

# AMERICAN BURN ASSOCIATION

## MULTICENTER TRIALS GROUP

### What is the ABA-MCTG?

The Multicenter Trials Group of the American Burn Association is a multidisciplinary group of ABA members committed to advancing burn care through research. The group first began meeting in 2001 and to date the group has completed three retrospective chart reviews and one prospective randomized trial. Five new studies are proposed for 2004.

### When does the ABA-MCTG meet?

The group meets at each ABA annual meeting. This fall, the group will have an interim conference in conjunction with the West Coast Burn Conference (see below).

### Who can attend?

Any interested ABA member is welcome to attend MCTG meetings and participate in MCTG studies.

### How does one propose or participate in a study?

Studies are proposed at MCTG meetings. The principal investigator is asked to give a short presentation about the study. Participants have the opportunity to offer suggestions and comments. Sites interested in participating are put on a contact list that is given to the investigator. The study is conducted by the principle investigator(s), who is responsible for all facets of the research from design through data analysis. Issues such as authorship and data ownership should be agreed upon by participating sites prior to study initiation. Investigators are expected to abide by federal and institutional regulations concerning the responsible and ethical conduct of human studies research.

### How do I get involved?

Email Linda Edelman, Intermountain Burn Trauma Center, at [Linda.Edelman@hsc.utah.edu](mailto:Linda.Edelman@hsc.utah.edu) to get on our mailing list. Please state if you would also like to be added to our Yahoo Group.

### MULTICENTER TRIALS GROUP IS ON YAHOO

A website for the ABA-MCTG is currently being planned (see below). Until that website is a reality, a Yahoo group has been opened to handle email and files that are of interest to individuals participating in the MCTG. Communicating through the yahoo group will make the information you contribute to the work of the ABA-MCTG available to all members of the group automatically. You may post files to the group page as well. You may customize your membership to receive all emails, to receive a single group of messages on a daily basis, or only see the messages when you log on to the yahoo group.

At this time, Linda Edelman, Jeffrey Saffle and I have "moderator" designations. If you are interested in being a part of the yahoo group, you may simply email one of us and ask to be invited, then follow Yahoo directions for establishing your identity with the yahoo group function. If you already make use of yahoo groups, you may simply be added to this group. I hope you'll find this a simple and useful way to keep abreast of the ABA-MCTG activity. In my experience, participating in a yahoo group does NOT expose you to Spam.

Nathan Kemalyan, MD

[kemalyan@thesurgicalcenter.com](mailto:kemalyan@thesurgicalcenter.com)

### ABA-MCTG WEBSITE-Coming soon!

The website will be accessible to all members of the MCTG and will list the sites, contact information, website links (if applicable) and also will list all current studies (including all source documents, protocols etc.). Also, retrospective reviews will be available at the site (starting with the elderly study as the test study) in order to enter all the data from each participating site while on-line. Concerns for HIPPA compliance and such will be addressed as the website is constructed. Also, a group chat site (as being put together at the YAHOO site) will be incorporated into the website. Dan Caruso, MD

[daniel\\_caruso@medprodoctors.com](mailto:daniel_caruso@medprodoctors.com)



**ABA Multicenter Trials Group Interim Conference**

September, 2004  
Napa California

Due to the vast number (and quality) of the studies put forward at this year's American Burn Association meeting, we are arranging an interim meeting for all interested in participating in the burn Multicenter Trials Group. The meeting will be held on Sunday, September 12 and, if necessary, Monday, September 13 in Napa, California in conjunction with the West Coast Burn Conference. The multicenter trials group meeting will concentrate on the planning, conduct, and participation in one of the trials proposed at the ABA. Each of the proposed trials will be presented by the principal investigator. Please plan on attending this meeting if you are interested in participating in or proposing a burn-related multicenter research project.

The exact location of the meeting will depend on the number of participants. Please contact Dr. Tina Palmieri MD ([tina.palmieri@ucdmc.ucdavis.edu](mailto:tina.palmieri@ucdmc.ucdavis.edu), phone 916-453-2050, or fax 916-453-2373) if you plan on attending. If you are interested in proposing a project or in participating in a specific project, include that in your reply. Responses are due no later than May 31, 2004.

**ABA-MCTG Meeting Minutes  
March 24, 2004  
Vancouver, BC**

The ABA-MCTG met during the 2004 ABA annual meeting. Dr. Jeffrey Saffle welcomed attendees and highlighted the successes of 2003. Completed and proposed studies are shown in the table below.

Individual investigators presented up-dates on MCTG studies that are completed and ongoing. Abstracts of recently completed studies are on pages 3-4.

Proposed new studies were discussed. Abstracts of these studies are discussed in detail elsewhere in this newsletter. These studies are presented in more detail below. Those interested in participating were asked to sign-up to receive information for any or all of the proposed studies.

The Arizona Burn Center presented information concerning the ABA-MCTG website they are constructing. Nathan Kemalyan volunteered to organize an ABA Multicenter Trials Yahoo Group.

An interim meeting was proposed for during the West Coast Burn Conference in Napa, CA in September.

<b>ABA-MCTG STUDIES</b>		
<b>Title</b>	<b>PI</b>	<b>Status</b>
EFFECTS OF OXANDROLONE ON LENGTH OF HOSPITAL STAY IN THE SEVERELY BURNED: A MULTI-CENTER PROSPECTIVE RANDOMIZED DOUBLE-BLIND TRIAL	Wolf	Closed to enrollment
BLOOD TRANSFUSION PRACTICES IN MAJOR BURN INJURY: A MULTICENTER STUDY	Palmieri	Closed to enrollment
DRG 272: DOES IT PROVIDE ADEQUATE BURN CENTER REIMBURSEMENT FOR THE CARE OF PATIENTS WITH TOXIC EPIDERMAL NECROLYSIS?	Kagan	Closed to enrollment
BURN MORTALITY IN PATIENTS AGE 75 OR GREATER*	Caruso	Accepting sites
PROSPECTIVE, RANDOMIZED TRIAL OF RESTRICTIVE VS. LIBERAL BLOOD TRANSFUSION POLICY IN BURNS >20% TBSA*	Palmieri	Accepting sites
A RETROSPECTIVE REVIEW OF DRG 504*	Kagan	Accepting sites
EFFICACY OF DECADRON FOR THE PREVENTION OF REINTUBATION IN BURNED CHILDREN*	Greenhalgh	Accepting sites
A MULTICENTER REVIEW OF FUNGAL INFECTIONS IN BURN PATIENTS*	Saffle	Accepting sites
A PROSPECTIVE STUDY OF THE EFFECTIVENESS OF ALBUMIN USE DURING THE FIRST 24 HOURS FOLLOWING BURN INJURY*	Cairns	Protocol in planning stage

\*Studies discussed in detail on pages 4-5. Please contact Principal Investigator for participation details.

## COMPLETED ABA-MCTG STUDIES

### EFFECTS OF OXANDROLONE ON LENGTH OF HOSPITAL STAY IN THE SEVERELY BURNED: A MULTI-CENTER PROSPECTIVE RANDOMIZED DOUBLE-BLIND TRIAL

Principal Investigator: Steve Wolf MD  
Co-Investigators: Edelman, Kemalyan, Donison, Cross, Underwood, Palmieri, Lawless, Spence, Goodwin, Noppenberger, Voigt, Edwards, Caruso, Foster, Hildebrand, Jeng, Crean, Purdue, Hunt, Burris, Warner, Hatfield, Klein, Baker, Cairns, Kessler, Yowler, Tutolo, Mazingo, Perrin, Benjamin, Villareal, Saffle

*The MCTG 's first prospective randomized trial was completed in 2003. This study involved 17 burn centers from across the U.S. The abstract was presented at the ABA 2004 meeting and a manuscript is in process.*

Severe burns induce a number of pathophysiologic deficits, among them catabolism of lean mass with resultant weakness and prolonged wound healing. These deficits then lead to protracted hospitalizations to affect recovery. Oxandrolone is an anabolic agent which has been shown to decrease lean mass catabolism and improve wound healing in the severely burned. We performed a rigorous multi-center double-blind prospective randomized clinical trial testing the effects of oxandrolone treatment on length of hospital stay among other clinical outcomes. We planned to enroll 150 subjects between 18 and 70 years of age with burns between 20 and 60% TBSA requiring at least one excision and grafting operation, randomized between oxandrolone 10mg BID every 12 hours or placebo beginning five days into hospitalization. Length of hospital stay was used as the primary outcome indicator. At the interim analysis, we found a significant difference in total length of hospitalization and length of hospitalization/% TBSA burn in favor of oxandrolone treatment (see table).

	Placebo (n = 32)	Oxandrolone (n = 43)	p- value
LOS / %TBSA	0.88 (0.69 - 1.32)	0.70 (0.53 - 0.88)	0.02
LOS	35 (23.5 - 49.5)	23 (13 - 36)	0.01
% TBSA	34.3 (25.5 - 46.8)	33.8 (24.0 - 42.0)	0.42

We conclude that oxandrolone treatment benefits the severely burned shown here for the first time with level I evidence. Further analysis of subgroups and secondary outcome measures are pending.



### BLOOD TRANSFUSION PRACTICES IN MAJOR BURN INJURY: A MULTICENTER STUDY

Principal Investigator: Tina L. Palmieri MD  
Co-Investigators: Caruso, Foster, Cairns, Gamelli, Mazingo, Kagan, Wahl, Kemalyan, Fish, Gomez, Sheridan, Faucher, Latenser, Gibran, Klein, Solem, Saffle, Morris, Jeng, Voigt, Howard, Greenhalgh

Abstract presented at the ABA 2004 meeting.

The use of blood transfusions to augment hemodynamic status has become a common practice, with over 11 million units of red blood cells transfused in more than 3 million patients every year in the United States. Traditionally, blood transfusions have been administered when the patient's hemoglobin is less than 10 g/dL or hematocrit less than 30%. Limited data exists regarding the effects of a restrictive blood transfusion policy in burn patients.

To evaluate burn center transfusion practices, we reviewed the actual use of blood transfusion in patients with burn injury >20% TBSA admitted to a member of the Burn Multicenter Trials Group over a one year period. Data was collected from 23 different burn centers on a total of 666 patients. Mortality was related to age, TBSA burn, presence of inhalation injury, and the number of units of PRBC transfused. Although this study suggests that blood transfusions influence outcome, it does not provide direct evidence that maintenance of a lower transfusion trigger improves survival. A prospective, randomized, multicenter study is needed to determine the appropriate blood transfusion threshold for burn patients.



### DRG 272: DOES IT PROVIDE ADEQUATE BURN CENTER REIMBURSEMENT FOR THE CARE OF PATIENTS WITH TOXIC EPIDERMAL NECROLYSIS?

Principal Investigator: Richard J. Kagan MD

Co-Investigators: Edelman, Saffle, Gamelli

Abstract presented at the ABA 2004 meeting.

Patients with Toxic Epidermal Necrolysis (TENS) are often referred to Burn Centers for wound and intensive care management. Unless they undergo a surgical procedure, patients with this diagnosis are assigned to DRG 272 to determine hospital reimbursement. In 2002, this DRG had an average length of stay of 5.2 days and an average national reimbursement by the Center for Medicare and Medicaid Services of \$4,416. The purpose of this study was to compare demographics, resource utilization, and hospital charges and reimbursement for all patients admitted to participating burn centers between 1998 and 2002 that were assigned to this DRG; and to evaluate the effect of surface area involvement on the dependent variables.

Results: Patients in DRG 272 with TENS have significantly greater resource utilization and hospital charges than NON-TENS patients assigned to this DRG. Patients with TENS involving  $\geq 20\%$  TBSA have significantly greater resource consumption and hospital charges than do TENS patients with smaller surface area involvement.

### ABA-MCTG PUBLICATIONS

Warner, P.M., Kagan, R.J., Yakuboff, K.P., Kemalyan, N., Palmieri, T.L., Greenhalgh, D.G., Sheridan, R.L., Mozingo, D.W., Heimbach, D.M., Gibran, N.S., Engrav, L., Saffle, J.R., Edelman, L.S., Warden, G.L. (2003). *Current Management of Purpura Fulminans: A Multicenter Trial*. J Burn Care and Rehabilitation. 24 (3):119-126.

Palmieri, T.L., Greenhalgh, D.G., Saffle, J.R., Spence, R.J., Peck, M.D., Jeng, J.C., Mozingo, D.W., Yowler, C.J., Sheridan, R.L., Ahrenholz, D.H., Caruso, D.M., Foster, K.N., Kagan, R.J., Voigt, D.W., Purdue, G.F., Hunt, J.L., Wolf, S., Molitor, F. (2002). *A Multicenter Review of Toxic Epidermal Necrolysis Treated in U.S. Burn Centers at the End of the Twentieth Century*. J Burn Care Rehabilitation. 23(2):87-96.

## PROPOSED ABA-MCTG STUDIES

Contact the Principal Investigator or Research Coordinator if you are interested in participating in a study

### BURN MORTALITY IN PATIENTS AGE 75 OR GREATER

Principal Investigator: Dan Caruso MD  
[Daniel\\_Caruso@medprodoctors.com](mailto:Daniel_Caruso@medprodoctors.com)

The care and management of burn patients is ever evolving with the continual improvement of equipment, medication, wound care products and superior treatment protocols. These advances have lead to significant increases in the survival rate of burn patients, most dramatically in the latter quarter of the 20th century. Overall survival rates have increased substantially across all total body surface area (TBSA) stratifications. However, this increase in survival has not been distributed across the age continuum. The mortality rate in the elderly population has shown little or no improvement based upon our data showing that elderly patients, over the age of 75, have a higher mortality versus patients 55 to 75.

The Arizona Burn Center survival rates from 1997 through 2000 were compared with burn patient survival data published in 1971 from the National Burn Information Exchange. An analysis revealed that overall survival had improved from 83% in 1971 to 96% for the aforementioned three-year period. Survival rates for patients age 0-59 years were improved throughout all TBSA ranges. Patients age 60-74 had improved survival rates until the TBSA reached 40%, and then no survival advantage existed. Finally, in patients 75 years and older, survival rates were nearly identical to those of thirty years ago, throughout all the TBSA ranges.

The purpose of this study is to determine the mortality rate of patients age 75 or greater that were admitted to burn centers that are members of the American Burn Association Multicenter Trials Group from 1993 through 2003. The presence of preexisting medical diagnosis that may impact mortality will be noted. In addition this study is designed to capture multiple variables from the individual's hospitalization that may also significantly impact mortality. This information will be analyzed for potential unique predictors of mortality.

## **PROSPECTIVE, RANDOMIZED TRIAL OF RESTRICTIVE VS. LIBERAL BLOOD TRANSFUSION POLICY IN BURNS >20% TBSA**

Principal Investigator: Tina L. Palmieri MD  
[tina.palmieri@ucdmc.ucdavis.edu](mailto:tina.palmieri@ucdmc.ucdavis.edu)

The retrospective review of transfusion practices involving 666 patients from 23 burn units that was recently conducted by participants in the ABA-MCTG suggested that blood transfusions negatively impact burn survival and supported the need for a prospective, randomized, multicenter study to determine the appropriate blood transfusion threshold for burn patients. Therefore we are proposing a prospective randomized trial of restrictive vs. liberal blood transfusion policy in burn patients.

The hypothesis of the study is that a restrictive approach to red blood cell transfusion (hemoglobin maintained at 7-8 g/dL) is associated with increased survival compared to a liberal approach (maintaining hemoglobin >9 g/dL) in patients with burns >20% TBSA.

Study Design and Treatment Protocols. This is a prospective, randomized trial to compare patient outcomes as they relate to transfusion strategies. Burn patients admitted with the above criteria will be assigned to one of two treatment groups (restrictive versus liberal transfusion strategy). Patients assigned to the restrictive strategy of transfusion will receive blood transfusions to maintain hemoglobin levels in the range of 7-8 g/dL. In the liberal transfusion group, hemoglobin concentrations will be maintained >9 g/dL. The patients will receive blood transfusions one unit at a time with a hemoglobin measurement taken after each unit of blood transfused.

The primary outcome measure will be death from all causes in the 30 days after randomization. Secondary outcomes include: mortality rate during hospitalization, length of stay in the burn intensive care unit, length of time on mechanical ventilation, organ dysfunction, time to 50% and 90% burn wound healing, and number of infectious episodes. A total of 400 patients (based on power calculations) are currently planned for this study. Interim safety analysis will be performed after 200 patients are enrolled.



## **A RETROSPECTIVE REVIEW OF DRG 504**

Principal Investigator: Richard Kagan MD  
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Diagnosis Related Groups (DRG's) are the basis for hospital reimbursement from Medicare, certain state Medicaid plans, and some non-government payers. The 504 DRG (Extensive Burns with Skin Grafts) is commonly used by burn center hospitals for reimbursement when patients have burns involving >20% total body surface area (TBSA) and full-thickness (3<sup>rd</sup> degree) burns involving >10% TBSA. Unlike the other DRG's for burn injury, which take into account the presence of inhalation injury, this DRG does not do so. The hypothesis of this study is that patients with extensive burns requiring skin grafts have greater hospital resource consumption when there is an associated inhalation injury and that this results in inadequate hospital reimbursement for patients with this condition and comorbid diagnosis.

We would therefore like to perform a chart review of all patients admitted to The University Hospital from January 2000 through December 2002 who were assigned DRG 504 to examine the differences in the clinical diagnoses, treatment, and outcome of those patients with and without burn injuries. Our hypothesis is that DRG 504 does not adequately reflect the extensive resource utilization for patients with smoke inhalation injury who are more likely to require prolonged ventilatory support and ICU care.



## **EFFICACY OF DECADRON FOR THE PREVENTION OF REINTUBATION IN BURNED CHILDREN**

Principal Investigator: David Greenhalgh MD  
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Burn patients have a high rate of endotracheal intubation because of airway edema. Once the patient is intubated, there is a significant risk with the development of stridor and a need for reintubation after extubation. There are protocols in many burn units to give steroids after extubation with the hope of reducing stridor and reintubation. No study, however, supports their use. Since so many of our patients are intubated for edema, we have the potential for proving or disproving the efficacy of steroid prophylaxis for the prevention of

the need for reintubation. Since children are at the highest risk (due to their smaller airways) the study will focus on children 8 years old or less. By including several burn centers, we should be able to answer the question of whether dexamethasone can reduce the need for reintubation after extubation in burned children.

**Study Design:** The proposal is to perform a prospective, randomized, double blind, placebo-controlled, multicenter study. Patients who are randomized to steroid treatment will be treated with dexamethasone 0.5 mg/kg (maximum, 10 mg) with the first dose 6-12 hours before extubation, then every 6 hours for 6 total doses. Those patients randomized to placebo will receive normal saline at the same volume as the steroid. The pharmacy will perform the randomization, maintain "blinded" records and prepare the solutions. All other management of the airway and pulmonary status will be according to the usual treatment in that center. The decision to extubate, treatment of stridor and the decision to reintubate will be based on the usual protocols in that unit. The incidence of reintubation, and the treatment of stridor will be documented. If the patient does require reintubation they may be re-entered into the study for a second randomization. Any complications potentially related to the treatment of steroids should be documented.



### **A MULTICENTER REVIEW OF FUNGAL INFECTIONS IN BURN PATIENTS**

Principal Investigator: Jeffrey Saffle MD  
[Linda.Edelman@hsc.utah.edu](mailto:Linda.Edelman@hsc.utah.edu)

Infections remains the major cause of mortality in patients hospitalized with burn injuries. Over the past two decades, the incidence and clinical severity of bacterial infections in burn patients have been significantly reduced. In contrast, fungal infections have increased in clinical importance. Burn injuries are frequently listed as a major risk factor for fungal infections.

Progress in the effective treatment of fungal infections in burn patients has been slowed by a near-total lack of agreement regarding the best methods of treatment. No standard exists for the performance of routine surveillance cultures, or for systemic or topical treatment of infections.

**Objectives:** This study will determine and describe the various regimens used for diagnosis and treatment of fungal infections in burn patients by various burn centers in the United States.

**Patient Selection Criteria:** The records of all burn patients with positive qualitative or quantitative routine or fungal cultures will be reviewed at participating sites. Participating centers will be asked to describe their standard methods of surveillance for infections in burn patients. Data will be recorded on individual patients, including the site(s) of infection, organism(s) encountered, methods of determining infection, methods of systemic and topical treatment, and outcomes. We anticipate that at least 300 patient records can be obtained within a year.



### **A PROSPECTIVE STUDY OF THE EFFECTIVENESS OF ALBUMIN USE DURING THE FIRST 24 HOURS FOLLOWING BURN INJURY**

Principal Investigator: Bruce Cairns MD  
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Even though Albumin has been used for decades, an almost inconceivable amount of controversy regarding its effectiveness exists. We are developing a protocol that prospectively examines albumin use within the first 48 hours of burn injury during burn shock resuscitation. Our goal is to better define how albumin really is given (what indication, formulation, rate) in the clinical scenario that reportedly (by our survey data) most often triggers its use.

Please contact Dr. Bruce Cairns if you have an interest in participating in the development of this protocol (or would like to take the survey that we have already given out).

This newsletter was constructed amateurishly by Linda Edelman, who is a data cruncher not a graphic designer!! Please email her with suggestions (kind or otherwise!) or content that you would like included in future editions. Linda can be reached via email ([Linda.Edelman@hsc.utah.edu](mailto:Linda.Edelman@hsc.utah.edu)) or phone (801-585-2489).