (11 with pre-existing CKD) and 5 with ESRD. Patients with CKD and ESRD more likely ($p<0.001$) required CRRT, however there were no statistical differences in total fluid administration and total fluid balance and time of CRRT initiation within first 48h among those groups. Hospital mortality was 48% and increased proportional to the severity of PH:

from 28% in mild, to 67% in moderate and 80% in severe PH. There were no significant differences between survivors and non-survivors in AKI incidence, fluid management and timing of CRRT initiation. Deceased patients required more time on pressors (5.3 vs.2.6 days,$p<0.05$) and were more likely to develop atrial fibrillation (46% vs.12%,$p<0.005$). **Conclusions:** Pre-existing PH is associated with dramatically poor outcomes in patients with SS. Contemporary SS management remains associated with high mortality in this patient subset and requires further study with respect to optimization of clinical strategies among this patient population.

12. No Difference in Clearance and Survival between Continous Hemofiltration and Hemodiafiltration at the Same Net Effluent in Patients with Septic Acute Kidney Injury

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Background: The mortality of the ICU patients with acute renal failure (ARF) is still high. It was reported that adding a dialysis dose to continuous veno-venous hemofiltration (CVVHF) increased their survival. By the way, hemofiltration is more proper for clearance of inflammatory mediators than hemodialysis in sepsis. **Hypothesis:** We tested whether continuous veno-venous hemodiafiltration (CVVHDF) is really better than CVVHF at the same net effluent according to their body weight in the ICU patients with septic ARF. **Methods:** CVVHDF was performed by Prisma (Hospal-Gambro) with multiflow 100 at the dialysate flow rate 20ml/kg/hour, in addition to the replacement fluid flow rate 20ml/kg/hour. In contrast, replacement fluid flow rate of CVVHF was 40ml/kg/hour. Patient's removal rate was individually adjusted by attending staff considering clinical status. **Results:** In this prospective randomized pilot study, 100 patients were assigned to CVVHF (n=47, M:F=25:22, age 64±15 years) or CVVHDF (n=49, M:F=30:19, age 65±11 years). There was no difference in baseline characteristics such as age, sex, body weight, serum creatinine, BUN, beta-2 microglobulin, APACHE II and SOFA score between two groups. All parameters were significantly decreased at 72 hours after the initiation of CVVHF or CVVHDF, compared with the baseline values. However, there was no significant difference of reduction ratio in serum creatinine (45% in CVVHF vs. 54% in CVVHDF, p=NS), blood urea nitrogen (45% vs. 54%, p=NS), beta-2 microglobulin (22% vs. 17%, p=NS), APACHE II (24% vs. 22%, p=NS) and SOFA score (12% vs. 10%, p=NS) between two groups. Seven, twenty-eight, and sixty days survivals (%) were 70, 45 and 25 in CVVHF and 67, 47 and 31 in CVVHDF groups (p=NS), respectively. **Conclusions:** In conclusion, none of CVVHF and CVVHDF was better than the other mode in clearance of waste products and survival at the same net effluent in this study. In the future, large scaled randomized prospective study will be necessary to distinguish better one from the other to give greater survival change to the critically ill patients with septic ARF.

13. Ultra-High Capacity Continuous Hemofiltration Treated Severe Cerebral Malaria Accompanied with Multiple Organ Failure Successfully: A Case Report and Literature Review

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Purpose: To study the effect of ultra-high capacity continuous hemofiltration (quantity of replacement fluid: 100ml /kg/h) in a patient with severe cerebral malaria accompanied with multiple organ failure. **Methods:** Through the literature and this case, we analyzed the pathogenesis, clinical characteristics of encephalic subtertian malaria accompanied with multiple organ failure, especially the role of the ultra-high capacity continuous hemofiltration. **Results:** The state of this patient with severe cerebral malaria deteriorated after the onset. He became comatose rapidly, and acute renal failure, type 1 respiratory failure, upper gastrointestinal bleeding, cardiac insufficiency and hepatic inadequacy came all in a short time. The therapeutic regimen composed of the anti-malaria thearapy, symptomatic treatment and the ultra-high capacity continuous hemofiltration made this patient recovered. **Conclusion:** We found that in the salvage of severe cerebral malaria accompanied with multiple organ failure, we could not only using the etiologic and symptomatic treatment, but alse we could use the ultra-high capacity continuous hemofiltration as soon as possible, which may increase the achievement ratio of this disease. The possible mechanism was that the ultra-high capacity

continuous hemofiltration could eliminate toxin continually, which may maintain the internal environment, protect endothelial cells, regulate immune function, maintain cardiovascular status, adjust the temperature, protect organ function and provide nutrition support.

14. Effects of Early Continuous Renal Replacement Therapy on Survival and Recovery of Renal Function in Sepsis Patients with Acute Kidney Injury

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Objective: To study the effects of the initiation time of continuous renal replacement therapy (CRRT) on survival and recovery of renal function in sepsis patients with acute kidney injury (AKI). **Methods:** We assigned sepsis patients with AKI to CRRT in the form of predilution continuous venovenous hemofiltration (CVVH). Patients were characterized as "early" or "late" starters, based upon whether the blood urea nitrogen (BUN) was less than or greater than 25 mmol/L, prior to CRRT initiation. The primary outcome measures were survival rate within 28 days and the recovery of renal function during hospital. **Results:** Of the 106 enrolled patients, 45 were early starters and 61 were late starters. The two groups had similar demographic characteristics and received the treatment for an average of effluent flow 45.8 and 49.6 ml/kg/h, respectively ($P = 0.35$). The mean BUN of the early and late starters was 18.3 and 36.5 mmol/L, respectively ($p < 0.001$). The primary study outcome, survival rate within 28 days was 64.3% in early starters and 38.1% in late starters. At 28 days, 6.8% of survivors in early start of CVVH, as compared with 14.4% of survivors in late start of CVVH, were still receiving renal-replacement therapy. Among hospital survivors, there was no difference in the days of hospital stay between two groups, but 59.7% of those in early start of CVVH recovered renal function compared with 13.2% of those in late start of CVVH (P=0.001). **Conclusions:** This study indicates that an earlier initiation of CRRT, may improve the rate of survival and renal recovery among sepsis patients with AKI.

15. Sustained Low Efficiency Dialysis (SLED) in the Control of Hyperammonaemia in Methylmalonic Acidaemia

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Objectives: Hyperammonaemia is associated with significant mortality and morbidity. Patient outcome may be related to the rapidity of serum ammonia clearance. While conventional haemodialysis effectively clears ammonia, therapy may be complicated by haemodynamic instability, and, rebound in serum ammonia levels on the completion of dialysis. We describe the use of SLED in the control of neonatal hyperammonaemia. **Methods:** Two infants presented with lethargy, hypothermia, respiratory distress and metabolic acidaemia. Serum ammonia levels (micromoles/Litre) at presentation were 340 (Patient 1) and 264 (Patient 2). Fluid resuscitation, supranormal dextrose loading and antibiotic administration were undertaken. Methylmalonic acidaemia was diagnosed in both cases and cyanocobalamin and carnitine were administered. Serum ammonia levels continued to increase. SLED was initiated. Venous access was achieved using a 6.5 Fr double lumen catheter. A Frensenius 2008K dialysis machine (modified for use in infants) was deployed with a FX Paed haemodialyser in Patient 1 and a F3 haemodialyser in Patient 2. Blood flows of 10 – 60 millilitres per minute were employed countercurrent to a dialysate flow of 100 – 500 millilitres per minute. Anticoagulation was achieved using a continuous infusion of heparin (10 – 30 units/kg/hr) to maintain an activated clotting time of 150 – 165s. Intra-arterial blood pressure measurement and ECG monitoring were conducted continuously. Blood gas analysis, and, ammonia and electrolyte measurement was performed 1-2 hourly during the SLED session. In the 24 hour period after the completion of dialysis serum ammonia measurement was performed 2-4 hourly. Ammonia levels less than 200 were considered non-toxic **Results:** In patient 1 the pre-SLED serum ammonia was 605. After 7 hrs of therapy (ammonia half-life = 4.1 hrs) the serum ammonia was 200. Patient 2 had a pre-treatment serum ammonia of 554. Non toxic levels (180) were attained after 4.75 hrs of therapy (ammonia half-life = 3.1 hrs). Total treatment duration was 12 hours and 7 hours respectively. Both patients were clinically stable during dialysis. Neither patient manifested an

increase in serum ammonia post SLED.
Conclusions: SLED may offer rapid control of hyperammonaemia without haemodynamic compromise, rebound hyperammonaemia, or, the need to employ a continuous mode of renal replacement therapy post dialysis.

16. Successful Treatment Of Hyperammonemia By Continuous Veno-venous Hemodiafiltration In A Newborn Patient With Ornithine Transcarbamylase Deficiency

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Background and Aims: Ornithine transcarbamylase (OTC) deficiency is known as one of the most common disorders of urea cycle metabolism and causes hyperammonemia in newborns with inherited disease. We experienced a case of a 3-day old baby with OTC deficiency. The baby looked healthy in the first two days of life but abruptly developed lethargy and seizures. On admission, serum electrolyte levels were as follows: sodium 153 mmol/L, potassium 6.0 mmol/L and chloride 116 mmol/L. Arterial blood gas analysis showed low ionized calcium and magnesium levels (2.82 mg/dL, range: 4.5-5.2; 0.88 mg/dL, range: 1.09-1.46, respectively), high lactate and pCO2 levels (5.6 mmol/L, range: 0.5–1.6; 58 mmHg, range 35-45, respectively), and low pH level (7.2, range: 7.35-7.45). The patient's serum ammonia level was more than 1700 _g/dL (range: 0-45 _g/dL). Continuous renal replacement therapy (CRRT) with the mode of continuous veno-venous hemodiafiltration (CVVHDF) was immediately performed to correct the elevated ammonia level. Seizure control was achieved after the ammonia level decreased. Therefore, CRRT should be included as one of the treatment modalities for newborns with inborn errors of metabolism, especially hyperammonemia. Here, we report on one case of successfully treated hyperammonemia by CRRT in a neonate with OTC deficiency.

17. Clinical Study of CRRT for Acute Encephalopathy with AKI or with Multiple Organ Failure(MOF)

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Introduction: In Japan, acute encephalopathy (AC) concerned with viral infection (eg.influenza virus or rota virus and so on) is higher incidence than any other countries. We can see multiple organ failure including AKI in AC patients who need CRRT , because AC leads to SIRS or Sepsis. Instead of early conventional treatment, AC patients were severe neurological prognosis. But sometimes we experienced that patients performed CRRT were better neurological prognosis than conventional therapy. We studied 16 AC patients who were performed CRRT. Patients: There were 16 AC patients who performed CRRT from 1997 to 2008. We excluded AC patients who were infected E. Coli(O-157) or Yersinia Pseudo tuberculosis and so on. **Purpose**: We studied efficacy of CRRT for various factors. The factors are age, sex, cause of virus, indication of CRRT, mortality, kidney injury, kind of blood purification, neurological and kidney prognosis. **Result)** Average age was 4 years and 5 months. There were 9 male patients and 7 female patients. Kind of virus was Influenza virus (4 cases), Rota virus (4 cases), RS virus (1 case), varicella(1case), HHV6(1 case) and unknown(3 cases). According to pediatric RIFLE criteria, 15 patients were failure, only one patient who was ARDS was normal kidney function, so called non renal indication. Kind of CRRT were CHDF(14 cases), CHF(1 case), PEX(3 cases) and PMX-DHP(3 cases). Mortality was 31.3% (survivor 11/16). There were10 patients whose kidney function were normal. There was a patient whose kidney function worsened to CKD stage 2(eGFR=60~89). In level of gross motor function (walk, sit, bedridden), 2 patients worsened. In level of mental retardation (mild, middle, severe) 3 patients worsened. **Conclusion)** It is necessary for AC patients who complicated with MOF to perform CRRT. We thought CRRT made better neurological prognosis than conventional therapy. But further study is necessary.

18. Impacts of Early Continuous Renal Replacement Therapy in Critically Ill Patients with Rapidly Progressive Acute Kidney Injury

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Background and Aims: The optimal time to initiate continuous renal replacement therapy (CRRT) in patients with acute kidney injury (AKI) remains elusive. In addition, it has been unclear as to which parameters should be considered for the decision to start CRRT. Here, we evaluated retrospectively the optimal timing of CRRT stratified by various clinical and laboratory parameters and its association with clinical outcomes in patients with rapidly progressive AKI. A retrospective study was performed on the data of 658 AKI patients received CRRT in intensive care unit (ICU) of Seoul National University Hospital from October 2007 to January 2010. Rapidly progressive AKI was defined as >2-fold increase of serum creatinine or >50% reduction of hourly urine output during 24h prior to initiation of CRRT. Data included RIFLE criteria, SOFA score, APACHE II score, and number of organ failures. Timing of CRRT was stratified into 'early' and 'late' by median value of BUN and creatinine levels at the start of CRRT, and also by median urine output during 6h, 12h, and 24h before the initiation of CRRT. The clinical outcomes assessed included duration of RRT, ICU stay, hospital stay and 90 day-mortality. There were no significant differences in outcomes of patients between early and late group stratified by median value of creatinine at the start of CRRT. However, in terms of BUN, 90 day mortality rate was significantly higher for late group in univariate analysis (p=0.02), but not in multivariate analysis. When the patients were stratified by urine output before CRRT, patients with lower urine output during 6h and 12h before CRRT had significant higher multivariate-adjusted, 90 day-mortality. (6h: OR 1.45, 95% CI 0.99-2.15, P=0.005, 12h: OR 1.69, 95% CI 1.14-2.39, P=0.008). Finally, when CRRT was started at 'Failure' stage of RIFLE criteria compared with 'Injury' stage, the multivariate adjusted OR for death was 1.74 (95% CI 1.15-2.64). Duration of RRT, ICU stay and hospital stay had no significant differences between 'early' and 'late' group. Our data suggest that early CRRT may have survival benefit in critically ill patients with rapidly progressive AKI, and urine output is the most important parameter for the decision to start CRRT.

19. CRRT Removes More Oxalate than Conventional Hemodialysis in Primary Hyperoxaluria

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Background and Aims: Kidney failure, caused by hyperoxaluria, is followed by high oxalate concentrations in blood and systemic deposition of calcium oxalate with severe end organ damage and death (systemic oxalosis) . Oxalate removal by conventional hemodialysis is usually not able to match the rate of oxalate production. Therefore, intensive therapy with hemodialysis 5-6 days of the week for 3-4 hour per session, sometimes with addition of nightly peritoneal dialysis may be required to minimize the effects of systemic oxalosis. Efficient oxalate removal is especially important following transplantation when accumulated tissues stores are mobilized, and can cause injury to the renal allograft. CRRT may have a role in this situation to facilitate more oxalate removal. We compared oxalate removal by conventional hemodialysis with CRRT in a patient with poor renal allograft function. A 48 year Caucasian male with primary hyperoxaluria type 1 had persistently elevated serum oxalate levels after liver-kidney transplantation. His liver enzymes were normal but he was noted to have rising serum creatinine. His transplant kidney biopsy showed acute tubular necrosis and abundant calcium oxalate deposits, consistent with recurrent oxalate nephropathy. He was initiated on high volume CVVH at 6 liters per hour using Prismaflex. Serum and effluent oxalate levels were measured while he was on CVVH, which was continued for a total of 7 days. Oxalate estimation was done by enzymatic method based on reduction of oxalate by oxalate oxidase (normal range <1.8 umol/L). The serum and effluent oxalate levels, volume of the effluent and the oxalate removed/day were as depicted in the table. He was subsequently switched over to 6 days/week hemodialysis for 3.5 hours with blood flow rate of 350 ml/min and dialysate flow rate of 600 ml/min using Revaclear Polyflux dialyzer. Serum and dialysis effluent oxalate were measured over the next 3 days and the results are shown in the table.

The oxalate removal on CVVH was found to be more than conventional daily dialysis in the index patient's case. CRRT warrants consideration in primary hyperoxaluria patients with renal failure.

(table on following page)

	Day on CVVH							Day on HD		
	1	2	3	4	5	6	7	1	2	3
Plasma oxalate (umol/L)	28.4	19.7	17.4	20.9	24.4	17.8	22.2	31.4	26.8	29.2
Dialysate effluent oxalate (umol/L)			17.3	13.3	18.8	19.1	22.3	8.9	9.3	9.7
Effluent volume (L)	30	144	144	144	144	144	84	126	126	126
Oxalate removal /day (umol /day)			2491.2	1915.2	2707.2	2750.4		1121.4	1171.8	1222.2

20. Femoral Catheterization for Short-Term Dialysis Vascular Access During CRRT

Bing Tang, Hong Ye, Zhiping Sun, Xia Shen, Junwei Yang, Nanjing University, Naning, Jiang Su, China

Purpose: To observe the clinical characteristic of femoral catheterization during continuous renal replacement therapy (CRRT) . **Methods:** Between Feb 2008 and Nov 2010, 195 patients were involved in this study by the retrospective analyses method at our center. Most of they underwent with interval CRRT treatment(6 to 12 hours per day ,dose average 4L/hour). Among them 172/195_88.2%_patients were employed femoral catheterization_the other employed arterio-venous fistulas or jugular catheterization. Most of 172 patients employed femoral catheterization received the breathing machine treatment or can not lie on the back. 16 cm catheter_doublelumen noncuffed, nontunneled hemodialysis catheter was inserted at the bedside , not under ultrasound guidance. Catheter acute malfunction_catheter-related infections and duration of catheterization were assessed. **Results:** Among 172 patients employed femoral catheterization ,Catheter acute malfunction was 3/172_1.75%_.The catheter-related infections was 1.5 per 1000 catheter-days. The duration of catheterization was 5.2 days average. **Conclusion:** The use of femoral veins catheter is a convenient and effective method for short-term dialysis vascular access during CRRT.

21. Instilling Confidence and Competence: CRRT Training and Trouble Shooting in the Simulation Lab

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Background: Maintaining competence with low volume high risk treatment modalities such as continuous renal replacement therapy can be a monumental issue. Educational plans usually include initial training by the company educators and then hands-on experience. However, when the number of patients requiring this treatment is limited, hands on experience is not always available. **Methods:** To work around this, educators encourage the nurses to practice setting up the machine during down time during the shift or to come in for practice sessions. These solutions did not work for us. Our physicians and nurses did not feel comfortable using this equipment on critically ill patients. To avoid transferring the patient to another facility, we had to devise a solution. Our solution was utilization of the simulation lab. Using moderate and high fidelity manikins, we were able to simulate real life conditions; setting up the machine, attaching it to the patient and troubleshooting alarms. **Conclusions:** What makes this simulation different from the usual "wet labs" is that we use porcine blood during the simulation. This use of blood allows us to troubleshoot alarms not attainable when saline is used. This presentation reflects the planning, implementation, and evaluation of the program.

Targeted Interventions

22. Myoglobin Removal Using High Volume Hemofiltration in Patients with Oliguric Acute Kidney Injury

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Purpose: Rhabdomyolysis with myoglobinemia can result in precipitation of acute kidney injury (AKI). It has been recommended that in high risk patients myoglobin be removed from the circulation with extracorporeal therapy to decrease renal exposure and lessen the risk of AKI. Given the size of the molecule (17 KD), however, it remains controversial whether or not significant clearance can be obtained beyond that achieved through both renal and extra-renal mechanisms. Previous studies have been small and contradictory. We examined myoglobin removal in a series of 6 patients with oliguric AKI treated with high volume hemofiltration. **Methods:** Oliguric AKI patients with rhabdomyolysis received pre-filter hemofiltration at a rate of 45 ml/kg/hour using a polysulfone filter with a molecular size cut-off of 65 KD. Oliguric patients were selected to eliminate the effects of urinary clearance. Myoglobin levels were measured in pre- and postfilter serum and in the effluent at times 2 hours, 12 hours, and 24 hours after the start of hemofiltration. Filters were not routinely changed during the study period. Sieving coefficients were calculated using the mean of the pre- and postfilter blood samples and the effluent concentration. **Results:** Most patients were male (5/6) and all had 24-hour urine outputs less than 100 ml. The mean myoglobin level at the start of hemofiltration was 18,500 ng/ml. The mean sieving coefficient for the 18 timed samples was 0.15. With a mean replacement fluid rate of 75 ml/minute for the group, the mean myoglobin clearance was only 11.3 ml/min. There was a non-significant (10%) decrease in myoglobin levels across the filter. **Conclusion:** Despite the use of high volume hemofiltration, the removal of myoglobin was negligible. In patients with normal renal function, the anticipated amount of extracorporeal removal would not likely significantly impact renal exposure to myoglobin. Whether filters with larger molecular weight cut-offs would improve the efficiency of removal needs to be determined. This study also raises concern about the efficiency of hemofiltration in sepsis since many inflammatory mediators are of similar size to myoglobin.

23. BNP is a Predictive Marker of Mortality in AKI Patient

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Purpose: Brain natriuretic peptide (BNP) level which measured at ICU admission is useful in evaluating heart failure, but its role in evaluating patients with AKI requiring CRRT is unclear. An independent predictor of mortality in critically ill patients and is useful in evaluating heart failure. **Methods:** We retrospectively reviewed the medical records of all ICU patients who received CRRT at Dong-A university hospital from March 2010 to September 2010. The prognostic values of BNP for the mortality during CRRT were investigated, and their cutoff values for death were determined. **Results:** The total number of patients who required CRRT in ICU was 43. The mean BNP levels of the 19 patients who died were significantly higher than that of those who survivrd (2180 versus 750pg/mL; $P<0.05$). The area under the curve was 0.87 and optimal threshold for BNP was 1389pg/mL. Patients with BNP levels more than the threshold of 1389pg/mL is the independent factor predicting mortality during CRRT (odds ratio 39.6; 95 CI, 5.79-271). **Conclusions:** Among critically ill patients, BNP level more than 1389pg/mL is an independent marker of mortality in patients during CRRT. A large scaled, prospective randomized multi-center trials are needs to confirm the validation of the optimal threshold and independent predictive power of BNP in the critical care setting.

24. Effect of Timing of Initiation of CRRT on ICU Mortality in Critically Ill Children for Management of Acute Renal Failure and / or Fluid Overload

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Purpose: Early initiation of CRRT in critically ill children requiring CRRT may have survival benefit. Our objective was to evaluate the effect of early initiation in a sub-group of critically ill children requiring CRRT for management of acute renal failure (ARF) and / or fluid overload (FO). **Methods:** We performed a retrospective review of all non-ECMO patients who underwent CRRT in our ICU between Jan 1,

2000 and Jul 31, 2009. Patients initiated on CRRT for management of ARF and / or FO were included in the study. Survivors were compared with non-survivors with respect to the Ti (timing of initiation measured as time from ICU admission to CRRT initiation) and other predictor variables. Also, early initiators (Ti < 3 days) were compared with late initiators (Ti > 3 days) with respect to ICU mortality. **Results:** A total of 251 patients underwent non-ECMO CRRT in our ICU during the specified time period. 190 of these met the criteria for inclusion, with an overall mortality of 47%. Ti was significantly lower among survivors compared to non-survivors (3.7 + 0.5 Vs. 6.8 + 1.1 days, p-value 0.01). Other significant predictors of non-survival were higher FO, higher severity of illness scores, oncologic diagnosis and worsening pRIFLE at CRRT Initiation. Age, weight and presence of shock were similar between the two groups. Multivariate logistic regression analysis identified Ti (OR 1.047), FO category (OR 1.294), Severity of Illness (OR 1.023) and presence of Oncologic diagnosis (OR 3.380) as independent predictors of mortality. Early initiators had a significantly lower mortality rate compared with late initiators (38% Vs. 60%, p-value 0.003). Kaplan Meier plots were consistent with improved survival among early initiators (Logrank p-value 0.05). **Conclusion:** In our cohort of critically ill children with ARF and/or FO, timing of initiation was an independent predictor of mortality. We observed a statistically significant difference in survival rates between early and late initiators with early initiation providing a survival advantage.

25. Biological effects of High Volume Hemofiltration (HVHF) on Kidney Endothelial and Tubular Epithelial Cell Alterations Induced by Septic Plasma

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Background: The mechanisms of sepsis-induced acute kidney injury (AKI) seem to be related not only to hypoperfusion, but also to a direct detrimental activity of circulating mediators on kidney cells. We previously demonstrated that plasma of septic patients induce apoptosis and functional alterations of kidney epithelial cells. Moreover, sepsis is associated with a microvascular derangement that may contribute to AKI and MODS. The aim of this study was to investigate the efficiency of HVHF to remove from septic plasma mediators involved in AKI. **Methods:** We selected 5 patients with sepsis-associated AKI (IVOIRE study) and we evaluated the effects of their plasma collected at different time points after the start of HVHF (70 ml/Kg/h restitution fluids, 1.9 m2 polyethersulfone membrane) on leukocyte adhesion (PMN and PBMC), apoptosis (TUNEL and caspase activities) and functional alterations of human tubular epithelial and endothelial cells. Data were correlated with plasma levels of von Willebrand factor-vWF, TNF-alpha, Fas-Ligand and CD40-Ligand, **Results:** Septic plasma collected after 1 h HVHF induced PMN and PBMC adhesion on endothelial and tubular cells through ICAM-1 and CD40. On endothelial cells, septic plasma induced a cytotoxic effect and significantly reduced angiogenesis. Plasma levels of vWF were elevated during HVHF, suggesting an endothelial dysfunction. On tubular cells, septic plasma induced apoptosis through Fas up-regulation and caspase activation. Moreover, septic plasma induced the loss of polarity and the altered expression of megalin and of the tight junction protein ZO-1. All these effects were significantly reduced incubating cells collected after 6 h HVHF in comparison to 1 h HVHF. By contrast no significant differences were observed incubating cells with plasma collected after 12 h and 72 h in respect to 6 h. Plasma levels of TNF-alpha, Fas-Ligand and CD40-Ligand had a similar time-course behaviour. **Conclusions:** Septic plasma induced leukocyte adhesion, apoptosis and functional alterations of endothelial and tubular epithelial cells. These effects may be ascribed to detrimental circulating mediators that can be removed in the first hours of HVHF. However, unexplored mechanisms (membrane adsorption, polarization, etc.) may interfere with convective-driven solute removal, thus limiting the long-term efficiency of HVHF.

26. Solute Clearance in CRRT: Comparing Measured Effluent Volume to Actual Delivered Dose

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Background and Purpose : Substantial efforts have been made towards defining the dose threshold of continuous renal replacement therapy (CRRT) associated with improved survival in critically ill patients with acute kidney injury. Published studies have based dose of CRRT on small solute clearance, expressed as total effluent volume (TEV) per weight and unit time (ml/kg/hr). These studies have not compared CRRT dose based on the measured TEV to the actual delivered dose as determined by direct quantitative measurement of the solute in the effluent. The purpose of this study was to determine whether the measured TEV corrected for pre-dilution replacement fluid (RF) accurately estimates actual delivered small solute clearance. **Methods:** We retrospectively analyzed data that had been prospectively collected for 200 patients enrolled in a randomized controlled trial comparing survival with a prescribed effluent rate of 20 ml/kg/hr (standard dose) to 35 ml/kg/hr (high dose) using pre-dilution continuous venovenous hemodiafiltration (CVVHDF). Filters were changed every 72 hours. Effluent urea nitrogen (EUN) and creatinine (ECr) levels, and TEV were obtained daily. Estimated effluent dose was defined as the TEV corrected for the pre-dilution effect of the RF. Actual delivered dose was calculated as: (EUN/BUN) multiplied by TEV for urea and (ECr/SCr) multiplied by TEV for creatinine. **Results:** Complete data were available for 165 patients. The difference in actual delivered dose for the standard dose compared to the high dose group was statistically significant for both measured urea and creatinine clearances ($p<0.0001$). For the standard dose group, there was no difference between the estimated effluent dose and actual delivered urea and creatinine clearances. For the high dose group, estimated dose based on TEV differed significantly from both the delivered urea clearance by 7.1% ($p<0.0001$), and the creatinine clearance by 13.9 % ($p<0.0001$).
Conclusion: Direct measurement of solute clearance is indicated if providing pre-dilutional CVVHDF.

27. Regional Low-Concentrated Citrate Anticoagulation Versus Heparin Anticoagulation in Continuous Venovenous Hemofiltration

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Background: In Continuous Venovenous Hemofiltration (CVVH) heparin or other systemic anticoagulants are necessary to prevent filter clotting. A disadvantage of the use of heparin is the potential harm of an elevated bleeding risk. Regional citrate anticoagulation seems to be a promising alternative. Because of some reported lethal events with high concentrated citrate dosages (12-14%) we developed a protocol based on low concentrated citrate (0.3%) for CVVH. We compared the efficacy and safety of this protocol with our heparin protocol. The difference in filter lifespan was our primary outcome. **Methods:** In a general 14-bed closed-format Intensive Care Unit (ICU) 35 patients receiving heparin anticoagulation for CVVH and 37 patients receiving low concentrated citrate were included in a partially prospective and retrospective cohort study. Heparin was dosed according to weight and bleeding risk. **Results:** The patient basic characteristics were similar. The median filter lifespan was significantly longer in the citrate group (42.8 hrs versus 30.9 hrs, $p=0.001$). The most apparent reason for interruption of CVVH in the heparin group was filter clotting but in the citrate group maximum filter lifespan. In the citrate group the relative urea and creatinine clearance was significantly better compared to the heparin group (-57.7% versus -33.3%, $p<0.001$ for urea and -55.7% versus -40.6%, $p<0.001$ for creatinine). The need for packed red blood cells (RBC) per CVVH day was higher in the citrate group, but this difference was not significant. In the heparin group control of plasma sodium and plasma bicarbonate concentration was significantly better. Though not significant we found a difference in survival on the ICU in favor of citrate (51.4% versus 40%, $p=0.36$). **Conclusion:** Low concentrated citrate is a satisfactory anticoagulant for CVVH because of a longer filter lifespan and shorter 'down-time' which resulted in a significantly more effective urea and creatinine clearance. The need for more RBC per CVVH day in the citrate group compared to the heparin group, although it is not significant, is an unexpected finding, needing further analysis.

28. Early Continuous Haemodiafiltration (CVVHDF) in Septic Patients. Six Years of Experience

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Introduction: In critically ill patients dysfunction of many organs develops during of the first 24 hours of recognised septic shock. However renal dysfunction, which is represented by high creatinine, water and sodium retention, is often observed after 48 or more hours, in spite of the facts in literature saying that early kidney injury (AKI) can exist without the change in creatinine level. Those facts forced us to implement early CVVHDF in septic shock during 24 hours after admission. **Material and Method** : Between 2004-2010 in our department early CVVHDF was introduced in 46 patients before 24h of admission with septic shock without clinical and biochemical signs of renal failure: mean level of creatinine was 1.08 mg/dl, mean daily urine output was 2370 ml, mean age was 58, mean Apache score was 23 points. Standard ultrafiltration rate was 35 ml/kg/h. The second group of patients consisted of 48 people, here CVVHDF was introduced after 48h of admission with recognition of clinical and biochemical signs of renal failure: mean creatinine level was 1.8 mg/dl, mean daily urine output was 430 ml, mean age was 58 years, mean Apache score was 23 points. Results of treatment in both groups were compared in table below. T-student test and Chi2 were used, $p<0.05$ was recognised as statistically significant. **Results :**Results are shown in table below. **Conclusion :**Lower mortality was observed in group <24 h, but it was not statistically significant.

Variables	CVVHDF < 24h	CVVHDF > 48h	p
Number of Patients	46	48	ns
Age in years	53	53	ns
Apache score	23	23	ns
Creatinine [mg/dl]	1.08	1.80	0.08
Urine output daily [ml/24h]	2370	430	0.07
Ultrafiltration [ml/kg/h]	35	35	ns
Mortality	16/46 [34.7%]	19/48 [39.5%]	0.06

29. Fluid Overload and Fluid Removal in Pediatric Patients on CRRT Predicts Pediatric ICU Mortality

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Purpose: In pediatric patients fluid overload (FO) at continuous renal replacement therapy (CRRT) initiation is a risk factor for mortality, but whether fluid removal during CRRT improves outcome is unknown. We hypothesized that the ability to achieve a negative fluid balance on CRRT would be associated with reduced mortality. **Methods:** Retrospective single-center cohort of all PICU patients requiring CRRT from 07/2006-09/2010 (n= 144). Percent FO was determined by a published standard: (fluid in-fluid out from ICU admission to CRRT initiation)/ICU admission weight). Net fluid removal during CRRT was recorded and % FO at CRRT discontinuation was calculated: (CRRT discontinuation weight-ICU admission weight)/ICU admission weight). Degree of FO was compared between ICU survivors and non-survivors, and multivariate analysis was conducted controlling for age and severity-of-illness (PRISM III score). **Results**: Overall ICU mortality for this cohort was 56%. Percent FO (mean±SD) at CRRT initiation was significantly lower in survivors compared to non-survivors (12.8±14.4 vs 28.8±28.2, $p<0.0001$). Percent FO at CRRT discontinuation was also significantly lower in survivors compared to non-survivors (2.8±13.5 vs 13.8±20.5, $p=0.0003$). In multivariate analysis, each percent rise in FO conferred a mortality OR of 1.04 (95%CI 1.01-1.07) at CRRT initiation, and 17.15 (95%CI 1.096-268) at CRRT discontinuation. Although the net fluid balance during CRRT did not differ between groups, more survivors achieved an even or net negative balance compared to non-survivors (51.6% vs 32.5%, $p=0.0208$). After adjusting for %FO at CRRT initiation, %FO at CRRT discontinuation did not independently predict mortality (OR 6.326, 95%CI 0.352-110.6). **Conclusion**: Our data demonstrates an association between mortality and the degree of FO at both CRRT initiation and discontinuation. We also demonstrate the ability to achieve a negative fluid balance on CRRT can predict survival. However, the prognostic value of FO at CRRT discontinuation may primarily be related

to degree of FO at CRRT initiation. Thus, prevention of FO, perhaps by earlier initiation of CRRT or by conservative goal-directed fluid management, may be a more effective clinical strategy than attempting fluid removal after it is already established.

30. Slow Continuous Ultrafiltration Using the Aquadex System in an Infant

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Background and Aims: Although fluid overload is a common life-threatening consequence of acute kidney injury (AKI) in infants, the technique of slow continuous ultrafiltration (SCUF) is rarely utilized due to limited vascular access and the lack of appropriate equipment. Since the Aquadex Flex Flow Fluid Removal System (CHF solutions) is designed to provide SCUF using small peripheral venous catheters and has a very small extracorporeal blood volume (30ml), we hypothesized that it would be well suited for use in infants with severe fluid overload. In this report a 4 month old male with autosomal recessive polycystic kidney disease underwent SCUF using the Aquadex system after he developed ultrafiltration failure while on peritoneal dialysis (PD). Prior to initiating SCUF, the patient was 20% above his 5 kg dry weight despite optimization of his PD regimen. He was suffering from severe respiratory distress and was receiving only 10% of his estimated caloric needs owing to fluid restriction. Due to a lack of suitable vascular access for hemodialysis, SCUF was initiated with the Aquadex system using a 5-french double lumen central venous catheter placed in the left saphenous vein. Using a blood flow of 20ml/min and an ultrafiltration rate of 20 to 40ml/hr resulted in 1500mL of ultrafiltration in a 72 hour period. Anticoagulation was provided with a low dose heparin drip (4 units/kg/hr) infused pre-filter into the Aquadex circuit and was monitored using activated clotting times. The patient tolerated the procedure well with no hemodynamic instability or electrolyte abnormalities. After 72 hours of SCUF therapy, the patient's respiratory distress had resolved, and his nutritional status was subsequently optimized with liberalization of fluid intake. To our knowledge, this is the first documented use of the Aquadex system to provide SCUF in infants. Given the association between significant fluid overload and increased mortality rate in the setting of AKI, the Aquadex system may provide a much needed alternative therapeutic intervention in this patient population.

RRT Research

31. Coupled Plasma Filtration Adsorption (CPFA) Combine with High Volume Hemofiltration (HVHF) Is Not Superior to HVHF Alone in the Treatment of Septic Shock

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Introduction: Coupled plasma filtration adsorption (CPFA), using a sorbent once the separation between plasma and blood has been obtained with a plasma filter, has been designed to non-selectively remove inflammatory mediators released in sepsis and septic shock. The aim of this study was to investigate whether early application of CPFA combined with high volume hemofiltration (HVHF) is superior to HVHF alone in the treatment of septic shockl. **Methods:** Sixteen 24 h-fasted, anesthetized, invasively monitored, mechanically ventilated female sheep received 1.5 g/kg body weight of feces into the abdominal cavity to induce sepsis. Ringer_s lactate (RL)+ hydroxyethyl starch solution (volume ratio=1:1) was titrated to maintain cardiac filling pressures at baseline levels throughout the experiment. Four hours after feces injection, animals were randomized in two groups to receive either CPFA with HVHF (n = 8) or HVHF alone (n = 8). Hemofiltation rate was 150 ml/kg/hour with a four-pump hemofiltration machine (Lynda, Bellco, Mirandola, Italy). Sublingual area microcirculation was evaluated with side dark-field videomicroscopy (Microscan, MicroVision Medical) at baseline and after 6, 12, 18 and 24 hours. Functional capillary density (FCD) and proportion of perfused vessels (PPV) were calculated. Experiments were pursued until the sheep's spontaneous death or a maximum of 24 hours. **Results:** Core body temperature was lower in the CPFA group than in the HVHF alone group. Mean arterial pressure and systemic

vascular resistance index were lower in the CPFA than in the HVHF group. Cardiac index, pulmonary arterial pressure, pulmonary vascular resistance and respiratory system resistance were higher in the CPFA group than in the HVHF group. PaO2/FiO2 was lower in the CPFA than in the HVHF group. Arterial blood lactate concentration was higher in the CPFA than in the in the HVHF group. FCD and PPV were lower in the CPFA group than in the HVHF group. Arterial IL-6 concentrations were lower in the CPFA group than that in the HVHF group. There was no significant difference in survival time between the two groups. **Conclusion:** In this clinically relevant septic shock model, despite of higher cardiac index, CPFA showed lower mean arterial pressure, lower systemic vascular resistance, higher pulmonary arterial pressure, lower PaO2/FiO2 ratio, higher lactate concentrations and lower IL-6 concentrations compared with HVHF group. CPFA combined with HVHF is not superior to HVHF alone and even worse hemodynamics and gas exchange in the treatment of septic shock.

32. Mortality Rate and Renal Recovery in Critically Ill Patients with Acute Kidney Injury Treated with Prolonged Intermittent Renal Replacement Therapy versus CRRT

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Background: Prolonged intermittent renal replacement therapy (PIRRT) is a promising renal replacement therapy for critically ill patients with unstable hemodynamics who had acute kidney injury (AKI). It provides solute removal and hemodynamic stability equivalent to continuous renal replacement therapy (CRRT) but significantly lower cost. The aim of the present study was to compare the 28-day mortality rate, renal recovery rate and hemodynamic status between PIRRT and CRRT in these patients. **Methods:** Sequential critically ill patients with AKI undergoing acute dialysis with CRRT (2004-2007), or PIRRT (2008-2010) were analyzed. PIRRT defined as prolonged duration of intermittent hemodialysis or hemodiafiltration at least 8 hours per session. The primary outcome was death from any cause by day 28. The secondary outcomes were renal recovery and hemodynamic stability as measured by the ratio of mean arterial blood pressure and vasopressor score during treatment. **Results:** Among the 94 recruited patients, 46 received PIRRT and 48 received CRRT. The mean age was 59.1 + 19.1 year, and 57.4% were male. Baseline characteristics of the patients in the two groups were similar. Mean APACHE II scores at the time of RRT initiation were comparable (28.3 + 5.0 in PIRRT, 28.2 + 4.8 in CRRT, P= 0.89). The rate of death from any cause by day 28 was 47.8% in PIRRT and 66.7% in CRRT (P=0.10). There was no significant difference between the two groups in the rate of recovery of kidney function among the survivors. The ratio of mean arterial blood pressure and vasopressor score at treatment initiation, at 4 hr, 8 hr, 12hr, 24 hr, and 48 hr after treatment initiation were not significantly different between the studied groups. **Conclusions:** Compared with CRRT, prolonged intermittent renal replacement therapy in critically ill patients with severe AKI was not associated with a change in mortality rate, rate of renal recovery and hemodynamic stability.

33. Down-Time and Filter Efficacy Affect the Delivering of a Prescribed Dose in Continuous Renal Replacement Therapies

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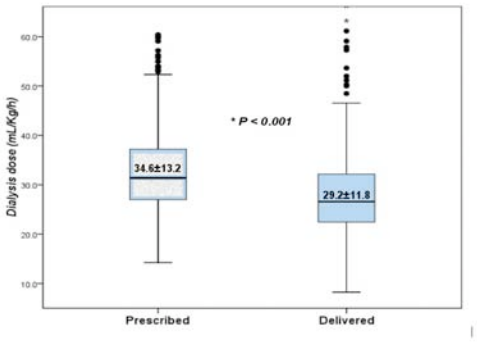
Objective: Time off renal replacement therapy (down- time) and low filter efficacy due to clotting constitute important factors that lead to failure delivering a prescribed dose in critically ill patients with acute kidney injury (AKI). These factors are not usually assessed and the total effluent volume adjusted for effective time of treatment is usually consider as delivered dose in continuous renal replacement therapies (CRRT). We assessed the impact of down-time and filter efficacy on the gap between prescribed and delivered dose. **Methods:** We prospectively analyzed data from 305 treatments in 54 critically ill patients with AKI treated with pre-dilution continuous venous-venous hemodiafiltration (CVVHDF) at the University of California San Diego Medical Center from September 2009 to March 2010. Regional citrate was used as an anticoagulation strategy in all treatments. All patients were prescribed a 2700 ml/hr effluent rate. Estimated dose was expressed as mL/Kg/h of observed effluent (adjusted for effective time of treatment). Delivered dose was expressed as mL/Kg/h and was derived from the observed effluent times the

actual sieving coefficient (effluent urea nitrogen/blood urea nitrogen). CRRT down-time was defined as the time off CRRT (hours) per day. Filter efficacy was determined by filter clearance using effluent urea nitrogen/plasma urea nitrogen ratio (FUN/BUN) at the beginning of each treatment and then each 12 hr. Percentage (%) of delivered dose was calculated by delivered dose/prescribed dose x 100%. **Results:** 10% of all the treatments had a median (IQR) down-time of 2.0 (1.0-5.1) hours per day. The mean FUN/BUN ratio was 0.9±0.1. Delivered dose assessed by measuring effluent urea nitrogen was significantly lower than prescribed dose, 29.1±11.8 versus 34.5±13.2 mL/kg/hr, p< 0.001 (Figure 1). A significant correlation was found between FUN/BUN ratio and the percentage of delivered dose (r2 =0.25; p < 0.001) whereas the down-time did not affect the percentage of the delivered dose (r2 =0.11; p = 0.062). **Conclusion:** Delivered dose of CRRT is lower than prescribed dose. Filter efficacy has significant impact on the percentage of delivered to prescribed dose. We recommend monitoring solute clearances to optimize delivering a prescribed dose in critically ill patients treated with CRRT.

Figure 1 - Mean prescribed and delivered dose (adjusted for effective time of treatment and filter efficacy).



34. Blood Pressure Profile In Diabetic Patients On Peritoneal Dialysis

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Background: Blood pressure (BP) varies during the course of the day and is characterized by a marked decrease of systolic and diastolic BP nocturnally (dippers). Non dipping is associated with a higher incidence of cardiovascular disease and a poor long-term survival. Numerous studies have shown that non dipping is common in patients with either diabetes mellitus or chronic kidney disease. **Purpose:** To accurately measure the average BP of patients on peritoneal dialysis (PD) and to compare the differences in BP profiles between diabetics and non diabetics. **Methods:** PD patients with stable dry weight, blood pressure and medications for the last 3 months were included into the study. All patients had their 24-hour Ambulatory Blood Pressure Monitoring (ABPM) recorded. Dippers were defined as a fall in SBP/DBP > 10% during night-time BP recordings. **Results:** 46 patients were eligible for this study. Their mean age was 45 ± 13 years and mean duration on PD was 31.6 ± 25.6 months. 43 patients (93.5%) had hypertension and 16 patients (34.8%) had diabetes. The group mean systolic BP (SBP) was 139 ± 21mm Hg and mean diastolic BP (DBP) was 87 ± 15mm Hg and the mean arterial pressure (MAP) was 104 ± 16mm Hg. **Conclusion:** Our study showed that despite being on PD, BP was not well controlled in our patients. 93.7% of diabetics were non dippers and therefore at higher risk of poor long term outcomes. The diabetics were older, had a lower diastolic BP with a higher pulse pressure and thereby increasing their cardiovascular risk.

	Diabetics	Non diabetics	P value
Number of patients	16	30	
Age (yrs)	54 ± 13	40 ± 11	p < 0.001
Mean SBP (mm Hg)	139 ± 18	139 ± 23	p = 0.975
Mean DBP (mm Hg)	80 ± 14	90 ± 14	p = 0.025
Mean MAP (mm Hg)	100 ± 13	107 ± 16	p = 0.171
Mean PP (mm Hg)	59 ± 17	49 ± 14	p = 0.035
Non dippers (%)	15 (93.7)	16 (53.3)	p = 0.007

35. The Use of Standard Kt/V for Dialysis Dose Assessment in Acute Kidney Injury

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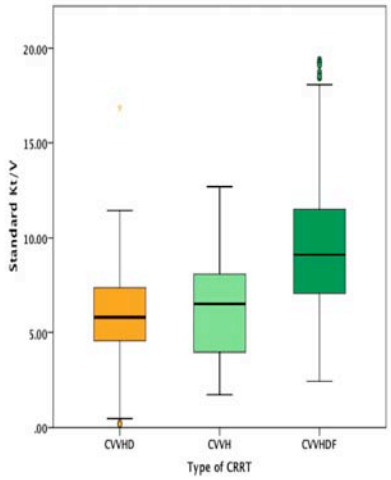
Objectives: Standard Kt/V (StdKt/V) is used to measure dialysis efficiency across different types of therapies of variable frequency in patients on chronic dialysis. In acute kidney injury (AKI) the assessment of dialysis dose across modalities has been limited to effluent volume in CRRT while single pool (spKt/V) or equilibrated (eKt/V) are used for IHD, making comparisons across modalities difficult. We evaluated the utility of StdKt/V equation to compare the efficiency of IHD and CRRT in patients with AKI. **Methods:** We analyzed data from 1,538 CRRT 24 hr sessions in 244 criticall- ill patients with at least 48 hr on CRRT and from 610 IHD sessions in 254 critically-ill patients from 5 centers included in the PICARD study. Delivered dose was calculated by using StdKt/V Leypoldt et al. equation for IHD; for continuous modalities StdKt/V was computed for each type of CRRT as shown by Diaz-Buxo JA and Perez J. We compared the efficacy of the following treatment regimens: IHD (1 to 7 treatments per week), CVVH, CVVHD and CVVHDF. **Results:** A good correlation was found between spKt/V (Daugirdas equation) and Leypoldt et al StdKt/V equation ($r2 = 0.961$; $p < 0.001$). Frequency of intermittent hemodialysis sessions ranged from 1 to 7 treatments per week. Higher frequency of IHD treatments per week was associated with increased delivered StdKt/V (median [IQR]): from 1.83 (1.50 - 2.15) for 3 treatments per week to 3.15 (2.60-3.97) for 6 treatments per week. A significant correlation was found between dose expressed as mL/kg/hr and StdKt/V ($r2 =0 .976$; $p < 0.001$). CVVHDF offered the highest efficiency among continuous renal replacement therapies (Figure 1; $p < 0.001$). Median (IQR) delivered StdKt/V in CRRT was higher than in a modeled 7 days per week IHD (7.6 [5.6 - 9.9] vs. 4.6 [3.6 5.8]; $p < 0.001$].) **Conclusions:** Standard Kt/V allows comparison of delivered dose across different modalities of RRT and treatment schedules as it is normalized for the duration and frequency of therapy. Additional studies are required to evaluate the utility of StdKt/V for molecules other than urea nitrogen, and correlate delivered dose with outcomes in AKI.

Figure 1 - Comparative efficiency of continuous therapies (CVVH, CVHHD, and CVVHDF)



36. Evaluation of Hemodialysis Efficacy Using Real-time Conductivity Monitoring And Calculations From Urea Measurements

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Background: Hemodialysis (HD) adequacy is strongly correlated with clinical outcome. Real-time conductivity monitoring, using sodium flux rather than urea, allows the repeated assessment of Kt/V during HD sessions. We compared real-time Kt/V with traditional blood-side urea Kt/V and urea reduction ratio (URR). **Methods:** We analyzed 2242 HD sessions in 418 hospitalized patients from 2 academic medical centers. The patients were treated with HD with or without heparin anticoagulation for acute kidney injury (AKI, n=906 sessions) or as chronic maintenance therapy (n=1327 sessions). Real-time Kt/V was obtained from Fresenius 4008® dialysis machine, and blood-side variable-volume single-pool Kt/V (spKt/V) was calculated using the second generation formula of Daugirdas. **Results:** Mean and SD real-time Kt/V was 1.25±0.47, mean spKt/V was 1.40±0.46, and mean URR was 67.8±0.3%. There were 1055 sessions (47.1%) with real-time Kt/V <1.2, 765 sessions (34.1%) with spKt/V <1.2, and 787

sessions (35.1%) with URR <65%. Both spKt/V and URR moderately correlated with real-time Kt/V (r=0.668, 0.652, and p=0.000, 0.000, respectively). However, there was a statistically significant difference between overall real-time Kt/V and spKt/V (-0.14±0.38, p=0.000). Lower real-time Kt/V was associated with larger post-HD weight (r=0.444, p=0.000), lower blood flow (r=0.383, p=0.000), and higher post-HD urea level (r=0.499, p=0.000), but not with AKI (p=0.173). In addition, the urea volume of distribution derived from anthropometric formula and from spKt/V only weakly correlated with each other (r=0.18, p=0.000). The anthropometric method was significantly larger than spV (46.6±14.9 L vs 37.7±21.3 L, respectively, p=0.000). **Conclusion:** Our results show that real-time Kt/V is lower than spKt/V and these 2 measurements are moderately correlated. The difference between the two could be accounted for by the overestimation of urea volume of distribution by the anthropometric formula, which is applied to the real-time Kt/V calculation. Moreover, the discrepancy is present in both acute and chronic settings, suggesting that dialysis delivery can be monitored with real-time Kt/V and periodically confirmed with spKt/V in hospitalized patients.

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37. Effective Removal of MPO-ANCA from Circulation of Patients with Vasculitides by A Novel Double-filtration Plasmapheresis Therapy Using Two Fraction Plasma Separators Combination

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Purpose: To investigate the ability to remove different plasma proteins by double-filtration plasmapheresis(DFPP) using various primary separator and secondary separator combinations; based on it, to propose a novel DFPP therapy, and test its ability to eliminate MPO-ANCA from circulation of patients with vasculitides. **Methods:** Seven patients diagnosed as vasculitides with serum MPO-ANCA positive were enrolled and received 20 sessions DFPP. Three kinds of plasma filters were used to serve as primary and secondary filter, one plasma separator MPS07 and two plasma fraction separators EC50W, EC20W. There were three combinations: MPS07/EC50W combination, MPS07/EC20W combination, and EC50W/EC20W combination; in each combination, the former was used as primary filter, and the latter was used as secondary filter. Double volume of plasma was processed, and 30-40g human albumin was supplemented during each session. One patient received 3 sessions DFPP using MPS07/EC50W, 1 patient received 3 sessions DFPP using MPS07/EC20W, and the other 5 patients received 14 sessions DFPP using EC50W/EC20W. During DFPP, waste plasma was discarded in intermittent way. When the pressure pre-secondary filter reached the threshold value to discard plasma, 800ml normal saline was flushing the secondary filter to force filtration of plasma proteins accumulated in filter, before waste plasma was discarded. Sieving coefficients (SC) of albumin, IgA, IgG and IgM were measured for 3 filters, as well as reduction percentage of plasma proteins concentrations, MPO-ANCA titer by single session DFPP. **Results:** MPS07 filter was well permeable for all above-mentioned plasma proteins (SC>0.6); while EC50W filter was well permeable for albumin and IgG, less permeable for IgA, and little permeable for IgM(SC 0.06); EC20W filter was permeable for only small proportion of albumin and IgG, much less for IgA, and impermeable for IgM(SC 0.03). Single session of DFPP had no effect on serum albumin level, but had diverse effects on other proteins concentration depending on filters combinations and proteins' type. During DFPP using MPS07/EC50W, decline of IgM, IgA, and IgG was 89.7±5.4%, 61.7±14.8%, and 30.5±9.0% respectively. During DFPP using MPS07/EC20W, decline of IgM, IgA, and IgG was 94.2±3.1%, 96.2±2.3%, and 64.7±21.0% respectively. During DFPP using EC50W/EC20W, decline of IgM, IgA, and IgG was 2.8±12.9%, 90.9±4.4%, and 43.5±13.8%, respectively. Reduction percentage of MPO-ANCA titer by single session DFPP using EC50W/EC20W was 34.6±14.3%. Forced filtration of plasma in secondary filter by normal saline flushing before waste plasma discarding could raise the ratio of IgG/albumin concentration in waste plasma by 24.2%. **Conclusions:** According to sieving coefficients of three kinds of filters for different plasma proteins, DFPP using EC50W/EC20W filters is better for removal of pathogens like IgG. With more selective removal of IgG, less loss of other larger useful molecules, it is effective to reduce serum ANCA titer.

38. CRRT in Parallel With ECMO Circuit: Clinical Trial of a Circuit Connection in Adult Patients

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Purpose: Acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT) is a common complication in patients on extra-corporeal membrane oxygenation (ECMO). Acquisition of a vascular access is a challenge in these critically ill patients. Connection of CRRT circuit in parallel to the ECMO circuit circumvents the need for further vascular access and this has been shown to be safe and effective in the pediatric population. However, the aforementioned access and return connections of CRRT on ECMO are very varied and have not been well reported in adult population. The aim of this study was to assess the clinical safety and efficacy of a connection of CRRT in parallel to ECMO in our institution. **Methods:** A total of 8 adult patients, over a period of 6 months, with CRRT on ECMO was assessed. In our institution, the CRRT access line was connected to the ECMO access line, immediately after it had left the patient extra-corporeally and before the centrifugal pump. Next, the return line of the CRRT was connected to the ECMO return line, at the point after the membrane oxygenator and just before it entered the patient. Detailed data including the ECMO pump (revolution per minute), blood flow rate, arterial line pressure, CRRT blood flow rate, and effluent flow rate were recorded. In addition, the CRRT access, return, filter and transmembrane pressures were monitored. **Results:** We found that at ECMO blood flow rate of less than 5 L/min, the CRRT machines functioned efficiently within their pre-determined pressure limits of less than -250 mmHg for the access pressure and less than +250 mmHg for the return pressure. Importantly, the CRRT machines achieved the preset targets for solute clearance and fluid balance. **Conclusion:** Our study shows that with this simple connection as described above, it allows for a safe and effective use of CRRT on ECMO, without the need for an additional vascular access. Future studies, exploring various other methods of connection in a larger population will give us further insight into the management of CRRT on ECMO circuits in adult patients.

39. Increased Surface Coverage Area of Polyvinylpyrrolidone on Polysulfone Hemofilter Membrane Improves Biocompatibility by Suppressing Cell Adhesion during Continuous Hemofiltration

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Background and aims: Continuous renal replacement therapy (CRRT) is a well-accepted treatment modality of acute renal failure in the field of intensive care. Since hemofilter used for CRRT contacts with blood for a long time during the treatment, clotting and cell adhesion within the membrane and/or air-trap chambers frequently occurs, which leads to inadequate solute removal, increased cost for the circuit and filter, time loss for staffs, and risks of troubles. The purpose of the present study was to compare two types of membranes with different surface coverage area of polyvinylpyrrolidone (PVP) on blood cell adhesion. **Methods:** We evaluated hemofilters by using ex vivo continuous hemofiltration (CHF) experiments for 24 hrs which mimicked clinical situation. To compare modified polysulfone membrane (SHG, Toray medical, Tokyo, Japan) on which PVP coverage area increased with conventional polysulfone membrane (SH, Toray medical, Tokyo, Japan), the change in the transmembrane pressure during CHF experiments, reduction of water and protein permeability, and blood cell adhesion after CHF were evaluated. **Results:** Transmembrane pressure of SH was significantly higher than that of SHG ($n=5$, $P<0.05$). Water permeability of both hemofilters reduced after CHF in the same manner. Protein concentration in the filtrate was higher in SHG. Hemoglobin concentration and lactate dehydrogenase activity of the solution eluted from the hemofilter after 24 hrs of CHF by triton X-100 were significantly higher in SH than SHG ($n=5$, $P< 0.05$), indicating that blood cell adhesion of red blood cells and leucocytes was less in SHG (the membrane of increased PVP coverage area). **Conclusions:** Modified polysulfone membrane (SHG) with increased PVP coverage area on their surface reduced blood cell adhesion.

Epidemiology and Patient Characteristics

40. Identifying Quality and Safety Indicators to Monitor Continuous Renal Replacement Therapy (CRRT) Practice

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Background: CRRT has become a standard therapy option in intensive care units (ICUs). The many potential complications related to CRRT may contribute to morbidity and mortality of patients. Despite the high risk nature of CRRT, there are scarce published recommendations for evaluating the safety and quality of CRRT practice. **Purpose:** To identify and measure clinical parameters which may serve as potential CRRT quality and safety indicators. **Methods:** Identified CRRT quality indicators were retrospectively measured from a convenient sample of 62 treatment days from 15 patients. CRRT using the NxStage® System One (Lawrence, MA) in two ICUs at an academic medical center where nephrologists prescribe therapy and CRRT-qualified ICU nurses monitor and manage patients. **Results:** The primary mode was CVVHD (73%) versus CVVH (27%). Time from order to therapy initiation ranged from 50 to 820 minutes (average 268 minutes) reflecting varying urgency levels and time needed for central access. Actual dialysate and replacement therapy fluid (TF) rates delivered compared to ordered rates revealed 93% TF target achieved (range 76% to 99%). Reasons for circuit down time included catheter change time, frequent access pressure alarms, transport time, circuit failure due to clotting or access issues. The Kt/V dose orders averaged 1.12 (range .78 to 1.55). Compliance with fluid balance parameter documentation was high. The internal jugular vein site was the most common access site (86%). Compliance with protocol orders for 1) laboratory monitoring revealed 22/967 (2.8%) errors of omission and 153/967 (16%) additional tests costing $1,157; 2) electrolyte replacement medications revealed 22/224 (9.8%) errors of omission and 1/224 (<1%) additional dose errors. Days of anticoagulation (AC) use included citrate (19%), heparin (3%), and none (78%). Normothermia was observed in 82% of CRRT days with fluid warmer (82%) and warming blanket (50%) use.
Conclusion: Standards and thresholds for CRRT quality monitoring are essential for safe practice and interpretation of patient outcomes related to CRRT. Additional quality indicators recommended include efficacy of fluid balance target achieved and review of adverse events/deaths with CRRT to rule out contribution of potential CRRT complication. CRRT quality monitoring can guide improvement of practice, safety, and resource utilization issues and trends.

41. Does Renal Angina Exist in Critically Ill Children?

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Background: Early recognition of acute kidney injury (AKI) may expedite treatment and improve outcomes. While serum and urine biomarkers identify AKI before a rise in serum creatinine, prompt diagnosis of AKI may be missed because the disease process lacks the physical signs and symptoms to identify patients at-risk for AKI, which would trigger biomarker assessment. Identification of the at-risk AKI phenotype, or a recently proposed state of 'renal angina', may make the use of biomarkers more effective and optimize initiation of therapeutic regimens. **Purpose:** We aim to test the risk factors and laboratory markers of the proposed renal anginal equivalent and the associated hazard tranches for escalating risks of developing AKI in children with systemic inflammatory response syndrome (SIRS), shock, or septic shock. Secondary aims include correlating the angina tranches with length of stay, duration of mechanical ventilation, the use of renal replacement therapy (RRT), and mortality. **Methods:** A single center, retrospective review of all children admitted to the pediatric intensive care unit (PICU) with SIRS, shock, or septic shock from 2005-2010. Risk factors to be tabulated include: admission PRISM (Pediatric Risk of Mortality) III score, admission SIRS criteria, stem cell or solid organ transplantation, mechanical ventilation (MV), kidney function (creatinine, urine output, degree of fluid overload (FO), pRIFLE score, and RRT), inotrope score, nephrotoxic medications, inflammatory markers, neurologic dysfunction, and thrombocytopenia. Renal angina hazard tranches include: Severe) Estimated creatinine clearance (eCCl) decrease of 25% with MV and one or more vasoactive medications, High) Increase in creatinine of 0.3 mg/dl over baseline, eCCl decrease of 25-50%, or 10% FO of in patients with heart failure or after stem cell

transplantation, Moderate) eCCl decrease > 50% or 15% FO over in patients admitted to the ICU. **Results:** Initial sampling of our pediatric database identified 913 children with SIRS, shock, or septic shock. Demographic data is shown in the table below. **Conclusion:** By studying this large sample of pediatric patients, we aim to validate and/or modify the renal angina hazard index which will potentiate the power of AKI biomarkers, expediting early and reliable diagnosis of AKI, which may ultimately improve outcomes.

Category	Survivors	Non-survivors	p-value
% (n)	86.4 (789)	13.6 (124)	
Male, % (n)	54.7 (432)	50 (62)	0.428
PRISM-III	9 [5-14]	23 [13-32]	<.001
Age (months)	53 [13-156]	37 [10-161]	0.346
Admission Source (total), % (n)			
Ward (328)	83.2 (273)	16.8 (55)	<.001*
ER (376)	92.3 (347)	7.7 (29)	<.001^
Transport (109)	78.0 (85)	22 (24)	
Clinic (16)	75.0 (12)	25.0 (4)	
OR (60)	88.3 (53)	11.7 (7)	
MRT - Rapid response (24)	79.2 (19)	20.8 (5)	
Mechanical Ventilation (MV), % (n)			
% (n)	49.2 (388)	94.4 (117)	
HFOV (High frequency MV), % (n)	13.1 (51)	48.7 (75)	

42. Fluid Status and Clinical Outcomes in Critically Ill Children with Sepsis: A Retrospective Analysis

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Purpose: Maintenance of fluid balance is an important component of care for children in the pediatric intensive care unit (PICU). Previous studies show that degree of fluid balance in PICU patients affects multiple organ systems. However, limited supporting data has led to variability in fluid management strategies and the epidemiology of current fluid management practices in the PICU is not well described. The aim of this study is to describe the epidemiology of acute resuscitative and late fluid administration, and assess associations between degree of daily and cumulative fluid accumulation and outcomes in septic PICU pts. **Methods**: Retrospective review of patients with sepsis admitted to Texas Children's Hospital (TCH) PICU during 2009 (n=38). Demographics, anthropometric measures, vital signs, lab data and fluid balance at specified time points were obtained by integration of PICU database and medical records. Predictor variables were acute resuscitative fluids (defined as 60cc/kg in first 1 hr of admission) and late fluid administration (defined by percentage of fluid overload (FO) validated from the Prospective Pediatric CRRT registry). Pulmonary outcomes were FiO2, mean airway pressure, and PEEP. Cardiac outcomes were SBP, heart rate, shock index and administration of pressors. Serum creatinine changes defined kidney function using pRIFLE and AKI criteria. Hospital LOS and survival data were obtained. Data were controlled for disease severity by PRISM-III. **Results**: Mean volume of fluid received during the first 24 hrs of admission was significantly greater in non-survivors than survivors (257.6 vs 160.4 cc/kg; p=0.004). Non-survivors achieved a significantly higher degree of %FO during the first 24 hrs of admission than survivors (17.5% vs 5.6%; p<0.001). Overall median (25-75%ile) PRISM-III was 1.3 (0.4-5.0) and shock index was 1.6 (1.1-2.2). In sub-group analysis of patients in the upper 50th%ile of PRISM-III, the mean %FO remained significantly higher in non-survivors than survivors (p=0.008). **Conclusions**: Mean fluid volume received and %FO at 24 hrs after admission were associated with mortality in septic PICU patients. Results of this study could inform treatment guidelines for optimal fluid administration and management of fluid overload in septic children.

43. Mortality Due To Acute Kidney Injury Associated With Malaria

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Background: The objective of this study was to determine the prevalence, clinical features, risk factors for the mortality in patients of acute kidney injury (AKI) associated with malaria.. **Methods:** A retrospective study carried out at our Institute. All patients admitted to the Institute during the six year period between January 2003 and October 2009 were reviewed. Those who suffered from malarial AKI were selected for further study. **Results:** 664 AKI patients were admitted. Of them 70 patients (10.54%) had AKI due to malaria. All malarial AKI patients were infected with Plasmodium falciparum. The number of deaths were 8 (out of 70, 11.42%). Table 1: Mortality indicators **Conclusion:** The mortality due to complicated malaria can be reduced with early referral to a centre equipped with facilities to tackle AKI and pulmonary oedema. Conservative management was possible with non-oliguric patients but oliguric patients deserve timely initiation of dialysis. Pulmonary oedema and cerebral malaria were the two major determinants of outcome of death in malarial AKI patients.

Indicator	Surviving group (n= 62)	Indicator Surviving group (n= 62) Expired group (n= 8)
Age (years)	37.22 + 12.67	33.25 + 9.42
Haemoglobin (g/dL)	8.63 + 2.72	7.2 + 0.72
Platelet count (/mm3)	96428.57 + 70965.16	45000 + 21213.32
Serum creatinine (mg/dL)	4.54 + 2.42	5.02 + 1.06
Serum bilirubin (mg/dL)	16.82 + 13.64	18.1 + 12.43
Oliguria	38 (61.29%)	8 (100%)*
Glasgow coma scale <8	24 (33.70%)	8 (100%)*
Jaundice	52 (83.87%)	8 (100%)
Hyponatraemia	24 (38.7)	8 (100%)*
*p value: significant		

44. Clinical Analysis of Acute Kidney Injury in 1113 Cases After Cardiac Valve Replacement Surgery

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Purpose: To investigate the incidence and risk factors of acute kidney injury(AKI) after different types of cardiac valve replacement surgery. **Method:** A single cohort of 1113 patients who received cardiac valve replacement surgery from April 2009 to March 2010 in Zhongshan hospital, Fudan University were prospectively analyzed. Multivariate Logistic regression analysis was used to evaluate possible risk factors associated with post-operative AKI. AKI was defined as a relative 50% increase or an absolute mol/L in serum creatinine within 48 hours and (or) urineμincrement of 26.4 volume < 0.5mL _ kg-1 _ h-1 up to 6h. **Results:** Of the 1113 patients, the incidence of AKI was 33.24%. In-hospital mortality of AKI patients was 6.49%, which was 5.373 times higher than that of non-AKI patients ($P < 0.01$). The incidence of AKI of patients who simultaneously received cardiac valve replacement and coronary artery bypass grafting was 75.00%, which was significantly higher than other types of valve replacement surgery ($P < 0.01$). Unconditional multivariate Logistic regression analysis revealed that male, old age, long cardiopulmonary bypass (CPB) time ($\geq$ 120min) and combined with coronary artery bypass grafting surgery were the independent predictors of AKI episodes, the corresponding OR values were 1.455, 2.110, 1.768 and 2.994, respectively. **Conclusions:** AKI is a common and serious complication after cardiac valve replacement surgery. Patients who received combined cardiac surgery as valve replacement and coronary artery bypass grafting have higher incidence of AKI. Old age, male sex, long CPB time ($\geq$ 120min) and combined with coronary artery bypass grafting surgery were the independent risk factors of post-operative AKI for patients underwent cardiac valve replacement surgery.

45. Incidence, Predictors, and Outcomes of Withdrawal of Life-sustaining Therapy in ICU Patients Receiving CRRT

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Purpose: The aim of this study was to determine the incidence, predictors, and outcomes of

withdrawal of life-sustaining therapy in ICU patients receiving CRRT. **Methods:** Case-control study of 200 consecutive ICU patients that received CRRT for acute kidney injury. Demographic and clinical characteristics were abstracted retrospectively. Baseline comorbidity was determined using the Charlson comorbidity index (CCI). Severity of illness at the time of CRRT initiation was determined by the Sequential Organ Failure Assessment (SOFA) score. Patients were stratified into two groups based on the decision to withdraw or continue life-sustaining therapy during the course of ICU admission. Demographic and clinical characteristics at the time of CRRT initiation were compared between the two groups to determine predictors of withdrawal of care. Data are presented as mean (SD). **Results:** Life-sustaining ICU care was withdrawn in 31% (62 of 200) of patients. Baseline characteristics including age, gender, race, comorbidity (CCI), ICU type and hospital days prior to CRRT did not significantly differ between groups. Severity of illness (SOFA) at the time of CRRT initiation was significantly higher in the withdrawal of therapy group [14.1 (0.4)] compared to the full therapy group [12.4 (0.3), p=0.002]. Liver failure was significantly associated with withdrawal of care compared to full care (OR 2.4, 95% CI 1.2 to 4.6). Hospital mortality was 97% (60 of 62) in the withdrawal of therapy group and 36% (49 of 138) in the full therapy group (p<0.0001). Interestingly, the duration of CRRT and hospital length of stay did not differ between those patients who had therapy withdrawn and those who died despite full care. **Conclusion:** Life-sustaining therapy was withdrawn in nearly one-third of ICU patients undergoing CRRT for acute kidney injury. Liver failure and higher ICU severity of illness at CRRT initiation were significant predictors of withdrawal of care.

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46. Etiology and Clinical Outcome of Acute Kidney Injury Admitting to Medicine Service: Single Tertiary Care Center Experience

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Background: Acute kidney injury (AKI) is a serious complication that commonly found in clinical practice. There is limited epidemiological report of AKI in Thailand. Objective: To determine the epidemiology, severity, the need for renal replacement therapy (RRT) and clinical outcome of AKI patients admitted to medicine service. **Method:** All medical records of the patients who were hospitalized to medicine department, including ICU admission, Siriraj hospital between January 1, 2010 and June 30, 2010 were reviewed. The retrieved data included demographic data, etiology and severity of AKI, mode of RRT, serum creatinine at baseline, peak, and prior to discharge. **Results:** There were 7,533 patients admitted during this period. AKI was detected in 914 patients (12.1 percent). Severity of AKI stratified by AKIN (Acute Kidney Injury Network) classification was stage 1 in 28.7 percent, stage 2 in 23.4 percent and stage 3 in 47.9 percent. Etiology of AKI was pre-renal cause in 514 patients (56.2 percent), intrinsic-renal cause in 383 patients (41.9 percent) and post-renal cause in 12 patients (1.3 percent). Sepsis was the most common cause of AKI (41.0 percent), followed by hypovolemia (20.9 percent) and cardiorenal syndrome (7.9 percent). Eighty eight patients (9.6 percent) with AKI required RRT that the mode included intermittent hemodialysis (46.6 percent), continuous RRT (30.7 percent), sustained low efficiency dialysis (19.3 percent) and peritoneal dialysis (3.4 percent). At discharge or death, 75.8% of these patients remained on dialysis. Mortality rate was higher in AKI patients with higher AKIN staging ($p < 0.001$). Sixty seven percent of the patient who required RRT died, compare with who did not required RRT (40 percent), $p < 0.001$. Risk factors for hospital mortality consisted of age more than 50 years, severity of AKI, underlying malignancy, sepsis, liver failure and need for RRT. **Conclusion:** Sepsis is still common cause of AKI in the patients admitted to medicine service and contributes to high mortality. Severity of AKI according to AKIN classification is associated with mortality rate.

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47. Effect of Early Versus Late Initiation of CRRT on the Duration of Need for CRRT in Critically Ill Children

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Purpose of Study: Delayed renal recovery is considered as one of the complications of renal

replacement therapy in critically ill patients. The purpose of this study was to evaluate the effect of timing of initiation of CRRT on renal recovery in critically ill children admitted to the ICU. **Methods:** We performed a retrospective review of all non-ECMO patients who underwent CRRT in our ICU between Jan 1, 2000 and Jul 31, 2009. Patients dying within 48 hours of discontinuation of CRRT were excluded from the study. We used Td (duration of need for CRRT) as a surrogate marker for time to renal recovery and compared early initiators (started on CRRT within 3 days of admission to ICU) with late initiators (beyond 3 days after admission to ICU) with respect to Td. We also examined predictor variables with respect to patients with Td < 5 days versus Td > 5 days. **Results:** A total of 251 patients underwent non-ECMO CRRT in our ICU during the specified time period. 151 of these met the criteria for inclusion, with a median Td of 4.5 days. Td was significantly lower in early compared to late initiators (Median 3.8 Vs. 6.1 days, p-value 0.0372). The sub-group initiated on CRRT for acute renal failure and/or fluid overload showed a similar trend (Median 5.4 Vs. 7.1 days, p-value 0.0916). Time to event (discontinuation of CRRT) plots showed a significant difference (Logrank p-value 0.03) as well, with early initiators coming off of CRRT sooner. Patients with Td > 5 days had higher severity of illness scores at admission and were more likely to have fluid overload > 15% and worsening pRIFLE scores at CRRT initiation. Age, weight, underlying diagnoses and admission pRIFLE were similar in both Td groups. **Conclusion:** In our cohort of patients, we did not see evidence for prolongation of need for CRRT with early initiation. On the contrary, we observed a statistically significant decrease in duration of CRRT with early initiation.

48. A Retrospective Study of Percent Fluid Overload (%FO) in NICU CRRT Patients

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Introduction: Percent FO in CRRT is now being one of the important factor effects mortality in pediatric patients as recent studies demonstrate, but these are almost about “P”ICU cases. There have been very few reports of CRRT in “N”ICU which reference to percent FO. We report relationship between percent FO and AKI stage of NICU CRRT patients in our hospital. **Methods:** 13 cases were performed CRRT in our NICU from April 2002 to May 2010. A retrospective chart review was done of these patients. Patients background were ; Birth weight : 1940g(646-3550), Gestational age : 31weeks (25-40),Body weight when CRRT introduced: 1988.5g(678-3520), Age : 4.5 days(1-187), Mean serum creatinine (sCr) at the beginning of CRRT : 1.25±0.52mg/dl. Their underlying diagnosis (overlapping) was persistent pulmonary hypertension of the newborn (8 cases), Sepsis(6 cases), severe asphyxia (3 cases), meconium aspiration syndrome (2 cases), fetal hydrops (2 cases), inborn error of metabolism (1 case), Liver failure (1 case), CINCA(chronic infantile neurological,cutaneous,and articular) syndrome(NOMID; neonatal onset multisysteminc inflammatory disease) (1 case), gastrointestinal breeding (1 case). CRRT modality was CHF (3 cases) and CHDF (13 cases). Combination therapy was PMX-DHP (6 cases), plasma exchange (2 cases) and ECMO (1 case). **Results:** Median percent FO was 22.3 percent(1.9-55.2) and mortality was 84.6 percent. AKI stage evaluated RIFLE by sCr were 5 normal(N), 3 risk(R), 3 injury(I) and 2 failure(F) cases. **Conclusions:** There is no significance between percent FO, RIFLE AKI stage and mortality in this study. Much more investigations about CRRT including percent FO and AKI criteria of babies in “N”ICU will be needed.

49. Acute Kidney Injury (AKI) incidence and severity in the Intensive Care Unit: impact of AKI on admission in 3 classification systems

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Background: AKI is associated with significantly increased morbidity and mortality. Until recently, there was a lack of a uniform definition for AKI. Standardization has led to the acceptance of the RIFLE (Risk, Injury, Failure, Loss, ESRD) criteria and subsequent Acute Kidney Injury Network (AKIN) system, as well as the recent proposal of the Kidney Disease: Improving Global Outcomes (KDIGO)

classification to unify the RIFLE and AKIN systems. The epidemiology and prognostic value of the new KDIGO system are not known. **Purpose:** The aim of this prospective study is to compare the incidence, severity, and outcomes of AKI defined by the three different classifications in a broad population of critically ill patients. **Methods:** We analysed the prospectively collected data of 115 consecutive adults admitted the ICU of a large urban tertiary referral hospital. We assessed the incidence, stages, and outcomes of AKI defined by the 3 systems. Changes of serum creatinine (not urine output) were assessed for all three classifications during the first 7 days of ICU admission, excluding ESRD patients, those initiated on acute RRT prior to or immediately on ICU admission, and those discharged from ICU in less than 24 hours. **Results:** Incidence and outcome of AKI varied depending on the criteria (see **Table 1**). The RIFLE and KDIGO classifications led to similar total incidences of AKI (83.4% vs. 84.3%), associated with increased hospital mortality averaging 48.9%. The AKIN classification had a much lower incidence of AKI (45.2%) than the RIFLE and KDIGO systems. The differing performance and apparent underdiagnosis of AKI by AKIN is explained by the high prevalence of AKI on admission to our ICU (>80% of total AKI cases). This phenomenon suggests that staging of AKI based on the detection of dynamic increases in serum creatinine within 48 h intervals misses patients who are already at their peak serum creatinine on admission to ICU (and often improving with resuscitation). The number of AKI cases present on admission to ICU out of the total number of AKI cases for each of the classifications are as follows: RIFLE, 78/96 (81.5%), KDIGO, 86/97 (88.6%), and AKIN 47/52 (90.3%). The overall incidence of renal replacement therapy was 23%. The number and percent of RRT cases among the stage III groups for each classification are as follows: RIFLE, 27/45 (60%), KDIGO 27/45 (60%) and AKIN 27/31 (87.1%). The RIFLE and KDIGO systems identify similar patient populations, with some additional cases added to the RIFLE system by the KDIGO modification. Overall, the AKIN classification identified fewer cases of AKI, but AKIN-defined cases were of greater severity, with a higher mortality and proportion of stage III patients (87.1%) requiring RRT. **Conclusions:** The three most recent definitions of AKI are all notable for a correlation between severity of AKI and outcomes, but have limitations in case ascertainment, depending on the availability of appropriate reference creatinine data. In particular, we found that the AKIN classification failed to identify many patients with AKI on ICU admission, compared to either the RIFLE of KDIGO systems.

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50. Clinical Characteristics and Outcomes of Patients with Acute Kidney Injury in a Tertiary Care Center in Sri Lanka

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Background and Aims: Acute Kidney Injury is an important cause of morbidity and mortality among hospitalized patients. We studied the clinical characteristics and outcomes of patients referred for specialist nephrology care at the National Hospital of Sri Lanka which is the largest tertiary care centre in the country. A retrospective observational study was conducted among patients fulfilling Acute Kidney Injury Network Criteria over a period of four months from July 2010 to October 2010. A total of 68 patients were enrolled. Admissions were mainly direct (67.6%) while there were 22 (32.4%) transfers from local hospitals. The mean age of the population was 49 (standard deviation = 17.6) with a mean body mass index of 20.26 (standard deviation = 2.29). Half of the patients had preceding co morbidities with 35% of them having pre existing diabetes mellitus. Commonest identified etiology among the study population was sepsis (41.2%) with leptospirosis (29.4%) as the second commonest. Among other identified etiologies were snake bites (8.8%), crush injuries (5.9 %) and rapidly progressive glomerulonephritis (5.9 %). Among septic causes urine sepsis was the commonest with a frequency of 20.6 % , among others were wound infections (8.8 %) and chest infections (5.9%). 58 patients required renal replacement therapy with 46 receiving hemo dialysis and 12 receiving acute peritoneal dialysis. 20 patients (29.4%) made a complete recovery while 28 (41.2%) made only a partial recovery. Of the patients who made a complete recovery 70 % were below the age of 55 compared to those over 55 (30%) which however was not statistically significant ($p= 0.13$). The absence of co morbidities predicted a worse outcome with only 5.9 % achieving complete remission ($p < 0.01$). None

of the patients with pre morbid diabetes mellitus made a complete recovery ($p < 0.01$). **Conclusions:** Sepsis remains the commonest cause of acute kidney injury with older age and the presence co morbidities predicting a poorer outcome.

51. Intensive Care Unit (ICU) Patient And Renal Survival By Modality Of Renal Replacement Therapy (RRT): An Analysis Adjusting For Time-Varying Modality Exposure And Illness-Severity

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Introduction: Modalities of RRT for ICU patients include prolonged intermittent RRT (PIRRT), continuous RRT (CRRT), and intermittent hemodialysis (iHD). Observational studies of outcome by modality often only adjust for baseline illness-severity and initial modality choice, and do not account for changes in modality exposure or illness-severity over time. Consequently, CRRT is often associated with worse outcomes than other modalities. **Purpose:** To estimate of risk of patient death and renal death (i.e. death or dialysis) by modality for all acute kidney injury (non-ESRD) patients were treated at our ICU with RRT between 1.1.02 and 31.12.08. **Methods:** The Marginal Structural Modeling (MSM) technique of Robins was used to account for time-varying modality exposure and also time-varying illness severity that may affect previous modality exposure while also affecting subsequent modality choice (Stata/MP 11.0). Data for analysis was in the form of a cross-sectional time-series. Variables for analysis included patient demographics, year of admission, lead-time between ICU admission and RRT inception, APACHE4 and SOFA at ICU admission, and daily SOFA scores while in the ICU. Primary exposure was RRT modality. Primary outcomes were assessed at hospital discharge. A one-day lag for attribution of outcomes to modality was used. **Results:** 142 patients were studied, who received 841 patient-days of PIRRT, 208 of CRRT, and 81of iHD. Mean+/- SD age 58.4+/- 15.4 yrs, APACHE4 risk-of death 70.6+/- 27.6%, lead-time 1.7+/- 3.1d. Patient death and renal death at hospital discharge were 39% and 49%, respectively. PIRRT and iHD were combined to improve model stability. The unadjusted and fully adjusted RR (95% CI) of PIRRT/iHD relative to CRRT for death were 0.8(0.3-2.5) and 1.3 (0.5 - 3.6), and for renal death were 1.2 (0.4-3.4) and 1.4 (0.5-3.9). **Conclusion:** Adjusting for time-varying modality exposure and illness-severity yields plausible estimates of mortality risk, and may be a preferred technique to point treatment (e.g. Cox) models.

52. Citrate Toxicity in Continuous Veno-venous Hemodiafiltration (CVVH) With Citrate Anticoagulation Predicts Mortality

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Background: Acute kidney injury (AKI) is associated with significant mortality in critically ill patients. Citrate used for anticoagulation in CVVH can accumulate in patients with severe liver disease. We have previously shown an association between liver dysfunction and citrate toxicity. We hypothesized that citrate toxicity would be associated with significantly greater mortality in patients on CVVH. **Methods:** This is a retrospective study of 372 patients receiving CVVH at URMC between 1/1/2006 and 7/24/2009. Treatment was initiated with a dilute (0.5% citrate) citrate-contain replacement solution prefilter at 1L/hr and 0 calcium dialysate at 1 L/hr. Calcium gluconate was infused intravenously. Citrate toxicity was defined as greater or equal to one, or greater or equal to two occurrences of a total to ionized calcium ratio (T/I) of > 2.5. Demographic data, lab values and presence or absence of citrate toxicity were compared between patients who died and those who survived. **Results:** 243 patients (65%) of the cohort died. 116 of the 372 (31%) were toxic by 1 T/I ratio and 59 (16%) by 2 T/I ratios. Mortality was 79% in patients with citrate toxicity by 1 T/I ratio and 81% in those with 2 T/I ratios. On bivariate analysis using mortality as the outcome, factors associated with mortality included alkaline phosphatase, international normalized ratio (INR), phosphorus (phos), partial thromboplastin time, total bilirubin and citrate toxicity by either 1 or 2 T/I ratios. On multivariate backward elimination logistic regression analysis, factors that remained significantly associated with mortality included citrate toxicity by 1 or 2 T/I ratios (OR 2.93), Age (OR 1.020) , INR (OR 2.17) and lower phos (OR 0.875) **Conclusions:** Citrate toxicity is

independently associated with high risk for mortality in patients undergoing CVVH with citrate anticoagulation. An elevated INR, suggestive of reduced hepatic synthetic function, is also predictive of mortality. It is possible that the liver dysfunction noted in patients with citrate toxicity, and their high prevalence of multi-organ system failure might contribute to their elevated mortality risk.

53. Magnesium, Intradialytic Hypotension and Muscle Cramps in Chronic Hemodialysis Patients

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Background and Aims: Few studies have reported a role of magnesium (Mg) on intradialytic hypotension (IDH) in chronic hemodialysis (HD) patients. However, an interaction between Mg, IDH and muscle cramps has not been studied. The present study evaluated the effect of different concentrations of dialysate Mg on IDH and muscle cramps. Fifty five ESRD patients with a mean age of 60 years (range 25-87), 31 males and 24 females on HD were studied. Patients were initially dialyzed with dialysate Mg of 0.75mEq/L then with dialysate Mg of 1.00mEq/L. The patients received HD with each dialysate for at least 3 months. Blood pressure (BP) measurements were obtained from three consecutive dialysis sessions with each dialysate Mg concentration. Mean values of the BP measurements were taken for analysis. To identify patients with IDH, we utilized KDOQI guideline which defines IDH as a decrease in systolic blood pressure (SBP) by ≥20 mmHg or a decrease in mean arterial blood pressure (MAP) by 10 mmHg. Monthly pre-HD laboratory data, before and after the change in dialysate Mg were used for analysis. A single nephrology fellow conducted two in-person questionnaires on all 55 patients. The severity of cramps was evaluated on a 0-10 scale, with 10 rated as maximal severity. Data are summarized in the table below (mean+SD): No significant correlation was observed between serum Mg level and the lowest SBP or lowest MAP during HD treatment. In patients with serum Mg >2.0 mg/dL, the number of patients with IDH decreased significantly with higher dialysate Mg (x2 4.24, p=0.04). No statistically significant difference in IDH was found in relation to gender, race, diabetes and ESRD etiology. In conclusion, increasing dialysate Mg to 1.00mEq/L may decrease IDH and muscle cramps in HD patients.

Variables	Mg 0.75 mEq/L	Mg 1.00 mEq/L	P value
Serum Mg mg/dL	1.89±0.27	2.1±0.3	<0.0001
Serum Ca mg/dL	8.93±0.89	9.30±1.07	<0.005
KT/V	1.81±0.71	1.70±0.31	NS
Pre dialysis SBP mmHg	139±19	135±17	NS
Lowest SBP during HD mmHg	115±21	115±17	NS
Lowest MAP during HD mmHg	81±16	80±12	NS
Dialysate temperature Centigrade	36.74±0.37	36.72±0.39	NS
Intradialytic UF Kg	2.99±0.91	2.92±0.97	NS
Cramp severity	5.2±3.6	3.9±4	<0.01

54. Patient Perceptions of Risk Factors for Chronic Kidney Disease and Methods of Delaying Progression of the Disease in a Tertiary Care Setting in Sri Lanka

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Background: Sri Lanka has seen a steady rise in the incidence of Chronic Kidney Disease (CKD) in the last two decades. Limited availability of health care resources in the country makes early recognition and delaying progression of the disease imperative. Patient education plays an important role in accomplishing success in this conservative care approach. Disease-educated patients are more likely to follow proper treatment and cope more successfully with their diagnosis, and participate in health care decisions that affect their outcomes. **Method:** A descriptive cross sectional study design with an interviewer administered questionnaire was used to assess patients' perceptions on risk factors for CKD and methods of delaying progression.

Participants were CKD stage 3 and 4 patients followed up at the University Medical Unit, National Hospital of Sri Lanka which is a major tertiary care referral centre in Sri Lanka. **Results:** The study population (n=162) was mainly male (63%) with a mean age of 49 years (SD – 15.39), while most had received a secondary education (40.7%) with a low income level (43.8%). Most participants identified diabetes mellitus (75%) as a risk factor for the development of CKD while hypertension (45.7%) was selected less frequently. Control of proteinuria (88%), blood pressure (67.9%), glycemia (87.7%), lipids (66.7%) and quitting smoking (76%) were associated by participants as possible methods of reducing progression. Use of angiotensin converting enzyme inhibitors (ACE I) and angiotensin receptor blockers (ARB) for slowing progression (28%) was less known. Almost all (96.3%) of the study population were aware they had CKD though 86.4% did not know their last serum creatinine value. Out of 56.8 % of diabetics with CKD, 72.8% were unaware of their last sugar value. Self reported patient practices also deferred from their knowledge on methods of slowing progression of the disease. Only 27.2 percent of patients checked their blood pressure regularly though the majority of them were aware of the importance of controlling blood pressure to reduce progression. Most admitted to adhering to a well controlled diet (61.7%) and being compliant with drugs(97.5%) as advised by the medical practitioner. Majority of patients did not take regular exercise (77.8%) though they were aware of it being beneficial. **Conclusions:** Patient awareness on risk factors for CKD and methods that delay progression was good though their practices deferred from what was perceived to be beneficial. Patients need to be educated on the importance of the use of ACE I/ARB which may increase their compliance. Health education should also aim at reiterating and encouraging the practice of accepted methods of reducing progression of CKD and not merely imparting knowledge.

55. LONG-TERM OUTCOME OF ACUTE TUBULAR NECROSIS

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Purpose: Recovery of renal function after acute tubular necrosis (ATN) is an important clinical determinant of patient morbidity and mortality. This study aimed to determinate long-term outcome and risk factors for lack of renal recovery **Method:** We studied 33 consecutive ATN patients, discharged alive from our hospital between October 75 and December 2005 and followed-up until December 2008. **Results**: There were 10 males and 23 females with mean ages 40.21 ± 14.1 years.The main etiologies of ATN were: Surgical in one case (3%); Nephrotoxic in 10 cases (30.3%); Septic in 4 cases (12.1%), and Medical in 18 case (54.5%). Classification with RIFLE system found: two cases at Risk (6.1%), three cases at Injury (9.1%), 26 cases at Failure (78.8%), 2 cases at Loss (6.1%) and no case at End-stage.
At hospitalization: 20 patients hade oliguria (60.6%), needed dialysis in 22 cases (66.7%) and 7 patients needed hospitalization in intensive care unit. The mean duration of hospitalization stay was 25 days (5 – 60 days). At hospitalization discharge functional situation was: 8 normal renal functions; 5 mild; 8 moderate; 8severe renal insufficiency and 4 end-stage renal diseases. We noted total recovery of renal function in 8 cases (24.2%), partial recovery in 22 cases (66.7%) and no recovery in 3 cases (9.1%). The median time since the ATN episode was 3.24 years (1 -10). At the end of the study period: mean serum creatinine was 201.3 ± 13 µmol/l, serum creatinine < 120 µmol/l in 23 cases (69.7%); 120 < serum creatinine < 300 µmol/l and serum creatinine < 300 µmol/l in 5 cases (15.1%). Poor prognostic factors included hypertension, previous chronic renal failure, 2 and 3 Rifle score, and when renal function at discharge superior them 120µmol/l **Conclusion:** Long-term outcome after ATN were favourable. If critically ill patients with normal renal function prior to the renal insults survive the precipitating cause of ATN, the overwhelming majority will recover sufficient renal function.

56. EARLY NEPHROLOGY REFERRAL INFLUENCES ON MORTALITY OF DIALYSIS PATIENTSS IN DEVELOPING COUNTRY

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Purpose: To evaluates the influence of early referral to nephrology of the patients with

chronic renal failure in the mortality of the patients who start dialysis. **Methods:** There were included 186 patients who started dialysis from January 2005 to December 2005. Patients who started dialysis after acute renal failure were excluded. Clinical and analytical data were determined for each patient at the start of dialysis and during the follow-up. Early (ER) and late referral (LR) were defined by the time of first nephrology encounter greater than or less than 3 months respectively, before dialysis initiation. Mortality analysis and global and annual during the first five years of follow-up survival analysis were carried out. **Results:** Of the 186 patients, 95 (51.1%) were referred late and 91 (48.9%) were early referred. There were no differences in gender, cause of ESRD and mean follow-up between ER and LR patients. The overall mortality rate for the 186 patients was 23.7% at the end of the study. The survival rate for ER versus LR group at 1 year, 2 years, 3 years, 4 years, and 5 years were respectively 88.1% vs 84.1%, 82.1% vs 79.6% and 73.7% vs 66.9%. In multivariate analysis by cox model regression, only the age > 50 years ($p = 0.0015$), diabetes ($p = 0.01$), hypertension ($p = 0.03$), vascular cerebral accident ($p = 0.025$), arterite of inferior member ($p = 0.003$), Charlson score ($p < 0.001$) and serum creatinine level > 950 µmol/l at the start of dialysis ($p = 0.005$) were significant predictors factors of mortality. Nevertheless, in successive models fitting after 5 years of follow-up the variable ER not influenced in any way the mortality rate 5 years later. **Conclusions:** It is concluded that early referral to the nephrologists in developing country don't influenced short and long-term mortality. Pre-ESRD care of patients treated by nephrologists was also less than ideal, can explicated by lack of the means available. Meanwhile, pre-ESRD educational efforts need to target patients, generalists, and nephrologists.

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57. Acute Kidney Injury Associated with High Mortality Compared with Chronic Hemodialysis Patients in the Medical Intensive Care Unit

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Purpose: Acute kidney injury (AKI) complicates about 5% of hospital admissions and 30% of admissions to intensive care units (ICU). Despite great advances in renal replacement technique (RRT), mortality from AKI remains over 50%. This retrospective study aimed to investigate the epidemiology and mortality of patients complicated with AKI compared with chronic hemodialysis who were admitted to the medical ICU. **Methods:** Using data from Bundang Medical center, we identified patients who were treated with hemodialysis in the ICU. ESRD group which contain patients who have been treated by hemodialysis more than 3 months before admission and AKI group included AKI patients requiring hemodialysis without a previous hemodialysis experience prior to admission. The patients who have been transferred out before clinical resolution were excluded. SOFA (Sequential Organ Failure Assessment) score at admission was calculated in all identified patients. **Results:** Total number of identified patients was 91 (ESRD group 35, AKI group 56). 71.4 % were males and the mean age was 60.8±15.5 years. The main diagnoses at admission were sepsis (49.5 %), cerebrovascular disease (20.9%), cardiac disease (13.2%), and liver disease (3.3%). In AKI group, continuous renal replacement therapy (CRRT) was more frequently used (62.5% vs. 14.3%, $p<0.05$). Compared with AKI group, those with ESRD had significantly more diabetes (65.7% vs 39.3%), hypertension (91.4% vs. 46.4%), and cardiac disease (22.9% vs. 7.1%) ($p<0.05$). Mean age, hospital day and total SOFA score were not significantly different between the groups. However, liver (0.70±1.14 vs. 0.11±0.53) and coagulation system score (1.16±1.32 vs. 0.57±0.98) were significantly higher in AKI group ($p<0.05$). In-hospital mortality in AKI group was 58.9%, and was significantly higher than ESRD group (25.7%) ($p<0.05$). In multivariate analysis, age, liver and coagulation system score of SOFA were significant affecting factors to mortality ($p<0.05$). In Kaplan-Meier method, patient survival in ESRD was significantly higher than the AKI ($p<0.05$). **Conclusion:** The mortality rate in ESRD group was significantly lower than AKI group although ESRD group included higher rate of diabetes, hypertension and cardiac disease. The higher mortality rate in AKI group is likely associated with poor functions of liver and coagulation system at admission.

Research in AKI

58. Red Blood Cell Distribution Width (RDW) is an Independent Predictor of All-cause Mortality in Acute Kidney Injury Patients on Continuous Renal Replacement Therapy

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Purpose: A potential independent association was recently demonstrated between high red blood cell distribution width (RDW) and the risk of all-cause mortality in patients with cardiovascular disease, although the underlying mechanism remains unclear. However, there have been no reports on the relationship between RDW and mortality in acute kidney injury (AKI) patients treated with continuous renal replacement therapy (CRRT). In this study, we assessed whether RDW is associated with mortality in AKI patients on CRRT treatment in the intensive care unit (ICU). **Methods:** We conducted a retrospective cohort study in 632 patients with AKI who were treated with CRRT at the ICU of Severance Hospital, Yonsei University Health System between August 2007 and September 2009. We collected baseline demographic data, Acute Physiology And Chronic Helath Evaluation version II(APACHE II) scores, biochemical parameters, echocardiographic data, and patient outcomes. Following CRRT treatment, 28-day and 90-day all-cause mortality were evaluated. **Results:** Excluding 162 patients who had insufficient data for analysis, a total of 470 patients were included. RDW level was significantly correlated with white blood cell (WBC) count, hemoglobin (Hb), and total cholesterol. Patients with high RDW levels exhibited significantly higher 28-day and 90-day mortality rates than patients with low RDW levels ($p<0.05$). High RDW, high C-reactive protein (CRP), low mean arterial pressure (MAP), low albumin, low total cholesterol, and high APACHE II scores at the initiation of CRRT treatment were risk factors for 28-day and 90-day all-cause mortality in univariate analysis. In multivariate Cox proportional hazard analyses, RDW at CRRT initiation remained as an independent predictor for 28-day and 90-day all-cause mortality (per 1% increase, adjusted HR 1.071, $P<0.01$, and HR 1.079, $p<0.01$) after adjusting for demographic data, APACHE II score, biochemical parameters including CRP, and echocardiographic parameters. **Conclusions:** Our study demonstrates that increased RDW is independently associated with all-cause mortality in AKI patients on CRRT treatment in the ICU.

59. Increased Accumulation of Iron in Lysosomes of the Proximal Tubular Cells of Hp 2-2 Diabetic Mice

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Purpose: One-third of all patients with diabetes (DM) will develop end stage renal disease within 20 years DM onset. Its well know that diabetic patients with the Haptoglobin 1-1 (Hp 1-1) are more protected than haptoglobin 2-1 (Hp 2-1) and Haptoglobin 2-2 (Hp 2-2) in developing diabetic nephropathy. Iron is a metal oxidant capable of generating reactive oxygen species and has been postulated to contribute to diabetic nephropathy. Iron accumulates within proximal tubular (PCT) lysosomes in several models of renal disease and may play role in the progression of kidney disease. Vitamin E may play a protective role in the progression of diabetic nephropathy. In this study, electron microscopy and energy disoersive X-ray spectrometry was used to confirm the presence of iron in lysosomes. **Methods:** Samples of kidney tissue from the control and experimental diabetic mice (Hp 1-1 DM, Hp 2-1, Hp 2-2) with and without treatment with vitamin E, were routinely prepared for transmission electron microscopy (TEM). Areas showing positive Perls' stain were considered as containing more iron compounds and were ultra-thin cut and viewed through a JEOL 100SX electron microscope.. At least 4 glomeruli per sample plus the adjacent tubuli were examined. Clusters of iron-containing lysosomes (siderosomes) were seen mostly in the proximal tubules. The siderosomes were identified by the presence of typical electron-dense ferritin and hemosiderin within single-membrane bound bodies. To confirm the presence of iron in these organelles, Energy-dispersive x-ray spectroscopy (EDS-EDAX) was used. **Results:** Three groups of mice were compared: Hp 1-1 and Hp 2-1, Hp 2-2. Light microscopy examinations of glomeruli and PCT, disclosed significant increased in glomerular area in in Hp2-2 DM vs 1-1 DM (4852.9±308 VS 3176±99 um2 ,$p<0.05$)

respectively , which decreased significantly by VitamineE in Hp2-2DM (4852.9±308 VS 4024.8±163 um2,p<0.05). Oxidative stress markers was measured by 4HNE immunostaining in glomeruli and PCT and was significantly increase in Hp 2-2 DM vs Hp1-1 DM (573001±55647 vs 408115.77±31259,p<0.05) which was decreased significantly by Vit. E in Hp2-2 DM(573001±55647 vs 30588±74231,p<0.05). There was impressive increase in ferritin in Lysosome of PCT cells of Hp2-2DM vs Hp1-1DM(0.194±0.01vs0.116=005%area) and decreased significantly by vit.E in Hp2-2DM(0.194 ±0.01 vs 0.13±0.007,p<0.05). **Conclusion:** 1:Increased iron accumulation within lysosome of proximal tubular cells of diabetic Hp 2-2 mice VS Hp 1-1 diabetic mice.2: Increased iron accumulated as ferritin in Hp 2-2 DM, is associated with increased oxidative stress and glomerular and tubular damage.

60. Acute Kidney Injury is Common Following Many But Not All Major Non-Cardiac Surgeries

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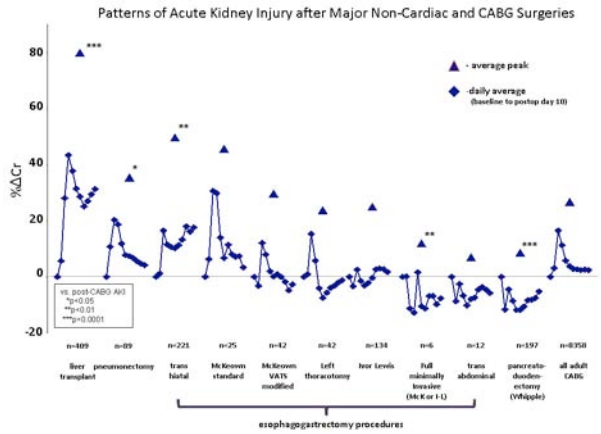
Backgound: Acute kidney injury following cardiac surgery (CSA-AKI), is a common serious complication. While a perception exists that major non-cardiac procedures are rarely affected, we and others have reported high AKI rates following liver transplant and pneumonectomy relative to cardiac procedures (eg. aortocoronary bypass (CABG)). However, AKI rates after other major non-cardiovascular thoracic and abdominal surgical procedures have not been described. Therefore, we tested the hypothesis that AKI complicates esophagogastrectomy and other major gastrointestinal surgeries. **Methods**: With IRB approval, demographic, renal, and procedural data were gathered for consecutive liver transplant, pneumonectomy, esophagogastrectomy, and pancreatoduodenectomy (Whipple) surgery procedures at a single institution from 1996 to 2010. Selected procedures included routine postoperative daily serum creatinine determinations and cohorts sufficient to assess AKI. Esophagogastrectomy procedures were subdivided by surgical approach. Peak postoperative fractional serum creatinine (%deltaCr) was selected as the primary AKI variable, defined as the difference between the preoperative and the highest postoperative serum creatinine as a percentage of the preoperative value. **Results:** 409 liver transplant, 89 pneumonectomy, 197 Whipple and 1076 esophagogastrectomy procedures met inclusion criteria. Relative to a contemporary sample of CABG surgery patients (n=8358), %deltaCr was comparable or higher for liver transplant, peumonectomy, and most esophagogastrectomy procedures (Figure). However, AKI was notably infrequent following Whipple procedures. **Conclusions:** Non-cardiac surgery-associated AKI (NCSA-AKI) is a significant problem following many but not all of the major surgical procedures assessed. Our data confirms that creatinine rise following several non-cardiac surgeries is more significant than previously appreciated and appears predictable by procedure. AKI varied by surgical technique/esophageal segment resected for esophagogastrectomy procedures, appearing less prevalent with less invasive approaches. AKI was notably less severe following Whipple procedures. Observational studies of NCSA-AKI are challenging due to smaller sample sizes and an often ad hoc approach to postoperative renal function monitoring relative to cardiac procedures. For these reasons, NCSA-AKI may also be less apparent to the clinician. Prospective studies are needed to confirm these findings and validate their importance relative to other outcomes (e.g., 30d mortality). Furthermore, our findings suggest other major non-cardiac surgery settings (e.g., orthopedic, neurosurgical, gynecology) warrant investigation for NCSA-AKI.



61. Morbidity and Mortality of Acute Kidney Injury in 3287 Patients Undergoing Cardiovascular Surgery in China

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Purpose: Acute kidney injury (AKI) is a complex and common problem in patients after cardiovascular surgery(CVS), which is often associated with elevated risks for dialysis and mortality. The aim of this study is to summarize incidence of AKI and in-hospital mortality in patients after receiving CVS, and to find risk factors related with them. **Methods:** A total of 3287 patients undergoing CVS were erolled in this objective study from January 2009 to June 2010 in Zhongshan hospital, Fudan University. Logistic regression was performed to seek out possible independent risk factors associated with AKI morbidity and mortality. AKI was defined according to Acute Kidney Injury Network (AKIN) classification. **Results:** Overall, 1165 (35.4%) of 3287 patients had AKI, with 878 (26.7%), 91 (2.8%), 196 (6.0%) in AKI stage 1, 2 and 3, respectively, according to AKIN classification; 86 / 3287 (2.6%) patients received hemodialysis; The total in-hospital mortality was 71 / 3287 (2.16%), of which, in-hospital mortality in AKI stage 1, 2 and 3 were 14 / 878 (1.6%), 4 / 91(4.4%), 47 / 196 (24.0%), respectively; By multivariate logistic regression analysis (forward: conditional), acute kidney injury was independenly associated with old age, male, heart transplanatation as CVS type, long cardiopulmonary bypass (CPB) time, worse New York Heart Association(NYHA) classifications and hypertension, while duration in hospital and intensive care unit (ICU), worse AKIN classifications and non-hemodialysis treatment were possible risk factors for in-hospital mortality in AKI patients after CVS. **Conclusion:** This study indicates a high incidence of AKI in patients after CVS. Old age, male, heart transplanatation as CVS type, long CPB time, worse NYHA classifications and hypertension were possible independent risk factors for AKI, while duration in hospital and ICU, worse AKIN classifications and non-hemodialysis treatment were associated with in-hospital mortality among AKI patients after CVS.

62. The Prognostic Value of AKIN Criteria Combined with APACHE II and SOFA Scoring System in Patients after Cardiac Surgery

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Purpose: To explore the prognostic value of Acute Kidney Injury Network (AKIN) criteria combined with Acute Physiology and Chronic Health Evaluation II(APACHE II) and Sequential Organ Failure Assessment(SOFA) scoring system in acute kidney injury after cardiac surgery. **Methods**: Clinical data of 993 patients who underwent open-heart surgery in Zhongshan Hospital, Fudan University from April to August 2009 were prospectively collected. AKI after cardiac surgery was classified by AKIN staging system. APACHE II and SOFA scores were evaluated in the 1st 24h after surgery. The three systems in predicting in-hospital mortality were evaluated by logistic regression analysis, and tested by receiver operating characteristic (ROC) curve and Hosmer-Lemeshow goodness-of-fit test. **Results**: A total of 309 / 993 (31.1%) cases developed AKI. The median time when AKI was diagnosed and serum creatinine recheached its' peak level were 1d and 2d, respectively; Both APACHE II and SOFA scores in AKI patients were much higher than those in non-AKI patients ($P < 0.01$), which were positively correlated with AKIN classifications (APACHE II $r = 0.37$, $P < 0.01$; SOFA $r = 0.42$, $P < 0.01$); The mortality increased corresponding to the severity of kidney injury, APACHE II and SOFA scores; By univariate logistic regression analysis, APACHE II ≥ 19, AKIN stage 3 and SOFA ≥ 7 were all possible risk factors for in-hospital mortality, with their areas under the ROC curve being above 0.8; Futher multivariate logistic regression analysis indicated that APACHE II ≥ 19(OR = 4.26) and AKIN stage 3(OR = 76.15) were independent predictors of in-hospital mortality. **Conclusions:** AKI can be classified by AKIN criteria in the early stage after cardiac surgery. The APACHE II and SOFA scores evaluated in the 1st 24h after operation could discern the severity of patients' illness. Three models all presented good discrimination and calibration in predicting patients' outcome, while APACHE II ≥ 19 along with AKIN stage 3 were independent predictors of in-hospital mortality.

63. Role of the First 24-hour Urine in Predicting In-Hospital Mortality Among Patients with Acute Kidney Injury occurring After Cardiovascular Surgery

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Purpose: Acute kidney injury (AKI) in patients after cardiovascular surgery (CVS) is often associated with decreased urine and elevated risks for dialysis and mortality. This study is to evaluate the role of the first 24-hour urine in predicting in-hospital mortality among patients with AKI occurring after CVS. **Methods:** A total of 1165 patients who suffered from AKI after CVS were enrolled in this study from January 2009 to June 2010 in Zhongshan hospital, Fudan University, Shanghai, China. The parameters included demographic characteristics, body mass index, the first 24-hour urine (divided into quartiles: the first, second, third and fourth 6-hour urine), co-morbidity (diabetes and hypertension) and other parameters. Logistic regression was performed to evaluate predicting value of quartiles of the first 24 hour in mortality among patients with post-operative AKI. **Results:** Among 1165 AKI patients, the first, second, third and fourth 6-hour urine were (818.2±507.4) ml, (514.8±328.9)ml, (478.7±303.1)ml and (538.8±342.5)ml, respectively ($P < 0.05$). A total of 65 in-hospital deaths occurred among patients with AKI after CVS. By multivariate logistic regression analysis (forward: conditional), inverse associations were observed in the first and the fourth 6-hour urine with in-hospital mortality in AKI patients after operation; When adjusted by age, gender, BMI and co-morbidity (including diabetes and hypertension), only the first 6-hour urine was independently related with patients' mortality. **Conclusion:** This study indicates that compared with the other three quartiles of the first 24-hour urine, the first 6-hour urine may be the most important and independent variable in predicting in-hospital mortality in AKI patients after receiving CVS.

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64. Combination of Endotoxin Activity Assay and Plasma NGAL Measurement in Sepsis and Acute Kidney Injury

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Background: Sepsis is frequently complicated with acute kidney injury (AKI) and evaluation of endotoxiemia is important for the management of septic AKI patients. The endotoxin activity assay (EAA) is the only FDA approved rapid ex vivo diagnostic test that utilizes the biological response of patient neutrophils to an immunological complex of endotoxin. So far, a number of basic and clinical investigations have demonstrated the role of neutrophil activation in AKI. However, it is unclear whether the EAA assay, which is based on neutrophil response to stimuli, will be influenced by AKI. **Method:** Thirty six severe AKI patients admitted to the ICU of our university hospital were analyzed. All the patients were treated by CRRT (AKIN stage 3). EAA and plasma NGAL measurement was conducted at the time of CRRT initiation, and 24 and 48 hr after. **Results:** At CRRT initiation, EAA showed a wide range of values [low <0.4 (n=15), intermediate 0.4-0.6 (n=14), high >0.6 (n=7)]. 31 of 36 AKI patients (86%) showed higher plasma NGAL (>150 ng/ml). Degree of renal dysfunction did not have any significant impact on EA values (BUN $R2=0.016$, Cre $R2=0.008$). Nine patients had severe gram-negative rod infections that eventually caused septic shock during the observation period. The highest EA values and plasma NGAL of these septic shock patients for 48 hr were significantly higher than the other AKI patients [EAA 0.80 (0.61-1.02) vs 0.41 (0.31-0.54), $P<0.05$; plasma NGAL 827 (652-1956) vs 360 (255-475), $P<0.05$]. Combination of EAA and plasma NGAL could discriminate septic shock with high sensitivity and specificity (Cut-off value of EA>0.6 and NGAL>500; sensitivity 87.5% and specificity 92.9%, ROC-AUC 0.957). **Conclusion**: Our data demonstrated that EAA was not influenced by AKI, which can potentially induce neutrophil activation. Combination of EAA and plasma NGAL is a useful diagnostic tool for septic shock in AKI patients.

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65. Rapid Determination of Kidney Function in Dogs with Acute Kidney Injury Using a Portable Fiber Optic Fluorescence Ratiometric Analyzer

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Purpose: Rapid determination of glomerular filtration rate (GFR) in acute kidney injury (AKI) is important for diagnosis and determination of disease severity. **Methods:** We have developed a fiber optic fluorescence ratiometric kidney function analyzer allowing point of care determination of GFR and plasma volume within 60 min. of fluorescent probe administration using a two compartment model. This novel system consists of dual LED excitation sources, two PMTs, a sub-millimeter optical fiber, and computer hardware with software handling control, data acquisition, and analysis capabilities. Using optimized fluorescence marker/reporter molecules, highly conjugated freely filterable 5 kDa Aminofluorescein-dextran and non-filterable 150 kDa 2-sulfohexamine-rhodamine-dextran, and ratiometric analysis for determination of GFR in dogs we compared 60 min. fluorescence-determined to 6 hour Iohexol GFR values obtained in healthy laboratory dogs under normal physiologic conditions and following gentamicin-induced AKI over a wide range of GFR values. **Results:** Excellent correlation existed between the two methods of GFR determination (r=0.91). Finally, no apparent toxic effects were noted following repeated administration of both fluorescent markers over a 4-month period to study the same dogs repetitively. **Conclusions:** Based on the success of these pilot studies we anticipate progression to a phase I human study with rapid point of care monitoring of GFR and plasma volume.

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66. Microvesicles Derived from Endothelial Progenitor Cells Protect Kidneys From Ischemia-Reperfusion Injury Through Horizontal RNA Transfer to Target Renal Resident Cells

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Background : Bone marrow-derived stem cells are known to reverse acute kidney injury (AKI) through paracrine mechanisms. Endothelial progenitor cells (EPCs) are potent pro-angiogenic stem cells able to stimulate tissue repair. We previously demonstrated that microvesicles (MVs), small biologically active particles carrying genetic information, released from EPCs induce angiogenesis through horizontal RNA transfer. The aim of this study was to evaluate whether the administration of EPC MVs may prevent AKI in a rat model of ischemia-reperfusion injury (IRI). **Methods:** EPCs were isolated from peripheral blood of healthy volunteers. MVs were isolated by ultracentrifugation and characterized for protein and RNA content. Wistar rats were treated as follows: 1) Sham; 2) IRI (renal pedicle clamping for 45 min); 3) IRI + 10 μg/ml EPC MVs; 4) IRI + 10 μg/ml EPC MVs pre-treated with 1U/ml RNase. Renal function and histology were evaluated. In vitro, we studied the effects of EPC MVs on isolated kidney endothelial, tubular epithelial and CD133+ progenitor cells. In selected experiments, MVs were isolated from EPCs subjected to the knock-down of Dicer, the intracellular enzyme essential for microRNA (miRNA) production. **Results:** After injection, EPC MVs localized within peritubular capillaries and tubular cells and protected rats from IRI-induced AKI (decrease of serum creatinine/BUN levels and of histologic tubular injury) MVs significantly reduced apoptosis (TUNEL), sustained tubular proliferation (BrDU and PCNA) and inhibited leukocyte infiltration. All these protective effects were not observed when MVs were pre-treated with RNase or produced by EPCs subjected to Dicer knock-down, suggesting a key role for mRNA and miRNA carried by MVs. In vitro, EPC MVs inhibited hypoxia-induced apoptosis of kidney endothelial and epithelial cells by up-regulating genes involved in cell proliferation, differentiation, angiogenesis and inhibition of inflammation. In addition, MVs induced the differentiation of CD133+ renal progenitors towards an endothelial phenotype. **Conclusions:** EPC MVs induced a protective effect on AKI following experimental IRI. This effect may be ascribed to the transfer of mRNAs and miRNAs from MVs to target renal resident cells. Our results suggest that EPC MVs could be exploited as a potential new therapeutic approach for ischemic AKI.

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67. Reduced Creatinine Production in Septic Patients Warrants Careful Clinical Application

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Background: Doi et al. reported that sepsis

markedly reduced creatinine production (Pc) in a cecal ligation and puncture of nephrectomized mouse model. Reduced Pc may hinder the elevation of serum creatinine (SCr) and thus the diagnosis of acute kidney injury (AKI). This finding has not yet been validated in humans. **Methods:** This is a retrospective study of patients treated with CVVHDF from June 2008 to August 2010 at an academic medical center. Sepsis was defined as ≥ 2 SIRS signs suspected or known to be caused by a bacterial or fungal infection. All patients had serum and effluent samples analyzed for urea nitrogen and creatinine every 12 hours during therapy. Once patients were in steady state, we computed Pc using the following equation (Fig. 1), where CMR = creatinine mass removed by CVVHDF, T = treatment duration, BW = body weight, = averaged SCr, and DW = the lowest BW recorded during the entire study period. Subscript 0 and T denote at the beginning and end of treatment-day, respectively. Every SCr was adjusted according to the cumulative daily fluid balance. **Results:** There were total 221 treatment-days in steady-state in 65 patients (mean age±SD was 55.7±14.9 years, 81.5% male). Pc was lower in septic patients (Table 1). Higher Pc was significantly associated with male gender (R=0.23, p=0.003), African Americans, non-ESRD CKD, HIV infection (R=0.27, p=0.000), and higher BW (R=0.16, p=0.041), but not with inotropic use (p=0.268), intubated status (p=0.069), or age (p=0.460). **Conclusion:** Our results show that creatinine production is altered in septic patients requiring CVVHDF. Additional studies are required to ascertain the mechanism for reduced creatinine production. Creatinine levels may underestimate severity of renal dysfunction in septic patients requiring dialysis and should be used with caution as a marker of AKI in sepsis.

Pc (mg/day)	Septic (N=143)	Non-Septic (N=31)	p-Value
Mean±SD	536.0±361.8	710.5±230.4	0.011

Figure:

$$\frac{CMR}{T/24} - \frac{BW_0 \times (SCr_0 - SCr_T)}{T/144} - \frac{SCr_T \times (BW_0 - BW_T)}{T/240} + 0.38 \times \overline{SCr} \times DW$$

68. Greater Increase in Urinary Hepcidin Predicts Protection from Acute Kidney Injury After Cardiopulmonary Bypass

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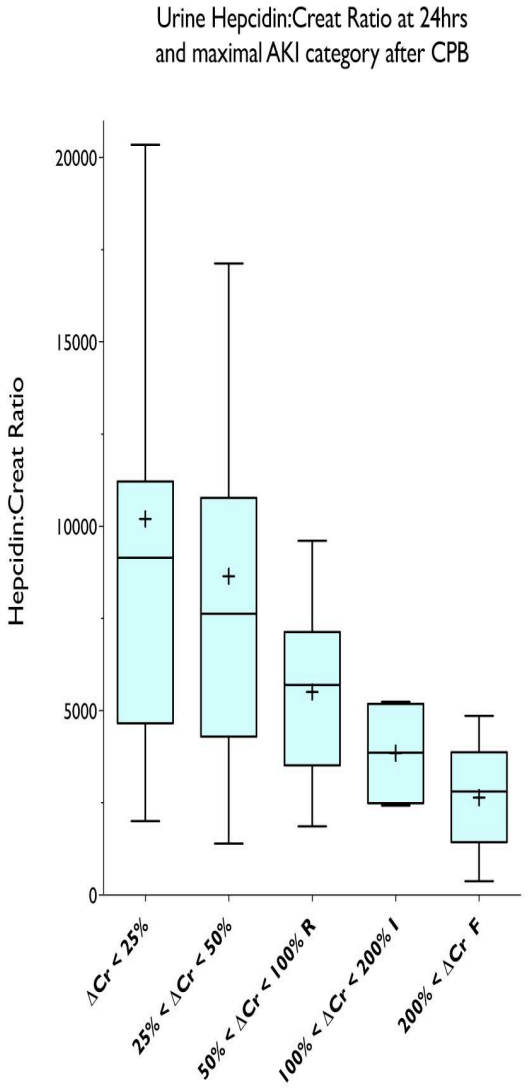
Background: Acute kidney injury (AKI) is a common and serious complication of cardiopulmonary bypass (CPB). Hepcidin, a peptide regulator of iron availability has been identified as a potential biomarker of AKI after CPB. We sort to investigate this association in 93 patients undergoing CPB enrolled in a clinical trial. **Methods:** Hepcidin was measured by enzyme-linked immunoassay in serum and urine samples at baseline, immediately post-operatively and at 24hrs. 25 patients developed AKI by RIFLE-Risk criteria in the first 5 days. **Results:** Serum hepcidin, urinary hepcidin, urinary hepcidin:creatine ratio and fractional excretion of hepcidin were significantly elevated post-op and at 24hrs ($p<0.0001$ vs. baseline). However, absolute urinary hepcidin and urinary hepcidin:creatinine ratio were significantly lower at 24hrs in patients with RIFLE ≥Risk compared to those without AKI ($p=0.0009$ & $p<0.0001$ respectively). Serum hepcidin levels and immediately post-op urinary hepcidin were not associated with AKI. Receiver operator characteristic analysis showed that lower 24hr urine hepcidin and hepcidin:creatinine ratio were sensitive and specific predictors of AKI, area under curve of 24hr urine hepcidin:creatinine ratio for diagnosis of RIFLE Risk or greater was 0.77, 0.84 for RIFILE Injury or greater. **Conclusion:** The intriguing finding that urinary hepcidin is higher in patients who do not go on to develop AKI and the central biological role of hepcidin in iron metabolism identifies hepcidin as an important subject for AKI research.



69. Ablation of Nur77 Gene Expression Protects Against Acute Kidney Injury

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Background: Early detection and intervention are the keys to abate Acute Kidney Injury (AKI) and facilitate faster recovery of kidney function. In the present study, we have identified the rapid induction of Nur77 during ischemia-reperfusion-induced AKI in mice. Nur77, an orphan nuclear receptor family member exhibits both pro-apoptotic and pro-survival functions depending upon the cellular context. **Purpose:** To evaluate the function of Nur77 during AKI. **Methods:** Bilateral renal ischemia reperfusion injury (IRI) was induced on 8-10 weeks old male mice (C57B6/J- Nur77+/+ and Nur77-/-) by clamping the renal pedicles. Serum Creatinine and Blood urea nitrogen (BUN) levels were obtained. Quantitative PCR (qPCR) and immunohistochemistry were performed on 24h post IRI tissues to analyze the extent of kidney injury and inflammation. Nur77 repression by 9 cis-Retinoic Acid (RA) was achieved by administering 10 mg/kg body weight, 4h prior to the induction of renal IRI or pretreatment of in vitro cultured Renal Proximal Tubular Epithelial Cells (RPTECs) with 1 uM 9 cis-RA. In vitro IRI was performed by overlaying RPTECs with mineral oil for 1h followed by reperfusion. **Results:** Intra renal expression of Nur77 was rapidly induced as early as 3h post ischemia reperfusion and most abundantly in the renal medulla. Nur77-/- mice exhibited lower serum creatinine ($P<0.0001$) and BUN ($P<0.0001$) and preserved kidney morphology as compared to Nur77+/+ mice, 24h post IRI. Nur77-/- kidneys also had significantly fewer apoptotic cells. 9 cis RA pretreatment potently blocked the induction of Nur77 during IRI in kidney tissues and also in the RPTECs, as assessed by qPCR. There was a concomitant decrease in the serum creatinine and BUN levels and less apoptosis in the RA treated mice compared to the vehicle control. Overall there was a drastic reduction of neutrophil infiltration in the kidneys in the absence or reduction of Nur77 expression. **Conclusion**: Nur77 is an early induced gene upon kidney injury in mice as well as in the RPTECs upon hypoxia and is pro-apoptotic. Nur77 expression during AKI is deleterious and presents a novel therapeutic target. Furthermore pharmacological ablation of Nur77 expression via prior exposure to retinoids prevents tubular epithelial cell apoptosis, inflammation and protects mice from renal IRI.

70. The Incidence and Outcome of Acute Kidney Injury in NICU

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Background: Acute kidney injury (AKI) is an important complication, especially in the critically ill patients. But there are few reports of

AKI in neonate. We report AKI in single Neonatal Intensive Care Unit (NICU), in Japan. **Methods**: From September 2007 to August 2010, we investigate all patients admitted to NICU of Kurashiki Central Hospital in Japan. According to AKIN criteria, patients were diagnosed AKI by their maximal serum creatinine (sCr) over 1.5mg/dl during their first 48hrs life or increasement of their sCr >0.3 mg/dl than the latest data, or low urine output (under 0.5 ml/kg/hr, over 24hrs). **Results**: Total patients were 1059, include 563 males and 496 females (the ratio is 1.20), 453 low birth weight infants, 96 very low birth weight infants, 117 extremely low birth weight infants. The average gestational ages were 35 weeks (22-42 weeks). 6.3% of patients had an episode of oligourea and 14.8% patients increased their sCr during the NICU stay. The incidence of AKI was 14.8% (n=157) of all patients, 6.6% in low birth weight infants, 18.8_ in very low birth weight infants, and 75.2% in extremely low birth weight infants. And the mortality of all of the 1059 patients was 4.4% (47/1059). The mortality of AKI patients was higher than non AKI patients (n=30) significantly 17.8% vs. 4.4%, P<0.001). We performed continuous hemodialysis in 4 cases and peritoneal dialysis in 5 cases. **Conclusions:** The incidence of AKI in NICU was high, especially in ELBW infants. The mortality of AKI patients was higher than non-AKI patients.

71. Vacular Calcification Scores on Plain Radiographs of Hands and Pelvis is Associated with Arterial Stiffness, Inflammation, Nutrition in Hemodialysis Patients

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Background: Vascular calcification(VC) have been shown to independent predictors of cardiovascular mortality in hemodialysis(HD) patients. Various VC scores have been evaluated in HD patients using plain radiographic films of the pelvis and hands. The presence of VC in HD patients is associated with increased stiffness of arteries. The purpose of this study was to analysis the association of VC and arterial stiffness, inflammation, nutrition in HD patients. **Methods:** We studied for 101 stable HD patients. All patients underwent both hands and pelvis X-ray. All patients were carried out to measurement of the carotid-femoral pulse wave velocity (PWV), the ankle brachial index (ABI) and augmentation index (AI). The presence of calcifications were analysed as a score (0 to 8) according to the number of arterial sites with calcifications on both hands and pelvis X-ray. Laboratory tests such as albumin, calcium, phosphate, iPTH, C-reactive protein, homocysteine, lipid profile were measured. **Results:** Sixty of 101 patients (Diabetes 48 patients) were male. The mean age was 55.7 ± 13.2 years and the mean HD duration was 185±55.8 months. The study patients were grouped according to VC scores to three groups. Group 1 (61 patients) was not investigation of VC and group 2 (25 patients) had VC score of 1 to 4 and group 3 (14 patients) had VC score of 4 to 8. The serum albumin had significant negative correlation with C-reactive protein and VC scores ($p<0.05$). The comparisons of different groups showed that PWV and ABI of group 3 were significantly increased than group 1 and 2 ($p<0.05$). AI was not significant difference among three groups. C-reactive protein and homocysteine were not significant difference among three groups. There was positive correlation between C-reactive protein and PWV ($p < 0.05$) and not correlation between homocysteine and PWV. **Conclusion:** The presence of vascular calcifications on plain X-ray of both hands and pelvis in HD patients may be associated with increased arterial stiffness, inflammation and nutrition. Hence, we thought that VC scores of the pain X-ray of hands and pelvis may be important for estimate of cardiovascular diseases and mortality in HD patients.

72. Antigen Specific Cellular Response in Patients with Hepatitis C virus Infection and its Association with HLA Alleles

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Background & Objectives: Host genetic diversity is believed to contribute to the spectrum of clinical outcomes in hepatitis C virus (HCV) infection. The present study aimed at finding out the frequencies of HLA class I alleles of HCV infected individuals from western India (Maharashtra state). **Methods:** Forty three clinically characterized anti-HCV positive patients from Maharashtra were studied for HLA A, B, C alleles by PCR- sequence specific primer

(SSP) typing method and compared with 67 and 113 ethnically matched, anti-HCV negative healthy controls from western India(Maharashtra state). **Results:** Our analysis revealed an association of HLA alleles HLA A*03 (OR= 16.69, EF, 0.44, P=7.9E-12), A*32 (OR= 1474, EF 0.21, P=1.8E-9), HLA B*15 (OR=14.11, EF 0.39, P=2.18E-10), B*55 (OR= 12.09,EF 0.07, P=0.005), Cw*16 (OR= 7.45, EF 0.12, P=0.001), Cw*18 (OR= 402, EF 0.05, P=0.003), with HCV infection, chronicity. **Conclusions:** Our results suggest that the establishment of viral persistence in patients is due to a failure of the immune response and is associated with HLA class 1 allele mainly A*03, A*32, B*15, B*55, Cw*16, Cw*18 restricted individuals, as indicated by the absence of a significant T-cell response thus this proves that associated haplotype influence HCV infection as a host genetic factor

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