Consensus Conference on Sepsis and Infection

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Problem for Burns

- Burn Patients already have some level of systemic inflammation
- SIRS definition too inclusive (most burn patients fit SIRS criteria)
- Current definitions will not help clinical trials

Goal

- Develop and publish standardized definitions for sepsis and infection related diagnoses for the burn population

Benefits

- Consistent definitions will lead to better clinical trial design
- Communicate to colleagues that burn patients have specific sepsis-related diagnoses
- Create recognition for the ABA and its members (that we are players in clinical trials for sepsis)
- Improve the recognition of JBCR

Process

- Two “rapporteurs” per topic
  - Examine literature
  - Seek advice and opinions
  - Provide “Draft Definition”
- Met in Tucson 1/20/07
  - Discuss definitions
  - Agree on definitions

Process

- Create document
  - Evaluate by e-mail
  - Feedback to DG
  - Agree on changes
    - Summary presented in Research Session (Friday, March 22)
- Publish in JBCR

Systemic Inflammatory Response Syndrome (SIRS)

Jeffrey Saffle, Jim Holmes IV

- SIRS occurs frequently in burns but it does not necessarily trigger a change in management
- In most patients it resolves, if it recurs or persists then it should trigger a response
- Currently, there is no (level 1) evidence that SIRS has prognostic value for burns
- It should not be used for study categorization
- The concept of change over time is essential

Sepsis

Richard Gamelli, Tina Palmieri

- Key Issues
  - Many parameters are typical for burn patients
  - Definition should be age specific (children have different parameters
  - Factors that impact skeletal muscle catabolism should be considered

Sepsis
Richard Gamelli, Tina Palmieri

- Burn Sepsis Criteria
  - A change in the burn patient that
    - Triggers the concern of a suspected infection
    - Antibiotics are usually initiated
    - It is a presumptive diagnosis
    - It should trigger a search for a source of infection
    - It has to be confirmed with an identification of infection
    - This is the link to other definitions of infection
    - There is a requirement for clinical interpretation
    - For instance, immediately post-op these factors apply

Sepsis
Richard Gamelli, Tina Palmieri

- Trigger (entrance criteria) (the trigger may be interpreted as SIRS) – at least 3 of the following:
  - Temperature >39^{o} or <36.5^{o} C
  - Progressive tachycardia
    - Adults >110 bpm
    - Children >2 SD above age-specific norms (85% age adjusted max heart rate)
  - Progressive tachypnea
    - Adults
      - >25 bpm not ventilated
      - Minute ventilation >12 l/min ventilated
    - Children >2 SD above age-specific norms (85% age adjusted max respiratory rate)

Sepsis

Richard Gamelli, Tina Palmieri

- Definition
  - Thrombocytopenia
    - Adults
      - <100,000/υl
      - >25% decrease in platelet count within 24 hours
  - Hyperglycemia (in the absence of pre-existing diabetes mellitus)
    - Untreated plasma glucose >200 mg/dl (or equivalent mM/l)
    - Insulin resistance – examples include:
      - >7 units of insulin/hour
      - Significant resistance to insulin (increase in insulin requirements >25%)

Sepsis

Richard Gamelli, Tina Palmieri

- Definition
  - Inability to continue enteral feedings for a period of 24 hours
    - Abdominal distension
    - High gastric residuals
    - Uncontrollable diarrhea
    - Discontinuation of enteral feedings

Sepsis

Richard Gamelli, Tina Palmieri

- Required - Documented infection (as defined later)
  - Culture positive infection
  - Pathologic tissue source identified
  - Clinical response to antimicrobials

Severe Sepsis

- Sepsis plus organ dysfunction
- Drop with explanation

Septic Shock

Jureta Horton, Ron Tompkins

- Shock has hemodynamic parameters that are defined in “Sepsis Bundles”
- Septic shock includes the above definitions plus Sepsis

Septic Shock

Jureta Horton, Ron Tompkins

- Persistent hypotension despite adequate fluid resuscitation and/or Lactate > 4 mmole (36 mg/dl)
- Surviving Sepsis Campaign Resuscitation Goals
  - CVP > 8-12 mmHg
  - Mean arterial pressure $\geq$ 65 mmHg
  - Urine output $\geq$ 0.5 ml/kg/hr
  - CVP (SVC) or MV O_2 Saturation $\geq$ 70%

Septic Shock

Jureta Horton, Ron Tompkins

- 2001 SCCM/ESICM/ACCP/ATP/SIS International Sepsis Definitions Conference
  - "in adults … a state of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes."
  - Hypotension (despite adequate volume resuscitation)
    - SBP < 90 mmHg
    - MAP < 60 mmHg
    - Reduction in SBP < 40 mmHg from baseline

Septic Shock

Jureta Horton, Ron Tompkins

- 2001 SCCM/ESICM/ACCP/ATP/SIS International Sepsis Definitions Conference
  - Children > 2 SD below normal for age
  - Tachycardia (may be absent in hypothermia) with signs of decreased perfusion
    - Decreased peripheral pulses compared to central pulses
    - Altered alertness
    - Flash capillary refill or refill > 2 seconds
    - Mottled or cool extremities
    - Decreased urine output (< 1 ml/kg/hr)

Smoke Inhalation Injury

Daniel Traber, David Mozingo

- Inhalation Injury – Not all Inhalation Injury is the same
  - CO poisoning may or may not occur in the presence of inhalation injury
  - Upper Airway Injury may or may not occur in the presence of inhalation injury
- Inhalation Injury (Injury caused by toxic products of combustion below the glottis)

Smoke Inhalation Injury

Daniel Traber, David Mozingo

- Yes or No diagnosis
  - We are developing a criteria for inclusion into a study
  - History of combustion is necessary
  - Bronchoscopy (all found below glottis)
    - Evidence of carbonaceous material
    - Signs of edema, ulceration
    - Erythema or carbon staining in the absence of evidence of other signs of injury may not be an indicator

Smoke Inhalation Injury

Daniel Traber, David Mozingo

- Factors that are not reliable
  - Singed hair
  - Soot in the saliva
  - Facial burns
  - Carbon monoxide poisoning

Smoke Inhalation Injury

Daniel Traber, David Mozingo

- Inhalation Severity System – to be developed

Multiple Organ Dysfunction Syndrome (MODS)

Edwin Deitch, Cleon Goodwin

- Do not use ACCP/SCCM Consensus Criteria
- Do not initiate MODS assessment until acute resuscitation completed (day 3)
- Scores should grade the degree of organ failure over a spectrum of values
- One of the 4 MODS scoring systems should be used
- Time to recovery is important (an outcome variable)

Multiple Organ Dysfunction Syndrome (MODS)

Edwin Deitch, Cleon Goodwin

- MODS Scoring System
  - Simple
  - Use commonly available criteria
  - Unlikely to confounded by the unique characteristics of burn patients
  - Failure to heal should be part of the assessment

Multiple Organ Dysfunction Syndrome (MODS)
Edwin Deitch, Cleon Goodwin

- Recommend
  - Marshall MODS Scoring System (as modified by Cook)

    Or
  - SOFA Scoring System
  - Glue grant has examined Marshall and Denver Scores
    - We need to assess their results
  - The Marshall Scoring System should be used until further data indicates a better system
    - Modify Marshall Score based on Glue Grant and Purdue data

Multiple Organ Dysfunction Syndrome (MODS)
Edwin Deitch, Cleon Goodwin

- Unresolved issues
  - Glasgow coma score used by Marshall and SOFA – should we keep it?
    - This is a difficult question that needs further evaluation
    - Use of GCS Motor Score may be helpful
  - Scoring systems need to be applied over a time period (ie. Burn patients have a long period of hospital stay so which score is used?)
  - Do we need a Severity Score
  - We should consider validating these scores

Pneumonia

David Herndon, Art Sanford, Jim Gallagher, James Jeng

- Clinical Diagnosis: 2 of the following:
  - Chest x-ray – new and persistent infiltrate, consolidation, or cavitation
  - Sepsis (defined above)
  - Sputum – change or purulent
  - There are diagnoses that may mimic pneumonia (ARDS, tracheo-bronchitis, chest contusion)

Pneumonia

David Herndon, Art Sanford, Jim Gallagher, James Jeng

- Microbiologic Data – the clinical diagnosis can be modified *post hoc* with the microbiologic data into one of three categories
  - **Confirmed –** clinical + pathogen isolated
  - **Probable –** clinically present without microbiological confirmation
  - **Possible –** abnormal CXR with uncertain cause with low or moderate clinical suspicion, but with microbiologic definite criteria met or pathogen identified

Pneumonia

David Herndon, Art Sanford, Jim Gallagher, James Jeng

- Positive Microbiology
  - Bronchoalveolar lavage – $\geq 10^4$ organisms
    - Blind is OK
  - Protected specimen brush – $\geq 10^3$ organisms
    - Blind brush is OK
  - We recognize that there are other criteria for special organisms that we may not include in the diagnosis
  - (The burn wound can be a source of the pathogens spread hematogenously)

Blood Stream Infection

David Ahrenholz, Alice Neely

- One of two criteria
  - (1) Patient has a recognized pathogen (defined as a microorganism not usually regarded as a common skin contaminant, i.e. diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, or micrococci) cultured from two or more blood cultures, or one positive blood culture, in the presence of sepsis (as defined above)

Blood Stream Infection

David Ahrenholz, Alice Neely

- One of two criteria
  - (2) Patient has a common skin contaminant cultured from two or more blood cultures drawn on separate occasions (including one drawn by venipuncture) and the patient has clinical signs of sepsis

Blood Stream Infection
David Ahrenholz, Alice Neely

- There are instances when some of these criteria may not apply
  - Culture techniques may miss infections
  - Patients on antibiotics (cultures may be negative)
  - The role of single positive blood cultures needs to be clarified
  - Some organisms act differently in BSI
- Appendix
  - Techniques for obtaining blood cultures
  - Techniques for dealing with patients on antibiotics
  - Primary infection – no other cause identified

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Utilize definitions of Centers for Disease Control with modifications
- There may be overlap with other types of infections
- Liberal definitions will avoid missing catheter-related infections

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Clinical Definitions
  - Localized catheter colonization
    - Significant growth of a microorganism (>15 CFU) from the catheter tip, SQ segment or catheter hub
    - In the absence of bacteremia
  - Exit site inflammation
    - Erythema or induration within 2 cm of the catheter exit site
    - Absence of concomitant bloodstream infection
    - Without concomitant purulence or necrosis

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Clinical Definitions
  - Clinical exit site infection
    - Tenderness, erythema, or undue site induration >2 cm from the catheter site
    - Absence of concomitant bloodstream infection (BSI)
    - Without concomitant purulence or necrosis
  - Infusate-related BSI
    - Concordant growth of the same organism from the infusate and from the blood cultures (preferably drawn percutaneously)
    - No other apparent source of infection

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Clinical Definitions
  - Catheter-related BSI (or Catheter infection with BSI)
    - Bacteremia/fungemia in a patient with an intravascular catheter
    - Microbial growth from at least one blood culture from another uninvolved vein/artery
    - Clinical manifestation of infection
    - No other source of infection

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Clinical Definitions
  - Catheter-related BSI (or Catheter infection with BSI)
    - One of the following should be present
      - >15 CFU/catheter segment on semiquantitative culture analysis or $>10^3$ CFU/catheter segment on quantitative culture analysis whereby the the same organism is isolated from the catheter segment and peripheral blood
      - Simultaneous quantitative blood cultures with a >5:1 ratio central venous catheter versus peripheral blood draw
      - Differential period of central venous catheter growth versus peripheral blood culture growth of >2 hours

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Clinical Definitions
  - Catheter-related infection
    - Vascular access device that terminates at or close to the heart or one of the great vessels
      - Umbilical artery or vein catheters are considered central lines
    - BSI is considered to be associated with a central line if the line was in use during the 48-hour period before development of the BSI

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- There is no difference between Catheter-related or Catheter-associated infection (this needs discussion)

Catheter-related Infection

Michael Shay O'Mara, Steven Wolf

- Surveillance Definitions for Primary BSIs
- (Modified from National Nosocomial Infections Surveillance System)
  - Laboratory-confirmed BSI
    - Criterion 1 – Patient has recognized pathogen cultured from one or more blood cultures
    - Criterion 2 – Patient has a common skin contaminant cultured from 2 or more blood cultures drawn on separate occasions
    - Criterion 3 – Positive antigen for a recognized pathogen in blood (H flu, S pneumo, N mening, Group B Strept)
  - Findings not related to an infection at another site

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Key Points
  - All skin surfaces and wounds have bacteria
  - Bacterial balance defines patient/bacterial interaction
  - Other nonbacterial pathogens can cause disease

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Wound Colonization
  - Bacteria present on the wound surface without sepsis
  - This is not an infection

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Invasive Infection
  - Pathogen present in the wound at high concentrations (frequently $>10^5$ pathogens/g tissue)
  - Invasion or destruction of unburned skin/tissue
  - This may occur with or without sepsis
  - Burn wound invasive infections are life threatening and need urgent treatment (usually wound excision)
  - A description of Pseudomonas/Fungal/Herpes invasion should be mentioned

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Presence of pathogens in a burn wound at concentrations sufficient in conjunction with depth, surface area involved and age of patient to cause suppurative separation of eschar or graft loss, invasion of adjacent unburned tissue or cause the systemic response of sepsis syndrome

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Cellulitis
  - Bacteria present in the wound and/or wound eschar at high concentrations
  - Examination of surrounding tissue reveals advancing erythema, induration, warmth, tenderness
  - Sepsis must be presence
  - Redness around the wound may not require treatment

Burn Wound Infection/Sepsis

Gary Purdue, Warren Garner

- Diagnosis
  - Objective (discussion)
    - Quantitative biopsy (Can be used to confirm but is not reliable It may help with identifying organism)
    - Quantitative swab (poor test but may help with identifying organism)
    - Tissue histology
  - Subjective
    - Pain, erythema, color changes
    - Unexpected change in the appearance or depth of the wound
    - Systemic changes
    - Premature separation of burn eschar

Urosepsis

Barbara Latenser, Charles Yowler

- Modified CDC Criteria (an uncommon cause of sepsis in burns)
- Catheterization changes the issue
  - Sepsis and
  - 1) One of the following:
    - Urgency, frequency, dysuria, suprapubic tenderness
    - Urine culture $\geq 10^5$ cfu/ml with no more than 2 species of organisms

Urosepsis

Barbara Latenser, Charles Yowler

- Modified CDC Criteria
  - 2) Two of the following (we will not use for burns)
    - Sepsis
    - Urgency, frequency, dysuria, suprapubic tenderness
    - Any of the following
      - Positive dipstick for leukocyte esterase and/or nitrate
      - Pyuria ($\geq$10 WBCs/υl or $\geq$3 WBCs/high power field of unspun urine)
      - Organisms seen on Gram stain of unspun urine
      - Two urine cultures with repeated isolation of the same uropathogen with $\geq 10^2$ cfu/ml in nonvoided specimen
      - Two urine cultures with $\leq 10^5$ cfu/ml of single uropathogens in a patient being treated with appropriate antimicrobial therapy

Urosepsis

Barbara Latenser, Charles Yowler

- Candiduria (symptomatic, extremely rare)
- (Put in discussion)
  - Sepsis
  - $>10^4$ yeast
  - No other source

Conclusion

- Send out main conclusions
- Address
  - Justifications
  - Appendices